A study of mechanisms involved in the pathogenicity of *Enterococcus faecalis* by DNA microarrays

En studie av mekanismer involvert i *Enterococcus faecalis* patogenisitet ved hjelp av DNA mikromatriser

Philosophiae Doctor (PhD) Thesis

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Ås 2010

Thesis number 2010:54
ISSN 1503-1667
ISBN 978-82-575-0964-4

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ACKNOWLEDGEMENT

The work presented in this thesis was carried out during the period 2007-2010 at the Laboratory of Microbial Gene Technology and Food Microbiology (LMG), Department of Chemistry, Biotechnology and Food Science, The Norwegian University of Life Sciences. The work was financially supported by a grant from the European Union Sixth Framework Program under contract LSHE-CT-2007-037410.

First of all, I wish to express my sincere gratitude to my two supervisors at LMG, Dr. Ingolf F. Nes and Dr. Dag Anders Brede. Ingolf, I really appreciate the opportunity you have given me. Throughout my time at LMG, your door has always been open. Thank you for all the good times we have shared. Thank you Dag, for taking me in under your wing when I needed it. You have been a true inspiration to me from the day we started working together. Your seemingly endless knowledge gives me something to reach for as a scientist. I would also like to thank my co-supervisors Dr. Lars Snipen, Dr. Rob Willems and Dr. Ågot Aakra, and my other co-authors for your contribution and collaboration.

My past and present colleagues at LMG, I thank you all for contributing to a stimulating and supporting working environment. Special thanks to Heidi, Daniel, Zhian and Morten: Heidi and Daniel, for welcoming me to the lab, sharing your knowledge and being good friends, Zhian, for being my "big brother" and always looking out for me, and Morten, for enduring my endless girl talk, straightening out my messy thoughts and sharing my Mekoro.

Finally, I would like to thank my family and friends for their encouragement. Thanks to my parents and my brother for believing in me. I am where I am today thanks to you. This is your day as well!

Ås, October 2010

Margrete Solheim

SUMMARY

Traditionally considered a harmless commensal of the mammalian gastrointestinal tract, *Enterococcus faecalis* now rank among the leading causes of nosocomial infections worldwide. Several genetic determinants enhancing the virulence of *E. faecalis* have been characterized, but none of these appears to be indispensible for the pathogenicity of the organism. In this context, the focus of this thesis has been to acquire in-depth knowledge about the specific traits contributing to the success of this versatile pathogen, with DNA microarrays as the main working tool.

Microarray-based comparison of gene content in *E. faecalis* isolated from Norwegian infants, contributed new insight into the genomic repertoire of commensal *E. faecalis*. Moreover, comparative genomic analysis of a larger collection of isolates identified a set of lineage-enriched genes which may contribute to the fitness of hospital-associated high-risk *E. faecalis* clonal complex 6 (CC6) strains. Preponderance of phage-related genes among the CC6-enriched genes, suggested a role of genome flexibility in hospital adaptation. Furthermore, significant enrichment of genes encoding surface-related structures may lead to antigenic variation, and may thus supply CC6 strains with a means to evade certain mechanisms of host defense.

E. faecalis is intrinsically robust and has a unique ability to adapt to changing environments. Since the pathogenic potential of the bacterium may not only relay on the presence and absence of specific genetic traits, but also on gene regulation, transcriptional profiles were obtained for *E. faecalis* in the presence of bile, NaCl-induced osmotic shock and growth in urine. In general, these studied highlighted the importance of rapid adaptations in the expression of genes related to energy metabolism, transport systems, cell envelope rearrangements and general stress mechanisms in response to host-relevant growth environments. Moreover, the transcriptional analyses provided clues to hitherto undiscovered mechanisms of resistance associated with the various growth conditions investigated.

SAMMENDRAG

Enterococcus faecalis, som tradisjonelt sett har vært ansett som en harmløs del av tarmfloraen hos pattedyr, verserer nå på listen over de vanligste årsakene til sykehusinfeksjoner verden over. En rekke genetiske trekk som bidrar til alvorligheten av en *E. faecalis* infeksjon har blitt karakterisker, men ingen av disse har vist seg å være nødvendige for organismens evne til å forårsake sykdom. På bakgrunn av dette, har fokus for arbeidet omtalt i denne avhandlingen vært å tilegne seg en bedre forståelse av faktorene som bidrar til suksessen til denne allsidige patogenen, men DNA mikromatriser som hovedverktøy.

Mikromatrise-baserte sammenligning av geninnhold i *E. faecalis* isolert fra norske spedbarn, ga økt innsikt i det genetiske repertoaret hos kommensale *E. faecalis*. Videre, ble det ved hjelp av komparative genomanalyser av en større gruppe isolater identifisert et sett med gener som var anriket blant stammer tilhørende høyrisiko-gruppen klonalt kompleks 6 (CC6). Stammer tilhørende denne gruppen er svært utbredt som årsak til infeksjoner, og da en stor andel av de anrikede genene var lokalisert innefor fag-relaterte områder på kromosomet, kan det tyde på at genomfleksibilitet spiller en viktig rolle i tilpasningen til sykehusmiljøet. Videre utgjorde også gener som koder for overflatestrukturer en signifikant andel av de anrikede genene. Variasjon i disse strukturene kan gi variasjon i antigenisitet, og dermed bidra til at bakterien unnslipper enkelte av vertens forsvarsmekanismer.

E. faecalis er en hardfør organisme, og i tillegg svært tilpasningsdyktig. Differensiell regulering av ulike gener kan, på samme måte som forskjeller i geninnhold, bidra til bakteriens patogene potensiale. Transkripsjonsprofiler av *E. faecalis* dyrket i nærvær at galle, under NaCl-indusert osmotisk stress og i urin understreket viktigheten av tilpasninger i genekspresjon innenfor de funksjonelle kategoriene energimetabolisme, transport, cellevegg/-membran, samt generelle stressmekansimer under disse vertsrelevante vekstforholdene. Videre, ga analysene et innblikk inn i hittil ukjente resistensmekanismer assosiert med de spesifikke vekstbetingelsene.

LIST OF PAPERS

Paper I

Solheim M, Aakra Å, Vebø HC, Snipen L and Nes IF. (2007). Transcriptional responses of *Enterococcus faecalis* V583 to bovine bile and sodium dodecyl sulfate. *Applied and Environmental Microbiology*. Sep; 73(18):5767-74.

Paper II

Solheim M, Aakra Å, Snipen L, Brede DA and Nes IF. (2009). Comparative genomics of *Enterococcus faecalis* from healthy Norwegian infants. *BMC Genomics*. Apr 24;10:194.

Paper III

Vebø HC, Solheim M, Snipen L, Nes IF and Brede DA. (2010). Comparative genomic analysis of pathogenic and probiotic *Enterococcus faecalis* isolates and their transcriptional responses to growth in human urine. *PLoS ONE* 5(8): e12489. doi:10.1371/journal.pone.0012489.

Paper IV

Solheim M, Brekke MC, Snipen L, Willems RJL, Nes IF and Brede DA. (2010). Comparative genomic analysis reveals significant enrichment of genes encoding virulence-related surface proteins in hospital-associated clonal complex 6 *Enterococcus faecalis*. Submitted.

Paper V

Solheim M, Mathiesen T, Snipen L, Nes IF and Brede DA. Transcriptomic analysis reveals that the enterococcal polysaccharide antigen (Epa) constitutes a major factor in *Enterococcus faecalis* intrinsic resistance to high level NaCl-induced osmotic stress. Manuscript.

Other related papers by the author not included in the thesis:

Snipen L, Nyquist OL, Solheim M, Aakra Å and Nes IF. (2009). Improved analysis of bacterial CGH data beyond the log-ratio paradigm. *BMC Bioinformatics*. 2009 Mar 19; 10:91.

Dørum G, Snipen L, Solheim M and Sæbø S. (2009). Rotation testing in gene set enrichment analysis for small direct comparison experiments. *Statistical Applications in Genetics and Molecular Biology*. 8(1):Article34.

Dørum G, Snipen L, Solheim M and Sæbø S. Smoothing Gene Expression Data With Network Information Improves Consistency of Regulated Genes. Submitted.

1. INTRODUCTION

Enterococci constitute a part of the normal intestinal flora of humans, of which only sporadic reports of infections in immunocompromised patients existed until the 1980s [1]. During the last decades, however, *Enterococcus faecalis* and *E. faecium* have concurrently emerged as clinically important pathogens. A dozen different enterococcal virulence factors have been characterized, but despite great efforts, no discriminatory markers for separation between pathogenic and non-pathogenic strains of enterococci have been identified. Enterococcal pathogenicity most likely involves an orchestrated interplay between the presence of various genetic determinants and the transcriptional regulation of these factors in response to changing environments encountered during the infection process. In the work associated with this thesis, DNA microarrays were used as a tool to further explore the mechanisms behind the two-faced character of *E. faecalis*.

1.1. The enterococci

The term "enterococcus" was first used by Thiercelin in 1899 to described bacteria observed in pairs and short chains in human feces [2]. The same year, a case of acute endocarditis, caused by what most likely was enterococci, was reported [3]. The term "*Enterococcus*/enterococcal group" was first used by Sherman to describe streptococci that grew at 10 and 45 ºC, at pH 9.6, in 6.5 % NaCl and survived heating to 60 ºC for 30 min [4], and the group included all three enterococcal species described at the time; *Streptococcus faecalis*, *S. faecium* and *S. durans*. Since then, more than 25 species have been proposed to be part of the genus (Figure 1).

The enterococci are defined as Gram-positive facultative anaerobe catalase-negative cocci that occur singly, in pairs or in short chains. They can be distinguished from other gram-positive cocci on the basis of an array of phenotypic tests, which in addition to the aforementioned growth conditions, includes production of pyrrolidonylarylamindase, hydrolysis of esculin in the presence of bile, production of leucine aminopeptidase and hemolytic activity on trypticase soy 5 % sheep blood agar [5]. Under most conditions,

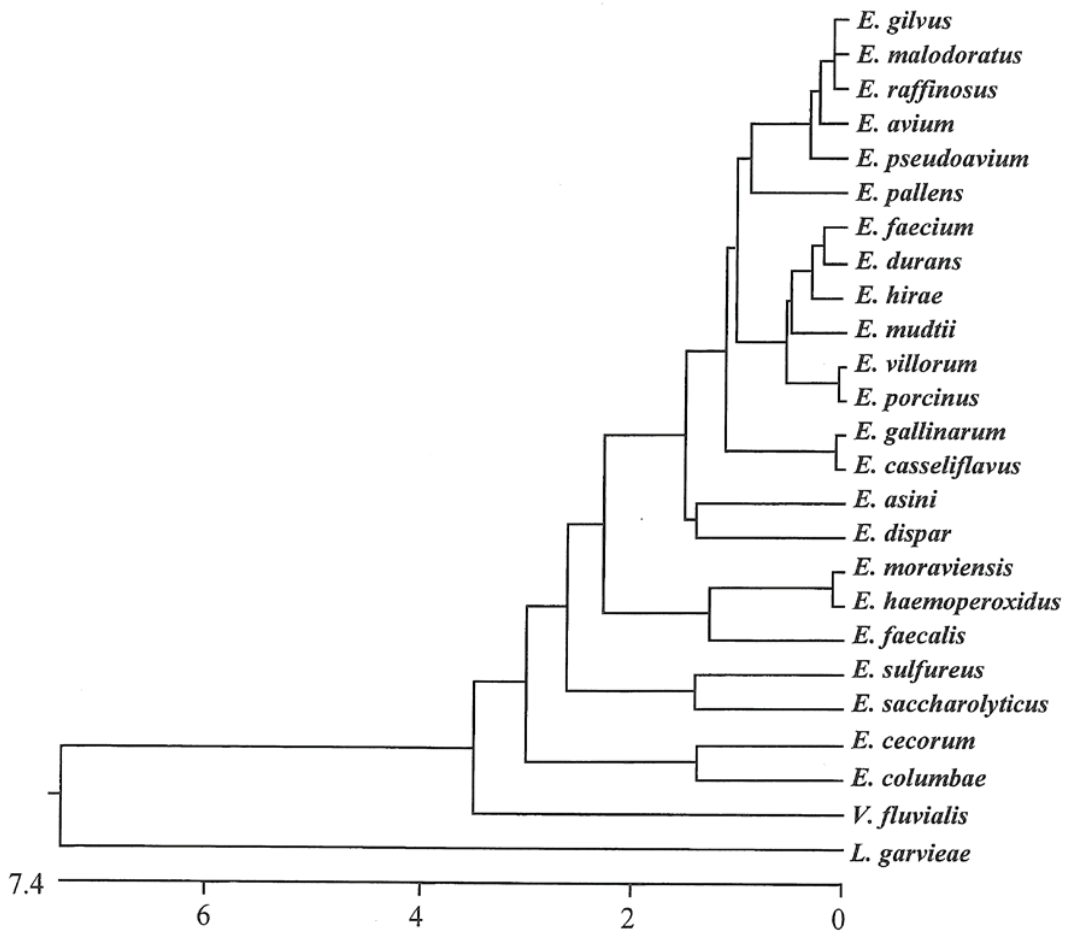

Figure 1. A dendrogram showing the phylogenetic inter-species relationships of the *Enterococcus* genus and some related species of Gram-positive cocci, based on 16S rRNA sequence analysis. Adapted from [6] .

enterococci metabolize glucose through homolactic fermentation with L-lactic acid as the prevalent end product. However, it has also been demonstrated that certain enterococci can perform respiration with oxygen as the terminal electron acceptor in the presence of heme [7].

Enterococci are commonly found as part of the intestinal flora in most mammals and birds, while less frequently isolated from other body sites, such as the oral cavity, the urinary tract, the female genitalia, and from blood [8]. Outside of their normal habitat, enterococci also occur in natural environments (soil and water), often as an indicator of fecal contamination,

and in foods [9]. Since the early 1990s, however, the enterococci have received increasing attention mainly due to their emergence as nosocomial pathogens.

1.1.1. Enterococci as members of the human intestinal flora

Enterococcal species, along with approximately 1000-1200 other species of anaerobic and aerobic bacteria, are part of the normal intestinal flora of humans [10]. Although the most abundant coccoide Gram-positive bacterium in the gastrointestinal (GI) tract, enterococci constitute < 1 % of the total intestinal microflora of most human adults [11]. The percentage of enterococci in the intestines varies with both age and diet, and the abundance of enterococci generally decreases with age. Among the enterococcal species described, *E. faecalis* and *E. faecium* are most commonly isolated from human feces [8]. The numbers of *E. faecalis* in human stool range from 10^5 to 10^7/g compared with 10^4 to 10^5/g for *E. faecium* [8]. Other species, such as *E. durans* and *E. avium* have only occasionally been detected in human feces [8].

1.1.2. Enterococci in foods

The industrial importance of enterococci is mainly based on their fermenting properties and proteolytic and esterolytic activities, which all play major roles in the ripening and flavor development of a selection of Mediterranean cheeses and sausages [12,13,14]. Traditionally, the source of enterococci in foods is thought to be derived from fecal contamination. The numbers of enterococci range from 10^1/g to more than 10^7/g in certain varieties of cheese [14]. *E. faecalis* and *E. faecium* are the most prevalent enterococcal species isolated from fermented food products [15]. In addition to their role in ripening and aroma development, fermentative end products such as lactic acid provide protection against spoilage by nonacidophilic microorganisms [13,14]. Certain enterococcal strains also have the advantage of producing bacteriocins (antimicrobial peptides) active against food spoilage microorganisms and pathogens such as *Listeria* [16], and the addition of starter cultures that produce bacteriocins with antilisterial activity has been suggested as a means of preservation of fermented foods [12,14].

1.1.3. Enterococci as probiotics

The term probiotics refers to dietary supplements of live microorganisms that have a beneficial effect on the health and well being of the consumer [17]. Although lactobacilli are the most common organisms distributed as probiotics, a few enterococcal products also exist. The probiotic fermented milk product Gaio contains 2×10^8 *E. faecium* and 7×10^8 *Streptococcus thermophilus*/ml, and is proposed to lower the blood pressure, reduce the blood-sugar levels of diabetics, relieve headaches, improve the intestinal flora and lower the blood cholesterol [18]. Moreover, the *E. faecium* strain SF68, also known as Bioflorin, has been used to treat diarrhea and is regarded as an alternative to antibiotic treatment [19]. Other probiotic products containing *Enterococcus* spp. include CausidoR [14], Idoform (Ferrosan Norge AS) and Symbioflor [20], and the beneficial effects of these products have also been well documented. Nevertheless, the use of enterococci as probiotics remains controversial, especially due to the risks of transfer of antimicrobial resistance traits and virulence genes to human commensal strains. Hence, for future references, whole genome sequencing of enterococcal strains considered used as probiotics should perhaps be requested.

1.2. Enterococcal genomes and genetic islands

The characteristics of all living organisms are essentially determined by information contained within DNA, which is passed along from parent to offspring, through generations. Consequently, deciphering the genetic sequence of an organism is a main key to understanding its whole existence. The power of DNA sequencing as a research tool has stimulated dramatic advances in the DNA sequencing technology, concurrently allowing ever more genomes to be sequenced, and thus making comparative genomics a focal point for the study of any form of life.

The first initiative to study comparative genomics of enterococci came with the identification and sequencing of a pathogenicity island (PAI) in the virulent *E. faecalis* MMH594 [21]. PAIs are defined as genetic island containing genes coding for virulence-associated traits. The 153-kb MMH594-PAI consists of 129 open reading frames (ORFs), and includes genes coding for the broad-spectrum toxin cytolysin, the enterococcal surface protein (Esp) and an

aggregation substance. In addition, a number of genes specifying properties that have been hypothesized to be advantageous in gastrointestinal colonization, including a bile salt hydrolase, new metabolic pathways and a Gls24-like starvation-inducible protein are present on the island. Microarray-based assessment of PAI-content in a set of clinical *E. faecalis* isolates revealed high degree of variation [22]; an observation in agreement with previous studies [23,24]. A putative *esp*-containing PAI has also been described in *E. faecium* [25].

The first complete enterococcal genome sequence was reported in 2003 [26]. *E. faecalis* V583 was the first vancomycin-resistant clinical isolate in the U.S., originally reported by Sahm *et al.* [27]. V583 contained three circular plasmids, including two pheromone-responsive conjugative plasmids, in addition to the bacterial chromosome (Figure 2). Interestingly, more than 25 % of the V583 genome corresponded to mobile and/or exogenously acquired DNA [26]. In addition to a PAI with a 17-kb deletion including parts of the *cyl* locus and *esp* compared to the prototype found in MMH594, seven integrated phage regions, three conjugative elements and a *vanB* vancomycin resistance locus were identified in the V583 genome.

Since the publication of the V583 genome sequence, several other *E. faecalis* genomes have been sequenced [20,28,29], and comparative genomics suggest that *E. faecalis* strains V583 and OG1RF represent extremes regarding chromosome size (~ 3.2 and 2.7 Mb, respectively) [26,29]. Furthermore, the diversity and genetic relationship within the species have been studied using DNA-based typing techniques, such as multilocus sequence typing (MLST) [30,31], and comparative genomic hybridization (CGH) [23,32,33]. The *E. faecalis* MLST scheme defines sequence types (STs) based on the allelic variation at seven housekeeping loci [31]. Clonal complexes (CC) are defined as groups of isolates where the members share a minimum of five loci with at least one other ST in the group. Population structure studies by MLST have defined distinct CC of *E. faecalis* associated with the hospital environment (CC6, CC9, CC28 and CC40) [31]. The microarray-based comparisons of gene content have revealed that the inter-strain diversity observed, was mainly associated with the mobile genomic elements described in V583 (Figure 2, lane 4); an observation which has later been supported by information obtained through whole-genome sequencing [29]. Genome sequences of other enterococcal species have also been published. The first *E. faecium* genome was announced in 2000; however, the sequence of *E. faecium* TX0016 (DO) has not

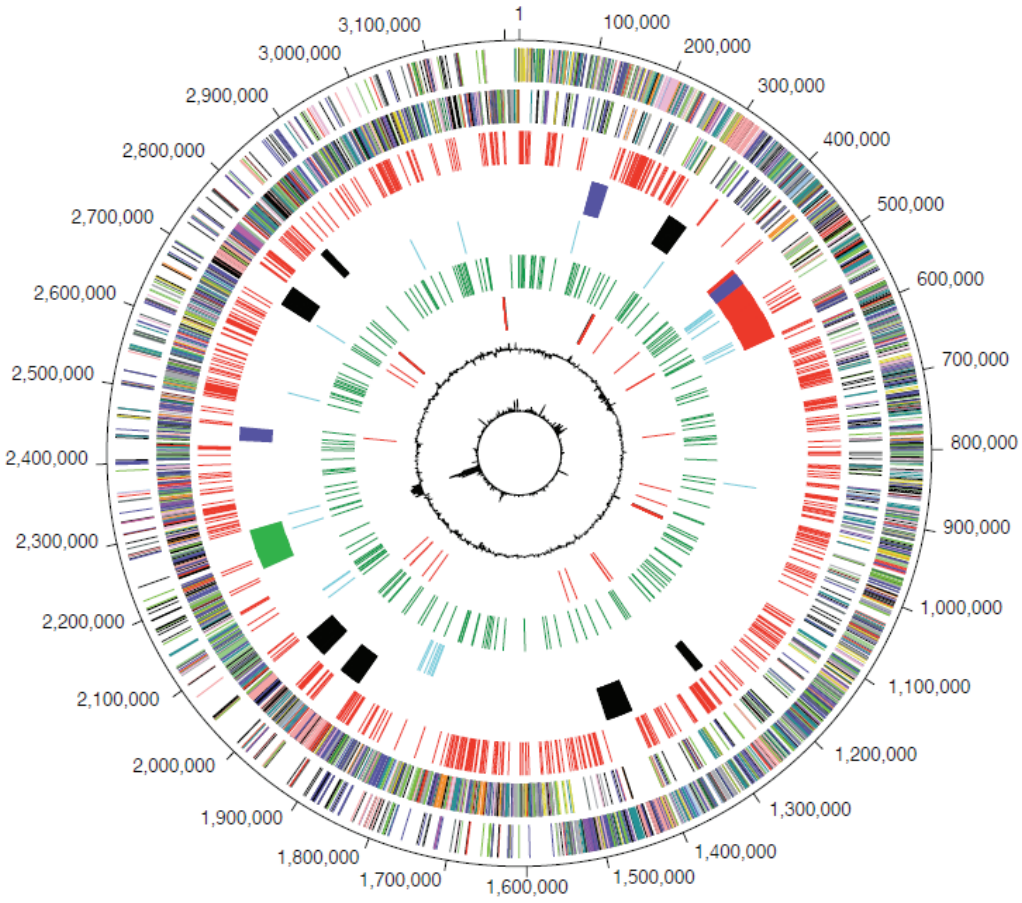

Figure 2: **Circular representation of the chromosome of *E. faecalis* strain V583.** From outer to inner lanes: 1) Predicted coding regions on the plus strand color-coded by role categories: salmon, amino acid biosynthesis; light blue, biosynthesis of cofactors, prosthetic groups and carriers; light green, cell envelope; red, cellular processes; brown, central intermediary metabolism; yellow, DNA metabolism; green, energy metabolism; purple, fatty acid and phospholipid metabolism; pink, protein fate/synthesis; orange, purines, pyrimidines, nucleosides, nucleotides; blue, regulatory functions; grey, transcription; teal, transport and binding proteins; black, hypothetical and conserved hypothetical proteins, 2) predicted coding regions on the minus strand color-coded by role categories, 3) proteins conserved in amongst ten sequenced low-GC Gram-positive bacteria, 4) phage genes, black; genes located within the putative pathogenicity island, red; genes within the putative vancomycin resistant conjugative transposon, green; and integrated plasmid genes, blue, 5) transposase genes, blue, 6) predicted surface exposed proteins, green, 7) tRNAs in red and rRNA operons in black, 8) GC% curve in black, 9) atypical nucleotide composition curve in black. Adapted from [26].

yet been finished. More recently, a genome-sequencing project of seven *E. faecium* strains was initiated [34]. Eight more *E. faecium* genomes were also recently announced, simultaneously with the first three *E. casseliflavus* genomes and an *E. gallinarum* genome [28]. In addition, several on-going sequencing projects have been reported, the majority of which are associated with the Human microbiome project (HMBP) [35]. Thus, the number of available enterococcal genome sequences is likely to increase rapidly.

1.3. Enterococcal pathogenesis and virulence

Prior to identification of multi-resistant strains in the late 1970s, enterococci had long been considered as harmless commensals with low pathogenic potential, which only sporadically caused opportunistic infections in immunocompromised patients [1]. Over the past two decades, however, enterococci have emerged as a leading agent of nosocomial infections. Medical treatment is difficult, as enterococci have acquired or intrinsically evolved resistance mechanisms against the most commonly used antibiotics. As a result, enterococci are now considered to be one of the leading clinical challenges for physicians when identified as the cause of serious or life-threatening infections. The majority of enterococcal infections are caused by either *E. faecalis* or *E. faecium*; historically, the ratio of infections due to *E. faecalis* to those due to *E. faecium* was approximately 10:1. In the recent years however, there has been a progressive increase in the proportion of infections caused by *E. faecium*. This microbiological shift can most likely to be explained by the emergence of vancomycin- and ampicillin resistant enterococci (VRE and ARE, respectively) and *E. faecium* being the dominant species identified among VRE/ARE. Other enterococcal species, such as *E. durans*, *E. avium*, *E. gallinarium* or *E. casseliflavus* have only occasionally been reported as the cause of enterococcal infections [1].

1.3.1. Enterococcal infections

The enterococci are associated with a range of different clinical infections, and although primarily recognized as nosocomial pathogens, the enterococci are also capable of causing a variety of community-acquired infections. It was initially thought that most enterococcal infections were endogenous, *i.e.* they were attributable to the patient's own intestinal flora.

This hypothesis was supported by reports on translocation of intestinal enterococci from the GI tract to the mesenteric lymph nodes [36]. However, several later studies have suggested that transfer of resistant enterococcal strains between patients also frequently occur, most often due to direct contact with colonized or infected persons or contaminated surfaces, but occasionally also indirectly with hospital personnel as a source of intra-hospital spread [37].

Urinary tract infections

Urinary tract infection (UTI) is the type of infection most commonly caused by enterococci [38]. Enterococcal UTIs are usually hospital-acquired and affect patients with predisposing conditions, such as urinary tract malformations, urinary catheters or prolonged antibiotic treatment [39]. A significant proportion of nosocomial UTIs are associated with establishment of biofilm on medical devices. Biofilms are surface-associated, sessile bacterial communities, frequently embedded in extracellular polymeric substance (EPS). The formation of biofilms is a complex, stepwise process, which involve initial attachment to a surface, cell-to-cell interaction, microcolony formation, and maturation into a complex three-dimensional biofilm structure [40]. According to the National Institutes of Health, biofilms are involved in >80 % of all microbial infections in humans [41]. Enterococci are intrinsically resistance to many antibiotics, including aminoglycosides, cephalosporins and cotrimoxazole, which are the common drugs of choice for treatment of UTIs [39]. Enterococci in biofilms show increased resistance to antibiotics compared to planktonically growing enterococci, thus biofilm formation appear to be of great medical importance [42].

Bacteremia

Enterococci also rank among the leading causes of nosocomial bacteremia [38,43]. Hospital-acquired bloodstream infections usually occur among patients with severe underlying illnesses, who have undergone broad-spectrum antibiotic therapy and who have been exposed to prolonged hospitalization [44,45]. The source of bacteremia is most often the urinary tract, with catheterization as a factors associated with increased risk [44,46]: approximately 20 % of hospital-acquired bacteremia arises from the urinary tract. Other sources of bacteremia include the bilinary tract, intra-abdominal- or soft tissue infections and intravenous catheters [44,46]. As opposed to UTI, enterococcal bacteremia is often polymicrobial, *i.e.* multiple species can be isolated from the infection site [44].

Endocarditis

According to a recent study, enterococci are the third most common agent isolated from prosthetic valve endocarditis; accounting for 12 % of the cases [47]. Endocarditis is one of the most serious enterococcal infections [38], and it is believed that acute endocarditis is a result of bacteremia [48]. Among the factors associated with increased risk of endocarditis include advanced age and predisposing heart disease [48]. *E. faecalis* is a far more common cause of endocarditis than *E. faecium*, and most cases are seen among older men [38].

Other infections

Enterococci are also known to cause intra-abdominal and pelvic infections, wound and soft tissue infections, and less frequently meningitis and respiratory tract infections [46]. In case of such infections, enterococci are almost always isolates as one of several species associated with a polymicrobial infection [46].

1.3.2. Enterococcal virulence factors

A dozen putative virulence factors have so far been characterized in *E. faecalis* (Table 1). These genetic traits have been proposed as putative virulence factors because they **1**) have been found to be enriched in infection-derived enterococcal isolates, **2**) show increased expression in serum, and/or **3**) are associated with enhanced survival in infection models in various animal models or cultured cell lines.

To better understand the factors involved in an enterococcal infection, the disease can be looked at as a stepwise process (Figure 3) [49]. Environmental persistence is followed by an initial, asymptomatic colonization of the gastrointestinal tract by enterococcal strains possessing various traits, which enhance the ability of a virulent strain to outcompete indigenous commensal bacteria, thereby increasing the likelihood of disease. The next step in the pathogenesis of an enterococcal infection involve mechanisms of spread such as the translocation through or breaching of intestinal epithelium, and external infections by shedding microorganisms. The asymptomatic colonization and spread of strains with enhanced virulence potential is followed by subsequent infection and symptomatic disease. This final stage of an enterococcal infection is associated with factors thought to enhance

virulence at the level of toxicity or tissue damage, *i.e.* factors that affect disease severity, as opposed to disease probability.

Table 1. Putative enterococcal virulence factors. A list of the enterococcal virulence determinants associated with the different stages of an enterococcal infection. The column specifying occurrence refers to in which enterococcal species the trait has been characterized.

Function	Factor	Occurrence	References
1. Enhance colonization/	Antibiotic resistance	*E. faecalis* and *E. faecium*	[50]
Inhibit indigenous commensal bacteria	Cytolysin	*E. faecalis* and *E. faecium*	[51,52,53]
2. Adherence	Aggregation substance (AS)	*E. faecalis*	[54,55,56,57]
	Collagen binding adhesin (Ace)	*E. faecalis*	[58]
	Enterococcal surface protein (Esp)	*E. faecalis* and *E. faecium*	[59,60,61]
	E. faecalis/E. faecium antigen A (EfaA(EfmA))	*E. faecalis* (and *E. faecium*)	[62,63]
	Capsular polysaccharides (Cps)	*E. faecalis*	[64,65,66]
	Pilus	*E. faecalis* and *E. faecium*	[67,68,69,70,71,72]
	Collagen binding adhesin of *E. faecium* (Acm)	*E. faecium*	[73]
	Second collagen binding adhesin of *E. faecium* (Scm)	*E. faecium*	[69]
	E. faecium collagen binding protein A (EcbA)	*E. faecium*	[74]
	Serine-glutamate repeat containing protein A (SgrA)	*E. faecium*	[74]
3. Evasion of host defense	Cps	*E. faecalis*	[64]
	Gelatinase	*E. faecalis*	[75]
4. Tissue damage (direct or indirect)	AS	*E. faecalis*	[57]
	Cytolysin	*E. faecalis* and *E. faecium*	[51,52,53]
	Gelatinase	*E. faecalis*	[76,77,78,79]
	Serine protease	*E. faecalis*	[76,78]
	Hyaluronidase	*E. faecium*	[80]
	Extra cellular superoxide	*E. faecalis* and *E. faecium*	[81,82,83]
	Lipoteichoic acids (LTA)	*E. faecalis*	[84]

The ability of enterococci to respond to changing environments is likely to contribute to the survival of the organism through all stages of infection. Traits that may enhance the ability of enterococci to persist in the hospital environment include those that confer the ability to survive environmental stresses. Enterococci are intrinsically robust; capable of resisting a

variety of external stressors including heat, acid, oxidation and hyperosmolarity. They are also tolerant to detergents and prolonged desiccation. Prior to the publication of the first enterococcal genome sequence, most of the work conducted on *E. faecalis* stress responses involved proteomic analyses of global changes in protein expression during exposure to various stresses [85,86,87,88,89,90,91]. The first publication of a complete enterococcal transcriptional profile followed shortly after the release of the V583 genome [92], and more recently, genome-wide microarrays have been used to investigate gene expression under various infection-relevant growth conditions [93,94,95].

Traits that contribute to the second step in the enterococcal pathogenesis model include 1) factors that help in overcoming the biological barriers succeeding consumption, *i.e.* variations in pH, elevated osmolarity and relatively high concentrations of host produced substances like bile, 2) factors that confer growth advantages, such as antibiotic resistances and bacteriocin production, and 3) factors involved in adherence, such as surface-exposed

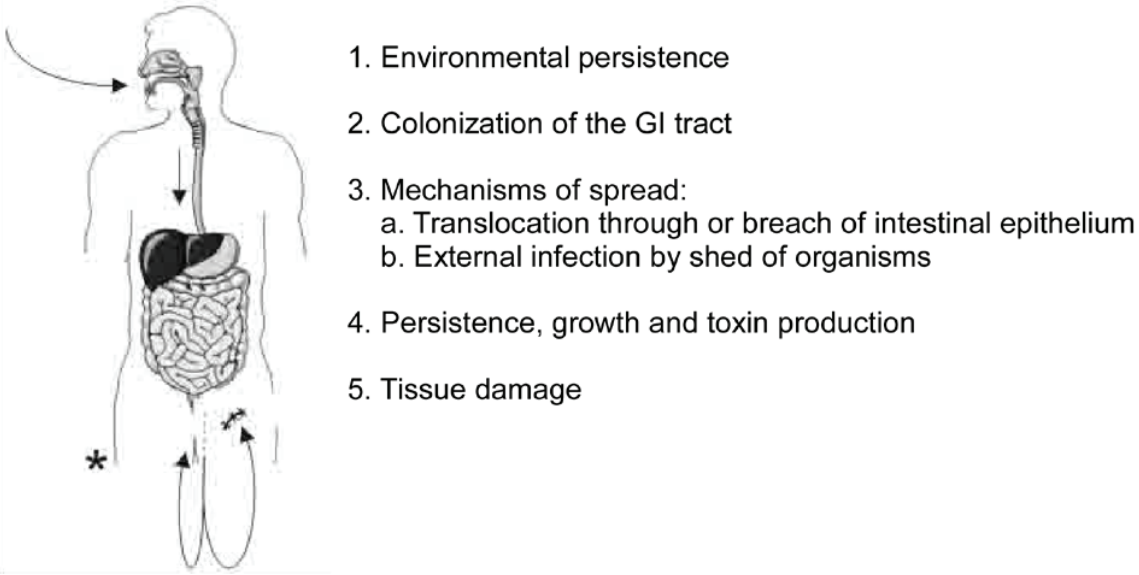

Figure 3: A stepwise model of the pathogenesis of enterococcal infections. Adapted from [49].

adhesins. Bacteria adhere to epithelial cells, endothelial cells, leukocytes or extracellular matrix [96]. A number of enterococcal adhesins have been identified that confer binding to mucosal and other epithelial surfaces. Aggregation substance (AS) is a surface-exposed

glycopeptid encoded on sex-pheromone plasmids, and is involved in cell aggregation and conjugation [57,97]. AS also mediate binding of enterococci to intestinal epithelium [98], renal epithelial cells [99], human neutrophils [56] and macrophages [55]. Moreover, AS augments internalization and intracellular survival of enterococci [100], and virulence of *E. faecalis* in a rabbit endocarditis model [101]. Another cell wall-associated protein, Esp, is involved in biofilm formation and has also been shown to contribute to the colonization and persistence of *E. faecalis* during ascending urinary tract infection [59]. Members of the MSCRAMM (microbial surface components recognizing adhesive matrix molecules)-subfamily of surface proteins have been shown to play a role in virulence both in *E. faecalis* and *E. faecium*. Ace (adhesin of collagen from *E. faecalis*) was the first enterococcal MSCRAMM to be characterized, and it was shown to mediate binding to collagen (type I and IV), dentin and laminin [58,102,103,104]. Recent evidence also suggested that Ace may promote *E. faecalis* phagocytosis and that Ace may possibly be involved in survival of enterococci inside phagocytic cells [58]. A structurally related MSCRAMM, Acm (adhesin of collagen from *E. faecium*), found in *E. faecium* was recently also reported to contribute to the pathogenesis of this bacterium [73]. Furthermore, the *E. faecium* specific adhesins Scm (second collagen binding adhesin of *E. faecium*), SgrA (serine-glutamate repeat containing protein A) and EcbA (*E. faecium* collagen binding protein A) have been described, and an implication of SgrA in biofilm formation has been accounted for, however, the exact role of these adhesins in enterococcal pathogenesis is yet to be determined [74]. *efaAfs* and *efaAfm* encoding the *E. faecalis* antigen A in *E. faecalis* and *E. faecium*, respectively, was originally characterized as an endocarditis-associated antigen, with an implication in adherence [63]. The *efaA* gene has since been found to constitute the solute binding receptor of a manganese transport system in *E. faecalis* coded for by the *efaCBA* operon [62]. Recently, pili have also been recognized as important virulence factors involved in adhesion in enterococci. *E. faecalis* possesses two pilin loci, designated the *ebp* locus (endocarditis and biofilm associated pili) [68] and the *bee* locus (biofilm enhancer in enterococci) [70]. An implication of Ebp in biofilm formation, endocarditis and ascending UTI has been reported [68,71]. Moreover, the *ebp* locus has been shown to be ubiquitous within the species [105]. The *bee* locus on the other hand, is located on a conjugative plasmid which was only sporadically detected (5%) among *E. faecalis* isolates. Also the *bee* locus has been shown to play a role in enhancing biofilm formation [72]. *E. faecium* harbors four distinct pilus-encoding loci [67,69]; pilin gene clusters (PGC) 1 to -4. PilA and PilB (PGC-1 and PGC-3, respectively)

were predominantly present in human hospital-acquired *E. faecium* isolates [67]; however, the role of *E. faecium* pili in pathogenesis remains to be investigated.

Capsular components play a crucial role in enterococcal pathogenicity by evasion of the host immune system, due to their complexity and their ability to confer resistance to complement-mediated phagocytosis. The enterococci are in possession of several capsular polysaccharides [64,106,107,108]. The *cps* (capsular polysaccharide) operon consists of 9 genes (*cpsC*-*cpsK*), of which eight genes are essential for capsule production [66]. Inactivation of *cps* genes resulted in isogenic mutants with enhanced susceptibility to phagocytic killing *in vitro* and reduced persistence in murine regional lymph nodes [64]. The *epa* (enterococcal polysaccharide antigen) cluster represents a rhamnose-containing polysaccharide which was originally identified in *E. faecalis* OG1RF [107]. According to a recent recharacterization, *epa* comprises 18 consecutive genes (*epaA*-*epaR*) in OG1RF [109]. Disruption of various genes within the *epa* cluster resulted in decreased biofilm formation and enterocyte translocation, reduced resistance to killing by polymorphonuclear leukocytes (PMNs), increased susceptibility to phage infection and reduced virulence in UTI and murine peritonitis models [108]. A third capsular polysaccharide found among both *E. faecalis* and *E. faecium* has also been reported [106].

Capsular polysaccharides and other cell wall components, such as lipoteichoic acids (LTA), can also provoke indirect damage to the host by the induction of inflammatory responses, *e.g.*, encapsulated enterococci have been shown to cause altered cytokine responses compared to unencapsulated strains [65]. Several secreted factors also have important implications in enterococcal pathogenicity through the induction of direct pathological damage. Cytolysin (Cyl) is a hemolytic toxin with bacteriocin activity [51]. The toxin is coded for by an eight gene operon localized on a pheromone-responsive plasmid or in the PAI of *E. faecalis*. Cytolysin is able to lyse a broad range of eukaryotic (human, horse and rabbit erythrocytes) and Gram-positive cells. Moreover, Cyl has been shown to contribute to virulence in several animal models [52,53]. The presence of cytolysin has also been shown to promote the appearance of *E. faecalis* in the blood stream [110]. Gelatinase (GelE) is an extracellular zinc metallo-endopeptidase, which is co-transcribed with the serine protease SprE and positively regulated by a quorum-sensing system encoded by the *fsr* locus [78]. GelE can hydrolyze a wide range of small biologically active peptides, including gelatin, casein and hemoglobin,

and have been shown to be enriched among clinical enterococcal isolates. Secreted bacterial proteases that damage host tissue may contribute to bacterial migration and spread. A more controversial virulence determinant is the *E. faecium* hyaluronidase (Hyl). Hyl is significantly more prevalent in *E. faecium* of clinical origin [80], and is thought to facilitate the spread of bacteria as well as their toxins and to increase invasiveness, through depolymerization of components of connective tissues [111]. The enterococci are also among the few prokaryotes that produce extracellular superoxide [81]. But whereas O_2^- -production is observed among most *E. faecalis* strains, it is limited to only a few strains among other enterococcal species. Reactive oxygen species, such as O_2^-, are intermediates produced during metabolism of molecular oxygen. *E. faecalis* generate superoxide via the respiratory chain, through reduction of oxygen by reduced demethylmenaquinone [112]. The production of extracellular superoxide also required a fermentable sugar [112]. Interestingly, the nutritional conditions in the mammalian GI tract apparently favor production of superoxide [112], and *E. faecalis* may thus be an important source of oxidative stress in the intestines. O_2^- exerts destructive effects on biological compounds such as lipids, proteins and nucleic acids, and may cause oxidative damage to membranes of host cells. A potential role of superoxide production by the intestinal microbiota in colon cancer has been suggested [113].

1.4. DNA microarray technology

High throughput DNA sequencing, as well as advances in fabrication and robotics during the 1990s led to the development of the DNA microarray technique, as an extension of existing macroarray techniques, such as Southern blots and dot blots [114]. As the majority or all of the predicted genes in a genome could be represented on a slide, the microarray technology provided a tool for genome-scale analysis, as opposed to the traditional one-by-one gene approaches. A DNA microarray is a two-dimensional matrix of DNA probes, usually arranged in a gridded manner on a glass slide or membrane. A typical microarray contains 10000-200000 spots. Each probe is designed to represent a defined target (gene, intergenic region etc.). The target is supplied in the form of DNA or reverse-transcribed RNA (cDNA), which under optimal conditions will hybridize specifically to its respective probe. When labeled with *e.g.,* a fluorophore, the amount of target bound to the probe can be quantified based on the signal emitted from the spot, when the fluorophore is excited through exposure

to light at the correct wavelength during scanning. Raw data from the scanning is stored as images, from which numerical information is extracted during the image analysis process. Currently, two major types of DNA chip technologies are in use; broadly termed one-channel and two-channel microarrays. Whereas one-channel microarrays are used to measure the absolute concentration of labeled target, two-channel microarrays estimate the relative abundance of target in test samples compared to control samples.

DNA microarrays have two main applications in microbiology [115]; the technology is mainly used to obtain quantitative information on the transcriptional activities (RNA) of all genes in a cell, and to a lesser extent for comparison of genetic content (DNA) between closely related species/strains. Transcriptional analysis reveals how global gene expression is modulated in response to changes in *e.g.,* cell growth, physiology and environment, while comparative genomic hybridization (CGH) measures differences in DNA copy numbers between a test and a reference genome. Other, more specific applications of microarray include definition of regulons, pathway engineering and single-nucleotide polymorphism (SNP) detection [115].

A number of manufactures is currently producing DNA microarrays, and the different types of arrays can be distinguished based on characteristics such as the nature of the probe (dsDNA, oligonucleotides etc.) and the surface material/matrix to which the probes are attached (glass, membrane etc.) [114]. Initially, PCR-based amplicon arrays and the high-density oligonucleotide Affymetrix arrays were the most commonly used systems. Further advances in the technology, leading to a drop in the costs associated with production, have since then made various oligonucleotide arrays widely applicable [116]. More recently, other platforms, such as Illumina have developed high-density bead arrays based on silica beads covered with hundreds of thousands of copies of specific oligonucleotide probes, which self assemble in microwells on either fiber optic bundles or planar silica slides. Localization of the different beads is accomplished by a decoding process of specific bead identifier sequences [114]. The Illumina bead arrays have successfully been applied to DNA methylation studies, gene expression profiling and SNP genotyping (references in [114]).

1.4.1. Microarrays in the future

Since its conception, the microarray technology has become one of the major tools in genomics. Nonetheless, during recent years the microarray technology has to some extent been caught up by advancing techniques, such as the next generation sequencing. In addition to assessing the gene content, high-throughput DNA sequencing has also provided a new method for mapping and quantifying microbial transcriptomes. Next-generation sequencing circumvents some of the inherent constraints associated with the microarray technology, including the need for knowledge about genome sequence, high background levels due to cross-hybridization and a limited dynamic range due to both background and saturation of signals. Currently, three main platforms for next-generation sequencing are on the marked: the Roche 454 sequencing technology, the Illumina GA technology and the ABI SOLiD technology, each associated with distinct advantages and disadvantages (reviewed in [116]), which must be carefully considered and taken into account when deciding on a sequencing technology. Sequencing-based transcriptomics has the potential to provide very high-definition transcriptional snapshots, and will undoubtedly increase our insight into microbial transcriptomes. Moreover, next-generation sequencing as opposed to microarrays also supplies information on regulatory RNA species, *e.g., cis*- and *trans*-acting RNAs (riboswitches and sRNA respectively) and antisense-RNA, thereby adding a new dimension to our understanding of microbial regulatory networks. However, the sequencing-based approaches are also associated with several challenges, including issues related to cDNA library construction (transcriptomics), bioinformatic challenges as a result of large datasets and coverage versus costs considerations (reviewed in [117]). Hence, whole-genome sequencing and sequencing-based transcriptomics currently require equipment, infrastructure and resources beyond those of most research groups, and sequencing of even a modest number of genomes/transcriptomes is thus in most cases an undertaking not feasible for a single laboratory. Microarray-based approaches therefore remain a relatively low cost alternative to sequencing. However, as the next generation sequencing technology is nascent, a transition from developmental phase to widespread use can be expected in the years to come, mirroring the early development of the microarray technology. Current efforts aim at reducing the cost of sequencing by several orders of magnitude, and such a reduction will further promote the sequencing-based technologies.

2. AIM OF STUDY

The main objective of the work presented in this thesis was to further explore the mechanisms behind *E. faecalis* pathogenicity, by means of genome-wide DNA microarrays.

The work included the following tasks:

- Assess the genetic diversity in a collection of *E. faecalis* baby isolates to obtain information about the genetic make-up of commensal *E. faecalis* and identify potential pathogen-specific genes.
- Examine differences in gene content in *E. faecalis* isolates to identify lineage-specific/-enriched genes associated with high-risk enterococcal clonal complex 6, which may potentially explain the survival and spread of this particular *E. faecalis* clone in the hospital environment.
- Investigate the global transcriptional responses of *E. faecalis* to the anionic detergent sodium dodecyl sulfate (SDS) and to bovine bile, and reveal common response mechanisms responsible for the observed cross-protection to SDS and the detergent-like activities of bile in *E. faecalis*.
- Investigate how NaCl-induced osmotic stress affects the global transcriptional activity of *E. faecalis*, and identify traits involved in growth and persistence under conditions relevant to the gastrointestinal environment, the natural habitat of the enterococci.
- Compare the genetic content and gene expression profiles of pathogenic and non-pathogenic strains of *E. faecalis* during growth in urine, to identify common traits important for survival, as well as individual characteristics explaining differences in pathogenic potential.

3. MAIN RESULTS AND DISCUSSIONS

E. faecalis has recently emerged as an important nosocomial pathogen and is thus of growing concern to the public health system. The high prevalence of virulence determinants among non-clinically relevant enterococci causes the contribution of the known enterococcal virulence factors to *E. faecalis* pathogenicity still to be a topic of debate. In this thesis, different aspects of enterococcal pathogenicity have been assessed using genome-wide microarrays. These include variations in gene content which may be relevant for host-association (paper II and IV) and clues about potentially important global gene regulation in the host-relevant growth environments bile and SDS (paper I), NaCl-induced osmotic stress (paper V) and urine (paper III).

Little information on the gene content of commensal *E. faecalis* was available. As a first initiative in an attempt to identify the genetic determinants responsible for the differences in life style between pathogenic and non-pathogenic *E. faecalis*, we decided to study genetic variation in a collection of community derived *E. faecalis* isolated from the feces of Norwegian infants (Paper II). Enterococci are among the first lactic acid bacteria to colonize the GI tract of a neonate. Thirty-one *E. faecalis* isolates, obtained from 11 healthy infants before the age of 12 months, were included in the study. These isolates were considered as legitimate representatives of commensal *E. faecalis* as they had been resident in the gut without causing any apparent negative effect to the health of the host. By MLST, the collection of baby isolates was resolved into 12 different sequence types (STs) and grouped into 11 genetic lineages, including 6 major clonal complexes (CCs) and 5 singletons at the time being. The baby isolates were also characterized with respect to antibiotic resistance and virulence properties. Tetracycline resistance was the most widespread resistance trait among the baby isolates (17/31). In accordance with previous reports [118,119,120,121,122,123], high prevalence of the virulence-associated genes *ace* (31/31), *agg* (27/31), *esp* (20/31), *cylL* (16/31), *gelE* (29/31) and *fsrB* (18/31) was also observed. The PCR screening correlated fairly well with the phenotypes detected in cytolysin - and gelatinase assays. The discrepancy between gelatinase genotype and phenotype could be attributed to the absence of the regulatory system *fsrABDC*. A subset of the isolates was further analyzed by CGH. The CGH data corroborated the importance of previously defined MGEs as the major source of

genomic diversity in *E. faecalis*. However, none of the MGEs were entirely divergent in all strains tested, and a block-wise pattern of present and divergent genes was consistent with modular evolution of these elements. Interestingly, the genetic variation observed in our collection of commensal *E. faecalis* was comparable to the diversity reported in a strain set thought to be representative of the major *E. faecalis* lineages [23], and although, MGEs was confirmed as a significant source of genomic diversity, our data also suggested other and more complex discriminatory factors to be involved in the evolution of *E. faecalis*. A total of 169 genes were divergent in all the isolates analyzed by CGH, and we hypothesized that these genes may represent potential *E. faecalis* pathogen-specific genes. Bayesian-based reconstruction of phylogenetic relationship suggested an overall correlation between MLST and gene content as revealed by CGH, and we therefore also advanced the idea of lineage-specific genes as contributors to the persistence and spread of *E. faecalis* in the hospital environment.

Further investigation of the hypotheses on pathogen-specific and lineage-specific genes was a natural continuation of the work presented in paper II. Hence, in paper IV, CGH was used to survey variation in gene content within 15 *E. faecalis* isolated in European hospital environments. Population structure studies by MLST had previously defined distinct clonal complexes (CC) of *E. faecalis* enriched in hospitalized patients (CC6, CC9, CC28 and CC40), designated high-risk enterococcal clonal complexes (HiRECCs), and in light of the Bayesian-based phylogenetic reconstruction conducted in paper II, a special focus was put on CC6. Of the 3219 V583 genes represented on the array, the number of genes classified as present ranged from 2359 (597/96) to 2883 (E4250) among the isolates genomotyped by CGH. During the course of the study, a number of draft genomes from *E. faecalis* sequencing projects was released, and BLASTN comparison against the V583 genome (ST6) was therefore also performed with 24 publicly available draft genomes, including the two CC6 strains TX0104 (ST2), which is an endocarditis isolate, and HH22 (ST6), the first known beta-lactamase producing *E. faecalis* isolate [124]. Analysis of the compiled data set (BLASTN and CGH), revealed a total of 1667 genes which were classified as present in all strains, thus representing the *E. faecalis* core genome. None of potential pathogen-specific genes identified in paper II were found to be present in all hospital-related isolates analyzed in paper IV, neither was any gene found to be unique to any HiRECC. In order to identify genes significantly enriched among CC6-strains, data from the present study were

supplemented with hybridization data from an additional 24 strains of various origins (Paper II, III and unpublished data). In addition to V583, data from a total of 63 strains were analyzed. By statistical testing (Fisher's exact test; $q < 0.01$), 252 genes were found to be more prevalent among CC6 strains than in non-CC6 strains. The majority of these genes were located within the previously defined mobile elements *phage03* (n=51), *efaB5* (n=34) and a *vanB* associated genomic island (n=55). Indeed, prophage-related genes constituted a predominant proportion of the CC6-enriched genes (55.5 %; $p < 2.2e-16$, Fisher's exact test). Notably, the two former elements had also previously been suggested to play a role in hospital adaptation [Leavis and Willems et al., unpublished data]. Moreover, a CC6-enriched genomic islet (EF3217 to -27), encoding a putative phage related element within the V583 genome, was identified. PCR screening revealed a number of polymorphisms in this locus across the species.

The enrichment of phage-related genes and genes located on other types of mobile elements among CC6-strains fits well with a newly emerging idea of hospital-enterococci as junkyards for MGEs [3rd ASM conference on enterococci, speaker S1-2:6]. The genome sequence of strain OG1RF revealed a number of genes unique to this strain compared to the V583 strain, including two CRISPR (clusters of regularly interspaced short palindromic repeats) elements. CRISPR elements are prokaryotic defense systems against bacteriophage infection [125,126]. A CRISPR locus generally consists of several noncontiguous direct repeats (23 to 47 base pairs (bp)) separated by unique spacer sequences (21 to 72 bp), and is often neighbored by *cas* (CRISPR-associated) genes [126]. The "specificity" of the CRISPR/Cas system, *i.e.* towards which phages it confers resistance, is directed by the spacers in a manner analogous to RNAi in eukaryotic organisms [125,126]. In OG1RF, only CRISPR1 was associated with *cas* genes. A third CRISPR locus has recently also been identified in *E. faecalis* [3rd ASM conference on enterococci, speaker S1-2:6]. According to the current hypothesis, enterococci devoid in CRISPR loci may benefit from uptake of various MGEs harboring *e.g.*, antibiotic resistance determinants, which may represent competitive advantages for pathogenic strains compared to non-pathogenic strains in a clinical setting. Indeed, preliminary analysis suggests that there is a negative correlation between the presence of antibiotic resistance determinants and CRISPR in the genomes of *E. faecalis*, and some CCs (CC6 and CC9) appear to be entirely devoid of CRISPR/cas systems [3rd ASM conference on enterococci, speaker S1-2:6].

Interestingly, EF3217 and EF3218 showed homology to genes with implications in DNA repair, hence, a potential role for these genes in protection against oxidative DNA damage induced in the hospital environment/ during infection is conceivable. Nevertheless, it is a significant impediment that a large proportion of the CC6-enriched genes codes for hypothetical proteins, to which no obvious function could be assigned. The lack of homology to genes of known function makes it difficult to deduce functionality, and further characterization of individual genes is thus required in order to distinguish their implications in enterococcal fitness. From the draft genomes of CC6 strains HH22 and TX0104, we also identified a CC6-enriched non-V583 locus associated with the *E. faecalis* PAI. One of the putative open reading frames located in this locus contained a known mucin-binding domain. Interestingly, surface related structures (including MSCRAMMs, internalin-like and WxL protein-coding genes) with putative implications in virulence were significantly overrepresented (9.1 %; $p = 0.036$, Fisher's exact test) among the CC6 enriched genes. We hypothesized that absence or divergence in these loci may result in antigenic variation, but again, further studies will be necessary to obtain clues on functionality.

In parallel with the genomic effort, we also wanted to explore other aspects of enterococcal pathogenicity through transcriptional profiling of *E. faecalis* in host-relevant growth environments. *E. faecalis* is the most abundant Gram-positive coccus in the gastrointestinal (GI) tract. In order to survive in their natural habitat, the bacterial flora residing in the intestines must tolerate relatively high concentrations of host-produced inhibitory compounds like bile. Bile is a digestive juice secreted by the liver and stored in the gallbladder, before released into the small intestines, where it plays a vital role in digestion and absorption of fats and fat-soluble vitamins. In paper I, the transcriptional response of *E. faecalis* V583 to bovine bile exposure was investigated. Growth in the presence of bovine bile induced extended lag phases, reduced growth rates and lower cell densities in the stationary phase of growth; the cell density of V583 grown in the present of 7.5 % bile was approximately one-fifth of the final OD_{600} of untreated cultures. Transcriptional profiling using genome-wide microarrays revealed 308 genes which were differentially transcribed in response to bovine bile. An enrichment of genes coding for proteins with membrane-associated functions and/or locations among the differentially expressed genes suggested that the membrane architecture and composition play a key role in *E. faecalis* bile tolerance. Particularly, the functional

categories of genes involved in fatty acid and lipid metabolism and signal transduction were strongly affected. Interestingly, the transcription of genes encoding two drug resistance transporters of the EmrB/QacA family was enhanced during treatment with bile. This was the first report of a proton motive force-dependent transport system involved in bile resistance in Gram-positive bacteria.

Detergents are surface-active chemicals used for cleaning purposes, and tolerance to detergents is important for bacterial persistence in the environment. Sodium dodecyl sulfate (SDS) is an anionic detergent. Significant cross-resistance has been reported between SDS and bile acids in *E. faecalis* [86]. Surfactant-based cleaning and disinfection may thus contribute to bacterial adaptation and resistance development, and the transcriptional response of *E. faecalis* to SDS has been considered relevant to the mechanisms involved in bile resistance. Paper I also examined the SDS-induced changes in gene expression in *E. faecalis* V583: a total of 209 genes showed differential transcription in *E. faecalis* V583 during treatment with 0.06 % SDS. Detergent activity was mainly reflected by enhanced transcription of genes with membrane-associated function or location, including several genes involved in type II fatty acid biosynthesis (FASII), as was also observed in response to bile. However, comparison of the transcriptional profiles of V583 during treatment with bile and SDS revealed 68 genes that were common between the two responses, of which only 38 genes showed similar expression patterns (either up- or down-regulated) to both treatments, and the FASII genes were not among them. Hence, although the observed cross protection between bile and SDS suggests overlapping toxicities, no obvious common mechanisms of resistance could be identified at the transcriptional level.

In light of the observed effects of the presence of bovine bile and SDS on growth and gene expression, growth experiments and transcriptional profiling were also performed with a mixture of the two detergents. On the basis of the reported cross-resistance between bile salt- and SDS-adapted cells both additive and synergistic effects on V583 were expected. However, the effect of the detergent mixture turned out to be partly antagonistic, *i.e.* the presence of bile seemed to abolish the inhibitory effects of SDS on the growth and transcription of V583. In paper I, we launched two alternative explanations to the observed antagonism, none of which was further investigated: 1) increased membrane stability as a

result of bile acids intercalating with membrane lipids, and 2) micelle-formation between bile acids and SDS, preventing SDS from adhering to the bacterial cell.

The gastrointestinal tract is also an environment associated with elevated osmolarity. The salinity of the small intestines is equivalent to 0.3M NaCl. Previous studies showed that *E. faecalis* was able to grow in 28.5 % NaCl, a concentration equivalent to the maximal amount of NaCl soluble in BHI broth. In paper V, the effect of NaCl on *E. faecalis* V583 was studied using genome-wide microarrays. A total of 515 genes were identified as differentially transcribed at one or more time points during the time course in V583 challenged with moderate osmolarity (6.5 % NaCl). The osmotic response of nonhalophilic bacteria is reportedly characterized by an initial uptake of potassium, with a concurrent increase in certain amino acids, in order to retain electrical neutrality [127]. Enterococci and other Gram-positives, however, have intrinsically high internal concentrations of potassium and a large pool of free amino acids [127,128], which may explain why this primary response was not as pronounced in *E. faecalis* as one could have expected. A partial induction of the *kpd* gene cluster encoding a K^+-uptake system was nevertheless observed. The second phase of osmoadaption involves accumulation of compatible solutes. The up-regulation of genes encoding two ABC transporters involved in the uptake of glycine betaine (EF0862 to -65 and EF2641 to -42) suggested that this is the primary osmoprotectant accumulated in *E. faecalis*. 6.5% NaCl induced a strict repression of the *gelE-sprE* operon encoding the virulence factors gelatinase and serine protease. A gelatinase-negative phenotype was also observed in the presence of salt. We hypothesized that the observed phenotype may be a product of ionic interference of the pheromone-receptor interaction required for the *fsr* autoregulatory circuit, however, follow-up experiments were not conclusive. The effect of NaCl on the bacterial cell envelope was reflected by a repression of the FASII genes, indicating lowered content of unsaturated fatty acids. Moreover, the *epa* gene cluster was also partially induced during elevated osmolarity. The role of Epa in osmoprotection was further confirmed by growth studies with *epa* mutants; the growth of an *epaB*- and an *epaE*-deficient mutants was significantly diminished compared to the wild type, in the presence of NaCl. We speculate that the induction of the *epa* cluster may be related to a NaCl-induced reduction in the membrane fluidity of V583, however, this hypothesis has not yet been further elaborated. Apparently, Epa also confers resistance to other cell envelope-active stressors, *i.e.* class IIa bacteriocins, ethanol, bile/bile acids and detergents, demonstrating a wider ranging role of

Epa in the physiological robustness and stress management of *E. faecalis*. This link between the intrinsic robustness of *E. faecalis* and its ability to perform as a human pathogen provides a new perspective on the underlying mechanisms by which Epa might act as a virulence trait.

In paper III, the global transcription profiles of two pathogenic (MMH594 and OG1RF) and one probiotic strain (Symbioflor 1) during cultivation in human urine were compared. Growth in urine partially mimics the milieu of the urinary tract, and identification of differentially expressed genes *in vitro* may thus represent a means to identify novel fitness factors required for this particular ecological niche. Moreover, we wanted to identify differential gene expression that may potentially explain differences in the ability to cause UTI observed between pathogenic- and non-pathogenic *E. faecalis*. Strains of different origins showed comparable growth characteristics, indicating that the pathogenic potential is not a result of different growth capacities. CGH was used to assess differences in gene content between the three test strains. Transcriptional activity in urine was compared to that in the rich medium 2xYT, and gene expression profiles were obtained after 5 (t_5) and 30 min. (t_{30}) exposure to urine. 2xYT was used as the reference medium, since it is believed to contain a minimum of potentially infection-relevant mammalian cues [129]. In addition, this was the reference conditions used in previous studies analyzing gene expression of *E. faecalis* in urine [129].

At the transcriptional level, overall similar expression patterns were observed between the three strains, with some distinct characteristics. The concentrations of glucose in urine from healthy humans are generally below the threshold for release of CCR [130,131]. However, of the loci known to be subjected to CCR [95,132], only genes involved in citrate metabolism (EF3215 to -22) were up-regulated in response to urine. In light of the abundance of citrate in human urine [133], this observation may however be significant. Moreover, the transcriptional data suggested that *E. faecalis* make use of available peptides and amino acids, as a source of other limited amino acids. Up-regulation of *efaABC* and two other genes encoding Mn^{2+}/Fe^{2+} transporters (EF1057 and EF1901), in addition to several other iron transporters may be indicative of iron- and manganese depletion. This notion was further supported by the induction of a MMH594-specific putative uptake system for manganese (EF0575 to -78) located on the pathogenicity island. Growth in urine also induced regulation of a large number of genes with a proven or predicted function in other stress responses in *E.*

faecalis. Particularly interesting was the stimulation of an oxidative stress response, which has previously been connected to *E. faecalis* survival in macrophages. Interestingly, low levels of Mn^{2+} have been reported as a regulator of oxidative stress regulons in other bacteria [62,134,135]. Another noteworthy characteristic of the *E. faecalis* response to urine was the differential transcription of genes implicated in biofilm formation: *bopABCD* (biofilm of plastic; EF0954 to -57) was partially up-regulated in OG1RF, while *srtA* (EF3056) was induced in MMH594 and Symbioflor 1. Knock-out mutant studies have also suggested a role for the *epa* locus (EF2177-2200), *salA* (EF3060), *salB* (EF0394) and *altA* (EF0799) in biofilm production [136,137], all of which were down-regulated in response to urine. These observations complemented an overall significant adaptation of genes with membrane-associated functions upon the encounter with urine, including an immediate up-regulation of genes involved in FASII which may relate to urine-induced changes in membrane composition.

Interestingly, OG1RF displayed what could be interpreted as a more rapid adjustment to urine as a growth medium: while the number of differentially expressed genes increased throughout the time course in MMH594 and Symbioflor 1, fewer genes were regulated in OG1RF after 30 min. than after 5 min. This rationale was further supported by the swift derepression of macromolecular biosynthesis in OG1RF, compared to the two other strains, which may be indicative of OG1RF holding adaptive advantages over the two other strains in this medium of growth. Although no direct comparison of the virulence potential of OG1RF and MMH594 has previously been conducted, OG1RF was recovered in higher numbers than V583, which is closely related to MMH594, from both kidney and bladder during mixed infection, and from the kidneys during mono-infection in a murine UTI model [29]. The encounter with urine also had a significant impact on the transcription of a number of proposed virulence-associated traits [26], however, among the established enterococcal virulence factors only the *fsr* operon showed differential transcription; a modest up-regulation of the *fsrABC* genes (EF1822 to -20) was observed in MMH594 at t_{30}. The *fsrA* gene was also up-regulated at t_5. The regulation of *fsrB* (EF1821) in MMH594 at t_{30} was however, not confirmed by real time quantitative PCR (QPCR), thus, the importance of this observation remains uncertain. On the other hand, QPCR revealed significant up-regulation of *fsrB* in OG1RF at t_{30}. As mentioned in the introduction, the *fsr* regulatory system is known to positively regulate *gelE-sprE* expression by quorum sensing. Quorum sensing regulatory cascades are characteristically

initiated by elevated expression of a regulatory unit (*fsr*), of which the prospective outcome would be a subsequent induction of the *fsr*-regulon, and hence, activation of genes encoding the secreted proteases GelE and SprE, among others [138]. Such a progression is in line with the work by Shepard and Gilmore [129]: by QPCR they found *gelE* to be 7-fold induced during logarithmic growth in urine. In summary, despite the failure to identify pathogen-specific *E. faecalis* genes, the overall similarity between the transcriptional responses of pathogenic and non-pathogenic strains to urine observed in paper III, implies that the pathogenic potential of different *E. faecalis* strains may in fact be determined by presence or absence of specific genes, rather than the level of expression of such traits.

However, although various *in vitro* conditions can be very carefully manipulated, they can never fully replicate the host environment; additional biological factors are present *in vivo* that most likely trigger further changes in the transcriptional activity of the pathogen. Interactions between *E. faecalis* and for example host surface proteins, phagocytic cells and local micro environments within the infected host will represent important aspects of an enterococcal infection, which is not accounted for in our *in vitro* experimental set-ups. Modified *in vitro* systems and/or animal models can thus potentially assist in further increasing our insight into the mechanisms of enterococcal pathogenicity. The first *in vivo* time course transcriptional analysis of *Listeria monocytogenes* was recently published [139]. Monitoring the gene expression during infection provides us with new knowledge on host-pathogen communication, and may thus be important for identification of novel targets for antibiotics and immunotherapy. Nevertheless, our *in vitro* urine study is a step in the right direction, as host-produced immune effector molecules such as secretory immunoglobulin A (IgA), proteins and low molecular weight sugars are released into urine as part of a constitutive host defense [140], and thus add a new aspect to the analysis of the transcriptional activity. Hence, paper III has provided novel insight into the factors involved in adaptation and survival of *E. faecalis* in an infection-relevant growth environment. It was particularly interesting to see the effect of urine on the gene expression of several genes with implications in biofilm formation. The clinical importance of biofilm formation in UTI is well documented, and the fact that cues in the urinary tract environment may promote biofilm formation is intriguing.

Table 2: *E. faecalis* V583 genes that were commonly differentially expressed under all the conditions investigated in papers I, III and V. ↑ = up-regulated, ↓ = down-regulated and NA = gene not present in this *E. faecalis* strain

ORF number	Gene product	Regulation					
		Bile	SDS	NaCl	Urine		
					MMH594	OG1RF	Symbioflor 1
EF0108	C4-dicarboxylate transporter, putative	↑	↑	↑	↓	↓	↑↓
EF0288	Hypothetical protein	↑	↑	↓	↓	↓	↓
EF2074	ABC transporter, ATP-binding protein	↑↓	↓	↓↑	↑	↑	↑
EF2075	ABC transporter, permease protein	↑↓	↓	↓↑	↑	↑	↑
EF2641	Glycine betaine/L-proline ABC transporter, ATP-binding subunit	↑	↑	↑	↓	↓	↓
EF2697	Conserved domain protein	↑	↓	↑	↑	↑	↑
EF2713	Cell wall surface anchor family protein	↓	↓	↓	↑	NA	NA
EF2875	Acetyl-CoA carboxylase, carboxyl transferase alpha subunit	↓	↑	↓	↑	↑	↑
EF2876	Acetyl-CoA carboxylase, carboxyl transferase beta subunit	↓	↑	↓	↑	↑	↓↑
EF2877	Acetyl-CoA carboxylase, biotin carboxylase	↓	↑	↓	↑	↑	↑
EF2878	(3R)-hydroxymyristoyl-(acyl-carrier-protein) dehydratase	↓	↑	↓	↑	↑	↑
EF2879	Acetyl-CoA carboxylase, biotin carboxyl carrier protein	↓	↑	↓	↑	↑	↑
EF2880	3-oxoacyl-(acyl-carrier-protein) synthase II	↓	↑	↓	↑	↑	↑
EF2883	Enoyl-(acyl-carrier-protein) reductase II	↓	↑	↓	↑	↑	↑
EF3283	Transcriptional regulator CtsR	↑	↑	↓↑	↑	↑	↑

Comparisons across the transcriptional analyses presented in papers I, III and V should be made with caution, due to different microarray platforms and varying stringency in the statistical methods applied to the different data sets. Nevertheless, it is noteworthy that of the 15 genes that showed differential transcription in response to all the experimental conditions in all the strains tested (Table 2), only one gene (EF3283) was induced in all three studies. EF3283 codes for CtsR, a well-known transcriptional regulator of stress responses, which negatively controls the expression of *clp* and heat-inducible chaperones in many Gram-positive bacteria [141]. The consensus CtsR recognition sequence was also detected upstream of *clpP*, *clpC* and *clpE* in *E. faecalis* [141]. An implication of the Clp proteins in the virulence and *in vivo* survival of several pathogens has been reported [142,143,144,145,146], with a proposed role for ClpP and the Clp ATPases in controlling the stability of key regulatory proteins [147]. In light of this role of the Clp proteins in adaption to atypical conditions, an overall induction of the *clp* genes in our experiments would make sense. Indeed, *clpP*, *clpC* and *clpE* were all induced upon the encounter with urine, and *clpE* also showed increased transcription during growth in NaCl. However, the coincident induction of CtsR conflict with the conception of CtsR as a repressor of the *clp* genes, rendering CtsR and its regulon an interesting target for future studies in *E. faecalis*.

4. CONCLUDING REMARKS AND FUTURE WORK

The work presented in this thesis provides new insight into different aspects of *E. faecalis* pathogenicity. Microarray-based comparative genomic analysis of *E. faecalis* identified a set of lineage-enriched genes which may contribute to the fitness of clonal complex 6 (CC6); one of several high-risk *E. faecalis* clonal complexes highly associated with the hospital environment. Preponderance of genes located within specific mobile genetic elements (MGEs) among the CC6-enriched genes, suggests a role of genome flexibility in hospital adaptation. Furthermore, significant enrichment of genes encoding surface-related structures may lead to antigenic variation, and may thus supply CC6 strains with a means to evade certain mechanisms of host defense.

Transcriptional analyses highlighted the importance of rapid adaptations in the expression of genes related to energy metabolism, active transport, cell envelope modification and general stress mechanisms in response to host-relevant growth environments. Moreover, the transcriptional profiling provided clues to hitherto undiscovered mechanisms of resistance associated with the various growth conditions investigated. Particularly interesting observations included:

- A potential involvement of multi drug resistance transporters of the EmrB/QacA family in *E. faecalis* bile resistance.
- The involvement of genes encoding a capsular rhamnose- containing polysaccharide (*epa*) in the ability of *E. faecalis* to cope with NaCl-induced osmotic stress.
- A potential role of the type II fatty acid biosynthesis pathway in adaptation to the cell envelop stress induced by various stressors, possibly through modifications of the membrane phospholipid composition.
- Biological cues present in urine apparently promote biofilm formation.

However, the microarray technology is a hypothesis-generating technology, and any functional clues inferred by the microarray data must therefore be further elaborated in follow-up studies. Such studies may involve knock out studies of interesting genes /gene clusters, and phenotypic characterization of the wild type-mutant pairs in animal infection models. Funding for characterization of potentially virulence-related transcriptional regulators has been applied for. Furthermore, transcriptional profiling of the transfer of *E.*

faecalis from rich to minimal medium may complement the data retrieved in paper III: at present, it is not possible to differentiate between changes in gene expression induced by biological cues in urine and a more general response to urine as a low nutrient growth medium. Comparison of the two gene expression profiles would thus add specificity to the observations made in paper III. Future work involving microarrays would benefit from the development of a novel array design. Due to the single strain array design, the current array is suboptimal for work with other strains than V583. Sequencing of additional *E. faecalis* genomes have provided insight into the genomic diversity of the species, and to take advantage of the available sequence information an *E. faecalis* pan-genome array is in planning. Such an array will provide us with an increased flexibility for analysis of both known and uncharacterized *E. faecalis* strains.

5. REFERENCES

1. Murray BE (1990) The life and times of the *Enterococcus*. Clin Microbiol Rev 3: 46-65.
2. Thiercelin ME (1899) Sur un diplocoque de l'intestin susceptible de devenir pathogène. C R Séances Société Biologie 51: 269-271.
3. Maccallum WG, Hastings TW (1899) A Case of Acute Endocarditis Caused by *Micrococcus Zymogenes* (Nov. Spec.), with a Description of the Microorganism. J Exp Med 4: 521-534.
4. Sherman JM (1937) The streptococci. Bacteriol Rev 1: 3-97.
5. Facklam RR, Carvalho MdGS, Teixeria LM (2002) History, taxonomy, biochemical characteristics and antibiotic suceptibility testing of enterococci. In: Gilmore MS, Clewell DB, Courvalin P, Dunny GM, Murray BE et al., editors. The Enterococci: pathogenesis, molecular biology and antibiotic resistance. Washington DC: ASM Press.
6. Facklam RR, M. Carvalho and L. M: Teixeira. (2002) History, Taxonomy, Biochemical Characteristics and Antibiotic susceptibility Testing of Enterococci. In: Gilmore MS, editor. Enterococci Pathogenesis, Molecular biology and Antibiotic Resistance Washington: ASM Press. pp. X, 439 s.
7. Ritchey TW, Seeley HW (1974) Cytochromes in *Streptococcus faecalis* var. *zymogenes* grown in a haematin-containing medium. J Gen Microbiol 85: 220-228.
8. Tannock GW, Cook G (2002) Enterococci as members of the intestinal microflora of humans. In: Gilmore MS, Clewell DB, Courvalin P, Dunny GM, Murray BE et al., editors. The Enterococci: Pathogenesis, Molecular Biology and Antibiotic resistance. Washington DC: ASM Press.
9. Aarestrup FM, Butaye P, Witte W (2002) Nonhuman reservoirs of enterococci. In: Gilmore MS, Clewell DB, Courvalin P, Dunny GM, Murray BE et al., editors. The enterococci: pathogenesis, molecular biology and antibiotic resistance. Washington: ASM Press.
10. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, et al. (2010) A human gut microbial gene catalogue established by metagenomic sequencing. Nature 464: 59-65.
11. Sghir A, Gramet G, Suau A, Rochet V, Pochart P, et al. (2000) Quantification of bacterial groups within human fecal flora by oligonucleotide probe hybridization. Appl Environ Microbiol 66: 2263-2266.
12. Foulquie Moreno MR, Sarantinopoulos P, Tsakalidou E, De Vuyst L (2006) The role and application of enterococci in food and health. Int J Food Microbiol 106: 1-24.
13. Ogier JC, Serror P (2008) Safety assessment of dairy microorganisms: the *Enterococcus* genus. Int J Food Microbiol 126: 291-301.
14. Franz CM, Stiles ME, Schleifer KH, Holzapfel WH (2003) Enterococci in foods - a conundrum for food safety. Int J Food Microbiol 88: 105-122.
15. Franz CM, Holzapfel WH, Stiles ME (1999) Enterococci at the crossroads of food safety? Int J Food Microbiol 47: 1-24.
16. Nes IF, Diep DB, Holo H (2007) Bacteriocin diversity in *Streptococcus* and *Enterococcus*. J Bacteriol 189: 1189-1198.
17. Williams NT Probiotics. Am J Health Syst Pharm 67: 449-458.
18. Bertolami MC, Faludi AA, Batlouni M (1999) Evaluation of the effects of a new fermented milk product (Gaio) on primary hypercholesterolemia. Eur J Clin Nutr 53: 97-101.

19. Cremonini F, Di Caro S, Santarelli L, Gabrielli M, Candelli M, et al. (2002) Probiotics in antibiotic-associated diarrhoea. Dig Liver Dis 34 Suppl 2: S78-80.
20. Domann E, Hain T, Ghai R, Billion A, Kuenne C, et al. (2007) Comparative genomic analysis for the presence of potential enterococcal virulence factors in the probiotic *Enterococcus faecalis* strain Symbioflor 1. Int J Med Microbiol 297: 533-539.
21. Shankar N, Baghdayan AS, Gilmore MS (2002) Modulation of virulence within a pathogenicity island in vancomycin-resistant *Enterococcus faecalis*. Nature 417: 746-750.
22. McBride SM, Coburn PS, Baghdayan AS, Willems RJ, Grande MJ, et al. (2009) Genetic variation and evolution of the pathogenicity island of *Enterococcus faecalis*. J Bacteriol 191: 3392-3402.
23. McBride SM, Fischetti VA, Leblanc DJ, Moellering RC, Jr., Gilmore MS (2007) Genetic diversity among *Enterococcus faecalis*. PLoS ONE 2: e582.
24. Shankar N, Baghdayan AS, Willems R, Hammerum AM, Jensen LB (2006) Presence of pathogenicity island genes in *Enterococcus faecalis* isolates from pigs in Denmark. J Clin Microbiol 44: 4200-4203.
25. Leavis H, Top J, Shankar N, Borgen K, Bonten M, et al. (2004) A novel putative enterococcal pathogenicity island linked to the *esp* virulence gene of *Enterococcus faecium* and associated with epidemicity. J Bacteriol 186: 672-682.
26. Paulsen IT, Banerjei L, Myers GS, Nelson KE, Seshadri R, et al. (2003) Role of mobile DNA in the evolution of vancomycin-resistant *Enterococcus faecalis*. Science 299: 2071-2074.
27. Sahm DF, Kissinger J, Gilmore MS, Murray PR, Mulder R, et al. (1989) In vitro susceptibility studies of vancomycin-resistant *Enterococcus faecalis*. Antimicrob Agents Chemother 33: 1588-1591.
28. Palmer KL, Carniol K, Manson JM, Heiman D, Shea T, et al. High-quality draft genome sequences of 28 *Enterococcus* sp. isolates. J Bacteriol 192: 2469-2470.
29. Bourgogne A, Garsin DA, Qin X, Singh KV, Sillanpaa J, et al. (2008) Large scale variation in *Enterococcus faecalis* illustrated by the genome analysis of strain OG1RF. Genome Biol 9: R110.
30. Kawalec M, Pietras Z, Danilowicz E, Jakubczak A, Gniadkowski M, et al. (2007) Clonal structure of *Enterococcus faecalis* isolated from Polish hospitals: characterization of epidemic clones. J Clin Microbiol 45: 147-153.
31. Ruiz-Garbajosa P, Bonten MJ, Robinson DA, Top J, Nallapareddy SR, et al. (2006) Multilocus sequence typing scheme for *Enterococcus faecalis* reveals hospital-adapted genetic complexes in a background of high rates of recombination. J Clin Microbiol 44: 2220-2228.
32. Aakra A, Nyquist OL, Snipen L, Reiersen TS, Nes IF (2007) Survey of genomic diversity among *Enterococcus faecalis* strains by microarray-based comparative genomic hybridization. Appl Environ Microbiol 73: 2207-2217.
33. Lepage E, Brinster S, Caron C, Ducroix-Crepy C, Rigottier-Gois L, et al. (2006) Comparative genomic hybridization analysis of *Enterococcus faecalis*: identification of genes absent from food strains. J Bacteriol 188: 6858-6868.
34. van Schaik W, Top J, Riley DR, Boekhorst J, Vrijenhoek JE, et al. Pyrosequencing-based comparative genome analysis of the nosocomial pathogen *Enterococcus faecium* and identification of a large transferable pathogenicity island. BMC Genomics 11: 239.
35. Peterson J, Garges S, Giovanni M, McInnes P, Wang L, et al. (2009) The NIH Human Microbiome Project. Genome Res 19: 2317-2323.

36. Wells CL, Jechorek RP, Erlandsen SL (1990) Evidence for the translocation of *Enterococcus faecalis* across the mouse intestinal tract. J Infect Dis 162: 82-90.
37. Moellering RC, Jr. (1992) Emergence of *Enterococcus* as a significant pathogen. Clin Infect Dis 14: 1173-1176.
38. Malani PN, Kauffman CA, Zervos MJ (2002) Enterococcal disease, epidemiology and treatment. In: Gilmore MS, Clewell DB, Courvalin P, Dunny GM, Murray BE et al., editors. The enterococci: Pathogenesis, Molecular Biology and Antibiotic Resistance. Washington DC: ASM Press.
39. Bitsori M, Maraki S, Raissaki M, Bakantaki A, Galanakis E (2005) Community-acquired enterococcal urinary tract infections. Pediatr Nephrol 20: 1583-1586.
40. O'Toole G, Kaplan HB, Kolter R (2000) Biofilm formation as microbial development. Annu Rev Microbiol 54: 49-79.
41. Lewis K (2001) Riddle of biofilm resistance. Antimicrob Agents Chemother 45: 999-1007.
42. Mohamed JA, Huang DB (2007) Biofilm formation by enterococci. J Med Microbiol 56: 1581-1588.
43. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, et al. (2004) Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 39: 309-317.
44. Garrison RN, Fry DE, Berberich S, Polk HC, Jr. (1982) Enterococcal bacteremia: clinical implications and determinants of death. Ann Surg 196: 43-47.
45. Stosor V, Peterson LR, Postelnick M, Noskin GA (1998) *Enterococcus faecium* bacteremia: does vancomycin resistance make a difference? Arch Intern Med 158: 522-527.
46. Malani PN, Kauffman CA, Zervis MJ (2002) Enterococcal disease, Epidemiology and treatment. In: Gilmore MS, Clewell DB, Courvalin P, Dunny GM, Murray BE et al., editors. The Enterococci: Pathogenesis, Molecular Biology and Antibiotic Resistance. Washington D.C.: ASM Press.
47. Wang A, Athan E, Pappas PA, Fowler VG, Jr., Olaison L, et al. (2007) Contemporary clinical profile and outcome of prosthetic valve endocarditis. JAMA 297: 1354-1361.
48. Fernandez Guerrero ML, Goyenechea A, Verdejo C, Roblas RF, de Gorgolas M (2007) Enterococcal endocarditis on native and prosthetic valves: a review of clinical and prognostic factors with emphasis on hospital-acquired infections as a major determinant of outcome. Medicine (Baltimore) 86: 363-377.
49. Pillar CM, Gilmore MS (2004) Enterococcal virulence - pathogenicity island of *E. faecalis*. Front Biosci 9: 2335-2346.
50. Arias CA, Murray BE (2008) Emergence and management of drug-resistant enterococcal infections. Expert Rev Anti Infect Ther 6: 637-655.
51. Booth MC, Bogie CP, Sahl HG, Siezen RJ, Hatter KL, et al. (1996) Structural analysis and proteolytic activation of *Enterococcus faecalis* cytolysin, a novel lantibiotic. Mol Microbiol 21: 1175-1184.
52. Jett BD, Jensen HG, Nordquist RE, Gilmore MS (1992) Contribution of the pAD1-encoded cytolysin to the severity of experimental *Enterococcus faecalis* endophthalmitis. Infect Immun 60: 2445-2452.
53. Chow JW, Thal LA, Perri MB, Vazquez JA, Donabedian SM, et al. (1993) Plasmid-associated hemolysin and aggregation substance production contribute to virulence in experimental enterococcal endocarditis. Antimicrob Agents Chemother 37: 2474-2477.

54. Sartingen S, Rozdzinski E, Muscholl-Silberhorn A, Marre R (2000) Aggregation substance increases adherence and internalization, but not translocation, of *Enterococcus faecalis* through different intestinal epithelial cells in vitro. Infect Immun 68: 6044-6047.
55. Sussmuth SD, Muscholl-Silberhorn A, Wirth R, Susa M, Marre R, et al. (2000) Aggregation substance promotes adherence, phagocytosis, and intracellular survival of *Enterococcus faecalis* within human macrophages and suppresses respiratory burst. Infect Immun 68: 4900-4906.
56. Vanek NN, Simon SI, Jacques-Palaz K, Mariscalco MM, Dunny GM, et al. (1999) *Enterococcus faecalis* aggregation substance promotes opsonin-independent binding to human neutrophils via a complement receptor type 3-mediated mechanism. FEMS Immunol Med Microbiol 26: 49-60.
57. Galli D, Lottspeich F, Wirth R (1990) Sequence analysis of *Enterococcus faecalis* aggregation substance encoded by the sex pheromone plasmid pAD1. Mol Microbiol 4: 895-904.
58. Lebreton F, Riboulet-Bisson E, Serror P, Sanguinetti M, Posteraro B, et al. (2009) *ace*, Which encodes an adhesin in *Enterococcus faecalis,* is regulated by Ers and is involved in virulence. Infect Immun 77: 2832-2839.
59. Shankar N, Lockatell CV, Baghdayan AS, Drachenberg C, Gilmore MS, et al. (2001) Role of *Enterococcus faecalis* surface protein Esp in the pathogenesis of ascending urinary tract infection. Infect Immun 69: 4366-4372.
60. Shankar V, Baghdayan AS, Huycke MM, Lindahl G, Gilmore MS (1999) Infection-derived *Enterococcus faecalis* strains are enriched in *esp*, a gene encoding a novel surface protein. Infect Immun 67: 193-200.
61. Tendolkar PM, Baghdayan AS, Gilmore MS, Shankar N (2004) Enterococcal surface protein, Esp, enhances biofilm formation by *Enterococcus faecalis*. Infect Immun 72: 6032-6039.
62. Low YL, Jakubovics NS, Flatman JC, Jenkinson HF, Smith AW (2003) Manganese-dependent regulation of the endocarditis-associated virulence factor EfaA of *Enterococcus faecalis*. J Med Microbiol 52: 113-119.
63. Lowe AM, Lambert PA, Smith AW (1995) Cloning of an *Enterococcus faecalis* endocarditis antigen: homology with adhesins from some oral streptococci. Infect Immun 63: 703-706.
64. Hancock LE, Gilmore MS (2002) The capsular polysaccharide of *Enterococcus faecalis* and its relationship to other polysaccharides in the cell wall. Proc Natl Acad Sci U S A 99: 1574-1579.
65. Thurlow LR, Thomas VC, Fleming SD, Hancock LE (2009) *Enterococcus faecalis* Capsular Polysaccharide Serotypes C and D and Their Contributions to Host Innate Immune Evasion. Infect Immun 77: 5551-5557.
66. Thurlow LR, Thomas VC, Hancock LE (2009) Capsular polysaccharide production in *Enterococcus faecalis* and contribution of CpsF to capsule serospecificity. J Bacteriol 191: 6203-6210.
67. Hendrickx AP, Bonten MJ, van Luit-Asbroek M, Schapendonk CM, Kragten AH, et al. (2008) Expression of two distinct types of pili by a hospital-acquired *Enterococcus faecium* isolate. Microbiology 154: 3212-3223.
68. Nallapareddy SR, Singh KV, Sillanpaa J, Garsin DA, Hook M, et al. (2006) Endocarditis and biofilm-associated pili of *Enterococcus faecalis*. J Clin Invest 116: 2799-2807.
69. Sillanpaa J, Nallapareddy SR, Prakash VP, Qin X, Hook M, et al. (2008) Identification and phenotypic characterization of a second collagen adhesin, Scm, and genome-

based identification and analysis of 13 other predicted MSCRAMMs, including four distinct pilus loci, in *Enterococcus faecium*. Microbiology 154: 3199-3211.
70. Schluter S, Franz CM, Gesellchen F, Bertinetti O, Herberg FW, et al. (2009) The high biofilm-encoding *bee* locus: a second pilus gene cluster in *Enterococcus faecalis*? Curr Microbiol 59: 206-211.
71. Singh KV, Nallapareddy SR, Murray BE (2007) Importance of the ebp (endocarditis- and biofilm-associated pilus) locus in the pathogenesis of *Enterococcus faecalis* ascending urinary tract infection. J Infect Dis 195: 1671-1677.
72. Tendolkar PM, Baghdayan AS, Shankar N (2006) Putative surface proteins encoded within a novel transferable locus confer a high-biofilm phenotype to *Enterococcus faecalis*. J Bacteriol 188: 2063-2072.
73. Nallapareddy SR, Singh KV, Murray BE (2008) Contribution of the collagen adhesin Acm to pathogenesis of *Enterococcus faecium* in experimental endocarditis. Infect Immun 76: 4120-4128.
74. Hendrickx AP, van Luit-Asbroek M, Schapendonk CM, van Wamel WJ, Braat JC, et al. (2009) SgrA, a nidogen-binding LPXTG surface adhesin implicated in biofilm formation, and EcbA, a collagen binding MSCRAMM, are two novel adhesins of hospital-acquired *Enterococcus faecium*. Infect Immun 77: 5097-5106.
75. Park SY, Shin YP, Kim CH, Park HJ, Seong YS, et al. (2008) Immune evasion of *Enterococcus faecalis* by an extracellular gelatinase that cleaves C3 and iC3b. J Immunol 181: 6328-6336.
76. Engelbert M, Mylonakis E, Ausubel FM, Calderwood SB, Gilmore MS (2004) Contribution of gelatinase, serine protease, and fsr to the pathogenesis of *Enterococcus faecalis* endophthalmitis. Infect Immun 72: 3628-3633.
77. Park SY, Kim KM, Lee JH, Seo SJ, Lee IH (2007) Extracellular gelatinase of *Enterococcus faecalis* destroys a defense system in insect hemolymph and human serum. Infect Immun 75: 1861-1869.
78. Qin X, Singh KV, Weinstock GM, Murray BE (2000) Effects of *Enterococcus faecalis fsr* genes on production of gelatinase and a serine protease and virulence. Infect Immun 68: 2579-2586.
79. Thurlow LR, Thomas VC, Narayanan S, Olson S, Fleming SD, et al. Gelatinase contributes to the pathogenesis of endocarditis caused by *Enterococcus faecalis*. Infect Immun.
80. Rice LB, Carias L, Rudin S, Vael C, Goossens H, et al. (2003) A potential virulence gene, hyl_{Efm}, predominates in *Enterococcus faecium* of clinical origin. J Infect Dis 187: 508-512.
81. Huycke MM, Joyce W, Wack MF (1996) Augmented production of extracellular superoxide by blood isolates of *Enterococcus faecalis*. J Infect Dis 173: 743-746.
82. Huycke MM, Abrams V, Moore DR (2002) *Enterococcus faecalis* produces extracellular superoxide and hydrogen peroxide that damages colonic epithelial cell DNA. Carcinogenesis 23: 529-536.
83. Huycke MM, Gilmore MS (1997) In vivo survival of *Enterococcus faecalis* is enhanced by extracellular superoxide production. Adv Exp Med Biol 418: 781-784.
84. Baik JE, Ryu YH, Han JY, Im J, Kum KY, et al. (2008) Lipoteichoic acid partially contributes to the inflammatory responses to *Enterococcus faecalis*. J Endod 34: 975-982.
85. Flahaut S, Benachour A, Giard JC, Boutibonnes P, Auffray Y (1996) Defense against lethal treatments and de novo protein synthesis induced by NaCl in *Enterococcus faecalis* ATCC 19433. Arch Microbiol 165: 317-324.

86. Flahaut S, Frere J, Boutibonnes P, Auffray Y (1996) Comparison of the bile salts and sodium dodecyl sulfate stress responses in *Enterococcus faecalis*. Appl Environ Microbiol 62: 2416-2420.
87. Flahaut S, Frere J, Boutibonnes P, Auffray Y (1997) Relationship between the thermotolerance and the increase of DnaK and GroEL synthesis in *Enterococcus faecalis* ATCC19433. J Basic Microbiol 37: 251-258.
88. Flahaut S, Hartke A, Giard JC, Auffray Y (1997) Alkaline stress response in *Enterococcus faecalis*: adaptation, cross-protection, and changes in protein synthesis. Appl Environ Microbiol 63: 812-814.
89. Flahaut S, Hartke A, Giard JC, Benachour A, Boutibonnes P, et al. (1996) Relationship between stress response toward bile salts, acid and heat treatment in *Enterococcus faecalis*. FEMS Microbiol Lett 138: 49-54.
90. Flahaut S, Laplace JM, Frere J, Auffray Y (1998) The oxidative stress response in *Enterococcus faecalis*: relationship between H2O2 tolerance and H2O2 stress proteins. Lett Appl Microbiol 26: 259-264.
91. Giard JC, Hartke A, Flahaut S, Boutibonnes P, Auffray Y (1997) Glucose starvation response in Enterococcus faecalis JH2-2: survival and protein analysis. Res Microbiol 148: 27-35.
92. Aakra A, Vebo H, Snipen L, Hirt H, Aastveit A, et al. (2005) Transcriptional Response of *Enterococcus faecalis* V583 to Erythromycin. Antimicrob Agents Chemother 49: 3989.
93. Bourgogne A, Thomson LC, Murray BE Bicarbonate enhances expression of the endocarditis and biofilm associated pilus locus, *ebpR-ebpABC*, in *Enterococcus faecalis*. BMC Microbiol 10: 17.
94. Vebo HC, Snipen L, Nes IF, Brede DA (2009) The transcriptome of the nosocomial pathogen *Enterococcus faecalis* V583 reveals adaptive responses to growth in blood. PLoS One 4: e7660.
95. Opsata M, Nes IF, Holo H Class IIa bacteriocin resistance in *Enterococcus faecalis* V583: The mannose PTS operon mediates global transcriptional responses. BMC Microbiol 10: 224.
96. Wilson M, editor (2002) Bacterial adhesion to host tissues : mechanisms and consequences
97. Galli D, Wirth R, Wanner G (1989) Identification of aggregation substances of *Enterococcus faecalis* cells after induction by sex pheromones. An immunological and ultrastructural investigation. Arch Microbiol 151: 486-490.
98. Sartingen S, Rozdzinski E, Muscholl-Silberhorn A, Marre R (2000) Aggregation Substance Increases Adherence and Internalization, but Not Translocation, of *Enterococcus faecalis* through Different Intestinal Epithelial Cells In Vitro. Infect Immun 68: 6044-6047.
99. Kreft B, Marre R, Schramm U, Wirth R (1992) Aggregation substance of *Enterococcus faecalis* mediates adhesion to cultured renal tubular cells. Infect Immun 60: 25-30.
100. Olmsted SB, Dunny GM, Erlandsen SL, Wells CL (1994) A plasmid-encoded surface protein on *Enterococcus faecalis* augments its internalization by cultured intestinal epithelial cells. J Infect Dis 170: 1549-1556.
101. Schlievert PM, Gahr PJ, Assimacopoulos AP, Dinges MM, Stoehr JA, et al. (1998) Aggregation and binding substances enhance pathogenicity in rabbit models of *Enterococcus faecalis* endocarditis. Infect Immun 66: 218-223.

102. Kowalski WJ, Kasper EL, Hatton JF, Murray BE, Nallapareddy SR, et al. (2006) *Enterococcus faecalis* adhesin, Ace, mediates attachment to particulate dentin. J Endod 32: 634-637.
103. Nallapareddy SR, Qin X, Weinstock GM, Hook M, Murray BE (2000) *Enterococcus faecalis* adhesin, *ace*, mediates attachment to extracellular matrix proteins collagen type IV and laminin as well as collagen type I. Infect Immun 68: 5218-5224.
104. Rich RL, Kreikemeyer B, Owens RT, LaBrenz S, Narayana SV, et al. (1999) Ace is a collagen-binding MSCRAMM from *Enterococcus faecalis*. J Biol Chem 274: 26939-26945.
105. Cobo Molinos A, Abriouel H, Omar NB, Lopez RL, Galvez A (2008) Detection of *ebp* (endocarditis- and biofilm-associated pilus) genes in enterococcal isolates from clinical and non-clinical origin. Int J Food Microbiol 126: 123-126.
106. Huebner J, Wang Y, Krueger WA, Madoff LC, Martirosian G, et al. (1999) Isolation and Chemical Characterization of a Capsular Polysaccharide Antigen Shared by Clinical Isolates of *Enterococcus faecalis* and Vancomycin-Resistant Enterococcus faecium. Infect Immun 67: 1213-1219.
107. Xu Y, Murray BE, Weinstock GM (1998) A cluster of genes involved in polysaccharide biosynthesis from *Enterococcus faecalis* OG1RF. Infect Immun 66: 4313-4323.
108. Xu Y, Singh KV, Qin X, Murray BE, Weinstock GM (2000) Analysis of a gene cluster of *Enterococcus faecalis* involved in polysaccharide biosynthesis. Infect Immun 68: 815-823.
109. Teng F, Singh KV, Bourgogne A, Zeng J, Murray BE (2009) Further characterization of the *epa* gene cluster and Epa polysaccharides of *Enterococcus faecalis*. Infect Immun 77: 3759-3767.
110. Huycke MM, Sahm DF, Gilmore MS (1998) Multiple-drug resistant enterococci: the nature of the problem and an agenda for the future. Emerg Infect Dis 4: 239-249.
111. Kayaoglu G, Orstavik D (2004) Virulence factors of *Enterococcus faecalis*: relationship to endodontic disease. Crit Rev Oral Biol Med 15: 308-320.
112. Huycke MM, Moore D, Joyce W, Wise P, Shepard L, et al. (2001) Extracellular superoxide production by *Enterococcus faecalis* requires demethylmenaquinone and is attenuated by functional terminal quinol oxidases. Mol Microbiol 42: 729-740.
113. Wang X, Allen TD, May RJ, Lightfoot S, Houchen CW, et al. (2008) *Enterococcus faecalis* induces aneuploidy and tetraploidy in colonic epithelial cells through a bystander effect. Cancer Res 68: 9909-9917.
114. Miller MB, Tang YW (2009) Basic concepts of microarrays and potential applications in clinical microbiology. Clin Microbiol Rev 22: 611-633.
115. Ye RW, Wang T, Bedzyk L, Croker KM (2001) Applications of DNA microarrays in microbial systems. J Microbiol Methods 47: 257-272.
116. van Vliet AH Next generation sequencing of microbial transcriptomes: challenges and opportunities. FEMS Microbiol Lett 302: 1-7.
117. Wang Z, Gerstein M, Snyder M (2009) RNA-Seq: a revolutionary tool for transcriptomics. Nat Rev Genet 10: 57-63.
118. Creti R, Imperi M, Bertuccini L, Fabretti F, Orefici G, et al. (2004) Survey for virulence determinants among *Enterococcus faecalis* isolated from different sources. J Med Microbiol 53: 13-20.
119. Eaton TJ, Gasson MJ (2001) Molecular screening of *Enterococcus* virulence determinants and potential for genetic exchange between food and medical isolates. Appl Environ Microbiol 67: 1628-1635.

120. Franz CM, Muscholl-Silberhorn AB, Yousif NM, Vancanneyt M, Swings J, et al. (2001) Incidence of virulence factors and antibiotic resistance among Enterococci isolated from food. Appl Environ Microbiol 67: 4385-4389.
121. Lempiainen H, Kinnunen K, Mertanen A, von Wright A (2005) Occurrence of virulence factors among human intestinal enterococcal isolates. Lett Appl Microbiol 41: 341-344.
122. Mannu L, Paba A, Daga E, Comunian R, Zanetti S, et al. (2003) Comparison of the incidence of virulence determinants and antibiotic resistance between *Enterococcus faecium* strains of dairy, animal and clinical origin. Int J Food Microbiol 88: 291-304.
123. Semedo T, Santos MA, Lopes MF, Figueiredo Marques JJ, Barreto Crespo MT, et al. (2003) Virulence factors in food, clinical and reference Enterococci: A common trait in the genus? Syst Appl Microbiol 26: 13-22.
124. Murray BE, Mederski-Samaroj B (1983) Transferable beta-lactamase. A new mechanism for in vitro penicillin resistance in *Streptococcus faecalis*. J Clin Invest 72: 1168-1171.
125. Barrangou R, Fremaux C, Deveau H, Richards M, Boyaval P, et al. (2007) CRISPR provides acquired resistance against viruses in prokaryotes. Science 315: 1709-1712.
126. Horvath P, Barrangou R CRISPR/Cas, the immune system of bacteria and archaea. Science 327: 167-170.
127. Csonka LN (1989) Physiological and genetic responses of bacteria to osmotic stress. Microbiol Mol Biol Rev 53: 121-147.
128. Huycke MM (2002) Physiology of enterococci. In: Gilmore MS, Clewell DB, Courvalin P, Dunny GM, Murray BE et al., editors. The Enterococci: Pathogenesis, molecular biology and antibiotic resistance. Washington DC: ASM Press.
129. Shepard BD, Gilmore MS (2002) Differential expression of virulence-related genes in *Enterococcus faecalis* in response to biological cues in serum and urine. Infect Immun 70: 4344-4352.
130. Deutscher J, Francke C, Postma PW (2006) How phosphotransferase system-related protein phosphorylation regulates carbohydrate metabolism in bacteria. Microbiol Mol Biol Rev 70: 939-1031.
131. Shaykhutdinov RA, MacInnis GD, Dowlatabadi R, Weljie AM, Vogel HJ (2009) Quantitative analysis of metabolite concentrations in human urine samples using C-13{H-1} NMR spectroscopy. Metabolomics 5: 307-317.
132. Blancato VS, Repizo GD, Suarez CA, Magni C (2008) Transcriptional regulation of the citrate gene cluster of *Enterococcus faecalis* Involves the GntR family transcriptional activator CitO. J Bacteriol 190: 7419-7430.
133. Wishart DS, Knox C, Guo AC, Eisner R, Young N, et al. (2009) HMDB: a knowledgebase for the human metabolome. Nucleic Acids Res 37: D603-610.
134. Horsburgh MJ, Clements MO, Crossley H, Ingham E, Foster SJ (2001) PerR controls oxidative stress resistance and iron storage proteins and is required for virulence in *Staphylococcus aureus*. Infect Immun 69: 3744-3754.
135. Jakubovics NS, Smith AW, Jenkinson HF (2002) Oxidative stress tolerance is manganese (Mn(2+)) regulated in *Streptococcus gordonii*. Microbiology 148: 3255-3263.
136. Kristich CJ, Nguyen VT, Le T, Barnes AM, Grindle S, et al. (2008) Development and use of an efficient system for random mariner transposon mutagenesis to identify novel genetic determinants of biofilm formation in the core *Enterococcus faecalis* genome. Appl Environ Microbiol 74: 3377-3386.

137. Mohamed JA, Teng F, Nallapareddy SR, Murray BE (2006) Pleiotrophic effects of 2 *Enterococcus faecalis sagA*-like genes, *salA* and *salB*, which encode proteins that are antigenic during human infection, on biofilm formation and binding to collagen type i and fibronectin. J Infect Dis 193: 231-240.
138. Bourgogne A, Hilsenbeck SG, Dunny GM, Murray BE (2006) Comparison of OG1RF and an isogenic *fsrB* deletion mutant by transcriptional analysis: the Fsr system of *Enterococcus faecalis* is more than the activator of gelatinase and serine protease. J Bacteriol 188: 2875-2884.
139. Camejo A, Buchrieser C, Couve E, Carvalho F, Reis O, et al. (2009) *In vivo* transcriptional profiling of *Listeria monocytogenes* and mutagenesis identify new virulence factors involved in infection. PLoS Pathog 5: e1000449.
140. Mulvey MA, Schilling JD, Martinez JJ, Hultgren SJ (2000) Bad bugs and beleaguered bladders: interplay between uropathogenic *Escherichia coli* and innate host defenses. Proc Natl Acad Sci U S A 97: 8829-8835.
141. Derre I, Rapoport G, Msadek T (1999) CtsR, a novel regulator of stress and heat shock response, controls clp and molecular chaperone gene expression in gram-positive bacteria. Mol Microbiol 31: 117-131.
142. Nair S, Milohanic E, Berche P (2000) ClpC ATPase is required for cell adhesion and invasion of *Listeria monocytogenes*. Infect Immun 68: 7061-7068.
143. Kajfasz JK, Martinez AR, Rivera-Ramos I, Abranches J, Koo H, et al. (2009) Role of Clp proteins in expression of virulence properties of *Streptococcus mutans*. J Bacteriol 191: 2060-2068.
144. Frees D, Chastanet A, Qazi S, Sorensen K, Hill P, et al. (2004) Clp ATPases are required for stress tolerance, intracellular replication and biofilm formation in *Staphylococcus aureus*. Mol Microbiol 54: 1445-1462.
145. Loughlin MF, Arandhara V, Okolie C, Aldsworth TG, Jenks PJ (2009) *Helicobacter pylori* mutants defective in the ClpP ATP-dependant protease and the chaperone ClpA display reduced macrophage and murine survival. Microb Pathog 46: 53-57.
146. Hanin A, Sava I, Bao Y, Huebner J, Hartke A, et al. Screening of in vivo activated genes in *Enterococcus faecalis* during insect and mouse infections and growth in urine. PLoS One 5: e11879.
147. Frees D, Savijoki K, Varmanen P, Ingmer H (2007) Clp ATPases and ClpP proteolytic complexes regulate vital biological processes in low GC, Gram-positive bacteria. Mol Microbiol 63: 1285-1295.

PAPER I

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Sept. 2007, p. 5767–5774 Vol. 73, No. 18
0099-2240/07/$08.00+0 doi:10.1128/AEM.00651-07

Transcriptional Responses of *Enterococcus faecalis* V583 to Bovine Bile and Sodium Dodecyl Sulfate▽†

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Received 22 March 2007/Accepted 18 July 2007

Resistance to bile is a prerequisite property of the gastrointestinal bacterial flora. Bile acids are powerful detergents, and resistance to sodium dodecyl sulfate (SDS) has therefore often been considered relevant to studies of bile resistance. We have studied the effects of bovine bile (BB) and SDS on *Enterococcus faecalis* V583 by traditional growth studies and microarrays. Transcriptional responses were studied by time course experiments. In the presence of BB (V583-BB) or SDS (V583-SDS), 308 and 209 genes were identified as differentially expressed at one or more time points, respectively. In V583 treated with both BB and SDS (V583-BB-SDS), 254 genes showed differential expression. Detergents exert their toxic effects primarily on the microbial membrane. The enrichment of differentially transcribed genes that encode proteins with membrane-associated functions and/or locations indicates a major impact of all three treatments on the integrity and functionality of the cell membrane. Two gene clusters involved in fatty acid biosynthesis were repressed in V583-BB and V583-BB-SDS and partly induced in V583-SDS. Furthermore, two EmrB/QacA family drug resistance transporters and a vacuolar-type ATPase were induced in V583-BB and V583-BB-SDS. None of the putative bile salt hydrolase homologs in V583 showed differential expression during the bile treatments. The transcriptional profile of V583-BB-SDS was qualitatively more similar to the response in V583-BB than to that in V583-SDS, suggesting that the presence of bile suppresses the effects of SDS in V583-BB-SDS. The overall results presented here indicate that different mechanisms are involved in detergent resistance in *E. faecalis*.

In order to survive in and colonize the gastrointestinal tract (GIT), a bacterium must overcome several biological barriers after consumption. Bacteria that survive the gastric acidity of the stomach transit to the intestine, where they encounter stress associated with variations in pH, low oxygen availability, elevated osmolarity, and relatively high concentrations of host-produced substances like bile. Bile is an aqueous solution whose major organic constituents are bile acids, cholesterol, and phospholipids (7). Bile acids are anionic-detergent-like biological compounds that are bactericidal because of their amphipathic structure (17). The primary bile acids are synthesized de novo from cholesterol in the liver and secreted as amino acid conjugates into the duodenum, where they aid in the digestion of fats and undergo enterohepatic circulation (17). During enterohepatic circulation, conjugated bile acids can undergo modifications by the intestinal microflora. Deconjugation of bile acids is catalyzed by bile salt hydrolases (BSHs), which hydrolyze the amide bond and liberate the glycine-taurine moiety from the steroid core (17).

Enterococcus faecalis is a natural member of the mammalian gastrointestinal bacterial flora. Previous work by Flahaut et al. (13, 14) demonstrated rapid killing of *E. faecalis* by a mixture of unconjugated bile salts (sodium cholate-sodium deoxycholate [1:1]) in vitro. However, *E. faecalis* is one of the most common lactic acid bacteria found in the GIT (12) and one of the predominant microbial species isolated from drainage devices used in biliary surgery (33). *E. faecalis* has also been isolated directly from the gallbladder (15). This indicates an inherent ability to tolerate high concentrations of bile under in vivo conditions. Several proteomic analyses of global changes in protein expression during bile salt exposure of gram-positive bacteria have been presented (13, 23, 31, 34). Bron et al. recently described a microarray-based approach for the identification of bile-responsive genes in *Lactobacillus plantarum* (9). Furthermore, random gene disruption strategies have been used to identify mutants that are more susceptible to bile salts than the wild-type strains in several gram-positive bacteria (6, 8, 20). In addition to emphasizing the effects of bile on membrane integrity and structure, these studies also suggested that bile imposes oxidative stress and DNA damage on the cell (summarized by Begley et al. [7]).

Sodium dodecyl sulfate (SDS) is an anionic detergent, and bacterial resistance to SDS has often been considered relevant to studies of bile resistance (13). Previous studies of bile salt and SDS stress responses in *E. faecalis* have shown significant cross-resistances between these two stress factors (13). This reported adaptation of *E. faecalis* to bile salts and SDS indicates that common resistance mechanisms are involved in the stress responses to these two detergents.

We have studied the susceptibility of *E. faecalis* V583 to bovine bile (BB) and SDS by using traditional growth studies and genome-wide microarrays. The aim of this work was to gain further insight into the effects of BB and SDS on growth and transcriptional events in V583. Since detergents exert their toxic effects primarily on the microbial membrane, it was expected that genes involved in cell membrane-associated functions would be affected by the detergent treatments. Moreover,

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† Supplemental material for this article may be found at http://aem.asm.org/.

▽ Published ahead of print on 27 July 2007.

in addition to genes related to DNA repair and oxidative response, proteins that take up or extrude bile and enzymes that modify and transform bile salts were also likely to play an important role in bile resistance.

MATERIALS AND METHODS

Bacterial strain and growth conditions. *E. faecalis* V583 (32) was grown aerobically overnight (ON) in brain heart infusion (BHI) broth (Oxoid) with shaking (300 rpm) at 37°C. For determination of the number of CFU/ml, BHI agar plates were used. SDS and BB (B3883; Sigma) were solubilized in water to obtain 10% (wt/vol) solutions. Filter-sterilized stock solutions were added to autoclaved medium.

SDS and BB treatments. For broth assays, ON cultures were inoculated (50× dilution) into BHI broth containing various concentrations of (i) BB (V583-BB), (ii) SDS (V583-SDS), or (iii) a combination of BB and SDS (V583-BB-SDS). Cell growth was measured spectrophotometrically and by viable cell counts. Growth experiments were performed with a Bioscreen instrument (Bioscreen C). For V583-SDS, each well contained 3 μl SDS to which 297 μl bacterial inoculum in BHI broth was added. The final concentrations of SDS were 0.01 to 0.1%. For V583-BB and V583-BB-SDS assays, 150 μl of the appropriate concentration of BB-containing BHI was added to each well. SDS was added as described above. Bacterial inoculum in BHI broth was then added to a total volume of 300 μl. The final bile concentrations were 1 to 7.5%. Wells containing BHI with equal amounts of sterile BB and SDS were used as negative controls. Cultures were incubated at 37°C (sample plates were shaken for 10 s prior to each measurement), and the optical density at 600 nm (OD_{600}) was measured at 30-min intervals for 24 h. All experiments were performed independently in triplicate. To determine the number of CFU/ml, viable cell counts were performed as follows. ON cultures in BHI were grown to an OD_{600} of ~0.2, split into four, and centrifuged, and the pellets were resuspended in (i) fresh BHI (V583-BHI), (ii) BHI containing 1% BB, (iii) BHI containing 0.06% SDS, or (iv) BHI containing 1% BB and 0.06% SDS. Samples were collected immediately after the addition of BB and/or SDS and after 2, 4, 6, and 8 h. The number of CFU/ml was estimated by averaging the colony counts in three replicates per treatment after 24 h of incubation at 37°C.

Sample collection. ON cultures were diluted 50× and grown in BHI to an OD_{600} of ~0.2, split into two, and centrifuged, and pellets were resuspended in 0.5 volume of fresh BHI. For each stress treatment, 0.5 volume of BHI (control) and 0.5 volume of BHI containing BB and/or SDS were added to the two cultures. The final concentrations of BB and SDS were 1% and 0.06%, respectively. The two cultures were then further incubated, and 10-ml samples were collected immediately after the addition of BB and/or SDS (t_0) and then after 10 (t_{10}), 20 (t_{20}), 30 (t_{30}), and 60 (t_{60}) min. Because of the difference in growth rate, samples were also collected after 120 min (t_{120}) for V583-BB and V583-BB-SDS and after 360 min (t_{360}) for V583-SDS. Samples were centrifuged at 5,000 rpm for 3 min in an Eppendorf 5804R tabletop centrifuge at 4°C, and pellets were flash frozen in liquid N_2 prior to RNA extraction.

Microarrays. The microarrays used in this study have been described previously by Aakra et al. (2). All PCR products, representing the predicted V583 open reading frames, were printed in three copies on each slide.

RNA isolation. Total RNA was isolated from the samples collected at the time points described above by means of the RNeasy Mini kit (QIAGEN) with on-column DNA digestions with RNase-free DNase I (QIAGEN) according to the manufacturer's recommendations or by FastPrep (Bio 101/Savant) as follows. Frozen cell pellets were thawed, and 350 μl lysis buffer RLT (RNeasy Mini Kit; QIAGEN) supplemented with 0.1% (vol/vol) β-mercaptoethanol (Sigma) was added to each cell suspension. The suspensions were transferred to 2-ml screw-cap FastPrep tubes (Qbiogene) containing 0.6 g acid-washed glass beads (<106 μm; Sigma) and 250 μl chloroform (Merck). Cells were lysed by shaking the tubes for 20 s at 6 m/s in an FP120 FastPrep bead beater (Bio 101/Savant). After a short spin, the water phases were transferred to Eppendorf tubes and the Eppendorf tubes were centrifuged for 2 min at 13,000 rpm (Biofuge Pico; Heraeus). The RNA-containing supernatants were then collected in new Eppendorf tubes. Pellets were resuspended in 350 μl β-mercaptoethanol-containing lysis buffer RLT, and the cell suspensions were transferred back to the FastPrep tubes with the glass beads for a second extraction to increase the overall RNA yield. A 250-μl volume of ethanol was then added to the supernatant fluids from the two extractions, and after mixing, each sample was applied to an RNeasy spin column (QIAGEN). The column was further washed and RNA eluted according to the RNeasy Mini kit protocol (QIAGEN), with DNA digestions as described above. The concentrations of the RNA samples were measured by using the NanoDrop (NanoDrop Technologies), and the quality was assessed by using the RNA 600 Nano LabChip kit and the Bioanalyzer 2100 (Agilent Technologies). Ten micrograms of each RNA sample was used for cDNA synthesis.

cDNA synthesis, fluorescent labeling, and hybridization. RNA was labeled with the FairPlay Microarray labeling kit (Stratagene) in accordance with the manufacturer's protocol, with the following modifications. For each labeling reaction, 10 μg of random hexamer primers (Amersham) and 10 μg of total RNA were initially preheated at 70°C for 10 min. A reverse transcription-PCR mixture (5× SuperScript III reaction buffer, a 20× deoxynucleoside triphosphate mixture, 0.1 M dithiothreitol, 20 U RNase block, and 520 U SuperScript III) was added to the annealed primers and RNA, and the reaction mixture was further incubated for 3 h at 46°C. After labeling, unincorporated dyes were removed from the samples by using the QIAquick PCR purification kit (QIAGEN). Prehybridization, hybridization, washing, and drying of the arrays were performed as described by Aakra et al. (2). Because of the reduced growth rates associated with growth in SDS, V583-SDS reached stationary phase after approximately 360 min while V583-BHI, V583-BB, and V583-BB-SDS reached stationary phase after approximately 120 min. We therefore chose to hybridize the t_{360} sample from V583-SDS against a sample that was harvested from faster-growing V583-BHI at a time point corresponding to the stationary phase. All of the other samples in the three experiments were cohybridized with control samples collected at the corresponding time points (e.g., V583-BB collected at t_{10} was hybridized along with V583-BHI collected at t_{10}). Four replicate hybridizations were performed with two separate batches of RNA. The two batches of RNA were obtained in two separate growth experiments. The Cy3 and Cy5 dyes (Amersham) used during cDNA synthesis were swapped in two of the four replicate hybridizations. Hybridized arrays were scanned at wavelengths of 532 nm (Cy3) and 635 nm (Cy5) with an Agilent G2505B scanner (Agilent Technologies). Fluorescence intensities and spot morphologies were analyzed with GenePix Pro 6.0 (Molecular Devices), and spots were excluded on the basis of slide or morphology abnormalities. Raw data from each array were preprocessed independently, and testing for differentially expressed genes was done by using a random-effect analysis-of-variance approach, as described by Aakra et al. (2). All genes were functionally classified according to The Institute for Genomic Research comprehensive microbial resource (http://cmr.tigr.org/tigr-scripts/CMR/CmrHomePage.cgi), and functional groups were tested for significant enrichment among the differentially expressed genes by using the Fisher exact test and a significance level of $P = 0.05$.

Microarray data accession number. The microarray data obtained in this study have been deposited in the ArrayExpress database (http://www.ebi.ac.uk/arrayexpress/) under accession number E-TABM-242.

RESULTS

Growth of *E. faecalis* V583 in the presence of SDS and BB. V583 was able to grow in BHI broth containing up to 7.5% BB and up to 0.1% SDS, with an extended lag phase, in addition to reduced growth rates and lower cell densities in the stationary phase of growth (Fig. 1A and B). In cultures treated with BB (V583-BB), the growth rates and final cell densities decreased with increasing concentrations of BB (Fig. 1A). The final cell density of V583 grown in medium containing 7.5% BB was approximately one-fifth of the final OD_{600} of untreated cultures (V583-BHI). However, V583-BHI and V583-BB with various concentrations of BB reached stationary phase after approximately the same time of growth. In V583 cultures treated with SDS (V583-SDS), growth rates decreased more drastically with increasing detergent concentrations than did those of V583-BB. On the other hand, the effect of SDS on cell density appeared to be more concentration dependent in V583-SDS. As opposed to V583-BB cultures, V583-SDS cultures containing less than 0.06% SDS were able to reach stationary-phase cell densities similar to those of V583-BHI cultures after prolonged incubation. In V583-SDS cultures containing higher concentrations of SDS, the stationary-phase cell densities decreased. The final cell density reached by V583 grown in the presence of 0.1% SDS was approximately half of

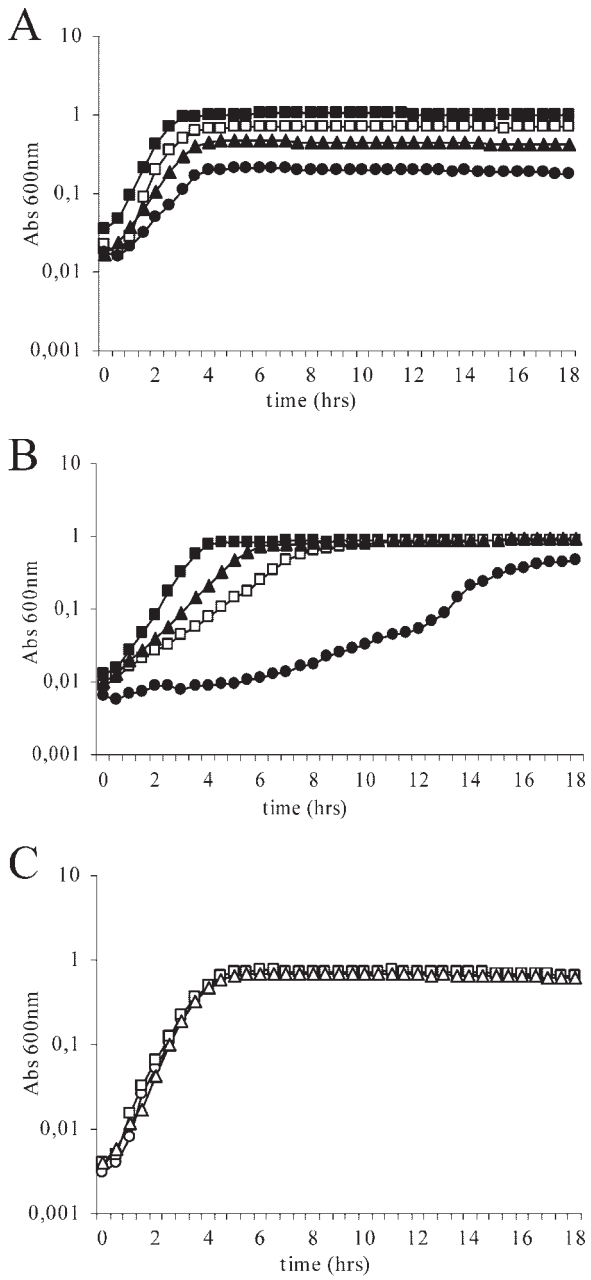

FIG. 1. Growth of *E. faecalis* V583 treated with BB (A; left untreated [■] or treated with 1 [□], 5 [▲], or 7.5% [●] BB), SDS (B; left untreated [■] or treated with 0.03 [▲], 0.06 [□], or 0.1% [●] SDS), or 1% BB plus SDS (C; 0 [○], 0.03 [□], or 0.06% [△] SDS). Abs, absorbance.

the final cell density of V583-BHI (Fig. 1B). These growth experiments suggest that BB and SDS affect *E. faecalis* V583 differently.

With the results of the V583-BB and V583-SDS growth experiments in mind, it was of interest to test the effects of mixtures of the two compounds on V583. Experiments were carried out by a constant amount of BB with various concentrations of SDS added to the BHI prior to inoculation. On the basis of the reported cross-resistance between bile salt- and SDS-adapted cells (13), both additive and synergistic effects on V583 were expected. However, the effect of the detergent mixture turned out to be partly antagonistic (Fig. 1C). The presence of BB seemed to abolish the inhibitory effects of SDS on V583 growth. Viable cell counts of V583 treated with selected concentrations of each detergent (1% BB, 0.06% SDS, and a mixture of 1% BB and 0.06% SDS) at different time points during growth confirmed the results obtained by OD measurements (data not shown).

Transcriptional profiling of V583-SDS, V583-BB, and V583-BB-SDS. A genome-wide amplicon-based microarray containing 3,160 genes (94.7% of the genes in the *E. faecalis* V583 genome) (2) was used for profiling of the transcriptional responses in V583-BB, V583-SDS, and V583-BB-SDS. Transcriptional events were studied by time course experiments. The time course experiments permitted us to investigate immediate responses, as well as adaptations to the more permanent presence of BB or/and SDS. We chose a stringent significance level of $P = 0.01$ for the determination of differential transcription. We also used a conservative Bonferroni correction to control the family-wise error rate under multiple testing to ensure a low false discovery rate. By these criteria, 308 genes were identified as differentially expressed at one or more of the six time points during the course of growth in V583-BB. In V583-SDS, 209 genes were differently expressed, while 254 genes showed differential expression when both compounds were present (V583-BB-SDS). Figure 2 contains the details. All functional groups were tested for significant enrichment among the differentially transcribed genes by using the Fisher exact test and a significance level of $P = 0.05$ (data not shown).

By comparison of the three different transcriptional profiles, 24 genes were identified as differentially expressed in V583-SDS, V583-BB, and V583-BB-SDS. Only two genes, EF0108 (C4-dicarboxylate transporter, putative) and EF0288 (hypothetical protein), were induced during all three treatments, while three genes (EF1027, which codes for a putative membrane protein; EF1207, which codes for a citrate carrier protein; and EF2983, which codes for a putative glutamyl-tRNA amidotransferase) were repressed. In addition, two genes that encode ABC transporters (EF2049 and -50) were both induced and repressed in V583-BB but only repressed in V583-SDS and V583-BB-SDS. Apparently, the expression profile of V583-BB-SDS was more similar to the expression profile of V583-BB than to that of V583-SDS (Fig. 3; see Tables S4, S6, and S7 in the supplemental material). Of the 24 commonly differentially expressed genes, 22 showed qualitatively similar responses to both V583-BB and V583-BB-SDS (see Table S4 in the supplemental material). Comparison of the transcriptional events in V583-SDS and V583-BB revealed 68 genes that were differentially expressed during both treatments, 38 of which showed similar expression patterns (either up- or down-regulated) in both experiments (see Table S5 in the supplemental material).

Interestingly, the two gene clusters EF0282 to -84 and EF2875 to -86, which encode proteins involved in type II fatty acid synthesis (FAS) in V583, were significantly repressed in V583-BB and V583-BB-SDS, while EF2875 to -80 and EF2883 showed increased transcriptional activity at t_{10} to t_{20} in V583-SDS (Fig. 4). This suggests that the presence of BB eradicated the stress imposed on FAS in V583-SDS. Other genes that were found to be induced in V583-BB and V583-BB-SDS but not induced in V583-

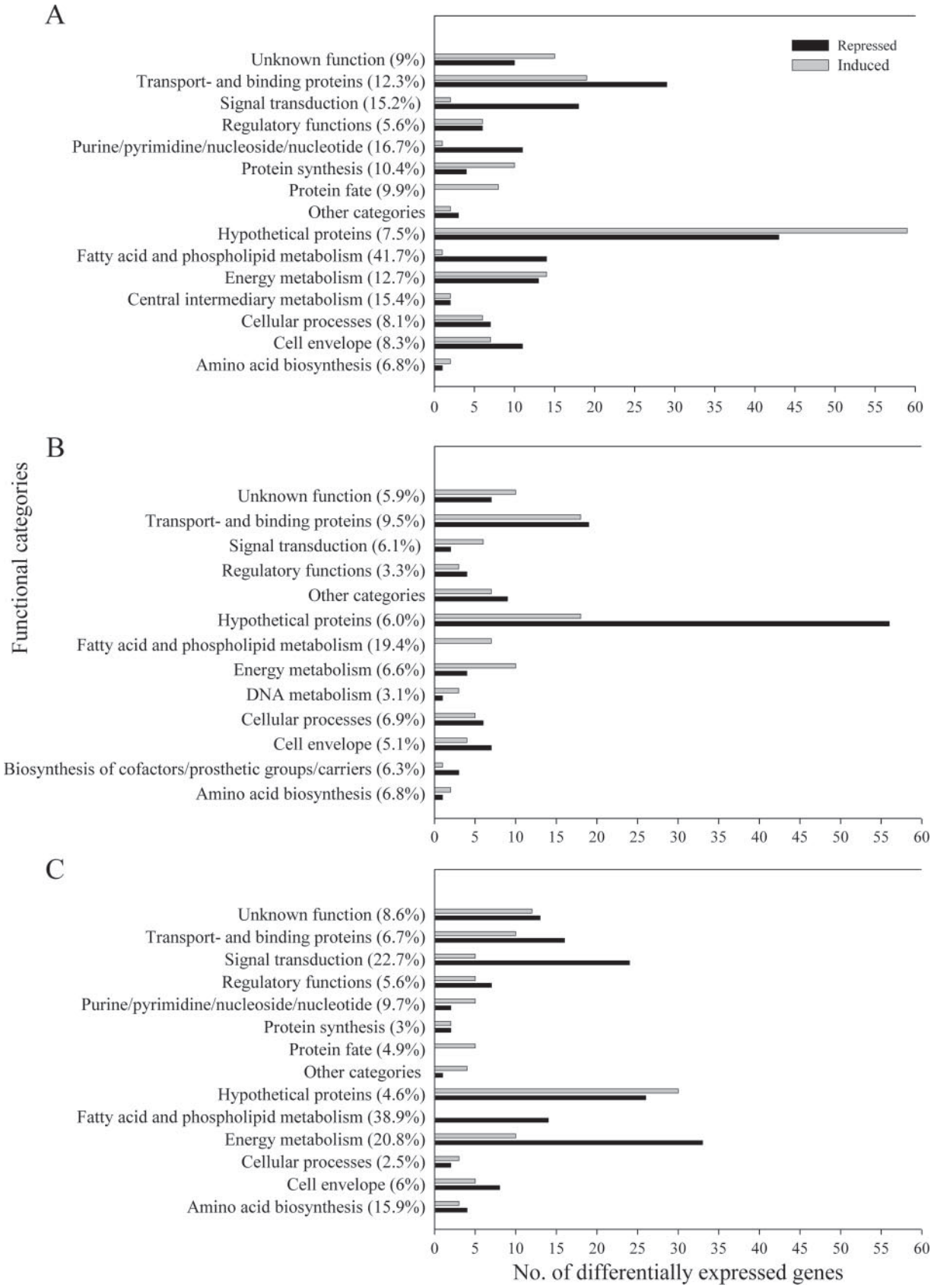

FIG. 2. Genes differentially expressed in V583-BB (A), V583-SDS (B), and V583-BB-SDS (C) grouped by functional classification according to The Institute for Genomic Research comprehensive microbial resource (http://cmr.tigr.org/tigr-scripts/CMR/CmrHomePage.cgi). Black bars refer to repressed genes, and gray bars refer to induced genes. Values in parenthesis are percentages of the total number of genes within each functional class in the genome. Functional classes with fewer than two regulated genes are gathered under "Other categories." Genes that were both up- and downregulated during the time course were counted twice.

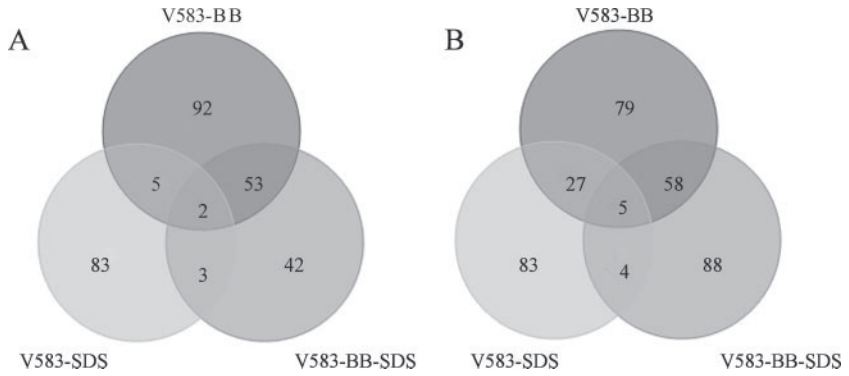

FIG. 3. Distribution of genes upregulated (A) and downregulated (B) in V583-BB, V583-SDS, and V583-BB-SDS. Genes that were both up- and downregulated during the time course were counted twice.

SDS were genes that encode two EmrB/QacA family drug resistance transporters (EF0420 and EF1814) and a vacuolar-type (V-type) ATPase (EF1492 to -1500).

For the $\log_2$ ratios of genes differentially expressed in V583-BB, V583-SDS, and V583-BB-SDS, see Tables S1 to S3 in the supplemental material.

DISCUSSION

In order to survive, the bacterial flora of the GIT must tolerate relatively high concentrations of host-produced inhibitory compounds like bile. Previous studies have shown strong cross-resistance between cells adapted to bile salts and the

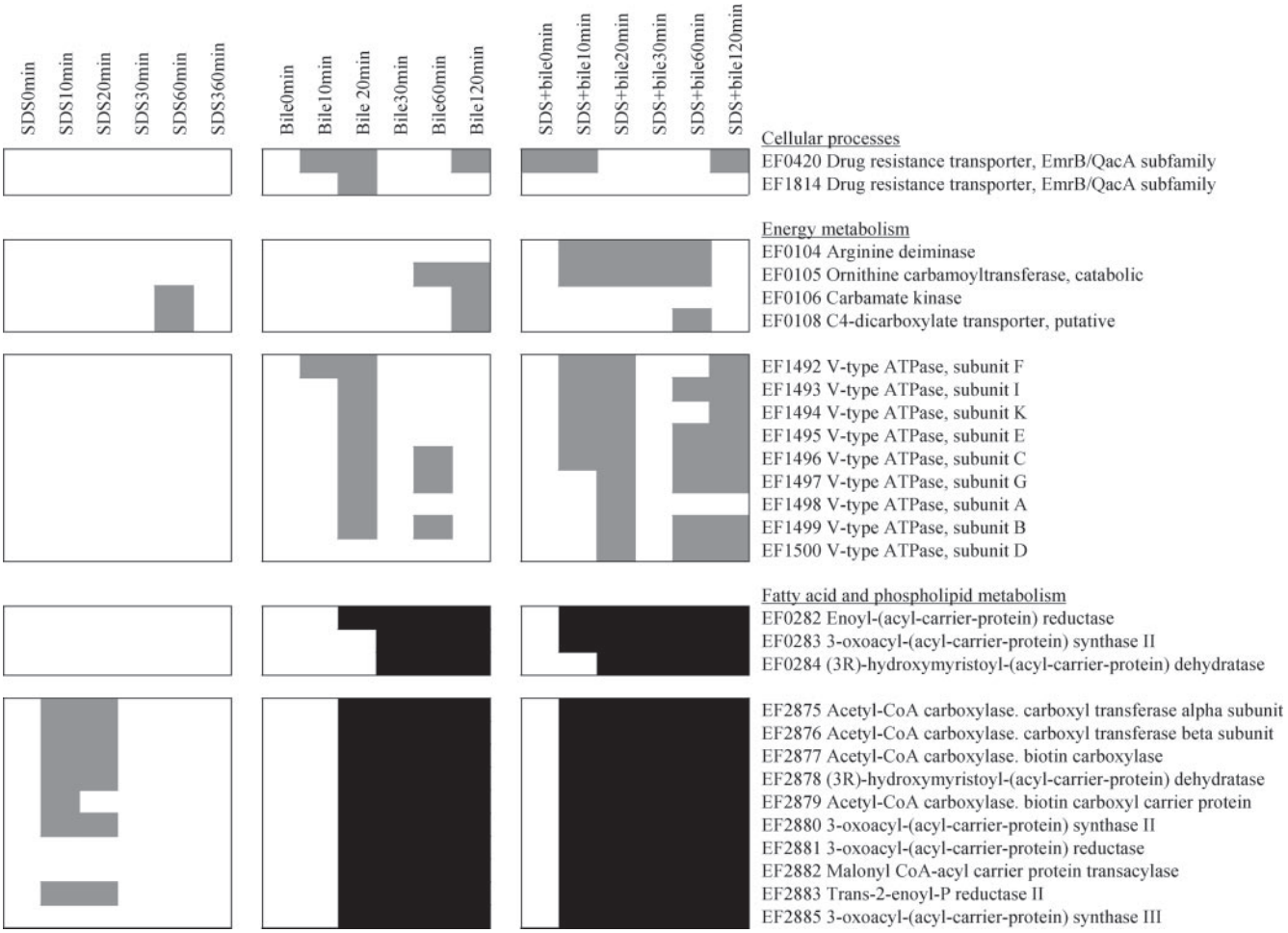

FIG. 4. Changes in mRNA levels of selected genes in V583-SDS, V583-BB, and V583-BB-SDS during the course of growth, represented in gray (induced), black (repressed), and white (no significant regulation). CoA, coenzyme A.

anionic detergent SDS (13), indicating that the physiological responses to bile salts and SDS are closely related in *E. faecalis*. The strain used in this study, V583, however, showed different responses to these compounds with respect to both growth and transcription.

V583 was able to grow in medium containing up to 7.5% BB and 0.1% SDS (Fig. 1A and B). Growth in 7.5% bile exceeds the physiological levels in the intestine (0.2 to 2%) (16). Previous susceptibility studies of *E. faecalis* have reported lower resistance to both bile salts and SDS (13, 14, 18), and the present results indicate large variations in resistance to these detergents within this species. The apparent divergent susceptibility to bile among *E. faecalis* strains may be a consequence of true strain-specific variation in bile resistance. A recently published microarray-based survey of genomic diversity in *E. faecalis* showed that regions corresponding to putative mobile genetic elements in V583 are missing in several *E. faecalis* strains (1), and one may suggest that genes within these mobile genetic elements could be required for the detergent resistance seen in V583. Divergent susceptibility may, however, also reflect particular traits of the mixture of bile acids used in the experiments reported (6, 7). Increased lag times associated with growth in the presence of SDS have previously been attributed to the time necessary to accumulate sufficient intracellular K^+ for logarithmic growth of gram-negative bacteria (4).

The addition of BB to cultures containing different concentrations of SDS apparently suppressed the inhibitory effects of SDS on growth in V583 (Fig. 1C). This observation may be explained by intercalation of bile acids with membrane lipids (22). As a consequence, the membrane may become more resistant to detergents because of enhanced lipid membrane stability. However, the enhanced resistance of V583 to SDS in the presence of BB might also be a result of bile acids and SDS forming micelles, preventing SDS from adhering to the bacterial cells (19). Such a rationale may, in turn, also explain the qualitatively similar responses in V583-BB and V583-BB-SDS.

To gain deeper insight into the BB and SDS resistance of V583, global transcriptional profiling was performed by use of DNA microarrays. The stress conditions applied caused significantly decreased growth compared to that of unstressed cultures. We decided to cohybridize the test samples with reference samples collected at the same time points and to correct for the differences in growth phase at only one time point, where the most obvious deviation in growth phase occurred (see Materials and Methods). This design allowed a direct comparison between stressed and nonstressed bacteria at a given time, as opposed to the use of a common reference, e.g., an untreated t_0 control sample, where differential expression may be an outcome of the stress conditions applied to the cells but also an effect of time. We therefore considered cohybridization of the treated samples with reference samples collected at the same time points as more precise than hybridization against a common reference. For the identification of significantly differentially expressed genes, the conservative Bonferroni correction was used as a strategy to reduce the occurrence of type I errors (false positives), at the expense of increasing type II errors (false negatives). To address the possible loss of information due to type II errors, an independent verification of the results for selected genes could be considered.

Testing for significant enrichment among the differentially expressed genes by using the Fisher exact test and a significance level of $P = 0.05$ (data not shown) showed that genes engaged in fatty acid and phospholipid metabolism were significantly enriched in all three treatments. Genes that encode the components of type II FAS are located in two separate clusters in the V583 genome (EF0282 to -84 and EF2875 to -86). Our data suggest that the type II FAS genes are a key target for both BB and SDS in V583. However, it was surprising to observe that the two compounds affect these genes so differently. Random gene disruption in *E. faecalis* has previously revealed bile-sensitive mutants that produce homologues of proteins involved in membrane composition and cell wall synthesis (20). Moreover, bile-induced changes in membrane composition have been reported in other gram-positive bacteria. In *Lactobacillus reuteri* (36), a fivefold reduction in the phospholipid fraction of the total membrane lipid content was seen in response to bile salts. Such a bile-induced decline in phospholipids is in line with the observed repression of genes involved in fatty acid and phospholipid metabolism in V583-BB and V583-BB-SDS. In *Streptococcus pneumoniae*, FabF and FabK are believed to be involved in the regulation of membrane fatty acid composition (26). These observations may be applicable to the induction of EF2880 (FabF2) and EF2883 (FabK) in V583-SDS. The high number of genes involved in membrane-associated functions with altered expression indicates a major impact of all three detergent treatments on the integrity and functionality of the cytoplasmic membrane.

Genes involved in energy metabolism were enriched among the genes differentially expressed in V583-BB-SDS (Fisher exact test; data not shown). The *bkd* operon (EF1658 to -63), which encodes the branched-chain α-keto acid dehydrogenase complex in V583, was downregulated at t_{120} in V583-BB-SDS. The branched-chain α-keto acid dehydrogenase complex catalyzes the oxidative decarboxylation of branched-chained α-keto acids with the concomitant reduction of NAD^+, supposedly generating the corresponding acyl coenzyme A and ATP via substrate level phosphorylation (39, 40). To our knowledge, there is no evidence linking the enterococcal *bkd* gene cluster to the biosynthesis of branched-chain fatty acids, as found in *Bacillus subtilis* (39). The repression of this operon in V583-BB-SDS should therefore not be correlated to the observed repression of genes involved in type II FAS.

In V583-BB and V583-BB-SDS, two gene clusters assigned to functions in energy metabolism were induced, EF0104 to -08 and EF1492 to -1500 (Fig. 4). EF0104 to -06 encode the three enzymatic steps of the arginine deiminase pathway, generating ATP through fermentative arginine catabolism (5). EF1492 to -1500 encode a V-type ATPase. V-type ATPases are membrane-bound proteins that function in active ion pumping at the expense of ATP hydrolysis. The induction of the gene cluster that encodes the V-type ATPase in V583-BB and V583-BB-SDS suggested that the generation of a proton gradient is important for survival of the cell during exposure to bile. Bile-mediated stress responses have previously been linked to maintenance of the proton motive force (PMF) in *L. plantarum* and *Bifidobacterium* sp. (9, 34, 35). Sánchez et al. recently proposed that increased ATPase activity in *Bifidobacterium animalis* is an

attempt to compensate for the PMF-dissipating and internal pH-decreasing effects of bile (35).

Another possible rationale for the cell to generate such a proton gradient in response to bile stress is the importance of PMF in the active extrusion of bile acids. The two drug resistance transporter genes EF0420 and EF1814 (drug resistance transporters, EmrB/QacA family proteins) (29) showed enhanced transcriptional activity in V583-BB and V583-BB-SDS (Fig. 4). Previous studies have shown that inactivation of efflux pumps has a deleterious effect on the ability of the bacterium to tolerate bile (24, 37), and bile resistance has been linked to ATP-dependent active efflux in gram-positive bacteria (41). However, EF0420 and EF1814 in *E. faecalis* are related to the known PMF-dependent efflux systems EmrB in *Escherichia coli* (25) and QacA in *Staphylococcus aureus* (10). EmrB has previously been reported to be involved in the active efflux of bile salts in *E. coli* (37), but to our knowledge, this is the first report of a PMF-dependent transport system linked to bile resistance in gram-positive bacteria.

A two-component system (EF3289 and -90; *croRS*) was induced in V583-BB and V583-BB-SDS at t_{20}. CroRS shows significant homology (60.4% similarity) to a bile-inducible two-component regulatory system in *Lactobacillus acidophilus* (30). The expression of *croRS* has recently been shown to be repressed when *E. faecalis* enters the stationary phase, implying that expression toward the end of the time course was not to be expected (21). Moreover, CroRS is believed to be involved in the regulation of the stress-inducible secreted protein SalB (EF0394) in *E. faecalis* (28). *salB* has previously been referred to as *sagA* and is identical to the disrupted locus in one of the bile-sensitive *E. faecalis* mutants identified by Le Breton et al. (20). s*alB* was predicted to encode a putative surface-exposed, virulence-related protein in V583 by Paulsen et al. (29). It has previously been shown that growth of *E. faecalis* strains in ox bile altered the physicochemical surface properties of the bacterium and resulted in increased adhesion to bile drainage materials (38). EF3245, which encodes a cell envelope-associated acid phosphatase, was induced at four and five of the six time points in V583-BB and V583-BB-SDS, respectively. Several other genes listed as putative virulence-related genes by Paulsen et al. (29) also showed significantly increased expression at one or more time points in V583-BB (see Table S1 in the supplemental material).

The gene cluster EF2977 to -83 was differentially transcribed at the same time points as EF3245. EF2977 to -81 encode a PTS system and a σ^{54}-dependent DNA-binding response regulator with significant homology to the *mpo* operon and its σ^{54}-dependent activator in *Listeria monocytogenes* (3). Inactivation of *mpoA* resulted in intermediate bacteriocin resistance in *L. monocytogenes*. The downregulation of EF2977 to -81 in V583-BB and V583-BB-SDS led us to the suggestion that exposure to bile enhances the tolerance to certain class IIa bacteriocins (11) in *E. faecalis*. Preliminary bacteriocin plate assays (27) performed with *Pediococcus acidilactici* (PacI) and *Lactobacillus sakei* (SakP) did show that while V583 was sensitive to PacI and SakP in the absence of bile, the presence of 2% bile rendered V583 significantly more resistant to these class IIa bacteriocins (results not shown).

In view of previous studies, our data imply that at least certain aspects of the response to bile are conserved among gram-positive bacteria. However, contrary to previous reports, this study does not reflect any impact of bile on DNA repair and oxidative response in *E. faecalis* V583. Intrinsic resistance to bile has also previously been associated with the presence of BSH activity in gram-positive bacteria (6, 8), but none of the putative *bsh* homologs in V583 (EF0521 and EF3005) showed significant differential expression in our experiments.

Comparison of the three different transcriptional profiles (V583-BB, V583-SDS, and V583-BB-SDS) revealed only 24 genes that were differentially transcribed in all three experiments. In V583-SDS and V583-BB, 68 genes were differentially expressed during both treatments, 38 of which showed similar expression patterns (either up- or downregulated) in both experiments (see Table S5 in the supplemental material). Cross-protection is generally regarded as a result of different stress conditions causing similar effects on cellular physiology. However, in a previous report by Flahaut et al. (13), the responses of *E. faecalis* to treatments with bile salts and SDS appeared to be less related on the protein level than suggested by the observed cross-resistance. The low number of commonly differentially expressed genes in the two transcriptional profiles presented here suggests that the responses to bile and SDS in *E. faecalis* involve different changes, also on the transcriptional level. So, although the toxicity pattern of bile acids resembles that of detergents such as SDS, a mechanism of resistance common to both remains to be established.

ACKNOWLEDGMENTS

This work was financially supported by grants from the Research Council of Norway to I.F.N.

We thank Bjørn E. Kristiansen, The Norwegian Microarray Consortium, Oslo, for printing and scanning of the microarray slides.

REFERENCES

1. **Aakra, A., O. L. Nyquist, L. Snipen, T. S. Reiersen, and I. F. Nes.** 2007. Survey of genomic diversity among *Enterococcus faecalis* strains by microarray-based comparative genomic hybridization. Appl. Environ. Microbiol. **73:**2207–2217.
2. **Aakra, A., H. Vebo, L. Snipen, H. Hirt, A. Aastveit, V. Kapur, G. Dunny, B. E. Murray, and I. F. Nes.** 2005. Transcriptional response of *Enterococcus faecalis* V583 to erythromycin. Antimicrob. Agents Chemother. **49:**2246–2259.
3. **Arous, S., K. Dalet, and Y. Hechard.** 2004. Involvement of the *mpo* operon in resistance to class IIa bacteriocins in *Listeria monocytogenes*. FEMS Microbiol. Lett. **238:**37–41.
4. **Aspedon, A., and K. W. Nickerson.** 1993. A two-part energy burden imposed by growth of *Enterobacter cloacae* and *Escherichia coli* in sodium dodecyl sulfate. Can. J. Microbiol. **39:**555–561.
5. **Barcelona-Andrés, B., A. Marina, and V. Rubio.** 2002. Gene structure, organization, expression, and potential regulatory mechanisms of arginine catabolism in *Enterococcus faecalis*. J. Bacteriol. **184:**6289–6300.
6. **Begley, M., C. G. Gahan, and C. Hill.** 2002. Bile stress response in *Listeria monocytogenes* LO28: adaptation, cross-protection, and identification of genetic loci involved in bile resistance. Appl. Environ. Microbiol. **68:**6005–6012.
7. **Begley, M., C. G. Gahan, and C. Hill.** 2005. The interaction between bacteria and bile. FEMS Microbiol. Rev. **29:**625–651.
8. **Bron, P. A., M. Marco, S. M. Hoffer, E. Van Mullekom, W. M. de Vos, and M. Kleerebezem.** 2004. Genetic characterization of the bile salt response in *Lactobacillus plantarum* and analysis of responsive promoters in vitro and in situ in the gastrointestinal tract. J. Bacteriol. **186:**7829–7835.
9. **Bron, P. A., D. Molenaar, W. M. De Vos, and M. Kleerebezem.** 2006. DNA micro-array-based identification of bile-responsive genes in *Lactobacillus plantarum*. J. Appl. Microbiol. **100:**728–738.
10. **Brown, M. H., and R. A. Skurray.** 2001. Staphylococcal multidrug efflux protein QacA. J. Mol. Microbiol. Biotechnol. **3:**163–170.
11. **Ennahar, S., T. Sashihara, K. Sonomoto, and A. Ishizaki.** 2000. Class IIa bacteriocins: biosynthesis, structure and activity. FEMS Microbiol. Rev. **24:**85–106.
12. **Facklam, R. R., M. Carvalho, and L. M. Teixeira.** 2002. History, taxonomy, biochemical characteristics and antibiotic susceptibility testing of entero-

cocci, p. 1–54. *In* M. S. Gilmore (ed.), The enterococci: pathogenesis, molecular biology and antibiotic resistance. ASM Press, Washington, DC.
13. **Flahaut, S., J. Frere, P. Boutibonnes, and Y. Auffray.** 1996. Comparison of the bile salts and sodium dodecyl sulfate stress responses in *Enterococcus faecalis*. Appl. Environ. Microbiol. **62:**2416–2420.
14. **Flahaut, S., A. Hartke, J. C. Giard, A. Benachour, P. Boutibonnes, and Y. Auffray.** 1996. Relationship between stress response toward bile salts, acid and heat treatment in *Enterococcus faecalis*. FEMS Microbiol. Lett. **138:**49–54.
15. **Flores, C., I. Maguilnik, E. Hadlich, and L. Z. Goldani.** 2003. Microbiology of choledochal bile in patients with choledocholithiasis admitted to a tertiary hospital. J. Gastroenterol. Hepatol. **18:**333–336.
16. **Hofmann, A.** 1998. Bile secretion and the enterohepatic circulation of bile acids, p. 937–948. *In* F. Feldman and M. Sleisenger (ed.), Sleisenger and Fordtran's gastrointestinal and liver disease, 6th ed. W. B. Saunders Co., Philadelphia, PA.
17. **Hofmann, A. F.** 1994. Bile acids, p. 677–718. *In* I. M. Arias (ed.), The liver: biology and pathobiology, 3rd. ed. Raven Press Ltd., New York, NY.
18. **Keyhani, J., E. Keyhani, F. Attar, and A. Haddadi.** 2006. Sensitivity to detergents and plasmid curing in *Enterococcus faecalis*. J. Ind. Microbiol. Biotechnol. **33:**238–242.
19. **Kimoto, H., S. Ohmomo, and T. Okamoto.** 2002. Enhancement of bile tolerance in lactococci by Tween 80. J. Appl. Microbiol. **92:**41–46.
20. **Le Breton, Y., A. Maze, A. Hartke, S. Lemarinier, Y. Auffray, and A. Rince.** 2002. Isolation and characterization of bile salts-sensitive mutants of *Enterococcus faecalis*. Curr. Microbiol. **45:**434–439.
21. **Le Breton, Y., C. Muller, Y. Auffray, and A. Rincé.** 2007. New insights into the *Enterococcus faecalis* CroRS two-component system obtained using a differential-display random arbitrarily primed PCR approach. Appl. Environ. Microbiol. **73:**3738–3741.
22. **Le Maire, M., P. Champeil, and J. V. Moller.** 2000. Interaction of membrane proteins and lipids with solubilizing detergents. Biochim. Biophys. Acta **1508:**86–111.
23. **Leverrier, P., D. Dimova, V. Pichereau, Y. Auffray, P. Boyaval, and G. Jan.** 2003. Susceptibility and adaptive response to bile salts in *Propionibacterium freudenreichii*: physiological and proteomic analysis. Appl. Environ. Microbiol. **69:**3809–3818.
24. **Lin, J., O. Sahin, L. O. Michel, and Q. Zhang.** 2003. Critical role of multidrug efflux pump CmeABC in bile resistance and in vivo colonization of *Campylobacter jejuni*. Infect. Immun. **71:**4250–4259.
25. **Lomovskaya, O., and K. Lewis.** 1992. Emr, an *Escherichia coli* locus for multidrug resistance. Proc. Natl. Acad. Sci. USA **89:**8938–8942.
26. **Lu, Y. J., and C. O. Rock.** 2006. Transcriptional regulation of fatty acid biosynthesis in *Streptococcus pneumoniae*. Mol. Microbiol. **59:**551–566.
27. **Mortvedt, C. I., and I. F. Nes.** 1990. Plasmid-associated bacteriocin production by a *Lactobacillus-sake* strain. J. Gen. Microbiol. **136:**1601–1607.
28. **Muller, C., Y. Le Breton, T. Morin, A. Benachour, Y. Auffray, and A. Rince.** 2006. The response regulator CroR modulates expression of the secreted stress-induced SalB protein in *Enterococcus faecalis*. J. Bacteriol. **188:**2636–2645.
29. **Paulsen, I. T., L. Banerjei, G. S. Myers, K. E. Nelson, R. Seshadri, T. D. Read, D. E. Fouts, J. A. Eisen, S. R. Gill, J. F. Heidelberg, H. Tettelin, R. J. Dodson, L. Umayam, L. Brinkac, M. Beanan, S. Daugherty, R. T. DeBoy, S. Durkin, J. Kolonay, R. Madupu, W. Nelson, J. Vamathevan, B. Tran, J. Upton, T. Hansen, J. Shetty, H. Khouri, T. Utterback, D. Radune, K. A. Ketchum, B. A. Dougherty, and C. M. Fraser.** 2003. Role of mobile DNA in the evolution of vancomycin-resistant *Enterococcus faecalis*. Science **299:**2071–2074.
30. **Pfeiler, E. A., M. A. Azcarate-Peril, and T. R. Klaenhammer.** 2007. Characterization of a novel bile-inducible operon encoding a two-component regulatory system in *Lactobacillus acidophilus*. J. Bacteriol. **189:**4624–4634.
31. **Phan-Thanh, L., and T. Gormon.** 1997. Stress proteins in *Listeria monocytogenes*. Electrophoresis **18:**1464–1471.
32. **Sahm, D. F., J. Kissinger, M. S. Gilmore, P. R. Murray, R. Mulder, J. Solliday, and B. Clarke.** 1989. In vitro susceptibility studies of vancomycin-resistant *Enterococcus faecalis*. Antimicrob. Agents Chemother. **33:**1588–1591.
33. **Saito, T., K. Senda, S. Takakura, N. Fujihara, T. Kudo, Y. Iinuma, T. Kiuchi, M. Tanimoto, and S. Ichiyama.** 2003. Biliary bacteria in living related liver transplant recipients: microbiology and rapid detection system using flow cytometry. Clin. Chem. Lab. Med. **41:**159–163.
34. **Sánchez, B., M. C. Champomier-Verges, P. Anglade, F. Baraige, C. G. de Los Reyes-Gavilan, A. Margolles, and M. Zagorec.** 2005. Proteomic analysis of global changes in protein expression during bile salt exposure of *Bifidobacterium longum* NCIMB 8809. J. Bacteriol. **187:**5799–5808.
35. **Sánchez, B., C. G. de los Reyes-Gavilan, and A. Margolles.** 2006. The F_1F_0-ATPase of *Bifidobacterium animalis* is involved in bile tolerance. Environ. Microbiol. **8:**1825–1833.
36. **Taranto, M. P., M. L. Fernandez Murga, G. Lorca, and G. F. de Valdez.** 2003. Bile salts and cholesterol induce changes in the lipid cell membrane of *Lactobacillus reuteri*. J. Appl. Microbiol. **95:**86–91.
37. **Thanassi, D. G., L. W. Cheng, and H. Nikaido.** 1997. Active efflux of bile salts by *Escherichia coli*. J. Bacteriol. **179:**2512–2518.
38. **Waar, K., H. C. van der Mei, H. J. Harmsen, J. E. Degener, and H. J. Busscher.** 2002. Adhesion to bile drain materials and physicochemical surface properties of *Enterococcus faecalis* strains grown in the presence of bile. Appl. Environ. Microbiol. **68:**3855–3858.
39. **Ward, D. E., R. P. Ross, C. C. van der Weijden, J. L. Snoep, and A. Claiborne.** 1999. Catabolism of branched-chain α-keto acids in *Enterococcus faecalis*: the *bkd* gene cluster, enzymes, and metabolic route. J. Bacteriol. **181:**5433–5442.
40. **Ward, D. E., C. C. van Der Weijden, M. J. van Der Merwe, H. V. Westerhoff, A. Claiborne, and J. L. Snoep.** 2000. Branched-chain α-keto acid catabolism via the gene products of the *bkd* operon in *Enterococcus faecalis*: a new, secreted metabolite serving as a temporary redox sink. J. Bacteriol. **182:**3239–3246.
41. **Yokota, A., M. Veenstra, P. Kurdi, H. W. van Veen, and W. N. Konings.** 2000. Cholate resistance in *Lactococcus lactis* is mediated by an ATP-dependent multispecific organic anion transporter. J. Bacteriol. **182:**5196–5201.

PAPER II

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Comparative genomics of *Enterococcus faecalis* from healthy Norwegian infants

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Published: 24 April 2009

BMC Genomics 2009, **10**:194 doi:10.1186/1471-2164-10-194

Received: 12 November 2008
Accepted: 24 April 2009

This article is available from: http://www.biomedcentral.com/1471-2164/10/194

Abstract

Background: *Enterococcus faecalis*, traditionally considered a harmless commensal of the intestinal tract, is now ranked among the leading causes of nosocomial infections. In an attempt to gain insight into the genetic make-up of commensal *E. faecalis*, we have studied genomic variation in a collection of community-derived *E. faecalis* isolated from the feces of Norwegian infants.

Results: The *E. faecalis* isolates were first sequence typed by multilocus sequence typing (MLST) and characterized with respect to antibiotic resistance and properties associated with virulence. A subset of the isolates was compared to the vancomycin resistant strain *E. faecalis* V583 (V583) by whole genome microarray comparison (comparative genomic hybridization (CGH)). Several of the putative enterococcal virulence factors were found to be highly prevalent among the commensal baby isolates. The genomic variation as observed by CGH was less between isolates displaying the same MLST sequence type than between isolates belonging to different evolutionary lineages.

Conclusion: The variations in gene content observed among the investigated commensal *E. faecalis* is comparable to the genetic variation previously reported among strains of various origins thought to be representative of the major *E. faecalis* lineages. Previous MLST analysis of *E. faecalis* have identified so-called high-risk enterococcal clonal complexes (HiRECC), defined as genetically distinct subpopulations, epidemiologically associated with enterococcal infections. The observed correlation between CGH and MLST presented here, may offer a method for the identification of lineage-specific genes, and may therefore add clues on how to distinguish pathogenic from commensal *E. faecalis*. In this work, information on the core genome of *E. faecalis* is also substantially extended.

Background

Enterococci are Gram-positive facultative anaerobic cocci with a low GC-content. They are natural inhabitants of the mammalian gastrointestinal (GI) tract and among the first lactic acid bacteria to colonize the intestines of a newborn [1]. During the last three decades, enterococci have emerged as important pathogens and as a major cause of nosocomial infections. The majority of hospital-acquired,

enterococcal infections is caused by *Enterococcus faecalis* [2]. Several putative virulence factors have been characterized in *E. faecalis* (reviewed in [2]), and their roles in pathogenicity have been established in various animal models [3-6] and cultured cell lines [7,8]. A large number of reports on enterococcal pathogenicity has focused on the presence or absence of these virulence determinants in enterococcal isolates from different origins [9-14]. The results have shown that several of the putative virulence traits are detected in enterococcal isolates independent of their origin, suggesting that these factors may not be crucial for enterococcal pathogenicity. However, a higher incidence of some of the virulence determinants in clinical isolates may indicate that these genes enhance the ability of *E. faecalis* to cause disease, as suggested by virulence studies on bacterial mutants in animal models [3].

The sequencing of the *E. faecalis* V583 genome (V583) [15] made global analyses of whole genome diversity within this species possible [16-18], by the use of microarray-based comparative genomic hybridization (CGH). The approximate size and composition of the *E. faecalis* core genome have been investigated on clinical, food and environmental isolates [17,18]. The CGH-approach has also been used to evaluate the dissemination of variable traits from the V583 genome within diverse lineages of the species [17]. Previous analyses have shown that the main genomic variation between the strains correspond to previously identified mobile genetic elements (MGEs) in V583 [17,18]. However, an effort to explore the gene content of commensal *E. faecalis* by CGH has not previously been made and little is known about genetic determinants that may explain the differences in life style between pathogenic and non-pathogenic *E. faecalis* strains.

The aim of this study was to investigate the genomic diversity among fecal *E. faecalis* isolated from healthy Norwegian infants by means of CGH. In an attempt to study genetic variability of commensal *E. faecalis* isolates, we used genome-wide DNA arrays to probe the presence of 3219 open reading frames (ORFs) from V583 and 10 ORFs representing a 17-kb deletion in the V583 pathogenicity island in our collection of community-derived Norwegian fecal *E. faecalis* baby isolates. The isolates were also characterized with respect to antibiotic resistance and properties associated with virulence, by PCR and phenotypic assays.

Methods

Stool samples

This study included 11 healthy Norwegian infants (7 male and 4 female) born in the Eastern part of Norway. The babies were all born in Oslo and Akershus Counties. Informed consent had been obtained from their parents. From infants A-C, stool samples were collected once each month during the first six months and once after 12 months from October 2004 to September 2005, while from infants D-K, samples were collected once during the first six months of life during 2002. All the samples were collected after mother and child had left the obstetric ward. All the infants were born by vaginal delivery and all were breast-fed during the period of sampling. None of the infants were treated with antibiotics during the sampling period. A total of 29 stool samples were collected.

Identification of enterococcal isolates and growth conditions

From each stool sample, two cultures were prepared: 1 g fecal material was homogenized in 1) 10 mL deMan-Rogosa-Sharpe (MRS; Oxoid) broth and 2) 10 mL Arroyo, Martin and Cotton broth (AMC; [19]), by vortexing. Serial dilutions were made and 100 μl of the 10^{-5} – 10^{-7} dilutions were plated on MRS- and AMC agar plates, respectively. MRS plates were incubated aerobically over night (ON) at 37°C, while AMC plates were incubated anaerobically ON at 37°C. Plates were then examined for growth, and colonies with different morphology and from different plates were picked and inoculated in 5 ml MRS- or AMC-broth, depending on which plates they were isolated from. The cultures were incubated as described above. Genomic DNA from each sample was isolated, and for identification, the 16S rRNA gene from each isolate was amplified and sequenced using general 16S rDNA primers (Additional file 1). PCR was accomplished using DyNAzyme™ II DNA Polymerase (Finnzymes). Thermocycling conditions were as follows: 2 min at 94°C; followed by 30 cycles of 30 s at 94°C, 30 s at 56°C, and 1.5 min at 72°C; followed by 10 min at 72°C. A total of 31 different *E. faecalis*-isolates were identified, and further analyzed in this study (Table 1). The 31 enterococcal isolates were isolated as part of two surveys of the content of lactic acid bacteria (LAB) in baby feces, hence, the culture media used were rich media, not particularly chosen to select for enterococci. In the present study, *E. faecalis* were grown aerobically ON in brain heart infusion broth (BHI; Oxoid) at 37°C.

MLST analysis

MLST was performed according to the scheme presented by Ruiz-Garbajosa et al. [20], using the ABI Prism Big dye Cycle Sequencing Ready Reaction kit (Applied Biosystems) in an ABI PrismTM 3100 Genetic Analyzer. Sequence types were defined by the allelic variation at the seven loci *aroE*, *gdh*, *gki*, *gyd*, *pstS*, *xpt* and *yqiL*. Isolates with the same sequence type are thought to be members of a single clone or lineage. Clonal complexes were defined as groups of isolates that differed in no more than two of the seven loci analyzed, by use of eBURST http://www.mlst.net[21]. Each clonal complex was designated after its ancestor sequence type (ST) or the representative

Table 1: Fecal *Enterococcus faecalis* isolates used in this study.

Infant	Isolate	MLST		CPS	Ab^R	Genotypes	Phenotypes
		ST	CC				
A	39A	91	S	-	-	*ace, agg, esp, fsrB, gelE*	GEL
A	88A	91	S	-	-	*ace, agg, esp, fsrB, gelE*	GEL
A	**92A**	**44**	**44**	**T1**	**-**	***ace, agg*** *	**-**
A	**111A**	**161**	**8**	**T1**	**aT**	***ace, agg, cylL, esp, gelE***	**CYL**
A	112A	64	8	-	T	*ace, agg, cylL, esp, gelE*	CYL
A	123A	64	8	-	T	*ace, agg, esp, gelE*	CYL
A	125A	64	8	-	aT	*ace, agg, cylL, esp, gelE*	CYL
A	157A	91	S	-	-	*ace, agg, esp, fsrB, gelE*	GEL
B	2B	30	30	-	aT	*ace, agg, esp, gelE*	-
B	75B	30	30	-	a	*ace, agg, esp, gelE*	-
B	132B	44	44	-	T	*ace, agg, cylL, fsrB, gelE*	GEL
B	**158B**	**6**	**2**	**T2**	**a**	***ace, agg, cylL, fsrB, gelE***	**CYL**
B	226B	6	2	-	-	*ace, agg, cylL, fsrB, gelE*	CYL
C	26C	44	44	-	T	*ace, agg, cylL, fsrB, gelE*	GEL
C	**29C**	**44**	**44**	**T1**	**aT**	***ace, agg, cylL, fsrB, gelE***	**CYL GEL**
C	34C	44	44	-	T	*ace, agg, cylL, fsrB, gelE*	GEL
C	105C	194	S	-	T	*ace, agg, esp, fsrB, gelE*	GEL
C	141C	44	44	-	aT	*ace, agg, esp, fsrB, gelE*	GEL
D	4	30	30	-	a	*ace, esp, gelE*	-
E	59	30	30	-	a	*ace, esp, gelE*	-
F	**62**	**66**	**S**	**T1**	**T**	***ace, agg, esp, gelE***	**-**
G	**85**	**30**	**30**	**T5**	**AG**	***ace, esp, gelE***	**-**
H	**105**	**16**	**S**	**T2**	**aEGT**	***ace, agg, cylL, esp, fsrB, gelE***	**CYL GEL**
I	135	16	S	-	aEGT	*ace, agg, cylL, esp, fsrB, gelE*	GEL
I	137	30	30	-	a	*ace, esp, gelE*	-
I	236	16	S	-	EGT	*ace, agg, esp, fsrB, gelE*	GEL
J	173	55	55	-	aET	*ace, agg, cylL, esp*	-
J	**189**	**162**	**72**	**T5**	**a**	***ace, agg, cylL, fsrB, gelE***	**CYL GEL**
J	199	162	72	-	-	*ace, agg, cylL, esp, fsrB, gelE*	GEL
K	**266**	**163**	**S**	**T2**	**aT**	***ace, agg, fsrB, gelE***	**-**
K	267	163	S	-	-	*ace, agg, cylL, esp, fsrB, gelE*	GEL

* Isolate 92A was not genotyped for the presence of *gelE*, and *fsrB* by PCR.

The isolates from infants A-C are listed chronologically, according to their time of isolation. Isolates that have been genomotyped by CGH are listed in bold. CS; community surveillance, MLST; multilocus sequence typing, ST; sequence type, CC; clonal complex, S; singleton, CPS; capsular locus polymorphism type, Ab^R; antibiotic resistance, A; ampicillin, E; erythromycin, G; gentamicin, T; tetracycline, *ace*; collagen-binding adhesin, *agg*; aggregation substance, *esp*; enterococcal surface protein, *frsB*;, *gelE*; gelatinase, *cylL*; cytolysin L, CYL; cytolysin activity, GEL; gelatinase activity.

ST that appeared with the highest frequency. All the MLST data from this study has been deposited into the *E. faecalis* MLST database http://efaecalis.mlst.net/.

Phenotypic assays

Cytolysin assay

Hemolytic activity was qualitatively detected by the use of blood agar plates supplemented with 5% (v/v) defibrinated horse blood, 1% (w/v) glucose and 0.03% (w/v) L-arginine (Sigma) [22]. Overnight cultures were diluted 1:100, spotted onto fresh plates and incubated at 37°C for 24 h. Zones of clearing around colonies indicated production of cytolysin.

Gelatinase assay

Detection of gelatinase activity was performed by the use of Todd-Hewitt (Oxoid) agar plates containing 3% gelatin [23]. Overnight cultures were diluted 1:100, spotted onto fresh plates and incubated at 37°C overnight, before they were placed at 4°C for 5 h. Zones of turbidity around colonies indicated hydrolysis of gelatin.

Antimicrobial susceptibility testing

BHI agar plates supplemented with 4 μg/ml ampicillin, 20 μg/ml chloramphenicol, 50 μg/ml erythromycin, 500 μg/ml gentamicin, 10 μg/ml tetracycline or 4 μg/ml vancomycin were used. The plates were inoculated by spotting 5 μl (10^6–10^7 CFU) overnight culture (1: 200) and incubated at 37°C overnight. Growth was interpreted as resistance to the antibiotic added to the medium.

Detection of genes encoding virulence factors and bacteriocin genes

The presence of *ace*, *agg*, *esp*, *cylL* and *gelE* were detected by means of polymerase chain reactions (PCR) as previously described [9,24]. Isolates were also tested for the presence of *iolE*, *iolR* and genes coding for the following bacterioc-

ins by PCR: enterocin A (EA), enterocin B (EB), enterocin P (EP), enterolysin A (EN), enterocin L50 (EL50) and enterocin 1071A and B (E1071A&B). Thermocycling conditions were as follows: 2 min at 94°C; followed by 30 cycles of 30 s at 94°C, 30 s at 50 ± 10°C, and 30 s at 72°C; followed by 10 min at 72°C. Primers are listed in Additional file 1.

API 50 CH for determination of fermentation patterns

Carbohydrate fermentation patterns were obtained for selected isolates with API 50 CH kits (BioMerieux) according to the manufacturer's instructions.

Comparative genomic hybridization

Microarrays

The microarrays used in this work contained 3219 open reading frames from the genome of *Enterococcus faecalis* V583 [15] represented by oligonucleotides (70-mers; probes). Of these 3219 ORFs, 3093 were chromosomal ORFs and 126 were located on plasmids. In addition, ten genes from the pathogenicity island (PAI) of *E. faecalis* MMH594 (deleted in the PAI of V583) were represented [25]. The 70-mer oligos were supplied by Invitrogen. The oligos were spotted in triplicates onto epoxy-coated glass slides (Corning). In order to reduce biases due to positional effects, the replicate spots were spotted at random positions within a subarray on the array. Alien reporter sequences (SpotReport®Alien® Oligo Array Validation System, Stratagene), without homology to any known nucleic acid sequences in public databases, were spotted as negative controls on the array. The microarray design has been deposited in the ArrayExpress database with the accession number A-MEXP-1069.

DNA isolation

For CGH, 9 isolates were chosen based on their representation of MLST sequence type diversity across the babies and of novel sequence types. Genomic DNA was isolated by using the FP120 FastPrep bead-beater (BIO101/Savent) and the QiaPrep MiniPrep kit (Qiagen) as follows: 10 mL overnight cultures were centrifuged for 5 min. at 6000 rpm in an Eppendorf 5804R tabletop centrifuge at 4°C, and pellets were resuspended in 250 μl RNaseA-containing Buffer P1 (100 μg/mL RNaseA). The cell suspensions were transferred to 2 mL screw cap FastPrep tubes (Qbiogene) containing 0.5 g acid-washed glass beads (< 106 μm) (Sigma). Cells were lysed by shaking the tubes for 20 s at 6 m/s in the FastPrep bead-beater. After a short spin, lysed cells were transferred to Eppendorf tubes and 250 μl Buffer P2 and 350 μl Buffer N3 was added to each tube. Then, the suspensions were centrifuged for 10 min. at 13000 rpm in a tabletop centrifuge (Biofuge Pico, Heraeus) at room temperature, before the supernatant fluids were loaded on to Qiaprep spin columns. The columns were washed again and genomic DNA was eluted according to the Qiaprep Spin MiniPrep kit protocol. Concentration and purity of the genomic DNA was measured using the NanoDrop spectrophotometer (NanoDrop Technologies). 5 μg genomic DNA was used for each labeling reaction.

Fluorescent labeling and hybridization

Genomic DNA was labeled and purified with the BioPrime Array CGH Genomic labeling System (Invitrogen) and Cyanine Smart Pack dUTP (PerkinElmer Life Sciences), according to the manufacturer's protocol.

Purified samples were then dried, prior to resuspension in 140 μl hybridization solution (5 × SSC, 0.1% (w/v) SDS, 1.0% (w/v) bovine serum albumin, 50% (v/v) formamide and 0.01% (w/v) single-stranded salmon sperm DNA) and hybridized for 16 h at 42°C to the *E. faecalis* oligonucleotide array in a Tecan HS 400 pro hybridization station (Tecan). Arrays were washed twice at 42°C with 2 × SSC + 0.2% SDS, and twice at 23°C with 2 × SSC, followed by washes at 23°C with 1) 0.2 × SSC and 2) H_2O. Two replicate hybridizations (dye-swap) were performed for each test strain. Hybridized arrays were scanned at wavelengths of 532 nm (Cy3) and 635 nm (Cy5) with a Tecan scanner LS (Tecan). Fluorescent intensities and spot morphologies were analyzed using GenePix Pro 6.0 (Molecular Devices), and spots were excluded based on slide or morphology abnormalities. All water used for the various steps of the hybridization and for preparation of solutions was filtered (0.2 μM) MilliQ dH_20.

Data analysis

Standard methods in the LIMMA package [26] in R http://www.r-project.org/, available from the Bioconductor http://www.bioconductor.org were employed for preprocessing and normalization. Within-array normalization was first conducted by subtracting the median from the log-ratios for each array. A standard loess-normalization was then performed, where smoothing was based only on spots with abs(log-ratio) < 2.0 to avoid biases due to extreme skewness in the log-ratio distribution. For the determination of present and divergent genes, a new method that predicts sequence identity based on array signals was used, as described by Snipen et al. [27]. A brief description of the method follows: Initially, all array probe sequences were queried against the fully sequenced V583 reference genome (R-genome) in a BLAST search. The value *Rb* for each probe was defined as the number of identical bases in the best local alignment found by blastn, divided by the probe length. Given the sequence identity *Rb* for each probe, the corresponding array signal *Ra* will in general correlate in a positive way, *i.e*. stronger sequence identity yields stronger array signal. This postulation also holds for the unsequenced sample genome (S-genome), where *Sa* denote the array signal and *Sb* the unknown sequence identity. The basic idea is that *Sb* can be predicted from *Sa* based on how sequence identity *Rb*

and array signal *Ra* relate to each other. A threshold of 0.75 was assigned to the *Sb*-values in order to obtain a categorical response of presence or divergence, *i. e.* genes with *Sb*-value > 0.75 were classified as present, while genes with *Sb*-value < 0.75 were classified as divergent. In a comparison with other methods for analyzing CGH data as reviewed by Carter et al. [28], the proposed method gave significantly better classification of present/divergent. Based on the fully sequenced genomes of V583 and OG1RF [15,29], tests gave sensitivity of 0.99 and specificity of 0.95 for detecting present probes based on CGH data.

Comparative phylogenomics

The relationship of the reference strain and the test strains based on the presence and divergence of genes was determined with Bayesian-based algorithms implemented through MR BAYES 3.1 [30], as previously described [31]. With samples and saves from every 40^{th} tree, 1.1×10^6 generations of four incrementally heated Markov chain Monte Carlos (MCMC) were performed on the CGH data by using an annealing temperature of 0.5, a burn-in of 100 000 MCMC generations and an 8-category distribution. Consensus trees and clade credibility values were visualized by using TreeView version 1.6.6 http://taxonomy.zoology.gla.ac.uk/rod/treeview.html.

Microarray data accession number

The microarray data have been deposited in the ArrayExpress database with the series accession number E-TABM-466.

Results

MLST – allelic variation in community-derived fecal E. faecalis *baby isolates*

The MLST analysis was performed on 31 *E. faecalis*-isolates, obtained from 11 healthy Norwegian infants during their first year of life. These isolates were considered as legitimate representatives of commensal *E. faecalis* as they have been resident in the gut without causing any apparent negative effect to the health of the host. Infants A-C were sampled once each month during the first six months and once after 12 months, and a total of 8, 5 and 5 different isolates were recovered from the respective infants over the period of sampling. Infants D-K were sampled once during the first six months of life and 1–3 different isolates were obtained from these infants. From the 31 isolates, 12 different sequence types (STs) were identified, of which four were novel STs (ST161, ST162, ST163 and ST194; Table 1). Of these novel STs, ST161 and ST162, were single-locus variants (SLV; differing from the ancestor ST in one allele) of ST64 and ST72, respectively. ST64 and ST161 belong to the previously defined clonal complex CC8. In addition to the ST161 (n = 1) isolate that was detected in one of the infants, three different isolates displaying ST64 (n = 3) were obtained from the same infant (A) during the same month. Other clonal complexes that were represented within our collection of isolates were CC2 (n = 2), CC30 (n = 6), CC44 (n = 6) and CC55 (n = 1). The remaining isolates were singletons.

Several STs were detected multiple times, within different infants: ST30 was found in 5 of the 11 infants, while ST44 occurred in three different infants, and ST16 and ST162 were both detected in two different infants. The number of different STs for the three infants (A-C) monitored over 12 months, ranged between 2 and 4. Some of these STs were detected only for a short period of time, while other STs persisted throughout the sampling period (Figure 1). No *E. faecalis* isolates were obtained from infant A and C at 12 months of age. This observation was probably due to the conditions for enterococcal selection not being stringent enough.

Distribution of virulence genes, bacteriocin genes and antibiotic resistance profiles

Single-concentration plate assays were used to assess resistance to ampicillin, chloramphenicol, erythromycin, gentamicin, tetracyline and vancomycin (see Table 1 and Additional file 2). Tetracycline resistance was the most prevalent resistance trait among the baby isolates (17/31). Moreover, a few of the isolates (n = 4) showed erythromycin- or high-level gentamicin resistance. All isolates were also examined for the presence of the putative virulence factors *ace*, *agg*, *cylL* and *esp* by means of PCR. *ace* was amplified from all isolates, while 27/31 isolates were *agg*$^+$. *esp* is known to be associated with the *E. faecalis* pathogenicity island (PAI) [25], and was detected in 20/31 of the isolates. Cytolysin has been shown to contribute to

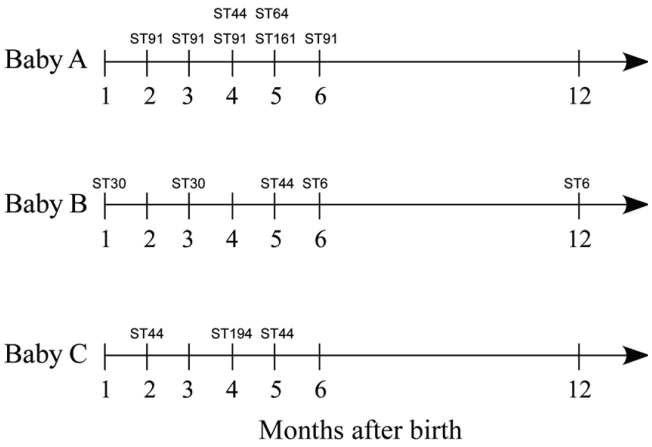

Figure 1
The different sequence types that were detected in infants A-C during their first year of life. ST; sequence type.

virulence in animal models of enterococcal infections, and *cylL*, encoding one of the structural subunits of enterococcal cytolysin was present in 16/31 of the isolates by PCR. Cytolysin production was detected in 9/31 of the isolates on blood agar plates. The isolates were also examined for gelatinase activity, which have been associated with virulence (reviewed in [2]). 15/31 isolates were gelatinase positive (GelE$^+$). Since the absence of the regulator (*fsrB*) can cause a lack of the gelatinase phenotype despite the presence of a positive *gelE* genotype [23], the isolates were also tested for the presence of *gelE* and *fsrB* by PCR. 29 of the isolates were *gelE*$^+$ and 18 were *fsrB*$^+$ (see Table 1 and Additional file 2). PCR-screening for content of bacteriocin genes among the test strains further discriminated between isolates with matching resistance profiles and virulence characteristics (see Additional file 2).

Comparative genomic hybridization analysis

Whole-genome CGH experiments on *E. faecalis* have previously shown that the main variations between the sequenced reference strain V583 and test strains relate to regions coding for integrated phages, plasmids and transposable elements in V583 [17,18]. In our experiments, 169 genes were classified as divergent in all 9 isolates, 121 of which are chromosomal genes in V583 (see Additional file 3). The majority of the divergent chromosomal genes are located within the following 6 previously identified mobile genetic elements (MGE) in V583: efaC2 (EF0127–66; n = 19), phage01 (EF0303–55; n = 9), phage03 (EF1417–89; n = 16), *vanB* resistance region as defined by [17] (EF2284–2334; n = 48), efaC1 (EF2512–46; n = 17) and phage07 (EF2936–55; n = 6). A large fraction of the 121 chromosomal genes code for hypothetical proteins (n = 70) or conserved hypothetical proteins/conserved domain proteins (n = 35). Apparently, a great proportion of the variable gene pool consists of hypothetical ORFs and this seems to be a common trait among prokaryotes [32]. None of the MGEs were entirely divergent in all of the commensal isolates, *e.g.* the content of PAI genes in the isolates varied from 36 to 118 present genes of the 123 PAI ORFs represented on the array (Figure 2), and similar patterns of present and divergent genes between isolates may suggest that MGE genes are often transferred in modules. The fact that only 48 of the plasmid-encoded genes on the array (n = 167; pTEF1, pTEF2 and pTEF3) were divergent in all the baby isolates is consistent with such an evolutionary scenario; however, the isolates have not been tested for plasmid content to further explore this hypothesis. The results of the microarray analysis were generally consistent with the phenotypic tests and the PCR analysis of the presence of virulence-associated genes, with a few exceptions only: the isolate 111A was *esp*$^+$ by PCR, but *esp*$^-$ by CGH. The same isolate was also *cylL*$^+$ by PCR and Cyl$^+$, but the entire cytolysin locus, except from PAIef0049, was divergent by CGH. The Cyl$^+$

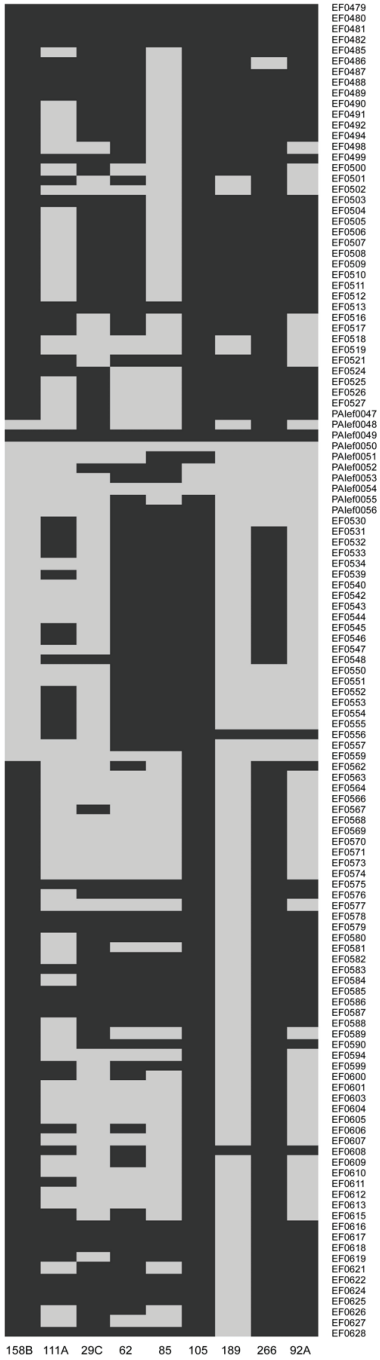

Figure 2
Presence and divergence of PAI genes (123 of 129 open reading frames represented on the microarray) in nine *E. faecalis* baby isolates, as detected by CGH. Genes PAIef**** correspond to EF**** genes in the PAI of strain MMH594 [25]. Putative enterococcal virulence genes located on the PAI include aggregation substance (*agg*; EF0485), cytolysin (*cyl*; EF0523–27 + PAIef0047–49) and enterococcal surface protein (*esp*; PAIef0056). Dark gray = present, light gray = divergent.

phenotypes of the isolates 158B and 189 were also inconsistent with the CGH data for some of the additional PAI genes on the array (PAIef0047–49). The observed inconsistencies between phenotypes/PCR and CGH may be due to sequence variations in the microarray-probe target sequences in the test stains.

Each of the fecal baby isolates showed a minimum of 76.5% presence of probes represented on the array (76.6% of the V583 genome). The CGH analysis classified 2092 of the 3093 chromosomal V583 ORFs as present in all 9 isolates. This set of shared genes is slightly higher than the core genomes that were previously reported for *E. faecalis* [17,18], probably due to the constricted environment and the limited geographical area, from which the isolates were obtained. The observed genetic variation among the investigated commensal *E. faecalis* shows that the genetic diversity is comparable to that among strains from other sources (food, clinical, environmental, animal husbandry etc) [17,18]. Our data confirmed the establishment of phage02 as a part of the *E. faecalis* core genome.

The *E. faecalis* V583 genome contains 35 probable phosphoenolpyruvate-dependent sugar phosphotransferase (PTS) systems and pathways for exploitation of 15 different sugars have been predicted [15]. Carbohydrate fermentation patterns obtained with API 50 CH kits for selected baby isolates whose gene content were also analyzed by CGH (see Additional file 4), showed only small differences in the metabolic capabilities of the test strains. Also, compared to API 50 CH results previously obtained for V583 [18], only minor variations were observed (see Additional file 4). These observations were supported by the high degree of conservation of genes encoding PTS components revealed by the CGH data. The recent publication of the *E. faecalis* OG1RF genome sequence revealed an *iol* operon that is not found in the V583 genome [29]. Interestingly, two of the baby isolates (111A and 105) were, according to the API assay, able to ferment myo-inositol. All the baby isolates were therefore surveyed for the presence of *iolE* and *iolR* by PCR. A total of 13 isolates, including 111A and 105, were both *iolE*$^+$ and *iolR*$^+$ (see Additional file 2). The presence of a partial *iol* operon in isolates 189 and 266 which were unable to ferment myo-inositol by the API assay is consistent with previous findings [29].

Phylogenomic analyses of the CGH data using Bayesian-based algorithms revealed a distinct clade containing seven of the nine community-derived baby isolates (Bayesian posterior probabilities [*PP*] = 1.0; Figure 3A). Initial branching within this clade was also fairly reliable (*PP* > 0.80). The remaining three isolates seemed to be more divergent, and V583 formed a distinct out-group. Based on this analysis, isolate 266 (ST163) appeared more closely related to V583 (ST6) than isolate 158B, which also displays ST6. Nevertheless, the Bayesian phylogeny suggested that the lineages defined by CGH generally correlated with those identified by MLST: Within the latter clade, the isolates 92A and 29C (ST44) formed one separate clade (Figure 3A). To further examine the correlation between MLST and CGH, additional CGH data obtained from the literature, in addition to unpublished data from five additional non-baby isolates of *E. faecalis* were included in the analysis. In this extended analysis, only genes (n = 3043) represented on all three arrays that were used in the different studies were considered. The clustering of identical STs was here further supported (*PP* > 0.55; see Additional file 5). Previous studies have suggested that genomotyping of *E. faecalis* by CGH is heavily influenced by extensive horizontal transfer of MGEs in *E. faecalis* [17]. To further analyze the effect of MGEs in our data set, the CGH data were reanalyzed after all core- and MGE genes had been removed from the gene list, as previously described [33]. The MGE genes comprised putative MGEs predicted in V583 [15], as well as an additional phage-related region identified by McBride et al. [17]. This revision left a list of 370 genes (see Additional file 6). Lindsay and coworkers [33,34] previously denominated such genes core variable (CV; all genes minus core genes minus MGE genes). The phylogenetic tree based on the content of CV genes in the isolates recovered a clade containing the same seven baby isolates as in the analysis with the entire probe set (*PP* = 0.92; Figure 3B).

Of the 370 CV genes, 145 genes code for hypothetical proteins. Among the remaining functionally annotated CV genes, many genes are predicted to code for surface-exposed proteins in E. faecalis, e.g. the cps locus coding for the capsule in E. faecalis [35]. The cps locus of E. faecalis consists of 11 genes (cpsABCDEFGHIJK) and insertional inactivation of genes in this locus have resulted in mutants with enhanced susceptibility to phagocytic killing [35]. Three different cps polymorphisms have been identified in E. faecalis so far: 1) type 2 (cps2) which includes all 11 genes, 2) type 5 (cps5) which includes all genes except cpsF and 3) type 1 (cps1) with only cpsA and cpsB present. All three polymorphisms were detected among our test strains, by CGH (Table 1). The cps type has previously been found to be invariant within MLST sequence types in E. faecalis [17], and our data is consistent with this finding. Analysis of the CGH data with respect to the cps type suggested that the E. faecalis PAI, or segments thereof, may be enriched among cps2-isolates. These observations support the hypothesis of convergence of enterococcal virulence determinants and cps2 by independent selection in E. faecalis [17].

Discussion

Enterococci are among the first bacteria to colonize the neonatal GI tract [1]. Though originally considered as harmless commensals, the enterococci now rank among

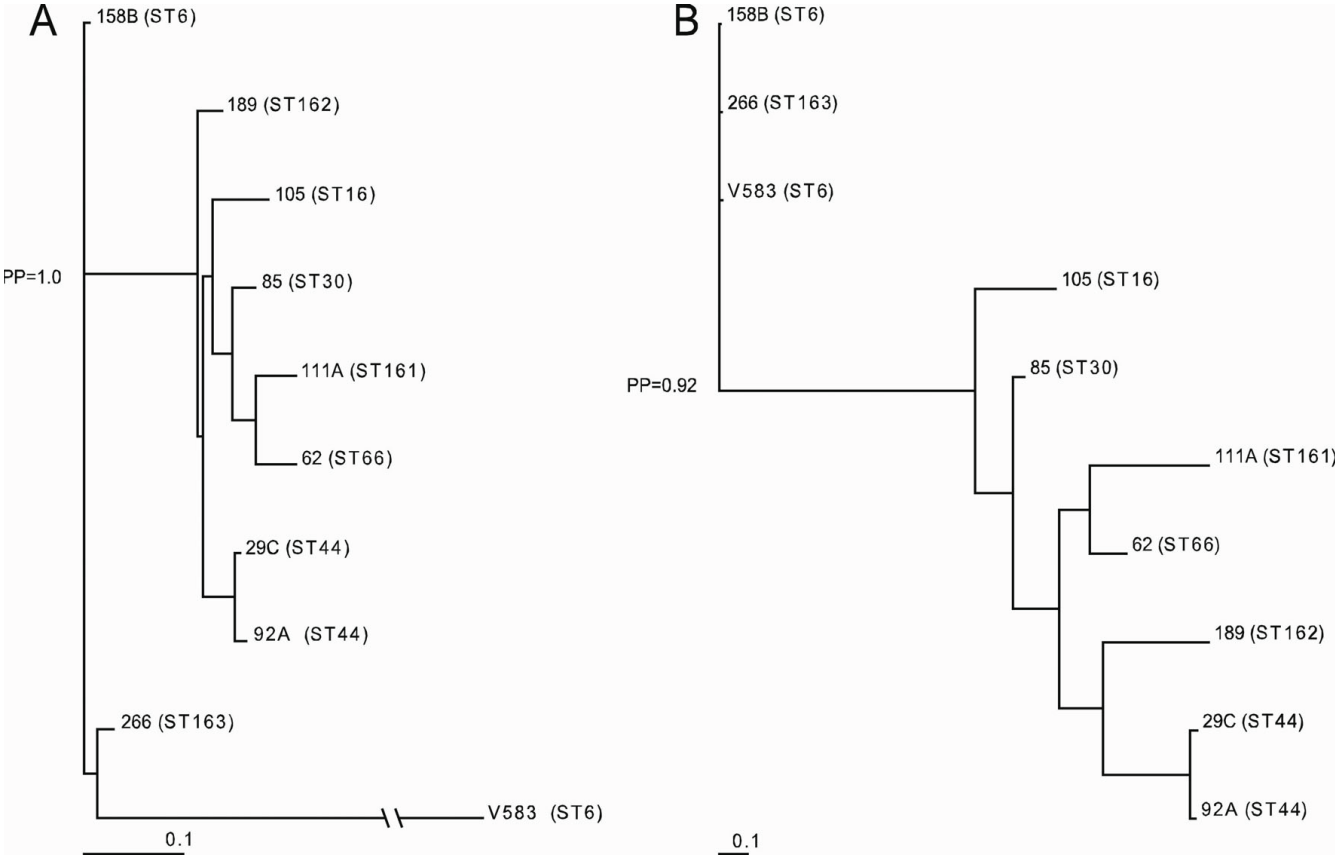

Figure 3
Phylogenomic relationship of community-derived fecal baby isolates based on (A) total microarray probe set and (B) core variable (CV) genes, as detected by CGH. Isolate names and sequence type (ST) are indicated at the end of the branches. Numerical values represent the posterior probability (*PP*) of support for internal branches.

the leading causes of nosocomial infections [36,37]. The present study was undertaken in an attempt to further explore the differences in the genetic make-up of *E. faecalis*. A total of 31 community-derived fecal baby isolates were sequence typed by MLST and characterized with respect to antibiotic resistance and properties associated with virulence. A subset of the isolates was genomotyped using genome-wide DNA microarrays.

By MLST analysis, the 31 baby isolates were resolved into 12 STs and grouped into 11 genetic lineages, including 6 major clonal complexes (CCs) and 5 singletons http://efaecalis.mlst.net/. Analyses with the MLST scheme employed in the present study have previously defined distinct clonal complexes of *E. faecalis* associated with the hospital environment, so-called high-risk enterococcal clonal complexes (HiRECC; CC2, CC9, CC40 and CC87) [20,38]. Of the isolates included in this study, only 158B and 226B (ST6) grouped into one of these complexes (CC2). These isolates were obtained towards the end of the sampling period, and may therefore have been introduced through habituation to solid food or from the environment through fecal-oral contamination. To our knowledge, none of the infants were admitted to the hospital during the period of sampling, however, hospital contact cannot be excluded as a source for ST6 isolates.

According to our results, several of the putative enterococcal virulence factors were widespread among the commensal baby isolates. These findings are in line with previous reports [11], and may reflect the adaptive functions that these factors can hold in non-virulent contexts, as indicated by Semedo et al. [11]. Several of the virulence traits and antibiotic resistant phenotypes were common for all the isolates within the clonal complexes; however, the strain set is too small to deduce statistically significant association of features with clonal identity of isolates.

Overall, our results highlight the importance of phenotypic assays to confirm genomics data as revealed by PCR and CGH. PCR confirmed the presence of *cylL* in the eight isolates that displayed hemolytic activity in our study,

however, *cylL* was also found to be present in an additional eight Cyl$^-$-isolates. A similar discrepancy between fermentation capabilities and the presence of *iolE* and *iolR* was also observed. Moreover, three isolates carrying both *gelE* and *fsrB* came out as GelE$^-$ in the plate assay. The confined genotype-phenotype correlation that is here reported, visualizes the need for phenotypic confirmation of genotypes.

esp which is known to be associated with the *E. faecalis* pathogenicity island (PAI) [25], was detected in two thirds of the commensal isolates by PCR. According to the CGH data, none of the baby isolates contained complete PAIs. These findings were as expected, considering that the PAI has been shown to be enriched among infection-derived enterococcal isolates [25]. More surprisingly, but consistent with a previous report [39], all the isolates studied contained some PAI genes. Several of the baby isolates showed similar patterns of present and divergent PAI genes (Figure 2). This suggests that the evolution of the enterococcal PAI may be driven by insertion and deletion of larger modules, as hypothesized in [39]. Shankar et al. also suggested that parts of the enterococcal PAI originate from pheromone-responsive plasmids, with subsequent indels of transposable elements driving the evolution of the PAI [39]. Indeed, conjugal transfer of a segment of the *E. faecalis* PAI has been demonstrated [40]. The CGH revealed a high degree of plasticity within all the MGEs represented on the microarray. These "mosaic structures" may reflect a complex evolutionary history of elements that have been frequently rearranged by horizontal gene transfer (HGT) and homologous recombination.

According to the CGH data presented here, a preliminary *E. faecalis* core genome consisting of 2092 (out of the 3093 chromosomal V583 ORFs) can be delineated. Compiled analysis of the data from Aakra et al. and McBride et al. [17,18] with the data from the present study produced a core genome estimate of 1722 genes. An additional 62 genes were only represented on one or two of the three different arrays used, but were defined as core genes in these experiments. Although the size of the core genome may fluctuate due to the stringency of the statistical methods used in the different studies, our data do add substantial information on the *E. faecalis* core genome.

In general, the genomic variation between isolates that are evolutionary -linked, *e.g.* isolates with the same ST, was expected to be lower than the variation between isolates that belong to different evolutionary lineages. Bayesian-based phylogenetic analysis confirmed these expectations (Figure 3A). McBride et al. previously reported genomotyping by CGH to be biased by the activity of MGEs in *E. faecalis* [17], and we therefore repeated the Bayesian analysis, using the CV genes, only. The phylogenetic analysis based on CV genes recovered the same patterns of relatedness as the analysis comprising all genes, with slight internal rearrangements of branches (Figure 3B). These rearrangements supported the hypothesis on the distribution of mobile elements as a source of genomic diversity in *E. faecalis*. Moreover, our data suggest that within lineages, most of the variation detected by CGH is due to MGEs. However, the conserved clade identified by the analyses based both on the CV genes and the complete gene-set, indicates that also other and more complex discriminatory factors contribute to the genomic diversity in *E. faecalis*. Since an overall correlation between CGH and MLST was revealed, it is reasonable to believe that genes contributing to the formation of clades, *i.e.* lineage-specific genes may be identified. In the 7 baby isolates that formed a clade in the phylogenetic analysis, we were able to recognize 137 genes that were divergent, but present in the remaining three isolates (including the reference strain). The majority of these genes were MGE genes located in phage03 (n = 39), phage06 (n = 28) and a phage-related region identified by McBride et al. [17] (EF2240–82/EF2335–51; n = 44). Lepage et al. have previously reported phage03 to be absent from several food isolates [16]. Since ST6 is part of CC2, which has been found to be significantly enriched among nosocomial isolates, phage03 may potentially represent an element associated with increased fitness in the hospital environment. The latter report also identified eight genes as potential markers for the V583/MMH594-lineage [16]. V583 and MMH594 both display ST6 [17], and five of the eight genes (EF2250, EF2253, EF2254, EF3155 and EF3252) were also present in the ST6-isolates (158B and LMGT3303; results not shown) analyzed by CGH in our study.

Comparative genome analyses have revealed that pathogen evolution often progresses through gene acquisition via HGT [32]. The 169 genes that were characterized as divergent in all the community-derived baby isolates by CGH may be potential pathogen-specific genes in *E. faecalis*, or genes that are specific to V583. However, additional CGH data from both pathogenic and non-pathogenic isolates are needed to address this issue. Vancomycin-resistant *E. faecalis* (VREfs) isolates appear to be widely spread in hospital environments, while isolation of VREfs from healthy volunteers rarely occurs [41-44]. Accordingly, the *vanB* operon was divergent in all the isolates studied by CGH in our lab (altogether 21 strains;[18] and results not shown). In addition to gene acquisition, pathoadaptive mutations via gene loss also plays an important role in evolution of bacteria [45]. A disadvantage of the comparative genomic analyses presented here, is that the comparison of gene content is based on a single reference strain (V583), only. The *E. faecalis* OG1RF genome showed that, in addition to a shared core of 2474

ORFs [29], both the V583 and the OG1RF genome carry unique genes, suggesting that the *E. faecalis* pan-genome will be further extended as more strains will be sequenced. The availability of additional *E. faecalis* genome sequences and the construction of a pan-species array would further increase the sensitivity of such approaches.

Conclusion

The data presented here suggest that the genetic variation among the investigated commensal *E. faecalis* is comparable to the genetic variation previously detected in a strain set thought to be representative of the major *E. faecalis* lineages. The widespread distribution of putative virulence determinants in the fecal baby isolates in this study supports the conception of enterococcal virulence, not as a result of any single virulence factor, but as a more complex process. Population structure studies of *E. faecalis* by MLST have identified so-called high-risk enterococcal clonal complexes (HiRECCs), defined as distinct genetic complexes that predominate among nosocomial infections. The failure to identify a shared set of pathogen-specific genes in *E. faecalis* so far opens up the possibility that the fitness and virulence of different HIRECCs may be due to genes that are unique within a lineage, but that the combined effects of the different gene-sets result in the same phenotype, *i.e*. infection. The observed correlation between CGH and MLST presented here, may offer a method for the identification of lineage-specific genes, and may therefore add clues on how to distinguish pathogenic from commensal *E. faecalis*.

Authors' contributions

MS participated in the design of the study, carried out the experimental work and drafted the manuscript. ÅAa participated in the design of the study and helped to draft the manuscript. LS proposed the statistical analysis and did the programming and statistical analysis in R. DAB and IFN participated in the design of the study and assisted in critical review of the manuscript. All authors read and approved the final manuscript.

Additional material

Additional File 1

Primers used in this study. *A table of primers used in this study.*
Click here for file
[http://www.biomedcentral.com/content/supplementary/1471-2164-10-194-S1.xls]

Additional File 2

Genotypic and phenotypic characteristics of* E. faecalis *baby isolates. *A table of the results from the phenotypic- and genotypic assays conducted in this study.*
Click here for file
[http://www.biomedcentral.com/content/supplementary/1471-2164-10-194-S2.xls]

Additional File 3

Genes divergent in all the baby isolates. *A table of genes that were classified as divergent in all the baby isolates analyzed by CGH.*
Click here for file
[http://www.biomedcentral.com/content/supplementary/1471-2164-10-194-S3.doc]

Additional File 4

Fermentation patterns from API 50 CH assays. *A table of results from fermentation profiling of selected* E. faecalis *baby isolates by API 50 CH.*
Click here for file
[http://www.biomedcentral.com/content/supplementary/1471-2164-10-194-S4.xls]

Additional File 5

The phylogenomic relationship of* E. faecalis *isolates based on gene content, as detected by CGH. *A phylogenetic tree based on CGH data from the present study, in addition to previously published CGH data from the literature.*
Click here for file
[http://www.biomedcentral.com/content/supplementary/1471-2164-10-194-S5.png]

Additional File 6

Core variable genes. *A table of genes that were classified as core variable by CGH.*
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Acknowledgements

This work was financially supported by the European Union 6th Framework Programme "Approaches to Control multi-resistant Enterococci: Studies on molecular ecology, horizontal gene transfer, fitness and prevention". Cathrine Herrera and Rønnaug Volden are acknowledged for the collection of the fecal baby isolates. We also acknowledge Zhian Salehian for technical assistance and Aksel Flack, The Norwegian Microarray Consortium, Oslo, for printing of the microarray slides.

References

1. Fanaro S, Chierici R, Guerrini P, Vigi V: **Intestinal microflora in early infancy: composition and development.** *Acta Paediatr Suppl* 2003, **91(441):**48-55.
2. Hancock LE, Gilmore MS: **Pathogenicity of enterococci.** In *Gram-positive pathogens* Edited by: Fischetti VA, Novick RP, Ferretti JJ, Portnoy DA, Rood JI. Washington DC: ASM Press; 2006:299-311.
3. Shankar N, Lockatell CV, Baghdayan AS, Drachenberg C, Gilmore MS, Johnson DE: **Role of *Enterococcus faecalis* surface protein Esp in the pathogenesis of ascending urinary tract infection.** *Infect Immun* 2001, **69(7):**4366-4372.
4. Chow JW, Thal LA, Perri MB, Vazquez JA, Donabedian SM, Clewell DB, Zervos MJ: **Plasmid-associated hemolysin and aggregation substance production contribute to virulence in experimental enterococcal endocarditis.** *Antimicrob Agents Chemother* 1993, **37(11):**2474-2477.
5. Jett BD, Jensen HG, Nordquist RE, Gilmore MS: **Contribution of the pAD1-encoded cytolysin to the severity of experimental *Enterococcus faecalis* endophthalmitis.** *Infect Immun* 1992, **60(6):**2445-2452.
6. Schlievert PM, Gahr PJ, Assimacopoulos AP, Dinges MM, Stoehr JA, Harmala JW, Hirt H, Dunny GM: **Aggregation and binding substances enhance pathogenicity in rabbit models of *Enterococcus faecalis* endocarditis.** *Infect Immun* 1998, **66(1):**218-223.

7. Kreft B, Marre R, Schramm U, Wirth R: **Aggregation substance of *Enterococcus faecalis* mediates adhesion to cultured renal tubular cells.** *Infect Immun* 1992, **60(1):**25-30.
8. Olmsted SB, Dunny GM, Erlandsen SL, Wells CL: **A plasmid-encoded surface protein on *Enterococcus faecalis* augments its internalization by cultured intestinal epithelial cells.** *J Infect Dis* 1994, **170(6):**1549-1556.
9. Eaton TJ, Gasson MJ: **Molecular screening of *Enterococcus* virulence determinants and potential for genetic exchange between food and medical isolates.** *Appl Environ Microbiol* 2001, **67(4):**1628-1635.
10. Lempiainen H, Kinnunen K, Mertanen A, von Wright A: **Occurrence of virulence factors among human intestinal enterococcal isolates.** *Lett Appl Microbiol* 2005, **41(4):**341-344.
11. Semedo T, Santos MA, Lopes MF, Figueiredo Marques JJ, Barreto Crespo MT, Tenreiro R: **Virulence factors in food, clinical and reference Enterococci: A common trait in the genus?** *Syst Appl Microbiol* 2003, **26(1):**13-22.
12. Creti R, Imperi M, Bertuccini L, Fabretti F, Orefici G, Di Rosa R, Baldassarri L: **Survey for virulence determinants among *Enterococcus faecalis* isolated from different sources.** *J Med Microbiol* 2004, **53(Pt 1):**13-20.
13. Franz CM, Muscholl-Silberhorn AB, Yousif NM, Vancanneyt M, Swings J, Holzapfel WH: **Incidence of virulence factors and antibiotic resistance among Enterococci isolated from food.** *Appl Environ Microbiol* 2001, **67(9):**4385-4389.
14. Mannu L, Paba A, Daga E, Comunian R, Zanetti S, Dupre I, Sechi LA: **Comparison of the incidence of virulence determinants and antibiotic resistance between *Enterococcus faecium* strains of dairy, animal and clinical origin.** *Int J Food Microbiol* 2003, **88(2–3):**291-304.
15. Paulsen IT, Banerjei L, Myers GS, Nelson KE, Seshadri R, Read TD, Fouts DE, Eisen JA, Gill SR, Heidelberg JF, *et al.*: **Role of mobile DNA in the evolution of vancomycin-resistant *Enterococcus faecalis*.** *Science* 2003, **299(5615):**2071-2074.
16. Lepage E, Brinster S, Caron C, Ducroix-Crepy C, Rigottier-Gois L, Dunny G, Hennequet-Antier C, Serror P: **Comparative genomic hybridization analysis of *Enterococcus faecalis*: identification of genes absent from food strains.** *J Bacteriol* 2006, **188(19):**6858-6868.
17. McBride SM, Fischetti VA, Leblanc DJ, Moellering RC Jr, Gilmore MS: **Genetic diversity among *Enterococcus faecalis*.** *PLoS ONE* 2007, **2(7):**e582.
18. Aakra A, Nyquist OL, Snipen L, Reiersen TS, Nes IF: **Survey of genomic diversity among *Enterococcus faecalis* strains by microarray-based comparative genomic hybridization.** *Appl Environ Microbiol* 2007, **73(7):**2207-2217.
19. Arroyo L, Cotton LN, Martin JH: **AMC Agar–A composite medium for selective enumeration of *Bifidobacterium longum*.** *Cultured Dairy Products Journal* 1995, **30:**12-15.
20. Ruiz-Garbajosa P, Bonten MJ, Robinson DA, Top J, Nallapareddy SR, Torres C, Coque TM, Canton R, Baquero F, Murray BE, *et al.*: **Multilocus sequence typing scheme for *Enterococcus faecalis* reveals hospital-adapted genetic complexes in a background of high rates of recombination.** *J Clin Microbiol* 2006, **44(6):**2220-2228.
21. Feil EJ, Li BC, Aanensen DM, Hanage WP, Spratt BG: **eBURST: inferring patterns of evolutionary descent among clusters of related bacterial genotypes from multilocus sequence typing data.** *J Bacteriol* 2004, **186(5):**1518-1530.
22. Booth MC, Bogie CP, Sahl HG, Siezen RJ, Hatter KL, Gilmore MS: **Structural analysis and proteolytic activation of *Enterococcus faecalis* cytolysin, a novel lantibiotic.** *Mol Microbiol* 1996, **21(6):**1175-1184.
23. Qin X, Singh KV, Weinstock GM, Murray BE: **Effects of *Enterococcus faecalis fsr* genes on production of gelatinase and a serine protease and virulence.** *Infect Immun* 2000, **68(5):**2579-2586.
24. Rich RL, Kreikemeyer B, Owens RT, LaBrenz S, Narayana SV, Weinstock GM, Murray BE, Hook M: **Ace is a collagen-binding MSCRAMM from *Enterococcus faecalis*.** *J Biol Chem* 1999, **274(38):**26939-26945.
25. Shankar N, Baghdayan AS, Gilmore MS: **Modulation of virulence within a pathogenicity island in vancomycin-resistant *Enterococcus faecalis*.** *Nature* 2002, **417(6890):**746-750.
26. Smyth GK, Speed T: **Normalization of cDNA microarray data.** *Methods* 2003, **31(4):**265-273.
27. Snipen L, Nyquist OL, Solheim M, Aakra A, Nes IF: **Improved analysis of bacterial CGH data beyond the log-ratio paradigm.** *BMC Bioinformatics* 2009, **10(1):**91.
28. Carter B, Wu G, Woodward M, Anjum M: **A process for analysis of microarray comparative genomics hybridisation studies for bacterial genomes.** *BMC Genomics* 2008, **9(1):**53.
29. Bourgogne A, Garsin DA, Qin X, Singh KV, Sillanpaa J, Yerrapragada S, Ding Y, Dugan-Rocha S, Buhay C, Shen H, *et al.*: **Large scale variation in *Enterococcus faecalis* illustrated by the genome analysis of strain OG1RF.** *Genome Biol* 2008, **9(7):**R110.
30. Ronquist F, Huelsenbeck JP: **MrBayes 3: Bayesian phylogenetic inference under mixed models.** *Bioinformatics* 2003, **19(12):**1572-1574.
31. Champion OL, Gaunt MW, Gundogdu O, Elmi A, Witney AA, Hinds J, Dorrell N, Wren BW: **Comparative phylogenomics of the food-borne pathogen *Campylobacter jejuni* reveals genetic markers predictive of infection source.** *Proc Natl Acad Sci USA* 2005, **102(44):**16043-16048.
32. Dobrindt U, Hacker J: **Whole genome plasticity in pathogenic bacteria.** *Curr Opin Microbiol* 2001, **4(5):**550-557.
33. Lindsay JA, Moore CE, Day NP, Peacock SJ, Witney AA, Stabler RA, Husain SE, Butcher PD, Hinds J: **Microarrays reveal that each of the ten dominant lineages of *Staphylococcus aureus* has a unique combination of surface-associated and regulatory genes.** *J Bacteriol* 2006, **188(2):**669-676.
34. Waldron DE, Lindsay JA: **Sau1: a novel lineage-specific type I restriction-modification system that blocks horizontal gene transfer into *Staphylococcus aureus* and between *S. aureus* isolates of different lineages.** *J Bacteriol* 2006, **188(15):**5578-5585.
35. Hancock LE, Gilmore MS: **The capsular polysaccharide of *Enterococcus faecalis* and its relationship to other polysaccharides in the cell wall.** *Proc Natl Acad Sci USA* 2002, **99(3):**1574-1579.
36. Richards MJ, Edwards JR, Culver DH, Gaynes RP: **Nosocomial infections in combined medical-surgical intensive care units in the United States.** *Infect Control Hosp Epidemiol* 2000, **21(8):**510-515.
37. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB: **Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study.** *Clin Infect Dis* 2004, **39(3):**309-317.
38. Kawalec M, Pietras Z, Danilowicz E, Jakubczak A, Gniadkowski M, Hryniewicz W, Willems RJ: **Clonal structure of *Enterococcus faecalis* isolated from Polish hospitals: characterization of epidemic clones.** *J Clin Microbiol* 2007, **45(1):**147-153.
39. Shankar N, Baghdayan AS, Willems R, Hammerum AM, Jensen LB: **Presence of pathogenicity island genes in *Enterococcus faecalis* isolates from pigs in Denmark.** *J Clin Microbiol* 2006, **44(11):**4200-4203.
40. Coburn PS, Baghdayan AS, Dolan GT, Shankar N: **Horizontal transfer of virulence genes encoded on the *Enterococcus faecalis* pathogenicity island.** *Mol Microbiol* 2007, **63(2):**530-544.
41. Coque TM, Tomayko JF, Ricke SC, Okhyusen PC, Murray BE: **Vancomycin-resistant enterococci from nosocomial, community, and animal sources in the United States.** *Antimicrob Agents Chemother* 1996, **40(11):**2605-2609.
42. Endtz HP, Braak N van den, van Belkum A, Kluytmans JA, Koeleman JG, Spanjaard L, Voss A, Weersink AJ, Vandenbroucke-Grauls CM, Buiting AG, *et al.*: **Fecal carriage of vancomycin-resistant enterococci in hospitalized patients and those living in the community in The Netherlands.** *J Clin Microbiol* 1997, **35(12):**3026-3031.
43. Gambarotto K, Ploy MC, Turlure P, Grelaud C, Martin C, Bordessoule D, Denis F: **Prevalence of vancomycin-resistant enterococci in fecal samples from hospitalized patients and nonhospitalized controls in a cattle-rearing area of France.** *J Clin Microbiol* 2000, **38(2):**620-624.
44. Torell E, Cars O, Olsson-Liljequist B, Hoffman BM, Lindback J, Burman LG: **Near absence of vancomycin-resistant enterococci but high carriage rates of quinolone-resistant ampicillin-resistant enterococci among hospitalized patients and non-hospitalized individuals in Sweden.** *J Clin Microbiol* 1999, **37(11):**3509-3513.
45. Maurelli AT: **Black holes, antivirulence genes, and gene inactivation in the evolution of bacterial pathogens.** *FEMS Microbiol Lett* 2007, **267(1):**1-8.

PAPER III

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PLoS one

Comparative Genomic Analysis of Pathogenic and Probiotic *Enterococcus faecalis* Isolates, and Their Transcriptional Responses to Growth in Human Urine

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Abstract

Urinary tract infection (UTI) is the most common infection caused by enterococci, and *Enterococcus faecalis* accounts for the majority of enterococcal infections. Although a number of virulence related traits have been established, no comprehensive genomic or transcriptomic studies have been conducted to investigate how to distinguish pathogenic from non-pathogenic *E. faecalis* in their ability to cause UTI. In order to identify potential genetic traits or gene regulatory features that distinguish pathogenic from non-pathogenic *E. faecalis* with respect to UTI, we have performed comparative genomic analysis, and investigated growth capacity and transcriptome profiling in human urine *in vitro*. Six strains of different origins were cultivated and all grew readily in human urine. The three strains chosen for transcriptional analysis showed an overall similar response with respect to energy and nitrogen metabolism, stress mechanism, cell envelope modifications, and trace metal acquisition. Our results suggest that citrate and aspartate are significant for growth of *E. faecalis* in human urine, and manganese appear to be a limiting factor. The majority of virulence factors were either not differentially regulated or down-regulated. Notably, a significant up-regulation of genes involved in biofilm formation was observed. Strains from different origins have similar capacity to grow in human urine. The overall similar transcriptional responses between the two pathogenic and the probiotic strain suggest that the pathogenic potential of a certain *E. faecalis* strain may to a great extent be determined by presence of fitness and virulence factors, rather than the level of expression of such traits.

Citation: Vebø HC, Solheim M, Snipen L, Nes IF, Brede DA (2010) Comparative Genomic Analysis of Pathogenic and Probiotic *Enterococcus faecalis* Isolates, and Their Transcriptional Responses to Growth in Human Urine. PLoS ONE 5(8): e12489. doi:10.1371/journal.pone.0012489

Editor: Markus M. Heimesaat, Charité, Campus Benjamin Franklin, Germany

Received May 19, 2010; **Accepted** July 11, 2010; **Published** August 31, 2010

Funding: HCV and DAB were financially supported by grants 142656 and 441392, respectively, from The Research Council of Norway, and MS by a grant from the European Union Sixth Framework Program under contract LSHE-CT-2007-037410. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

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Introduction

Once considered as harmless commensals of the intestinal tract, enterococci now rank among the leading causes of infections among hospital patients [1,2]. *Enterococcus faecalis* is among the most prevalent agents isolated from nosocomial urinary tract infections (UTIs), and is a common cause of chronic and recurrent UTIs, especially those associated with structural abnormalities and medical devices, such as urinary catheters [3]. The ability of *E. faecalis* to cause infection has been linked to inherent enterococcal traits, enabling the bacterium to tolerate harsh and diverse environments. In addition, several factors that may contribute to enterococcal virulence have been characterized (reviewed in [4]), and the role of these factors in pathogenicity have been further established in various animal models [5,6,7,8] and cultured cell lines [9,10]. However, a widespread distribution of putative virulence determinants in enterococcal isolates independent of origin has been reported [11,12,13,14,15,16], and to date, no single virulence factor has been demonstrated to be essential for enterococcal infections. The ability of *E. faecalis* to cause infection is therefore likely to involve an orchestrated interplay between the regulation of these putative virulence factors and various genetic determinants that govern adaptation of the bacterial cell physiology during the infection process. Cultivation in urine partly mimics the urinary tract environment, and identification of differentially expressed genes *in vitro* may therefore represent a potential means to identify novel fitness factors required for this particular ecological niche.

Shepard and Gilmore previously examined the effect of growth in urine on the expression of known and suspected enterococcal virulence factors by quantitative real-time PCR [17], and significant changes in *E. faecalis* virulence-associated gene expression were observed in response to the biological cues present in urine, compared to laboratory medium-growth. Furthermore, studies of other pathogens causing UTI have reported responses involving iron acquisition systems and genes involved in sugar and amino acid metabolism [18,19], which may indicate that bacteria suffer from glucose and iron limitation during growth in human urine.

In this report, we compare the global expression profiles of three *E. faecalis* strains during growth in human urine *in vitro*. The three

strains were chosen based on their origins; the Symbioflor 1 strain, included in a commercial probiotic product used for more than fifty years without any reports of infection [20], the hospital outbreak strain MMH594 holding most known virulence genes in its genetic repertoire [21,22], and finally the laboratory strain OG1RF which harbors some important virulence traits like *fsr* and *epa*, but is devoid of mobile genetic elements (MGEs) [23,24]. This latter strain is however capable of causing infection in *e.g.* mice [23,25], and has been extensively used as a model organism to investigate virulence ([4] and references therein). The aim of this work was to gain insight into genetic factors that make *E. faecalis* such a potent cause of human UTI. The study was designed to identify traits that distinguish pathogenic from non-pathogenic *E. faecalis*. Identification of such traits may ultimately contribute to development of strategies for prevention and treatment of *E. faecalis* UTI.

Results and Discussion

Growth capacity of different *E. faecalis* strains in urine and 2xYT

Escherichia coli associated with UTI normally grow well in urine, while non-uropathogenic strains do not [26]. To examine whether this also could be true for *E. faecalis*, six strains of nosocomial, UTI, commensal or probiotic origin were cultivated in urine and colony forming unit (CFU) counts performed (Figure 1). Only minor differences in growth capacity were observed between the various isolates, with generation times of around 48 minutes (doubling time of 48.6±3.7 min). MMH594 and V583 reached a slightly higher final cell density ($\sim 2.0\times10^8$ CFU/ml) compared to OG1RF and Symbioflor 1 ($\sim 1.2\times10^8$ CFU/ml), and even more so compared to Baby isolate 62 and 179Vet ($\sim 6.5\times10^7$ CFU/ml). These observations are consistent with a recent study by Carlos *et al.* [27], where strains from diverse origins, such as food and clinical strains, did not grow significantly different in urine. Furthermore, the growth capacity of MMH594 observed in the present study was in agreement with previous reports [17].

Since the initial growth experiments did not reveal any strains with a distinctively enhanced or reduced growth capacity in urine, two pathogenic strains MMH594 and OG1RF, and the probiotic strain Symbioflor 1 were selected for further investigation by comparative genomic analysis and transcriptional analysis.

Comparative genomic analysis

A comparative genomic analysis was conducted with emphasis on features that distinguish the three strains. The genomes of the strains used in the present study have previously been analyzed, and many aspects of the genomic composition have thus been accounted for (MMH594: [22,28]; OG1RF: [23,29]; Symbioflor 1: [20]. However, there are no sequence data publicly available for the Symbioflor 1 strain. Moreover, there existed no publicly available complete annotation for OG1RF. Thus, in order to obtain a detailed account of genetic variation and to validate the performance of our microarray, CGH was performed on the three strains (Figure 2, Figure 3 and Table S1). A total of 2284 genes were classified as present in all the strains tested. Not surprisingly, the clinical bacteremia isolate MMH594 showed the highest similarity to the reference strain V583 (94.7% genes in common). The presence of the entire pathogenicity island (PAI) in MMH594 was also confirmed [22,30]. For the two other test stains the similarity to the reference strain was significantly lower, with 2384 (74.1%) and 2371 (73.7%) of V583 genes represented on the array classified as present in OG1RF and Symbioflor 1, respectively.

Altogether, MMH594 contains 596 genes that appear to be divergent in OG1RF and Symbioflor 1. Major variations in the presence of all the previously defined mobile genetic elements (MGEs) [28,31] were observed between the three test strains. Except for *phage01* and *vanB*, all the MGEs seemed to be present in MMH594. *phage02* appear to be part of the *E. faecalis* core genome, while none of the other elements were found in OG1RF. This observation is consistent with the genome sequence available for OG1RF [23]. Symbioflor 1 contained certain genes/modules from *phage06*, but not the entire element. The rest of the MGEs were

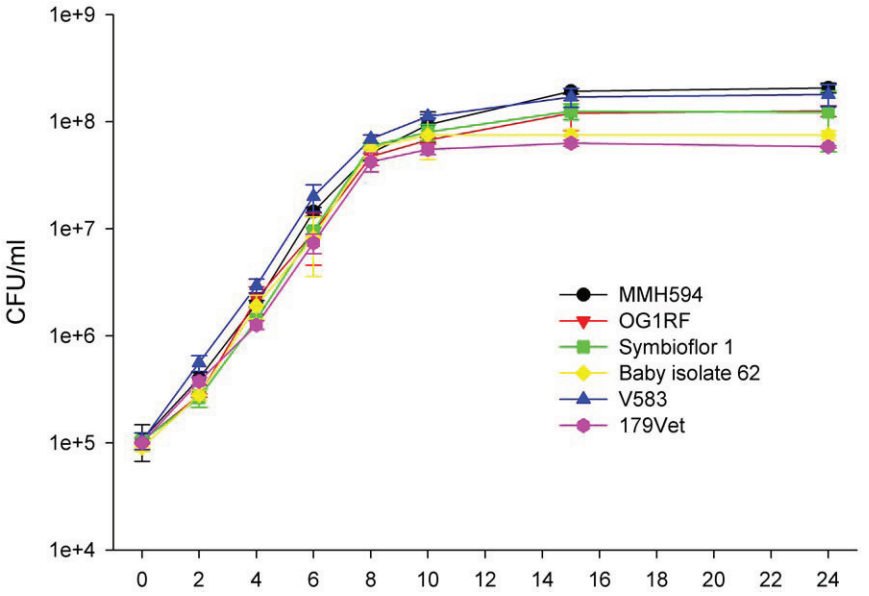

Figure 1. Growth of *E. faecalis* in urine. Characterization of growth of *E. faecalis* MMH594 (black circle), OG1RF (red triangle), Symbioflor 1 (green square), Baby isolate 62 (yellow diamond), V583 (blue triangle) and 179Vet (pink hexagon) in urine. The growth curves are represented by colony forming units per millilitre (CFU/ml) on the Y-axis, and hours as indicated on the X-axis. The growth curves correspond to the mean ± STD of two parallels.
doi:10.1371/journal.pone.0012489.g001

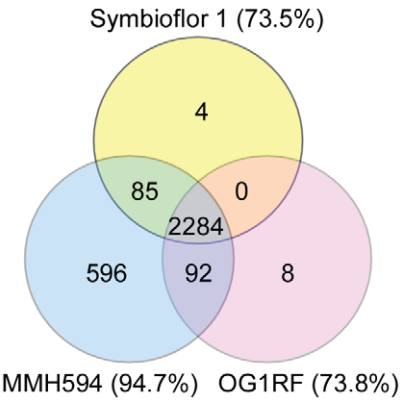

Figure 2. Gene content of *E. faecalis* MMH594, OG1RF and Symbioflor 1. Venn diagram showing the distribution of genes classified as present in the three test strains. The percentages indicated for each strain specify how large part of total probe set represented on the array that was classified as present in the corresponding strain.
doi:10.1371/journal.pone.0012489.g002

divergent by CGH in Symbioflor 1, which is consistent with previous reports [20]. Notably, Symbioflor 1 contains two major deletions in proximity to the *vanB* associated island and the efaB5 element (Figure 3 and Table S1). The latter deletion extends in the 5′ direction of efaB5 to EF1811 including the *fsr-gelE-sprE* virulence locus. The number of predicted OG1RF genes (2384) in common with V583 was significantly lower compared to 2474 genes identified in a previous report [23]. This instigated us to perform a more detailed analysis to identify the cause of this discrepancy. For this purpose we performed BLASTN comparison to V583 of 2558 genes (Table S2) predicted using EasyGene 1.2 [32], which showed an overall identity (~96.5%) between the CGH and the BLASTN analysis. An interactive Genewiz map [33] of OG1RF CGH and BLASTN (Genbank ABPI00000000) analysis compared with V583 is accessible at; http://ws.cbs.dtu.dk/cgi-bin/gwBrowser-0.91/edit.cgi?hexkey=6561d07e713b77fe75aa3403798e36c1. Moreover, BLASTN comparison of the annotated genes of V583 with the OG1RF genome sequence using 75% sequence identity across an entire CDS (Table S3) identified 2385 orthologous genes, confirming the results obtained by CGH and EasyGene 1.2 analysis.

Transcriptional analysis

A rich laboratory medium (2xYT) was used as the reference culture medium since it is considered to contain a minimum of infection relevant biological cues [17]. The growth capacity in urine was compared to that in the 2xYT medium by CFU counts (Figure S1). We found that growth in urine was slightly slower, and the cell density obtained was about one log lower than in 2xYT. For the transcriptional analysis, the three strains were grown in 2xYT to a cell density $\sim 1\times10^7$ before exposure to either pre-warmed urine or 2xYT (control). Samples were collected after 5 (t_5) and 30 (t_{30}) minutes growth. The obtained $\log_2$-ratios and q-values for the three strains during growth in urine compared to 2xYT are listed in Table S1.

Growth in urine vs. 2xYT triggers global transcriptional changes for both pathogenic and probiotic *E. faecalis*

The microarray results revealed changed expression in most functional gene categories for all three strains. At t_5, 713 genes were differentially expressed in MMH594, 735 in OG1RF and 730 in Symbioflor 1. 344 of these regulated genes were common for all three strains (Figure 4A). At t_{30}, the number of regulated genes increased dramatically to 1212 genes in MMH594 and 979 in Symbioflor 1. However, in OG1RF the number of regulated genes decreased to 574 after 30 minutes growth in urine. It is possible that the reduced number of regulated genes in OG1RF at t_{30} reflects a more rapid adjustment to the new growth environment, which potentially can be advantageous for the establishment of an infection. This notion was further supported by the swift derepression of macromolecular biosynthesis (*e.g.* protein synthesis) in OG1RF, compared to the two other strains. A total of 378 differentially expressed genes were common for MMH594, OG1RF and Symbioflor 1 at t_{30} (Figure 4B). Of the 596 genes that appeared unique to MMH594, 153 were differentially expressed at one or both time points during growth in urine. None of the genes unique to OG1RF or Symbioflor 1 were differentially expressed. The heat map in Figure 5 presents an overview of the regulated genes within each functional category for the three strains. An overview of the number of regulated genes within each functional category is given in Figure S2.

Transcription of metabolic pathways during growth in urine

Prior to the current study, no comprehensive investigation regarding which substrates or metabolic processes that confer growth of *E. faecalis* in urine existed. The transcriptome data (Table S1) was thus examined to identify metabolic pathways that showed specific responses during growth in urine.

With respect to carbon metabolism the genes encoding the main glucose uptake-system, mannose phosphoenolpyruvate phosphotransferase (PTS) *mptBACD* (EF0019-22) [34] were down-regulated in all three strains at t_{30}. This is consistent with a recent metabolomic investigation which showed that urine from healthy adults contains glucose concentrations in the range of 0.2–0.6 mM [35]. Such concentrations of glucose is below the threshold for release of carbon catabolite repression (CCR), and the cells thus initiate use of less preferred carbon and energy sources [36]. This implied that substrates besides glucose might play a role for growth of *E. faecalis* in urine. However, of the loci known to be subject to catabolite control protein A (CcpA) mediated CCR, only the genes encoding citrate metabolism (EF3322-15) [37] were positively modulated in MMH594 and OG1RF at both time points and at t_5 in Symbioflor1. At t_{30} EF3322-15 only showed a slightly (not statistically significant) enhanced expression in Symbioflor 1. The content of citrate in human urine is in the range of 1–2 mM [38], which suggests that citrate metabolism is important for *E. faecalis* during growth in urine.

PTS systems facilitate uptake of diverse sugars in *E. faecalis*. Two operons encoding a sucrose uptake PTS-system (EF1602-01) and sucrose metabolism (EF1603-04) showed consistent up-regulation in all three strains. Dietary sucrose is normally degraded in the intestinal lumen and absorbed as glucose and fructose, but a previous study has shown that even healthy individuals have µM sucrose content in their urine [39]. Moreover, the sugar content in urine increases with high sugar diet. Once sucrose is present in the bloodstream it is not metabolized further, but removed from the blood via the renal capillaries and excreted into the urine, reaching concentrations of 70 to 200 µM [39]. Interestingly, EF1603-04 knock-out mutants show reduced virulence in a *Caenorhabditis elegans* infection model [40,41]. All three strains showed elevated expression of the major facilitator family transporter (EF0082) proposed to function in import of phosphorylated sugars [42] and glycerol [43], which implies that such substrates might contribute to growth in urine.

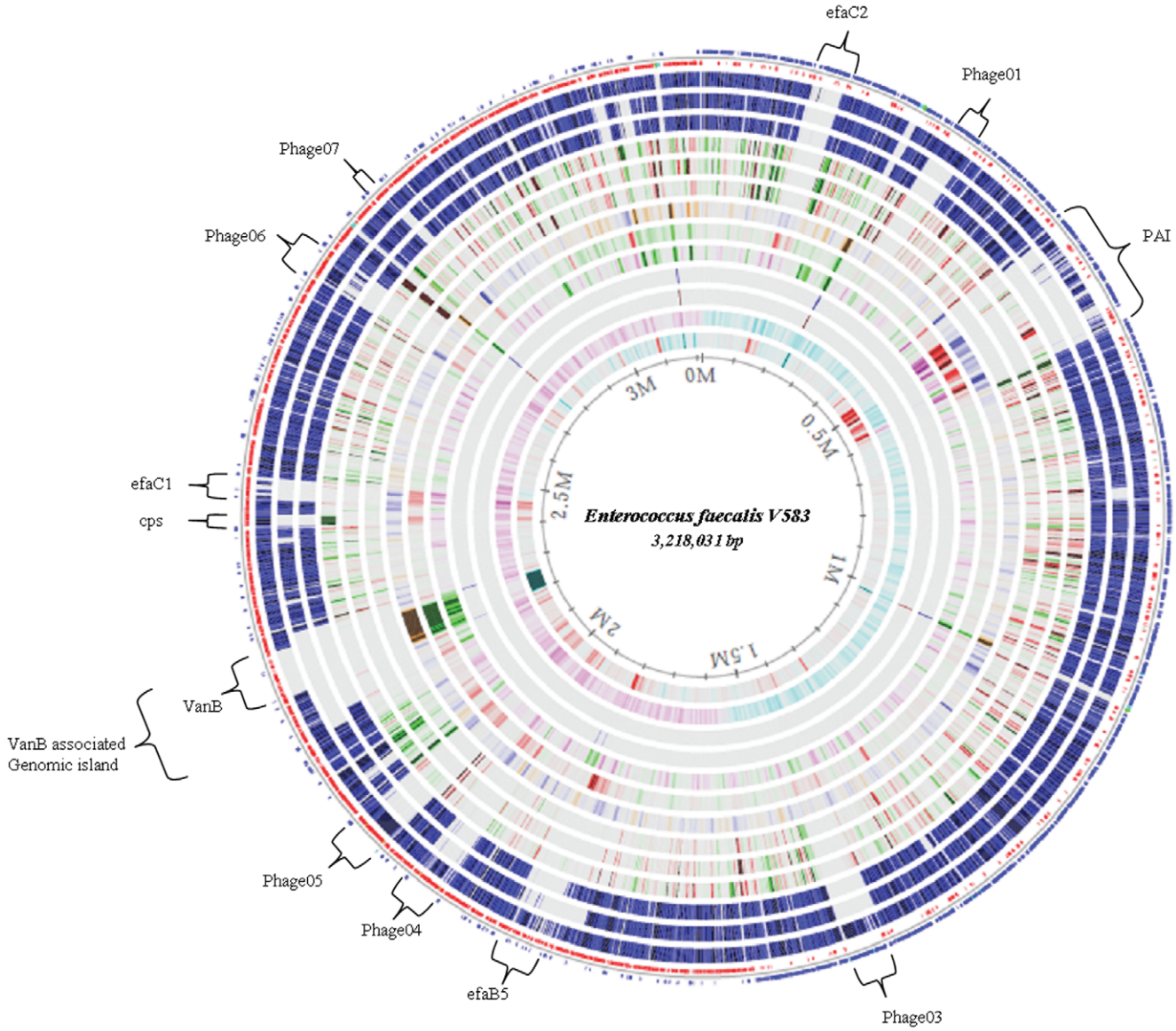

Figure 3. Genome-atlas presentation of CGH analysis and transcriptional responses to growth (t_{30}) in urine compared to 2xYT. Mobile genetic elements [28,31] are indicated by brackets. From outer to inner lanes: 1) V583 annotated CDS, 2) CGH MMH594, 3) CGH Symbioflor1, 4) CGH OG1RF, 5) Urine transcriptome MMH594, 6) Urine transcriptome Symbioflor1, 7) Urine transcriptome OG1RF, 8) Intrinsic curvature, 9) Stacking energy, 10) Position Preference, 11) Global direct repeats, 12) Global inverted repeats, 13) GC skew, 14) AT percent. Interactive Genewiz atlases of CGH and transcriptome data are available at; http://ws.cbs.dtu.dk/cgi-bin/gwBrowser/edit.cgi?hexkey=603430a081eb5be3f306e744e94b151a, and http://ws.cbs.dtu.dk/cgi-bin/gwBrowser/edit.cgi?hexkey=3068b894fb6b9e44d9c135a210950f52, respectively.
doi:10.1371/journal.pone.0012489.g003

Transcriptome analysis conducted on an *E. coli* asymptomatic bacteriuria strain revealed an important role of amino sugar and amino acids present in urine as growth substrates [44]. The transcription of *nagB* (EF0466) and *nagA-1* (EF1317) involved in N-acetyl glucosamine metabolism was elevated, implying that these substrates were utilized by *E. faecalis* during growth in urine. A massive down-regulation of *glmS* (EF2151), which is responsible for conversion of fructose-6P into glucosamine-6P using glutamine as a nitrogen source, could signify glutamine constraints.

Growth in urine also had an impact on pyruvate metabolic pathways and certain changes were strain specific. For OG1RF and Symbioflor 1, we observed increased expression of L-lactate dehydrogenase (*ldh*-1; EF0255), whereas expression of *adhE* (EF0900), involved in ethanol formation was reduced. The *pflAB* (EF1612 and EF1613) genes responsible for formate formation were reduced in MMH594 and Symbioflor 1 at t_{30}. In all strains the *lutABC* operon (EF1108-1110), involved in metabolism of L-lactate like substrates was up-regulated. The pyruvate dehydrogenase complex gene-cluster *pdhAB*, *aceF* and *lpdA* (EF1353-56) involved in acetyl-CoA biosynthesis showed consistent up-regulation in all three strains at t_{30}. Moreover, the *ackA* gene (EF1983) responsible for conversion of acetyl-phosphate to acetate and ATP was significantly down-regulated, perhaps as a consequence of increased acetate production due to elevated activity of the citrate metabolism (EF3322-15) [37]. It is thus conceivable that the increased acetyl-CoA formation serves to supply either the FASII biosynthesis, or the citrate metabolism.

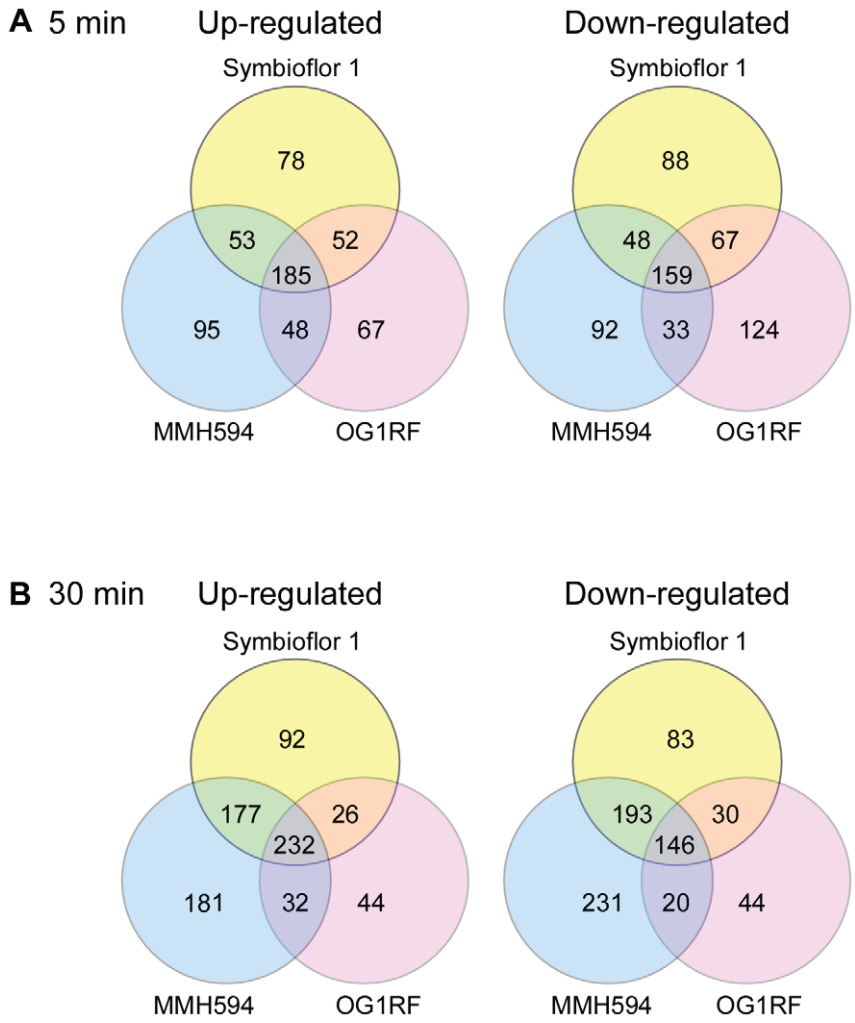

Figure 4. Distribution of differentially expressed genes during growth in urine. Venn diagram showing the number of unique and common up- and down-regulated genes in MMH594, OG1RF and Symbioflor 1 when grown in urine compared to 2xYT after A: 5 minutes (t_5) and B: 30 minutes (t_{30}).
doi:10.1371/journal.pone.0012489.g004

Transport and biosynthesis

Compared to the rich 2xYT medium the growth rates were significantly lower in urine, and moreover, the growth halted one order of magnitude below that in 2xYT (Figure S1). For *E. coli* it has been demonstrated that growth in urine is restricted by availability of one specific cofactor, namely iron [44]. We were thus interested to see whether the transcriptional responses with respect to transport and biosynthesis processes in *E. faecalis*, could reveal candidate nutrients or co-factors whose availability restrict growth of *E. faecalis* in urine.

Human urine contains significant amounts of creatine, creatinine, and glycine, while other amino acids like histidine, glutamine, methionine, proline, glutamate, arginine and branched chain amino acids (bcaa) are present at lower concentrations [45]. The CGH-results indicate that MMH594 and Symbioflor 1 have similar requirements for amino acids as OG1RF, which was shown to be auxotrophic for amino acids like histidine, isoleucine, methionine, and tryptophan [24]. Also, some *E. faecalis* strains require arginine, glutamate, glycine, leucine, or valine [24], and are capable of utilizing certain amino acids as energy and carbon source [46,47]. However, transcription of the genes encoding catabolism of arginine (EF0104-7 and EF0108) and serine (EF0097-100) was significantly reduced at t_{30}, indicating a shift towards protein synthesis rather than energy metabolism.

According to our data, the transcription of several genes encoding oligo-peptide ABC-transporters (EF0907, EF0909-12 and EF3110-06) was enhanced at t_{30}, while the transcription of three amino acid permease genes (EF0635, EF0929 and EF2377) and two operons encoding amino acid transporters (EF0247-46 and EF0761-60) was reduced in all three strains at the same time point (Table S1). These observations indicate that *E. faecalis* meets its demand for certain amino acids by acquiring oligo-peptides during growth in urine. However, the *gln*-operon encoding glutamine/glutamate transport system (EF1120-17) [48] was up-regulated in all strains at both time points, suggesting that glutamate/glutamine from urine were utilized. This was further supported by the observed reduced expression of the glutamine synthase operon *glnRA* (EF2160-59) in all three strains and glutamate synthase *gltA* (EF2560) in OG1RF and Symbioflor 1 at t_{30}. On the contrary, the increased expression of *cysK* (EF1584) implies that cysteine is scarce in urine, which also is in accordance to the metabolomic analysis of human urine [45].

An operon comprising a putative amino acid ABC transporter (EF0893-92) and a putative aspartate aminotransferase (EF0891) was

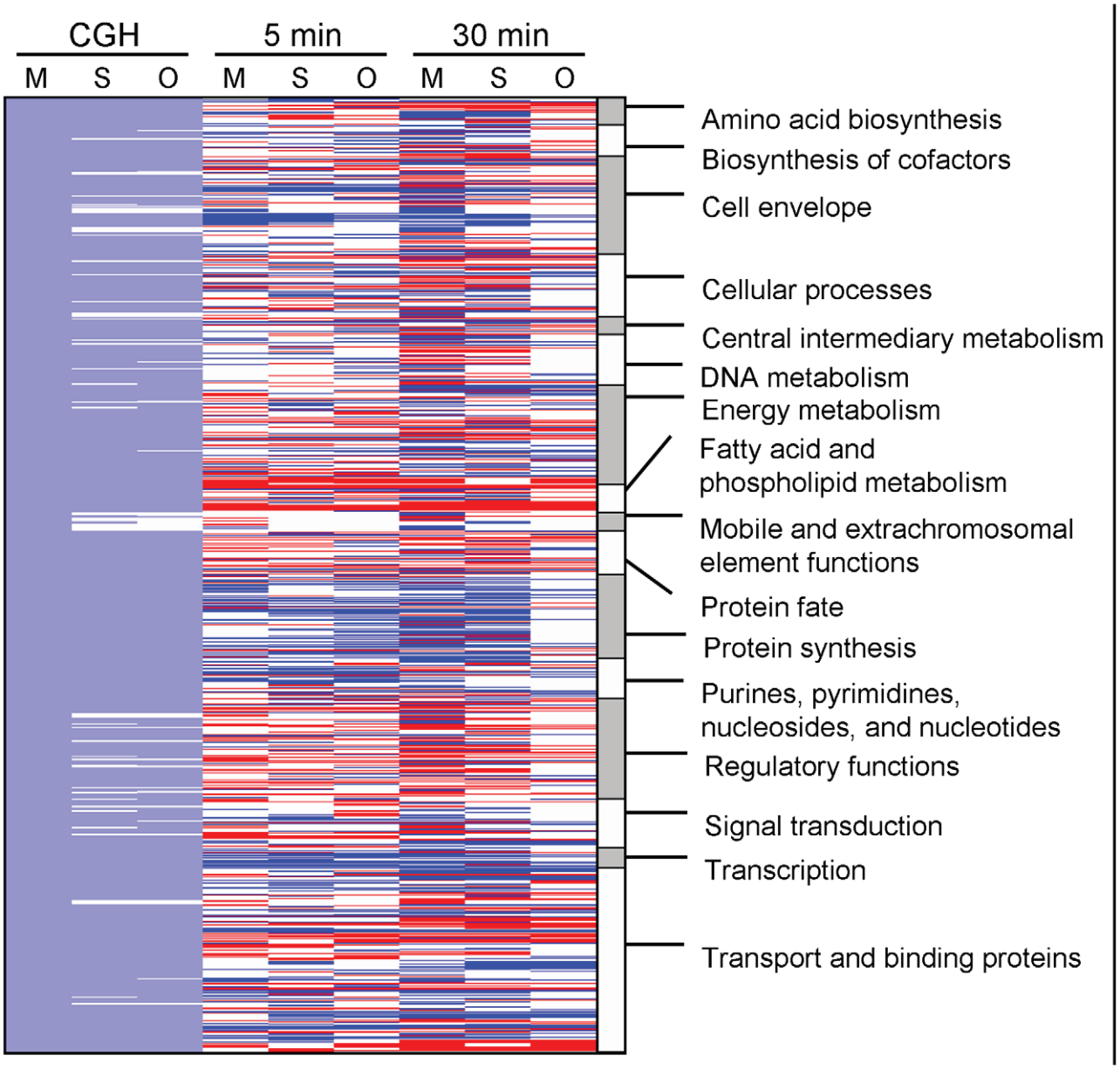

Figure 5. Heat map of CGH data and differentially expressed genes during growth in urine. Heat map visualizing the regulated genes in MMH594 (M), Symbioflor 1 (S) and OG1RF (O) when grown in urine compared to in 2xYT. The comparative genome hybridization (CGH) results for the respective regulated genes are shown in columns 1–3 (light blue: present gene, white: divergent gene). Genes found to be significantly regulated are indicated by either red (up-regulated), or blue (down-regulated). Genes regulated after growth for 5 minutes (t_5) in urine compared to in 2xYT are listed in columns 4–6 and after 30 minutes (t_{30}) in columns 7–9. The functional categories are sorted alphabetically (column 10). Significantly regulated hypothetical genes and genes encoding proteins with unknown function are not included in this heat map.
doi:10.1371/journal.pone.0012489.g005

highly up-regulated in all strains. The latter gene is predicted to facilitate the conversion of aspartate and alpha-ketoglutarate to oxaloacetate and glutamate, which may also in turn explain the down-regulation of the above mentioned *gltA*. Furthermore, the transcription of a gene encoding methionine synthase (EF0395) was enhanced in all three strains. These results are consistent with the metabolomic analysis of human urine which showed that aspartate is 5-fold more abundant than methionine [45]. These observations imply that aspartate might serve a key role for nitrogen metabolism of *E. faecalis* in urine. Thus, it appears that *E. faecalis* scavenge available peptides and amino acids, which in turn are sequentially hydrolyzed and transaminated in order to fuel the pool of depleted amino acids.

Urinary tract pathogenic bacteria like *E. coli* (UPEC), have pathogenic islands dedicated to acquisition of limited nutrients and biometals [49]. Manganese is one such factor which is essential for the fermentative metabolism of lactic acid bacteria (LAB) [50,51]. The up-regulation of the main manganese scavenging mechanism encoded by *efaCBA* (EF2074-76), accompanied by two other genes (EF1057 and EF1901) encoding Mn^{2+}/Fe^{2+} transporters in all strains at both time points is a clear indication that *E. faecalis* scavenged manganese. The content of manganese in human urine is in the nano molar range [52], while the optimal concentration for *E. faecalis* is in the micro molar range [53]. Thus manganese may be restrictive for the growth of *E. faecalis*. This in turn can

affect the virulence of the bacterium and *efaCBA* has indeed been shown to be implicated in virulence [54]. Notably, for MMH594 a potential auxiliary Mn-uptake system (EF 0575-78) [55], located within the PAI also showed highly elevated expression, indicating that PAI harboring strains might be better equipped to cope with manganese depleted environments.

In addition to the above mentioned Mn^{2+}/Fe^{2+} transporters, our experiments also revealed an enhanced expression of several other genes involved in iron transport; the *feoAB* (EF0475-76) and *ceuBCD* and *fatB* (EF3085-82) operons were up-regulated in all strains at t_{30}. Another gene involved in iron transport, *feuA* (EF0188) was down-regulated in all strains at t_5, but was up-regulated in MMH594 and OG1RF at t_{30}. Interestingly, a third iron transport encoding operon (EF0191-93) was down-regulated in all three strains at t_5, while up-regulated at t_{30} in OG1RF only. Iron is one of the main limiting factors for *E. coli* growth in urine and the addition of iron to urine increased the maximum growth extensively [18,19]. LAB, on the other hand comprise one of the very few groups of bacteria for which iron is not an essential growth factor [51]. Even so, our data suggest a potentially important role of iron acquisition and metabolism during growth in urine.

Stress response of *E. faecalis* towards exposure to urine

Proteomic analyses with systematic exposure to various stresses have previously identified six genes encoding general stress response proteins (GSPs) which were up-regulated in *E. faecalis* by a wide variety of environmental stimuli [56]. The enhanced expression of all the GSP-encoding genes at one or both time points in the present study indicates that the bacterium experienced a multitude of stress factors upon the encounter with urine. This impression was further substantiated by the significantly differential transcription of a large number of genes with a proven or predicted function in other stress responses in *E. faecalis* [112–120] (Table S1 and S4).

The gene encoding Gsp62 (EF0770; hypothetical protein) was the only GSP which showed a significantly enhanced expression in all strain at both time points. The stress- and starvation inducible *gls24* operon (EF0076-81) was significantly up-regulated at both time points in OG1RF and Symbioflor 1, while partly up-regulated in MMH594. Inactivation of *gls24* and *glsB* (EF0079 and -80, respectively) has been reported to have a pleiotrophic effect on cell morphology and stress tolerance in *E. faecalis* [57]. A *gls24* disruption mutant has also been shown to be highly attenuated in animal infection models [58,59]. MMH594 contains two additional *gls24*-like genes within the PAI (EF0604 and PAIef0055). Both gene were up-regulated at t_{30} and might possibly contribute to the fitness of MHH594 during growth in urine.

An organic hydroperoxide resistance protein, *ohr* (Gsp65; EF0453) was up-regulated in MMH594 at t_5, and in all three strains at t_{30}. An *ohr* mutant has previously been shown to be less resistant to the oxidative stress generated by 20 mM Tertiary-Butylhydroperoxide, suggesting that Ohr may be implicated in oxidative stress resistance in *E. faecalis* [60]. Interestingly, the microarray data revealed differentially expression of an arsenal of genes holding putative roles in oxidative stress response in *E. faecalis* (Table S1 and S4). The enhanced transcription of genes involved in oxidative stress response during exposure to urine is interesting. Especially in light of an observed adaptation to lethal challenges of H_2O_2 by pretreatment with sublethal concentrations of H_2O_2 [61], and a reported link between oxidative stress response and survival within macrophages in enterococci [62,63,64]. Furthermore, it has been demonstrated that purified lipoteichoic acids from *E. faecalis* induced proliferation and production of nitrous oxides and cytokines by a subpopulation of basal urothelial cells [65,66]. It is thus tempting to speculate that urine act as a cue to trigger oxidative stress-protection by *E. faecalis*, in order to render increased resistance against certain host defense mechanisms in the urinary tract.

Modifications to the cell envelope caused by growth in urine

When infecting a host, the integrity and composition of the cell envelope of the bacterium are important to avoid damage by the host defense systems [67,68]. In the case of *E. faecalis*, it has been demonstrated that important processes in the interaction with the host *e.g.* recognition by immune system mechanisms and innate immune evasion, involve specific cell envelope structures like lipotechioc acids [69], and cell wall and capsular polysaccharide determinants [70,71].

During growth in urine, signs of adaptation to this new growth environment were evident for several genes important for the cell membrane composition and surface related structures (Table S1). We observed an immediate response to urine by the up-regulation of two gene clusters (EF0282-84 and EF2886-75) responsible for type II fatty acid biosynthesis (FASII) and isomerization of membrane phospholipids. Most of these genes were up-regulated in all strains at t_5 and t_{30}. Interestingly, these gene clusters have previously been shown to be up-regulated in response to growth in blood [72] and to exposure to the cell membrane detergent SDS [73]. Furthermore, the FASII genes were down-regulated in response to exposure to NaCl (Solheim, unpublished data), bovine bile, and SDS and bovine bile in combination [73], indicating that several different external stressors triggers remodeling of the fatty acid composition in the cell membrane.

In addition to the FASII pathway, a regulation of three genes encoding lipases (EF0169, EF1683 and EF3191) and two genes encoding cardiolipin synthetases (EF0631 and EF1608) further indicates both degradation and processing of fatty acids (Table S1). It is possible that the lipolytic activity is connected to a modulation of the FASII genes, as it recently was demonstrated that *E. faecalis* can utilize available fatty acids from the environment in their membrane biogenesis [74]. However, there are only trace amounts of free fatty acids in urine [38], and it is therefore more likely that the remodeling of the fatty acid composition in the cell membrane is a more general stress response in *E. faecalis*, while the lipases may play a more specialized role in virulence. A recent study by Walecka and co-workers revealed that a higher percentage of invasive *E. faecalis* isolates produce lipases compared to non-invasive isolates [75], indicating a central role for lipase activity during invasive infection. Notably, Symbioflor 1 showed a more enhanced expression of genes encoding lipases compared to the pathogenic strains.

The ability of *E. faecalis* to adhere and develop biofilm is thought to be important for its potential to cause UTI and other infections [76]. In our experimental design, the cells were cultivated planktonically. We were thus interested in assessing whether genes implicated in adherence or biofilm formation would be modulated by human urine. The gene encoding the maltose PTS system *malT* (EF0958) and the cognate operon *bopABCD/malPBMR* (EF0957-54), are involved in biofilm formation [77,78], and were partly up-regulated in OG1RF at t_5. Another gene important for biofilm production and the initial attachment stage for binding to abiotic surfaces is a sortase A encoding gene, *srtA* (EF3056) [79,80]. This gene showed an enhanced expression in MMH594 at t_{30} and Symbioflor 1 at both time points. Interestingly, an *srtA* mutant showed a slightly attenuated virulence during UTI in mice [81]. However, among the genes encoding potential substrate proteins

of SrtA, only EF2713 was up-regulated at t_5 in MMH594, whereas EF3314 showed an enhanced expression in Symbioflor 1 at both t_5 and t_{30}. This latter gene encodes a protein recently shown to be important for the pathogenicity of *E. faecalis* [82], and it is noteworthy that the only strain which showed an enhanced expression of this gene, was the probiotic strain.

Mohamed *et al.* [83] demonstrated that a knockout mutant of the secreted antigen *salB* (EF0394) in OG1RF showed reduced biofilm formation in BHI, but enhanced biofilm production in the presence of serum or fibronectin. The authors also showed that the *salB* mutant was able to bind to the extra cellular matrix (ECM) proteins collagen type I and fibronectin, whereas wild type OG1RF did not bind these ECM proteins [83]. Furthermore, they showed that a *salA* (EF3060; secreted lipase) mutant also produced slightly less biofilm than wild type OG1RF, while binding to ECM was unaffected. During growth in urine *salA* was down-regulated in all strains at both time points, while *salB* was down-regulated in all strains at t_5, and in MMH594 at t_{30}. Mohamed and co-workers [83] speculated that under certain conditions a down-regulation of *salB* would be sufficient to see similar effects as was seen for the *salB* mutant, thus it is possible that the expression of *salB* and possibly also *salA* is reduced in response to urine in order to promote colonization of the urinary tract.

At t_5, a gene encoding the major autolysin of *E. faecalis*, *atlA* (EF0799) was down-regulated in all three strains. An *atlA* deletion mutant of OG1RF showed delayed biofilm formation, reduced attachment on plastic surfaces and longer chains than the wild type OG1RF [79,84]. AtlA is also essential for DNA release and biofilm accumulation, which is needed for the development of a mature biofilm in *E. faecalis* [79,85]. MMH594 and Symbioflor 1 contain a second peptidoglycan hydrolase encoding gene *atlB* (EF0355), which have been shown to compensate for the absence of AtlA in autolysis and cell separation [84]. *atlB* was down-regulated at t_{30} in MMH594, while not differentially expressed in Symbioflor 1. The lowered expression of *atlA* and *atlB* may also be connected to reduced cell wall synthesis indicated by down regulation of several genes responsible for peptidoglycan biosynthesis (Table S1), which again is consistent with the significantly lower growth rate in urine compared to 2xYT.

Bacterial surface proteins are key players in host-pathogen interactions [81]. Therefore, the change of membrane bound proteins might alter the bacterium's potential of causing an infection. Regulation of several genes encoding proteins bound to the cell membrane or cell surface *i.e.* membrane proteins and lipoproteins was observed for all three strains (Table S1). Moreover, most microbial surface components recognizing adhesive matrix molecules (MSCRAMMs) and cell-wall anchor family proteins [86] including the endocarditis- and biofilm-associated pilus (*ebp*) [87,88] were either down-regulated, or not differential regulated (Table S1).

A gene encoding a chitin binding protein (EF0362) and one encoding a chitinase (EF0361) were up-regulated in all three strains at t_5. The direct function for these genes in response to urine is not clear, however a homologous protein GbpA in *Vibrio cholerae* was shown to facilitate binding to the chitin monomer N-acetylglucosamine [89], a sugar residue found on the surface of epithelial cells [90,91,92], which line the cavities and surfaces of structures including the urinary tract. Hence, it is possible that biological cues in urine trigger the up-regulation of these genes as an initial step of adherence to uroepithelial cells. Interestingly, growth of *E. faecalis* V583 in blood triggered an even more enhanced transcription of these two genes [72], but a functional study of these genes would be required to elucidate any function related to enterococcal virulence.

Most of the genes within a cluster responsible for the production of a serotype-determining exopolysaccharide (EF2198-2177; *epa*) [93,94] were down-regulated both at t_5 and t_{30} in the three strains. An OG1RF Δ*epaB* mutant has previously been reported to show reduced virulence in mice [95], higher susceptibility to phagocytic killing [71], and decreased biofilm formation compared to the wild type [71,96]. Furthermore, Singh *et al.* recently showed that the *epaB* mutant was less competitive compared to the wild type in a model of UTI in mouse [97]. However, it is possible that the exopolysaccharide production is body-site dependent, and could be more pronounced in *E. faecalis* that have reached the glomerular basement membrane in kidneys, which is a preferred site for *E. faecalis* colonization [97,98].

The serotype 2 capsular polysaccharide (*cps*) [99], which constitutes an important virulence factor that enables *E. faecalis* to evade phagocytic killing, by masking the lipoteichoic acids [70], is absent in both OG1RF and Symbioflor 1 (Figure 3 and Table S1). Intriguingly, the *cps* gene cluster (EF2495-85) was down-regulated in MMH594 at t_{30}, which is similar to the response observed in V583 growing in blood [72]. It is tempting to speculate that a basal capsular polysaccharide production could be sufficient to protect *E. faecalis* from complement-mediated opsonophagocytosis, especially in infected tissues where micro-colonies or biofilm develop.

In sum, the human urine milieu appears to instigate a drastically altered composition of the cell envelope and cell surface structures, some of which might be advantageous or required for establishment of *E. faecalis* UTI.

Virulence traits and Regulatory genes

A number of genetic traits have been identified to contribute to virulence in *E. faecalis* [5,6,8,25,59,71,99,100,101,121,122]. The expression of selected virulence genes in MMH594 during growth in urine have previously been examined by real-time quantitative PCR (QPCR) [17]. More recently, a new QPCR study of the expression in several strains including MMH594 during growth in urine was published [102]. The two studies show some differences in gene expression in MMH594, *e.g.* of a gene encoding the enterococcal surface protein Esp (PAIef0056). Shepard and Gilmore [17] found an enhanced expression of *esp*, while Carlos *et al.* [102] found a reduced expression of the same gene. In the present study, we found that the *esp* gene was not significantly differentially expressed. Indeed, QPCR appear to be more sensitive and have a broader detection range than microarray, but the deviating results still seem to imply a problem when comparing these types of experiments. Shepard and Gilmore [17] reported a growth-phase dependent difference in the expression of the virulence genes tested. Hence, the differences observed between these three similar experiments are most likely due to the different methods used for cultivation. Our aim was to investigate the immediate effect on actively growing *E. faecalis* cells upon the first encounter of urine. We revealed a significant impact on the transcription of a number of virulence related traits connected to stress, co-factor acquisition, and cell surface structures (described above), and a summary of these genes can be found in Table S5.

The *fsr* quorum sensing system has been shown to coordinate expression of the virulence factors *gelE* (encoding a gelatinase) and *sprE* (encoding a serine protease) during infection of *C. elegans* and in mouse peritonitis models [25,101], and several other genes were differentially expressed in wild type OG1RF compared to an *fsrB* mutant, indicating a more complex regulatory network [103]. Consistent with previous observations [17], we detected a modest up-regulation of the *fsrABC* genes (EF1822-20) in MMH594 at t_{30}.

The *fsrA* gene was also up-regulated at t_5. In addition, the downstream *gelE* (EF1818) was down-regulated at t_5 in MMH594. No regulation of these genes was observed in OG1RF (the genes are divergent in Symbioflor 1). However, due to the fact that several of the *fsr*-genes had been excluded from the data analysis as a result of the number of functional spots in the latter strain (see Materials and methods), the expression of *fsrB* was verified by real time quantitative PCR (QPCR; Figure S3). The QPCR analysis of *fsrB* revealed that the $\log_2$-ratio was below the threshold for significant differential expression in MMH594. Differential expression of *fsrB* was however, observed in OG1RF. These results are in line with previous findings which suggest that growth in urine promotes transcription of the *fsr*-quorum sensing system [17]. Quorum sensing regulatory cascades are characteristically initiated by elevated expression of a regulatory unit, in this case the *fsr*-operon, of which the most likely consequence would be the subsequent induction of the *fsr*-regulon.

The PAI is significantly more prevalent among infection-derived isolates compared to *E. faecalis* from other sources [22,28,30,104]. Moreover, the contribution of PAI-related genes to the pathogenicity of *E. faecalis* has been experimentally determined for certain traits, such as *araC*, cytolysin, *esp* [5,100,105]. In the genome of the three strains used in this study only MMH594 contains the entire enterococcal PAI (129 genes, of which 125 were represented on the array). Fifteen PAI genes were down-regulated, while twenty PAI genes including manganese transporter (EF0575-77), *gls24* (EF0604) and a bile salt hydrolase (BSH; EF0521) were up-regulated in MMH594 at t_{30}. The latter gene was also the only PAI gene which showed an enhanced expression in Symbioflor 1. The BSH and the Gls24 starvation-inducible protein are factors that have been hypothesized to be advantageous in colonization of the gastrointestinal tract, and our results demonstrate that potential virulence-, stress- and fitness-genes located in the PAI do in fact respond to an infection-relevant milieu like urine. However, the exact function of these genes in the pathogenicity of *E. faecalis* remains to be elucidated. Moreover, transcripts were detected for a substantial number of PAI genes, implying that their mere presence and basal expression might also be important during UTI.

In conclusion, a significant proportion of the transcriptional responses seen during growth in urine were common for the three different strains examined, and the main differential regulation was observed among genes related to stress responses, energy metabolism, acquisition of trace metals, and a drastic modification of the cell envelope. Despite the failure to identify pathogen-specific *E. faecalis* genes, the overall similarity between the transcriptional responses of pathogenic and non-pathogenic strains presented here, implies that the pathogenic potential of an *E. faecalis* strain may in fact be determined by presence or absence of specific genes, rather than the level of expression of such traits.

Materials and Methods

Bacterial strains and growth conditions

Bacterial strains used in this study are listed in Table 1. The growth capacity of six *Enterococcus faecalis* strains was examined. Three of these strains were selected for transcriptional profiling based on their origin. For all experiments *E. faecalis* strains were streaked on a 2xYT agar plate (1% (w/v) yeast extract, 1.6% (w/v) tryptone and 1% (w/v) NaCl) and incubated at 37°C over night (ON). Four individual colonies were then inoculated into the same tube of 5 ml 2xYT medium and grown ON without shaking at 37°C. For growth in urine, human urine was collected from four healthy men and women who had no history of UTI or antibiotic use in the last 6 months. The urine was pooled with equal amounts from each volunteer, centrifuged at 12000×g and sterilized twice by filtration (0.22 µm-pore size). Since the composition of human urine may potentially be variable, samples were collected on three separate days for three replicate experiments and used within the next day.

Growth measurement

The six *E. faecalis* strains were pre-cultured as described above. ON cultures were diluted 1000× in either preheated urine (37°C) or in preheated 2xYT medium and incubated ON. These cultures were then diluted 1000× in either preheated urine or 2xYT, and cell growth was measured spectrophotometrically with a Bioscreen instrument (Bioscreen C) and by plating and colony forming units (cfu) counts. Growth experiments measured spectrophotometrically were performed in triplicates with a total volume of 300 µl of bacterial inoculum in fresh urine or 2xYT medium. Wells containing sterile urine/2xYT were used as negative controls. Cultures were incubated at 37°C and optical density 600 nm (OD_{600}) was measured at 15-min intervals for 24 hours. To determine CFU/ml, viable cell counts were performed as follows: ON cultures were inoculated (1000× dilution) in preheated urine. Samples were collected immediately after inoculation, and after 2, 4, 6, 8, 10 and 24 hours for 2xYT, and also after 15 hours for urine. The number of CFU/ml was estimated by averaging the colony count values in two replicates per strain after ON incubation at 37°C.

Table 1. Bacterial strains used in this study.

Strain	Country	Source	Isolation site	MLST		Characteristics	Reference
				CC	ST		
Baby isolate 62	Norway	Non-hospitalized person <1 year	Feces	S	66	Tet^R	[106]
MMH594	USA	Hospitalized patient	Blood	6	6	Ery^R,Gen^R, hospital outbreak	[21]
OG1RF	USA	Laboratory strain		21	1	Rif^R, Fus^R	[24]
Symbioflor 1	Germany	Non-hospitalized person	Feces	25	248	Probiotic	[20]
V583	USA	Hospitalized patient	Blood	6	6	Ery^R, Gen^R, Van^R	[123]
179Vet	Norway	Animal_dog	Urine	9	9	Multi-resistant*	[29]

CC = clonal complex; Ery = erythromycin; Fus = fusidic acid; Gen = gentamicin; MLST = multilocus sequence typing; R = resistance; Rif = rifampicin; S = singleton; ST = sequence type; Tet = tetracycline; Van = vancomycin.
*Tested against 16 different antibiotics, of which it was susceptible only to ampicillin.
doi:10.1371/journal.pone.0012489.t001

Cultivation and sampling prior to microarray analysis

The three selected *E. faecalis* strains, MMH594, OG1RF and Symbioflor 1 were pre-cultured as described above. The cultures were then diluted 1000× in 250 ml pre-warmed 2xYT medium and incubated further at 37°C. When the culture reached $OD_{600} = 0.1$ the cultures from each strain was split in two and centrifuged (10000×*g* for 3 min at 37°C). For the control cultures the pellets were resuspended in 100 ml pre-warmed 2xYT (37°C) whereas for the test culture the pellet was resuspended in 100 ml pre-warmed urine (37°C). Samples (45 ml) of each culture were collected immediately after the resuspension in urine (t_5), and after 30 min (t_{30}) by centrifugation (8000×*g* for 2 min at 37°C), and the pellets were immediately frozen in liquid nitrogen and kept at −80°C prior to RNA extraction.

RNA isolation, cDNA synthesis, fluorescent labeling and hybridization

Total RNA was isolated by FastPrep (Bio 101/Savant) and RNeasy Mini kit (QIAGEN) as previously described [72]. The concentrations of the RNA samples were measured by using the NanoDrop (NanoDrop Technologies), and the quality was assessed by using the RNA 600 Nano LabChip kit and the Bioanalyzer 2100 (Agilent Technologies). cDNA was synthesized and labeled with the Fairplay III Microarray labeling kit (Stratagene) according to the manufacturer's protocol, with the following modifications: For each labeling reaction, 10 µg of total RNA and 500 ng of random primers were initially preheated at 70°C for 10 min. A reverse transcription-PCR mixture (10× AffinityScript RT buffer, a 20× deoxynucleoside triphosphate mixture, 0.1 M dithiothreitol, 20 U RNase block, and Affinity-Script HC RT) was added to the annealed primers and RNA, and the reaction mixture was further incubated for 3 h at 42°C. After labeling, 1 µL of hydroxylamine (Sigma Aldrich) was added to quench the coupling reaction, and the reaction mixture was incubated 10 min. at room temperature. 70 µL RNase-free water was then added, and unincorporated dyes were removed from the samples by using the QIAquick PCR purification kit (QIAGEN). Labeled samples were then dried, prior to resuspension in 140 µl hybridization solution (5× SSC, 0.1% (w/v) SDS, 1.0% (w/v) bovine serum albumin, 50% (v/v) formamide and 0.01% (w/v) single-stranded salmon sperm DNA) and hybridized for 16 h at 42°C to the array in a Tecan HS 400 pro hybridization station (Tecan). Arrays were washed twice at 42°C with 2× SSC +0.2% SDS, and twice at 23°C with 2× SSC, followed by more stringent washes at 23°C with 0.2× SSC and with filtrated H_2O. Three replicate hybridizations were performed with three separate batches of RNA. The three batches of RNA were obtained in three separate growth experiments. The Cy3 and Cy5 dyes (Amersham) used during cDNA synthesis were swapped in two of the three replicate hybridizations. All samples in the three experiments were co-hybridized with control samples collected at equal time points (*e.g.* t_5 was hybridized along with t_5). Hybridized arrays were scanned at wavelengths of 532 nm (Cy3) and 635 nm (Cy5) with a Tecan scanner LS (Tecan). Fluorescent intensities and spot morphologies were analyzed using GenePix Pro 6.0 (Molecular Devices), and spots were excluded based on slide or morphology abnormalities.

Microarrays

The microarray used in this work has been described previously [106]. The microarray designs have been deposited in the ArrayExpress database with the accession numbers A-MEXP-1688 and A-MEXP-1765.

Data analysis

Downstream analysis was done by the LIMMA package (www.bioconductor.org) in the R computing environment (www.r-project.org). Preprocessing and normalization followed a standard procedure using methods described by Smyth & Speed [107]. Testing for differential expressed gene was done by using a linear mixed model as described in Smyth [108]. A mixed-model approach was chosen to adequately describe between-array variation and still utilize probe-replicates (3 replicates of each probe in each array). An empirical Bayes smoothing of gene-wise variances was conducted according to Smyth *et al* [109]. For each gene, the p-value was adjusted to control the false discovery rate; hence, all p-values displayed are FDR-adjusted (often referred to as *q*-values). A gene was found to be significantly regulated if $q<0.01$ and the $\log_2$-ratio was similar to or above 0.5, or similar to or below −0.5. Genes represented with less than 1 spot on one or more arrays were excluded from the final results (NA).

Comparative genomic hybridization

Genomic DNA was isolated by using the FP120 FastPrep bead-beater (BIO101/Savent) and the QiaPrep MiniPrep kit (Qiagen), as previously described [106], and then labeled and purified with the BioPrime Array CGH Genomic labeling System (Invitrogen) and Cyanine Smart Pack dUTP (PerkinElmer Life Sciences), according to the manufacturer's protocol. Standard methods in the LIMMA package [107] in R (http://www.r-project.org/), available from the Bioconductor (http://www.bioconductor.org) were employed for preprocessing and normalization. Within-array normalization was first conducted by subtracting the median from the log-ratios for each array. A standard loess-normalization was then performed, where smoothing was based only on spots with abs(log-ratio) <2.0 to avoid biases due to extreme skewness in the log-ratio distribution. For the determination of present and divergent genes a method that predicts sequence identity based on array signals was used, as described by Snipen *et al.* [110]. A threshold of 0.75 was used in order to obtain a categorical response of presence or divergence, *i.e.* genes with *Sb*-value >0.75 were classified as present, while genes with *Sb*-value <0.75 were classified as divergent. Genes with *Sb*-value = 0.75 remained unclassified.

Microarray data accession number

The microarray data have been deposited in the ArrayExpress database with the series accession number E-TABM-885.

OG1RF gene prediction

Gene prediction from OG1RF (Genbank ABPI00000000) was conducted with EasyGene 1.2 [32] using model "EF02", with R cut off value set at 2.

BLASTN comparison of *E. faecalis* V583 genes versus the OG1RF genome

BLASTN comparison was conducted for *E. faecalis* V583 (Genbank AE016830) against the OG1RF genome (Genbank ABPI00000000) as follows: the annotated V583 genes were blasted (BLASTN) against the entire OG1RF genome, and presence and divergence was predicted based on a score calculated as the number of identical nucleotides divided by the length of the query gene. Genes obtaining a score >0.75 were classified as present.

Real-time quantitative RT-PCR

Real time quantitative RT-PCR (QPCR) was used to validate the expression levels for selected genes. QPCR was performed on

Table 2. QPCR primers used in this study.

Target gene/primer name	Primer sequences (5′ → 3′)	Amplicon size (bp)	Reference
EF1821	F: TGA ACC TGT TCA GCC ATC TG	142	This study
	R: CAT CAG ACC TTG GAT GAC GA		
23S	F: CCT ATC GGC CTC GGC TTA G		[17]
	R: AGC GAA AGA CAG GTG AGA ATC C		

doi:10.1371/journal.pone.0012489.t002

a Rotor-Gene 6000 centrifugal amplification system (Corbett Research). cDNA was synthesized with 1 µg total RNA as template. In addition to the on-column DNase-treatment mentioned above, an off-column DNase treatment was conducted as follows: To each of the RNA preparations, 80 U RNasin, 20 U DNase 1 and 70 µl RDD buffer was added. The reaction was incubated at 37°C for 30 min., and DNase-treated RNA was extracted by performing a phenol:chloroform extraction as follows: 1:1:1 (v/v/v) phenol/chloroform/DEPC water was added, before the samples were centrifuged at 10000×g for 1 min. The aqueous layer was transferred to a tube containing 960 µl 96% ethanol and 40 µl 3M NaAc and incubated ON at – 20°C, before the RNA was precipitated by centrifugation at 10000×g for 30 min. at 4°C. RNA was then washed with 70% ethanol, dried by vacuum centrifugation and resuspended in 20 µl RNase-free water. The genes were quantified in triplicate. PCR amplification was performed at an annealing temperature of 60°C with 0.5 µl cDNA in a 25-µl reaction mixture containing 12.5 µl FastStart SYBR green Master (Rox; Roche) and 0.5 µM of each primer. The primers used are shown in Table 2. Upon completing PCR, melting curve analysis was used to determine whether there was detectable primer-dimer contribution to the SYBR green fluorescence measurement of amplified DNA. Differential expression was calculated by the Pfaffl method [111]. 23S was used as a reference.

Supporting Information

Figure S1 Characterization of growth of E. faecalis MMH594 (black circle), OG1RF (red triangle) and Symbioflor 1 (green square) in 2xYT (stippled lines) and urine (solid lines). The growth curves are represented by colony forming units per millilitre (CFU/ml) on the Y-axis, and hours as indicated on the X-axis. The growth curves correspond to the mean ± STD of two parallels.
Found at: doi:10.1371/journal.pone.0012489.s001 (0.10 MB TIF)

Figure S2 Distribution of differentially expressed genes in response to urine by functional classification. Overview of the number of up- and down-regulated genes in MMH594 (grey), OG1RF (purple) and Symbioflor 1 (green) at A) 5 minutes and B) 30 minutes. The functional categories are listed between the two bar-charts.
Found at: doi:10.1371/journal.pone.0012489.s002 (0.40 MB TIF)

Figure S3 The effect of urine on the expression of EF1821 (fsrB) in MMH594 an OG1RF as quantified by QPCR.
Found at: doi:10.1371/journal.pone.0012489.s003 (5.53 MB TIF)

Table S1 Microarray expression data and comparative genome hybridization of E. faecalis strains MMH594 (M), OG1RF (O) and Symbioflor 1 (S). Differences in gene content were analyzed using comparative genomic hybridization (*): present (1), divergent (0), unclassified (U). Gene expression after 5 (t5) or 30 (t30) minutes of growth in urine is relative to 2xYT. Significantly regulated genes are $q<0.01$ (bold), and log2-ratio $>\pm 0.5$). "NA" denotes non-expressed or excluded genes.
Found at: doi:10.1371/journal.pone.0012489.s004 (1.10 MB XLS)

Table S2 Gene prediction from OG1RF (Genbank ABPI00000000) conducted with EasyGene 1.2 [32] using model "EF02", with R cut off value at 2. Predicted genes are presented in nucleotide fasta format.
Found at: doi:10.1371/journal.pone.0012489.s005 (2.99 MB TXT)

Table S3 BLASTN comparison of E. faecalis V583 genes versus the OG1RF genome. The score was calculated as number of identical nucleotides identified by BLAST divided by query ORF length. ORFs obtaining a score >0.75 were classified as orthologous genes present in the OG1RF genome.
Found at: doi:10.1371/journal.pone.0012489.s006 (0.22 MB XLS)

Table S4 Differentially expressed genes with proven or predicted function in various stress responses in *E. faecalis*. Only significant $\log_2$-ratios are listed.
Found at: doi:10.1371/journal.pone.0012489.s007 (0.63 MB DOC)

Table S5 Differentially expressed genes with proven or predicted virulence function in *E. faecalis*. Only significant $\log_2$-ratios are listed.
Found at: doi:10.1371/journal.pone.0012489.s008 (1.20 MB DOC)

Acknowledgments

We thank Linda H. Godager for technical assistance with the real-time quantitative RT-PCR. We also acknowledge the Norwegian Microarray Consortium, Trondheim, for printing the microarray slides.

Author Contributions

Conceived and designed the experiments: HCV MS DAB. Performed the experiments: HCV MS. Analyzed the data: HCV MS LS IFN DAB. Contributed reagents/materials/analysis tools: LS IFN. Wrote the paper: HCV MS LS IFN DAB.

References

1. Richards MJ, Edwards JR, Culver DH, Gaynes RP (2000) Nosocomial infections in combined medical-surgical intensive care units in the United States. Infect Control Hosp Epidemiol 21: 510–515.

2. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, et al. (2004) Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 39: 309–317.

3. Gross PA, Harkavy LM, Barden GE, Flower MF (1976) The epidemiology of nosocomial enterococcal urinary tract infection. Am J Med Sci 272: 75–81.
4. Hancock LE, Gilmore MS (2006) Pathogenicity of enterococci. In: Fischetti VA, Novick RP, Ferretti JJ, Portnoy DA, Rood JI, eds. Gram-positive pathogens. Washington DC: ASM Press. pp 299–311.
5. Shankar N, Lockatell CV, Baghdayan AS, Drachenberg C, Gilmore MS, et al. (2001) Role of *Enterococcus faecalis* surface protein Esp in the pathogenesis of ascending urinary tract infection. Infect Immun 69: 4366–4372.
6. Chow JW, Thal LA, Perri MB, Vazquez JA, Donabedian SM, et al. (1993) Plasmid-associated hemolysin and aggregation substance production contribute to virulence in experimental enterococcal endocarditis. Antimicrob Agents Chemother 37: 2474–2477.
7. Jett BD, Jensen HG, Nordquist RE, Gilmore MS (1992) Contribution of the pAD1-encoded cytolysin to the severity of experimental *Enterococcus faecalis* endophthalmitis. Infect Immun 60: 2445–2452.
8. Schlievert PM, Gahr PJ, Assimacopoulos AP, Dinges MM, Stoehr JA, et al. (1998) Aggregation and binding substances enhance pathogenicity in rabbit models of *Enterococcus faecalis* endocarditis. Infect Immun 66: 218–223.
9. Kreft B, Marre R, Schramm U, Wirth R (1992) Aggregation substance of *Enterococcus faecalis* mediates adhesion to cultured renal tubular cells. Infect Immun 60: 25–30.
10. Olmsted SB, Dunny GM, Erlandsen SL, Wells CL (1994) A plasmid-encoded surface protein on *Enterococcus faecalis* augments its internalization by cultured intestinal epithelial cells. J Infect Dis 170: 1549–1556.
11. Eaton TJ, Gasson MJ (2001) Molecular screening of *Enterococcus* virulence determinants and potential for genetic exchange between food and medical isolates. Appl Environ Microbiol 67: 1628–1635.
12. Lempiainen H, Kinnunen K, Mertanen A, von Wright A (2005) Occurrence of virulence factors among human intestinal enterococcal isolates. Lett Appl Microbiol 41: 341–344.
13. Semedo T, Santos MA, Lopes MF, Figueiredo Marques JJ, Barreto Crespo MT, et al. (2003) Virulence factors in food, clinical and reference Enterococci: A common trait in the genus? Syst Appl Microbiol 26: 13–22.
14. Creti R, Imperi M, Bertuccini L, Fabretti F, Orefici G, et al. (2004) Survey for virulence determinants among *Enterococcus faecalis* isolated from different sources. J Med Microbiol 53: 13–20.
15. Franz CM, Muscholl-Silberhorn AB, Yousif NM, Vancanneyt M, Swings J, et al. (2001) Incidence of virulence factors and antibiotic resistance among Enterococci isolated from food. Appl Environ Microbiol 67: 4385–4389.
16. Mannu L, Paba A, Daga E, Comunian R, Zanetti S, et al. (2003) Comparison of the incidence of virulence determinants and antibiotic resistance between *Enterococcus faecium* strains of dairy, animal and clinical origin. Int J Food Microbiol 88: 291–304.
17. Shepard BD, Gilmore MS (2002) Differential expression of virulence-related genes in *Enterococcus faecalis* in response to biological cues in serum and urine. Infect Immun 70: 4344–4352.
18. Alteri CJ, Mobley HL (2007) Quantitative profile of the uropathogenic *Escherichia coli* outer membrane proteome during growth in human urine. Infect Immun 75: 2679–2688.
19. Russo TA, Carlino UB, Mong A, Jodush ST (1999) Identification of genes in an extraintestinal isolate of *Escherichia coli* with increased expression after exposure to human urine. Infect Immun 67: 5306–5314.
20. Domann E, Hain T, Ghai R, Billion A, Kuenne C, et al. (2007) Comparative genomic analysis for the presence of potential enterococcal virulence factors in the probiotic *Enterococcus faecalis* strain Symbioflor 1. Int J Med Microbiol 297: 533–539.
21. Huycke MM, Spiegel CA, Gilmore MS (1991) Bacteremia caused by hemolytic, high-level gentamicin-resistant *Enterococcus faecalis*. Antimicrob Agents Chemother 35: 1626–1634.
22. Shankar N, Baghdayan AS, Gilmore MS (2002) Modulation of virulence within a pathogenicity island in vancomycin-resistant *Enterococcus faecalis*. Nature 417: 746–750.
23. Bourgogne A, Garsin DA, Qin X, Singh KV, Sillanpaa J, et al. (2008) Large scale variation in *Enterococcus faecalis* illustrated by the genome analysis of strain OG1RF. Genome Biol 9: R110.
24. Murray BE, Singh KV, Ross RP, Heath JD, Dunny GM, et al. (1993) Generation of restriction map of *Enterococcus faecalis* OG1 and investigation of growth requirements and regions encoding biosynthetic function. J Bacteriol 175: 5216–5223.
25. Sifri CD, Mylonakis E, Singh KV, Qin X, Garsin DA, et al. (2002) Virulence effect of *Enterococcus faecalis* protease genes and the quorum-sensing locus *fsr* in *Caenorhabditis elegans* and mice. Infect Immun 70: 5647–5650.
26. Stamey TA, Mihara G (1980) Observations on the growth of urethral and vaginal bacteria in sterile urine. J Urol 124: 461–463.
27. Carlos AR, Santos J, Semedo-Lemsaddek T, Barreto-Crespo MT, Tenreiro R (2009) Enterococci from artisanal dairy products show high levels of adaptability. Int J Food Microbiol 129: 194–199.
28. McBride SM, Fischetti VA, Leblanc DJ, Moellering RC, Jr., Gilmore MS (2007) Genetic diversity among *Enterococcus faecalis*. PLoS One 2: e582.
29. Aakra A, Nyquist OL, Snipen L, Reiersen TS, Nes IF (2007) Survey of genomic diversity among *Enterococcus faecalis* strains by microarray-based comparative genomic hybridization. Appl Environ Microbiol 73: 2207–2217.
30. McBride SM, Coburn PS, Baghdayan AS, Willems RJ, Grande MJ, et al. (2009) Genetic variation and evolution of the pathogenicity island of *Enterococcus faecalis*. J Bacteriol 191: 3392–3402.
31. Paulsen IT, Banerjei L, Myers GS, Nelson KE, Seshadri R, et al. (2003) Role of mobile DNA in the evolution of vancomycin-resistant *Enterococcus faecalis*. Science 299: 2071–2074.
32. Larsen TS, Krogh A (2003) EasyGene - a prokaryotic gene finder that ranks ORFs by statistical significance. BMC Bioinformatics 4: 21.
33. Hallin PF, Binnewies TT, Ussery DW (2008) The genome BLASTatlas-a GeneWiz extension for visualization of whole-genome homology. Mol Biosyst 4: 363–371.
34. Hechard Y, Pelletier C, Cenatiempo Y, Frere J (2001) Analysis of sigma(54)-dependent genes in *Enterococcus faecalis*: a mannose PTS permease (EII^{Man}) is involved in sensitivity to a bacteriocin, mesentericin Y105. Microbiology 147: 1575–1580.
35. Shaykhutdinov R, MacInnis G, Dowlatabadi R, Weljie A, Vogel H (2009) Quantitative analysis of metabolite concentrations in human urine samples using $^{13}C\{^{1}H\}$ NMR spectroscopy. Metabolomics 5: 307–317.
36. Deutscher J, Francke C, Postma PW (2006) How phosphotransferase system-related protein phosphorylation regulates carbohydrate metabolism in bacteria. Microbiol Mol Biol Rev 70: 939–1031.
37. Blancato VS, Repizo GD, Suarez CA, Magni C (2008) Transcriptional regulation of the citrate gene cluster of *Enterococcus faecalis* Involves the GntR family transcriptional activator CitO. J Bacteriol 190: 7419–7430.
38. Wishart D, Knox C, Guo A (2009) HMDB: a knowledgebase for the human metabolome. 37(Database issue): D603-610. Nucleic Acids Res.
39. Tasevska N, Runswick SA, McTaggart A, Bingham SA (2005) Urinary sucrose and fructose as biomarkers for sugar consumption. Cancer Epidemiol Biomarkers Prev 14: 1287–1294.
40. Maadani A, Fox KA, Mylonakis E, Garsin DA (2007) *Enterococcus faecalis* mutations affecting virulence in the *Caenorhabditis elegans* model host. Infect Immun 75: 2634–2637.
41. Garsin DA, Sifri CD, Mylonakis E, Qin X, Singh KV, et al. (2001) A simple model host for identifying Gram-positive virulence factors. Proc Natl Acad Sci U S A 98: 10892–10897.
42. Riboulet-Bisson E, Sanguinetti M, Budin-Verneuil A, Auffray Y, Hartke A, et al. (2008) Characterization of the Ers regulon of *Enterococcus faecalis*. Infect Immun 76: 3064–3074.
43. Riboulet-Bisson E, Hartke A, Auffray Y, Giard JC (2009) Ers controls glycerol metabolism in *Enterococcus faecalis*. Curr Microbiol 58: 201–204.
44. Roos V, Klemm P (2006) Global gene expression profiling of the asymptomatic bacteriuria *Escherichia coli* strain 83972 in the human urinary tract. Infect Immun 74: 3565–3575.
45. Guo K, Li L (2009) Differential ^{12}C-/^{13}C-isotope dansylation labeling and fast liquid chromatography/mass spectrometry for absolute and relative quantification of the metabolome. Anal Chem 81: 3919–3932.
46. Deibel RH (1964) Utilization of arginine as an energy source for the growth of *Streptococcus faecalis*. J Bacteriol 87: 988–992.
47. Roon RJ, Barker HA (1972) Fermentation of agmatine in *Streptococcus faecalis*: occurrence of putrescine transcarbamoylase. J Bacteriol 109: 44–50.
48. Le Breton Y, Muller C, Auffray Y, Rince A (2007) New insights into the *Enterococcus faecalis* CroRS two-component system obtained using a differential-display random arbitrarily primed PCR approach. Appl Environ Microbiol 73: 3738–3741.
49. Lloyd AL, Rasko DA, Mobley HL (2007) Defining genomic islands and uropathogen-specific genes in uropathogenic *Escherichia coli*. J Bacteriol 189: 3532–3546.
50. MacLeod RA (1951) Further mineral requirements of *Streptococcus faecalis*. J Bacteriol 62: 337–345.
51. MacLeod RA, Snell EE (1947) Some mineral requirements of the lactic acid bacteria. J Biol Chem 170: 351–365.
52. Jarvisalo J, Olkinuora M, Kiilunen M, Kivisto H, Ristola P, et al. (1992) Urinary and blood manganese in occupationally nonexposed populations and in manual metal arc welders of mild steel. Int Arch Occup Environ Health 63: 495–501.
53. Low YL, Jakubovics NS, Flatman JC, Jenkinson HF, Smith AW (2003) Manganese-dependent regulation of the endocarditis-associated virulence factor EfaA of *Enterococcus faecalis*. J Med Microbiol 52: 113–119.
54. Singh KV, Coque TM, Weinstock GM, Murray BE (1998) In vivo testing of an *Enterococcus faecalis efaA* mutant and use of *efaA* homologs for species identification. FEMS Immunol Med Microbiol 21: 323–331.
55. Manson J, Gilmore M (2006) 7. Pathogenomics of *Enterococcus faecalis*. In: Hacker J, Dobrindt U, eds. Pathogenomics: genome analysis of pathogenic microbes. Weinheim: WILEY-VCH Verlag GmbH & Co. KGaA. pp 125–148.
56. Rince A, Flahaut S, Auffray Y (2000) Identification of general stress genes in *Enterococcus faecalis*. Int J Food Microbiol 55: 87–91.
57. Giard JC, Rince A, Capiaux H, Auffray Y, Hartke A (2000) Inactivation of the stress- and starvation-inducible *gls24* operon has a pleiotrophic effect on cell morphology, stress sensitivity, and gene expression in *Enterococcus faecalis*. J Bacteriol 182: 4512–4520.
58. Nannini EC, Teng F, Singh KV, Murray BE (2005) Decreased virulence of a *gls24* mutant of *Enterococcus faecalis* OG1RF in an experimental endocarditis model. Infect Immun 73: 7772–7774.

59. Teng F, Nannini EC, Murray BE (2005) Importance of *gls24* in virulence and stress response of *Enterococcus faecalis* and use of the Gls24 protein as a possible immunotherapy target. J Infect Dis 191: 472–480.
60. Rince A, Giard JC, Pichereau V, Flahaut S, Auffray Y (2001) Identification and characterization of *gsp65*, an organic hydroperoxide resistance (*ohr*) gene encoding a general stress protein in *Enterococcus faecalis*. J Bacteriol 183: 1482–1488.
61. Flahaut S, Hartke A, Giard JC, Benachour A, Boutibonnes P, et al. (1996) Relationship between stress response toward bile salts, acid and heat treatment in *Enterococcus faecalis*. FEMS Microbiol Lett 138: 49–54.
62. La Carbona S, Sauvageot N, Giard JC, Benachour A, Posteraro B, et al. (2007) Comparative study of the physiological roles of three peroxidases (NADH peroxidase, Alkyl hydroperoxide reductase and Thiol peroxidase) in oxidative stress response, survival inside macrophages and virulence of *Enterococcus faecalis*. Mol Microbiol 66: 1148–1163.
63. Verneuil N, Maze A, Sanguinetti M, Laplace JM, Benachour A, et al. (2006) Implication of (Mn)superoxide dismutase of *Enterococcus faecalis* in oxidative stress responses and survival inside macrophages. Microbiology 152: 2579–2589.
64. Giard JC, Riboulet E, Verneuil N, Sanguinetti M, Auffray Y, et al. (2006) Characterization of Ers, a PrfA-like regulator of *Enterococcus faecalis*. FEMS Immunol Med Microbiol 46: 410–418.
65. Elgavish A, Lloyd K, Reed R (1996) A subpopulation of human urothelial cells is stimulated to proliferate by treatment *in vitro* with lipoteichoic acid, a cell wall component of *Streptococcus faecalis*. J Cell Physiol 169: 42–51.
66. Elgavish A (2000) NF-kappaB activation mediates the response of a subpopulation of basal uroepithelial cells to a cell wall component of *Enterococcus faecalis*. J Cell Physiol 182: 232–238.
67. Jordan S, Hutchings MI, Mascher T (2008) Cell envelope stress response in Gram-positive bacteria. FEMS Microbiol Rev 32: 107–146.
68. Rowley G, Spector M, Kormanec J, Roberts M (2006) Pushing the envelope: extracytoplasmic stress responses in bacterial pathogens. Nat Rev Microbiol 4: 383–394.
69. Theilacker C, Kaczynski Z, Kropec A, Fabretti F, Sange T, et al. (2006) Opsonic antibodies to *Enterococcus faecalis* strain 12030 are directed against lipoteichoic acid. Infect Immun 74: 5703–5712.
70. Thurlow LR, Thomas VC, Fleming SD, Hancock LE (2009) *Enterococcus faecalis* capsular polysaccharide serotypes C and D and their contributions to host innate immune evasion. Infect Immun 77: 5551–5557.
71. Teng F, Jacques-Palaz KD, Weinstock GM, Murray BE (2002) Evidence that the enterococcal polysaccharide antigen gene (*epa*) cluster is widespread in *Enterococcus faecalis* and influences resistance to phagocytic killing of *E. faecalis*. Infect Immun 70: 2010–2015.
72. Vebø HC, Snipen L, Nes IF, Brede DA (2009) The transcriptome of the nosocomial pathogen *Enterococcus faecalis* V583 reveals adaptive responses to growth in blood. PLoS One 4: e7660.
73. Solheim M, Aakra A, Vebo H, Snipen L, Nes IF (2007) Transcriptional responses of *Enterococcus faecalis* V583 to bovine bile and sodium dodecyl sulfate. Appl Environ Microbiol 73: 5767–5774.
74. Brinster S, Lamberet G, Staels B, Trieu-Cuot P, Gruss A, et al. (2009) Type II fatty acid synthesis is not a suitable antibiotic target for Gram-positive pathogens. Nature 458: 83–86.
75. Walecka E, Bania J, Dworniczek E, Ugorski M (2009) Genotypic characterization of hospital *Enterococcus faecalis* strains using multiple-locus variable-number tandem-repeat analysis. Lett Appl Microbiol 49: 79–84.
76. Mohamed JA, Huang DB (2007) Biofilm formation by enterococci. J Med Microbiol 56: 1581–1588.
77. Hufnagel M, Koch S, Creti R, Baldassarri L, Huebner J (2004) A putative sugar-binding transcriptional regulator in a novel gene locus in *Enterococcus faecalis* contributes to production of biofilm and prolonged bacteremia in mice. J Infect Dis 189: 420–430.
78. Le Breton Y, Pichereau V, Sauvageot N, Auffray Y, Rince A (2005) Maltose utilization in *Enterococcus faecalis*. J Appl Microbiol 98: 806–813.
79. Guiton PS, Hung CS, Kline KA, Roth R, Kau AL, et al. (2009) Contribution of autolysin and Sortase a during *Enterococcus faecalis* DNA-dependent biofilm development. Infect Immun 77: 3626–3638.
80. Kristich CJ, Nguyen VT, Le T, Barnes AM, Grindle S, et al. (2008) Development and use of an efficient system for random mariner transposon mutagenesis to identify novel genetic determinants of biofilm formation in the core *Enterococcus faecalis* genome. Appl Environ Microbiol 74: 3377–3386.
81. Kemp KD, Singh KV, Nallapareddy SR, Murray BE (2007) Relative contributions of *Enterococcus faecalis* OG1RF sortase-encoding genes, *srtA* and *bps* (*srtC*), to biofilm formation and a murine model of urinary tract infection. Infect Immun 75: 5399–5404.
82. Creti R, Fabretti F, Koch S, Huebner J, Garsin DA, et al. (2009) Surface protein EF3314 contributes to virulence properties of *Enterococcus faecalis*. Int J Artif Organs 32: 611–620.
83. Mohamed JA, Teng F, Nallapareddy SR, Murray BE (2006) Pleiotrophic effects of 2 *Enterococcus faecalis sagA*-like genes, *salA* and *salB*, which encode proteins that are antigenic during human infection, on biofilm formation and binding to collagen type i and fibronectin. J Infect Dis 193: 231–240.
84. Mesnage S, Chau F, Dubost L, Arthur M (2008) Role of N-acetylglucosaminidase and N-acetylmuramidase activities in *Enterococcus faecalis* peptidoglycan metabolism. J Biol Chem 283: 19845–19853.
85. Thomas VC, Hiromasa Y, Harms N, Thurlow L, Tomich J, et al. (2009) A fratricidal mechanism is responsible for eDNA release and contributes to biofilm development of Enterococcus faecalis. Mol Microbiol 72: 1022–1036.
86. Sillanpaa J, Xu Y, Nallapareddy SR, Murray BE, Hook M (2004) A family of putative MSCRAMMs from *Enterococcus faecalis*. Microbiology 150: 2069–2078.
87. Singh KV, Nallapareddy SR, Murray BE (2007) Importance of the *ebp* (endocarditis- and biofilm-associated pilus) locus in the pathogenesis of *Enterococcus faecalis* ascending urinary tract infection. J Infect Dis 195: 1671–1677.
88. Nallapareddy SR, Singh KV, Sillanpaa J, Garsin DA, Hook M, et al. (2006) Endocarditis and biofilm-associated pili of *Enterococcus faecalis*. J Clin Invest 116: 2799–2807.
89. Jude BA, Martinez RM, Skorupski K, Taylor RK (2009) Levels of the secreted *Vibrio cholerae* attachment factor GbpA are modulated by quorum-sensing-induced proteolysis. J Bacteriol 191: 6911–6917.
90. Bjork S, Breimer ME, Hansson GC, Karlsson KA, Leffler H (1987) Structures of blood group glycosphingolipids of human small intestine. A relation between the expression of fucolipids of epithelial cells and the ABO, Le and Se phenotype of the donor. J Biol Chem 262: 6758–6765.
91. Finne J, Breimer ME, Hansson GC, Karlsson KA, Leffler H, et al. (1989) Novel polyfucosylated *N*-linked glycopeptides with blood group A, H, X, and Y determinants from human small intestinal epithelial cells. J Biol Chem 264: 5720–5735.
92. Kirn TJ, Jude BA, Taylor RK (2005) A colonization factor links *Vibrio cholerae* environmental survival and human infection. Nature 438: 863–866.
93. Xu Y, Murray BE, Weinstock GM (1998) A cluster of genes involved in polysaccharide biosynthesis from *Enterococcus faecalis* OG1RF. Infect Immun 66: 4313–4323.
94. Teng F, Singh KV, Bourgogne A, Zeng J, Murray BE (2009) Further characterization of the *epa* gene cluster and Epa polysaccharides of *Enterococcus faecalis*. Infect Immun 77: 3759–3767.
95. Xu Y, Singh KV, Qin X, Murray BE, Weinstock GM (2000) Analysis of a gene cluster of *Enterococcus faecalis* involved in polysaccharide biosynthesis. Infect Immun 68: 815–823.
96. Mohamed JA, Huang W, Nallapareddy SR, Teng F, Murray BE (2004) Influence of origin of isolates, especially endocarditis isolates, and various genes on biofilm formation by *Enterococcus faecalis*. Infect Immun 72: 3658–3663.
97. Singh KV, Lewis RJ, Murray BE (2009) Importance of the *epa* Locus of *Enterococcus faecalis* OG1RF in a Mouse Model of Ascending Urinary Tract Infection. J Infect Dis 200: 417–420.
98. Kau AL, Martin SM, Lyon W, Hayes E, Caparon MG, et al. (2005) *Enterococcus faecalis* tropism for the kidneys in the urinary tract of C57BL/6J mice. Infect Immun 73: 2461–2468.
99. Hancock LE, Gilmore MS (2002) The capsular polysaccharide of *Enterococcus faecalis* and its relationship to other polysaccharides in the cell wall. Proc Natl Acad Sci U S A 99: 1574–1579.
100. Ike Y, Hashimoto H, Clewell DB (1984) Hemolysin of *Streptococcus faecalis* subspecies zymogenes contributes to virulence in mice. Infect Immun 45: 528–530.
101. Qin X, Singh KV, Weinstock GM, Murray BE (2000) Effects of *Enterococcus faecalis fsr* genes on production of gelatinase and a serine protease and virulence. Infect Immun 68: 2579–2586.
102. Carlos AR, Semedo-Lemsaddek T, Barreto-Crespo MT, Tenreiro R (2009) Transcriptional analysis of virulence-related genes in enterococci from distinct origins. J Appl Microbiol.
103. Bourgogne A, Hilsenbeck SG, Dunny GM, Murray BE (2006) Comparison of OG1RF and an isogenic *fsrB* deletion mutant by transcriptional analysis: the Fsr system of *Enterococcus faecalis* is more than the activator of gelatinase and serine protease. J Bacteriol 188: 2875–2884.
104. Nallapareddy SR, Wenxiang H, Weinstock GM, Murray BE (2005) Molecular characterization of a widespread, pathogenic, and antibiotic resistance-receptive *Enterococcus faecalis* lineage and dissemination of its putative pathogenicity island. J Bacteriol 187: 5709–5718.
105. Coburn PS, Baghdayan AS, Dolan GT, Shankar N (2008) An AraC-type transcriptional regulator encoded on the *Enterococcus faecalis* pathogenicity island contributes to pathogenesis and intracellular macrophage survival. Infect Immun 76: 5668–5676.
106. Solheim M, Aakra A, Snipen LG, Brede DA, Nes IF (2009) Comparative genomics of *Enterococcus faecalis* from healthy Norwegian infants. BMC Genomics 10: 194.
107. Smyth GK, Speed T (2003) Normalization of cDNA microarray data. Methods 31: 265–273.
108. Smyth GK (2004) Linear models and empirical bayes methods for assessing differential expression in microarray experiments. Stat Appl Genet Mol Biol 3: Article3.
109. Smyth GK, Michaud J, Scott HS (2005) Use of within-array replicate spots for assessing differential expression in microarray experiments. Bioinformatics 21: 2067–2075.
110. Snipen L, Nyquist OL, Solheim M, Aakra A, Nes IF (2009) Improved analysis of bacterial CGH data beyond the log-ratio paradigm. BMC Bioinformatics 10: 91.
111. Pfaffl MW (2001) A new mathematical model for relative quantification in real-time RT-PCR. Nucl Acids Res 29: e45.

112. Giard JC, Laplace JM, Rince A, Pichereau V, Benachour A, et al. (2001) The stress proteome of *Enterococcus faecalis*. Electrophoresis 22: 2947–2954.
113. Laport MS, Lemos JA, Bastos Md Mdo C, Burne RA, Giambiagi-De Marval M (2004) Transcriptional analysis of the *groE* and *dnaK* heat-shock operons of *Enterococcus faecalis*. Res Microbiol 155: 252–258.
114. Giard JC, Hartke A, Flahaut S, Boutibonnes P, Auffray Y (1997) Glucose starvation response in *Enterococcus faecalis* JH2-2: survival and protein analysis. Res Microbiol 148: 27–35.
115. Riboulet E, Verneuil N, La Carbona S, Sauvageot N, Auffray Y, et al. (2007) Relationships between oxidative stress response and virulence in *Enterococcus faecalis*. J Mol Microbiol Biotechnol 13: 140–146.
116. Verneuil N, Rince A, Sanguinetti M, Posteraro B, Fadda G, et al. (2005) Contribution of a PerR-like regulator to the oxidative-stress response and virulence of *Enterococcus faecalis*. Microbiology 151: 3997–4004.
117. Verneuil N, Rince A, Sanguinetti M, Auffray Y, Hartke A, et al. (2005) Implication of *hypR* in the virulence and oxidative stress response of *Enterococcus faecalis*. FEMS Microbiol Lett 252: 137–141.
118. Verneuil N, Sanguinetti M, Le Breton Y, Posteraro B, Fadda G, et al. (2004) Effects of the *Enterococcus faecalis hypR* gene encoding a new transcriptional regulator on oxidative stress response and intracellular survival within macrophages. Infect Immun 72: 4424–4431.
119. Laplace JM, Hartke A, Giard JC, Auffray Y (2000) Cloning, characterization and expression of an *Enterococcus faecalis* gene responsive to heavy metals. Appl Microbiol Biotechnol 53: 685–689.
120. Giard JC, Verneuil N, Auffray Y, Hartke A (2002) Characterization of genes homologous to the general stress-inducible gene *gls24* in *Enterococcus faecalis* and *Lactococcus lactis*. FEMS Microbiol Lett 206: 235–239.
121. Teng F, Wang L, Singh KV, Murray BE, Weinstock GM (2002) Involvement of PhoP-PhoS homologs in *Enterococcus faecalis* virulence. Infect Immunw 70: 1991–1996.
122. Theilacker C, Sanchez-Carballo P, Toma I, Fabretti F, Sava I, et al. (2009) Glycolipids are involved in biofilm accumulation and prolonged bacteraemia in *Enterococcus faecalis*. Mol Microbiol 71: 1055–1069.
123. Sahm DF, Kissinger J, Gilmore MS, Murray PR, Mulder R, et al. (1989) In vitro susceptibility studies of vancomycin-resistant *Enterococcus faecalis*. Antimicrob Agents Chemother 33: 1588–1591.

PAPER IV

Comparative genomic analysis reveals significant enrichment of genes encoding virulence-related surface proteins in hospital-associated clonal complex 6 *Enterococcus faecalis*.

Running title: CC6-enriched genes in *Enterococcus faecalis*

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Abstract

Background. Enterococci rank among the leading causes of nosocomial infections. The failure to identify pathogen-specific genes in *Enterococcus faecalis* has led to a hypothesis where the virulence of different strains may be linked to strain-specific genes, and where the combined endeavor of the different gene-sets result in the ability to cause infection. Population structure studies by multilocus sequence typing have defined distinct clonal complexes (CC) of *E. faecalis* enriched in hospitalized patients (CC6, CC9, CC28 and CC40).

Results. In the present study, we have used a comparative genomic approach to investigate gene content in 63 *E. faecalis* strains, with a special focus on CC6. Statistical analysis using Fisher's exact test revealed 252 significantly enriched genes among CC6 strains. The majority of these genes were located within the previously defined mobile elements *phage03* (n=51)*, efaB5* (n=34) and a *vanB* associated genomic island (n=55). Moreover, a CC6-enriched genomic islet (EF3217 to -27), encoding a putative phage related element within the V583 genome, was identified. From the draft genomes of CC6 strains HH22 and TX0104, we also identified a CC6-enriched non-V583 locus associated with the *E. faecalis* pathogenicity island (PAI). Interestingly, surface related structures (including MSCRAMMs, internalin-like and WxL protein-coding genes) implicated in virulence were significantly overrepresented (9.1 %; $p = 0.036$, Fisher's exact test) among the CC6 enriched genes.

Conclusion. In conclusion, we have identified a set of genes with potential roles in adaptation or persistence in the hospital environment, and that might contribute to the ability of CC6 *E. faecalis* isolates to cause disease.

Background

For many years, *Enterococcus faecalis* was considered as an intestinal commensal, which only sporadically caused opportunistic infections in immunocompromised patients. During the last thirty years, however, *E. faecalis* has gained notoriety as one of the primary causative agents of nosocomial infections [1, 2], including urinary tract infections, endocarditis, intra-abdominal infections and bacteremia. The ability of *E. faecalis* to cause infection has been connected to inherent enterococcal traits, enabling the bacterium to tolerate diverse and harsh growth conditions. Moreover, several putative enterococcal virulence factors have been characterized (reviewed in [3]), and the role of these virulence factors in pathogenicity have been further established in various animal infection models [4-8] and cultured cell lines [9, 10]. On the other hand, a number of studies on enterococcal pathogenicity have shown that several of the putative virulence traits are present not only in infectious isolates but also in animal and environmental isolates [11-16]. This widespread distribution of putative virulence determinants in enterococcal isolates strongly suggest that enterococcal pathogenicity is not a result of any single virulence factor, but rather a more intricate process. Indeed, the virulence potential of the newly sequenced laboratory strain *E. faecalis* OG1RF was, despite its lack of several factors, comparable to that of the clinical isolate *E. faecalis* V583 [17]. Bourgogne et al. [17] proposed a scenario where the virulence of V583 and OG1RF may be linked to genes that are unique to each of the two strains, but where the combined endeavor of the different gene-sets result in the ability to cause infection.

Population structure studies of *E. faecalis* by multilocus sequence typing (MLST) have previously defined distinct clonal complexes (CC) of *E. faecalis* enriched in hospitalized patients (CC6, CC9, CC28 and CC40), designated high-risk enterococcal clonal complexes (HiRECCs) [18, 19]. In one of our previous studies, we reported an overall correlation

between MLST and Bayesian phylogenetic analysis of gene content as revealed by microarray-based comparative genomic hybridization (CGH) [20]. This observation led us to speculate whether the virulence of different HiRECCs may be due to lineage-specific gene sets. In the present study we have used the comparative genomics approach to further investigate variation in gene content within *E. faecalis*, with a special focus on CC6 (formerly known as CC2). This complex was chosen on the basis of previous Bayesian-based phylogenetic reconstruction [20]. CC6 is equivalent to the previously designated BVE complex, and comprises several clinically important *E. faecalis* isolates, including the first known beta-lactamase producing isolate HH22, the first U.S. vancomycin-resistant isolate V583, and pathogenicity island (PAI)-harboring clinical bacteremia isolate MMH594 [19, 21, 22]. This CC represents a globally dispersed hospital-associated lineage, and identification of CC6-enriched genes may unravel novel fitness factors implicated in survival and spread of *E. faecalis* clones in the hospital environment.

Results and discussion

Overall genomic diversity. To explore the genetic diversity among *E. faecalis*, BLAST comparison was performed with 24 publicly available sequenced draft genomes, including the two CC6 strains TX0104 (ST2), which is an endocarditis isolate, and HH22 (ST6; mentioned above) against the genome of strain V583, which is also a ST6 isolate. The number of V583 genes predicted to be present varied between 2385 (OG1RF) and 2831 (HH22) for the 24 strains (Table S1). In addition, we used CGH to investigate variation in gene content within 15 *E. faecalis* isolated in European hospital environments, with a special focus on a hospital-adapted subpopulation identified by MLST (CC6). Of the 3219 V583 genes represented on the array, the number of genes classified as present ranged from 2359 (597/96) to 2883

(E4250). Analysis of the compiled data set (*in silico* and CGH), revealed a total of 1667 genes which were classified as present in all strains, thus representing the *E. faecalis* core genome. None of the annotated V583 genes were found to be divergent in all the isolates analyzed.

Putative clonal complex 6-enriched elements. In a previous study [20], we identified a set of potential pathogen-specific genes, which were entirely divergent in a collection of commensal baby isolates. None of these genes were found to be present in all hospital-related isolates analyzed in the present study, neither was any gene found to be unique to any HiRECC. In order to identify genes specifically enriched among strains belonging to CC6, data from the present study were supplemented with hybridization data from an additional 24 strains of various origins ([20, 23] and M. Solheim, unpublished data). The additional data sets were obtained by hybridization to the same array as described above. All together, data from a total of 63 strains were analyzed, in addition to V583, and these strains are listed in Table 1. A genome-atlas presentation of the gene content in all the strains analyzed by CGH compared to the V583 genome is shown in Figure 1.

By Fisher's exact testing ($q < 0.01$), 252 genes were found to be more prevalent among CC6 strains than in non-CC6 strains (Table 2). The CC6-enriched genes included large parts of *phage03* (*p03*; n = 51), *efaB5* (n = 34) and a phage-related region identified by McBride et al. [24](EF2240-82/EF2335-51; n = 55), supporting the notion that the *p03* genetic element may confer increased fitness in the hospital environment [20]. Indeed, prophage-related genes constituted a predominant proportion of the CC6-enriched genes (55.5 %; $p < 2.2e-16$, Fisher's exact test). Interestingly, the Tn*916*-like *efaB5* element has previously also been suggested to play a role in niche adaptation (Leavis, Willems et al. unpublished data): CGH analysis identified an *efaB5*-orthologous element in *E. faecium* that appeared to be common

for HiREEC *E. faecalis* and CC17 *E. faecium*, a hospital-adapted subpopulation identified by MLST. To further confirm the presence of the relevant MGEs in *E. faecalis*, we used PCR combining internal primers with primers targeting the genes flanking *p03*, *efaB5* and the *vanB*-associated phage-related element in V583, to monitor conserved V583 junctions on either side of the elements in 44 strains (Table 1). Seven strains contained the junctions on both sides of *p03*, of which six strains were CC6-strains. Eleven strains were positive for the junctions on both sides of *efaB5*, including nine CC6-strains, while thirteen strains gave positive PCR for both junctions of the phage-related element surrounding *vanB*, of which eleven strains belonged to CC6. These results substantiate the theory of *p03*, *efaB5* and the *vanB*-associated phage as CC6-enriched elements.

A total of 178 of the 252 putative CC6-enriched genes identified here, were associated with previously defined MGEs identified in V583 [25]. In addition to *p03*, *efaB5* and the *vanB*-surrounding phage element, these included *p01* (n = 5), PAI (n = 7), *p04* (n = 21), *p06* (n = 1) and pTEF1 and pTEF2 (n = 5) (Table 2). In addition, a ten-gene cluster (EF3217-27) with significant GC skew compared to the genome-average (31.6 and 37.4 %, respectively), was found to be significantly more frequent in strains belonging to CC6 than in non-CC6 strains. The deviation in GC content suggests that this genetic element may also be of foreign origin. This notion was further supported by the sequence similarities of several of the genes with known phage-related transcriptional regulators (EF3221, EF3223 and EF3227). Moreover, EF3221 to -22 showed high degree of identity (> 85 %) to EfmE980_2492 to -93 of the newly sequenced *Enterococcus faecium* E980 [26]. EfmE980_2492 holds a domain characteristic of the aspartate aminotransferase superfamily of pyridoxal phosphate-dependent enzymes. Interestingly, EF3217 encodes a putative helicase, while EF3218 encodes a putative MutT protein, both with implications in DNA repair [27, 28]. A potential role of these genes in

protection against oxidative DNA damage induced in the hospital environment and during infection is plausible. To further investigate the presence of EF3217-27 in *E. faecalis*, 44 strains were screened by PCR (Table S2): 10 CC6-strains held all ten genes, while 19 strains including two CC6-strains were devoid of the entire element. Moreover, 2 strains contained EF3225 only, 3 strains contained EF3217-18, while 8 strains, including OG1RF, contained EF3226 only. The two latter patterns of presence and divergence of EF3217-27 were also obtained with BLASTN analysis of TX0104 and OG1RF, respectively, corroborating that these are indeed genuine polymorphisms in this locus. Notably, in the OG1RF genome five more genes (OG1RF_0214 to -18) are also located between the homologs of EF3216 and EF3230 [17], suggesting this locus may represent a hot spot for insertions. Partial sequencing across the junction between EF3216 and EF3230 suggested that several of the non-CC6 strains carry genes homologous to OG1RF_0214-18 in this locus (results not shown).

A constraint of the comparative genomic analyses presented here, is that the comparison of gene content is based on a single reference strain only (V583). To compensate, we conducted a CC6 pangenome analysis with the draft genomes of CC6-strains HH22 and TX0104 to identify putative CC6-enriched non-V583 genes. The pangenome analysis identified a total of 298 non-V583 ORFs in the HH22 and TX0104 (Table S3). Among these ORFs, one gene cluster was identified as particularly interesting (Fisher's exact; Table S3). This cluster of hypothetical ORFs were detected only in HH22 and TX0104, and consisted of eight genes according to the annotation of HH22 (HMPREF0346_1861-68), and six genes according the TX0104 annotation (HMPREF0348_0424-30; Figure 2). In the TX0104 draft genome HMPREF0348_0424-27 and HMPREF0348_0428-30 are located on two different contigs; contig 00034 and contig 00035, respectively. HMPREF0348_0427 and HMPREF0348_0428 are hence currently not completely sequenced; however, BLAST searches suggest that these

reading frames represent the two respective ends of a gene homologous to HMPREF0346_1863 in HH22. Sequencing across the gap confirmed this (Figure S1). Notably, HMPREF0348_0426 in TX0104 represented the best BLAST hit for all the three ORFs HMPREF0364_1864-66 in HH22, suggesting discrepancy in annotation between the two strains. The presence of the putative non-V583 CC6-enriched gene cluster among *E. faecalis* was further elucidated by PCR in our collection of strains (Table S2). Strains were screened for the presence of three individual genes (HMPREF0346_1861, HMPREF0346_1864 and HMPREF0346_1868) and the entire element, with primers hmpref0346_1868-F and hmpref0346_1861-R. Fisher's exact testing ($q < 0.01$) on the basis of the PCR data confirmed that the gene cluster was significantly enriched among CC6. Comparative sequence analysis of the flanking regions suggests that the gene cluster is located in the HH22 and TX0104 versions of the *E. faecalis* pathogenicity island [29]. Recently, a microarray-based assessment of PAI-content in a set of clinical *E. faecalis* isolates revealed high degree of variation within the island, and an evidently modular evolution of the PAI [30], which would be consistent with acquisition by an indel event of this locus in the PAI of TX0104, HH22 and other positive CC6 strains.

CC-6 enriched surface-related structures. Lepage et al. [31] have previously identified eight genes as potential markers for the V583/MMH594-lineage, of which all except one gene (EF2513) are found among the CC6-enriched genes in this study. Interestingly, several of these genes were later assigned to a recently classified family of surface proteins, with a C-terminal WxL domain, proposed to form multi-component complexes on the cell surface [32, 33]. Siezen et al. [33] termed these genes cell-surface complex (*csc*) genes and postulated a role in carbon source acquisition. Independently, Brinster et al. [32] showed that WxL domains are involved in peptidoglycan-binding. A total of nine WxL protein-coding genes,

divided into three clusters (EF2248 to -54, EF3153 to -55 and EF3248 to -53), were identified as putative CC6-enriched genes in the present study. Note that EF3153 to - 55 does not represent a complete *csc* gene cluster, as not all four *csc* gene families (*cscA – cscD*) are present in the cluster [33]. Interestingly, the OG1RF genome sequence revealed homologues loci encoding WxL-proteins corresponding to the gene clusters EF3153 to -55 and EF3248 to -53 in V583 (50-75 % sequence identity) [17]. Such homologs may possibly explain the divergence observed between CC6 and non-CC6 strains in the present study. Indeed, BLAST analysis with the OG1RF sequences against the *E. faecalis* draft genomes suggested that the OG1RF_0209-10 and OG1RF_0224-25 are widely distributed among non-CC6 *E. faecalis*. Given the putative function in carbon metabolism, the observed sequence variation may be related to substrate specificity.

In addition to the WxL domain, EF2250 also encodes a domain characteristic for the internalin family [32]. Internalins are characterized by the presence of N-terminal leucine-rich repeats (LRRs). The best characterized bacterial LRR proteins are InlA and InlB from *Listeria monocytogenes*, known to trigger internalization by normally non-phagocytic cells [34]. Two internalin-like proteins were identified in *E. faecalis* V583 (EF2250 and *elrA* (EF2686)) [34, 35]. Recently, Brinster et al. [35] presented evidence of that ElrA play a role in *E. faecalis* virulence, both in early intracellular survival in macrophages and by stimulating the host inflammatory response through IL-6 induction. Moreover, by quantitative real-time PCR Shepard and Gilmore [36] found that *elrA* was induced in *E. faecalis* MMH594 during exponential growth in serum and during both exponential and stationary growth in urine. Contradictory data have, however, been published for this and other strains using different methods [35, 37]. Although it is tempting to speculate that EF2250 contributes to the interaction with the mammalian host, the role of internalins in *E. faecalis* pathogenesis is still

not understood, and it may therefore be premature to extrapolate function solely on the basis of shared structural domains.

Glycosyl transferase family proteins are involved in the formation of a number of cell surface structures such as glycolipids, glycoproteins and polysaccharides [38]. *E. faecalis* is in possession of several capsular polysaccharides [39-41], with Cps and Epa being the best characterized. The *epa* (enterococcal polysaccharide antigen) cluster represents a rhamnose-containing polysaccharide which was originally identified in *E. faecalis* OG1RF [39]. The version of the *epa* cluster found in the V583 genome contains an insertion of four genes (EF2185 to -88) compared to OG1RF. This insertion appeared to be enriched among CC6. While EF 2185 and EF2187 encodes transposases of the IS256 family, the two remaining genes showed 100 % identity to the two respective ends of a racemase domain protein in *E. faecalis* TX0104. Neighboring the *epa* cluster, two glycosyl transferases (EF2170 and EF2167) proposed as potential virulence factors [25], are part of a three operon locus (EF2172-66), possibly associated with lipopolysachharide production. Five of the genes within this locus were also found to be enriched among CC6 in the present study.

Paulsen et al. [25] also listed other putative surface-exposed virulence genes, including a choline-binding protein (CBP; EF2662) and a putative MSCRAMM (microbial surface components recognizing adhesive matrix molecules; EF2347) that based on our analysis were found to be enriched in CC6. A role of CBPs in pneumococcal colonization and virulence has been established [42, 43]. A number of putative MSCRAMMs have been identified in *E. faecalis* [44], however, only Ace (adhesion of collagen from *E. faecalis*) has been characterized in detail: Ace was shown to mediate binding to collagen (type I and IV), dentin and laminin [45-47]. Lebreton et al. [48] recently presented evidence of an *in vivo* function of

Ace in enterococcal infections other than involvement in the interaction with extracellular matrix. It was demonstrated that an *ace* deletion mutant was significantly impaired in virulence, both in an insect model and in an *in vivo*-*in vitro* murine macrophage models. The authors suggested that Ace may promote *E. faecalis* phagocytosis and that it may also be possible that Ace is involved in survival of enterococci inside phagocytic cells. Also the structurally related MSCRAMM, Acm, found in *E. faecium* was recently reported to contribute to the pathogenesis of this bacterium [49].

Mucins are high molecular weight glycoproteins expressed by a wide variety of epithelial cells, including those of the gastrointestinal tract, and located at the interface between the cell and the surrounding environment [50]. The binding of bacteria to mucins through mucin-binding domain proteins is thought to promote colonization [51]. Diversity in the carbohydrate side chains creates a significant heterogeneity among mucins of different origin (*e.g.* different organisms or body sites), facilitating bacterial attachment to epithelial cells [51]. The non-V583 CC6-enriched gene cluster identified through *in silico* analysis in the present study harboured an ORF (HMPREF0346_1863 and HMPREF0348_0428 in HH22 and TX0104, respectively) with homology to known mucin-binding domain proteins.

In conclusion, we have identified a set of genes that appear to be enriched among strains belonging to CC6. Since a significant proportion (9.1 %; $p = 0.036$, Fisher's exact test) of these genes code for proteins associated with cell surface structures, absence of or divergence in these loci may lead to antigenic variation. Indeed, both MSCRAMMs and internalins have been identified as potential antigens of *E. faecalis* or other Gram-positive bacteria [52-54]. It is noteworthy that the genes encoding any of the established enterococcal virulence factors were not among the CC6-enriched genes. Surface structures that promote adhesion of

pathogenic bacteria to human tissue are also promising targets for creation of effective vaccines. However, functional studies of the individual CC6-enriched genes are required in order to distinguish their implications in enterococcal virulence.

Materials and methods

Bacterial strain and growth conditions. Bacterial strains used in this study are listed in Table 1. *E. faecalis* strains were grown overnight (ON) in brain heart infusion broth (BHI; Oxoid) at 37 º without shaking. All the strains have previously been sequence typed by the MLST scheme proposed by Ruiz-Garbajosa et al. [19].

Comparative genomic hybridization.

Microarrays. The microarray used in this work has been described previously [20]. The microarray design has been deposited in the ArrayExpress database with the accession number A-MEXP-1069 and A-MEXP-1765.

DNA isolation. Genomic DNA was isolated by using the FP120 FastPrep bead-beater (BIO101/Savent) and the QiaPrep MiniPrep kit (Qiagen) as previously described [20].

Fluorescent labeling and hybridization. Fifteen hospital-associated *E. faecalis* strains were selected for CGH based on their representation of MLST sequence types (STs) belonging to major CCs and potential HiRECCs, with a special focus on CC6, and their variety of geographical origins within Europe. Genomic DNA was labeled and purified with the BioPrime Array CGH Genomic labeling System (Invitrogen) and Cyanine Smart Pack dUTP (PerkinElmer Life Sciences), according to the manufacturer's protocol. Purified samples were

then dried, prior to resuspension in 140 µl hybridization solution (5× SSC, 0.1 % (w/v) SDS, 1.0 % (w/v) bovine serum albumin, 50 % (v/v) formamide and 0.01 % (w/v) single-stranded salmon sperm DNA) and hybridized for 16 h at 42 ºC to the *E. faecalis* oligonucleotide array in a Tecan HS 400 pro hybridization station (Tecan). Arrays were washed twice at 42 ºC with 2 × SSC + 0.2 % SDS, and twice at 23 ºC with 2 × SSC, followed by washes at 23 ºC with 1) 0.2 × SSC and 2) H_2O. Two replicate hybridizations (dye-swap) were performed for each test strain. Hybridized arrays were scanned at wavelengths of 532 nm (Cy3) and 635 nm (Cy5) with a Tecan scanner LS (Tecan). Fluorescent intensities and spot morphologies were analyzed using GenePix Pro 6.0 (Molecular Devices), and spots were excluded based on slide or morphology abnormalities. All water used for the various steps of the hybridization and for preparation of solutions was filtered (0.2 µM) MilliQ dH_20.

Data analysis. Standard methods in the LIMMA package [55] in R (http://www.r-project.org/), available from the Bioconductor (http://www.bioconductor.org) were employed for preprocessing and normalization. Within-array normalization was first conducted by subtracting the median from the log-ratios for each array. A standard loess-normalization was then performed, where smoothing was based only on spots with abs(log-ratio) < 2.0 to avoid biases due to extreme skewness in the log-ratio distribution. For the determination of present and divergent genes a method that predicts sequence identity based on array signals was used, as described by Snipen et al. [56]. A threshold of 0.75 was used in order to obtain a categorical response of presence or divergence, *i. e.* genes with Sb-value > 0.75 were classified as present, while genes with Sb-value < 0.75 were classified as divergent. Genes with Sb-value = 0.75 remained unclassified. All genes were tested for significant enrichment among the CC6-strains by using the Fisher's exact test.

Microarray data accession number. The microarray data have been deposited in the ArrayExpress database with the series accession number E-TABM-905.

Polymerase chain reaction. The presence of selected genes was verified by means of polymerase chain reactions (PCR). A similar approach was also applied to investigate the presence of selected mobile genetic elements (MGEs). Primers targeting the genes flanking the MGEs were combined with internal primers to monitor the presence of the junctions on either side of each MGE. PCR was carried out in 20 µl reaction volumes containing 1× buffer, 250 µM of each deoxynucleotide triphosphate and 1 U DyNAZyme II polymerase (Finnzymes). The reaction conditions included an initial denaturation step at 95 ºC and 35 cycles of 95 ºC for 30 s, 56-60 ºC for 30 s and 72 ºC for 1-5 min, followed by a final extension step at 72 ºC for 7 min. The primers used in this study are listed in Table 3.

Validation of microarray data by sequencing. Sequencing was performed using the ABI Prism Big dye Cycle Sequencing Ready Reaction kit (Applied Biosystems) in an ABI PrismTM 3100 Genetic Analyzer and primers listed in Table 3.

***In silico* comparison of *E. faecalis* draft genomes.** Whole genome blast comparison against the V583 reference genome was conducted for 24 *E. faecalis* strains whose draft genomes were publicly available (GenBank accession numbers in parenthesis; Table 1): *E. faecalis* ARO1/DG (ACAK01000000); *E. faecalis* ATCC 4200 (ACAG01000000); *E. faecalis* ATCC 29200 (ACOX00000000); *E. faecalis* CH188 (ACAV01000000); *E. faecalis* D6 (ACAT01000000); *E. faecalis* DS5 (ACAI01000000); *E. faecalis* E1Sol (ACAQ01000000); *E. faecalis* Fly1 (ACAR01000000): *E. faecalis* HIP11704 (ACAN01000000); *E. faecalis* HH22 (ACIX00000000); *E. faecalis* JH1 (ACAP01000000); *E. faecalis* Merz96

(ACAM01000000); *E. faecalis* OG1RF (ABPI01000001); *E. faecalis* R712 (ADDQ00000000); *E. faecalis* S613 (ADDP00000000); *E. faecalis* T1 (ACAD01000000); *E. faecalis* T2 (ACAE01000000); *E. faecalis* T3 (ACAF01000000); *E. faecalis* T8 (ACOC01000000); *E. faecalis* T11 (ACAU01000000); *E. faecalis* TuSoD ef11(ACOX00000000); *E. faecalis* TX0104 (ACGL00000000); *E. faecalis* TX1322 (ACGM00000000); *E. faecalis* X98 (ACAW01000000) [57, 58], as follows: the annotated V583 genes were blasted (BLASTN) against each genome, and presence and divergence was predicted based on a score calculated as number of identical nucleotides divided by the length of the query gene. Genes obtaining a score > 0.75 were predicted to be present.

CC6 pangenome content analysis. Among the newly released *E. faecalis* draft genomes were two CC6-strains; HH22 and TX0104. In order to extend the list of CC6-enriched genes beyond V583, we conducted a BLAST search using the annotated genes of these two strains as queries against the full genome sequences of the other draft genomes. Again, a cutoff of 75% identity to the query was used to distinguish present from divergent genes.

Authors' contributions

MS conceived and designed the study, carried out the experimental work, analyzed the data, assisted in the bioinformatic analysis and drafted the manuscript. MCB performed the experimental work and assisted in critical review of the manuscript. LS contributed analysis tools, performed the statistical and bioinformatic analyses and assisted in the critical review of the manuscript. RJLW conceived and designed the study, contributed material and assisted in critical review of the manuscript. IFN conceived the study, contributed material and assisted in critical review of the manuscript. DAB participated in the design and coordination of the

study, performed bioinformatic analysis and helped to draft the manuscript. All authors read and approved the final manuscript.

Acknowledgements

This work was financially supported by the European Union 6th Framework Programme "Approaches to Control multi-resistant Enterococci: Studies on molecular ecology, horizontal gene transfer, fitness and prevention" (LSHE-CT-2007-037410). We gratefully acknowledge the following researchers for kindly providing strains to this study: Dr. Lars B. Jensen, Dr. Barbara E. Murray, Dr. Ewa Sadowy, Dr. Arnfinn Sundsfjord and Dr. Atte von Wright. We also acknowledge Dr. David W. Ussery for contributing bioinfomatic tools and constructing the genome-atlas and Hallgeir Bergum at The Norwegian Microarray Consortium for printing of the microarray slides. Finally, we acknowledge the tremendous genome sequencing efforts made by Dr. Michael S. Gilmore and coworkers at the Stephens Eye Research Institute and Harvard Medical School, the Broad Institute, and the Human Microbiome-project represented by Dr. Barbara E. Murray and co-workers at Baylor College of Medicine, Dr. George Weinstock and coworkers at Washington University, and Dr. S. Shrivastava and co-workers at the J. Craig Venter Institute.

References

1. Richards MJ, Edwards JR, Culver DH, Gaynes RP: **Nosocomial infections in combined medical-surgical intensive care units in the United States**. *Infect Control Hosp Epidemiol* 2000, **21**(8):510-515.
2. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB: **Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study**. *Clin Infect Dis* 2004, **39**(3):309-317.
3. Hancock LE, Gilmore MS: **Pathogenicity of enterococci**. In: *Gram-positive pathogens.* Edited by Fischetti VA, Novick RP, Ferretti JJ, Portnoy DA, Rood JI. Washington DC: ASM Press; 2006: p. 299-311.
4. Shankar N, Lockatell CV, Baghdayan AS, Drachenberg C, Gilmore MS, Johnson DE: **Role of *Enterococcus faecalis* surface protein Esp in the pathogenesis of ascending urinary tract infection**. *Infect Immun* 2001, **69**(7):4366-4372.
5. Chow JW, Thal LA, Perri MB, Vazquez JA, Donabedian SM, Clewell DB, Zervos MJ: **Plasmid-associated hemolysin and aggregation substance production contribute to virulence in experimental enterococcal endocarditis**. *Antimicrob Agents Chemother* 1993, **37**(11):2474-2477.
6. Jett BD, Jensen HG, Nordquist RE, Gilmore MS: **Contribution of the pAD1-encoded cytolysin to the severity of experimental *Enterococcus faecalis* endophthalmitis**. *Infect Immun* 1992, **60**(6):2445-2452.
7. Schlievert PM, Gahr PJ, Assimacopoulos AP, Dinges MM, Stoehr JA, Harmala JW, Hirt H, Dunny GM: **Aggregation and binding substances enhance pathogenicity in rabbit models of *Enterococcus faecalis* endocarditis**. *Infect Immun* 1998, **66**(1):218-223.
8. Singh KV, Nallapareddy SR, Sillanpaa J, Murray BE: **Importance of the collagen adhesin ace in pathogenesis and protection against *Enterococcus faecalis* experimental endocarditis**. *PLoS Pathog*, **6**(1):e1000716.
9. Kreft B, Marre R, Schramm U, Wirth R: **Aggregation substance of *Enterococcus faecalis* mediates adhesion to cultured renal tubular cells**. *Infect Immun* 1992, **60**(1):25-30.
10. Olmsted SB, Dunny GM, Erlandsen SL, Wells CL: **A plasmid-encoded surface protein on *Enterococcus faecalis* augments its internalization by cultured intestinal epithelial cells**. *J Infect Dis* 1994, **170**(6):1549-1556.
11. Eaton TJ, Gasson MJ: **Molecular screening of *Enterococcus* virulence determinants and potential for genetic exchange between food and medical isolates**. *Appl Environ Microbiol* 2001, **67**(4):1628-1635.
12. Lempiainen H, Kinnunen K, Mertanen A, von Wright A: **Occurrence of virulence factors among human intestinal enterococcal isolates**. *Lett Appl Microbiol* 2005, **41**(4):341-344.
13. Semedo T, Santos MA, Lopes MF, Figueiredo Marques JJ, Barreto Crespo MT, Tenreiro R: **Virulence factors in food, clinical and reference Enterococci: A common trait in the genus?** *Syst Appl Microbiol* 2003, **26**(1):13-22.
14. Creti R, Imperi M, Bertuccini L, Fabretti F, Orefici G, Di Rosa R, Baldassarri L: **Survey for virulence determinants among *Enterococcus faecalis* isolated from different sources**. *J Med Microbiol* 2004, **53**(Pt 1):13-20.
15. Franz CM, Muscholl-Silberhorn AB, Yousif NM, Vancanneyt M, Swings J, Holzapfel WH: **Incidence of virulence factors and antibiotic resistance among Enterococci isolated from food**. *Appl Environ Microbiol* 2001, **67**(9):4385-4389.
16. Mannu L, Paba A, Daga E, Comunian R, Zanetti S, Dupre I, Sechi LA: **Comparison of the incidence of virulence determinants and antibiotic resistance between *Enterococcus faecium* strains of dairy, animal and clinical origin**. *Int J Food Microbiol* 2003, **88**(2-3):291-304.

17. Bourgogne A, Garsin DA, Qin X, Singh KV, Sillanpaa J, Yerrapragada S, Ding Y, Dugan-Rocha S, Buhay C, Shen H *et al*: **Large scale variation in *Enterococcus faecalis* illustrated by the genome analysis of strain OG1RF**. *Genome Biol* 2008, **9**(7):R110.
18. Kawalec M, Pietras Z, Danilowicz E, Jakubczak A, Gniadkowski M, Hryniewicz W, Willems RJ: **Clonal structure of *Enterococcus faecalis* isolated from Polish hospitals: characterization of epidemic clones**. *J Clin Microbiol* 2007, **45**(1):147-153.
19. Ruiz-Garbajosa P, Bonten MJ, Robinson DA, Top J, Nallapareddy SR, Torres C, Coque TM, Canton R, Baquero F, Murray BE *et al*: **Multilocus sequence typing scheme for *Enterococcus faecalis* reveals hospital-adapted genetic complexes in a background of high rates of recombination**. *J Clin Microbiol* 2006, **44**(6):2220-2228.
20. Solheim M, Aakra A, Snipen LG, Brede DA, Nes IF: **Comparative genomics of *Enterococcus faecalis* from healthy Norwegian infants**. *BMC Genomics* 2009, **10**:194.
21. Nallapareddy SR, Wenxiang H, Weinstock GM, Murray BE: **Molecular characterization of a widespread, pathogenic, and antibiotic resistance-receptive *Enterococcus faecalis* lineage and dissemination of its putative pathogenicity island**. *J Bacteriol* 2005, **187**(16):5709-5718.
22. Murray BE, Mederski-Samaroj B: **Transferable beta-lactamase. A new mechanism for in vitro penicillin resistance in *Streptococcus faecalis***. *J Clin Invest* 1983, **72**(3):1168-1171.
23. Vebø HC, Solheim M, Snipen L, Nes IF, Brede DA: **Comparative Genomic Analysis of Pathogenic and Probiotic *Enterococcus faecalis* Isolates, and Their Transcriptional Responses to Growth in Human Urine**. *PLoS ONE*, **5**(8):e12489.
24. McBride SM, Fischetti VA, Leblanc DJ, Moellering RC, Jr., Gilmore MS: **Genetic diversity among *Enterococcus faecalis***. *PLoS ONE* 2007, **2**(7):e582.
25. Paulsen IT, Banerjei L, Myers GS, Nelson KE, Seshadri R, Read TD, Fouts DE, Eisen JA, Gill SR, Heidelberg JF *et al*: **Role of mobile DNA in the evolution of vancomycin-resistant *Enterococcus faecalis***. *Science* 2003, **299**(5615):2071-2074.
26. van Schaik W, Top J, Riley DR, Boekhorst J, Vrijenhoek JE, Schapendonk CM, Hendrickx AP, Nijman IJ, Bonten MJ, Tettelin H *et al*: **Pyrosequencing-based comparative genome analysis of the nosocomial pathogen *Enterococcus faecium* and identification of a large transferable pathogenicity island**. *BMC Genomics*, **11**:239.
27. Bessman MJ, Frick DN, O'Handley SF: **The MutT proteins or "Nudix" hydrolases, a family of versatile, widely distributed, "housecleaning" enzymes**. *J Biol Chem* 1996, **271**(41):25059-25062.
28. Tuteja N, Tuteja R: **Prokaryotic and eukaryotic DNA helicases. Essential molecular motor proteins for cellular machinery**. *Eur J Biochem* 2004, **271**(10):1835-1848.
29. Shankar N, Baghdayan AS, Gilmore MS: **Modulation of virulence within a pathogenicity island in vancomycin-resistant *Enterococcus faecalis***. *Nature* 2002, **417**(6890):746-750.
30. McBride SM, Coburn PS, Baghdayan AS, Willems RJ, Grande MJ, Shankar N, Gilmore MS: **Genetic variation and evolution of the pathogenicity island of *Enterococcus faecalis***. *J Bacteriol* 2009, **191**(10):3392-3402.
31. Lepage E, Brinster S, Caron C, Ducroix-Crepy C, Rigottier-Gois L, Dunny G, Hennequet-Antier C, Serror P: **Comparative genomic hybridization analysis of *Enterococcus faecalis*: identification of genes absent from food strains**. *J Bacteriol* 2006, **188**(19):6858-6868.
32. Brinster S, Furlan S, Serror P: **C-terminal WxL domain mediates cell wall binding in *Enterococcus faecalis* and other gram-positive bacteria**. *J Bacteriol* 2007, **189**(4):1244-1253.
33. Siezen R, Boekhorst J, Muscariello L, Molenaar D, Renckens B, Kleerebezem M: ***Lactobacillus plantarum* gene clusters encoding putative cell-surface protein complexes for carbohydrate utilization are conserved in specific gram-positive bacteria**. *BMC Genomics* 2006, **7**:126.
34. Bierne H, Sabet C, Personnic N, Cossart P: **Internalins: a complex family of leucine-rich repeat-containing proteins in *Listeria monocytogenes***. *Microbes Infect* 2007, **9**(10):1156-1166.

35. Brinster S, Posteraro B, Bierne H, Alberti A, Makhzami S, Sanguinetti M, Serror P: **Enterococcal leucine-rich repeat-containing protein involved in virulence and host inflammatory response**. *Infect Immun* 2007, **75**(9):4463-4471.
36. Shepard BD, Gilmore MS: **Differential expression of virulence-related genes in *Enterococcus faecalis* in response to biological cues in serum and urine**. *Infect Immun* 2002, **70**(8):4344-4352.
37. Vebø HC, Snipen L, Nes IF, Brede DA: **The transcriptome of the nosocomial pathogen *Enterococcus faecalis* V583 reveals adaptive responses to growth in blood**. *PLoS One* 2009, **4**(11):e7660.
38. Paulson JC, Colley KJ: **Glycosyltransferases. Structure, localization, and control of cell type-specific glycosylation**. *J Biol Chem* 1989, **264**(30):17615-17618.
39. Xu Y, Murray BE, Weinstock GM: **A cluster of genes involved in polysaccharide biosynthesis from *Enterococcus faecalis* OG1RF**. *Infect Immun* 1998, **66**(9):4313-4323.
40. Hancock LE, Gilmore MS: **The capsular polysaccharide of *Enterococcus faecalis* and its relationship to other polysaccharides in the cell wall**. *Proc Natl Acad Sci U S A* 2002, **99**(3):1574-1579.
41. Huebner J, Wang Y, Krueger WA, Madoff LC, Martirosian G, Boisot S, Goldmann DA, Kasper DL, Tzianabos AO, Pier GB: **Isolation and Chemical Characterization of a Capsular Polysaccharide Antigen Shared by Clinical Isolates of *Enterococcus faecalis* and Vancomycin-Resistant Enterococcus faecium**. *Infect Immun* 1999, **67**(3):1213-1219.
42. Gosink KK, Mann ER, Guglielmo C, Tuomanen EI, Masure HR: **Role of novel choline binding proteins in virulence of *Streptococcus pneumoniae***. *Infect Immun* 2000, **68**(10):5690-5695.
43. Rosenow C, Ryan P, Weiser JN, Johnson S, Fontan P, Ortqvist A, Masure HR: **Contribution of novel choline-binding proteins to adherence, colonization and immunogenicity of *Streptococcus pneumoniae***. *Mol Microbiol* 1997, **25**(5):819-829.
44. Sillanpaa J, Xu Y, Nallapareddy SR, Murray BE, Hook M: **A family of putative MSCRAMMs from *Enterococcus faecalis***. *Microbiology* 2004, **150**(Pt 7):2069-2078.
45. Kowalski WJ, Kasper EL, Hatton JF, Murray BE, Nallapareddy SR, Gillespie MJ: ***Enterococcus faecalis* adhesin, Ace, mediates attachment to particulate dentin**. *J Endod* 2006, **32**(7):634-637.
46. Nallapareddy SR, Qin X, Weinstock GM, Hook M, Murray BE: ***Enterococcus faecalis* adhesin, *ace*, mediates attachment to extracellular matrix proteins collagen type IV and laminin as well as collagen type I**. *Infect Immun* 2000, **68**(9):5218-5224.
47. Rich RL, Kreikemeyer B, Owens RT, LaBrenz S, Narayana SV, Weinstock GM, Murray BE, Hook M: **Ace is a collagen-binding MSCRAMM from *Enterococcus faecalis***. *J Biol Chem* 1999, **274**(38):26939-26945.
48. Lebreton F, Riboulet-Bisson E, Serror P, Sanguinetti M, Posteraro B, Torelli R, Hartke A, Auffray Y, Giard JC: ***ace*, Which encodes an adhesin in *Enterococcus faecalis*, is regulated by Ers and is involved in virulence**. *Infect Immun* 2009, **77**(7):2832-2839.
49. Nallapareddy SR, Singh KV, Murray BE: **Contribution of the collagen adhesin Acm to pathogenesis of *Enterococcus faecium* in experimental endocarditis**. *Infect Immun* 2008, **76**(9):4120-4128.
50. Linden SK, Sutton P, Karlsson NG, Korolik V, McGuckin MA: **Mucins in the mucosal barrier to infection**. *Mucosal Immunol* 2008, **1**(3):183-197.
51. Styriak I, Ljungh S: **Binding of extracellular matrix molecules by enterococci**. *Curr Microbiol* 2003, **46**(6):435-442.
52. Hall AE, Gorovits EL, Syribeys PJ, Domanski PJ, Ames BR, Chang CY, Vernachio JH, Patti JM, Hutchins JT: **Monoclonal antibodies recognizing the *Enterococcus faecalis* collagen-binding MSCRAMM Ace: Conditional expression and binding analysis**. *Microbial Pathogenesis* 2007, **43**(2-3):55-66.

53. Nallapareddy SR, Singh KV, Duh R-W, Weinstock GM, Murray BE: **Diversity of ace, a Gene Encoding a Microbial Surface Component Recognizing Adhesive Matrix Molecules, from Different Strains of *Enterococcus faecalis* and Evidence for Production of Ace during Human Infections**. *Infect Immun* 2000, **68**(9):5210-5217.
54. Yu WL, Dan H, Lin M: **InlA and InlC2 of *Listeria monocytogenes* serotype 4b are two internalin proteins eliciting humoral immune responses common to listerial infection of various host species**. *Curr Microbiol* 2008, **56**(5):505-509.
55. Smyth GK, Speed T: **Normalization of cDNA microarray data**. *Methods* 2003, **31**(4):265-273.
56. Snipen L, Nyquist OL, Solheim M, Aakra A, Nes IF: **Improved analysis of bacterial CGH data beyond the log-ratio paradigm**. *BMC Bioinformatics* 2009, **10**(1):91.
57. Palmer KL, Carniol K, Manson JM, Heiman D, Shea T, Young S, Zeng Q, Gevers D, Feldgarden M, Birren B *et al*: **High Quality Draft Genome Sequences of 28 *Enterococcus* sp. Isolates**. *J Bacteriol*:JB.00153-00110.
58. Peterson J, Garges S, Giovanni M, McInnes P, Wang L, Schloss JA, Bonazzi V, McEwen JE, Wetterstrand KA, Deal C *et al*: **The NIH Human Microbiome Project**. *Genome Res* 2009, **19**(12):2317-2323.
59. Moellering RC, Jr., Weinberg AN: **Studies on antibiotic syngerism against enterococci. II. Effect of various antibiotics on the uptake of 14 C-labeled streptomycin by enterococci**. *J Clin Invest* 1971, **50**(12):2580-2584.
60. Huycke MM, Spiegel CA, Gilmore MS: **Bacteremia caused by hemolytic, high-level gentamicin-resistant *Enterococcus faecalis***. *Antimicrob Agents Chemother* 1991, **35**(8):1626-1634.
61. Sahm DF, Kissinger J, Gilmore MS, Murray PR, Mulder R, Solliday J, Clarke B: **In vitro susceptibility studies of vancomycin-resistant *Enterococcus faecalis***. *Antimicrob Agents Chemother* 1989, **33**(9):1588-1591.
62. Aakra A, Nyquist OL, Snipen L, Reiersen TS, Nes IF: **Survey of genomic diversity among *Enterococcus faecalis* strains by microarray-based comparative genomic hybridization**. *Appl Environ Microbiol* 2007, **73**(7):2207-2217.
63. Rice LB, Eliopoulos GM, Wennersten C, Goldmann D, Jacoby GA, Moellering RC, Jr.: **Chromosomally mediated beta-lactamase production and gentamicin resistance in *Enterococcus faecalis***. *Antimicrob Agents Chemother* 1991, **35**(2):272-276.
64. Wheeler SM, Foley GE: **Studies on the Streptococci (Enterococci) of Lancefield Group-D .2. Recovery of Lancefield Group D Streptococci from Antemortem and Postmortem Cultures from Infants and Young Children**. *American Journal of Diseases of Children* 1945, **70**(4):207-213.
65. Murray BE, Singh KV, Ross RP, Heath JD, Dunny GM, Weinstock GM: **Generation of restriction map of *Enterococcus faecalis* OG1 and investigation of growth requirements and regions encoding biosynthetic function**. *J Bacteriol* 1993, **175**(16):5216-5223.
66. Maekawa S, Yoshioka M, Kumamoto Y: **Proposal of a new scheme for the serological typing of *Enterococcus faecalis* strains**. *Microbiol Immunol* 1992, **36**(7):671-681.
67. Ackermann HW, Caprioli T, Kasatiya SS: **A large new *Streptococcus* bacteriophage**. *Can J Microbiol* 1975, **21**(4):571-574.
68. Domann E, Hain T, Ghai R, Billion A, Kuenne C, Zimmermann K, Chakraborty T: **Comparative genomic analysis for the presence of potential enterococcal virulence factors in the probiotic *Enterococcus faecalis* strain Symbioflor 1**. *Int J Med Microbiol* 2007, **297**(7-8):533-539.
69. Jacob AE, Hobbs SJ: **Conjugal transfer of plasmid-borne multiple antibiotic resistance in *Streptococcus faecalis* var. *zymogenes***. *J Bacteriol* 1974, **117**(2):360-372.
70. Clewell DB, Yagi Y, Dunny GM, Schultz SK: **Characterization of three plasmid deoxyribonucleic acid molecules in a strain of *Streptococcus faecalis*: identification of a plasmid determining erythromycin resistance**. *J Bacteriol* 1974, **117**(1):283-289.

71. Gardner P, Smith DH, Beer H, Moellering RC, Jr.: **Recovery of resistance (R) factors from a drug-free community**. *Lancet* 1969, **2**(7624):774-776.
72. Harrington SM, Ross TL, Gebo KA, Merz WG: **Vancomycin resistance, esp, and strain relatedness: a 1-year study of enterococcal bacteremia**. *J Clin Microbiol* 2004, **42**(12):5895-5898.
73. Manson JM, Keis S, Smith JM, Cook GM: **Characterization of a vancomycin-resistant *Enterococcus faecalis* (VREF) isolate from a dog with mastitis: further evidence of a clonal lineage of VREF in New Zealand**. *J Clin Microbiol* 2003, **41**(7):3331-3333.

Table 1. *Enterococcus faecalis* isolates used in this study. CC; clonal complex, CGH; comparative genomic hybridization, MLST; multilocus sequence typing, S; singleton, ST; sequence type.

Strain	Year	Country	Source	MLST		Application	Reference
				ST	CC		
HIP11704	2002	USA	Clinical	4	4	*In silico*	[59]
TX0104		USA	Clinical	2	6	*In silico*	[58]
609/96	1996	Poland	Wound	6	6	CGH, PCR	[18]
372-56	2007	Norway	Blood	6	6	CGH, PCR	
226B	2005	Norway	Feces	6	6	PCR	[20]
368-42	2007	Norway	Blood	6	6	PCR	
442/05	2005	Poland	CSF	6	6	PCR	[18]
E1828	2001	Spain	Blood	6	6	PCR	[19]
MMH594	1985	USA	Clinical	6	6	CGH[C], PCR	[60]
V583	1989	USA	Blood	6	6	CGH, PCR	[61]
158B	2005	Norway	Feces	6	6	CGH[B], PCR	[20]
HH22	≤1982	USA	Urine	6	6	*In silico*	[22]
LMGT3303				6	6	CGH[D], PCR	
E1834	2001	Spain	Blood	51	6	CGH, PCR	[19]
E4250	2007	Netherlands	Feces	183	6	CGH, PCR	
E1841	2001	Spain	Blood	9	9	CGH, PCR	[19]
Vet179	1999	Norway	Dog_urine	9	9	CGH[D], PCR	[62]
CH188	1980s	USA	Liver	9	9	*In silico*	[63]
E1807	2002	Spain	Feces	17	9	CGH, PCR	[19]
X98	1934		Feces	19	19	*In silico*	[64]
OG1RF	≤1975	USA	Oral	1	21	CGH[C], PCR	[65]
E1960	2001	Spain	Feces	8	21	CGH, PCR	[19]
T8	≤1992	Japan	Urine	8	21	*In silico*	[66]
2426/03	2003	Poland	Feces	21	21	CGH, PCR	[18]
ATCC 29200	≤1974	Canada	Urogenital	21	21	*In silico*	[67]
T1	≤ 1950			21	21	*In silico*	[66]
LMGT3406	1999	Denmark	Poultry_feces	22	21	CGH[D], PCR	
111A	2005	Norway	Feces	161	21	CGH[B], PCR	[20]
TX1322		USA		161	21	*In silico*	[58]
3339/04	2004	Poland	Blood	23	25	CGH, PCR	[18]
UC11/46		Finland	Feces	97	25	CGH, PCR	[12]
189	2002-2003	Norway	Feces	162	25	CGH[B], PCR	[20]
Symbioflor 1		Germany	Feces	248	25	CGH[C], PCR	[68]
T2	≤1992	Japan	Urine	11	28	*In silico*	[66]
E1188	1997	Greece	Blood	28	28	CGH, PCR	[19]
383/04	2004	Poland	Blood	87	28	CGH, PCR	[18]
E0152		Netherlands	Feces	30	30	CGH[D], PCR	
85	2008	Norway	Feces	30	30	CGH[B], PCR	[20]
597/96	1996	Poland	Ulcer	40	40	CGH, PCR	[18]
LMGT2333		Iceland	Fish	40	40	CGH[D], PCR	
JH1	≤1974	United Kingdom	Clinical	40	40	*In silico*	[69]
LMGT3209		Greece	Food_cheese	40	40	CGH[D], PCR	
1645	2007	Denmark	Blood	220	40	CGH, PCR	
29C	2004	Norway	Feces	44	44	CGH[B], PCR	[20]
92A	2005	Norway	Feces	44	44	CGH[B]	[20]
DS5	≤1974			55	55	*In silico*	[70]
E2370		Hungary	Wound	16	58	CGH, PCR	
105	2002-2003	Norway	Feces	16	58	CGH[B], PCR	[20]
D6		Denmark	Pig	16	58	*In silico*	[24]
E1Sol	1960s	Solomon Islands	Feces	93	93	*In silico*	[71]
Merz96	2002	USA	Blood	103	103	*In silico*	[72]
R712		USA	Clinical	103	103	*In silico*	[58]
S613		USA	Clinical	103	103	*In silico*	[58]
LMGT3405	1999	Denmark	Poultry_feces	116	116	CGH[D], PCR	
LMGT3407	1999	Denmark	Poultry_feces	34	121	CGH[D], PCR	
Fly1	2005	USA	Drosophila	101	101[A]	*In silico*	[24]
Vet138	1998	Norway	Dog_ear	164	119[A]	CGH[D], PCR	[62]
82	2008	Norway	Poultry_feces	65	S	CGH[D], PCR	
T11	≤1992	Japan	Urine	65	S	*In silico*	[66]
62	2002-2003	Norway	Feces	66	S	CGH[B], PCR	[20]
ATCC 4200	1926		Blood	105	S	*In silico*	
AR01/DG	2001	New Zealand	Dog	108	S	*In silico*	[73]
266	2002-2003	Norway	Feces	163	S	CGH[B], PCR	[20]

LMGT3143		Spain	Animal_wood pigeon	165	S	CGH[D], PCR	
LMGT3208		Greece	Food_cheese	166	S	CGH[D], PCR	
84	2008	Norway	Poultry_feces	249	S	CGH[D], PCR	
TuSoD ef11		USA	Clinical	364	S	*In silico*	[58]

[A]Clonal complexes were no predicted founder was proposed by eBURST.
[B]In Solheim et al. 2009.
[C]In Vebø et al. 2010.
[D]MS, unpublished work.

Table 2. V583 genes which were identified as significantly enriched among CC6-strains in the present study. CC; clonal complex, FDR; false discovery rate, p01; phage01, p03; phage03, p04; phage04, p06;phage06 and PAI; pathogenicity island.

ORF	Gene product	Mobile genetic element	CC6-strains present (n=10)	(%)	Non-CC6 strains present (n=54)	(%)	*q*-value (FDR)
EF0052	Hypothetical protein		8	(80)	3	(6)	4E-05
EF0053	DNA polymerase III, epsilon subunit		8	(80)	2	(4)	1E-05
EF0054	Hypothetical protein		8	(80)	2	(4)	1E-05
EF0112	Conserved domain protein		8	(80)	4	(7)	8E-05
EF0113	Hypothetical protein		8	(80)	4	(7)	8E-05
EF0126	Conserved hypothetical protein		8	(80)	5	(9)	2E-04
EF0315	Conserved hypothetical protein	*p01*	4	(40)	1	(2)	9E-03
EF0316	Hypothetical protein	*p01*	4	(40)	1	(2)	9E-03
EF0325	DNA polymerase, putative	*p01*	5	(50)	3	(6)	9E-03
EF0329	Conserved hypothetical protein	*p01*	5	(50)	3	(6)	9E-03
EF0330	SNF2 domain protein	*p01*	4	(40)	1	(2)	9E-03
EF0500	Conserved hypothetical protein	PAI	10	(100)	23	(43)	6E-03
EF0510	Single-strand binding protein	PAI	10	(100)	25	(46)	9E-03
EF0568	Potassium-transporting ATPase, subunit B	PAI	7	(70)	9	(17)	9E-03
EF0569	Potassium-transporting ATPase, subunit C	PAI	7	(70)	9	(17)	9E-03
EF0570	Sensor histidine kinase KdpD	PAI	7	(70)	9	(17)	9E-03
EF0574	Hypothetical protein	PAI	7	(70)	9	(17)	9E-03
EF0594	Hypothetical protein	PAI	7	(70)	9	(17)	9E-03
EF0967	Conserved domain protein		10	(100)	18	(33)	9E-04
EF1031	Phosphorylase family protein		10	(100)	19	(35)	1E-03
EF1329	HesA/MoeB/ThiF family protein		10	(100)	22	(41)	6E-03
EF1330	Hypothetical protein		10	(100)	20	(37)	2E-03
EF1331	ABC transporter, ATP-binding protein		10	(100)	20	(37)	2E-03
EF1332	Membrane protein, putative		10	(100)	20	(37)	2E-03
EF1333	ABC transporter, ATP-binding protein		10	(100)	20	(37)	2E-03
EF1334	AgrC domain protein		10	(100)	20	(37)	2E-03
EF1335	Sensor histidine kinase, putative		10	(100)	20	(37)	2E-03
EF1336	Response regulator		10	(100)	21	(39)	2E-03
EF1417	Site-specific recombinase, phage integrase family	*p03*	8	(80)	6	(11)	3E-04
EF1418	Hypothetical protein	*p03*	7	(70)	8	(15)	6E-03
EF1419	Conserved hypothetical protein	*p03*	6	(60)	2	(4)	8E-04
EF1423	Transcriptional regulator, Cro/CI family	*p03*	5	(50)	2	(4)	5E-03
EF1424	Hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1425	Hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1426	VrlI protein, putative	*p03*	7	(70)	6	(11)	2E-03
EF1428	Hypothetical protein	*p03*	6	(60)	5	(9)	6E-03
EF1429	Hypothetical protein	*p03*	7	(70)	7	(13)	4E-03
EF1430	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1433	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1434	DnaD domain protein	*p03*	8	(80)	6	(11)	3E-04
EF1435	Recombination protein U, putative	*p03*	8	(80)	6	(11)	3E-04
EF1436	Hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1443	Conserved hypothetical protein	*p03*	7	(70)	5	(9)	1E-03
EF1445	Replicase domain protein	*p03*	8	(80)	7	(13)	6E-04
EF1446	Hypothetical protein	*p03*	8	(80)	9	(17)	2E-03
EF1447	Conserved hypothetical protein	*p03*	8	(80)	5	(9)	2E-04
EF1448	Hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1449	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1450	Positive control factor, putative	*p03*	8	(80)	6	(11)	3E-04
EF1455	Terminase, large subunit, putative	*p03*	8	(80)	6	(11)	3E-04
EF1456	Conserved hypothetical protein TIGR01555	*p03*	7	(70)	5	(9)	1E-03
EF1457	Minor head protein	*p03*	8	(80)	5	(9)	2E-04
EF1458	Hypothetical protein	*p03*	8	(80)	5	(9)	2E-04
EF1459	Conserved hypothetical protein	*p03*	8	(80)	7	(13)	6E-04
EF1460	LysM domain protein	*p03*	8	(80)	5	(9)	2E-04
EF1461	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1462	Conserved hypothetical protein	*p03*	7	(70)	8	(15)	6E-03
EF1463	Hypothetical protein	*p03*	7	(70)	6	(11)	2E-03
EF1464	Conserved hypothetical protein	*p03*	8	(80)	5	(9)	2E-04
EF1465	Conserved hypothetical protein	*p03*	8	(80)	5	(9)	2E-04
EF1466	Conserved hypothetical protein	*p03*	7	(70)	6	(11)	2E-03
EF1467	Conserved hypothetical protein	*p03*	7	(70)	6	(11)	2E-03

ORF	Gene product	Mobile genetic element	CC6-strains present (n=10)	(%)	Non-CC6 strains present (n=54)	(%)	*q*-value (FDR)
EF1469	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1470	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1471	Conserved hypothetical protein	*p03*	8	(80)	8	(15)	1E-03
EF1472	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1473	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1474	LysM domain protein	*p03*	8	(80)	6	(11)	3E-04
EF1475	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1476	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1477	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1478	Conserved hypothetical protein	*p03*	8	(80)	7	(13)	6E-04
EF1479	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1480	Conserved hypothetical protein	*p03*	8	(80)	7	(13)	6E-04
EF1481	Hypothetical protein	*p03*	7	(70)	5	(9)	1E-03
EF1482	Hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1483	Conserved hypothetical protein	*p03*	8	(80)	8	(15)	1E-03
EF1484	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1485	Conserved hypothetical protein	*p03*	8	(80)	6	(11)	3E-04
EF1589	Acetyltransferase, GNAT family		10	(100)	25	(46)	9E-03
EF1825	Conserved domain protein		10	(100)	23	(43)	6E-03
EF1826	Alcohol dehydrogenase, zinc-containing		10	(100)	22	(41)	6E-03
EF1827	Conserved hypothetical protein		10	(100)	18	(33)	9E-04
EF1828	Glycerol uptake facilitator protein, putative		10	(100)	18	(33)	9E-04
EF1829	PTS system, IID component		10	(100)	18	(33)	9E-04
EF1830	PTS system, IIC component		10	(100)	18	(33)	9E-04
EF1833	PTS system component, authentic frameshift		10	(100)	22	(41)	6E-03
EF1834	galactose-6-phosphate isomerase, LacB subunit		10	(100)	22	(41)	6E-03
EF1835	galactose-6-phosphate isomerase, LacA subunit		10	(100)	22	(41)	6E-03
EF1836	PTS system, IIA component, putative		10	(100)	22	(41)	6E-03
EF1837	PTS system, IIB component, putative		10	(100)	22	(41)	6E-03
EF1838	PTS system, IIC component		10	(100)	22	(41)	6E-03
EF1844	Hypothetical protein		10	(100)	21	(39)	2E-03
EF1847	Site-specific recombinase, phage integrase family	*efaB5*	10	(100)	20	(37)	2E-03
EF1848	Hypothetical protein	*efaB5*	10	(100)	18	(33)	9E-04
EF1849	Conserved hypothetical protein	*efaB5*	10	(100)	22	(41)	6E-03
EF1851	Glycosyl hydrolase, family 35	*efaB5*	10	(100)	21	(39)	2E-03
EF1853	Hypothetical protein	*efaB5*	10	(100)	20	(37)	2E-03
EF1855	Transposase, IS256 family	*efaB5*	10	(100)	20	(37)	2E-03
EF1858	Aspartate 1-decarboxylase	*efaB5*	10	(100)	20	(37)	2E-03
EF1859	Pantoate--beta-alanine ligase	*efaB5*	10	(100)	20	(37)	2E-03
EF1860	3-methyl-2-oxobutanoate hydroxymethyltransferase	*efaB5*	10	(100)	20	(37)	2E-03
EF1861	Conserved domain protein	*efaB5*	10	(100)	20	(37)	2E-03
EF1863	Sensor histidine kinase	*efaB5*	10	(100)	20	(37)	2E-03
EF1864	DNA-binding response regulator	*efaB5*	10	(100)	20	(37)	2E-03
EF1867	Permease, putative	*efaB5*	10	(100)	20	(37)	2E-03
EF1868	ABC transporter, ATP-binding protein	*efaB5*	10	(100)	21	(39)	2E-03
EF1869	Permease, putative	*efaB5*	10	(100)	20	(37)	2E-03
EF1871	Thioredoxin family protein	*efaB5*	10	(100)	23	(43)	6E-03
EF1872	Conserved domain protein	*efaB5*	10	(100)	22	(41)	6E-03
EF1875	Conserved hypothetical protein	*efaB5*	10	(100)	21	(39)	2E-03
EF1876	Lipoprotein, NLP/P60 family	*efaB5*	10	(100)	20	(37)	2E-03
EF1877	Membrane protein, putative	*efaB5*	10	(100)	24	(44)	7E-03
EF1879	Conserved hypothetical protein	*efaB5*	10	(100)	21	(39)	2E-03
EF1880	Hypothetical protein	*efaB5*	10	(100)	20	(37)	2E-03
EF1881	Conserved domain protein	*efaB5*	10	(100)	20	(37)	2E-03
EF1882	Conserved hypothetical protein	*efaB5*	10	(100)	20	(37)	2E-03
EF1884	Transposase, IS116/IS110/IS902 family	*efaB5*	10	(100)	21	(39)	2E-03
EF1885	Hypothetical protein	*efaB5*	10	(100)	24	(44)	7E-03
EF1886	Transcriptional regulator, Cro/CI family	*efaB5*	10	(100)	22	(41)	6E-03
EF1887	Conserved hypothetical protein	*efaB5*	10	(100)	20	(37)	2E-03
EF1888	Hypothetical protein	*efaB5*	10	(100)	22	(41)	6E-03
EF1889	Conserved domain protein	*efaB5*	10	(100)	25	(46)	9E-03
EF1892	FtsK/SpoIIIE family protein	*efaB5*	10	(100)	24	(44)	7E-03
EF1894	Conserved hypothetical protein	*efaB5*	10	(100)	21	(39)	2E-03
EF1895	Conserved hypothetical protein	*efaB5*	10	(100)	20	(37)	2E-03
EF1897	Hypothetical protein		10	(100)	23	(43)	6E-03
EF1993	holin	*p04*	10	(100)	23	(43)	6E-03
EF1994	Conserved hypothetical protein	*p04*	10	(100)	25	(46)	9E-03
EF1995	Hypothetical protein	*p04*	10	(100)	24	(44)	7E-03
EF2006	Hypothetical protein	*p04*	10	(100)	24	(44)	7E-03
EF2012	Conserved hypothetical protein	*p04*	10	(100)	23	(43)	6E-03

ORF	Gene product	Mobile genetic element	CC6-strains present (n=10)	(%)	Non-CC6 strains present (n=54)	(%)	*q*-value (FDR)
EF2014	Coenzyme F420 hydrogenase domain protein	*p04*	10	(100)	12	(22)	8E-05
EF2015	Minor head protein, putative	*p04*	9	(90)	16	(30)	4E-03
EF2017	Terminase, large subunit, putative	*p04*	9	(90)	10	(19)	3E-04
EF2018	Conserved hypothetical protein	*p04*	10	(100)	5	(9)	7E-07
EF2019	Hypothetical protein	*p04*	10	(100)	4	(7)	3E-07
EF2020	Hypothetical protein	*p04*	10	(100)	4	(7)	3E-07
EF2022	Conserved domain protein	*p04*	10	(100)	5	(9)	7E-07
EF2027	Conserved hypothetical protein	*p04*	10	(100)	20	(37)	2E-03
EF2028	Hypothetical protein	*p04*	9	(90)	17	(31)	6E-03
EF2031	Conserved hypothetical protein	*p04*	10	(100)	23	(43)	6E-03
EF2032	Hypothetical protein	*p04*	10	(100)	23	(43)	6E-03
EF2033	Hypothetical protein	*p04*	10	(100)	14	(26)	2E-04
EF2034	Hypothetical protein	*p04*	10	(100)	21	(39)	2E-03
EF2039	Conserved hypothetical protein	*p04*	10	(100)	11	(20)	5E-05
EF2040	transcriptional regulator, Cro/CI family	*p04*	9	(90)	7	(13)	8E-05
EF2042	Conserved domain protein	*p04*	10	(100)	8	(15)	8E-06
EF2164	Membrane protein, putative		10	(100)	14	(26)	2E-04
EF2166	Membrane protein, putative		10	(100)	16	(30)	4E-04
EF2167	Glycosyl transferase, group 2 family protein		10	(100)	12	(22)	8E-05
EF2168	LicD1 protein, putative		10	(100)	14	(26)	2E-04
EF2169	Membrane protein, putative		10	(100)	12	(22)	8E-05
EF2170	Glycosyl transferase, group 2 family protein		10	(100)	23	(43)	6E-03
EF2174	Conserved domain protein		10	(100)	23	(43)	6E-03
EF2186	Conserved domain protein		10	(100)	16	(30)	4E-04
EF2188	Racemase domain protein		10	(100)	18	(33)	9E-04
EF2240	Site-specific recombinase, phage integrase family	*vanB*-ass. phage	10	(100)	8	(15)	8E-06
EF2241	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	7	(13)	4E-06
EF2243	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2244	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	5	(9)	8E-07
EF2245	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2247	Transcriptional regulator	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2248	Hypothetical protein	*vanB*-ass. phage	8	(80)	4	(7)	8E-05
EF2249	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2250	Conserved domain protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2251	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2252	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2253	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2254	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2255	Site-specific recombinase, phage integrase family	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2257	PTS system, IIC component, putative	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2258	Conserved domain protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2259	Phosphosugar-binding transcriptional regulator	*vanB*-ass. phage	10	(100)	6	(11)	2E-06
EF2260	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	6	(11)	2E-06
EF2261	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2262	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2263	Gluconate 5-dehydrogenase, putative	*vanB*-ass. phage	10	(100)	5	(9)	7E-07
EF2264	4-deoxy-l-threo-5-hexosulose-uronate ketol-isomerase	*vanB*-ass. phage	10	(100)	25	(46)	9E-03
EF2265	Carbohydrate kinase, pfkB family	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2266	2-dehydro-3-deoxyphosphogluconate aldolase/4-hydroxy-2-oxoglutarate aldolase, putative	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2267	PTS system, IIA component	*vanB*-ass. phage	10	(100)	6	(11)	2E-06
EF2268	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2269	PTS system, IID component	*vanB*-ass. phage	10	(100)	13	24	1E-04
EF2270	PTS system, IIC component	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2271	PTS system, IIB component	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2272	Glucuronyl hydrolase, putative	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2273	Transcriptional regulator, GntR family	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2275	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2276	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2277	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	5	(9)	7E-07
EF2278	Lipoprotein, NLP/P60 family	*vanB*-ass. phage	10	(100)	12	(22)	8E-05
EF2279	Membrane protein, putative	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2280	Conserved hypothetical protein	*vanB*-ass. phage	8	(80)	12	(22)	6E-03
EF2281	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	14	(26)	2E-04
EF2282	Conserved domain protein	*vanB*-ass. phage	10	(100)	6	(11)	2E-06
EF2335	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	12	(22)	8E-05
EF2337	Hypothetical protein	*vanB*-ass. phage	10	(100)	19	(35)	1E-03
EF2338	Transcriptional regulator, Cro/CI family	*vanB*-ass. phage	9	(90)	14	(26)	2E-03
EF2339	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2340	C-5 cytosine-specific DNA methylase	*vanB*-ass. phage	10	(100)	4	(7)	3E-07

ORF	Gene product	Mobile genetic element	CC6-strains present (n=10)	(%)	Non-CC6 strains present (n=54)	(%)	*q*-value (FDR)
EF2341	Hypothetical protein	*vanB*-ass. phage	10	(100)	5	(9)	7E-07
EF2342	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2343	FtsK/SpoIIIE family protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2344	Hypothetical protein	*vanB*-ass. phage	10	(100)	13	(24)	1E-04
EF2345	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	13	(24)	1E-04
EF2346	Conserved hypothetical protein	*vanB*-ass. phage	10	(100)	14	(26)	2E-04
EF2347	Cell wall surface anchor family protein	*vanB*-ass. phage	8	(80)	13	(24)	9E-03
EF2348	Hypothetical protein	*vanB*-ass. phage	9	(90)	4	(7)	7E-06
EF2349	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2350	Transcriptional regulator, Cro/CI family	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2351	Hypothetical protein	*vanB*-ass. phage	10	(100)	4	(7)	3E-07
EF2360	Hypothetical protein		10	(100)	22	(41)	6E-03
EF2385	Hypothetical protein		10	(100)	4	(7)	3E-07
EF2386	Hypothetical protein		10	(100)	4	(7)	3E-07
EF2387	chromosome partitioning ATPase, ParA family		10	(100)	4	(7)	3E-07
EF2388	Hypothetical protein		10	(100)	11	(20)	5E-05
EF2389	Hypothetical protein		10	(100)	12	(22)	8E-05
EF2662	Choline binding protein		7	(70)	2	(4)	1E-04
EF2807	Hypothetical protein	*p06*	6	(60)	4	(7)	4E-03
EF3099	Transporter accessory protein, putative		10	(100)	13	(24)	1E-04
EF3101	Conserved domain protein		10	(100)	10	(19)	3E-05
EF3102	Hypothetical protein		10	(100)	9	(17)	1E-05
EF3103	Membrane protein, putative		10	(100)	9	(17)	1E-05
EF3104	ABC transporter, ATP-binding protein		10	(100)	9	(17)	2E-05
EF3105	Hypothetical protein		10	(100)	10	(19)	3E-05
EF3153	Conserved hypothetical protein		8	(80)	9	(17)	2E-03
EF3154	Conserved hypothetical protein		10	(100)	7	(13)	4E-06
EF3155	Conserved hypothetical protein		8	(80)	1	(2)	3E-06
EF3161	Hypothetical protein		10	(100)	18	(33)	9E-04
EF3217	Helicase, putative	New genomic islet	10	(100)	3	(6)	3E-07
EF3218	Mutator MutT protein, putative	New genomic islet	10	(100)	5	(9)	7E-07
EF3220	Hypothetical protein	New genomic islet	8	(80)	3	(6)	3E-05
EF3221	Transcriptional regulator, Cro/CI family	New genomic islet	8	(80)	2	(4)	1E-05
EF3222	Hypothetical protein	New genomic islet	8	(80)	2	(4)	1E-05
EF3223	Hypothetical protein	New genomic islet	9	(90)	3	(6)	2E-06
EF3224	Hypothetical protein	New genomic islet	8	(80)	2	(4)	1E-05
EF3225	Conserved hypothetical protein	New genomic islet	8	(80)	2	(4)	1E-05
EF3226	Rep protein	New genomic islet	8	(80)	2	(4)	1E-05
EF3227	Conserved hypothetical protein	New genomic islet	8	(80)	2	(4)	1E-05
EF3241	Abortive phage resistance protein, putative		10	(100)	18	(33)	9E-04
EF3242	Abortive phage resistance protein, putative		10	(100)	17	(31)	6E-04
EF3243	Hypothetical protein		10	(100)	18	(33)	1E-03
EF3248	Hypothetical protein		8	(80)	5	(9)	2E-04
EF3250	Hypothetical protein		8	(80)	9	(17)	2E-03
EF3251	Hypothetical protein		8	(80)	9	(17)	2E-03
EF3252	Hypothetical protein		8	(80)	1	(2)	3E-06
EFA0028	Conserved domain protein	pTEF1	10	(100)	22	(41)	6E-03
EFB0014	Conserved hypothetical protein	pTEF2	10	(100)	19	(35)	1E-03
EFB0015	Hypothetical protein	pTEF2	9	(90)	16	(30)	4E-03
EFB0016	Hypothetical protein	pTEF2	9	(90)	17	(31)	6E-03
EFB0019	Conserved domain protein	pTEF2	9	(90)	17	(31)	6E-03

Table 3. Primers used in this study.

Target gene	Primer sequences (5' → 3')	Amplicon size (bp)	Application
ef1415	F:TGTTGCGGTTTCTGCATTAG	2818	PCR on junction between EF1415 and EF1417
ef1417	R:GCATCTCGATAGACAATTCG		PCR on junction between EF1415 and EF1417
ef1489	F:GAATCGAACTAGCATTTTTGGG	465	PCR on junction between EF1489 and EF1490
ef1490	R:ATGGAACGAACCATTGGAAA		PCR on junction between EF1489 and EF1490
ef1843	F:GGAGCCGTTAGACAGACAGC	2457	PCR on junction between EF1843 and EF1847
ef1847	R:GCTTGCTTTACAGCCTCAAGA		PCR on junction between EF1843 and EF1847
ef1895	F:GCACAACAAATTTCAATTCCA	4573	PCR on junction between EF1895 and EF1898
ef1898	R:ATTGAAGTGGTTCGCTACGG		PCR on junction between EF1895 and EF1898
ef2239	F:AACTGCTGTCAAGCGTAGCA	1252	PCR on junction between EF2239 and EF2240
ef2240	R:TGTGGCATTTTGGACTGTTG		PCR on junction between EF2239 and EF2240
ef2350	F:ATAACTGAGTGATTTTCACAATTGC	654	PCR on junction between EF2350 and EF2352
ef2352	R:GATCCGTGGAAGTTCCTCAA		PCR on junction between EF2350 and EF2352
ef3216	F:TCGGCGTTGAAGACTATGAA	-	Sequencing of junction between EF3216 and EF3230
ef3217	F:ATTGGGAATGACGGCTACAC	499	PCR
	R:TTGCGTATTTCGCAGCATAA		
ef3218	F:TCGCGTAGTAGGAGCAATCA	396	PCR
	R:TTTTGTTCAGTTCCCACACCT		
ef3220	F:AGCTTTTGGCGAAGGAGATT	495	PCR
	R:TTTATTGCGGGTTCCTCAGT		
ef3221	F:TGAACGAAAATGAAGGTGGT	196	PCR
	R:TCATCAATCTCCAACGCATC		
ef3222	F:CAAAGAAGAATCAGCCGATTAAA	183	PCR
	R:ATATTTGGGCATTTGCATGG		
ef3223	F:AATTGGGAAAAAGGGGTCAG	501	PCR
	R:TTCGTGATCTGCTTGTTGTTCT		
ef3224	F:GTTGGGCTGGACGTATGAAT	214	PCR
	R:TGTGGCTTTATAGGCTGTAGCA		
ef3225	F:ATTACTTCACCGCCCATGAC	474	PCR
	R:CGCTGGAAGTCTGCTCTTG		
ef3226	F:GATGATTTAACCGCACAAGGA	499	PCR
	R:TTTTTATTTCGAGCGGATGC		
ef3227	F:ACAGGAAGCCATTCACAAACT	162	PCR
	R:CTGATTCGTGGAAGTCCAACT		
ef3230	R:TCCTGACTTCCGTTCTGCTT	-	Sequencing of junction between EF3216 and EF3230
hmpref0346_1861	F:CGAGTTAGAGGAAGCGTTGG	630	PCR
	R:CCAGACAATTTGGGCGTACT		
hmpref0346_1864	F:GAAATTTTCTGAAAGTGAAGACAAGA	299	PCR
	R:TGATTAGCAGTCACAACAGCAA		
hmpref0346_1868	F:TGTACACAAGCTACCCGGATT	538	PCR
	R:TTCCCACCTGCGTCTATTTT		
hmpref0348_0427	R:GAGACTTCAACCACTCCACAAAAACC	-	Sequencing of gap between contig00034-35 in TX0104
hmpref0348_0428	F:CCTGTAGAAGTATTGTCCATTTTAACGCTATC		Sequencing of gap between contig00034-35 in TX0104

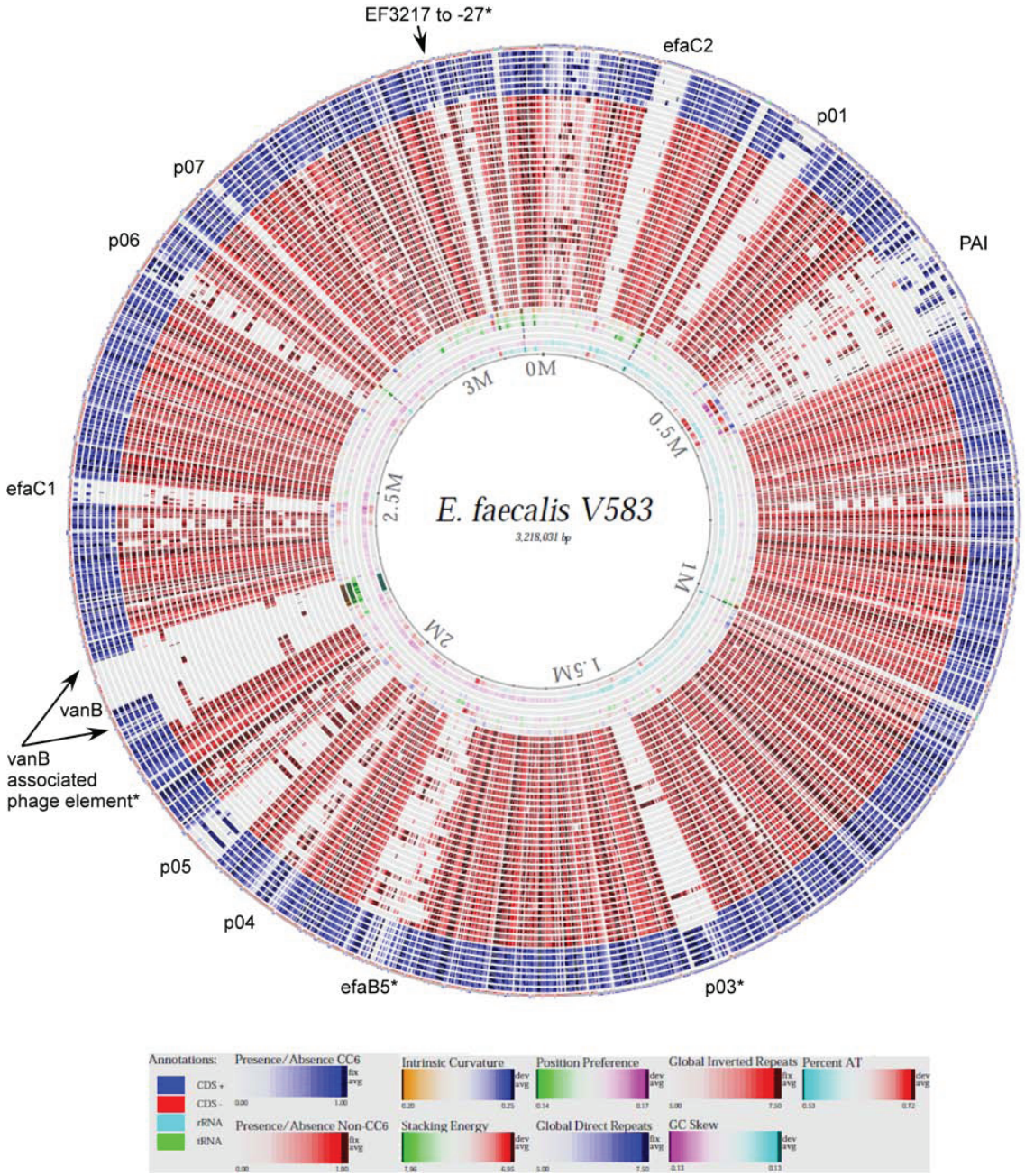
EF3217 to -27*
efaC2
p01
PAI
p07
p06
efaC1
0M
0.5M
1M
1.5M
2M
2.5M
3M
E. faecalis V583
3,218,031 bp
vanB
vanB
associated
phage element*
p05
p04
efaB5*
p03*
Annotations:
CDS +
CDS -
rRNA
tRNA
Presence/Absence CC6
Intrinsic Curvature
Position Preference
Global Inverted Repeats
Percent AT
Presence/Absence Non-CC6
Stacking Energy
Global Direct Repeats
GC Skew

Figure 1. Genome-atlas presentation of CGH data compared to the V583 genome and arranged by clonal relationship according to MLST. From inner to outer lanes: 1) percent AT, 2) GC skew, 3) global inverted repeats, 4) global direct repeats, 5) position preference, 6) stacking energy, 7) intrinsic curvature, 8) 189, 9) LMGT3208, 10) LMGT3407, 11) 92A, 12) 29C, 13) E1960, 14) 111A, 15) 105, 16) E2370, 17) 84, 18) 383/05, 19) E1188, 20) Vet179, 21) E1807, 22) LMGT3143, 23) LMGT3405, 24) OG1RF, 25) 2426/03, 26) LMGT3406, 27) 85, 28) E1052, 29) 1645, 30) E1841, 31) LMGT3209, 32) LMGT2333, 33) 597/96, 34) 62, 35) Vet138, 36) 266, 37) UC11/96, 38) Symbioflor 1, 39) 3339/04, 40) 82, 41) E1834, 42) E4250, 43) LMGT3303, 44) 158B, 45) MMH594, 46) 372-56, 47) 609/96 and 48) annotations in V583. Elements enriched in CC6 strains are indicated with an asterisk.

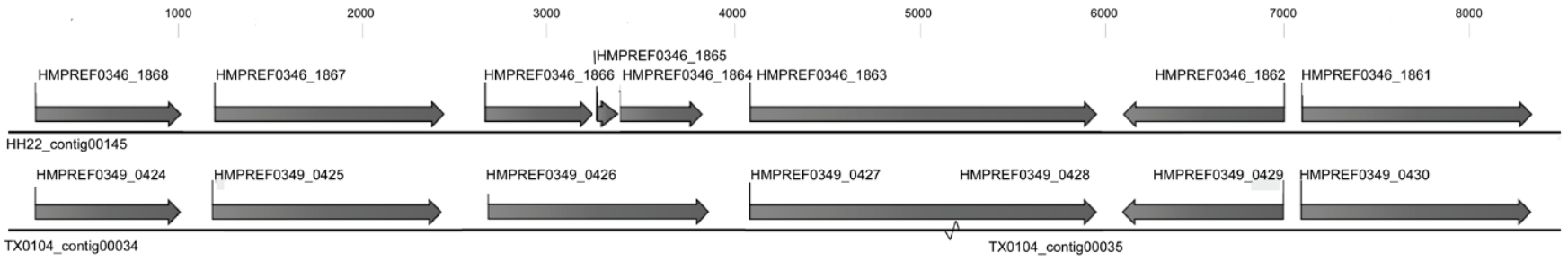

Figure 2. Schematic representation of a putative non-V583 CC6-enriched gene cluster, as annotated in the *Enterococcus faecalis* HH22 and TX0104 draft genomes (GenBank accession numbers ACIX00000000 and ACGL00000000, respectively)

Supplemental material

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TX0104 1    MKKFLNLCIFYVIRVKNKIKYNFKEEEMIKKILFGVVCIFAFGGMAITAFADDTLPIYGS  60
            MKKFLNLCIFYVIRVKNKIKYNFKEEEMIKKILFGVVCIFAFGGMAITAFADDTLPIYGS
HH22   1    MKKFLNLCIFYVIRVKNKIKYNFKEEEMIKKILFGVVCIFAFGGMAITAFADDTLPIYGS  60

TX0104 61   RIWFDLNGNGIQDQNEPSAPAIHFDKLAFTNKDLTVGFDYPGNNHLNAGSTTTPINSATA  120
            RIWFDLNGNGIQDQNEPSAPAIHFDKLAFTNKDLTVGFDYPGNNHLNAGSTTTPINSATA
HH22   61   RIWFDLNGNGIQDQNEPSAPAIHFDKLAFTNKDLTVGFDYPGNNHLNAGSTTTPINSATA  120

TX0104 121  VIEPKSAWVKQNLNKDWSEITDKAMETDDWTEYESVSKQFSDANPLMDNAEVPYRTGFGN  180
            VIEPKSAWVKQNLNKDWSEITDKAMETDDWTEYESVSKQFSDANPLMDNAEVPYRTGFGN
HH22   121  VIEPKSAWVKQNLNKDWSEITDKAMETDDWTEYESVSKQFSDANPLMDNAEVPYRTGFGN  180

TX0104 181  LNLANWIAQNVPEDSSYIN-----PSQLPKWLTITESNKASIVNSSQFSADGFYYFDNKA  235
            LNLANWIAQNVPEDSSYIN     PSQLPKWLTITESNKASIVNSSQFSADGFYYFDNKA
HH22   181  LNLANWIAQNVPEDSSYINYIYINPSQLPKWLTITESNKASIVNSSQFSADGFYYFDNKA  240

TX0104 236  PLQTVSGYYNLDGTFTESNDTQNPYVHSYAIANLGLIPHASIKLDMTTEQKISNPNKEIT  295
            PLQTVSGYYNLDGTFTESNDTQNPYVHSYAIANLGLIPHASIKLDMTTEQKISNPNKEIT
HH22   241  PLQTVSGYYNLDGTFTESNDTQNPYVHSYAIANLGLIPHASIKLDMTTEQKISNPNKEIT  300

TX0104 296  VTYTVKNDGTSDLENITLSDIDFPAFNLKSGEEKTFSVAQIPNQQGIINTTVQGDLNYYY  355
            VTYTVKNDGTSDLENITLSDIDFPAFNLKSGEEKTFSVAQIPNQQGIINTTVQGDLNYYY
HH22   301  VTYTVKNDGTSDLENITLSDIDFPAFNLKSGEEKTFSVAQIPNQQGIINTTVQGDLNYYY  360

TX0104 356  DQVYLNPDTGETSTTPQKPMHLLTVTDDKQVTVTYPTTKQSTITVRYMDEEGNQLIDPIT  415
            DQVYLNPDTGETSTTPQKPMHLLTVTDDKQVTVTYPTTKQSTITVRYMDEEGNQLIDPIT
HH22   361  DQVYLNPDTGETSTTPQKPMHLLTVTDDKQVTVTYPTTKQSTITVRYMDEEGNQLIDPIT  420

TX0104 416  KTDIVGKEYSTEQKTFDGYQFEKLTGNASGVFTENDQEIVYVYKKIDVLKEENKAQINKT  475
            KTDIVGKEYSTEQKTFDGYQFEKLTGNASGVFTE+DQEIVYVYKKIDVLKEENKAQINKT
HH22   421  KTDIVGKEYSTEQKTFDGYQFEKLTGNASGVFTESDQEIVYVYKKIDVLKEENKAQINKT  480

TX0104 476  SNTEFKEENKVNDSVKMDNTSTGKKIDKSLPRTGFNNNLVLNTLGSALLVVSFVGFTVVF  535
            SNTEFKEENKVNDSVKMDNTSTGKKIDKSLPRTGFNNNLVLNTLGSALLVVSFVGFTVVF
HH22   481  SNTEFKEENKVNDSVKMDNTSTGKKIDKSLPRTGFNNNLVLNTLGSALLVVSFVGFTVVF  540

TX0104 536  VIKRLKQDK 544
            VIKRLKQDK
HH22   541  VIKRLKQDK 549
```

Figure S1. Amino acid alignment of HMPREF0346_1863 in *Enterococcus faecalis* HH22 and its homologue in *E. faecalis* TX0104. The underlined region corresponds to a gap between ORFs HMPREF0348_0427 and HMPREF0348_0428 in the *E. faecalis* TX0104 draft genome, which was sequenced in the present study.

Table S1: BLAST comparison of *E. faecalis* genomes. The score was calculated as number of identical nucleotides identified by BLAST divided by query ORF length. ORFs obtaining a score > 0.75 were predicted to be present in the draft genome.

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0001	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0002	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0003	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0004	1	0.99	1	1	1	1	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF0005	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0006	0.98	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.97	0.97	0.96	1	0.99	0.99	0.99	0.99
EF0007	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0008	1	0.99	1	1	0.99	1	1	1	1	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF0009	1	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99
EF0011	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1
EF0012	1	0.99	0.99	1	0.99	0.98	0.99	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1
EF0013	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99
EF0014	1	1	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF0016	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	1
EF0017	1	1	1	1	1	1	1	1	0.96	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0018	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	0.99
EF0019	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0020	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0021	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.65	1	1
EF0022	1	1	0.99	1	1	1	0.99	1	0.99	1	0.99	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1
EF0024	1	0.99	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0025	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.9	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0026	1	1	1	0.99	1	1	1	1	1	0.76	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF0027	1	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99
EF0028	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	0.99	0.99
EF0029	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0030	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0031	1	0.99	0.99	0.99	0.96	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.99	0.99	0.99
EF0032	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0033	1	0.97	0.98	0.98	0.98	0.97	0.98	0.97	0.98	0.97	0.99	0.97	0.97	0.98	0.97	0.97	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98
EF0034	1	0.99	0.99	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0035	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.64	0.99	0.99	0.99	0.99
EF0036	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99
EF0037	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0038	0.65	0.99	0.99	0.99	1	1	1	1	0.99	0.99	1	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1
EF0039	1	0.99	0.99	1	0.99	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99
EF0040	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0041	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0042	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	0.99	1
EF0043	1	0.99	0.99	1	1	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0044	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	0.99	0.99	1	1
EF0045	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99
EF0046	1	1	1	0.99	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF0047	1	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.98	0.98
EF0048	1	0.99	1	1	1	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1
EF0049	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0050	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0051	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0052	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
EF0053	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
EF0054	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
EF0055	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1
EF0056	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1	1
EF0057	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1
EF0058	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	0.99	1	0.99	0.99	1	1
EF0059	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0062	0.68	0.94	0.98	0.94	0.99	0.61	0.95	0.99	0.98	0.93	0.94	0.98	0.94	0.94	0.94	0.94	0.99	0.94	0.93	0.94	0.93	0.99	0.98	0.99
EF0063	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1
EF0064	1	1	1	0.99	0.99	1	1	1	0.99	1	0.99	1	0.94	1	0.94	0.94	1	0.99	1	0.99	1	0.99	1	1
EF0065	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF0066	1	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.68	0.69	0.98	1	1	0.99	0.99	1	0.98	0.98
EF0067	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99
EF0068	1	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0.99	0	0	0	0	0	0	0.99	0.99	0	0
EF0069	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0071	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0073	1	0.91	1	0.99	0.99	0.92	0.93	0.99	1	0.92	0.98	0.99	0.93	1	0	0.93	0.99	0.93	1	0.92	1	1	0.99	0.99
EF0074	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
EF0076	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99
EF0077	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0078	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0079	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0	1	0.99	1	1	0.99	1	0.99	0.99	0.99
EF0080	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99
EF0081	1	1	0.99	0.99	1	0.99	0.99	1	0.99	0.98	0.99	0.99	1	0.99	0.69	1	1	1	0.99	1	1	0.98	1	1
EF0082	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1	0	1	1	1	1	1	1	1	1	1
EF0083	1	1	1	0.99	1	1	1	1	0.99	0.99	1	1	0.99	1	0	0.99	1	1	1	1	1	1	1	1
EF0084	1	0.96	0.97	0.98	0.99	1	0.99	0.98	0.96	0.96	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	1	1	0.99	1	0.98
EF0085	1	0.97	0.97	0.98	1	0.99	0.99	0.99	0.98	0.96	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF0086	1	0.92	0.92	0.94	1	0.99	1	0.99	0.94	0.93	1	0.99	1	0.99	1	1	0.99	0.94	1	1	0.99	0.99	0.99	0.99
EF0089	1	0.97	0.97	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99
EF0090	1	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0091	1	0.96	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.99	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98
EF0092	1	0.95	0.96	0.94	0.97	0.97	0.96	0.96	0.96	0.98	0.97	0.96	0.96	0.96	0.96	0.96	0.96	0.97	0.97	0.97	0.97	0.96	0.97	0.96
EF0093	1	0.67	0.8	0.78	0.82	0.82	0.78	0.7	0.82	0.82	0.83	0.76	0.95	0.82	0.75	0.75	0.75	0.81	0.79	0.95	0.69	0.78	0.81	0.75
EF0094	1	0.98	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0095	1	0.99	0.99	0.98	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF0096	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0097	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0098	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	1
EF0099	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0100	1	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF0101	1	0.98	0.99	0.98	0.99	0.99	0.99	1	0.99	0.98	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.98	0.99
EF0102	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0103	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99	1
EF0104	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF0105	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	1	1	1	0.99	1	1
EF0106	1	0.98	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1
EF0107	1	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0108	1	0.99	0.99	1	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1
EF0109	1	0.62	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0110	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0111	1	0.96	0.96	0.96	0.96	0.97	0.97	0.97	0.99	0.97	0.97	0.97	0.96	0.97	0.96	0.96	0.95	1	0.96	0.97	0.97	0.97	0.96	0.96
EF0112	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
EF0113	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
EF0114	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1
EF0115	1	0.98	0.98	0.99	0.99	0.98	1	0.98	0.78	0.99	0.99	0.98	0.99	0.99	0.99	0.99	1	1	0.99	0.98	0.98	0.99	1	1
EF0116	1	0.97	0.97	0.98	0.99	1	0.98	0.98	0.98	0.97	0.98	0.98	0.99	0.98	0.99	0.99	0.98	1	0.98	0.98	0.98	0.98	0.98	0.98
EF0117	1	0	0.99	0.99	1	1	0	0.99	0.99	0	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99
EF0118	1	0	0.99	0.99	0.99	0.99	0	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0119	1	0	0.98	0.98	0.99	0.99	0	0.99	0.98	0	0.98	0.99	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.99	0.99	0.99
EF0120	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0121	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0122	1	0	0.98	0	0	0.99	0	0	0	0	0.98	0	0.99	0	0.99	0.99	0	0.99	0	0	1	0	0	0
EF0123	0.39	0	0.99	0	0	0.99	0	0	0	0	0.99	0	0.99	0	0.36	0.36	0	0.99	0	0	0.38	0	0	0
EF0124	0.55	0.91	0.94	0.9	0.91	1	0.91	0.92	0.91	0.91	0.95	0.92	0.94	0.92	0.94	0.94	0.91	1	0	0.92	0.94	0.91	0.91	0.91
EF0125	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EF0126	1	0	0	0	0.13	1	0	0.13	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0.13	0
EF0127	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0128	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0129	0	0	0.14	0.14	0.14	0.29	0.14	0.39	0	0	0.12	0.65	0	0	0	0	0.14	0	1	0	0	0.14	0.14	0.14
EF0130	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0131	0	0	0	0.6	0	0.92	0	0.92	0	0	0.6	0.92	0	0	0	0	0	0	1	0	0	0	0	0
EF0132	0	0	0	0	0	0.93	0	0.93	0	0	0	0.93	0	0	0	0	0	0	1	0	0	0	0	0
EF0133	0	0	0.54	0	0	0.82	0	0.83	0	0	0	0.82	0	0	0	0	0	0	1	0	0	0	0	0
EF0134	0	0	0	0	0	0	0	0.93	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0135	0	0	0	0	0	0.51	0	0.7	0	0	0	0.51	0	0	0	0	0	0	1	0	0	0	0	0
EF0136	0	0	0	0	0	0.43	0	0.45	0	0	0	0.42	0	0	0	0	0	0	1	0	0	0	0	0
EF0137	0	0	0	0	0	0.79	0	0.67	0	0	0	0.79	0	0	0	0	0	0	1	0	0	0	0	0
EF0138	0	0	0	0	0	0.72	0	0.61	0	0	0	0.72	0	0	0	0	0	0	1	0	0	0	0	0
EF0139	0.06	0	0.23	0	0	0.86	0.06	0.84	0	0	0	0.85	0.23	0.06	0.23	0.23	0	0	1	0.06	0	0.06	0.06	0
EF0140	0	0	0	0	0	0.34	0	0.34	0	0	0	0.34	0	0	0	0	0	0	1	0	0	0	0	0
EF0141	0	0	0	0	0	0.86	0	0	0	0	0	0.86	0	0	0	0	0	0	1	0	0	0	0	0
EF0142	0	0	0	0	0	0	0	0.44	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0143	0	0	0.5	0	0	0.84	0	0.92	0	0	0	0.84	0	0	0	0	0	0	1	0	0	0	0	0
EF0144	0	0	0	0	0	0.38	0	0.38	0	0	0.26	0.38	0	0	0	0	0	0	1	0	0	0	0	0
EF0145	0	0.92	0.93	0.31	0	0	0	0.95	0.94	0	0	0.94	0.95	0	0.92	0.92	0.74	0.94	1	0	0	0	0.93	0.93
EF0146	0.24	0.9	0.82	0.88	0	0	0	0.64	0.52	0	0	0.9	0.9	0	0.9	0.9	0.9	0.82	0.88	0	0	0	0.88	0.91
EF0147	0	0	0	0	0	0	0	0.93	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0149	0.16	0.21	0.88	0.88	0	0.31	0.88	0.53	0	0	0.88	0.54	0.86	0	0.37	0.37	0.54	0.89	0.62	0	0	0.86	0.88	0.54
EF0150	0	0	0	0.6	0	0	0	0	0	0	0.6	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0151	0	0	0	0.89	0	0.19	0	0.18	0	0	0.89	0.19	0	0	0	0	0	0	1	0	0	0	0	0
EF0152	0	0	0	0.97	0	0.3	0	0.3	0	0	0.97	0.3	0	0	0	0	0	0	1	0	0	0	0	0
EF0153	0.5	0.43	0.43	0.73	0	0.62	0.62	0.44	0	0	0.94	0.49	0.43	0	0.44	0.44	0	0.43	1	0	0	0.43	0.62	0
EF0154	0	0	0	0.97	0	0.62	0	0.61	0	0	0.97	0.62	0	0	0	0	0	0	1	0	0	0	0	0
EF0155	0	0	0	0.92	0	0.74	0	0.74	0	0	0.92	0.74	0	0	0	0	0	0	1	0	0	0	0	0
EF0156	0	0	0	0.97	0	0.8	0	0.77	0	0	0.97	0.8	0	0	0	0	0	0	1	0	0	0	0	0
EF0157	0	0	0	0.96	0	0.41	0	0	0	0	0.96	0.41	0	0	0	0	0	0	1	0	0	0	0	0
EF0158	0	0	0	0.95	0	0.72	0	0.73	0	0	0.95	0.72	0	0	0	0	0	0	1	0	0	0	0	0
EF0159	0	0	0	0.92	0	0.46	0	0.46	0	0	0.92	0.46	0	0	0	0	0	0	1	0	0	0	0	0
EF0160	0	0	0	0.96	0	0.66	0	0.66	0	0	0.96	0.66	0.06	0	0	0	0.12	0	1	0	0	0	0	0.06
EF0161	0	0	0	0.93	0	0	0	0	0	0	0.93	0	0.73	0	0.73	0.73	0	0	1	0	0	0.72	0	0
EF0162	0	0	0	0.98	0	0.64	0	0.62	0	0	0.98	0.64	0	0	0	0	0	0	1	0	0	0	0	0
EF0163	0	0	0	0.97	0	0.4	0	0.4	0	0	0.97	0.4	0	0	0	0	0	0	1	0	0	0	0	0
EF0164	0	0	0	0.46	0	0.44	0	0.43	0	0	0.46	0.44	0	0	0	0	0	0	1	0	0	0	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0165	0.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0.5	0.5	0	0
EF0166	0.57	0	0.08	0	0.08	0.76	0	0.3	0	0	0.08	0.3	0.08	0	0.08	0.08	0	0	1	0	0.6	0.6	0	0
EF0167	1	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.9
EF0168	1	0.99	1	0.99	1	1	1	0.99	0.99	0.99	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1
EF0169	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0170	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1
EF0171	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99
EF0172	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1
EF0173	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0174	1	1	0.99	1	1	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	1	0.99	1	1
EF0175	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99
EF0176	1	0.99	1	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1	1
EF0177	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0178	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99
EF0179	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0180	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0183	1	0.39	0.99	0.7	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.38	0.99	0.99	0.39	0.99	0.99	0.99	0.99	0.98	0.39	0.39
EF0184	1	0	0.99	0	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0	0.99	0.99	0	0.98	0.99	0.99	0.99	0.99	0	0
EF0185	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0186	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0187	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0188	1	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99
EF0191	1	0.98	0.99	0.99	0.99	0.72	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0192	1	0.98	0.99	0.99	0.98	0.99	0.99	1	0.98	0.98	0.99	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.98	0.98	1	1
EF0193	1	0.98	0.99	0.99	1	0.86	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0194	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.94	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0195	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1
EF0196	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	1	1	0.99	1	0.99	0.99
EF0197	1	0.98	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	1	1	1	1	0.99	0.99	1	0.99	1	1
EF0198	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0199	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0200	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0201	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0202	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0203	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	0.73	1	1	1	1
EF0205	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0206	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0207	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.67	1	1	1	1
EF0208	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0209	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0210	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0211	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0212	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF0213	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0214	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0215	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0216	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0217	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0218	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0219	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0220	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0221	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0223	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0224	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0225	1	1	0.99	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99	0.98	1	1	1	1	1	0.99	1	1
EF0226	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0227	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0228	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0229	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0230	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0231	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0232	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0233	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0234	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0235	1	0.99	1	0.54	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF0236	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0237	1	1	1	0.99	1	0.99	1	0.99	1	0.99	1	0.99	1	1	1	1	0.99	1	1	1	1	1	0.99	0.99
EF0238	1	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99
EF0239	1	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.99	0.99	0.99	0.99	0.98	1	0.99	0.98	0.99	0.98	0.98	0.98
EF0241	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF0243	1	0.99	1	1	1	1	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99
EF0244	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.97	1	0.97	0.98	0.98	0.98	0.98	0.98	1	1	0.98	0.98	0.98	0.98	0.98
EF0245	1	0.98	0.97	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.98	1	0.99	0.99	0.98	0.99	0.98	0.98
EF0246	1	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0247	1	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99	1	1
EF0248	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0249	0.64	0.99	1	0.99	1	0.98	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	1	1	1
EF0250	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99
EF0251	1	0.99	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0252	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0253	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.5	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0255	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0256	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0257	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0258	1	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	1	1
EF0259	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0260	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF0261	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0262	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0263	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0264	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0265	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99
EF0266	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0267	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0268	1	0.99	0.99	0.99	0.96	0.99	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.97
EF0269	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	1	1	0.99	1	1	1	1	0.99	1	1	0.05	1	1
EF0270	1	0.99	1	0.99	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	0.59	1	1
EF0271	1	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99	0.99	1	1	1	0.99
EF0272	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF0273	1	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99
EF0274	1	0.97	0.97	0.99	0.97	0.97	0.96	0.99	0.99	0.97	0.99	0.99	0.98	0.97	0.98	0.98	0.97	0.99	0.98	0.99	0.97	0.98	0.97	0.97
EF0275	1	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0277	1	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.97	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98
EF0278	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0279	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF0280	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0281	1	0.98	0.98	0.98	0.98	0.97	0.98	0.98	0.98	0.99	0.97	0.98	0.98	0.98	0.98	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.97
EF0282	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0283	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0284	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1
EF0285	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1	1
EF0286	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0287	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0288	1	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF0289	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0290	1	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0291	0.51	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0292	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF0293	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.95
EF0294	1	0.99	0.99	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1
EF0295	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1
EF0296	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0297	1	0.98	0.98	0.98	0.98	0.98	0.97	0.98	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.98	0.98	0.99	0.98	0.98
EF0298	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0299	1	1	1	1	0.99	0.99	0.99	1	0.98	0.99	0.99	0.76	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.62	0.99
EF0300	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0301	1	1	1	0.99	1	1	1	0.99	1	1	1	0.99	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0302	0.95	0.94	0.95	0.95	0.95	0.94	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.94	0.95	0.95	0.95	0.95	0.95	0.95	0.94
EF0303	0	0	0	0.06	0.06	0.98	0	0.06	0	0	0.06	0	0.06	0	0.06	0.06	0	0	0	0	0.06	0	0.06	0.06
EF0304	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0305	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0306	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0307	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0308	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0309	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0310	0	0	0	0	0	0.99	0	0.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.48
EF0311	0	0.98	0	0	0	0.97	0	0	0.91	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0312	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0313	0	0	0.76	0.83	0	0.9	0	0.85	0.91	0	0	0.78	0	0	0	0	0.79	0	0	0	0.85	0	0	0
EF0314	0	0.95	0	0	0	0.97	0	0	0.73	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0315	0	0.73	0	0	0	0.74	0	0	0.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0316	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0317	0	0.95	0	0	0	0.95	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0318	0	0.64	0	0	0	0.89	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0319	0	0.99	0	0	0	0.97	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0320	0	1	0	0	0	0.98	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0321	0	1	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0322	0	1	0	0	0	0.97	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0323	0	0.69	0	0	0	0.71	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0324	0	0.95	0	0	0	0.98	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0325	0	0.95	0	0	0.36	0.94	0.36	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0326	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0327	0	0.97	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0328	0	0.94	0	0	0	0.93	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0329	0	0.93	0	0	0	0.93	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0330	0	0.95	0	0	0.52	0.97	0.52	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0331	0	0.92	0	0	0	0.86	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0332	0.64	0.66	0	0	0	0.88	0.47	0	0	0	0	0	0	0	0	0	0	0	0.47	0	0	0	0	0
EF0333	0	0	0	0	0	0.91	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0334	0	0	0	0	0	0.95	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0335	0	0	0	0	0	0.98	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0336	0	0	0	0	0	0.97	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0337	0	0	0	0	0	0.82	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0338	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0339	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0.64	0	0	0.64	0	0	0	0.64
EF0340	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0341	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0342	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0343	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0344	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0345	0	0	0	0	0	0.95	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0346	0	0	0	0	0	0.92	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0347	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0348	0	0.02	0	0	0	0.99	0	0	0.02	0	0	0.02	0	0	0	0	0	0	0.02	0	0	0	0	0
EF0349	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0350	0	0.18	0	0	0	0.99	0	0	0.18	0	0	0.33	0	0	0	0	0.33	0	0.18	0	0	0	0	0.38
EF0351	0	0.74	0	0	0	0.79	0	0	0.63	0	0	0.72	0	0	0	0	0.17	0	0.61	0	0	0	0	0.72
EF0352	0.24	1	0	0	0	1	0	0	0.09	0.23	0.25	0.1	0.54	0	0.54	0.54	0	0	0.23	0	0	0	0.23	0.09
EF0353	0	1	0	0	0	1	0	0	0	0	0.63	0	0	0	0	0	0	0	0	0	0	0	0	0
EF0354	0	1	0.89	0.95	0	1	0	0.76	0	0	0.86	0	0.89	0	0.89	0.89	0	0	0	0	0	0.87	0	0.87
EF0355	0.47	0.48	0.93	0.96	0.47	0.59	0.59	0.96	0.48	0	0.96	0.91	0.57	0	0.57	0.57	0.94	0	0	0	0.89	0.57	0.47	0.91
EF0356	0.77	0.75	0.75	0.74	0.75	0.6	0.75	0.75	0.74	0.74	0.75	0.75	0.75	0.75	0.41	0.39	0.75	0.77	0.75	0.74	0.75	0.72	0.75	0.75
EF0357	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.84	0.98	1	0.99	0.99	0.99	0.98	0.99	0.98
EF0358	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99
EF0359	1	0.99	0.98	0.98	0.97	0.97	0.98	0.97	0.98	0.98	0.97	0.97	0.98	1	0.98	0.98	0.98	0.97	0.98	0.97	0.97	0.98	0.97	0.98
EF0360	1	0.99	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.97	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.97	0.98	0.99	0.98	0.99
EF0361	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.56	0.99	0.99	0.99	0.99	1
EF0362	1	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1
EF0363	0.69	0.69	0	0.66	0.69	0.69	0.56	0.64	0.56	0	1	1	0.69	0	0.69	0.69	0.66	0	1	0.46	0.56	0.66	0.69	0.66
EF0365	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.93	1	0.99	0.99	0.99	0.99
EF0366	1	0.93	0.99	0.99	0.99	1	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	1	1	1	1	1	0.99	1	1
EF0367	1	0.98	0.99	0.99	0.98	1	0.99	1	0.99	0.95	0.99	1	0.99	0.99	0.99	0.99	1	1	0.98	0.99	0.99	0.99	0.99	1
EF0368	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.98	0.99	0.98	0.98	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0369	1	0.99	1	0.99	1	1	1	1	0.56	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF0370	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.68	0.99	1	0.99	0.99
EF0371	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0372	1	0.99	1	1	1	0.99	0.99	1	1	0.98	1	1	0.98	0.99	0.98	0.98	0.99	1	1	0.99	1	0.99	1	0.99
EF0373	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0374	1	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF0375	1	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1
EF0376	1	0.27	0.87	0.93	1	0.99	1	1	0.87	0.89	0.99	1	0.95	1	0.95	0.95	1	0.9	1	1	1	1	1	1
EF0377	1	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0378	1	0.44	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0379	1	0	0	1	1	1	1	1	0	0	0.99	1	0	1	0	0	1	1	1	1	0	0	0	1
EF0380	1	0	0	1	1	1	1	1	0	0	1	1	0	1	0	0	1	1	1	1	0	0	0	1
EF0381	1	0.97	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.98	0.98	0.99
EF0382	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0383	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0384	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0385	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0386	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	1	0.99	1	1	1	0.99
EF0387	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0388	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0389	1	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	1	1	0.99	1	1	0.99	1	1	1	1	1	1	0.99
EF0390	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.97	1	0.99	0.99
EF0392	1	0.29	0.18	0.99	0.99	1	1	0.99	0.99	0.16	0.99	0.99	0.16	1	0.16	0.15	0.99	1	0.99	0.96	0.99	0.99	0.99	0.99
EF0393	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0394	1	0.74	0.71	0.94	0.98	0.98	0.93	0.94	0.98	0.7	0.98	0.94	0.94	0.94	0.94	0.94	0.98	0.98	0.98	0.94	0.98	0.98	0.98	0.98
EF0395	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.98	0.99	0.98	0.99
EF0396	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF0397	1	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.99	0.98	0.99	0.98	0.98	1	1	0.98	0.99	0.98	0.98	0.98	1
EF0398	1	1	1	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	1
EF0399	1	0.99	1	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	0.99	1	0.99	1	1	0.99	1	0.99
EF0400	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0401	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0402	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0403	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF0404	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99
EF0405	1	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.98	1	0.98	0.99	0.99	0.98	0.99	0.99
EF0406	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0407	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1
EF0408	1	0.99	0.99	0.98	0.99	1	0.99	1	0.99	0.97	0.99	1	0.99	0.99	0.99	0.99	0.98	1	1	0.99	0.99	1	0.99	0.98
EF0409	1	1	1	0.99	1	0.65	1	1	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	1	0.99
EF0411	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	0.99	1	1
EF0412	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0413	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0414	1	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0415	1	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99
EF0417	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF0418	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99
EF0419	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	1	1	1	1	0.99	1	0.98	1	0.99	0.99	0.99	0.99
EF0420	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0421	1	0.99	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0422	1	0.99	1	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	0.99	1	0.99
EF0423	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0424	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	1
EF0425	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0426	1	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	1	0.99	1
EF0428	1	0	0	1	1	1	1	1	0	0.99	1	1	0	1	0	0	1	1	1	1	1	1	1	1
EF0429	1	0	0	1	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0	0.99	0	0	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0430	1	0	0	1	1	0.99	1	1	0	1	1	1	0	1	0	0	1	1	0.99	1	1	1	1	1
EF0431	1	0	0	1	1	1	1	1	0	0.99	1	1	0	0.99	0	0	1	1	1	1	0.99	1	0.99	1
EF0432	1	0	0	0.99	1	1	1	1	0	0.99	1	1	0	0.99	0	0	0.99	1	1	0.99	1	1	1	0.99
EF0433	1	0	0	0.99	1	0.99	0.99	0.99	0	0.99	0.99	0.99	0	1	0	0	0.99	1	0.99	0.99	1	1	1	0.99
EF0434	1	0	0	1	0.99	1	0.99	0.99	0	0.99	0.99	0.99	0	0.99	0	0	1	1	0.99	0.99	1	0.99	1	1
EF0435	1	0	0	0.99	1	0.99	1	0.99	0	0.99	0.99	0.99	0	0.99	0	0	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0436	1	0	0	0.98	0.99	0.98	0.99	0.97	0	0.98	0.97	0.97	0	0.99	0	0	0.99	1	0.97	0.99	0.98	0.99	0.98	0.99
EF0437	1	0	0	0.99	0.99	1	0.99	0.99	0	1	0.99	0.99	0	0.99	0	0	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0438	1	0	0	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0	0.99	0	0	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF0439	1	0.99	0.99	1	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1
EF0440	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0441	1	0.95	0.96	0.96	0.96	0.96	0.96	1	0.96	1	1	1	1	1	1	1	0.96	1	0.96	1	1	0.95	1	0.96
EF0442	1	0.96	0.96	0.97	0.96	0.97	0.98	0.98	0.96	0.97	0.99	0.98	0.96	1	0.96	0.96	0.97	1	0.96	0.98	0.97	0.96	0.97	0.97
EF0443	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1
EF0444	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.91	1	1	0.96	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0445	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0446	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0447	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0448	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0449	1	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.99
EF0450	1	0.98	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.96	0.99	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.99
EF0451	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0	0.99	0.98	0.99	0.98	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1
EF0452	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0453	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0454	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	0.99
EF0455	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0456	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	0.99	1	0.99	1
EF0457	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0458	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	1	1	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99
EF0459	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0460	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0461	1	0.99	1	0.99	0.99	0.99	1	0.55	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99
EF0462	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0463	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0464	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0465	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0466	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0467	1	0.99	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0468	0.99	0.99	0.99	0.99	0.99	0.99	0	0.98	0	0	0.99	0.98	1	0.98	1	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99
EF0469	1	0.99	1	1	1	1	0.04	0.99	0.03	0.04	1	1	1	1	1	1	1	1	0.99	1	1	0.99	1	1
EF0470	1	0.99	0.99	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF0471	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	1	1	1	0.99	1	1	1	1	1	1	0.99	1	0.99	1
EF0472	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	1	0.99	1
EF0473	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0475	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0476	1	0.98	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0477	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	0.99
EF0478	0.99	0.91	0	0.98	0.98	0.98	1	0.98	0	0	1	0.98	0.98	0	0.98	0.98	0.98	0	1	0	0.98	0.98	0.98	0.98
EF0479	1	0.99	0	1	1	1	1	1	0	0	1	1	1	0	1	1	1	0	1	0	1	1	1	1
EF0480	1	1	0	1	1	1	1	1	0	0	1	1	1	0	1	1	1	0	1	0	1	1	1	1
EF0481	1	0.95	0	0	0.85	1	1	1	0	0	1	1	1	0	1	1	0	0	1	0	0.95	1	0.97	0
EF0482	0.86	1	0	0	0.86	1	1	1	0	0	1	1	1	0.28	0.87	1	0	0	1	0	1	1	1	0
EF0485	0.16	0.22	0.96	0.95	0	0.33	1	0.56	0	0	1	0.55	0.94	0	0.41	0.41	0.55	0.96	0.53	0	0	0.94	0.95	0.55
EF0486	0.52	0.73	0.96	0.94	0	0.97	1	0.96	0	0	0.55	0.98	0.94	0	0.84	0.83	0.96	0.94	0.22	0	0	0.94	0.96	0.94
EF0487	0.99	0.71	0	0	0	0.84	1	0.99	0	0	0.99	0.99	0	0	0.98	0.98	0.97	0	0	0	0	0	0.48	0
EF0488	1	0	0	0	0	1	1	0.7	0	0	1	1	0	0	1	1	0	0	1	0	0	0	1	0
EF0489	0.98	0	0	0	0	0.98	1	0.98	0	0	0.63	0.98	0	0	0.98	0.98	0	0	0.99	0	0	0	0.98	0
EF0490	0.94	0.48	0.48	0.47	0	0.94	0.72	0.38	0	0	0.94	0.94	0.47	0	0.93	0.9	0	0.47	0.94	0.13	0	0.47	0.93	0
EF0491	0.98	0	0	0	0	0.99	1	0.42	0	0.05	0.41	0.99	0	0	0.88	0.88	0	0	0.99	0	0	0	0.99	0
EF0492	0.99	0	0	0	0	0.99	1	0.22	0	0	0.41	0.98	0	0	0.98	0.98	0	0	0.98	0	0	0	0.98	0
EF0493	0.99	0	0	0	0	0.99	1	0.99	0	0	0.25	0.99	0	0	0.99	0.99	0	0	1	0	0	0	0.99	0
EF0494	1	0	0	0	0	1	1	0.77	0	0	1	0.99	0	0	0.99	0.99	0	0	0.98	0	0.46	0	0.99	0
EF0495	0.99	0	0	0	0	0.99	1	0.99	0	0	0.33	0.99	0	0	0.98	0.98	0	0	1	0	0.58	0	0.99	0
EF0496	1	0	0	0	0	0.99	1	1	0	0	1	0.99	0	0	1	1	0	0	1	0	1	0	0.99	0
EF0497	1	0	0	0	0	1	1	0.33	0	0	1	0.99	0	0	1	1	0	0	1	0	1	0	1	0
EF0498	1	0	0	0	0	1	1	0	0	0	1	0	0	0	1	1	0	0	1	0	1	0	0	0
EF0499	1	0.72	0.72	0.6	0.49	1	1	1	0.49	0.48	0.71	0.7	0.53	0.49	1	1	0.49	0.73	0.7	0.49	1	0.49	0.7	0.53
EF0500	1	0.99	0	0	0	0.99	1	0.3	0	0	0.31	0.98	0	0	0.99	0.99	0	0	0.99	0	0.99	0	0.99	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0501	0.32	0.76	0	0	0	0.32	1	0.99	0	0	1	0.76	0	0	0.76	0.76	0	0	0.76	0	0.76	0	0.76	0
EF0502	0.97	0.51	0	0	0	0.96	1	0.73	0	0	0.43	0.97	0.5	0	0.5	0.48	0	0	0.97	0	0.97	0	0.97	0
EF0503	0.66	0.95	0.19	0	0	0.97	1	0.9	0	0	0.67	0.98	0.98	0	0.95	0.95	0	0	0.98	0	0.99	0	0.99	0
EF0504	0.56	0.48	0.99	0	0	0.56	1	0.99	0	0	0	0.99	1	0	0	0	0	0	0.99	0	0.99	0	0.99	0
EF0505	0.89	0.73	1	0	0	0.89	1	0.76	0.89	0	1	1	1	0	0	0.51	0	0	1	0	0.99	0	0.99	0
EF0506	0.46	0.38	0.94	0	0	0.99	1	0.72	0.99	0	0.61	0.94	0.99	0	0.33	0.79	0	0	0.98	0	0.99	0	0.99	0
EF0507	0.98	0.98	0	0	0	0.99	1	0.98	0.98	0	0.7	0	0.98	0	0.98	0.98	0	0	0.98	0	0.98	0	0.99	0
EF0508	1	1	0	0	0	0.96	1	0.96	0.96	0	1	0	1	0	1	1	0	0	1	0	0.99	0	0.97	0
EF0509	1	1	0	0	0	0	1	0	0.56	0	1	0	0.98	0	0.98	0.98	0	0	1	0	0.98	0	0	0
EF0510	0.98	0.98	0.61	0.47	0	0.99	1	0.99	0.99	0	0.71	0.61	1	0	1	1	0	0.47	0.98	0	1	0	0.99	0.46
EF0511	0.99	0.99	0.82	0.81	0	0.96	1	0.87	0.99	0	0.81	0	0.87	0	0.87	0.87	0	0.82	0.99	0	0.99	0	0.99	0.82
EF0512	1	0.55	0	0	0	1	1	0.99	1	0	0	0	0.99	0	0.24	0.24	0	0	1	0	1	0	1	0
EF0513	0.99	0.67	0	0	0	0.99	1	1	1	0	0	0	1	0	0.78	0.78	0	0	1	0	1	0	1	0
EF0514	1	1	0.81	0.77	0.99	1	1	0	0.99	0	0.9	1	1	0	0.83	0.79	0.77	0	0.39	0.99	0.76	0.82	0.76	0.77
EF0516	0.68	1	0.68	1	1	0.68	1	0.68	1	0.68	1	0.68	0.68	0.68	0.68	0.68	1	0.52	1	1	1	1	1	1
EF0517	0.64	1	0.64	1	1	0.64	1	0.64	1	0.64	1	0.64	0.64	0.64	0.64	0.64	1	0.64	1	1	0.82	1	1	1
EF0518	0.23	0	0	0.42	0	0.81	1	0.81	1	0	1	0	0	0	0	0	0	0	1	1	1	0	0	0
EF0519	0	0.21	0.23	0.25	0.25	0	1	0	0.77	0	1	0	0	0	0.21	0.21	0.25	0	1	0.77	1	0.22	0.22	0.25
EF0520	0.39	0.39	0.49	0.47	0.47	0.38	1	0	0.99	0	1	0.39	0.39	0	0.38	0.39	0.47	0	1	0.99	0.96	0.43	0.43	0.47
EF0521	1	0	0	1	1	1	1	1	1	0	1	1	0	0	0	0	1	0	1	1	1	1	1	1
EF0522	1	1	0.81	0.77	0.99	1	1	0	0.99	0	0.9	1	1	0	0.83	0.79	0.77	0	0.39	0.99	0.76	0.82	0.76	0.77
EF0523	0.97	0.96	0.98	0.97	0.34	0.97	1	0.98	0	0.35	1	0.35	0.35	0	0.35	0.35	0.35	0.97	0.88	0.34	1	0.35	0.35	0.35
EF0524	0	0	0.21	0	0	0	1	1	0	0	1	1	1	0	0	0	0.98	0	1	0	1	0	0	1
EF0525	0	0	0	0	0	0	1	1	0	0	1	1	1	0	0	0	1	0	1	0	1	0	0	1
EF0526	0	0	0	0	0	0	1	1	0	0	1	1	1	0	0	0	0.99	0	0.99	0	1	0	0	1
EF0527	0	0	0	0	0	0	1	1	0	0	1	1	1	0	0	0	1	0	0.99	0	1	0	0	1
EF0528	0	0	0	0	0.12	0	0.98	0.98	0	0	0.98	0.98	0.98	0	0	0	0.98	0	0.97	0	0.98	0	0	0.98
EF0529	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EF0530	0	0	0	1	1	1	1	1	0	0	1	1	0	0	0	0	0	0	1	0	1	0	1	1
EF0531	0	0	0	1	1	1	1	1	0	0	1	1	0	0	0	0	0	0	1	0	1	0	1	1
EF0532	0	0	0	0.99	0.99	0.99	1	0.99	0	0	1	0.99	0	0	0	0	0	0	1	0	0.99	0	0.99	0.99
EF0533	0	0	0	1	1	1	1	1	0	0	1	1	0	0	0	0	0.91	0	1	0	1	0	1	1
EF0534	0	0	0	0.64	0.64	0.64	1	0.64	0	0	1	0.64	0	0	0	0	0.97	0	1	0.8	0.64	0	0.64	0.64
EF0536	0	0.36	0.36	0.7	0.7	0.7	1	0.7	0	0	1	0.7	0.36	0	0.36	0.36	0.68	0	1	0.63	0.7	0.14	0.7	0.7
EF0538	0.44	0.5	0.8	0.52	0.51	0.51	1	0	0	0	1	0.51	0.5	0	0.5	0.5	0	0.52	1	0	0.51	0	0.51	0.51
EF0539	1	1	0	1	1	1	1	1	0	0	1	1	0	0	0	0	0	0.1	1	0	1	0	1	1
EF0540	1	1	0.48	0.99	0.99	0.99	1	1	0.49	0.34	1	0.99	0.34	0.34	0	0.34	0.34	0.49	1	0.34	0.99	0.34	0.98	0.99
EF0541	1	1	0.11	1	0.99	0.99	1	1	0.11	0.11	1	0.99	0.11	0.11	0.11	0.11	0.11	0.11	1	0.11	0.99	0.11	0.99	1
EF0542	1	1	0	1	1	1	1	1	0	0	1	1	0	0	0	0	0	0	1	0	1	0	1	1
EF0543	1	1	0	0.99	0.99	0.99	1	0.99	0	0	1	0.99	0	0	0	0	0	0	1	0	0.99	0	0.99	0.99
EF0544	1	1	0	1	1	1	1	0.99	0	0	1	1	0.68	0	0.68	0.68	0	0.97	1	0	1	0	0.99	1
EF0545	1	1	0	0.99	0.99	0.99	1	0.98	0	0	1	0.99	0	0	0	0	0	0.98	1	0	0.99	0	0.99	0.99
EF0546	0.97	0.97	0	0.97	0.97	0.97	0.99	0.99	0	0	0.99	0.99	0.46	0	0.46	0.46	0	0.99	1	0	0.97	0	0.94	0.97
EF0547	0.98	0.98	0	0.98	0.98	0.98	1	0.99	0	0	0.98	0.98	0	0	0	0	0	0	1	0	0.98	0	0.98	0.98
EF0548	0.96	0.97	0	0.99	0.99	0.99	1	0.99	0	0	0.99	0.99	0	0	0	0	0	0	1	0	0.99	0	0.99	0.99
EF0549	1	0.99	0	1	1	1	1	1	0.96	0	1	1	1	0	1	1	0	0.96	1	0.14	1	0	1	1
EF0550	1	1	0	1	1	1	1	1	0	0	1	0.03	0.03	0	0.03	0.03	0	0	1	0	1	0	1	1
EF0551	1	1	0	1	1	1	1	1	0	0	1	0	0	0	0	0	0	0	1	0	1	0	1	1
EF0552	1	1	0.14	1	1	1	1	1	0	0.14	1	0.14	0.14	0.14	0.14	0.14	0.14	0.14	1	0.14	1	0	1	1
EF0553	1	1	0.24	1	1	1	1	1	0	0.41	1	0.41	0.41	0.41	0.41	0.41	0.41	0.4	1	0.4	1	0	1	1
EF0554	1	1	0.36	0.99	0.99	0.99	1	0.99	0.37	0.37	0.99	0.36	0.36	0.36	0.36	0.36	0.36	0.36	1	0.36	0.99	0.36	0.99	0.99
EF0555	1	1	0.19	1	1	1	1	1	0.19	0.19	1	0.19	0.19	0.19	0.19	0.19	0.19	0.19	1	0.19	1	0.19	1	1
EF0556	1	1	0	1	1	1	1	1	0	0	1	0	0	0	0	0	0	0	1	0	1	0	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0557	1	1	0	0.99	0.99	0.99	1	0.99	0	0.6	0.99	0	0	0	0	0	0	0	1	0	0.99	0	0.99	0.99
EF0559	1	1	0	0.06	0.06	0.06	1	0.06	0	0	0.06	0.05	0	0	0	0	0	0	1	0	0.05	0	0.05	0.06
EF0561	0.95	0.98	0	0	0	0	1	0.97	0	0	0.98	0.97	0.98	0	0	0	0.98	0	0.61	0	0.98	0	0	0.98
EF0562	0.84	1	0	0	0	0	1	0	0	0	0	0.95	0	0	0	0	0	0.95	0	0	0	0	0	0
EF0563	1	1	0	0	0	0	1	0	0	0	0	0.97	0	0	0	0	0	0.97	1	0	0	0	0	0
EF0564	1	0.99	0	0	0	0	1	0	0	0	0	0.93	0	0	0	0	0	0.93	1	0	0	0	0	0
EF0566	1	1	0	0	0	0	1	0	0	0	0	0.94	0	0	0	0	0	0.94	0.99	0	0	0	0	0
EF0567	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0568	1	1	0.08	0.08	0.08	0.08	1	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	1	0.08	0.08	0.08	0.08	0.08
EF0569	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0570	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0571	1	1	0.3	0.3	0.3	0.3	1	0.3	0.3	0.29	0.3	0.3	0.29	0.29	0.29	0.29	0.29	0.3	1	0.29	0.29	0.3	0.29	0.29
EF0573	0.12	0.16	0	0	0	0	0.41	0	0	0	0	0	0	0	0	0	0	0	0.16	0	0	0	0	0
EF0574	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0575	1	1	0.51	0.99	0.99	0.99	1	0.99	0.51	0.51	0.99	0.51	0.99	0.51	0.99	0.99	0.51	0.51	1	0.51	0.99	0.51	0.99	0.99
EF0576	1	1	0.63	0.98	0.98	0.98	1	0.98	0.63	0.63	0.98	0.63	0.98	0.63	0.98	0.98	0.63	0.63	1	0.63	0.98	0.63	0.98	0.98
EF0577	1	1	0.57	0.98	0.98	0.98	1	0.98	0.57	0.57	0.98	0.57	0.98	0.57	0.98	0.98	0.57	0.57	1	0.57	0.98	0.57	0.98	0.98
EF0578	1	0.99	0	1	1	1	1	1	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	1
EF0579	1	1	0	1	1	1	1	1	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	1
EF0580	1	1	0	1	1	1	1	1	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	1
EF0581	1	1	0.04	0.99	0.99	0.99	1	0.99	0.04	0	0.99	0	0.99	0	0.99	0.99	0	0.04	1	0	0.99	0	0.99	0.99
EF0582	1	1	0	0.98	0.98	0.98	1	0.98	0	0	0.98	0	0.98	0	0.98	0.98	0	0	1	0	0.98	0	0.98	0.98
EF0583	1	1	0.04	0.99	0.99	0.99	1	0.99	0.1	0.14	0.99	0.14	0.99	0.14	0.99	0.99	0.1	0.14	1	0.14	0.99	0.1	0.99	0.99
EF0584	1	1	0.21	0.99	0.99	0.99	1	0.99	0.21	0.21	0.99	0.21	0.99	0.21	0.99	0.99	0.21	0.21	1	0.22	0.99	0.21	0.99	0.99
EF0585	1	1	0.72	0.96	0.96	0.96	1	0.96	0.72	0.72	0.96	0.72	0.96	0.72	0.96	0.96	0.72	0.72	1	0.72	0.96	0.72	0.96	0.96
EF0586	1	1	0	0.98	0.98	0.98	1	0.98	0	0	0.98	0.66	0.98	0	0.98	0.98	0	0.66	1	0	0.98	0	0.98	0.98
EF0587	1	1	0	0.97	0.97	0.97	1	0.97	0	0	0.97	0	0.97	0	0.97	0.97	0	0	1	0	0.97	0	0.97	0.97
EF0588	1	0.99	0.49	0.97	0.97	0.97	0.99	0.97	0.49	0.49	0.97	0.49	0.97	0.49	0.97	0.97	0.49	0.49	1	0.49	0.97	0.49	0.97	0.97
EF0589	1	0.99	0.66	0.96	0.96	0.96	1	0.96	0.66	0.65	0.96	0.65	0.96	0.66	0.96	0.96	0.66	0.66	1	0.66	0.96	0.66	0.96	0.96
EF0590	1	1	0	0.98	0.98	0.98	1	0.97	0	0	0.98	0	0.98	0	0.98	0.98	0	0	1	0	0.98	0	0.98	0.98
EF0592	0.54	0.53	0	0	0	0	0.56	0	0.01	0	0	0	0	0	0	0	0	0	0.32	0	0	0	0	0
EF0594	0.95	0.95	0	0	0	0	0.95	0	0	0	0	0	0	0	0	0	0	0	0.95	0	0	0	0	0
EF0595	0.69	0.69	0	0.66	0.69	0.69	0.56	0.64	0.56	0	1	1	0.69	0	0.69	0.69	0.66	0	1	0.46	0.56	0.66	0.69	0.66
EF0598	1	1	0	0	0	0	1	0	0	0	0	0	0.95	0	0	0.95	0	0	1	0	0.04	0	0.04	0
EF0599	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0600	0.22	1	0	0	0	0	1	0	0.5	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0601	0	1	0	0	0	0	1	0	0.66	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0602	0.7	1	0	0	0.7	0.7	1	0.7	0	0	0	0.7	0.7	0	0.37	0.7	0	0	1	0	0.29	0.7	0.66	0
EF0603	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0604	0.55	1	0.55	0.48	0.48	0.48	1	0.48	0.55	0.55	0.48	0.48	0.55	0.55	0	0.55	0.55	0.53	1	0.55	0.48	0.55	0.48	0.48
EF0605	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0606	0.65	1	0.65	0.65	0.65	0.65	1	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	1	0.65	0.65	0.65	0.65	0.65
EF0607	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0608	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0609	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0610	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0611	0	0.55	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0612	0	1	0	0.46	0.46	0.46	1	0.46	0	0	0.46	0	0.46	0	0.46	0.46	0	0	1	0	0.46	0	0.46	0.46
EF0613	0	1	0	0.92	0.92	0.92	1	0.92	0	0	0.92	0	0.92	0	0.95	0.95	0	0	1	0	0.92	0	0.92	0.92
EF0615	0	1	0.94	0	0	0	1	0.97	0	0	0	0.97	0.99	0	0	0	0.97	0	1	0.96	0	0	0.97	0.97
EF0616	0	1	0	0.98	0.98	0.98	1	0.98	0	0	0.98	0	0.98	0	0.98	0.98	0	0	1	0	0.98	0	0.98	0.98
EF0617	0	1	0	1	1	1	1	1	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	1
EF0618	0	1	0	0.98	0.98	0.98	1	0.98	0	0	1	0	0.98	0	0.98	0.98	0	0	1	0	0.98	0	0.98	0.98

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0619	0	0.99	0	0.94	0.94	0	1	0.94	0	0	1	0	0.94	0	0.94	0.94	0	0	1	0	0.94	0	0.94	0.94
EF0621	0	0.99	0	0.95	0.95	0	1	0.95	0	0	1	0	0.95	0	0.95	0.95	0	0	1	0	0.95	0	0.95	0.95
EF0622	0.32	1	0	0.97	0.97	0	1	0.97	0	0	1	0	0.97	0	0.97	0.97	0	0	1	0	0.97	0	0.97	0.97
EF0623	0.82	1	0	0.96	0.96	0	1	0.96	0	0	1	0	0.96	0	0.96	0.96	0	0	1	0	0.96	0	0.96	0.96
EF0624	0.74	1	0	0.97	0.97	0	1	0.97	0	0	1	0	0.97	0	0.97	0.97	0	0	1	0	0.97	0	0.97	0.97
EF0625	0.4	1	0	0.87	0.87	0.14	1	0.87	0	0	1	0	0.87	0	0.87	0.87	0	0	1	0	0.87	0	0.87	0.87
EF0626	0.73	1	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0627	0.77	0.99	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0
EF0628	0.77	0.99	0	0.32	0.32	0.32	1	0.32	0.15	0.15	1	0.15	0.32	0.15	0.32	0.32	0.15	0.15	1	0.15	0.32	0.15	0.32	0.32
EF0629	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99
EF0630	1	0.99	1	1	1	1	0.99	1	1	0.99	0.99	1	1	0.99	1	1	0.99	0.99	0.99	1	1	1	1	1
EF0631	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0633	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0634	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0635	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0636	1	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1
EF0637	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0638	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0639	1	0.99	1	0.97	0.99	1	0.99	0.94	0.99	0.99	0.9	1	0.99	0.99	0.99	0.99	0.99	0.99	0.89	1	1	0.86	0.87	0.99
EF0640	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0641	1	0.6	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1
EF0642	1	0.99	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0643	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0644	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	1	1	1	0.99	1	1	0.99	0.99	1	1	1	1	0.99	1
EF0645	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0646	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF0647	1	0.92	1	0.99	1	0.99	1	0.99	0.99	0.78	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99
EF0648	1	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	0.99
EF0650	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF0651	1	0.99	1	0.99	1	0.99	0.99	0.99	1	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99
EF0652	1	0.99	0.99	0.99	0.99	0.99	0.96	1	0.99	0.99	0.99	1	0.98	0.77	0.98	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0653	1	1	1	0.99	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99
EF0654	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1
EF0655	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF0656	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0657	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0658	1	0.99	0.98	1	0.99	0.98	0.99	1	0.98	0.98	0.98	1	0.98	0.99	0.98	0.98	0.53	0.98	0.98	0.99	0.98	0.99	0.98	1
EF0659	1	1	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF0660	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0661	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF0662	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0663	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1	0.99	1
EF0664	1	0.99	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF0665	1	0.99	1	1	1	1	1	1	1	1	0.99	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0666	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.98	0.99
EF0667	1	0.99	0.98	1	0.99	0.99	0.99	1	0.98	0.99	0.98	1	0.98	1	0.98	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.99	1
EF0668	1	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.99
EF0669	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99
EF0670	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0671	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.96	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0672	1	1	1	1	1	0.99	1	1	0.99	0	0.99	1	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	1
EF0673	1	0.99	0.99	0.96	0.95	0.99	0.96	0.96	0.95	1	1	1	0.99	0.96	0.99	0.99	0.99	1	0.43	0.99	0.99	0.99	0.99	0.96
EF0674	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0675	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF0676	1	0.99	0.99	1	1	0.99	1	1	0.99	0.98	0.99	1	1	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1
EF0677	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0678	1	0.54	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.53	0.98	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.98	0.99	0.99
EF0679	1	0.98	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.99
EF0680	1	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99
EF0681	1	1	0.99	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1
EF0682	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1
EF0683	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0684	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.94	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF0685	1	0.93	1	1	1	1	1	1	0.94	0.92	1	1	0.94	1	0.94	0.94	1	0.94	1	1	1	1	1	1
EF0686	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.97	1	0.97	0.97	0.99	0.98	0.99	1	1	1	1	1
EF0687	1	0.99	1	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	1
EF0688	1	0.99	1	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	1	0.99	1	1	1	1
EF0689	1	0.98	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	1	1	0.99
EF0690	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	0.99
EF0691	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0692	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.66	0.99	0.99	0.99
EF0693	1	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99
EF0694	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99
EF0695	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0696	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0697	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0698	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0699	1	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0700	0.88	0.99	0.99	1	1	1	0.99	0.99	0.99	1	0.99	1	1	1	1	1	0.99	1	0.99	1	1	0.99	1	1
EF0701	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0702	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.54	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1
EF0703	1	0.98	0.99	1	1	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	1	1
EF0704	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF0705	1	0.99	1	1	1	1	1	0.99	1	1	0.99	0.51	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0706	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF0707	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0708	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0709	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0710	1	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF0711	1	0.98	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.98	0.99	1	0.98	0.99	0.98	0.98	0.98	0.99	0.98	1	0.98	0.98	0.98	0.99
EF0713	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF0714	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99	0.98	0.99	0.99	0.99	0.98	1	1	0.99	0.99	0.99	0.99
EF0715	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1
EF0716	1	0.98	0.98	0.99	1	0.99	0.99	0.99	0.98	0.98	0.99	0.99	1	0.99	1	1	1	0.98	1	0.93	0.99	0.97	0.99	0.99
EF0717	1	0.98	1	0.99	1	0.95	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.9	0.99	0.99	0.99	0.99
EF0718	1	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1
EF0719	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99
EF0720	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0721	0.5	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0722	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0723	1	0.97	0.99	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	1	0.97	1	0.97	0.95	0.97	0.97
EF0724	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1
EF0725	1	0.96	0.97	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.97	0.99	0.97	0.97	0.98	1	0.96	1	0.96	0.97	0.96	0.96
EF0726	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0727	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.98	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0728	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0730	1	1	1	1	1	1	1	0.92	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0731	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0732	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0733	1	0.99	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0734	1	0.99	0.99	1	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF0735	1	0.99	0.99	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1
EF0737	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0738	1	0.95	0.96	0.95	0.95	0.95	0.97	1	0.95	0.97	0.95	1	0.94	0.95	0.94	0.94	0.94	0.95	0.97	0.95	0.95	0.98	0.95	0.95
EF0739	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.98	0.99
EF0740	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0741	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.99
EF0742	1	1	1	1	1	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	1
EF0743	1	0.98	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.97	0.99	0.99	0.98	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0744	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1	0.99	1	1	1	0.99
EF0745	1	0.98	0.99	0.98	0.98	0.98	0.98	0.98	1	0.99	0.96	0.98	0.99	0.99	1	1	0.81	0.98	1	0.98	1	0.96	1	0.98
EF0746	1	0.97	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.98	0.99
EF0747	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1
EF0748	1	0.99	0.99	0.99	0.92	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.94	0.99
EF0750	1	0.98	0.99	0.99	0.99	0.99	0.98	0.98	1	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0751	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF0752	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99
EF0753	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0754	1	0.99	0.99	1	0.99	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1
EF0755	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF0756	1	0.99	1	1	1	1	1	1	1	0.98	1	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	1
EF0757	1	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1
EF0758	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF0759	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0760	1	0.99	1	1	1	0.99	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF0761	1	0.99	1	0.99	1	1	0.99	0.99	1	0.99	0.99	0.78	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99
EF0762	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.65	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99
EF0763	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0764	1	0.98	0.99	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.99	0.98	0.98
EF0765	1	1	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	0.98	0.93	1
EF0766	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0767	1	1	0.99	0.98	0.99	0.99	1	0.99	0.99	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.98	1	0.98	0.99	0.98	0.99	0.98	0.98
EF0768	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	1	0.99	1
EF0769	1	0.98	1	1	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1
EF0770	0.92	0.96	0.98	0.87	0.86	0.99	0.99	1	0.99	0.98	0.99	1	0.89	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.86	0.99
EF0771	0.92	0.99	0.99	1	0.99	0.99	0.99	0.99	0.91	0.99	0.99	0.88	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF0773	1	0.99	0.99	0.99	1	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF0774	1	0.99	1	1	0.99	0.99	1	1	0.99	0.99	1	1	1	0.99	1	1	0.99	1	1	1	1	1	1	1
EF0775	0.52	0.62	0.87	0.96	0.57	0.72	0.89	0.87	0.94	0.69	0.48	0.87	0.72	0.86	0.45	0.52	0.56	1	0.54	0.87	0.94	0.57	0.71	0.96
EF0776	1	0.99	1	1	1	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	1
EF0778	1	0.97	1	0.99	1	1	1	1	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0779	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.8	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0780	1	0.98	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.98	0.98	0.99	0.98	0.99
EF0781	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0782	0.85	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0783	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99
EF0784	1	0.99	1	1	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1
EF0785	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	0.99
EF0786	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0787	1	0.98	0.98	0.98	1	0.99	1	0.98	1	0.99	1	0.98	0.98	0.99	0.98	0.98	0.99	1	1	0.99	0.99	1	0.99	0.98
EF0789	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99
EF0790	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0791	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0792	1	0.99	0.99	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1
EF0793	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1
EF0794	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	1	1	1	0.99	0.99	1	0.99	0.99
EF0795	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0796	1	0.99	1	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0797	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0798	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99
EF0799	0.48	0.49	0.99	0.99	0.58	0.59	0.99	0.99	0.99	0.98	0.49	0.99	0.99	0.99	0.49	0.49	0.99	0.99	0.48	0.99	0.99	0.99	0.99	0.99
EF0801	1	0.86	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF0802	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0803	1	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1
EF0804	1	0.98	0.99	1	1	1	1	0.99	0.99	0.96	0.99	0.99	0.97	0.99	0.97	0.97	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF0805	1	0.99	0.99	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	0.99
EF0806	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	1	1	1	0.99	1	0.99
EF0807	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0808	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0809	1	0.99	1	0.99	0.98	0.98	0.99	0.98	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	1	0.99	1	0.99
EF0810	1	0.99	0.99	0.99	0.42	0.42	0.42	0.99	0.42	0.98	0.42	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.42	0.42	0.42	0.99
EF0811	1	0.98	0.99	0.99	0.35	0.35	0.35	0.99	0.35	0.99	0.35	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.35	0.35	0.36	0.99
EF0812	1	0.99	1	0.99	0.24	0.24	0.24	1	0.32	0.99	0.24	1	1	1	1	1	1	0.99	0.99	1	0.24	0.24	0.36	0.99
EF0813	1	0.99	0.99	0.99	0.72	0.72	0.58	0.99	0.58	0.99	0.72	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.72	0.58	0.72	0.99
EF0814	1	1	1	1	0.33	0	0	1	0	0.99	0	1	1	1	1	1	1	1	1	1	0	0	0	1
EF0815	1	1	0.99	0.99	0.27	0.27	0.26	1	0.26	0.99	0.27	1	1	0.99	1	1	1	0.99	1	1	0.26	0.26	0.26	0.66
EF0816	1	0.99	0.99	0.99	0.49	0.14	0.14	0.99	0	0.99	0.42	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.14	0	0.14	0.99
EF0817	1	0.99	1	0.99	0.53	0.53	0.53	0.99	0.53	1	0.53	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.53	0.53	0.53	0.99
EF0818	0.86	0.99	0.99	1	0.05	0.05	0.05	0.99	0.05	0.99	0.05	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0	0.05	0	1
EF0819	1	0.99	1	1	0.99	0.99	0.99	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1	0.99	1	1
EF0820	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0821	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.91	0.98	1	0.98	0.98	1	0.99	0.99	1	0.99	0.99	0.99	0.99
EF0822	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0823	0.82	0.55	0.85	0.85	0.86	0.86	0.84	0.87	0.84	0.84	0.86	0.85	0.86	0.87	0.84	0.8	0.85	1	0.86	0.85	0.86	0.85	0.86	0.86
EF0824	1	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.99	0.98	1	0.98	0.98	0.98	0.98	0.98	0.98
EF0825	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	1
EF0826	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1
EF0827	1	0.98	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98
EF0828	1	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1
EF0829	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0830	0.79	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF0831	1	1	1	1	1	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0832	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0833	1	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.98	0.99	0.98	0.98
EF0834	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	0.99	1	0.99	1
EF0835	1	0.99	1	1	1	1	1	1	1	0.98	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	0.98	0.99	1
EF0836	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.96	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	1	1	0.99	1	0.99
EF0837	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	1
EF0838	0.99	0.97	0.98	0.77	0.98	0.97	0.98	0.87	0.65	0.98	0.98	0.49	0.57	0.99	0.87	0.86	0.37	0.99	0.16	0.63	0.98	0.53	0.78	0.43
EF0839	0.98	0.98	0.99	0.86	0.99	0.9	0.99	0.1	0.75	0.54	0.99	0.35	0.57	0.99	0.8	0.6	0.54	0.62	0.71	0.99	0.42	0.75	0.56	0.45
EF0840	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99
EF0841	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0842	1	0.99	0.99	1	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	1	0.99	0.99	1	1	0.99	0.99	0.98	1	0.98	1
EF0843	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99
EF0844	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF0845	1	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0846	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0847	1	0.96	0.97	0.98	0.98	0.98	0.98	0.98	0.97	0.96	0.97	0.98	0.97	0.98	0.97	0.97	0.98	1	0.98	0.97	0.98	0.98	0.98	0.98
EF0848	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0849	1	0.98	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	1
EF0850	1	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1	0.99	1	1	1	0.99
EF0851	1	0.98	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0852	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0853	1	0.96	0.96	0.95	0.98	0.98	0.99	1	0.98	0.95	1	1	0.96	1	0.96	0.96	0.95	0.99	0.99	0.94	1	1	1	0.95
EF0854	1	0.97	0.98	0.99	0.99	0.99	0.99	1	1	0.98	0.99	1	0.97	1	0.97	0.97	0.99	0.99	0.98	0.99	1	1	1	0.99
EF0855	1	0.96	0.97	1	1	1	1	1	1	0.97	0.99	1	0.98	1	0.98	0.98	1	1	0.99	1	1	1	1	1
EF0856	1	0.95	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.99	0.99	0.97	0.99	0.97	0.97	0.99	0.98	0.98	0.99	0.98	0.99	0.98	0.99
EF0857	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0858	1	0.45	0.45	0.45	0.98	0.98	0.45	0.45	0.97	0.45	0.94	0.45	0.45	0.94	0.45	0.45	0.45	1	0.45	0.98	0.45	0.46	0.45	0.45
EF0859	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.98	0.99
EF0860	0.96	0.98	1	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF0861	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	1	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0862	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0863	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0864	1	1	1	1	1	1	1	0.99	1	1	0.99	0.99	1	0.99	1	1	1	1	1	1	1	1	1	1
EF0865	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	1	1	1	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0867	1	0.98	0.99	1	1	1	1	1	0.99	0.99	0.99	1	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0868	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0869	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99	0.99
EF0871	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF0872	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0873	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0875	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	1	1
EF0876	0.7	0.97	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0877	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1
EF0878	1	0.48	0.99	1	1	1	0.99	1	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	1
EF0879	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	1	1	0.99	1	1	1	1	1
EF0880	1	0.98	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.97	0.98	0.97	0.97	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0881	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0882	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	1
EF0883	1	0.99	0.99	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF0884	1	0.98	0.99	0.99	0.99	0.99	1	1	0.98	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0885	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.68	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0886	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0887	1	0.99	0.98	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	0.99	0.99	1	0.99	1	1
EF0888	0.85	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0889	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	1	0.98	0.98	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0890	1	0.98	0.98	1	0.97	0.99	0.99	1	0.97	0.98	0.99	1	0.97	0.98	0.97	0.97	1	1	0.97	0.98	0.99	0.98	0.99	1
EF0891	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0892	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99
EF0893	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	1
EF0895	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0896	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	0.99	1	0.99	1
EF0897	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF0898	0.56	0.56	0.57	0.57	0.57	0.57	0.57	0.56	0.57	0.57	0.57	0.56	0.56	0.57	0.56	0.56	0.57	1	0.57	0.57	0.57	1	0.57	0.57

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0899	1	0.99	1	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0900	1	0.92	1	1	1	1	0.99	0.99	1	0.99	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99	1	1
EF0901	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF0902	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF0903	1	0.99	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1
EF0904	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0905	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.92	0.99	0.99	0.99	0.99
EF0906	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	1	1
EF0907	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	1	1	0.98	0.99	0.99	1	0.99	1
EF0908	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	0.99	1	1
EF0909	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0910	1	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0911	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1
EF0912	1	1	0.99	1	1	1	0.99	0.99	0.59	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF0913	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF0914	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0915	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0916	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0917	1	0.99	0.99	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF0918	1	0.98	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	1	1	0.99	0.98	0.99	0.99
EF0919	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	1	0.99	0.98	1	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0920	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.54	0.92	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0921	1	0.99	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.96	0.99	0.98	0.98	0.99	0.98	0.98	0.98	1	0.99	0.98	0.99	0.99	0.99	0.98
EF0922	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1
EF0923	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF0924	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0925	1	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99
EF0926	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0927	1	0.98	0.99	0.99	1	1	0.99	1	1	0.98	0.98	1	1	0.99	1	1	0.99	1	0.99	1	0.99	1	0.99	0.99
EF0928	1	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1
EF0929	1	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	0.99
EF0930	1	1	1	1	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1
EF0931	1	0.16	0.16	0.16	1	1	0.92	0.16	0.16	1	0.99	0.16	0.99	0.16	0.99	0.99	0.16	0.99	0.99	1	1	0.16	1	0.16
EF0932	1	0.99	0.99	0.99	1	1	0.99	1	0.99	0.98	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF0933	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0934	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0935	1	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.98	1	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	1	0.99	0.98
EF0936	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.98	0.99	0.98	0.98	0.98	0.99
EF0937	1	1	1	0.99	1	1	0.99	0.99	1	1	1	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF0938	0.93	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	0.99	1
EF0939	1	0.99	1	1	0.98	0.98	1	1	1	1	0.98	1	0.99	1	0.99	0.99	1	1	0.97	0.99	0.99	1	0.99	1
EF0940	1	0.99	1	1	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	1	1
EF0941	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0942	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF0943	1	0.97	0.99	1	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	1
EF0944	1	0.98	1	0.99	0.98	0.98	0.98	0.99	0.98	1	1	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0945	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0946	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0947	1	0.99	1	1	0.99	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0948	1	0.98	0.99	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.98	1	0.98	0.99	0.98	0.99	0.98	0.98
EF0949	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99
EF0950	1	0.99	1	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.98	0.98	1	0.99	1	1	0.98	1	0.98	0.98	0.99	0.99	0.99	0.98
EF0951	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	1	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF0953	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF0954	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0955	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0956	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0957	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF0958	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0959	1	0.56	0.81	0.99	0.95	0.95	0.79	0.8	0.81	1	0.82	0.81	0.99	0.8	0.99	0.99	0.99	1	0.81	0.99	0.82	0.99	0.82	0.99
EF0960	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99
EF0961	1	0.98	0.98	0.98	0.99	0.99	0.98	0.98	0.98	1	1	0.98	0.99	0.98	0.99	0.99	0.98	1	0.98	0.97	1	0.99	1	0.98
EF0962	1	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	1	1	0.98	0.99	0.98	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.98
EF0963	1	0.99	0.98	0.99	0.99	0.99	1	0.99	0.98	1	1	0.99	0.97	0.99	0.97	0.97	0.99	1	1	0.99	1	1	1	0.99
EF0964	1	0.99	0.99	0.98	1	1	1	0.98	0.97	1	1	0.98	0.99	0.97	0.99	0.99	0.98	1	0.99	0.98	1	0.98	1	0.98
EF0965	1	0.99	1	0	1	0.99	0.99	0	0	1	1	0	0.99	0	0.99	0.99	0	1	0.99	0	0.99	0	0.99	0
EF0966	1	0.99	0.99	0.43	0.99	0.99	1	0.43	0.43	1	1	0.43	0.99	0.43	0.99	0.99	0.43	1	1	0.43	0.99	0.43	0.99	0.43
EF0967	1	0.99	0.99	0.09	0.12	0.12	1	0.1	0	1	0.99	0.1	0.12	0	0.12	0.12	0.09	0.99	0.12	0.09	0.1	0.09	0.1	0.09
EF0968	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0969	1	0.99	1	0.99	1	1	0.99	0.99	1	1	1	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF0970	1	1	0.99	1	1	1	1	0.9	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	0.99	1	1
EF0971	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF0972	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF0973	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0974	1	0.99	0.98	1	0.98	0.98	0.98	1	0.98	0.98	1	1	0.98	0.98	0.98	0.98	1	1	0.98	0.98	0.98	0.99	0.98	1
EF0976	1	0.99	1	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1
EF0977	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0978	1	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF0979	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.98	1	0.98	0.99
EF0980	1	1	1	1	1	1	1	0.99	1	1	1	0.99	1	0.99	1	1	1	1	1	1	0.99	1	0.99	1
EF0981	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF0982	1	0.98	0.99	0.99	0.98	0.98	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF0983	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.98	0.98	0.99	1	0.98	0.98	0.98	0.98	0.99	1	0.99	1	0.98	1	0.98	0.99
EF0984	1	0.99	0.98	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.97	0.99	0.99
EF0985	1	0.99	0.99	0.99	1	1	1	1	0.99	1	1	1	1	0.99	1	1	0.99	1	1	1	1	1	1	0.99
EF0986	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.99	0.99
EF0987	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF0988	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0989	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF0990	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0991	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.94	1	0.99	0.94	0.99	0.94	0.94	0.99	1	0.94	1	0.98	1	0.98	0.99
EF0992	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF0993	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF0994	1	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF0995	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1
EF0996	1	1	1	1	1	1	1	1	1	1	1	0.95	1	1	1	1	1	1	1	1	1	1	1	1
EF0997	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF0998	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF0999	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1000	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1001	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1002	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	1	1	1
EF1003	1	0.56	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1004	1	0.99	1	1	0.99	0.99	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1
EF1005	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1006	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1007	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1008	1	0.99	1	1	1	1	1	1	0.99	1	1	1	0.75	1	1	1	1	1	1	1	1	1	1	1
EF1009	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1010	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1012	0.82	0.93	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.97	0.99	1	0.96	0.72	0.99	1	1	1	1	1	1	0.99
EF1013	1	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.17	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1014	1	1	0.99	1	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0	0.99	1	1	0.99	1	1	0.99	1	1
EF1015	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.98	0.99	0.99	0	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1016	1	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1	0.99	0.99	0	0.99	0.99	1	1	1	1	1	1	0.99
EF1017	0.81	0.91	1	0.98	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	1	0.98	0.99	0.69	0.98	1	0.99	0.99	0.99	0.99	0.99	0.98
EF1018	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF1019	1	1	1	1	1	1	1	1	1	0.99	1	1	0.9	1	0.9	0.9	1	1	1	1	1	1	1	1
EF1020	1	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	0.84	1	1	1	1
EF1021	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF1022	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1023	1	0.99	0.99	1	1	1	0.99	1	0.98	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1024	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1025	1	0.99	1	1	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1
EF1026	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	1
EF1027	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1028	1	0.99	1	0.99	1	1	0.99	1	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1029	1	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	1	0.98	0.98	0.99	0.98	0.99	0.99
EF1030	1	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.98
EF1031	1	1	0	0	0	0	0	0	0	0.99	1	0	0	1	0	0	0	1	0	1	1	1	1	0
EF1032	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1033	0.85	0.81	0.98	0.98	0.98	0.98	0.85	0.98	0.79	0.85	0.98	0.98	0.96	0.86	0.82	0.82	0.98	0.89	0.97	0.85	0.86	0.98	0.86	0.98
EF1034	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.8	0.99	0.99	0.99	0.99	0.99	0.99
EF1035	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.98	0.99	1	0.99	1	0.99
EF1036	1	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	1	1	1	1	0.92	1	1	1	1	1
EF1037	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1
EF1038	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1
EF1039	1	0.99	1	1	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1
EF1040	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99
EF1041	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1042	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99
EF1043	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	1
EF1044	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1045	1	0.99	1	1	1	1	1	0.99	1	0.99	1	0.99	1	0.99	1	1	1	1	1	0.62	1	1	1	1
EF1046	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1047	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99
EF1048	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF1049	0.93	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1050	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1051	1	0.98	0.99	1	1	1	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1052	1	0.68	0.96	0.97	0.67	0.67	0.99	0.92	0.92	0.87	0.96	0.9	0.9	0.98	0.97	0.97	0.98	1	0.67	0.99	0.9	0.89	0.68	0.98
EF1053	1	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.2	0.99	1	1	1	1	1	1	1	1
EF1054	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1055	1	0.99	0.98	0.99	0.99	0.99	0.98	0.99	1	0.99	0.98	0.99	0.98	1	0	0.98	0.99	1	1	0.99	1	0.98	1	0.99
EF1056	1	0.98	0.95	0.98	0.98	0.98	0.97	0.98	0.99	0.94	0.98	0.98	0.99	0.99	0	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.99	0.98
EF1057	1	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.46	0.99	1	1	1	1	1	0.99	1	1
EF1058	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	0	1	1	1	0.99	0.99	0.99	1	0.99	1
EF1059	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	1	0.99	1	0.27	0.99	1	1	1	1	1	1	1	1
EF1060	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.17	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1061	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1062	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1063	1	1	0.99	1	0.99	0.99	0.99	0.99	0.98	1	1	0.99	1	0.99	0	1	1	1	0.99	1	1	1	1	1
EF1064	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.84	0.92	1	0.99	0.99	0.99	0	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1065	0.99	0.62	0.96	1	0.52	0.5	0.96	0.58	0.5	0	0.99	0.7	0.5	0.96	0	0.96	1	1	1	0.96	0.96	0.96	0.55	1
EF1066	1	1	0.99	1	0.97	0.99	0.99	0.99	0.99	0.94	0.99	0.9	0.99	0.99	0.37	0.99	1	1	1	1	0.99	1	0.99	1
EF1067	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
EF1068	1	0.99	0.99	1	1	1	0.99	1	0.99	0.99	0.99	1	1	0.99	0.04	1	1	1	1	1	0.99	0.99	0.99	1
EF1069	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1070	0.85	0.95	0.99	0.47	0.99	0.99	0.99	0.53	0.39	0.69	0.52	0.67	0.53	0.99	0.06	0.95	0.71	1	0.48	0.99	0.99	0.52	0.56	0.27
EF1071	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	1	1	0.99	0.99	0.99	1	0.99	1
EF1072	1	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1073	1	0.61	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.98	0.99
EF1074	1	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.99	1	0.98	1	0.99	0.99	0.99	0.99
EF1075	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	1	0.99	1	0.99	1	1	0.99	1	0.99
EF1076	1	0	0	0.99	0.99	0.99	0	0	0.99	0	0.99	0	0	0.99	0	0	0.99	1	0.99	0	0	0.99	0	0.99
EF1077	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99	0.99
EF1078	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1080	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1081	1	0.98	0.98	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99
EF1082	1	0.97	0.98	0.98	1	1	0.96	0.98	0.98	0.96	0.99	0.98	0.99	0.98	0.99	0.99	0.98	1	0.99	0.99	0.98	0.98	0.98	0.98
EF1083	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	0.99
EF1084	1	0.99	0.99	0.99	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1085	1	0.99	0.98	1	1	1	0.99	0.99	0.98	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1
EF1086	1	0.98	0.98	1	0.99	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	1	1	0.99	0.99	0.99	1	0.99	1
EF1088	1	0.98	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.98	0.99	0.99	0.99	1
EF1089	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1090	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF1091	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1092	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1093	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1094	1	0.99	0.97	0.99	0.98	0.98	0.98	0.99	0.98	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.98	0.99	0.99
EF1095	1	0.98	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF1096	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1097	1	0.99	1	1	1	1	1	1	0.99	0.98	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF1098	1	0.98	1	0.99	1	1	1	1	0.99	0.99	1	1	1	0.99	1	1	0.99	1	1	1	1	1	1	0.99
EF1099	0.54	0.52	0.97	0.54	0.54	0.54	0.75	0.57	0.56	0.97	0.82	0.97	0.97	0.98	0.55	0.55	0.69	0.76	0.54	0.55	0.54	0.56	0.69	0.54
EF1100	1	0.98	0.99	1	0.98	0.98	0.98	0.99	0.3	0.99	0.99	0.99	0.98	0.99	0.06	0.98	1	1	0.99	0.99	0.98	0.99	0.99	1
EF1101	1	0.98	0.98	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0	0.99	0.98	1	0.99	0.99	0.98	0.98	0.98	0.98
EF1102	1	0.99	0.91	1	0.99	0.99	0.99	0.99	0.91	0.97	1	0.99	0.99	0.99	0	0.99	1	1	1	0.99	0.91	1	0.91	1
EF1103	0.57	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1104	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	0	1	1	1	1	1	1	1	1	1
EF1105	1	0.97	0.98	0.98	0.97	0.97	0.98	0.98	0.99	0.98	0.99	0.98	0.99	0.98	0	0.99	0.98	0.97	0.97	0.98	1	0.98	1	0.98
EF1106	1	1	1	1	1	1	1	1	0.98	1	0.99	1	0.98	1	0	0.98	1	1	1	1	0.99	1	0.99	1
EF1107	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	0	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1108	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1109	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1110	1	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1111	1	0.99	1	1	1	1	1	1	0.99	0.99	0.7	1	1	0.99	0.16	1	1	1	1	1	1	1	1	1
EF1112	1	0.94	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1113	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1114	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	0	1	1	1	1	0.99	0.99	1	0.99	1
EF1115	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	1	1	0.99	1	0	0.99	1	0.99	1	0.99	1	1	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1116	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.06	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1117	1	1	0.98	1	0.98	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.98	0.98	0.16	0.98	1	0.98	1	1	0.98	0.99	0.98	1
EF1118	1	1	0.99	1	0.99	0.99	1	1	0.99	0.98	0.99	1	1	0.99	0.16	1	1	1	0.99	0.98	0.99	1	0.99	1
EF1119	1	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99
EF1120	0.58	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.6	0.99	1	1	0.98	1	0.99	1	0.99	1
EF1121	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0	1	1	1	1	1	1	0.99	1	1
EF1122	0.7	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0	1	0.99	1	0.98	0.99	0.98	0.99	0.98	0.99
EF1123	1	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0	0.99	0.99	1	0.98	0.98	0.98	0.98	0.98	0.99
EF1124	1	0.99	1	1	0.99	1	1	1	1	0.99	1	1	1	1	0	1	1	1	1	1	1	1	1	1
EF1125	0.63	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	0	1	0.99	1	1	0.99	1	0.99	1	0.99
EF1126	1	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.98	0.99
EF1127	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF1128	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1129	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1
EF1130	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99
EF1131	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0	0.99	0.99	0.98	0.98	1	0.99	0.99	0.99	0.99
EF1132	0.99	0.98	1	1	0.99	0.99	1	1	0.98	1	0.99	1	0.99	1	0	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1133	1	0.98	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0	0.99	0.98	0.99	0.99	1	1	0.99	0.99	0.98
EF1134	0.9	0.98	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.07	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF1135	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1136	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.97	0.99	0.99	0.99	0.99
EF1137	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	0	1	1	1	0.99	1	0.99	0.99	0.99	1
EF1138	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.48	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1139	1	1	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0	1	0.99	1	1	1	1	1	1	0.99
EF1140	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1141	1	0.98	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0	0.99	1	1	0.99	0.99	0.98	0.99	0.98	1
EF1142	1	1	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.17	0.99	0.99	1	0.99	1	1	0.99	1	0.99
EF1143	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1144	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1145	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	1	0.99	1	0.99	0	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF1146	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
EF1147	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1148	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1149	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
EF1150	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1151	1	0.99	0.99	0.99	1	0.99	1	1	1	0.98	0.99	1	0.99	1	0	0.99	0.99	1	0.97	0.99	0.99	0.99	0.99	0.99
EF1152	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0	1	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1153	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1154	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0	0.99	1	1	0.99	0.98	0.99	1	0.99	1
EF1155	1	1	1	0.99	1	1	0.99	1	1	1	0.99	1	1	1	0	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1156	1	0.98	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1157	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99
EF1158	1	0.98	0.99	0.99	0.99	0.99	1	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1159	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1160	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1161	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.97	0.98	0.98	0.99	1	0.99	0.99	0.98	0.99	0.98	0.99
EF1162	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1163	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1164	1	0.98	0.98	0.96	0.99	1	0.99	0.98	0.99	0.88	0.95	0.98	0.95	0.99	0.98	0.98	0.97	0.97	0.91	0.99	0.97	0.92	0.98	0.95
EF1165	1	0.99	0.99	0.99	0.99	1	0.99	0.95	0.99	0.96	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99
EF1166	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF1167	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1
EF1168	1	1	1	1	1	1	1	1	0.99	1	0.99	1	1	1	1	0.69	1	1	1	1	0.65	1	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1169	1	0.98	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.98	0.99
EF1170	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.77
EF1171	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1172	1	0.97	1	0	1	1	1	0	0	0.98	0.99	0	0	0	0	0	0	1	0.99	0	1	0	1	0
EF1173	1	0.99	1	0	1	1	1	0	0	0.99	0.99	0	0	0	0	0	0	1	1	0	1	0	1	0
EF1174	1	0.97	1	0	1	1	1	0	0	0.98	1	0	0	0	0	0	0	1	1	0	1	0	1	0
EF1175	1	0.98	1	0.67	1	1	1	0.67	0.71	0.99	1	0.67	0	0.67	0	0	0.67	1	1	0	1	0	1	0.71
EF1176	1	0.98	0.98	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF1177	1	0.99	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.96	0.98	0.99	0.98	0.98	0.98	0.98	0.98	1	0.98	0.98	0.98	0.98	0.98	0.98
EF1179	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1180	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF1181	1	0.97	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	1	1	1	1	0.99	1	1	1	0.98	0.99	0.98	0.98
EF1182	1	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1183	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF1184	1	0.99	0.99	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF1185	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF1186	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1187	1	0.97	0.98	1	0.99	1	0.98	1	0.97	0.99	1	1	0.98	0.99	0.98	0.98	1	1	0.98	0.99	0.99	1	0.99	1
EF1188	1	1	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99
EF1189	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1190	1	1	0.99	0.99	0.99	1	0.99	1	1	1	0.99	1	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1191	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.99	1	0.98	0.99	0.91	0.99	0.99	0.99
EF1192	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1193	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1194	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1195	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1196	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF1197	1	1	0.99	1	0.99	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	0.99	1	0.99	1
EF1198	1	0.97	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.98	1	0.98	0.98	0.98	1	0.98	0.98
EF1199	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1200	1	0.99	0.99	0.98	0.99	1	0.99	0.98	0.99	0.99	0.99	0.98	0.99	1	0.99	0.99	0.98	1	0.99	1	0.99	1	0.99	0.98
EF1201	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1202	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1203	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1	1	1	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1204	1	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1205	1	0.99	0.99	0.99	1	1	1	1	0.63	0.99	1	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99
EF1206	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99
EF1207	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.78	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1209	0.65	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF1210	1	0.98	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.97	0.98	0.98	0.99	0.99	0.99	0.99	0.98	1	0.99	0.98	0.99	0.98	0.99	0.98
EF1211	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1212	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1213	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1214	1	0.98	0.99	1	0.99	1	0.99	1	0.99	1	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1
EF1215	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1216	1	0.97	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1217	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1218	1	0.99	1	1	1	1	0.99	1	1	1	1	1	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF1219	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF1220	1	0.98	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF1221	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1222	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.48
EF1223	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1224	0.78	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	0.99	0.99	0.99	1	0.99	0
EF1225	1	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	1	0.99	0.99	0.99	0.99	0
EF1226	1	1	0.99	1	1	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0
EF1227	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99	0
EF1228	1	0.99	0.99	1	0.99	1	1	1	0.97	0.99	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1	0.99	0
EF1229	1	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.98	0.97	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0
EF1230	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
EF1231	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.45
EF1232	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	0
EF1233	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0
EF1234	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0
EF1235	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0
EF1236	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0
EF1237	1	1	0.99	1	0.99	1	0.99	1	0.99	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	0
EF1238	0.61	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0
EF1239	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0
EF1240	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.1
EF1241	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	0.99	1	0.57
EF1242	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1243	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1244	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.98	0.99
EF1246	1	0.99	0.99	0.86	1	0.99	0.99	0.82	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1247	1	1	1	0.9	1	1	0.99	1	0.86	0.83	1	1	0.88	1	1	1	1	1	1	1	0.81	1	1	0.98
EF1248	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1249	1	0.75	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1250	1	0.98	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1251	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1253	1	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.98	0.99	0.98
EF1254	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	1	0.83	0.84	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1255	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	1
EF1257	1	0.99	0.98	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1258	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1259	1	0.99	0.99	1	1	0.99	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1260	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1	1	1	1	1	0.99	0.99	1	0.99	1
EF1261	0.58	0.99	0.99	0.99	0.93	0.99	0.99	0.99	0.57	0.96	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1262	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1263	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.98	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1264	1	1	1	1	0.99	0.99	1	0.99	0.66	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	1	1	1	0.99	0.99
EF1265	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1266	1	0.98	0.99	0.97	0.97	0.98	0.98	0.98	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.97	1	0.97	0.97	0.97	0.97	0.97	0.97
EF1267	1	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.97	0.98	0.97	0.97	0.98	1	0.99	0.98	0.99	0.98	0.99	0.98
EF1268	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1269	1	1	0.99	0.99	0.98	1	0.99	1	0.98	0.98	0.99	1	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1270	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1271	1	1	1	0.99	1	1	1	1	1	0.98	1	1	1	0.99	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1272	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1273	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1274	1	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	0.99	1	0.99	1	0.99	1
EF1275	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF1276	1	1	1	1	1	0.99	1	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1
EF1277	1	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.98	0.99
EF1278	1	1	0.98	0.96	0.96	0.97	0.97	0.97	0.96	0.93	0.98	0.97	0.98	0.97	0.98	0.98	0.96	1	0.97	0.92	0.99	0.96	0.99	0.96
EF1279	1	1	0.98	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1280	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1281	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF1282	1	1	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1283	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1284	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1285	1	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1286	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1287	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1288	0.79	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1289	1	1	0.99	1	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.98	1	0.98	0.98	1	1	0.99	0.99	0.99	1	0.99	1
EF1290	1	1	0.99	0.98	0.99	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.98	1	0.99	1	0.99	0.98	0.99	0.98
EF1291	1	1	0.98	0.98	0.94	0.98	0.94	0.95	0.95	0.94	0.99	0.95	0.98	0.99	0.98	0.98	0.98	1	0.94	0.95	0.95	0.98	0.95	0.98
EF1292	1	1	0.99	1	1	0.99	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1
EF1293	1	1	0.97	0.97	0.92	0.98	0.98	0.98	0.98	0.98	0.99	0.94	0.98	0.98	0.98	0.98	0.97	1	0.98	0.98	0.94	0.98	0.98	0.97
EF1295	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1296	1	1	0.99	0.99	1	1	0.99	0.98	0.98	0.98	1	0.98	0.99	1	0.99	0.99	0.99	1	0.98	1	0.99	1	0.99	0.99
EF1297	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1298	1	1	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98	0.99	1	0.98	0.98	0.99	0.98	0.99	0.99
EF1299	1	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1
EF1300	1	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1301	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1302	1	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1303	1	1	0.99	1	1	1	1	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF1304	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1305	1	1	1	0.99	0.99	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99
EF1306	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1307	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1308	0.52	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1309	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1
EF1310	1	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	1	1	1	1	1	0.99	1	1	0.99	1	0.99	1	0.99
EF1311	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1312	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1313	1	1	0.99	1	0.99	1	0.89	1	1	1	1	1	1	1	0.63	0.63	1	1	0.99	1	0.99	1	0.99	1
EF1314	1	1	0.99	0.99	0.99	0.99	0.95	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1315	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	0.99	1	1
EF1316	1	1	0.99	1	1	0.99	0.99	1	0.98	0.99	1	1	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99	1
EF1317	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1318	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1319	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1320	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	0.99	1	1
EF1321	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.67	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1322	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1
EF1323	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1324	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	0.99	1	0.99
EF1325	1	1	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	0.99	1	0.99	1
EF1326	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1327	0.74	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1328	1	1	1	0.99	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	0.99
EF1329	1	1	0	0	0.79	0	0.79	0	0	0.99	0	0	0	0	0	0	0	1	0	0	0	0.79	0	0
EF1330	1	1	0	0	0.87	0	0.83	0	0	0.87	0	0	0	0	0	0	0	0.87	0	0	0	0.87	0	0
EF1331	1	1	0	0	1	0	1	0	0	0.99	0	0	0	0	0	0	0	1	0	0	0	1	0	0
EF1332	1	1	0	0	1	0	0.99	0	0	0.99	0	0	0	0	0	0	0	1	0	0	0	1	0	0
EF1333	1	1	0.07	0.13	1	0.13	1	0	0.07	0.98	0.13	0.13	0.12	0.13	0.12	0.07	0.13	1	0	0.13	0.13	1	0.13	0.13

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1334	1	1	0	0	1	0	1	0	0	0.99	0	0	0	0	0	0	0	1	0	0	0	1	0	0
EF1335	1	0.92	0	0	0.99	0	1	0	0	0.99	0	0	0	0	0	0	0	1	0	0	0	1	0	0
EF1336	1	1	0	0	0.99	0	1	0	0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0
EF1337	1	1	0.99	0	0.97	0.97	1	0	0	0.96	0.97	0	0.98	0	0.98	0.98	0	1	0.99	0	1	0.98	1	0
EF1338	1	1	0.99	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.95	0.93	0.99	0.99	0.99	0.86	0.99
EF1339	1	0.97	1	1	0.99	1	1	0.95	0.99	0.96	0.99	0.92	0.99	1	0.99	0.99	1	1	0.99	1	1	0.98	1	0.83
EF1340	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1341	0.89	1	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.97	1	0.99	0.99	0.99	0.99	1
EF1342	1	1	0.98	1	0.99	0.99	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1
EF1343	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1344	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1345	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1346	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.97	0.99	1	0.99	0.99
EF1347	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1348	1	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.57
EF1349	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1350	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.98	0.98	0.98	0.98	0.99
EF1351	1	1	0.99	0.99	0.99	1	1	1	0.98	0.98	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.98	0.99	0.98	0.99
EF1352	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1353	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF1354	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1355	0.67	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1
EF1356	0.5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1357	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1358	1	1	0.99	1	1	1	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF1359	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99
EF1360	0.9	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1361	1	1	1	0.99	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	0.99
EF1362	1	1	0.98	0.99	0.99	0.98	0.53	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	1	0.98	0.99
EF1363	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1364	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.92	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1365	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1366	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1367	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1368	1	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1369	1	1	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF1370	1	0.71	0.99	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1
EF1371	1	1	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1372	1	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1
EF1373	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1374	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1375	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF1376	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99	0.99
EF1377	1	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1378	1	1	0.99	1	1	0.99	1	1	0.98	0.99	0.99	1	1	1	1	1	1	1	1	1	0.97	0.97	0.97	1
EF1379	1	1	0.99	1	0.99	1	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.84	1
EF1380	1	1	0.98	0.99	0.98	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99
EF1381	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF1382	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1383	1	1	0.99	0.99	0.99	1	0.99	1	1	0.98	0.99	1	1	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99
EF1384	1	1	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF1385	1	1	1	0.99	1	0.99	1	0.99	1	1	1	0.99	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1386	1	1	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1387	1	1	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.98	0.99	0.98	0.99
EF1388	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.98	0.99	0.98	0.98	1	1	1	1	0.99	0.99	0.99	1
EF1389	0.91	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.7	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1390	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1391	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1392	1	1	1	0.99	0.97	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1393	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1394	1	1	0.99	0.99	0.99	1	1	1	1	0.98	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1395	1	1	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.98	0.99	0.99	0.98	1	0.98	0.99	0.99	0.99	0.99	0.98
EF1396	1	1	0.98	0.99	0.98	0.99	0.99	0.98	0.99	0.98	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1397	1	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99
EF1398	1	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1399	1	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1400	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1401	1	1	0.98	0.94	1	0.95	0.95	0.97	0.95	0.97	0.94	0.97	1	0.97	1	1	0.94	1	0.95	0.95	1	1	1	0.94
EF1402	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1403	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99
EF1404	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.98	0.99	0.99
EF1405	1	1	1	1	0.99	0.99	1	1	1	1	0.99	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	0.99	1	1
EF1406	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1407	1	1	0.98	0.96	0.97	0.97	0.97	0.96	0.97	0.99	0.97	0.96	0.97	0.97	0.97	0.97	0.96	1	0.96	0.97	0.97	0.97	0.97	0.96
EF1408	0.49	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1409	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF1410	0.88	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1411	1	1	1	1	0.99	1	0.99	1	1	0.99	0.99	1	0.79	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	1
EF1412	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF1413	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.97	0.99	1	0.46	0.99	0.46	0.46	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1414	0.73	0.73	0.72	0.72	0.72	0.73	0.73	0.72	0.72	0.72	0.72	0.72	0.72	0.73	0.72	0.72	0.72	0.73	0.72	0.73	0.73	0.72	0.73	0.72
EF1415	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1416	0.69	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1417	0.96	0	0	0	0	0	0	0	0	0.94	0	0	0	0	0.93	0.93	0	0	0	0	0	0	0	0
EF1418	0.94	0	0	0	0	0	0	0	0	0.9	0	0	0	0	0.89	0.89	0	0	0	0	0	0	0	0
EF1419	0.96	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF1420	0.95	0	0.09	0	0.09	0	0.09	0.09	0.09	0.09	0	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0	0	0.09	0	0.07
EF1421	0.94	0.18	0	0	0	0.18	0	0	0.2	0.94	0	0	0.22	0	0.95	0.95	0	0	0	0	0	0	0	0
EF1422	0.99	0.15	0	0	0	0	0	0	0	0.24	0	0	0	0	0.24	0.24	0	0	0	0	0	0	0	0
EF1423	0.95	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF1424	0.99	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0.98	0.98	0	0	0	0	0	0	0	0
EF1425	0.99	0	0	0	0	0	0	0	0	0.97	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1426	0.99	0	0	0	0	0	0	0	0	0.96	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1427	0.99	0	0	0	0	0	0	0	0	0.97	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1428	0.97	0	0	0	0	0.57	0	0	0	0.97	0	0	0	0	0.97	0.97	0	0	0.57	0	0	0	0	0
EF1429	0.97	0	0	0	0	0.79	0	0	0	0.98	0	0	0	0	0.97	0.97	0	0	0.79	0	0	0	0	0
EF1430	0.97	0	0	0	0	0	0	0	0	0.96	0	0	0	0	0.95	0.95	0	0	0	0	0	0	0	0
EF1431	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF1432	0.8	0	0	0	0	0	0	0	0	0.8	0	0	0	0	0.8	0.8	0	0	0	0	0	0	0	0
EF1433	0.99	0	0	0	0	0	0	0	0	0.99	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1434	1	0	0	0	0.3	0	0	0	0	1	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1435	0.98	0	0	0	0	0	0	0	0	0.35	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1436	0.98	0	0	0	0	0	0	0	0	0.98	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1437	0.98	0.71	0.71	0	0.84	0.5	0	0	0	0.97	0.72	0	0	0	1	1	0.88	0	0	0.88	0	0	0	0.88
EF1438	0.43	0	0	0	0	0	0	0	0	0.94	0	0	0	0	1	1	0.9	0	0	0.9	0	0.93	0	0.9
EF1439	0.96	0	0	0	0	0	0	0	0	0.98	0	0	0	0	1	1	0	0	0	0	0	0	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1440	0.12	0	0	0	0.11	0.11	0	0.11	0.56	0.15	0.52	0	0	0	0.57	0.57	0.15	0	0	0.15	0	0.12	0	0.56
EF1441	0	0	0	0	0	0	0	0	0.95	0	0	0	0.12	0	0.99	0.99	0.11	0	0	0.11	0	0	0	0.93
EF1442	0	0	0	0	0.93	0	0	0	0.92	0	0	0	0	0	0.93	0.93	0	0	0	0	0	0	0	0
EF1443	0.23	0.1	0.11	0.11	0.1	0.11	0	0.11	0.09	0.23	0.09	0	0.09	0	0.55	0.55	0.11	0	0.55	0.11	0.1	0	0.36	0.11
EF1444	0.93	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.93	0	0
EF1445	0.99	0	0	0	0	0	0	0	0	0.91	0	0	0	0	0.98	0.98	0	0	0	0	0	0	0	0
EF1446	0.89	0	0.76	0.22	0	0	0	0.69	0.27	0.94	0	0	0	0	0.99	0.99	0.74	0	0	0.74	0	0.19	0	0.74
EF1447	0.88	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1448	0.98	0.52	0.52	0	0.52	0.52	0	0	0	0.97	0	0	0	0	1	1	0	0	0	0	0	0.68	0	0
EF1449	0.97	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1450	0.99	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1451	0.98	0	0	0	0	0	0	0	0	0.97	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF1452	0.99	0	0.21	0	0.21	0	0.05	0	0	0.96	0.22	0	0.21	0	0.21	0.21	0	0	0	0	0	0.22	0	0
EF1453	1	0	0	0	0	0	0	0	0	0.98	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF1454	0.99	0	0	0	0	0	0	0	0	0.91	0	0	0	0	0.93	0.93	0	0	0	0	0	0	0	0
EF1455	0.91	0.04	0	0	0	0	0	0	0	0.93	0	0	0	0	0.94	0.94	0	0	0	0	0	0	0	0
EF1456	0.96	0	0	0	0	0	0	0	0	0.89	0	0	0	0	0.88	0.88	0	0	0	0	0	0	0	0
EF1457	0.95	0	0	0	0	0	0	0	0	0.98	0	0	0	0	0.98	0.98	0	0	0	0	0	0	0	0
EF1458	0.99	0	0	0	0	0	0	0	0	0.97	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1459	1	0	0	0	0	0	0	0	0	0.99	0	0	0.61	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1460	0.97	0	0	0	0	0	0	0	0	1	0	0	0	0	0.97	0.97	0	0	0	0	0	0	0	0
EF1461	0.84	0	0	0	0	0	0	0	0	0.98	0	0	0	0	0.96	0.96	0	0	0	0	0	0	0	0
EF1462	1	0	0	0	0	0	0	0	0	0.97	0	0	0	0	0.91	0.91	0	0	0	0	0	0	0	0
EF1463	0.88	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0.85	0.85	0	0	0	0	0	0	0	0
EF1464	0.84	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0.84	0.84	0	0	0	0	0	0	0	0
EF1465	0.97	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1466	0.69	0	0	0	0	0	0	0	0	0.9	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1467	0	0	0	0	0	0	0	0	0	0.85	0	0	0	0	0.98	0.98	0	0	0	0	0	0	0	0
EF1468	0.89	0	0	0	0	0	0	0	0	0.89	0	0	0	0	0.92	0.92	0	0	0	0	0	0	0	0
EF1469	0.98	0	0	0	0	0	0	0	0	0.97	0	0	0	0	0.98	0.98	0	0	0	0	0	0	0	0
EF1470	1	0	0	0	0	0	0	0	0	0.97	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1471	1	0	0	0	0	0	0	0	0	0.97	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1472	1	0	0	0	0	0	0	0	0	0.98	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1473	0.97	0	0	0	0	0	0	0	0	0.95	0	0	0	0	0.86	0.86	0	0	0	0	0	0	0	0
EF1474	0.99	0	0	0	0	0	0	0	0	0.99	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1475	1	0	0	0	0	0	0	0	0	0.99	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1476	0.98	0	0	0	0	0	0	0	0	0.99	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1477	0.99	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1478	0.99	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0.99	0.99	0	0	0	0	0	0	0	0
EF1479	0.98	0	0	0	0	0	0	0	0	0.99	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1480	0.99	0	0	0	0	0	0	0	0	0.99	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1481	0.59	0.12	0.13	0.1	0	0.12	0	0	0	0.58	0.56	0	0.1	0.1	1	1	0.1	0.13	0.13	0	0	0.1	0.13	0.1
EF1482	0.96	0	0	0	0	0	0	0	0	0.93	0.64	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1483	1	0.58	0.61	0.66	0	0.58	0.68	0	0	1	0.67	0	0.68	0	1	1	0.66	0	0	0	0	0	0	0.68
EF1484	0.98	0	0	0	0	0	0	0	0	0.98	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1485	0.98	0	0	0	0	0	0	0	0	0.98	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1486	0.56	0.63	0.63	0.63	0.59	0.63	0.63	0.79	0.78	0.89	0.81	0.61	0.82	0.63	1	1	0.63	0.63	0.78	0.63	0.82	0.63	0.63	0.63
EF1487	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1488	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0
EF1489	0.92	0.92	0.63	0	0.63	0.92	0	0	0.91	0.93	0	0	0	0	1	1	0.93	0	0.94	0.93	0	0	0	0.93
EF1490	1	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF1491	0.63	1	0.98	0.99	0.99	1	1	0.99	1	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1492	1	1	0.99	1	1	1	1	0.99	1	0.99	1	0.99	1	0.99	1	1	1	1	0.99	0.99	1	1	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1493	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1494	0.86	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1495	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1496	1	1	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.98	0.98	0.98	0.98	0.98
EF1497	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF1498	0.98	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1499	0.97	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	1
EF1500	1	1	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99	1
EF1501	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.97	1	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF1502	1	1	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.98	0.98	0.98	0.98	0.99
EF1503	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1504	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF1505	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1506	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.13	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	0.99
EF1507	1	1	0.92	0.92	0.93	0.92	0.92	0.92	0.92	0	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.94	0.92	0.92
EF1508	0.56	1	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF1509	1	1	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0	0.99	0.98	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF1510	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1
EF1511	1	1	0.99	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	0.99	1	1
EF1512	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99	1
EF1513	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1515	1	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	1	1	1	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1516	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.55	0.99	0.99	0.99
EF1517	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1518	1	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99
EF1519	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1521	1	0.89	0.99	0.99	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99
EF1522	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1523	1	1	0.98	1	0.98	0.99	0.97	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	1	1	0.99	0.99	0.98	0.98	0.98	1
EF1524	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99
EF1525	1	1	1	0.99	0.99	1	1	1	1	0.74	0.99	0.93	0.99	1	1	1	1	1	1	1	1	1	1	1
EF1526	1	1	0.99	0.99	0.94	1	1	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99	0.99	1	1	1	1	1	1	0.99
EF1527	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1528	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1529	1	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1531	1	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1	1	1	0.7	1	0.99
EF1532	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99
EF1533	0.88	1	0.98	0.88	1	0.99	1	0.94	0.99	0.98	1	1	0.98	1	0.99	0.99	1	1	0.85	0.99	0.88	0.99	0.99	1
EF1534	1	1	0.98	0.98	0.97	1	1	0.99	0.99	1	1	0.94	0.98	1	0.99	0.99	0.98	1	0.96	1	0.99	1	0.89	1
EF1535	1	1	0.99	1	1	1	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	0.99	0.99	1	0.99	1
EF1536	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1537	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1538	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1539	1	1	1	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	1	1	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1540	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1541	1	1	0.99	0.99	1	1	0.99	0.99	1	1	1	0.99	1	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99
EF1542	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1543	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1
EF1544	1	1	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.98	0.99	0.98	0.99	0.99
EF1545	0.8	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1546	1	1	0.99	0.99	1	1	1	0.98	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99
EF1547	1	1	1	0.99	1	0.99	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99
EF1548	1	1	0.99	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1549	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1550	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1551	1	1	1	0.99	1	0.98	0.98	0.98	0.97	1	1	0.98	0.97	1	0.97	0.97	0.99	1	1	0.99	0.99	1	0.99	0.99
EF1552	0.81	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1553	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1554	1	1	0.97	0.96	0.86	0.85	0.98	0.99	0.99	0.98	0.98	0.99	0.94	0.99	0.99	0.99	0.89	0.96	0.99	0.99	0.99	0.99	0.94	0.99
EF1555	1	1	0.99	1	1	1	0.99	0.99	1	0.99	0.99	0.98	0.88	1	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF1556	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF1557	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	0.99
EF1558	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1559	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	1	0.98	1	0.98	0.98	1	0.98	1	0.99	1	0.99	1	1
EF1560	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1561	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF1562	0.59	0.74	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1
EF1563	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.54	0.99
EF1564	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1565	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1566	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1567	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	1	0.99	0.99	1	0.99	0.99	0.99	1
EF1568	1	1	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98
EF1569	1	1	0.99	1	0.99	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99	1	1	1	1
EF1570	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	0.99
EF1571	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF1572	1	1	0.99	1	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF1573	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF1574	1	1	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.98
EF1575	0.67	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99
EF1576	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	1	0.98	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1577	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.99
EF1578	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1579	1	1	1	1	1	1	1	0.99	1	1	1	0.99	0.99	1	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF1580	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	1	0.99	0.99	0.99	0.99	1	0.99	1
EF1581	0.74	1	0.99	0.99	0.99	0.99	0.99	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1582	1	1	0.99	0.99	1	1	1	0.95	0.99	0.99	1	0.99	0.93	0.99	0.98	0.98	0.99	1	0.98	0.99	0.99	0.94	0.99	0.99
EF1583	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1584	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1585	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1586	1	1	0.99	1	1	1	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	1	1
EF1587	1	1	0.99	1	0.98	1	0.98	1	0.98	0.98	1	1	0.99	0.98	0.99	0.99	1	1	0.98	0.98	0.99	0.98	0.99	1
EF1589	1	1	1	0.99	1	0.27	0.27	0.27	0.27	0.99	0.27	0.27	0.99	1	0.99	0.99	0.99	1	0.99	1	0.27	0.99	0.27	0.99
EF1590	1	1	1	1	1	1	1	0.99	1	1	1	0.99	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1
EF1591	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF1592	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1
EF1593	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1594	1	1	1	1	0.99	0.99	0.99	1	1	0.98	0.99	1	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	1
EF1595	1	1	1	1	1	1	1	1	0.99	0.98	1	1	0.99	1	0.99	0.99	1	1	1	1	0.98	1	0.98	1
EF1596	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1597	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.73	0.99	0.99	0.99	0.99	0.99
EF1598	0.54	1	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.98	0.99
EF1599	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99
EF1601	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.08
EF1602	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.76	1	1	0.23
EF1603	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1	1	0.99	1	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1604	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.94	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0
EF1605	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1606	1	1	0.98	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.98	0.98	0.98	0.98
EF1607	1	1	0.98	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.99	1	0.98	1	1	0.98	1	0.99	0.99	0.98	0.99	0.98	0.99
EF1608	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF1609	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1610	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1611	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	1
EF1612	1	1	0.99	1	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1
EF1613	0.81	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1614	0.39	0.57	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1
EF1615	0.55	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1616	1	1	0.98	0.99	0.99	0.99	1	1	1	0.98	1	1	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.98
EF1617	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	1	0.99	1	0.99
EF1618	1	1	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1619	1	1	1	1	1	1	0.99	1	1	0.99	1	1	0.98	0.99	0.98	0.98	1	0.99	1	1	1	0.99	1	0.99
EF1620	1	1	0.99	1	1	1	1	1	0.99	0.98	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99
EF1621	1	1	0.99	0.99	0.98	0.97	0.98	0.99	0.98	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.99
EF1622	1	1	0.98	0.98	0.99	0.99	0.99	0.97	0.98	0.99	0.99	0.98	1	0.98	1	1	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.98
EF1623	1	1	0.99	1	0.99	0.99	1	0.99	0.98	0.98	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.98
EF1624	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1625	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99
EF1626	1	1	0.99	1	1	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF1627	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF1629	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1630	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1632	0.75	1	0.99	1	0.99	0.99	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1
EF1633	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1634	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99	1	0.99	0.99	0.99	1
EF1635	0.94	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1637	1	1	0.99	1	0.99	1	0.99	1	0.99	0.98	0.99	1	0.98	0.99	0.98	0.98	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF1638	1	1	0.98	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99
EF1639	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1640	1	1	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.99
EF1641	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF1643	1	1	0.99	0.98	0.85	0.98	0.96	0.95	1	0.83	0.98	0.87	0.95	0.99	1	1	0.99	0.94	0.96	0.99	0.95	0.99	0.96	0.99
EF1644	1	1	0.99	0.99	0.99	0.99	1	0.93	0.99	0.99	1	0.93	0.99	1	1	1	0.99	0.99	1	0.99	0.98	0.99	0.99	1
EF1645	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99
EF1646	1	1	0.99	0.99	0.99	0.65	1	1	0.99	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1647	1	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	1	1	0.99	0.99	1	1	1	1	0.99
EF1648	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	1	1	0.99	0.99
EF1649	0.56	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	1	1	1	0.99
EF1650	0.81	0.92	0.99	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF1651	1	1	0.99	0.98	0.99	0.98	0.99	0.98	0.99	0.99	0.98	0.98	1	0.98	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF1652	1	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1653	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99
EF1654	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.92	0.99	0.99	0.99	0.99
EF1655	1	1	0.98	0.98	0.99	0.99	0.54	0.98	0.99	0.98	0.99	0.98	1	0.98	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1656	0.98	1	0.99	0.67	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF1657	1	1	0.98	0.98	0.98	0.98	1	0.98	0.99	0.99	0.98	0.98	1	0.98	1	1	0.98	0.75	0.99	0.98	0.98	0.98	0.98	0.99
EF1658	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1659	0.91	0.72	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1660	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1661	0.53	1	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.98	1	0.98	1	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98
EF1662	1	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1663	1	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99
EF1664	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.97	1	0.99	1	0.99	1	1	0.99	1	1	1	1	1	1	0.99
EF1665	0.75	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1666	0.44	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1667	0.54	1	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99
EF1668	1	1	1	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.98	1	1	0.99	0.99	0.99	0.98	0.98	0.98	0.98	1
EF1669	1	0.87	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.98	0.98	1	0.98	1	1	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98
EF1670	1	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	1	1	1	0.99
EF1671	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1672	1	1	0	0.99	1	0.99	0.99	1	0	0	1	1	1	0.99	1	1	0.99	1	1	0.99	1	1	1	0
EF1673	1	1	0.52	1	0.97	0.99	1	0.99	0.49	0.5	1	0.99	1	0.99	1	1	1	1	1	1	0.99	0.97	0.99	0.5
EF1674	1	1	0.98	0.98	0.97	0.99	0.98	0.99	0.98	0.98	0.98	0.99	1	0.97	1	1	0.98	0.99	0.99	0.97	0.97	0.97	0.97	0.98
EF1675	1	0.61	1	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF1676	1	1	0.98	1	1	1	1	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	1	1	1	1	1	1	1	0.99
EF1677	1	1	0.99	1	0.99	0.98	1	0.98	1	0.98	0.99	0.98	0.39	1	0.39	0.39	1	1	0.99	1	0.99	0.99	0.99	0.99
EF1678	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1679	0.84	1	0.99	1	1	1	0.99	0.99	1	0.99	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1
EF1680	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1681	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1682	0.94	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	0.99
EF1683	1	1	1	0.99	0.98	0.99	0.99	1	1	0.99	1	1	1	0.99	1	1	0.99	1	0.99	0.99	0.98	0.98	0.98	0.99
EF1684	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99
EF1685	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.98	0.99	1	0.99	1	1	0.99	0.99	1	0.99	1	1	1	0.98
EF1686	1	1	0.99	0.99	0.99	0.99	0.99	0.96	0.99	0.99	0.99	0.96	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1687	1	1	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	0.99
EF1688	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1689	1	1	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.98	0.98	0.98	0.98
EF1690	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1691	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1692	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1693	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1694	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1695	1	1	0.99	1	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	1	0.98	0.98	0.98	0.99
EF1698	1	1	0.99	1	1	1	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	1	1	0.99	0.98	1	1	1	0.99
EF1699	1	1	1	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	0.99
Ef16SA	1	1	1	1	1	1	1	1	0.87	1	1	1	1	1	0.59	1	1	1	1	1	1	1	1	0.55
Ef16SB	1	1	1	1	1	1	1	1	0.87	1	1	1	1	1	0.59	1	1	1	1	1	1	1	1	0.55
Ef16SC	1	1	1	1	1	1	1	1	0.87	1	1	1	1	1	0.59	1	1	1	1	1	1	1	1	0.55
Ef16SD	1	1	1	1	1	1	1	1	0.87	1	1	1	1	1	0.59	1	1	1	1	1	1	1	1	0.55
EF1700	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	1	0.99	1	0.99	0.99	0.99	1
EF1701	1	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF1702	1	1	0.97	0.98	0.98	0.98	0.99	0.98	0.97	0.98	0.98	0.98	1	0.98	1	1	0.98	1	0.99	0.99	0.98	0.98	0.98	0.98
EF1703	1	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1704	0.97	0.99	0.99	0.99	0.97	0.99	0.99	0.98	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99
EF1705	1	0.95	0.99	0.99	0.99	1	0.96	0.98	0.99	0.93	0.99	0.99	0.98	1	1	1	1	0.99	0.92	1	0.94	0.91	0.99	0.9
EF1706	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1707	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1708	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1709	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.98	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1710	1	1	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.99
EF1711	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1712	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1713	0.5	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1714	1	1	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.98	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.99
EF1715	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	1
EF1716	0.87	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF1717	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF1718	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF1719	1	1	0.99	1	1	1	1	1	0.99	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF1720	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.86	0.99	0.99	0.99	0.99
EF1721	1	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1	0.99
EF1722	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1723	1	1	0.99	0.99	1	1	1	1	1	0.99	1	0.99	1	0.99	1	1	0.99	1	1	1	1	1	1	1
EF1724	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1725	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1
EF1726	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	0.99
EF1727	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	0.98	0.99	1	0.99	0.99	0.99	0.99
EF1728	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF1730	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1731	1	1	0.99	1	0.98	0.98	0.99	0.98	0.99	0.99	0.98	0.99	1	0.99	1	1	1	0.99	0.99	0.99	0.98	0.98	0.98	0.98
EF1732	1	1	0.98	1	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	1	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1733	0.63	1	0.99	1	0.99	1	1	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99
EF1734	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1735	1	1	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	1
EF1736	1	1	0.99	1	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	1	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1737	1	1	0.99	1	0.98	1	0.99	0.98	1	0.98	0.98	1	1	1	1	1	1	1	0.99	0.98	0.98	0.98	0.98	0.99
EF1738	1	1	0.99	0.99	0.99	0.99	1	0.98	0.99	0.98	0.99	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF1739	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1740	1	1	0.99	0.97	0.98	0.97	0.97	0.97	0.99	0.98	0.98	0.97	1	0.98	1	1	0.97	0.98	0.99	0.98	0.98	0.98	0.98	0.96
EF1741	0.41	1	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.98	1	0.98	1	1	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99
EF1743	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF1744	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1745	1	1	1	0.99	0.99	1	1	1	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1746	1	1	1	1	1	1	0.99	1	0.99	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1
EF1747	1	1	1	1	1	1	1	0.99	1	0.99	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99
EF1748	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF1749	1	1	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	0.99	0.98	0.98	0.98	0.99
EF1750	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1
EF1751	1	1	0.99	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF1752	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1
EF1753	0.53	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1754	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99	1	1	0.99	1	1
EF1755	1	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	0.99	0.99	0.99	1	1	1	1
EF1756	0.88	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1
EF1757	1	1	0.99	0.99	1	1	0.99	0.99	0.99	1	1	0.99	1	0.99	1	1	0.99	1	1	1	1	0.99	1	1
EF1758	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1759	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF1760	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.96	0.99	0.99	0.99	0.94	0.99	1	0.95
EF1761	1	1	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99	1	1
EF1762	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	1	1
EF1763	0.62	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1
EF1764	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1765	1	1	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.98	1	0.99	1	0.99	1	1	0.98	0.96	0.99	0.99	0.98	0.99	0.98	0.99
EF1767	1	1	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.98	0.98	0.99	0.98	0.99	0.98

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1768	1	1	0	0.99	0	1	0	0.99	0	0.99	0	0.99	1	0.99	1	1	0.99	0	0	0.99	0	0.99	0	0
EF1769	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.98	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98
EF1770	1	1	0.98	1	0.99	1	1	0.99	0.99	0.99	0.99	0.98	1	1	1	1	1	1	0.99	0.98	0.99	0.99	0.99	1
EF1771	1	1	0.99	0.99	1	1	0.99	0.99	1	0.99	1	1	1	1	1	1	0.99	1	0.99	1	1	0.99	1	1
EF1772	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF1773	1	1	0.98	0.98	0.98	1	1	0.98	0.98	0.98	0.98	0.98	1	0.98	1	1	0.98	0.99	0.98	0.98	0.98	0.98	0.98	1
EF1774	1	0.98	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1775	1	1	0.98	0.98	0.98	0.98	0.99	0.98	0.97	0.98	0.98	0.98	1	0.98	1	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98
EF1776	1	1	0.95	0.98	0.96	0.97	0.93	0.99	0.98	0.98	0.97	0.97	1	0.98	1	1	0.98	0.96	0.96	0.94	0.96	0.99	0.96	0.98
EF1777	1	1	0.98	0.99	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98
EF1778	1	0.79	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1779	1	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.97	0.99	0.98	1	0.98	1	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98
EF1780	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1781	1	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1782	1	0.68	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF1783	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF1784	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1785	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	1
EF1786	1	1	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.98	1	0.98	1	1	0.98	1	0.98	0.99	0.98	0.99	0.98	0.98
EF1787	1	1	0.98	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	1	0.99	1	1	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1789	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1790	0.82	1	0.98	0.99	0.99	0.98	0.99	1	0.98	0.98	0.98	0.99	1	0.98	1	1	0.99	1	0.98	0.99	0.99	1	0.99	0.99
EF1791	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1792	1	1	0.99	0.98	0.99	0.99	0.99	1	0.99	0.97	0.99	0.98	1	0.99	1	1	0.98	1	0.99	0.99	0.99	1	0.99	0.99
EF1793	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1794	1	1	0.97	0.99	0.99	1	1	0.98	0.98	0.98	0.99	0.99	1	0.98	1	1	0.99	1	0.98	0.99	0.99	0.98	0.99	0.99
EF1796	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1797	1	1	0.99	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	1	0.98	0.99	1	1	1	1
EF1798	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.98	0.99	0.99	0.99	0.99
EF1800	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1801	1	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF1802	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1803	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF1804	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1805	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.6	0.99
EF1806	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1807	1	1	0.99	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1808	0.38	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.9	0.99
EF1809	1	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99
EF1810	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	1	1	0.99	1	0.99	1	0.96
EF1811	0.71	1	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.98	1	0.98	1	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.98
EF1812	0.65	1	0.97	0.98	0.96	0.98	0.99	0.34	0.96	0.42	0.96	1	1	0.97	1	0.99	0.98	1	0.96	1	0.96	0.36	0.96	0.42
EF1813	1	1	0.99	0.99	1	0.99	0.99	0.36	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	1	0.99	1	0.36	1	0.99
EF1814	1	1	0.99	0.99	0.99	0.99	0.94	0	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0	0.99	0.99
EF1815	1	1	1	0.99	0.99	0.99	0	0	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0	0.99	1
EF1816	0.67	1	0.99	0.99	0.99	0.99	0	0	1	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99
EF1817	1	1	0.99	0.99	0.98	0.98	0	0	0.99	0.99	0.98	0.99	1	0.98	1	1	0.99	0.99	0.98	0.99	0.98	0	0.98	0.98
EF1818	1	1	0.99	0.63	0.99	0.99	0	0	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0	0.99	0.99
EF1820	1	0.96	0.99	0	0.8	0.99	0	0	0.99	0.95	0.8	1	0.98	0.99	0.92	0.92	0.99	0.99	0.8	0.99	0.75	0	0.8	0.98
EF1821	1	1	0.99	0	0	0.99	0	0	0.99	0.99	0	0.99	1	0.99	1	1	0.99	0.99	0	0.99	0	0	0	0.99
EF1822	1	1	1	0	0	1	0	0	1	0.99	0	0.99	1	0.99	1	1	1	0.99	0	0.99	0	0	0	0.4
EF1823	1	1	0.98	0.15	0.15	0.98	0.15	0.15	0.98	0.99	0.15	0.43	1	0.98	1	1	0.97	0.98	0.15	0.99	0.15	0.15	0.15	0.15
EF1824	0.67	1	0.99	0	0	0.38	0	0	0.99	0.99	0	0	1	0.99	1	1	0.99	0.99	0	0.99	0	0	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1825	1	1	0.99	0	0	0	0	0	0.99	0.98	0	0	1	0.99	1	1	0.99	1	0	0.99	0	0	0	0
EF1826	1	1	0	0	0	0	0	0	1	0.99	0	0	1	1	1	1	1	1	0	1	0	0	0	0
EF1827	1	1	0	0	0	0	0	0	0.97	0	0	0	1	0.97	1	1	0.97	0.97	0	0.97	0	0	0	0
EF1828	1	1	0.1	0.1	0.1	0.1	0.1	0.1	1	0.1	0.1	0.1	1	1	1	1	1	1	0.1	1	0.1	0.1	0.1	0.1
EF1829	1	1	0.17	0.17	0.17	0.17	0.17	0.17	0.99	0.17	0.17	0.17	1	0.99	1	1	0.99	0.99	0.17	0.99	0.17	0.17	0.17	0.17
EF1830	1	1	0	0	0	0	0	0	0.99	0	0	0	1	1	1	1	1	1	0	1	0	0	0	0
EF1831	1	1	0	0	0	0	0	0.29	0.99	0	0	0.48	1	0.97	1	1	0.99	0.97	0	0.97	0	0.29	0	0
EF1833	1	1	0	0	0	0	0	0	0.99	0	0	0.98	1	0.99	1	1	0.99	0.99	0	0.99	0	0	0	0
EF1834	1	1	0	0.7	0.7	0.7	0	0.7	0.99	0	0	0.99	1	0.99	1	1	1	1	0	0.99	0.7	0.7	0.7	0.7
EF1835	1	1	0	0.64	0.64	0.64	0	0.64	1	0	0	1	1	1	1	1	1	1	0	1	0.64	0.64	0.64	0.64
EF1836	1	1	0	0	0	0	0	0	1	0	0	1	1	1	1	1	1	1	0	1	0	0	0	0
EF1837	1	1	0	0	0	0	0	0	1	0	0	0.99	1	0.99	1	1	0.99	0.99	0	0.99	0	0	0	0
EF1838	1	1	0	0	0	0.1	0.11	0	0.99	0	0	1	1	1	1	1	0.99	0.99	0	0.99	0	0	0	0
EF1839	1	1	0	0	0	0.75	0.99	0	0.99	0	0	0.99	1	0.99	1	1	0.99	0.99	0	0.99	0	0	0	0
EF1840	1	1	0	0.48	0	0.96	0.96	0	0.11	0	0	0.96	1	0.96	1	1	0.96	0.96	0	0.96	0	0	0	0
EF1841	1	1	0	0.98	0.75	0.98	0.98	0	0.99	0.08	0.75	0.98	1	0.98	1	1	0.98	0.99	0.75	1	0.75	0	0.75	0
EF1843	1	1	0.41	0.99	0.99	1	1	0	0.99	0.89	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0	0.99	0.98
EF1844	1	1	0	0	1	0	0	0	0	0.99	1	0	1	0	1	1	0	0	1	0.99	1	0	1	0
EF1846	1	1	0.82	0.84	0.98	0.84	0.97	0	0.8	0.97	0.98	0.97	1	0.85	1	1	0.84	0.97	0.98	0.96	0.98	0	0.98	0.83
EF1847	1	1	0	0	1	1	0	0	0	0.64	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1848	1	1	0	0	1	1	0	0	0	0.54	1	0	1	0	1	1	0	0	1	0	0.61	0	0.61	0
EF1849	1	1	0	0	1	1	0.85	0.85	0	0	1	0.85	1	0.45	1	1	0	0	1	0	0.8	0.85	0.82	0
EF1850	1	1	0	0	1	1	0.86	0.86	0	0	1	0.86	1	0.3	1	1	0	0	1	0	0.86	0.86	0.86	0
EF1851	1	1	0.69	0.69	1	1	0.56	0.69	0.56	0.69	1	0.69	1	0.69	1	1	0.69	0.69	1	0.69	1	0.56	1	0.69
EF1852	1	1	0.18	0.18	1	1	0.18	0.18	0.18	0.18	1	0.18	1	0.18	1	1	0.18	0.18	1	0.18	1	0.18	1	0.18
EF1853	1	1	0	0	0.99	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1855	1	1	0	0	1	1	0.14	0	0	0.18	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1856	1	0.99	0	0	1	0.96	0.71	0.99	0	0	0	0.99	0.96	0	0.57	0.99	0	0	0.69	0	0.47	0.99	0.91	0
EF1857	1	1	0	0	1	1	0	0	0.71	0	1	0	1	0	1	1	0	0.72	1	0	1	0	1	0
EF1858	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1859	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1860	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1861	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1862	1	1	0	0.63	1	1	0.42	0.61	0.52	0	0.64	0.7	1	0	1	1	0.63	0	1	0.34	1	0.64	1	0.63
EF1863	1	1	0	0	1	1	0	0	0	0	1	0	0.83	0	1	1	0	0	1	0	1	0	1	0
EF1864	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1866	1	1	0	0.07	1	1	0.22	0.35	0	0	1	0.35	1	0	1	1	0.35	0	1	0	1	0	1	0.35
EF1867	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1868	1	1	0.19	0.19	1	1	0.19	0.19	0.19	0.19	1	0.19	1	0.19	1	1	0.19	0.19	1	0.19	1	0.19	1	0.16
EF1869	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1870	1	1	0	0	1	0.16	0	0	0	0	0.16	0	1	0	1	1	0	0	0.16	0	0.16	0	0.16	0
EF1871	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1872	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1873	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1874	1	0.95	0	0.98	0.54	1	0.41	0.9	0.99	0	1	0.66	1	0	0.68	0.68	0.98	0	1	0.34	0.54	0.98	0.54	0.98
EF1875	1	1	0	0	1	1	0	0	0.52	0	1	0	1	0.39	1	1	0	0	1	0	1	0.52	1	0
EF1876	1	1	0.57	0	1	1	0.57	0.55	0.56	0.53	1	0.57	1	0.55	1	1	0	0	1	0.57	1	0.58	1	0
EF1877	1	1	0.42	0	1	1	0.42	0.42	0.37	0.38	1	0.42	1	0.4	1	1	0	0	1	0.42	1	0.42	1	0
EF1878	0.74	0.44	0.69	0	1	1	0.69	0.69	0.69	0.72	1	0.69	1	0.72	1	1	0	0	1	0.69	1	0.69	1	0
EF1879	0.99	1	0.57	0	1	1	0.57	0.56	0.61	0.65	1	0.57	1	0.6	1	1	0	0	1	0.57	1	0.67	1	0
EF1880	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1881	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1882	1	1	0.63	0	1	1	0.63	0.64	0.65	0.64	1	0.63	1	0.69	1	1	0	0	1	0.63	1	0.63	1	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1883	0.69	1	0	0	1	1	0	0	0.75	0.76	1	0	1	0.74	1	1	0	0	1	0	1	0	1	0
EF1884	1	1	0.27	0	1	1	0	0	0.06	0.12	1	0	1	0	1	1	0	0	1	0.27	1	0	1	0
EF1885	1	1	0	0	1	0.93	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	0.93	0
EF1886	0.68	1	0.53	0.17	1	1	0.53	0.53	0.61	0.59	1	0.53	1	0.65	1	1	0	0	1	0.53	1	0.61	1	0
EF1887	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1888	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1889	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1890	1	1	0.67	0	1	1	0.67	0.65	0.7	0.64	1	0.67	1	0.68	1	1	0	0	1	0.67	1	0.67	1	0
EF1891	1	1	0	0	1	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1892	0.54	1	0.48	0.24	1	1	0.48	0.48	0.47	0.46	1	0.48	1	0.51	1	1	0	0	1	0.48	1	0.49	1	0
EF1893	1	1	0	0	1	0.99	0	0	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0
EF1894	0.89	1	0	0	1	1	0.58	0.55	0.57	0.58	1	0.58	1	0.65	1	1	0	0	1	0.58	1	0.61	1	0
EF1895	0.84	1	0	0	1	1	0	0	0.58	0.64	1	0	1	0.68	1	1	0	0	1	0	1	0	1	0
EF1896	0.7	0.59	0	0	0.99	0.99	0	0.8	0.44	0.03	0.99	0.12	1	0.59	1	1	0	0	0.99	0	0.99	0.8	0.99	0
EF1897	1	1	0	0	1	1	0.19	0.69	0	0.6	1	0.19	1	0	1	1	0	0.19	1	0	1	0.69	1	0
EF1898	1	1	0.99	0.99	1	1	0.99	0.99	0.99	1	1	0.99	1	0.99	1	1	0.99	0.99	1	0.99	1	0.99	1	0.99
EF1899	1	1	0.99	0.99	1	0.99	1	0.99	0.97	0.99	0.99	0.99	1	1	1	1	0.99	1	1	0.99	1	0.99	1	1
EF1900	1	1	0.98	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	1	1	0.98	1	0.97	0.98	0.97	0.98	0.97	0.98
EF1901	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF1902	1	1	0.98	0.99	0.98	0.99	0.99	0.98	0.99	0.99	1	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.99
EF1903	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1904	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.87	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1905	0.93	0.63	0.94	0.97	0.98	0.95	0.95	0.97	0.97	0.94	1	0.97	1	0.97	0.94	0.92	0.97	0.99	0.95	1	0.98	0.95	0.98	0.97
EF1906	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	1	0.99	0.99	1	0.99	1	0.99
EF1907	1	1	1	1	1	1	0.99	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99
EF1908	1	1	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99
EF1909	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1910	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1911	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99
EF1912	1	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	1	0.99	1	1
EF1913	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1914	1	1	0.99	1	0.99	1	0.99	1	1	0.99	1	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1
EF1915	1	1	0.99	1	1	1	0.99	0.99	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1	1
EF1916	1	1	0.99	1	0.99	1	1	0.99	0.99	0.99	1	1	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1917	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	1
EF1918	1	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF1919	1	1	0.98	0.98	0.99	1	0.99	0.98	0.99	0.97	0.98	0.98	0.97	0.99	0.97	0.97	0.98	1	0.99	0.98	0.99	0.98	0.99	0.99
EF1920	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1921	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	0.99	1	1	0.99	1	1	1	1
EF1922	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF1923	1	1	0.81	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1925	0.79	1	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF1926	1	1	0	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.99	1	0.99	0.99	0.98	0.98	0.98	0.99
EF1927	1	1	1	1	0.99	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF1928	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1929	1	1	0.99	1	1	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99
EF1931	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1932	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.98	0.99	0.99	0.99
EF1933	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	1	0.99	1	0.99
EF1934	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1935	1	1	0.99	0.42	0.98	0.99	0.99	0.99	1	0.97	0.99	0.99	0.99	0.42	0.99	0.99	0.42	1	0.99	0.99	1	0.99	0.99	0.99
EF1936	1	1	0.99	1	0.98	0.99	1	1	1	0.98	0.98	0.98	0.99	1	0.99	0.99	1	1	0.99	1	0.98	1	0.98	0.99
EF1937	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.98	0.98	0.99	1	0.99	0.98	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1938	1	1	1	1	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99
EF1939	1	1	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.99	1	0.98	1	1	0.98	1	0.99	0.99	0.98	0.99	0.98	0.99
EF1940	1	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF1941	1	1	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.98	1	0.99	0.98	0.98	0.99	0.98	0.98
EF1943	1	1	0.99	0.54	0.99	0.99	0.99	0.99	1	1	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1944	0.78	0.6	0.83	0.85	0.81	0.81	0.8	0.8	0.83	0.79	0.83	0.85	0.83	0.8	0.84	0.76	0.85	1	0.83	0.8	0.81	0.83	0.81	0.83
EF1945	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1946	1	1	1	1	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1
EF1947	1	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	1
EF1948	1	1	0.94	0.99	0.94	0.99	0.99	0.94	0.94	0.95	0.99	0.94	0.95	0.99	0.95	0.95	0.99	1	0.94	0.99	0.94	0.94	0.94	0.93
EF1949	1	1	0.98	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99
EF1950	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1951	1	1	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.98	0.98	0.98	0.99
EF1952	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1
EF1953	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1954	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1955	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1956	1	0.59	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1
EF1958	1	1	0.99	1	1	0.99	0	1	0.99	0.99	1	0.99	0.99	0	0.99	0.99	1	1	1	0	1	1	1	0.99
EF1959	1	1	1	1	1	0.99	0.1	1	0.99	0.99	1	1	0.99	0.1	0.99	0.99	1	1	0.99	0.1	1	1	1	0.99
EF1961	0.89	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99
EF1962	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99
EF1963	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1964	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1965	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF1966	1	1	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	0.98	0.99	0.98	0.98	0.98	1	0.99	0.99	0.99	0.98	0.99	0.99
EF1967	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1968	1	1	1	1	1	0.99	0.99	1	0.99	1	1	1	1	0.98	1	1	1	1	0.99	1	1	1	1	0.99
EF1969	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	1	0.99	1	0.99	1	0.99	0.99
EF1970	0.52	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1971	1	1	0.99	1	0.99	0.99	1	1	1	0.98	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99
EF1972	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1973	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF1974	0.86	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1975	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	1	1
EF1976	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99
EF1977	1	1	1	1	1	0.99	1	1	1	0.98	1	1	1	0.98	1	1	1	1	1	1	1	1	1	0.98
EF1978	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF1979	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99
EF1980	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF1981	0.58	0.62	0.59	0.99	0.59	0.99	0.98	0.99	0.59	0.6	0.59	0.98	1	0.98	0.4	0.71	0.99	1	0.59	0.59	0.59	0.99	0.59	0.59
EF1982	1	1	1	1	0.95	1	0.99	1	0.99	1	0.99	0.99	0.99	1	0.22	0.99	1	1	0.99	0.99	1	1	0.98	0.99
EF1983	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0	0.99	0.99	1	0.99	0.99	1	0.95	0.94	0.99
EF1984	1	1	1	1	0.99	1	0.99	1	1	0.99	1	1	1	1	0	1	1	0.99	1	1	0.99	1	0.99	1
EF1985	1	1	0.97	1	0.99	0.97	0.97	1	0.97	0.99	1	0.99	0.99	0.97	0	0.99	1	0.97	0.99	0.97	0.99	1	0.99	1
EF1986	1	1	0.99	1	0.99	1	0.99	1	0.99	0.99	1	1	1	0.99	0	1	1	1	1	0.99	0.99	1	0.99	1
EF1987	1	1	0.73	0.99	0.69	0.99	0.99	1	0.73	0.74	0.98	1	0.74	0.74	0	0.74	0.99	0.74	0.74	0.74	0.99	0.99	0.99	0.99
EF1988	1	1	0.3	0.98	1	1	0.98	1	0	0	0.98	1	0.3	0	0.3	0.3	0.98	0	0	0	0.98	0.98	0.98	0.98
EF1989	1	1	0	0.99	1	1	0.99	0.99	0	0	0.99	1	0	0	0	0	0.99	0	0	0	0.99	0.99	0.99	0.99
EF1990	1	1	0	1	0.97	0.97	0.99	0.99	0	0	0.99	0.97	0	0	0	0	1	0	0	0	0.97	0.99	0.99	0.99
EF1991	1	1	0.86	1	1	1	1	1	0.86	0.86	1	1	0.86	0.86	0.86	0.86	1	0.86	0.86	0.86	1	1	1	1
EF1992	0.66	0.74	0.49	0.91	0.96	0.97	0.74	0.72	0.95	0	1	0.53	0.69	0	0.69	0.69	0.91	0	0	0	0.94	1	0.99	0.74
EF1993	1	1	0	0	0.99	0.99	0	0	0.85	0	1	0	0	0	0	0	0	0	0	0	1	1	1	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF1994	1	1	0.58	0.56	0.99	0.99	0	0	0.95	0	1	0	0	0	0	0	0	0	0	0	1	1	1	0
EF1995	1	1	0.64	0	1	1	0.5	0.5	0.83	0	1	0	0.62	0	0.62	0.62	0	0	0	0	0.95	1	1	0.5
EF1996	1	1	0.9	0.13	1	0.88	0	0.13	0.6	0	1	0	0.68	0	0.68	0.68	0.13	0	0	0	0.92	1	1	0
EF1998	1	1	0.97	1	1	1	0	0.96	0.15	0	1	0.13	0	0	0	0	1	0	0.07	0	0.97	1	1	0
EF2000	1	0.62	0.98	1	1	0.51	0	0.98	0.52	0	0.86	0.44	0	0	0	0	1	0	0	0	0.99	1	1	0
EF2001	1	0.99	0.5	0.81	0.99	0.99	0	0.9	0.51	0.4	0.64	0.59	0	0	0	0	0.99	0	0	0	0.47	0.99	0.99	0
EF2002	1	1	0	1	1	1	0	0.91	0	0	1	0.9	0	0	0	0	1	0	0	0	0	1	1	0
EF2003	1	0.55	0	0.96	0.96	0.96	0	0.86	0	0	0.96	0.87	0	0	0	0	0.96	0	0	0	0	0.96	0.96	0
EF2004	1	1	0	1	0.99	1	0	0.73	0	0	1	1	0	0	0	0	1	0	0	0	0	1	1	0
EF2005	1	1	0	0.99	0.99	0.99	0	0.78	0.22	0	0.99	0.99	0	0	0	0	0.99	0	0.22	0	0	0.99	0.99	0.22
EF2006	1	1	0	0.96	0.96	0.96	0	0.9	0	0	0.96	0.96	0	0	0	0	0.96	0	0	0	0	0.95	0.96	0
EF2007	1	1	0	0.99	0.99	0.99	0	0.86	0	0	0.99	0.88	0	0.1	0	0	0.99	0	0	0	0	0.99	0.78	0
EF2008	1	1	0	0.96	0.96	0.96	0	0.69	0	0	0.96	0.69	0	0	0	0	0.96	0	0	0	0	0.96	0.96	0
EF2009	1	1	0	0.98	0.98	0.98	0	0.65	0	0	0.98	0.64	0	0	0	0	0.98	0	0	0	0	0.98	0.98	0
EF2010	1	0.99	0	0.97	0.97	0.97	0	0	0	0	0.97	0	0	0	0	0	0.97	0	0	0	0	0.97	0.97	0
EF2011	1	0.99	0	0.99	0.99	0.99	0	0.72	0	0	0.99	0.72	0	0	0	0	0.99	0	0	0	0	0.99	0.99	0
EF2012	1	0.99	0	0.98	0.98	0.99	0	0.73	0	0	0.98	0.72	0	0	0	0	0.98	0	0	0	0	0.98	0.98	0
EF2013	1	0.91	0	0.93	0.93	1	0	0.96	0	0	0.93	0.93	0	0	0	0	0.93	0	0	0	0	0.93	0.93	0
EF2014	1	1	0	0	0	1	0	0.93	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2015	1	0.65	0	0.5	0.5	0.98	0	0.54	0	0	0.5	0.51	0	0	0	0	0.5	0	0	0	0	0.5	0.5	0
EF2016	1	0.3	0	0.89	0.89	0.89	0	0.81	0	0	0.89	0.82	0	0	0	0	0.89	0	0	0	0	0.89	0.89	0
EF2017	1	0.38	0	0	0	0	0	0	0	0.04	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2018	1	1	0	0	0	0.62	0.47	0	0	0	0	0	0	0	0	0	0	0	0.47	0	0	0	0	0
EF2019	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2020	1	1	0	0	0	0	0	0	0	0	0	0.06	0	0	0	0	0	0	0	0	0	0	0	0.08
EF2021	1	1	0.88	0	0.85	0.64	0.77	0.77	0	0	0.88	0.64	0.88	0	0.88	0.88	0	0	0	0	0.77	0.88	0	0.65
EF2022	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2023	1	1	0.95	0.95	0.97	0.94	0.98	0.95	0	0	0.9	0.94	0.95	0	0.93	0.93	0.95	0	0	0.21	0.95	0.94	0.21	0.95
EF2024	1	0.54	0.94	0.93	0.97	0.98	0.93	0.97	0	0	0.39	0.98	0.96	0	0	0	0.94	0	0	0.94	0.93	0.99	0.92	0.94
EF2025	1	1	0.58	0.99	0.98	0.99	0.99	0.99	0	0	0.98	0.99	1	0	1	1	0.99	0.44	0.44	0.58	0.99	0.98	0.98	0.99
EF2026	1	1	0.8	0.81	0.89	0.82	1	0.93	0	0	0.77	0.82	0.87	0	0.87	0.87	0.81	0	0.7	0.74	0.88	0.87	0.88	0.81
EF2027	1	0.97	0	0.95	0.12	0.11	1	1	0	0	0.11	0.11	0.54	0	0.54	0.54	0.95	0	0	0.11	0.11	0.11	0.11	0.93
EF2028	1	1	0	1	0	0	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1
EF2029	1	1	0	0.99	0.94	0	0.99	1	0	0	0.23	0	0.29	0	0.29	0.29	0.99	0	0	0	0	0	0	1
EF2031	1	1	0	0.99	0	0	0.99	0.99	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0	0	0.99
EF2032	1	1	0	0.97	0.16	0	0.97	0.97	0	0	0	0	0	0	0	0	0.97	0	0	0	0	0	0	0.97
EF2033	1	1	0	0.46	0.98	0	0.47	0.46	0	0	0	0	0.98	0	0.98	0.98	0.68	0	0	0.68	0	0.69	0	0.68
EF2034	1	1	0.2	0.99	0.96	0.19	0.97	0.99	0	0	0.2	0.2	0.21	0	0.21	0.21	0.99	0	0	0	0.2	0.2	0.2	0.98
EF2036	1	1	0.88	1	0.88	0.88	1	0.99	0	0	0.87	0.88	0.88	0	0.88	0.88	1	0	0	0	0.88	0.87	0.88	0.99
EF2037	1	0.37	0.95	1	0.95	0.95	0.86	0.85	0	0.34	0.93	0.95	0.95	0	0.95	0.95	1	0	0	0.33	0.7	0.96	0.95	0.85
EF2038	1	0.74	0	0.97	0.98	0.98	0.95	0.95	0	0	0.98	0.98	0	0	0	0	0.97	0	0	0	0.95	0.98	0.98	0.95
EF2039	1	1	0	0.72	0.72	0.72	0	0	0	0	0.72	0.82	0	0	0	0	0.72	0	0	0	0	0.72	0.72	0
EF2040	1	0.6	0	0.58	0.58	0.58	0	0.35	0.37	0	0.58	0.58	0	0	0	0	0.58	0	0	0	0.37	0.58	0.58	0
EF2041	1	0.78	0	0.95	0.96	0.96	0	0	0	0	0.95	0.96	0	0	0	0	0.95	0	0	0	0	0.96	0.96	0
EF2042	1	0.98	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2043	1	0.77	0	0.97	0.97	0.97	0.98	0.95	0	0	0.97	0.97	0	0	0	0	0.97	0	0	0	0.95	0.97	0.97	0.95
EF2044	1	1	0.99	1	0.98	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	1	1	0.99	1	0.98	1	0.98	1
EF2045	1	1	0.98	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0	0.99	1	1	0.98	0.99	0.99	1	0.99	0.99
EF2046	1	1	0.99	1	0.99	1	1	1	0.99	0.98	0.99	1	1	1	0	1	1	1	1	1	0.99	1	0.99	1
EF2047	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.98	1	0.99	0.99	1	0	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF2048	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF2049	1	1	0.93	0.97	0.99	0.99	0.97	0.98	0.93	0.99	0.97	0.99	0.97	0.99	0	0.97	0.97	1	0.97	0.97	1	0.98	1	0.97
EF2050	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.47	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2051	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.85	1	0.99	0.99	0.99
EF2052	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0	0.99	1	0.99	0.99	0.98	0.98	1	0.98	0.99
EF2055	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	0.61	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2056	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.96	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2057	1	1	1	1	1	1	1	1	1	1	1	0.62	0.99	1	0.99	0.99	1	1	1	1	0.99	1	1	1
EF2058	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2059	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99
EF2060	1	1	1	1	1	1	1	1	1	0.99	1	1	1	0.99	1	1	1	1	0.99	0.99	1	1	0.99	1
EF2061	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2062	1	1	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.98	0.98	0.98	1	0.99	0.99	0.99	0.98	0.98	0.99
EF2063	1	1	0.98	1	0.98	0.99	0.98	1	0.99	0.99	0.99	0.98	1	0.99	1	1	1	1	0.99	0.99	0.99	1	0.98	0.98
EF2064	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.67	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99
EF2065	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2066	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99	0.99	1	1	0.99
EF2067	1	1	0.99	1	1	1	1	1	0.99	0.99	0.99	1	1	0.99	1	1	1	1	1	0.99	0.99	1	0.99	1
EF2068	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1
EF2069	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.99	0.99	0.97	0.98	0.98	0.98	0.98	0.99	1	0.99	0.95	0.99	0.99	0.99	0.99
EF2070	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1
EF2071	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	1
EF2072	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	0.99	1	1	1	1	0.99	1	0.99	1	1	0.99
EF2073	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2074	1	1	1	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	0.99	0.99	1	1	1
EF2075	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2076	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1
EF2077	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99
EF2078	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	1	0.99	1	1
EF2079	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99
EF2080	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	1
EF2081	1	1	0.98	0.98	0.99	0.98	0.99	0.98	0.99	0.97	0.99	0.99	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.98	0.99	0.99
EF2082	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF2083	1	1	1	1	1	0.99	0.99	1	0.77	0.99	1	1	1	1	1	1	1	1	0.78	1	1	1	0.99	1
EF2084	0.92	0.92	0.63	0	0.63	0.92	0	0	0.91	0.94	0	0	0	0	0.93	0.93	0.92	0	1	0.92	0	0	0	0.92
EF2085	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2086	0	0	0	0	0	0.9	0	0	0	0	0	0	0	0	0	0	0.3	0	1	0.3	0	0	0.42	0.3
EF2087	0	0	0	0	0	0.65	0	0	0	0	0.52	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2088	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2089	0	0	0	0	0	0.7	0	0	0	0	0.7	0	0	0	0	0	0	0	1	0	0	0	0.85	0
EF2090	0.07	0.07	0.07	0.07	0.07	0.46	0	0.07	0	0	0.43	0	0	0	0	0	0.07	0	1	0	0.07	0.07	0.42	0
EF2091	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2092	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2093	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2094	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2095	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0
EF2096	0	0	0	0	0	0.98	0	0	0	0	0.08	0	0	0	0	0	0	0	0.89	0	0	0	0	0
EF2097	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2098	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2099	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2100	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2101	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2102	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2103	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2104	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2105	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2106	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2107	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2108	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2109	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2110	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2111	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2112	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2113	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2114	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2115	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0.46	0	0	0
EF2116	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2117	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2118	0.39	0.53	0.23	0.08	0.23	0.56	0	0.5	0	0.43	0	0	0.51	0	0.51	0.51	0.22	0	0.39	0.22	0.5	0.41	0	0.22
EF2119	0	0.45	0	0	0	0	0	0	0	0.44	0.51	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2120	0	0.51	0.52	0	0	0	0	0.51	0	0	0.47	0	0.48	0	0.48	0.48	0	0.43	0.42	0	0.51	0	0.45	0.42
EF2121	0	0.91	0.92	0	0	0.95	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2122	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2123	0	0.86	0.87	0	0	0.91	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2124	0	0	0.89	0	0	0	0	0.89	0	0	0	0	0	0	0	0	0	0	0	0	0.24	0.86	0	0
EF2125	0	0.82	0.82	0	0.4	0.46	0	0	0	0	0.87	0	0.73	0	0.73	0.73	0	0	0	0	0	0	0	0
EF2126	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2127	0	0	0	0	0	0.95	0	0	0	0	0	0	0	0	0	0	0	0	0.94	0	0	0	0	0
EF2128	0.7	0.84	0.76	0.73	0.78	0.97	0.7	0.74	0	0	0.77	0.76	0.77	0	0.77	0.77	0.78	0	0.97	0.78	0.75	0.73	0.75	0.78
EF2129	0.11	0.11	0.18	0.18	0.11	0.18	0.11	0.18	0.18	0.17	0.18	0.18	0.11	0.11	0.11	0.11	0.18	0.11	0.98	0.11	0.18	0.17	0.11	0.17
EF2130	0	0.34	0.34	0	0.34	0.32	0	0	0	0	0.35	0.34	0	0	0	0	0	0	1	0	0.34	0.35	0.3	0
EF2131	0	0	0.7	0.71	0	0.71	0	0.7	0.7	0	0.71	0.71	0	0	0	0	0.7	0	0.99	0	0.7	0	0	0
EF2132	0	0	0.37	0.34	0	0.33	0	0.33	0.34	0	0.33	0.34	0	0	0	0	0.33	0	0.99	0	0.33	0	0	0
EF2133	0	0	0	0	0	0.91	0	0	0	0	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0
EF2134	0.85	0	0	0	0	0.95	0	0	0	0.82	0	0	0	0	0.81	0.81	0	0	0.95	0	0	0	0	0
EF2135	0.17	0.17	0	0.17	0.17	0.73	0	0.17	0	0	0	0	0	0	0	0	0.17	0	0.76	0	0	0	0	0.17
EF2136	0.58	0	0	0	0	0.97	0	0	0	0.58	0	0	0	0	0.58	0.58	0	0	1	0	0	0	0	0
EF2137	0	0	0	0	0	0.98	0	0	0	0	0	0	0.65	0	0.65	0.65	0	0	0.98	0	0	0	0	0.65
EF2138	0	0	0	0	0	0.98	0	0	0	0	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0
EF2139	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0
EF2140	0	0	0	0	0	0.61	0	0	0	0	0	0	0	0	0	0	0	0	0.83	0	0	0	0	0
EF2141	0.25	0	0	0.31	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2142	0.23	0	0	0	0	0	0	0.15	0	0.22	0	0	0	0	0.22	0.22	0.14	0	0	0	0.15	0	0	0
EF2143	0.62	0	0	0	0	0	0	0	0	0.62	0	0	0	0	0.65	0.65	0	0	0	0	0	0	0	0
EF2144	0	0	0	0	0	0.57	0	0	0	0	0	0	0	0	0	0	0	0	0.56	0	0	0	0	0
EF2145	0	0	0	0	0	0.98	0	0	0	0	0	0	0	0	0	0	0	0	0.98	0	0	0	0	0
EF2146	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF2147	1	1	0.99	1	1	0.99	0.99	1	1	0.98	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	0.99
EF2148	1	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.98
EF2149	1	1	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	1	0.98	1	0.98	0.98	0.98	1	0.98	0.99	0.99	0.98	0.98	0.98
EF2150	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99
EF2151	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99
EF2152	0.51	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	1
EF2153	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2154	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.98	0.99	0.99	0.99
EF2155	1	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.9	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.99	0.98
EF2156	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2157	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1	1	1	0.99	1	1
EF2158	1	1	0.98	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.98	1	0.98	0.98	0.98	0.98	0.98	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2159	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2160	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1	1
EF2161	1	1	0.98	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2162	1	1	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.98	1	0.98	0.99	0.99	0.99	0.99	0.98
EF2163	1	1	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.99	0.98	0.98	0.99	0.98
EF2164	1	1	0.97	0	0.23	0	0.97	0	0.91	0	0.23	0	0	0	0	0	0	1	0.18	0.99	0.98	0	0	0.92
EF2165	1	1	0.98	0.94	0.94	0.98	0.96	0.94	0.95	0.93	0.94	0.94	0.96	0.93	0.96	0.96	0.94	0.99	0.93	0.99	0.97	0.96	0.95	0.94
EF2166	1	1	0.99	0	0	0.99	0	0	0	0	0	0	0.99	0	0.99	0.99	0	0.99	0	0	0.96	0	0	0
EF2167	1	1	0.95	0.08	0.08	0.99	0.08	0.08	0.08	0.08	0.08	0.08	0.99	0.08	0.99	0.99	0.08	0.95	0.08	0.08	0.08	0.08	0.08	0.08
EF2168	1	1	0.97	0	0	1	0.08	0	0.57	0	0	0	1	0	1	1	0	1	0	0.07	0.61	0.08	0.08	0.57
EF2169	1	1	1	0.1	0.17	0.94	0.11	0.1	0	0.1	0.17	0.1	1	0.1	1	1	0.1	1	0.16	0.09	0.44	0.09	0.07	0
EF2170	1	1	0.99	0.42	0.16	0.98	0.7	0.42	0.66	0.44	0.16	0.42	0.99	0.42	0.99	0.99	0.42	0.99	0.16	0.57	0.73	0.57	0.57	0.65
EF2171	1	1	0.99	0	0	1	1	0	0.97	0	0	0	0.98	0	0.98	0.98	0	1	0	0.55	1	0.56	0.56	0.5
EF2172	1	1	0.99	0	0	1	0.99	0	0.99	0	0	0	0.99	0	0.99	0.99	0	0.98	0	0.95	0.98	0.95	0.95	0.98
EF2173	0.69	0.69	0	0.66	0.69	0.69	0.56	0.64	0.56	0	1	1	0.69	0	0.69	0.69	0.66	0	1	0.46	0.56	0.66	0.69	0.66
EF2174	1	1	1	0.47	0.13	0.42	0.98	0.47	0.49	0.43	0.13	0.48	0.07	0.69	0.07	0.07	0.48	1	0.13	0.98	0.07	0.61	0.07	0.49
EF2175	1	1	1	0.22	0	0.99	1	0.22	0.98	0.06	0	0.22	0.82	0.22	0.82	0.82	0.22	1	0	1	0.82	1	0.83	0.82
EF2176	1	1	0.99	1	0.2	1	0.99	1	0.99	0.99	0.2	1	0	1	0	0	1	1	0.2	1	0	1	0	0
EF2177	1	1	1	0.99	0.96	1	1	0.99	0.99	0.99	0.96	0.99	1	0.99	1	1	0.99	1	0.96	1	0.73	0.99	0.99	0.99
EF2178	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99
EF2179	1	1	1	1	0.99	0.99	1	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2180	1	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2181	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2182	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2183	1	1	1	1	1	1	1	1	1	0.5	1	1	1	1	1	1	1	1	1	0.99	0.99	1	0.99	1
EF2184	1	1	0.99	1	0.99	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2185	0.69	0.69	0	0.66	0.69	0.69	0.56	0.64	0.56	0	1	1	0.69	0	0.69	0.69	0.66	0	1	0.46	0.56	0.66	0.69	0.66
EF2186	0.89	0.89	0.89	0.12	0.12	0	0.89	0	0.12	0	0.12	0.11	0	0	0	0	0.12	0.89	0.89	0.89	0.89	0.12	0.12	0.12
EF2187	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EF2188	0.99	0.99	0.98	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0.99	0.99	0.99	0.99	0	0	0
EF2189	1	1	0.99	0.9	0.9	0.91	0.99	0.9	0.88	0.9	0.91	0.9	0.9	0.9	0.9	0.9	0.9	1	0.99	0.99	0.99	0.91	0.9	0.91
EF2190	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2191	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	0.99
EF2192	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	1
EF2193	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	0.99	0.99	1	0.99	1	0.99	1	0.99
EF2194	1	1	1	0.99	1	1	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1
EF2195	1	1	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2196	1	1	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.98	0.98	0.99	0.99
EF2197	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2198	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	1
EF2199	1	1	0.99	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	0.98
EF2200	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98
EF2201	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2202	1	1	0.99	1	1	1	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1
EF2203	1	1	1	1	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	0.99	1	1	0.99	0.99	0.99
EF2204	1	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	0.98	0.99	0.98	0.98	0.99	0.99	1	0.99	1	0.99	0.99	0.99
EF2205	1	1	0	0.99	0.99	0.99	0.99	0.98	0	0.99	0.99	0.98	0	0.99	0	0	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99
EF2206	1	1	0.99	1	0.99	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.59	0.99	0.99	0.99	1	0.99	0.99	0.99
EF2207	1	1	1	1	1	0.99	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99
EF2208	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2209	1	1	0.99	0.99	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	1	1
EF2210	1	1	0.98	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.98	1	0.99	0.99	0.99	0.99	0.98
EF2211	1	0.82	0.95	0.91	1	1	1	1	0.94	0.94	1	1	0.97	1	1	1	1	0.87	1	1	0.91	1	0.95	0.95

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2212	1	0.94	0.99	0.99	0.98	0.99	0.99	0.93	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.94	0.99	0.99	0.99
EF2213	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2214	1	1	0.99	1	0.99	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2215	1	1	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.98	0.98
EF2216	1	1	0.98	0.99	0.98	0.99	0.99	0.99	0.98	0.97	1	0.99	0.98	1	0.98	0.98	0.99	1	1	0.99	1	0.98	0.98	0.98
EF2217	0.58	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2218	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2219	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.87	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98
EF2220	1	1	1	1	1	1	1	1	1	0.98	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1
EF2221	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2222	1	1	1	1	0.99	1	1	1	0.99	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	0.99	0.99	1
EF2223	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1
EF2224	0.53	0.56	0.58	0.67	0.67	0.66	0.96	0.57	0.51	0	0.57	0.59	0	0.91	0	0	0.79	0.77	0.64	0	0.82	0.58	0	0.52
EF2225	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	0.99	0.99	1	0.99	0.99	0.98
EF2226	1	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF2227	1	1	0.99	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	0.99	1	0.99
EF2228	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2229	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0
EF2230	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0
EF2231	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0
EF2232	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0
EF2233	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	0
EF2234	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0
EF2235	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.25
EF2236	1	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	1	1	1	0.99	0.4
EF2237	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	1	1	1	1	0
EF2238	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.09
EF2239	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.35
EF2240	1	1	0	0	0.09	0	0	0	0	0	0	0	0.07	0	0.07	0.07	0	0.86	1	0	0.06	0.06	0	0
EF2241	1	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.83	1	0	0	0	0	0
EF2243	1	1	0.32	0	0.51	0	0	0	0.54	0	0	0.4	0	0	0	0	0	0.24	1	0	0	0	0	0
EF2244	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2245	1	1	0.22	0	0.26	0	0	0	0.27	0	0	0.21	0	0	0	0	0	0	1	0	0	0	0	0
EF2247	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2248	0.35	0.36	0	0	0	0	0	0	0	0	0	0	0	0	0.12	0.16	0	0	0.65	0	0	0	0	0
EF2249	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2250	0.83	0.83	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2251	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2252	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2253	1	1	0.43	0.12	0.11	0.11	0.12	0.12	0.33	0.33	0.12	0.12	0.14	0.12	0.14	0.14	0.12	0.12	1	0.12	0.12	0.12	0.12	0.12
EF2254	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2255	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2257	1	1	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.04	0.07	0.07	0.07	1	0.07	0.07	0.07	0.07	0.07
EF2258	1	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2259	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2260	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2261	1	1	0.44	0	0	0	0	0	0	0.44	0	0	0.44	0	0.44	0.44	0.44	0	1	0.44	0	0	0	0
EF2262	1	1	0.43	0.43	0.43	0.42	0.43	0.43	0.43	0.43	0.43	0.42	0.42	0.42	0.42	0.42	0.43	0.43	1	0.42	0.42	0.42	0.43	0.53
EF2263	1	1	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	1	0.75	0.75	0.75	0.75	0.75
EF2264	1	1	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.79	0.8	0.79	0.79	0.8	0.8	1	0.8	0.79	0.8	0.79	0.8
EF2265	1	1	0.65	0.64	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	1	0.65	0.65	0.65	0.65	0.65
EF2266	1	1	0.67	0.67	0.68	0.68	0.67	0.67	0.67	0.67	0.67	0.67	0.67	0.7	0.67	0.67	0.68	0.67	1	0.67	0.67	0.68	0.67	0.68
EF2267	1	1	0	0.25	0.25	0.25	0.77	0.25	0	0	0.77	0	0.25	0	0.25	0.25	0	0	1	0	0.25	0	0.25	0.25

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2268	1	1	0	0.38	0.38	0.04	0.39	0.38	0	0	0.39	0	0.38	0	0.38	0.38	0	0	1	0	0.38	0	0.38	0.38
EF2269	1	1	0	0.76	0.76	0	0.74	0.76	0	0	0.74	0	0.76	0	0.76	0.76	0	0	1	0	0.76	0	0.76	0.76
EF2270	1	1	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	1	0.06	0.06	0.11	0.06	0.06
EF2271	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2272	1	1	0.28	0.28	0.22	0.22	0.22	0.28	0.22	0.28	0.22	0.28	0.28	0.28	0.28	0.28	0.28	0.28	1	0.28	0.22	0.22	0.22	0.28
EF2273	1	1	0.17	0.17	0	0	0	0.17	0	0.17	0	0.17	0.17	0.17	0.17	0.17	0.17	0.17	1	0.17	0	0	0	0.17
EF2275	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2276	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2277	1	1	0.12	0	0.68	0.68	0.12	0	0.2	0.48	0.68	0.12	0.68	0.4	0.68	0.68	0	0	1	0.12	0.68	0.12	0.68	0
EF2278	1	1	0.55	0	0.78	0.78	0.55	0.56	0.55	0.54	0.78	0.55	0.78	0.55	0.78	0.78	0	0	1	0.55	0.78	0.56	0.78	0.12
EF2279	1	1	0.41	0	0.67	0.67	0.42	0.41	0.37	0.4	0.67	0.42	0.67	0.4	0.67	0.67	0	0	1	0.41	0.67	0.42	0.67	0
EF2280	0.7	0.44	0.69	0	0.92	0.92	0.69	0.69	0.69	0.71	0.92	0.69	0.92	0.71	0.92	0.92	0	0	0.95	0.69	0.91	0.7	0.91	0
EF2281	1	1	0.65	0	0.91	0.91	0.65	0.65	0.55	0.66	0.91	0.65	0.91	0.7	0.91	0.91	0	0	1	0.65	0.91	0.67	0.91	0
EF2282	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2283	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2284	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2285	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2286	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2287	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2288	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2289	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2290	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2291	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2292	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2293	0	0.96	0	0	0	0	0	0	0	0	0.72	0	1	0	0.72	0.72	0	0	0	0	0	0	0	0
EF2294	0	0.95	0	0	0	0	0	0	0	0	0.74	0	1	0	0.74	0.74	0	0	0	0	0	0	0	0
EF2295	0	0.95	0	0	0	0	0	0	0	0	0.7	0	1	0	0.7	0.7	0	0	0	0	0	0	0	0
EF2296	0	0.96	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2297	0	0.58	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2298	0	0.96	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2299	0	0.95	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0.06	0.06	0	0
EF2300	0	0.18	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2302	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2303	0	0.04	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2304	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2305	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2306	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2307	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0.11	0	0.11	0	0	0	0	0
EF2308	0	0	0	0	0	0	0	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0
EF2309	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2310	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2311	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2312	0	0.47	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2313	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2314	0	0.11	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2315	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2316	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2317	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2318	0	0.08	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2319	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2320	0	0.54	0	0	0	0	0	0	0	0	0	0.08	1	0	0	0	0	0	0	0	0	0	0	0
EF2321	0	0.46	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2322	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2323	0	0.63	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2324	0	0.58	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2325	0.3	0.3	0	0	0.3	0.3	0.32	0	0	0	0.33	0	0.63	0	0.3	0.32	0	0	0.29	0	0.3	0	0.3	0
EF2326	0.19	0.19	0	0	0.19	0.19	0	0	0	0	0.29	0	0.23	0	0.19	0.23	0	0	0.19	0	0.19	0	0.19	0
EF2327	0	0.57	0	0	0	0	0	0	0	0	0	0	0.89	0	0	0	0	0	0	0	0	0	0	0
EF2328	0	0.6	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2329	0	0.18	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2330	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2331	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2332	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2333	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2334	0	0.17	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
EF2335	1	1	0.62	0	0.78	0.78	0.62	0.63	0.63	0.64	0.78	0.62	0.78	0.67	0.78	0.78	0	0	1	0.62	0.78	0.62	0.78	0
EF2336	0.69	1	0.73	0	0.91	0.91	0.73	0.73	0.74	0.77	0.91	0.73	0.91	0.8	0.91	0.91	0	0	1	0.73	0.91	0.77	0.91	0
EF2337	1	1	0	0	0.86	0.8	0	0	0	0	0.86	0	0.86	0	0.86	0.86	0	0	1	0	0.86	0	0.8	0
EF2338	0.72	1	0.53	0	0.92	0.92	0.53	0.53	0.61	0.59	0.92	0.53	0.92	0.66	0.92	0.92	0	0	1	0.53	0.92	0.56	0.92	0
EF2339	1	0.87	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2340	1	1	0	0	0	0	0	0.3	0.3	0	0	0	0	0.31	0	0	0.3	0	1	0.3	0	0	0	0.3
EF2341	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2342	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2343	0.79	1	0.54	0	0.63	0.63	0.54	0.53	0.53	0.52	0.63	0.54	0.63	0.57	0.63	0.63	0	0	1	0.54	0.63	0.54	0.63	0
EF2344	1	1	0	0	0.82	0.82	0	0	0	0	0.82	0	0.82	0	0.82	0.82	0	0	1	0	0.82	0	0.82	0
EF2345	1	1	0	0	0.89	0.89	0.65	0.6	0.58	0.58	0.89	0.65	0.89	0.65	0.89	0.89	0	0	1	0.65	0.89	0.6	0.89	0
EF2346	0.84	1	0	0	0.89	0.89	0.6	0.59	0.59	0.62	0.89	0.6	0.89	0.71	0.89	0.89	0	0	1	0.6	0.89	0.62	0.89	0
EF2347	0.7	0.7	0	0	0.83	0.83	0	0.73	0.44	0.03	0.83	0.12	0.84	0.62	0.84	0.84	0	0	1	0	0.83	0.73	0.83	0
EF2348	1	0.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.87	0	0	0	0	0
EF2349	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2350	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2351	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.71	1	0	0	0	0	0
EF2352	1	1	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.99	1	0.99	0.99	0.99	0.98	0.98
EF2353	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1
EF2354	1	1	0.99	0.99	0.98	0.97	0.98	0.99	0.97	0.99	0.99	0.83	0.99	1	0.99	0.99	0.99	0.85	1	0.99	0.99	0.99	0.99	0.99
EF2355	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	0.99	0.99	0.99
EF2357	1	1	1	1	1	0.99	0.99	1	1	0.98	1	0.99	0.98	1	0.98	0.98	1	1	1	1	1	1	1	1
EF2359	1	0.69	0.99	0.37	0.99	0	0.38	0.99	0	0.99	0	0.99	0.99	0	0.54	0.99	0.37	0	1	0	0.37	0.37	0.99	0.37
EF2360	1	1	1	0	0.99	0	0	0.98	0	0.99	0	0.98	0.99	0	0.54	0.99	0	0	1	0	0.35	0	0.99	0
EF2361	1	1	0.99	0.99	1	1	1	0.99	0.99	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2362	1	1	1	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99
EF2363	1	1	1	1	1	0.98	1	1	1	1	0.98	1	1	0.98	1	1	1	0.98	1	0.98	0.98	1	1	1
EF2364	0.9	1	1	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF2365	1	1	1	1	1	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	1	0.99	0.99	1	0.99
EF2366	1	0.91	1	1	1	1	0.92	0.97	0.99	1	1	1	1	1	1	0.99	1	1	1	1	0.97	1	0.99	1
EF2367	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2368	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	0.99
EF2369	1	1	0.99	1	1	1	1	1	0.98	0.98	1	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	0.99	0.98
EF2370	1	1	0.99	0.99	0.99	1	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2371	1	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	0.99	0.99
EF2372	0.71	1	0.99	0.99	1	1	0.99	0.99	0.99	0.98	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99
EF2373	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2374	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF2376	1	1	0.53	0.54	0.53	0.53	0.54	0.54	0.53	0.53	0.54	0.54	0.54	0.98	0.54	0.54	0.54	0.54	1	0.54	0.54	0.54	0.53	0.52
EF2377	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98
EF2378	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2379	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2380	1	1	0.99	0.99	1	0.99	1	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99
EF2381	1	1	0.98	0	1	0.98	0.98	0.98	1	1	1	0.98	0.98	1	0.98	0.98	0	1	1	1	0.98	0.98	1	0
EF2382	1	1	0.98	0	0.99	0.99	0.99	1	0.98	0.98	1	0.99	0.99	0.99	0.99	0.99	0	0.97	1	1	0.99	1	0.99	0
EF2383	1	1	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.98	0.98	0	0.99	1	0.99	0.99	0.99	0.99	0
EF2384	1	1	0.96	0	1	1	0.99	0.96	0.86	0.96	0.96	0.99	0.95	0.99	0.95	0.95	0	0.98	1	0.97	1	0.96	0.98	0
EF2385	1	1	0	0	0	0	0	0.7	0	0	0	0	0	0	0	0	0	0	1	0	0	0.7	0	0
EF2386	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
EF2387	1	1	0	0	0	0	0	0	0	0	0	0	0.07	0	0.07	0.07	0	0	0.99	0	0	0	0.07	0
EF2388	1	1	0.92	0	0	1	0	0	0	0	0	0	0	0.99	0	0	0	0	1	0	0	0	0	0
EF2389	1	1	0.71	0	0.38	1	0	0	0	0	0	0	0	0.98	0	0	0	0	1	0	0.38	0	0	0
EF2390	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2391	1	1	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.98
EF2392	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99
EF2393	1	0.99	0.99	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99
EF2394	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.98	0.98
EF2395	1	0.99	1	1	0.99	1	1	1	0.99	0.99	0.99	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	0.99	1
EF2396	1	1	1	0.99	1	1	0.99	1	0.99	1	1	0.99	1	1	1	1	0.99	0.99	1	0.99	1	1	0.99	1
EF2397	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2398	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99
EF2399	1	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99
Ef23SA	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.45	0.67	1	1	1	1	1	1	1	1
Ef23SB	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.45	0.67	1	1	1	1	1	1	1	1
Ef23SC	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.45	0.67	1	1	1	1	1	1	1	1
Ef23SD	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.45	0.67	1	1	1	1	1	1	1	1
EF2400	1	0.99	0.98	1	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	1	0.99	0.99	0.99	0.99	0.98
EF2401	1	0.99	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.97	0.98	0.98	0.97	0.98	0.97	0.97	0.98	0.99	1	0.98	0.98	0.98	0.98	1
EF2403	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2404	1	0.98	1	0.98	0.97	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.6	0.98	0.98	1	0.99	0.99	0.98	0.98	0.94
EF2405	0.99	0.95	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.94	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.84
EF2406	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99
EF2407	1	0.98	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99
EF2408	0.73	0.8	0.99	1	0.99	1	0.99	0.99	0.99	0.73	1	1	0.8	1	0.8	0.8	1	0.84	1	0.99	0.99	0.99	0.66	1
EF2409	1	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99
EF2410	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2411	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF2412	1	0.99	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	1	0.99	1
EF2413	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF2414	1	0.99	1	1	0.99	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	0.99
EF2415	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2416	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2417	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99
EF2419	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1
EF2420	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2421	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99
EF2422	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.53	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2423	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	1
EF2424	1	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99
EF2425	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99
EF2426	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2427	1	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99
EF2428	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2429	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2430	1	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	1
EF2431	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99
EF2432	1	0.99	1	1	1	1	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	1
EF2433	1	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	1	1	1	0.99	0.99	0.99	0.99
EF2434	1	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2435	1	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99
EF2436	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99
EF2437	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2438	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF2439	1	0.99	1	1	0.95	1	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1
EF2440	1	0.99	0.98	0.99	0.91	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF2441	0.58	0.99	0.99	1	0.99	1	0.99	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	0.99	1	1	1	0.99
EF2442	1	0.99	1	1	1	1	1	1	0.98	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	0.99	0.99
EF2443	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2444	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2445	1	0.98	0.98	0.99	0.99	0.96	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.98	0.98	0.94	0.99	0.99	0.98
EF2446	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2447	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2448	1	0.99	1	1	0.99	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF2449	1	0.97	0.96	0.97	0.97	0.97	0.98	0.98	0.97	0.98	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.98	0.97	0.98	0.97	0.98
EF2450	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1
EF2451	1	1	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99
EF2452	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2453	1	0.99	1	0.99	1	1	0.99	0.99	1	1	0.99	0.99	1	0.99	1	1	0.99	0.99	1	1	1	0.99	1	1
EF2454	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF2455	1	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2456	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2457	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99
EF2458	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF2459	0.46	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	0.99
EF2460	1	1	1	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.54	0.99	0.99	1	0.99
EF2461	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1	1	0.99	0.99	0.99
EF2462	1	1	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1	1	1	1	0.99	0.99	1	1	0.99	0.99	1	1
EF2463	1	0.98	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99
EF2464	1	0.93	0	0.99	0.99	1	0	0.99	0.99	0.95	0	0.99	0	0.99	0	0	0.99	1	0.99	0.99	0	0.99	0	0
EF2465	1	0.9	0	1	1	1	0	1	1	0.95	0	1	0	1	0	0	1	1	1	1	0	1	0	0
EF2466	0.35	0.31	0.02	0.76	0.62	0.96	0.02	0.76	0.62	0.66	0.02	0.69	0.02	0.76	0.02	0.02	0.76	0.91	0.35	0.79	0.01	0.76	0.01	0.02
EF2467	1	0.94	0.74	1	1	1	0.74	1	0.95	0.95	0.74	1	0.75	1	0.75	0.75	1	1	1	1	0.74	1	0.74	0.74
EF2469	1	0.97	1	1	1	1	1	1	0.97	0.97	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.97
EF2470	0.88	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.95	0.99	0.99	0.99
EF2471	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2472	1	0.99	0.98	0.98	0.99	1	1	0.98	0.99	0.98	1	0.99	0.99	1	0.99	0.99	0.98	1	0.99	0.99	0.99	0.98	0.99	0.98
EF2473	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2474	1	0.99	0.98	0.99	1	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.99	0.98	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.98	0.99
EF2475	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99
EF2476	1	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	1	0.99	1
EF2477	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1
EF2478	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2479	1	0.96	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.6	0.97	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.98	0.97	0.98	0.98	0.96
EF2480	1	0.12	0.99	0	0.99	0.99	0.99	0.07	1	0	0.99	0	0	0	0	0	0.09	1	1	0.09	1	0	0	0.09
EF2481	1	0.96	0.98	0.96	0.99	1	0.99	0.96	0.98	0.97	0.99	0.97	0.91	0.98	0.98	0.98	0.96	1	0.98	0.97	0.99	0.97	0.96	0.97
EF2483	1	0.95	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.89	1	0.99	0.99
EF2484	1	0.98	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	1	0.97	0.98	0.97	0.97	0.98	1	1	0.97	0.99	0.98	0.99	0.98

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2485	1	0.99	1	0	1	0.99	0.99	0	0	0.99	1	0	0	0	0	0	0	1	1	0	0.98	0	0	0
EF2486	1	0.98	0.99	0.22	0.99	0.99	1	0.22	0.22	0.97	0.99	0.22	0.22	0.22	0.22	0.22	0.22	1	0.99	0.22	0.99	0.22	0.22	0.22
EF2487	1	0.98	0.99	0	0.98	1	1	0	0	0.98	1	0	0	0	0	0	0	1	1	0	0.99	0	0	0
EF2488	1	0.97	0.99	0	0.97	1	1	0	0	0.99	1	0	0	0	0	0	0	1	1	0	1	0	0	0
EF2489	1	0.99	1	0	1	1	0.99	0	0	0.98	1	0	0	0	0	0	0	1	1	0	1	0	0	0
EF2490	1	0	1	0	0.56	0.56	1	0	0	0	1	0	0	0	0	0	0	1	1	0	1	0	0	0
EF2491	1	0.98	0.98	0	0.99	0.99	0.99	0	0	0.98	1	0	0	0	0	0	0	1	1	0	0.99	0	0	0.07
EF2492	1	0.97	0.99	0	0.99	0.99	0.99	0	0	0.98	1	0	0	0	0	0	0	1	1	0	0.99	0	0	0
EF2493	1	0.96	1	0	1	1	0.99	0	0	0.97	1	0	0	0	0	0	0	1	0.98	0	1	0	0	0
EF2494	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF2495	1	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	0.99	0.99
EF2496	1	0.99	0.99	0.98	0.99	0.99	1	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.64	0.99	0.99
EF2497	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	1	0.99	0.99	0.99
EF2498	1	0.98	0.98	0.99	0.99	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	1	0.99
EF2499	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2500	1	0.99	0.99	0.99	0.97	0.97	0.98	0.99	0.99	0.97	0.98	1	0.97	0.97	0.97	0.97	0.99	1	0.98	0.97	0.99	0.99	0.98	0.98
EF2501	1	0.99	0.98	0.98	0.98	0.99	1	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	1	1	1	1	1	0.98	0.99
EF2502	1	0.98	0.98	1	1	1	1	1	0.98	0.99	0.98	1	0.98	0.98	0.98	0.98	1	1	1	1	1	1	0.98	0.98
EF2503	1	0.99	0.99	1	1	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	1	1	1	1	0.99	0.99
EF2504	1	0.98	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF2505	0.64	0.65	0.79	0.67	0.81	0.98	0.65	0.75	0.74	0.65	0.84	0.81	0.78	0.75	0.74	0.78	0.75	1	0.84	0.77	0.84	0.75	0.79	0.77
EF2507	1	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF2508	1	0.98	0.99	0.99	1	1	1	0.99	0.99	0.99	1	1	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99
EF2509	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF2511	1	0.99	0.99	0.98	0.99	0.99	1	0.98	0.99	0.99	0.97	0.98	0.99	0.98	0.99	0.99	0.98	1	0.98	1	0.98	0.98	0.98	0.99
EF2512	0	0	0	0.59	0	0.89	0	0.89	0	0	0.59	0.89	0	0	0	0	0	0	0.55	0	0	0	0	0
EF2513	0	0	0	0.38	0	0.93	0	0.94	0	0	0.38	0.93	0	0	0	0	0	0	0.37	0	0	0	0	0
EF2514	0	0	0	0.61	0	0.97	0	1	0	0	0.61	0.97	0	0	0	0	0	0	0.62	0	0	0	0	0
EF2515	0	0	0	0.68	0	0.92	0	0.97	0	0	0.68	0.92	0.21	0	0	0	0.2	0	0.69	0	0	0	0	0.21
EF2516	0	0	0	0.46	0	0.97	0	0.97	0	0	0.46	0.97	0	0	0	0	0	0	0.44	0	0	0	0	0
EF2517	0	0	0.1	0.73	0	0.93	0	0.98	0	0	0.73	0.93	0	0	0	0	0	0	0.73	0	0	0	0	0
EF2518	0	0	0	0.98	0	0.43	0	0	0	0	0.98	0.43	0	0	0	0	0	0	0.96	0	0	0	0	0
EF2519	0	0	0	0.79	0	0.97	0	0.97	0	0	0.79	0.97	0	0	0	0	0	0	0.79	0	0	0	0	0
EF2520	0	0	0	0.72	0	0.97	0	0.93	0	0	0.72	0.97	0	0	0	0	0	0	0.75	0	0	0	0	0
EF2521	0	0	0	0.62	0	0.97	0	0.96	0	0	0.62	0.97	0	0	0	0	0	0	0.62	0	0	0	0	0
EF2522	0	0	0	0.31	0	0.93	0	0.93	0	0	0.31	0.93	0	0	0	0	0	0	0.29	0	0	0	0	0
EF2523	0	0	0	0.19	0	0.88	0	0.94	0	0	0.19	0.88	0	0	0	0	0	0	0.18	0	0	0	0	0
EF2524	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2525	0	0	0	0	0	0	0	0.97	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2526	0	0	0	0	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2527	0	0	0	0	0	0.92	0	0.99	0	0	0.23	0.92	0	0	0	0	0	0	0.38	0	0	0	0	0
EF2528	0	0	0.53	0	0	0.88	0	0.99	0	0	0	0.88	0	0	0	0	0	0	0.91	0	0	0	0	0
EF2529	0	0	0	0	0	0.71	0	0.82	0	0	0	0.71	0	0	0	0	0	0	0.43	0	0	0	0	0
EF2530	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2531	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2532	0	0	0	0	0	0.87	0	1	0	0	0	0.87	0	0	0	0	0	0	0.67	0	0	0	0	0
EF2533	0.13	0.13	0.36	0.35	0	0.91	0	0.87	0.13	0.06	0.35	0.91	0	0	0	0	0	0	0.85	0	0.05	0.05	0	0
EF2534	0	0	0	0	0	0.68	0	1	0	0	0	0.68	0	0	0	0	0	0	0.62	0	0	0	0	0
EF2535	0	0	0	0	0	0.67	0	1	0.1	0	0	0.67	0	0	0	0	0	0	0.66	0	0	0	0	0
EF2536	0	0	0	0	0	0.63	0	1	0	0	0	0.63	0	0	0	0	0	0	0.56	0	0	0	0	0
EF2537	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2538	0	0	0	0	0	0.88	0	0.99	0	0	0	0.89	0	0	0	0	0	0	0.8	0	0	0	0	0
EF2539	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0.93	0	0	0	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2540	0	0	0.53	0	0	0.84	0	0.86	0	0	0	0.84	0	0	0	0	0	0	0.9	0	0	0	0	0
EF2541	0	0	0.53	0	0	0.96	0	0.96	0	0	0	0.96	0	0	0	0	0	0	0.94	0	0	0	0	0
EF2542	0	0	0	0.62	0	0.93	0	0.93	0	0	0.62	0.93	0	0	0	0	0	0	0.91	0	0	0	0	0
EF2543	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2544	0	0.15	0	0	0	0	0	0	0	0	0	0.14	0	0	0	0	0	0	0	0	0	0	0	0
EF2545	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2546	0	0	0.05	0.05	0.33	0.03	0	0.05	0.05	0	0	0	0.26	0	0.26	0.26	0	0	0	0	0.05	0	0	0
EF2547	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF2548	1	0.99	0.99	0.98	0.97	0.98	1	0.98	0.99	0.98	0.97	0.98	0.97	0.98	0.97	0.97	0.98	1	0.99	1	1	0.98	0.98	0.98
EF2549	1	1	1	0.99	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	1	0.99
EF2550	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99
EF2552	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	0.99	0.99
EF2553	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2554	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2555	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1
EF2556	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1
EF2558	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99
EF2559	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2560	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.99	0.99	0.99	0.99
EF2561	1	0.98	0.98	1	1	1	1	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	0.98
EF2562	1	0.99	0.99	1	1	0.99	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	0.99	0.99
EF2563	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	1	1	0.78	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.98
EF2564	1	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98
EF2565	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98
EF2566	1	0.99	0.98	1	0.99	0.99	0.99	1	0.98	0.97	1	1	0.99	0.99	0.99	0.99	1	0.98	1	1	0.99	1	0.98	0.98
EF2567	1	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.99	0.99	0.98	1	0.98	1	1	0.99	0.98	1	1	0.99	0.98	0.98	1
EF2568	1	0.97	0.98	1	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	1	0.99	0.99	0.98	0.99
EF2569	1	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.98	1	0.98	1	0.98	0.98	0.98	0.98
EF2570	1	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.98	0.98	1	1	0.99	1	0.99	0.99	0.99	0.98
EF2571	1	0.98	0.98	0.99	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.98	0.99	0.98	0.98
EF2572	1	0.99	0.98	0.99	1	1	0.99	1	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	0.99	0.99
EF2573	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF2574	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99
EF2575	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF2576	1	0.96	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2577	1	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	1	0.99	1	0.99	1	0.99	0.99
EF2578	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99
EF2579	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2580	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2581	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF2582	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	0.99
EF2583	1	0.99	0.98	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.98	0.99
EF2584	0.43	0.38	0.57	0.63	0.58	0.65	0.63	0.57	0.57	0.49	0.63	0.57	0.63	0.6	0.55	0.54	0.6	1	0.61	0.55	0.63	0.63	0.63	0.63
EF2585	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99
EF2586	1	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	1	0.99
EF2587	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	1	0.99
EF2588	0.99	0.99	0.99	0.98	0.98	1	0.99	0.98	0.99	0.99	0.99	1	1	1	1	1	0.98	1	1	0.98	0.98	0.98	0.99	0.99
EF2589	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	0.98	0.99	0.98	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF2590	1	0.99	0.99	1	0.99	1	1	1	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.98	1	1	0.99	0.99	0.99	1	0.99	1
EF2591	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	0.99
EF2592	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99
EF2593	0.84	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2594	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2595	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99
EF2597	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF2598	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	1
EF2599	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2601	1	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99
EF2602	1	1	0.99	1	1	1	1	1	0.99	0.99	0.99	1	1	0.99	1	1	1	1	1	0.99	1	1	1	0.99
EF2603	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.99	0.99
EF2604	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1
EF2605	1	0.99	0.99	1	1	0.99	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	0.99	1	0.99	1	1	1
EF2606	1	0.98	0.98	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	0.98
EF2607	1	0.99	0.99	0.99	1	1	0.99	0.99	1	1	1	0.99	1	0.99	1	1	0.99	1	1	1	1	0.99	1	1
EF2608	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2609	1	0.99	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2610	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2611	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF2612	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2613	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2614	1	1	1	1	1	0.99	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	0.99	1	1	0.99	1
EF2615	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2616	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.99	1	0.99	1	1	0.99	1	1	1	0.99	0.99	1	0.99
EF2617	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2618	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	1	1	1	0.99	0.99	0.99
EF2619	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	0.99
EF2620	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2621	1	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	0.95	1	1	1	0.99	0.99	1	1	1
EF2622	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	1
EF2623	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.93	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2624	1	0.85	0.85	0.98	1	0.99	0.99	0.99	0.99	0.97	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.97	0.97	0.99	0.99	0.99
EF2625	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	0.99
EF2626	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF2627	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1
EF2628	1	0.96	0.96	0.98	0.98	0.99	0.98	0.98	0.97	0.97	0.99	0.98	0.97	0.98	0.97	0.97	0.98	1	0.98	0.97	0.48	0.98	0.97	0.96
EF2629	1	0.54	0.94	0.97	0.96	0.99	0.97	0.97	0.96	0.96	0.99	0.97	0.99	0.97	0.99	0.99	0.97	1	0.98	0.98	0.96	0.97	0.95	0.94
EF2630	1	0.97	0.97	1	0.99	0.99	1	0.99	0.98	0.98	0.99	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.98	0.99
EF2631	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99
EF2632	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EF2633	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.96	0.99	0.99	0.99	0.99
EF2634	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2636	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	0.99	0.99
EF2637	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.94	1	1	1	0.99	1
EF2638	1	1	1	1	1	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1
EF2639	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2640	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99
EF2641	1	0.99	1	1	0.99	0.99	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF2642	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99
EF2643	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.85	0.99	0.85	0.85	0.99	1	0.99	1	1	0.99	0.99	1
EF2644	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF2645	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	1	1
EF2646	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99
EF2647	1	0.99	0.99	1	1	0.99	1	1	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99
EF2648	1	0.96	0.98	0	1	1	0.99	0	0.98	0.99	1	0	0.98	0	0.98	0.98	0	1	0.99	0.99	0.99	0	0.98	0.98
EF2649	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2650	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2651	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2652	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF2653	1	0.99	0.99	1	1	0.99	1	1	0.99	0.99	0.99	1	1	0.99	1	1	1	1	0.99	1	0.99	1	0.99	0.99
EF2654	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1
EF2655	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2656	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2657	1	0.99	1	1	1	1	0.94	1	0.99	1	1	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	1	1	0.99
EF2658	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99
EF2659	1	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1	1	0.99
EF2661	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99
EF2662	0.53	0	0	0	0	0	0	0.24	0	0	0	0.24	0	0.24	0	0	0.24	0.51	0	0	0	0	0	0
EF2663	1	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	0.97	1	0.97	0.97	0.97	0.97	0.97	0.97
EF2664	1	0.98	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	0.99	1	0.99	0.99	1	0.99
EF2665	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2666	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.98
EF2667	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	1	0.99	0.99	1	1	0.99
EF2668	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	1	1	0.99
EF2669	1	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.98	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99
EF2670	1	0.99	0.99	1	1	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	0.99	1
EF2671	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1
EF2672	1	1	1	1	1	1	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	1
EF2673	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2674	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2675	1	0.98	0.97	0.98	0.99	0.99	0.98	0.98	0.99	0.97	0.98	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.98
EF2677	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.54	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF2678	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF2679	1	0.99	0.98	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF2680	1	0.77	0.99	0.99	0.99	0.78	0.99	0.99	0.78	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.78	0.99	0.99	0.99	0.99	0.78
EF2681	1	0.99	0.99	1	1	0.99	1	1	0.92	0.99	1	1	1	1	1	1	1	1	1	1	1	0.94	1	0.99
EF2682	1	0.06	0.06	0.99	0.99	0.99	0.99	0.97	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.06
EF2683	1	0.17	0.17	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.17
EF2684	1	0.26	0.26	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.26
EF2685	1	0	0	1	0.99	0.99	0.99	1	1	0.99	1	1	0.98	1	0.98	0.98	1	1	1	1	1	1	0.99	0
EF2686	1	0	0	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0
EF2687	1	0	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0
EF2688	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2689	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2690	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2691	1	0.99	0.99	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99
EF2692	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99
EF2693	1	0.97	0.97	0.97	0.96	0.97	0.98	0.96	0.98	0.98	0.96	0.98	0.97	0.97	0.97	0.97	0.97	1	0.98	0.96	0.98	0.96	0.98	0.97
EF2694	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2695	1	0.98	0.98	1	0.99	1	0.98	1	0.98	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	0.98
EF2696	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1
EF2697	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2698	1	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	1	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	0.99
EF2699	1	1	1	1	0.97	1	0.98	1	1	1	1	1	0.98	1	0.98	0.97	1	1	1	1	0.98	1	1	1
EF2700	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.98	0.99	1	1	0.99	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99
EF2701	1	0.98	0.98	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99
EF2702	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2703	1	0.99	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	1	0.99	1	1	0.99	0.99
EF2704	1	0.98	0.98	1	0.99	0.98	0.98	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.98
EF2705	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2706	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	1	1	1	1	1	1	1	1
EF2707	0.89	0.69	1	0.86	1	0.87	0.86	0.91	0.87	0.83	0.87	0.86	0.9	0.91	0.85	0.85	0.86	0.86	0.99	0.86	0.87	0.86	0.87	0.87
EF2708	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF2709	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2710	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2711	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2712	1	0	1	0	0	1	0	0	0	0	0.99	0	1	0	1	1	0	1	0	0	1	0	0	0
EF2713	1	0	0.99	0	0	1	0	0	0	0	0.99	0	0.99	0	0.99	0.99	0	1	0	0	1	0	0	0
EF2715	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2716	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1
EF2718	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2719	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2720	1	0.98	0.98	0.99	0.99	1	0.98	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.99
EF2721	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99
EF2722	1	0.99	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99
EF2723	1	0.98	1	1	0.99	0.99	0.99	1	0.99	0.98	1	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.98	1	0.99	0.99
EF2724	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98
EF2725	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.68	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2727	1	0.98	0.99	0.98	0.99	1	0.99	0.98	0.99	0.98	0.97	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99
EF2728	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99
EF2729	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF2730	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2731	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2732	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	1	1	0.99	0.99	1
EF2733	1	1	0.99	1	0.99	1	1	1	0.99	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1
EF2734	1	0.98	0.99	1	0.99	0.98	0.99	1	0.99	0.98	0.99	1	0.98	0.99	0.98	0.98	1	0.98	0.99	0.99	0.99	1	0.99	0.99
EF2735	1	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.98	1	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.99	1	0.99	0.99
EF2736	1	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99
EF2738	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.52	0.52	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2739	1	0.99	1	0.99	0.99	0.56	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	1	1	0.99	1	0.99	1	1
EF2740	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.94	0.98	0.99
EF2741	1	0.99	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	1	0.6	1	0.99	0.99	1	1	0.99
EF2742	1	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	0.99
EF2743	1	0.99	1	0.99	0.99	0.99	0.99	1	1	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF2744	1	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF2746	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	0.99
EF2747	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99
EF2748	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99
EF2749	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99
EF2750	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF2751	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2752	1	0.99	1	0.99	1	0.99	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	1
EF2754	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1
EF2755	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99
EF2756	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2757	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF2758	1	0.99	0.99	0.99	1	1	1	1	1	0.99	1	1	1	0.99	1	1	0.99	1	0.99	1	1	1	1	1
EF2759	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.98
EF2760	0.93	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2761	0.93	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2762	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1
EF2763	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2764	1	0.99	0.99	1	1	0.99	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	0.99	1	0.99	1	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2765	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.98	0.99	0.98	1
EF2766	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	1	0.99	0.98
EF2767	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.61
EF2768	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF2769	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF2770	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2771	1	0.98	0.99	1	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	0.99
EF2772	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2773	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1
EF2774	1	0.99	0.99	0.98	0.99	1	1	1	1	0.99	0.99	1	0.99	0.98	0.99	0.99	0.98	1	0.99	1	0.99	1	0.99	0.99
EF2775	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	0.98
EF2776	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2777	1	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.99	0.98	0.98	0.98	1
EF2778	1	0.99	0.98	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.98	0.99	0.99	0.99	1	0.99	1	1
EF2780	1	0.98	0.97	0.97	0.99	0.98	0.98	0.97	0.98	0.98	0.97	0.98	0.97	0.97	0.97	0.97	0.97	0.98	0.98	0.97	0.99	0.97	0.99	0.97
EF2781	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF2782	1	0.98	0.99	1	0.99	1	0.99	1	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99
EF2783	0.85	0.94	0.98	0.46	0.99	0.98	0.98	0.52	0.39	0.69	0.51	0.66	0.52	0.98	0.06	0.94	0.7	0.98	0.47	0.98	0.98	0.52	0.55	0.27
EF2784	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1
EF2785	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2786	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1	1	0.99	0.99	0.99	1	1	0.99	1	0.99
EF2787	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2788	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2789	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2790	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1	0.99	1	0.99	1	1
EF2791	1	0.99	0.98	0.98	1	0.99	0.99	0.98	0.99	0.98	0.99	0.99	1	0.98	1	1	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99
EF2792	1	0.98	0.99	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1
EF2793	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF2794	1	0	0.99	0.97	0.99	0.98	1	0.99	0.99	0.99	0.97	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0	0.99	0.2	0.96
EF2795	1	0	1	0.13	1	0.13	1	0.99	0.99	0.99	0.13	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.11	0.14	0.99	0.13	0.18
EF2796	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF2797	1	0.99	0.98	0.98	1	0.99	0.98	0.99	0.98	1	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	1
EF2798	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2800	0.69	0.69	0	0.66	0.69	0.69	0.56	0.64	0.56	0	1	1	0.69	0	0.69	0.69	0.66	0	1	0.46	0.56	0.66	0.69	0.66
EF2801	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2802	0.46	0.47	0.91	0.94	0.47	0.49	0.58	0.94	0.45	0	0.94	0.91	0.57	0	0.57	0.57	0.92	0	0	0	0.89	0.57	0.46	0.92
EF2803	0	0.97	1	0.94	0	0.95	0	0.74	0	0	0.9	0	0.93	0	0.93	0.93	0	0	0	0	0	0.86	0	0.86
EF2804	0	1	1	0.98	0	0.99	0	0	0	0	0.97	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2805	0.54	1	0.89	0.84	0.82	1	0.52	0.41	0.61	0.54	0.87	0	0.52	0	0.54	0.54	0.54	0	0	0	0.6	0.6	0.6	0.52
EF2806	0	1	0	0.66	0	0.99	0	0.27	0	0	0.83	0	0	0	0	0	0.77	0	0	0	0	0	0	0
EF2807	0	1	0	0.23	0	0.89	0	0.22	0	0	0.21	0.12	0	0	0	0	0.22	0	0	0	0	0	0	0
EF2809	0.21	1	0.21	0.96	0.21	0.21	0	0.9	0.84	0	0.9	0.75	0	0	0	0	0.21	0	0	0	0.21	0.21	0.21	0
EF2810	0.5	0.5	0.49	0.51	0.5	0.46	0	0.5	0.88	0	0.8	0.76	0	0	0	0	0.5	0	0	0	0.5	0.5	0.5	0
EF2811	0.5	0.47	0.98	0.77	0.51	0.51	0	0.99	0.99	0.78	0.6	0.19	0	0	0	0	0.51	0	0	0	0.94	0.51	0.51	0
EF2812	0	0	0.96	0.99	0	0.55	0	0.98	0.87	0	0.97	0	0	0	0	0	0	0	0	0	0.98	0	0	0
EF2813	0	0	0.79	1	0	0.97	0	0.39	0.85	0	0.39	0	0	0	0	0	0	0	0	0	0.39	0	0	0
EF2814	0	0	0.98	1	0	1	0	0	0.85	0	0.09	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2815	0	0	0.99	1	0	1	0	0.51	0.78	0	0	0	0	0	0	0	0	0	0	0	0.52	0	0	0
EF2816	0	0	0.99	1	0	0.86	0	0.66	0.8	0	0.75	0	0	0	0	0	0	0	0	0	0.66	0	0	0
EF2817	0	0	0.97	1	0	0.86	0	0.46	0.86	0	0.43	0	0	0	0	0	0	0	0	0	0.46	0	0	0
EF2818	0	0	0.98	1	0	0.48	0	0.97	0.83	0	0.97	0	0	0	0	0	0	0	0	0	0.97	0	0	0
EF2819	0	0	1	1	0	0	0	1	0.88	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0
EF2820	0	0	0.98	0.99	0	0.16	0	0.98	0.84	0	0.98	0	0	0	0	0	0	0	0	0	0.98	0	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2821	0	0	0.99	1	0	0.38	0	0.99	0.89	0	0.99	0	0	0	0	0	0	0	0	0	0.99	0	0	0
EF2822	0	0	0.99	0.99	0	0.3	0	0.99	0.88	0	0.98	0	0	0	0	0	0	0	0	0	0.99	0	0	0
EF2823	0	0	0.99	0.99	0	0.58	0	0.99	0.94	0	1	0	0	0	0	0	0	0	0	0	0.98	0	0	0
EF2824	0	0	1	1	0	0	0	1	0.9	0.19	0.99	0	0	0	0	0	0	0	0	0	1	0	0	0
EF2825	0	0	0.98	0.94	0	0	0	0.99	0.89	0	0.97	0	0	0	0	0	0	0	0	0	0.99	0	0	0
EF2826	0	0	0.98	0.98	0	0	0	0.99	0.93	0	0.99	0	0	0	0	0	0	0	0	0	0.99	0	0	0
EF2828	0	0	0.96	0.95	0	0.96	0	0.95	0.96	0.66	0.94	0.94	0	0	0	0	0.96	0	0.27	0	0.95	0	0	0.96
EF2829	0.71	0.15	0.93	0.23	0.15	0.15	0	0.69	0.21	0.7	0.15	0	0.15	0	0.69	0.69	0.74	0	0	0.74	0.15	0.23	0	0.74
EF2830	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.89	0	0
EF2831	0.52	0	0.38	0	0.34	0	0	0.3	0	0.54	0	0	0	0	0.52	0.52	0.32	0	0.52	0.32	0.3	0.52	0	0.38
EF2832	0	0	0	0	0	0	0	0	0.88	0	0	0	0	0	0	0	0.79	0	0	0	0	0	0	0
EF2833	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2834	0	0	0.94	0.95	0	0.95	0.14	0.93	0.95	0	0.93	0.86	0	0	0	0	0.9	0	0.94	0	0	0	0	0.94
EF2835	0	0	0.9	0.96	0	0.95	0	0.9	0.95	0	0.95	0.97	0	0	0	0	0.95	0	0	0	0.9	0	0	0
EF2836	0	0	0.98	0.97	0	0.93	0	0.98	0.7	0	0.71	0.97	0	0	0	0	0.7	0	0	0	0.98	0	0	0
EF2837	0	0	0.87	0.86	0	0.97	0	0.87	0.87	0	0.88	0.86	0	0	0	0	0.91	0	0	0	0.87	0	0	0
EF2838	0.54	0.54	0.91	1	0.54	0.93	0.54	0.91	0.97	0.53	0.99	0.93	0.54	0.54	0.54	0.54	0.93	0.54	0.53	0.53	0.91	0.53	0.54	0.53
EF2839	0	0	0.46	1	0	0.46	0	0.5	0.17	0.16	0.17	0.45	0	0	0	0	0.45	0	0	0	0.44	0	0	0
EF2840	0	0	0.96	0.98	0	0.97	0	0.98	0.97	0	0.98	0.98	0	0	0	0	0.97	0	0.71	0	0.98	0	0	0
EF2841	0	0	0.4	0.77	0	0.98	0	0.95	0.98	0	0.75	0.77	0	0	0	0	0.75	0	0.3	0	0.95	0	0	0
EF2842	0	0.71	0.85	0.96	0.71	0.92	0	0.98	0.93	0	0.85	0.96	0	0	0	0	0.92	0	0	0	0.98	0.71	0.71	0
EF2843	0	0.74	0.99	0.97	0.73	0.98	0	0.98	0.97	0	0.98	0.98	0	0	0	0	0.97	0	0	0	0.98	0.73	0.73	0.49
EF2844	0	0	0.94	0.99	0	0.99	0	0.98	0.98	0	0.94	0.98	0	0	0	0	0.98	0	0	0	0.98	0	0	0
EF2845	0	0	0.89	1	0	0.82	0	0.78	0.66	0	0	0.65	0	0	0	0	0.66	0	0	0	0.78	0	0	0
EF2846	0	0	0.97	1	0	0.97	0	0.99	0.99	0.71	0	0	0	0	0	0	0	0	0	0	0.99	0	0	0
EF2847	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2848	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2849	0	0	0.95	1	0	0	0.85	0.85	0	0	0.84	0	0	0	0	0	0	0	0	0	0.74	0	0	0.85
EF2850	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2851	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2852	0	0.39	0.99	1	0.37	0.49	0.93	0.93	0.49	0	0.5	0.37	0	0	0	0	0.54	0	0.15	0	0.75	0.37	0.37	0.93
EF2853	0	0	0.98	1	0	0.98	0.74	0.74	0.99	0	0.74	0	0	0	0	0	0.75	0	0	0	0.99	0	0	0.74
EF2854	0	0	0	1	0	1	0.87	0.87	1	0	0.86	0	0	0	0	0	0	0	0	0	0.89	0	0	0.87
EF2855	0	0	0.99	1	0.24	0.98	0	0.99	0.98	0	0.24	0	0	0	0	0	0	0	0	0	0.99	0	0	0
EF2856	1	1	1	1	1	0.85	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF2857	1	0.99	0.99	0.99	0.99	0.99	0.99	0.92	0.99	0.99	0.99	0.93	0.92	0.99	0.92	0.92	0.92	0.99	0.99	0.99	0.99	0.92	0.99	0.99
EF2858	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2859	1	1	0.99	0.98	1	0.98	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF2860	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1
EF2861	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1
EF2862	1	0.99	1	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	0.99	1	0.99	1
EF2863	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF2864	1	0.99	0.97	0.99	1	0.99	0.98	0.98	0.96	0.97	0.98	0.98	0.99	0.98	0.99	0.99	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.97
EF2866	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	1	1	1	1	0.99	1	0.99	0.99	0.99	0.99	1
EF2867	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF2868	1	0.99	0.99	1	1	1	0.74	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	0.99
EF2869	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2870	1	0.99	0.99	0.99	0.98	0.99	0.65	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99
EF2871	1	1	1	0.99	1	0.99	0.99	1	1	1	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1
EF2872	1	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	1	0.99	1	0.99
EF2873	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	1	1	0.99	1	1	1	1	1	0.99	0.99	0.99	0.99	1
EF2874	1	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1
EF2875	1	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2876	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	1
EF2877	1	0.99	1	0.99	1	0.99	1	1	0.99	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF2878	1	1	1	1	1	1	1	1	1	0.98	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2879	1	0.98	0.99	1	0.99	1	0.99	1	0.99	0.98	0.98	0.99	0.98	1	0.98	0.98	0.99	1	0.99	0.98	0.99	1	0.99	0.98
EF2880	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	1	1	1	1	1	0.99	1	1
EF2881	1	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.98	0.98	0.99
EF2882	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2883	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99
EF2884	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2885	1	0.99	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99
EF2886	1	1	1	1	0.99	1	0.99	1	0.99	1	0.99	1	1	1	1	1	1	0.99	1	0.99	1	1	1	1
EF2888	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2889	1	0.98	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	1	1	1	0.99	1	0.99	1	0.99	0.99
EF2890	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2891	1	0.99	0.99	1	0.99	1	0.99	1	0.98	0.99	1	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF2892	1	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	1	0.99	1	1	1	1	1	1	0.99	1	0.99	1	0.99	0.99
EF2893	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2894	1	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	1
EF2895	1	0.97	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.99	0.98	1	0.98	0.98	0.99	0.98	0.99	0.98
EF2896	1	1	0.99	0.99	1	0.98	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF2898	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	1
EF2899	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2900	1	1	1	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF2901	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	1	0.99	1	1
EF2902	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.58	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2903	1	0.99	1	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99
EF2904	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99
EF2905	0.55	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	1	1	1
EF2906	1	0.98	0.98	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2907	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99
EF2908	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF2909	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2910	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2911	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	0.99	0.99	0.99
EF2912	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	0.99	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99
EF2913	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	1	0.99	1	1	1	0.99	1	0.99	1	0.99	0.99
EF2914	1	0.99	0.99	1	1	1	1	0.99	1	1	1	1	1	0.99	1	1	0.99	1	1	0.99	1	0.99	1	0.99
EF2915	1	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99
EF2916	1	0.98	0.97	0.98	0.98	0.98	0.97	0.98	0.97	0.97	0.98	0.97	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.97	0.96	0.98	0.97	0.98
EF2917	1	0.98	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	0.99
EF2918	1	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99
EF2919	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2920	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2921	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2922	1	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1
EF2923	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2924	1	0.99	1	1	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99	1
EF2925	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF2926	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.65	0.99	0.78	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2927	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99
EF2928	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	1
EF2929	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2930	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2931	1	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98
EF2932	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	1	0.99	1	1
EF2933	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.98
EF2934	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99
EF2935	0.8	0.99	0.99	1	0.99	1	1	1	0.99	0.98	0.99	1	1	0.99	1	1	1	1	1	0.99	0.99	1	0.99	0.99
EF2936	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2937	0	0	0.54	0	0	0	0	0.48	0	0	0	0	0	0	0	0	0.48	0	0.53	0.54	0	0	0	0
EF2938	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2939	0.48	0.48	0.48	0.49	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.48	0.49
EF2940	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2941	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2942	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2943	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2944	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2945	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2946	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2947	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2948	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2949	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2950	0	0	0	0	0	0	0	0	0	0.83	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2951	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2952	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2953	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2954	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EF2955	0	0.08	0.11	0	0.53	0.53	0	0.11	0	0.77	0.11	0	0.11	0	0.11	0.11	0.08	0.1	0	0.08	0.53	0	0	0.08
EF2956	1	0.99	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF2957	1	0.99	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	0.99
EF2958	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF2959	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	1	0.99	1	0.99
EF2960	1	0.98	0.99	0.99	0.98	0.99	1	0.99	0.99	0.98	0.99	0.99	0.98	1	0.98	0.98	0.99	1	0.99	0.99	1	0.99	1	0.98
EF2961	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2962	1	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.98	0.99	0.98
EF2963	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF2964	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2965	1	0.99	1	0.99	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	1
EF2966	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.98	0.98
EF2967	1	0.96	0.95	0.98	0.98	0.98	1	1	0.96	0.96	0.98	1	0.99	1	0.99	0.99	0.98	0.96	0.99	1	0.98	1	0.98	0.95
EF2968	1	0.89	0.81	0.99	0.99	0.99	0.99	1	0.81	0.81	0.99	0.99	0.91	0.99	0.91	0.91	0.99	0.98	0.99	0.99	0.99	1	0.99	0.81
EF2969	0.93	0.96	0.95	1	1	1	1	1	0.95	0.95	1	1	1	1	1	1	1	1	1	1	1	1	1	0.95
EF2970	1	0.93	0.93	1	0.99	1	1	1	0.95	0.91	1	0.99	0.97	1	0.97	0.97	0.96	0.97	0.96	0.96	0.99	1	0.99	0.95
EF2972	1	0.97	0.99	1	0.99	0.99	1	1	0.98	0.96	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	0.98
EF2973	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99
EF2974	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	1	0.99	0.99
EF2975	0.98	0.98	0.98	0.86	1	0.9	0.99	0.11	0.75	0.54	0.98	0.35	0.56	0.99	0.8	0.6	0.54	0.62	0.71	0.99	0.42	0.75	0.56	0.45
EF2976	1	0.97	0.97	0.77	0.98	0.98	0.98	0.87	0.65	0.97	0.98	0.49	0.56	0.98	0.86	0.86	0.37	0.99	0.16	0.63	0.98	0.53	0.78	0.43
EF2977	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2978	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF2979	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	0.91	1	1	1	1
EF2980	1	0.98	0.98	0.98	1	0.98	1	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	1	1	0.99	1	0.99
EF2981	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.81	0.98	0.99	0.99	0.99	0.99	0.99	0.98
EF2982	1	0.98	0.98	0.99	0.99	0.99	0.98	1	1	0.98	1	1	0.99	1	0.99	0.99	1	0.98	0.99	1	0.98	1	0.98	0.99
EF2983	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.99
EF2984	1	0.98	0.99	1	1	1	0.99	1	0.98	0.98	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.98

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF2985	1	0.98	0.99	0.71	0.99	0.99	0.99	1	0.98	0.98	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	1	0.98	1	0.98	0.99
EF2986	1	0.99	0.99	1	1	1	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	1	1	1	1	1	1	1
EF2987	1	0.98	0.99	0.86	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2988	1	0.99	1	1	1	1	1	1	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.98	1	0.99	0.99	1	0.99	1
EF2989	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1
EF2990	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.98	0.98	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.98	1	0.98	1
EF2991	1	1	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	1	1	1	1
EF2992	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF2994	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99
EF2995	1	0.99	0.99	1	0.99	1	1	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99
EF2996	1	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	1	0.99	1	0.98
EF2997	1	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99
EF2999	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99
EF3000	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3001	1	0.97	0.98	0.99	1	0.99	0.99	0.99	0.99	0.96	0.98	0.99	1	0.99	1	1	0.98	0.97	0.98	0.99	1	0.98	1	0.98
EF3002	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.98	0.99	0.98	0.99
EF3003	1	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.91	0.98	0.91	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.98	0.97	0.98	0.97	0.98
EF3004	1	0.98	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3005	1	0	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0
EF3006	1	0.95	0.98	0.99	0.98	0.99	0.99	0.98	0	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.99	0	0.99	0.95
EF3007	1	0	0.97	0.97	0.98	0.97	0.98	0.98	0.98	0.97	0.99	0	0.98	0.99	0.98	0.98	0.99	0.97	0.99	0.99	0.98	0.98	0.98	0
EF3008	1	0.98	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.3	0.99	0.98	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.99
EF3009	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1
EF3010	0.71	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99
EF3011	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.42	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3012	1	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3013	1	0.98	0.98	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.99	1	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.98	0.98
EF3014	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3015	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3016	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3018	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3019	1	0.98	0.98	1	0.99	1	0.99	0.99	0.99	0.96	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.97	0.99	0.99	0.99	0.99
EF3020	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	0.99	0.99	1	1	1	0.48
EF3021	1	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.78	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.99	1	0.99	0.99
EF3022	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3023	0.75	0.04	0.04	0.87	0.78	0.88	0.93	0.99	0.87	0.76	0.74	0.8	0.74	0.83	0.75	0.75	0.74	0.04	0.04	0.75	0	0.75	0	0.04
EF3024	1	0	0	0.99	0.94	0.99	0.99	0.99	0.95	0.98	0.98	0.99	0.97	0.99	0.97	0.97	0.99	0	0	0.99	0	0.99	0	0
EF3025	1	0.98	1	1	0.99	1	0.99	0.99	0.99	0.98	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3027	1	0.98	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.98
EF3028	1	0.98	0.99	0.99	0.99	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99
EF3029	1	0.45	0.45	0.45	1	0.45	0.45	1	0.45	0.45	0.45	1	0.45	0.45	0.45	0.45	0.45	0.45	1	1	1	0.45	1	0.45
EF3030	1	0.43	0.43	0.43	1	0.43	0.43	1	0.43	0.43	0.43	1	0.43	0.43	0.43	0.43	0.43	0.43	1	1	1	0.43	1	0.43
EF3031	1	0.5	0.49	0.5	1	0.49	0.49	1	0.49	0.5	0.49	1	0.5	0.5	0.5	0.5	0.5	0.5	1	1	1	0.49	1	0.49
EF3032	1	0	0	0	0.99	0	0	0.99	0	0	0	0.99	0	0	0	0	0	0	0.99	0.99	0.99	0	0.99	0
EF3033	1	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	1	1	1	0	1	0
EF3034	1	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	1	1	1	0	1	0
EF3035	1	0.99	0.99	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3036	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99
EF3037	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1
EF3039	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3040	1	1	1	1	1	1	1	1	1	1	1	1	1	0.96	1	1	1	1	1	1	1	1	1	1
EF3041	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99
EF3042	1	0.17	0.17	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.17	0.99	0.17	0.17	0.99	0.99	0.3	0.99	0.99	1	0.99	0.17

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF3043	1	0	0	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0	0	0.98	0.99	0	0.99	0.99	0.99	0.99	0
EF3044	1	0.17	0.17	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.17	1	0.17	0.17	0.99	0.99	0.17	0.99	1	0.99	1	0.17
EF3045	1	0.15	0.37	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.15	0.99	0.15	0.15	1	0.99	0.15	0.99	1	0.99	1	0.15
EF3046	1	0.14	0	0.97	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0	0.97	0	0	0.98	0.99	0.14	0.98	0.98	0.97	0.98	0
EF3047	1	0	0	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0	0.97	0	0	0.98	0.99	0	0.98	0.98	0.98	0.98	0
EF3048	1	0	0	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0	0.98	0	0	0.98	0.99	0	0.98	0.98	0.98	0.98	0
EF3049	1	0	0	0.99	1	0.99	1	1	1	0.99	0.99	1	0	0.99	0	0	0.99	1	0	0.99	0.99	0.99	0.99	0
EF3050	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3051	1	0.98	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99
EF3052	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3053	1	0.99	0.99	1	1	1	1	1	0.99	0.99	1	1	0.98	0.99	0.98	0.98	0.99	0.98	0.99	1	0.99	0.99	0.99	0.99
EF3054	1	0.99	0.99	0.97	0.98	0.97	0.98	0.97	0.99	0.97	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98
EF3055	1	1	1	1	1	1	1	0.99	0.92	0.99	1	0.99	1	1	1	1	1	0.99	1	1	1	1	1	0.99
EF3056	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	1	0.99	0.99	1	0.99	0.99
EF3057	1	0.98	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3058	1	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.98	1	0.99	1	1	0.98	1	0.99	0.98	1	1	1	0.98
EF3059	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3060	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.95	0.99	0.99
EF3061	1	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.98
EF3062	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3063	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF3064	1	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3065	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3066	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3067	1	0.98	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.98
EF3068	1	0.99	0.99	1	0.99	1	1	1	1	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3069	1	0.98	0.98	1	0.99	1	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	0.99
EF3070	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3071	1	1	1	0.97	0.95	0.97	0.99	0.99	1	1	1	0.99	1	1	1	1	1	1	0.96	0.96	0.99	0.98	0.99	0.99
EF3072	1	0.99	0.97	1	0.98	1	0.99	0.98	1	0.98	1	0.98	0.98	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99
EF3073	1	0.97	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98
EF3074	1	0.26	0.41	0.98	0.68	0.98	0.99	0.98	0.27	0.19	0.98	0.98	0.23	0.98	0.18	0.23	0.98	0.24	0.65	0.66	0.9	0.99	0.99	0.27
EF3075	1	0.24	0.19	0.51	0.17	0.51	0.51	0.51	0.19	0.2	0.11	0.51	0.1	0.27	0.18	0.19	0.38	0.33	0.33	0.27	0.99	0.39	0.77	0.27
EF3076	0.99	0.92	0.88	0.97	0.97	0.97	0.97	0.99	0.89	0	0.96	1	0.9	0.94	0.18	0.18	0.97	0.91	0.38	1	0.91	0.96	0.48	0.91
EF3078	1	0.97	0.98	0.99	0.99	0.99	0.99	1	0.98	0.98	1	1	0.99	0.98	0.99	0.99	0.99	0.98	1	0.99	0.99	1	0.99	0.98
EF3079	1	0.92	0.97	1	0.99	1	1	0.99	0.98	0.97	0.99	0.99	1	0.99	1	1	1	0.98	0.99	0.99	0.99	0.98	0.99	1
EF3080	1	0.97	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.98	0.99	0.99
EF3081	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3082	1	0.99	0.99	0.99	1	0.99	1	1	0.98	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	1
EF3083	1	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.98	1	0.98	1
EF3084	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3085	1	0.99	0.99	1	0.99	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF3086	1	0.98	0.99	0.99	0.99	0.99	1	1	0.99	0.98	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	0.99	1	0.99
EF3087	0.86	0.56	0.99	1	1	1	0.98	0.52	0.99	0.95	0.99	0.99	0.94	0.99	0.94	0.94	0.99	1	0.55	0.96	0.55	0.99	0.55	0.55
EF3088	0.93	0.66	0.98	0.96	0.96	0.96	0.97	0.56	0.98	0.99	0.96	0.96	1	0.96	1	1	0.96	1	0.65	1	0.65	0.96	0.65	0.66
EF3089	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3090	1	0.95	0.96	0.98	0.98	0.99	0.96	0.98	0.98	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.98	0.98	0.98	0.98	0.97
EF3091	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3092	1	0.98	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0	0.98	0.99	1	0.98	0.98	0.98	0.98	0.98	0.98
EF3093	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1
EF3094	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.6	0.6	0.98	1	0.98	0.98	0.98	0.98	0.98	0.98
EF3095	1	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3096	0.82	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF3097	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3099	1	1	0	0	0	0	0	0	0	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0
EF3100	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EF3101	0.79	0.79	0	0	0	0.21	0	0	0	0.79	0.21	0.17	0.79	0	0.79	0.79	0	0.79	0.22	0	0	0	0	0
EF3102	1	1	0	0	0	0	0	0	0	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0
EF3103	1	1	0	0	0	0	0	0	0	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0
EF3104	1	1	0	0	0	0	0	0	0	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0
EF3105	1	0.99	0	0	0	0	0	0	0	1	0	0	1	0	1	1	0	1	0	0	0	0	0	0
EF3106	1	0.99	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.91	0.99	0.98
EF3107	1	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	1	1	0.99	1	1	0.99	1	1
EF3108	1	1	0.99	0.99	0.99	0.99	1	1	0.99	1	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3109	1	0.99	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF3110	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	0.99	1	0.99	1	1
EF3111	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3112	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1	1	1	1	0.99	1	1	0.99	1	0.99	1	1
EF3113	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3114	1	0.99	0.99	1	1	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	1
EF3115	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3116	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3117	1	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.98	0.99	0.98	0.99
EF3118	1	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3119	1	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3120	1	0.98	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.66
EF3121	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3122	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3123	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3124	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3125	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3126	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF3127	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3129	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF3130	1	0.99	1	0.99	1	1	1	1	0.99	0.98	1	1	0.98	0.99	0.98	0.98	0.99	1	1	1	1	1	1	0.99
EF3131	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98
EF3132	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3133	1	0.98	0.97	0.99	0.99	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	1	1	0.99	0.98	0.99	0.98	0.99	0.98
EF3134	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF3135	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3136	1	0.99	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF3137	1	0.99	1	1	0.99	1	1	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1
EF3138	1	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.99
EF3139	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.98	1
EF3140	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3141	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3142	1	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3144	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF3145	1	0	0.98	0	0	0	0	0.99	0	0.27	0	0.99	0.27	1	0.27	0.27	0.99	0.99	0	1	1	0	1	0
EF3146	1	0	0	0	0	0	0	1	0	0	0	0.77	0	1	0	0	1	1	0	1	1	0	1	0
EF3148	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF3149	1	0.99	0.98	0.99	0.99	0.99	0.99	1	0.98	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99
EF3150	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3151	1	0.98	0.98	0.98	0.97	0.98	0.98	0.99	0.98	0.97	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98
EF3152	1	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	1	0.98	0.98	1	0.99	1	0.98
EF3153	0.95	0.66	0.68	0.69	0.65	0.69	0.66	0.69	0.67	0.69	0.21	0.69	0.96	0.68	0.96	0.96	0.68	0.97	0.68	0.67	0.24	0.69	0.24	0.68

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF3154	1	0.77	0.77	0.72	0.69	0.72	0.68	0.76	0.76	0.77	0.22	0.76	0.72	0.73	0.72	0.72	0.73	0.71	0.73	0.69	0.25	0.72	0.25	0.81
EF3155	1	0.6	0.15	0.61	0.63	0.61	0.61	0.15	0.15	0.16	0.62	0.59	0.63	0.63	0.63	0.63	0.63	0.63	0.63	0.23	0.62	0.61	0.62	0.62
EF3156	1	0.97	0.97	0.99	0.98	0.99	0.98	0.99	0.97	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.97	0.99	0.99	0.99	0.97
EF3157	1	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3158	1	0.98	0.98	0.99	0.98	0.99	0.98	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.97	0.98	0.97	0.99	0.97	0.98
EF3160	1	0	0	0	0	0	1	0	0	0	0	0	0	0.99	0	0	0.99	1	0	0	1	0.99	1	0
EF3161	1	0.99	0	0.99	1	0.99	0.16	0.15	0	0	0.15	0.15	0	0.16	0	0	0.16	1	0	0.15	1	0	1	0.99
EF3163	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3164	1	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3165	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.97	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	1	0.99	0.98	0.98	0.98	0.98	0.98
EF3166	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3167	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF3168	1	0.99	1	1	1	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	1	0.99	1	0.99
EF3169	1	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3170	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3171	1	0.99	1	1	1	1	1	0.99	1	0.99	1	0.99	1	0.99	1	1	0.99	1	1	1	1	0.99	1	1
EF3172	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3173	1	0.98	1	0.86	0.48	0.86	0.99	1	0.99	0.86	0.87	0.99	0.86	0.98	0.86	0.86	0.86	1	0.99	1	0.99	0.99	0.99	1
EF3174	1	0.98	1	1	1	1	1	1	1	0.99	1	1	1	1	1	0.99	1	1	0.96	1	0.99	0.99	0.99	1
EF3175	1	0.99	1	1	1	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99
EF3176	1	0.98	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.97	0.99	0.97	0.97	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99
EF3177	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99
EF3178	1	0.96	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.97	0.99	0.99	0.99	0.99	0.99
EF3179	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.98	0.98
EF3180	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3181	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.98
EF3182	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF3183	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3184	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.98	0.98
EF3185	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	0.99
EF3186	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1
EF3187	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF3188	1	0.98	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.83	0.83	0.83	0.83	0.83	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3189	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1
EF3191	1	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	1	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99
EF3192	1	0.99	1	0.98	0.99	0.98	0.99	1	0.99	0.99	0.99	1	0.98	0.98	0.98	0.98	0.99	0.98	0.99	1	0.98	0.99	0.98	0.98
EF3193	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3194	1	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1
EF3196	0.83	0.98	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	1
EF3197	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3198	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99
EF3199	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	1	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
EF3200	1	1	1	1	1	1	0.99	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1
EF3201	1	0.99	0.98	1	0.99	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99
EF3202	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99
EF3203	1	1	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99
EF3204	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF3205	1	0.99	1	1	1	1	1	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1
EF3206	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3207	1	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.98	0.98
EF3208	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99
EF3209	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	1	0.98	0.98	1	0.99	1	0.99	1	1	1	0.99
EF3210	1	0	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF3211	1	0.24	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.99
EF3212	1	0	1	1	1	1	1	1	0.99	0.99	1	1	1	0.99	1	1	1	1	1	0.99	1	1	1	0.99
EF3213	1	0.32	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3214	0.98	0.25	0.97	0.97	0.96	0.97	0.97	0.96	0.96	0.97	0.96	0.96	0.97	0.96	0.97	0.97	0.96	0.96	0.97	0.97	0.97	0.97	0.97	0.97
EF3215	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EF3216	1	0	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.98
EF3217	1	0.99	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.6
EF3218	1	0.99	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.99
EF3220	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
EF3221	1	0	0	0.7	0	0	0.68	0.55	0	0	0.55	0.55	0	0	0	0	0.7	0	0	0	0	0	0	1
EF3222	1	0	0	0	0	0	0.37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
EF3223	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
EF3224	1	0	0	0	0.68	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
EF3225	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
EF3226	1	0	0	0	0.55	0	0	0.1	0	0	0.1	0.1	0	0	0	0	0	0	0	0	0	0	0	1
EF3227	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
EF3228	1	0	0	0	0	0	0	0	0.54	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
EF3230	1	1	0.99	1	0.98	1	0.99	1	0.99	1	0.99	1	0.99	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1
EF3231	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3232	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3233	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF3234	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.98	0.97	0.99	0.98	0.98	0.98	0.98	0.98
EF3235	1	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3236	1	0.98	0.97	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.99	0.98	0.98	0.99	0.98	0.99	0.98	0.99	0.99	0.99	0.98
EF3237	1	0.99	1	1	0.99	1	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	0.99	1	1	0.99	1	1
EF3238	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99
EF3239	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF3240	1	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	1	0.98	0.98	0.98	0.98	0.98	0.97
EF3241	1	0.94	0	0	0	0	0	0.99	0.99	0	1	0.99	0	0	0	0	0	1	0.99	1	0	0	0	0
EF3242	1	0.99	0	0	0	0	0	0.99	0.99	0	0.99	0.99	0	0	0	0	0	1	0.99	0.99	0	0	0	0
EF3243	1	0.94	0.37	0.37	0.37	0.37	0.37	0.94	0.96	0.37	0.96	0.94	0.37	0.37	0.37	0.37	0.37	1	0.96	0.97	0.37	0.37	0.37	0.37
EF3244	0.99	1	1	1	0.99	1	0.99	0.99	1	1	1	0.99	1	1	1	1	0.99	1	1	1	0.99	1	1	0.99
EF3245	1	0.98	0.99	0.98	0.98	0.98	0.98	0.98	0.99	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.98	1	0.99	0.98	0.98	0.98	0.98	0.98
EF3247	1	0.51	0.92	0.8	0.98	0.21	0.21	0.76	0.98	0.9	0.8	0.51	0.97	0.73	0.97	0.97	0.73	1	0.99	0.77	0.97	0.78	0.21	0.73
EF3248	1	0.21	0.2	0.21	0.41	0.41	0.41	0.41	0.2	0.73	0.41	0.41	0.2	0.41	0.2	0.19	0.32	1	0.41	0.41	0.2	0.21	0.2	0.41
EF3249	1	0	0.36	0.95	0.96	0.95	0.97	0.96	0.47	0.67	0.97	0.95	0.33	0.95	0.33	0.33	0.95	1	0.97	0.97	0.96	0.95	0.95	0.95
EF3250	1	0.2	0.43	0.45	0.53	0.52	0.53	0.47	0.43	0.41	0.53	0.53	0.98	0.53	0.98	0.95	0.53	0.99	0.53	0.53	0.43	0.46	0.45	0.53
EF3251	1	0	0	0	0	0	0	0	0	0.07	0	0	0.98	0	0.98	0.98	0	0.97	0	0	0	0	0	0
EF3252	1	0.22	0.11	0.23	0.3	0.23	0.23	0.25	0.1	0.19	0.3	0.25	0.25	0.24	0.26	0.26	0.25	0.48	0.22	0.39	0.23	0.23	0.22	0.24
EF3253	1	0.94	0.94	0.98	0.98	0.98	0.97	0.97	0.94	0	0.98	0.97	1	0.98	0.23	0.23	0.96	1	0.39	0.9	0.94	0.97	0.51	0.96
EF3254	1	0.95	0.97	0.98	0.97	0.98	0.97	0.97	0.97	0.95	0.97	0.97	0.97	0.96	0.97	0.97	0.97	0.97	0.97	0.98	0.97	0.97	0.97	0.97
EF3255	0.87	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98
EF3256	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3257	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1	1	0.99	0.99	0.99	0.99
EF3258	1	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3259	1	0.98	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF3260	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3261	1	0	0	0	0	1	1	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0	1	0
EF3262	1	0	0	0	0	1	1	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0	1	0
EF3263	1	0.98	1	1	1	1	1	1	1	1	1	1	0.96	1	0.96	0.96	1	1	0.99	0.99	1	1	1	1
EF3264	1	0	0	0	1	1	0.98	0.86	0	0	1	0.87	0	0.88	0	0	1	1	0.99	0.98	1	0.99	1	1
EF3265	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3266	1	0.96	0.97	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF3267	1	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	1	1	1	1	0.99	0.99	1	0.99	1	1
EF3268	1	0.99	0.99	0.98	0.98	0.99	0.99	1	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.98	1	1
EF3269	1	0.98	0.98	0.99	0.99	0.98	1	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.98	0.98	0.99	0.98	0.98
EF3270	1	0.98	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF3271	1	0.97	0.97	0.23	0.97	0.99	0.98	1	0.98	0.97	1	1	0.23	0.99	0.23	0.23	1	1	1	1	0.98	0.99	1	1
EF3272	1	0	0	0	0	0	1	1	0.99	0	1	1	0	1	0	0	0.99	1	1	1	1	0	0.99	0.99
EF3273	1	0	0	0	0	0	1	1	1	0	1	1	0	1	0	0	1	1	1	1	1	0	1	1
EF3274	1	0	0	0	0	0	0.99	0.99	0.98	0	0.99	0.99	0	0.99	0	0	0.99	1	0.99	0.99	0.99	0	0.99	0.99
EF3275	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.98	0.98	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99
EF3276	1	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3277	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF3278	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	0.99	0.99	0.99	0.99	1	0.99
EF3279	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3280	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF3281	1	0.99	0.99	0.99	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.98	1	0.98	0.99	0.99	0.98	0.98	0.98
EF3282	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3283	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3284	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3285	1	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.49	0.99	0.99	0.99
EF3286	1	0.99	0.99	0.99	1	1	1	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	1	0.99	0.99	0.99	0.99
EF3287	0.68	0	0	1	0	0	0.88	1	0.87	0.32	0	0.88	0.99	1	0.56	0.56	0.88	0	0	0	0	0.88	1	0.88
EF3289	1	1	1	1	1	1	0.99	0.99	1	0.99	1	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1
EF3290	1	0.99	1	1	0.99	0.99	1	1	1	0.99	0.99	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF3292	1	0.99	0.99	0.99	0.99	0.98	0.98	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.98	1	0.99	0.98	0.99	0.99	0.98	0.98
EF3293	1	0.84	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3294	1	0.99	0.99	0.98	0.98	0.98	0.98	0.99	0.99	0.99	0.98	0.99	0.98	0.98	0.98	0.98	0.99	1	0.98	0.99	0.98	0.98	0.99	0.99
EF3295	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99
EF3296	1	0.99	0.99	1	0.99	1	1	1	1	0.99	1	1	1	1	1	1	0.99	1	0.99	0.99	1	1	0.99	0.99
EF3297	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3298	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF3299	1	0.99	1	0.99	1	0.99	1	1	0.99	0.99	0.99	1	1	1	1	1	1	1	0.99	0.99	1	0.99	1	1
EF3300	1	0.99	1	0.99	1	0.99	0.99	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1
EF3301	1	0.98	0.98	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.92	0.95	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3302	0.8	0.52	0.82	0.86	1	0.82	1	0.97	0.82	0.8	0.82	0.97	0.85	0.99	0.79	0.8	0.97	0.97	1	1	0.86	0.86	0.97	0.97
EF3303	1	0.99	0.99	0.99	1	1	1	1	0.99	1	1	1	1	0.99	1	1	1	0.99	0.99	1	1	0.99	1	1
EF3304	1	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3305	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	0.99	1	1
EF3306	1	0.99	1	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99	1	1	1	1	0.99	1	1	1	1	0.99	0.99	0.99
EF3307	1	0.99	1	0.99	1	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.82	0.83	0.99	1	0.99	0.99	1	0.99	0.99	0.99
EF3308	1	1	1	0.99	1	1	0.99	1	1	1	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1
EF3309	1	0.99	1	1	1	1	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3310	1	0.99	0.98	0.99	0.98	0.99	0.99	0.98	0.98	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.98	1	0.99	0.99	0.99	0.99	0.98	0.98
EF3311	1	0.99	1	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	1	0.99	0.99
EF3312	1	0.99	0.99	0.99	0.99	1	0.99	1	0.99	1	0.99	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	1	0.99	1	1
EF3313	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3314	0.58	0.59	0.72	0.72	0.72	0.72	0.72	0.72	0.61	0.67	0.61	0.72	0.59	0.72	0.63	0.58	0.73	0.62	0.6	0.72	0.72	0.72	0.72	0.72
EF3315	1	0.98	0.99	0.98	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	1	0.99	0.99	0.99	0.99
EF3316	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.99	0.99	0.51	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3317	1	0.99	1	0.99	1	1	1	1	0.71	0.99	0.99	1	0.99	1	0.99	0.99	1	1	0.99	0.99	1	1	1	1
EF3318	0.6	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	1	1
EF3319	1	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99
EF3320	1	0.99	0.99	0.99	0.99	1	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	0.99	0.99	0.99
EF3321	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EF3322	1	1	0.99	1	0.99	1	1	1	0.99	0.99	1	1	0.99	1	0.99	0.99	1	1	0.99	1	0.99	1	1	1
EF3323	1	0.99	0.99	1	1	0.99	1	1	0.99	0.99	1	1	1	1	1	1	1	1	0.99	1	1	1	1	1
EF3324	1	0.99	0.99	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3325	1	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99
EF3326	1	1	0.99	1	0.99	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3327	1	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3328	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99
EF3329	1	0.99	1	0.99	0.99	1	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	0.99	0.99
EF3330	1	0.99	0.99	1	1	1	0.99	1	0.99	1	1	1	0.99	1	0.99	0.99	1	0.99	1	1	1	1	1	1
EF3331	1	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	1	0.99	0.99	1	1	1	1	1	1	1	0.99	0.99	0.99	1	1
EF3332	1	1	1	1	1	1	0.99	1	1	1	0.99	1	1	1	1	1	1	1	1	1	1	1	1	1
EF3333	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ef5SA	1	1	1	0.72	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ef5SB	1	1	1	0.72	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ef5SC	1	1	1	0.72	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ef5SD	1	1	1	0.72	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
EFA0001	1	0.57	0.95	0.43	0	0	0	1	0.38	0	0.34	0.96	0.37	0	0.38	0.38	0.96	0	0.37	0.38	0	0	0.34	0.43
EFA0002	1	0.46	0.5	0.99	0	0	0	1	0	0	0	0.98	0.56	0	0	0	0	0.56	0.56	0	0	0	0.54	0.98
EFA0003	0.67	0.61	0.7	0.99	0.43	0.43	0.43	1	0.61	0.43	0.69	0.99	0.69	0.43	0.69	0.69	0.61	0.66	0.7	0.61	0.55	0.43	0.7	0.99
EFA0004	0.99	0	0	0.99	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0.16	0.99
EFA0005.1	1	0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1
EFA0006	1	1	0.81	0.76	1	0.98	0.99	0	0.99	0	0.86	1	1	0	0.82	0.8	0.76	0	0.4	0.99	0.76	0.82	0.76	0.76
EFA0007	0	1	0	0	0	1	1	1	0	0	0.7	1	1	0	0	1	0	0	1	0	1	0	0	0
EFA0008	0.26	0	0	0	0.25	0.75	0.25	0.75	0.25	0	0.54	0	0.25	0	0.24	0.24	0	0	0	0.26	0.54	0	0	0
EFA0009	1	1	0.81	0.76	1	0.98	0.99	0	0.99	0	0.86	1	1	0	0.82	0.8	0.76	0	0.4	0.99	0.76	0.82	0.76	0.76
EFA0010	0	0.74	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFA0012	0	0.77	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFA0013	1	1	0.81	0.76	1	0.98	0.99	0	0.99	0	0.86	1	1	0	0.82	0.8	0.76	0	0.4	0.99	0.76	0.82	0.76	0.76
EFA0014	0.08	0.09	0	0	0.07	0	0.08	0	0.08	0	0.08	0.08	0.08	0	0.07	0.07	0	0	0.08	0.08	0.08	0	0	0
EFA0015	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFA0016	1	0.44	0.34	0.34	0.31	0.43	0.44	0	0.29	0	0.34	0.43	0.43	0	0.55	0.43	0.34	0	0.29	0.43	0.43	0.43	0.43	0.34
EFA0017	1	1	1	0.19	0.42	0	0	1	0.41	0.54	0.19	1	0.52	0.44	1	1	0.44	0.41	0.42	0.69	0.41	0.68	0	0.44
EFA0019	1	1	1	0.26	0	0.54	0.53	1	0.54	0	0.38	1	0.54	0	1	1	0.25	0.26	0.53	0	0.53	0	0.54	0.25
EFA0020	1	0.97	0.97	0.76	0	0.11	0	0.97	0	0	0.75	0.97	0.65	0	0.97	0.97	0	0.75	0.73	0.74	0.76	0.7	0.74	0.72
EFA0021	1	0.97	0.97	0.71	0	0.6	0	0.97	0.4	0	0.72	0.97	0.68	0	0.97	0.97	0	0.72	0.72	0.72	0.72	0	0.71	0.71
EFA0022	1	1	1	0.73	0	0	0	1	0	0	0.64	1	0	0	1	1	0	0	0	0	0	0	0	0
EFA0024	0.47	0.38	0.99	0	0	0.95	0.94	0.68	0.94	0	0.57	1	0.94	0	0.3	0.79	0	0	0.94	0	0.93	0	0.94	0
EFA0025	1	0.46	0.64	0	0	0.65	0.64	0.49	0.65	0	0.65	0.64	0.64	0	0	0.32	0	0	0.64	0	0.63	0	0.64	0
EFA0026	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFA0028	1	0.79	0.79	0	0	0.79	0.79	0.79	0	0	0	0.79	0.79	0	0	0	0	0	0.79	0	0.8	0	0.8	0
EFA0029	1	0.27	0.27	0	0	0.27	0.27	0.27	0	0	0	0.26	0.27	0	0	0	0	0	0.27	0	0.27	0	0.27	0
EFA0030	0.67	0.42	0.16	0	0	0.42	0.41	0.36	0	0	0.28	0.42	0.42	0	0.42	0.43	0	0	0.42	0	0.4	0	0.41	0
EFA0031	0.98	0.51	0	0	0	0.97	0.97	0.73	0	0	0.4	0.97	0.5	0	0.5	0.5	0	0	0.97	0	0.97	0	0.99	0
EFA0032	0.62	0.99	0	0	0	0.62	0.77	0.77	0	0	0.77	0.71	0	0	0.99	0.99	0	0	0.71	0	0.71	0	0.99	0
EFA0033	0.99	0.99	0	0	0	0.99	0.99	0.3	0	0	0.31	0.98	0	0	0.99	0.99	0	0	0.99	0	0.99	0	0.99	0
EFA0034	1	0.73	0.72	0.6	0.49	1	1	1	0.49	0.49	0.71	0.7	0.53	0.49	1	1	0.49	0.73	0.7	0.49	1	0.49	0.7	0.53
EFA0035	1	0	0	0	0	1	1	0.34	0	0	1	1	0	0	1	1	0	0	1	0	1	0	1	0
EFA0036	1	0	0	0	0	1	1	0.99	0	0	1	1	0	0	1	1	0	0	0.99	0	1	0	0.99	0
EFA0037	0.98	0	0	0	0	1	0.99	1	0	0	0.35	1	0	0	0.99	0.99	0	0	0.99	0	0.55	0	1	0
EFA0038	0.99	0	0	0	0	0.99	0.99	0.77	0	0	0.99	0.99	0	0	0.99	0.99	0	0	0.98	0	0.46	0	1	0
EFA0039	0.99	0	0	0	0	0.99	0.99	1	0	0	0.22	1	0	0	0.99	0.99	0	0	0.99	0	0	0	1	0
EFA0040	0.99	0	0	0	0	0.99	0.99	0.22	0	0	0.41	0.99	0	0	0.98	0.99	0	0	0.99	0	0	0	0.98	0
EFA0041	0.98	0	0	0	0	0.98	1	0.42	0	0.05	0.41	0.99	0	0	0.88	0.88	0	0	0.99	0	0	0	0.99	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EFA0042	0.99	0.62	0.62	0.62	0	0.99	0.99	0.67	0	0	0.99	0.99	0.62	0	0.6	0.6	0	0.62	0.99	0.12	0	0.62	0.99	0.11
EFA0043	1	0	0	0	0	1	0.98	1	0	0	0.64	0.99	0	0	1	1	0	0	0.99	0	0	0	0.98	0
EFA0044	1	0	0	0	0	1	1	0.7	0	0	1	1	0	0	1	1	0	0	1	0	0	0	1	0
EFA0045	1	0.71	0	0	0	0.84	0.99	1	0	0	0.99	0.99	0	0	0.99	0.99	0.96	0	0	0	0	0	0.48	0
EFA0046	0.55	0.77	0.95	0.97	0	1	0.97	0.94	0	0	0.55	0.97	0.98	0	0.87	0.87	0.94	0.97	0.22	0	0	0.97	0.98	0.97
EFA0047	0.25	0.23	0.56	0.56	0.02	0.34	0.56	0.4	0.02	0.02	0.58	0.99	0.97	0	0.2	0.2	0.97	0.56	0.21	0.02	0.02	0.55	0.56	0.98
EFA0048	1	0.83	0	0.99	0	0	0	1	0.57	0	0.77	1	1	0	0.83	0.83	0	0	1	0	0	0	0.83	0.99
EFA0050	1	0.99	0	0	0	0	0	1	0	0	0	1	1	0	0.99	0.99	0	0.96	0.97	0	0	0	0	0.97
EFA0051	0.99	0.99	0	0	0	0	0	1	0	0	0	0.99	0.99	0	0.99	0.99	0	0.36	0.36	0	0	0	0.99	0.36
EFA0052	0.28	0.98	0.86	0.91	0	0	0	0.72	0.55	0	0	0.97	0.97	0	0.98	0.98	0.97	0.86	0.91	0	0	0	0.92	0.97
EFA0053	0.12	0.94	0.95	0.3	0	0	0	1	0.96	0	0	0.98	0.99	0	0.94	0.94	0.74	0.94	1	0	0	0	0.96	0.95
EFA0054	1	0	0	0	0	0	0	1	0	0	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0
EFA0056	1	1	0.81	0.76	1	0.98	0.99	0	0.99	0	0.86	1	1	0	0.82	0.8	0.76	0	0.4	0.99	0.76	0.82	0.76	0.76
EFA0057	0	0	0	0.72	0	1	0	0.66	0	0	0.67	0	0	0	0	0	0	0	0	0	0.67	0	0	0
EFA0058	0.09	0	0	0	0	1	0	0.98	0	0	0.93	0.28	0	0	0	0	0	0	0.53	0	0.23	0	0	0
EFA0059	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EFA0060	1	1	0	0	0	1	1	0	0	0	1	0	1	0	0	1	0	0	0.96	0	0	0	0	0
EFA0061	1	1	0	0	0	1	1	0	0	0	1	0	1	0	0	1	0	0	0.86	0	0	0	0	0
EFA0062	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EFA0063	1	1	0.81	0.76	1	0.98	0.99	0	0.99	0	0.86	1	1	0	0.82	0.8	0.76	0	0.4	0.99	0.76	0.82	0.76	0.76
EFA0065	1	1	1	0	0.28	0	0	0	0	0	1	0	1	0	1	1	0	0	0	0	0	0	0	0
EFA0066	1	1	1	0	0.35	0	0	0	0	0	1	0	1	0	1	1	0.38	0	0.37	0	0	0	0	0
EFA0067	1	1	1	0.11	0.11	0.11	0.11	0.11	0.12	0.12	1	0.11	1	0.11	0.79	1	0.11	0.12	0.11	0.12	0.11	0.12	0.11	0.11
EFA0069	1	1	1	0.4	0.4	0.4	0.4	0.4	0.4	0.4	1	0.4	1	0.4	1	1	0.4	0.4	0.39	0.4	0.4	0.4	0.4	0
EFA0070	1	1	1	0.55	0.55	0.55	0.55	0.55	0.55	0.55	1	0.55	1	0.55	1	1	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.1
EFA0071	1	1	1	0	0	0	0	0	0	0	1	0	1	0	1	1	0	0	0	0	0	0	0	0
EFA0072	1	1	1	0	0	0	0	0	0	0	1	0	1	0	1	1	0	0	0	0	0	0	0	0
EFA0073	0.49	0.17	0.94	0.97	0.97	0.97	0	0.9	0.96	0	0.9	0.97	0.9	0	0.9	0.9	0	0.91	0.95	0.93	0.97	0	0.97	0.97
EFA0074	0.84	0.98	0.89	0.98	0.98	0.98	0.44	0.72	0.96	0	0.92	0.98	0.92	0	0.92	0.92	0	0.96	0.97	0.17	0.98	0	0.98	0.98
EFA0075	1	0.98	0.77	0.95	0.95	0.95	0	0.87	0	0	0.96	0.83	0.96	0	0.96	0.96	0.7	0	0.92	0.79	0.95	0	0.95	0.99
EFA0076	1	1	0	0	0	0	0	1	0	0	0.97	0.97	0.97	0	0.97	0.97	0	0	0.97	0	0	0	0	1
EFA0078	1	0.7	0.71	0.99	0.7	0.7	0.7	0.54	0.71	0.7	0.99	0.98	0.7	0.7	0.99	0.99	0.71	0.72	0.98	0.72	1	0.7	0.7	0.99
EFA0079	1	0	0	0.98	0	0	0	1	0	0	0.99	0.98	0.99	0	0.99	0.99	0	0	0.99	0	1	0	0	0.98
EFA0080	1	0.68	0.45	0.99	0	0	0	1	0.36	0	0.97	0.97	0.99	0	0.97	0.97	0.35	0.45	0.97	0.35	1	0	0.58	0.99
EFA0081	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
EFA0082	1	1	0.99	0	0	0	0	1	0	0	0	1	0	0	0	0	0.99	0	0	0	0	0	0	0
EFA0083	1	1	0.99	0.49	0	0	0	1	0	0	0.49	1	0	0	0	0	0.99	0.04	0.59	0	0	0	0.59	0
EFB0001	0.96	0.57	0.37	0.7	0	0	0	0.73	0.38	0	0.72	0.38	1	0	0.96	0.96	0.38	0	0.99	0.38	0	0	0.71	0.7
EFB0003	0.99	0.19	0.42	0.57	0	0	0	0.64	0	0	0	0.57	1	0	0	0	0	0.98	0.98	0	0	0	0.64	0.56
EFB0004	0.8	0.62	0.7	0.68	0.44	0.44	0.44	0.68	0.62	0.44	0.69	0.67	0.99	0.44	0.69	0.69	0.62	0.99	0.99	0.62	0.54	0.44	0.69	0.68
EFB0005	0.99	0	0	0	0	0	0	0.11	0	0	0	0	0.99	0	0	0	0	0.99	0.99	0	0	0	0.11	0
EFB0005.1	0.99	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0
EFB0007	0.97	0.97	0.96	0.96	0	0	0	0.99	0.96	0	0	0.46	0.97	0	0.97	0.97	0.97	0.98	0.97	0	0	0	0.96	0.97
EFB0008	0.19	0.94	0.97	0	0	0	0	0.99	0.97	0	0	0.99	0.99	0	0.94	0.94	0.71	0.96	0.99	0	0	0	0.97	0.94
EFB0009	0	0.92	0.92	0.81	0	0	0	0.96	0.92	0	0	0.95	0.99	0	0.92	0.92	0.69	0.92	0.98	0	0	0	0.91	1
EFB0010	0.27	0.87	0.97	0.87	0	0	0	0.6	0.51	0	0	0.86	0.86	0	0.87	0.87	0.87	0.97	0.87	0	0	0	0.86	0.87
EFB0011	0.16	0.22	0.97	0.95	0	0.33	0.95	0.56	0	0	0.95	0.56	0.94	0	0.41	0.41	0.55	0.97	0.53	0	0	0.94	0.96	0.55
EFB0012	1	1	1	1	0	0.62	0.62	0.97	0	0	0.62	0.62	1	0	0.49	1	0	1	0.62	0	0	1	0.27	0.08
EFB0013	0.99	0.99	0.99	0.98	0	0	0	0.99	0	0	0	0	0.99	0	0	0.99	0	0.99	0	0	0	0.99	0	0
EFB0014	1	1	1	1	0	0	0	0.99	0	0	0	0	1	0	0	1	0	1	0	0	0	1	0	0
EFB0015	1	0.99	0.99	0.99	0	0	0	1	0	0	0	0	1	0	0	1	0	0.99	0	0	0	0.99	0	0
EFB0016	1	0.99	0.98	0.99	0	0	0	1	0	0	0	0	0.99	0	0	0.99	0	0.99	0	0	0	1	0	0
EFB0017	0.71	0.88	0.99	0.88	0	0	0	0.88	0	0	0	0	0.88	0	0	0.88	0	0.88	0	0	0	0.98	0	0

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EFB0018	0.98	0.91	0.98	0.98	0	0	0	0.98	0	0	0	0	0.98	0	0	0.98	0	0.98	0	0	0	0.98	0.67	0
EFB0019	0.99	0.99	0.99	0.99	0	0	0	0.99	0	0	0	0	0.99	0	0	0.99	0	0.99	0	0	0	0.99	0.31	0
EFB0020	0.98	0.98	0.99	0.98	0	0.04	0	0.99	0.04	0.04	0	0.04	0.94	0.04	0.05	0.94	0.04	0.98	0	0.04	0	0.98	0.08	0
EFB0021	0.99	0.95	1	0.99	0	0	0	0.99	0	0	0.84	0	0.99	0	0.99	0.99	0	0.99	0	0	0	1	0.07	0
EFB0022	0.99	0.98	0.99	1	0	0	0	1	0	0	0.98	0	1	0	1	1	0	0.98	0	0	0	1	0.99	0
EFB0023	0.95	0.98	0.99	0.98	0	0	0	0.99	0	0	0.98	0	0.97	0	0.97	0.97	0	0.98	0	0	0	0.99	0.66	0
EFB0024	0.83	0.98	0.98	0.99	0	0	0	1	0	0	0.98	0	0.99	0	0.99	0.99	0	0.98	0	0.56	0	1	0	0
EFB0025	0.99	0.99	0.99	0.98	0	0	0	0.98	0	0	0.98	0	0.96	0	0.96	0.96	0	1	0	0.23	0	0.95	0.13	0
EFB0026	0.99	0.99	0.99	0.98	0	0	0	0.99	0	0	0.99	0.05	0.98	0	0.98	0.98	0	0.99	0.05	0.98	0	0.98	0.1	0
EFB0027	0.99	0.97	0.99	0.98	0	0	0	0.99	0	0	0.99	0	0.99	0	0.99	0.99	0	0.98	0	0.98	0	0.98	0	0
EFB0029	0.56	1	1	1	0	0	0	0.95	0	0	1	0	0.96	0	0.96	0.96	0	0.99	0	0.96	0	0.95	0	0
EFB0030	0.5	0.99	0.89	0.88	0	0	0	0.88	0	0	0.88	0	0.88	0	0.88	0.88	0	0.98	0	0.88	0	0.88	0.13	0
EFB0031	0.78	0.98	0.82	0.82	0	0	0	0.81	0	0	0.82	0	0.82	0	0.82	0.82	0	0.82	0	0.8	0	0.81	0	0
EFB0032	1	0.46	1	0.98	0	0	0	0.64	0	0	0.99	0.62	0.99	0	0.99	0.99	0	0.99	0.73	0.99	0	0.99	0	0.73
EFB0033	0.8	0.8	0.92	0.91	0	0.28	0	0.8	0	0	0.92	0.8	0.58	0	0.8	0.8	0	0.93	0.86	0.92	0.89	0.67	0.89	0.86
EFB0034	0.9	0.92	0.92	0.78	0	0.58	0	0.92	0.39	0	0.79	0.92	0.66	0	0.92	0.92	0	0.8	0.8	0.8	0.79	0	0.78	0.78
EFB0035	0.98	0.09	0.98	0.97	0	0.09	0	0.07	0.09	0	0.99	0	0.83	0	0.99	0.99	0	1	0.99	0.98	0.09	0	0	0.98
EFB0036	0.99	0.92	0.99	0.99	0	0.92	0	0.93	0.91	0	0.99	0	0.67	0	0.99	0.99	0	1	0.99	0.98	0.92	0	0.93	0.98
EFB0037	0.99	0.73	0.99	0.99	0	0.74	0	0.74	0.73	0	0.99	0.69	0.69	0	0.74	0.74	0	0.99	0.99	0.99	0.73	0	0.74	0.99
EFB0038	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0.2	0	0	0
EFB0040	1	0.28	0.98	1	0	0	0	0.25	0	0	1	0.28	1	0	0.28	0.28	0	1	1	0.99	1	0	0	1
EFB0041	0.98	0	1	1	0	0	0	1	0	0	1	0	1	0	0	0	0	1	1	1	0.98	0	0	1
EFB0042	0.98	0	0.99	0.99	0	0	0	0.98	0	0	0.99	0	0.98	0	0	0	0	1	0.99	0	0.98	0	0	0.98
EFB0043	0.97	0.56	0.97	0.98	0.56	0.56	0.56	0.98	0.56	0.56	0.98	0.56	0.99	0.56	0.56	0.56	0.56	1	0.98	0.56	0.98	0.56	0.56	0.99
EFB0044	0.98	0	0.97	0.95	0	0.38	0	0.97	0	0	0.94	0	0.96	0	0	0	0	1	0.94	0	0.94	0	0	0.96
EFB0045	0.98	0.82	0.98	0.98	0	0.83	0.82	0.85	0.82	0	0.83	0	0.8	0	0.8	0.8	0	0.98	0.82	0	0.99	0	0.82	0.8
EFB0046	0.99	0	0.99	0.99	0	0	0	0.95	0	0	0.95	0	0	0	0	0	0	0.99	0.96	0	0.99	0.82	0	0
EFB0047	0.62	0.3	0.98	0.99	0.23	0.98	0.29	0.99	0.25	0.23	0.98	0.23	0.25	0.23	0.25	0.25	0.23	0.99	0.26	0.23	0.99	0.23	0.23	0.23
EFB0048	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFB0049	0	0.99	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFB0050	0	1	0	0	0	0	0	0	0.02	0	0	0	0	0	0	0	0	0	0	0.02	0	0	0	0
EFB0051	0.05	0.94	0	0	0	0.05	0	0	0	0	0.05	0.03	0.05	0	0.05	0.05	0	0	0.05	0	0	0	0	0
EFB0052	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EFB0053	0.1	0.88	0	0	0	0.1	0	0	0	0	0.1	0.1	0.1	0	0.1	0.1	0	0	0.11	0	0	0	0	0
EFB0054	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFB0055	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFB0056	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFB0057	0.52	1	0	0	0	0.52	0	0	0	0	0.99	0	0	0	0	0	0	0	0.99	0	1	0	0	0
EFB0058	0.66	0.63	0.28	0.14	0.14	0.11	0	0.66	0.44	0	0.83	0.63	0.1	0	0.63	0.63	0	0	0.63	0	0.74	0.28	0.74	0.14
EFB0059	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFB0060	0.93	0.7	0.93	0.7	0.7	0.7	0.7	0.93	0.95	0.7	0.97	0.71	0.7	0.7	0.71	0.71	0.96	0.91	0.93	0.92	0.93	0.7	0.7	0.7
EFB0061	0.78	0.73	0.79	0.49	0.5	0.5	0.49	0.79	0.87	0.49	0.89	0.49	0.49	0.49	0.73	0.73	0.85	0.78	0.49	0.87	0.78	0.49	0.75	0.56
EFB0062	0.61	0.73	0.61	0.4	0	0	0	0.61	0.68	0	0.38	0.38	0.4	0	0.73	0.73	0.7	0.61	0.51	0.69	0.61	0	0.73	0.4
EFB0063	0.97	0.6	0.9	0.87	0	0.43	0	0.95	0.96	0	0.95	0.95	0.95	0	0.46	0.46	0.94	0	0.98	0.94	0.48	0	0.95	0.87
EFB0064	1	1	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	1	0.11	1	1	0.11	0.11	0.99	0.11	0.11	0.11	0.11	0.11
EFB0065	0.99	0.99	0	0	0.14	0	0	0	0	0	0	0	1	0	0.99	0.99	0	0	0.99	0	0.14	0.14	0.14	0
EFC0001	0.53	0.6	0.96	0.68	0.44	0.44	0.44	0.93	0.6	0.45	0.92	0.69	0.92	0.44	0.92	0.92	0.6	0.66	0.93	0.6	0.96	0.45	0.92	0.68
EFC0002	1	1	0.81	0.76	0.99	0.98	0.99	0	0.99	0	0.85	1	0.99	0	0.82	0.8	0.76	0	0.4	0.99	0.76	0.82	0.76	0.76
EFC0003	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFC0004	1	0.29	0	0	0	1	0	0	0	0	1	0.8	1	0	0.83	0.86	0	0	1	0	0	0	0	0
EFC0005	0	0	0	0	0	0	0	0	0	0	1	0.71	0	0	0	0	0	0	0	0	0	0	0	0
EFC0006	0.52	0.04	0.53	0.5	0.03	0	0.04	0.53	0.53	0	0.96	0.96	0.04	0	0.5	0.5	0.53	0.53	0.52	0.52	0.52	0	0	0.5
EFC0007	1	1	0.81	0.76	1	0.98	0.99	0	0.99	0	0.86	1	1	0	0.82	0.8	0.76	0	0.4	0.99	0.76	0.82	0.76	0.76

ID	HH22	TX0104	ARO1DG	ATCC29200	ATCC4200	CH188	D6	DS5	E1Sol	Fly1	HIP11704	JH1	Merz96	OG1RF	R712	S613	T1	T11	T2	T3	T8	TUSoD	TX1322	X98
EFC0008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EFC0009	0.49	0.17	0.94	0.97	0.97	0.97	0	0.9	0.96	0	0.9	0.96	0.9	0	0.9	0.9	0	0.9	0.95	0.92	0.97	0	0.97	0.97
EFC0010	0.84	0.95	0.88	0.96	0.96	0.96	0.45	0.72	0.94	0	0.9	0.96	0.9	0	0.9	0.9	0	0.94	0.96	0.15	0.96	0	0.96	0.96
EFC0011	1	0.47	0.7	0.48	0.47	0.47	0	0	0	0	0.47	0.47	0.47	0	0.47	0.47	0	0.47	0.89	0.43	1	0	0.98	0.47
EFC0012	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.97	0	1	0	0.98	0
EFC0013	1	0	0.97	0	0	0	0	1	0.92	0	0	0	0	0	0	0	0.99	0	0.99	0.99	1	0	0	0
EFC0014	1	0	0.98	0	0	0	0	0.98	0.98	0	0	0	0	0	0	0	0.98	0.12	1	0.98	1	0	0	0
EFC0015	1	0.7	0.95	0.71	0.7	0.7	0.7	0.97	0.92	0.7	0.91	0.71	0.7	0.7	0.71	0.71	0.93	0.95	0.95	0.95	1	0.7	0.7	0.71
EFC0016	1	0.72	0.98	0.48	0.49	0.49	0.48	0.97	0.85	0.48	0.88	0.48	0.48	0.48	0.72	0.72	0.87	0.98	0.48	0.85	1	0.48	0.75	0.53
EFC0017	1	0	1	0	0	0	0	0.99	0	0	0.98	0	0	0	0	0	0	0.99	0	0	1	0	0	0
EFC0018	1	0	1	0.14	0	0	0	1	0.11	0	0.14	0	0	0	0	0	0	0.99	0.12	0.11	1	0	0	0
EFC0019	1	0	0.96	0	0	0.43	0	0.96	0	0	0.21	0	0	0	0	0	0	0.97	0.95	0	1	0	0	0

Table S2: PCR screening. Strains in bold were analyzed by comparative genomic hybridization in the present study. A = animal, C = clinical, CC = clonal complex, CS = community surveillance, DEN = Denmark, DEU = Germany, ESP = Spain, FIN = Finland, F = food, GRE = Greece, HS = hospital surveillance. HUN = Hungary, NED = The Netherlands, NOR = Norway, POL = Poland, ST = sequence type.

Strain	Country	ST	CC	Junction EF1415-EF1417	Junction EF1489-EF1490	Junction EF1843-EF1847	Junction EF1895-EF1898	Junction EF2239-EF2240	Junction EF2350-EF2352	EF3217	EF3218	EF3220	EF3221	EF3222	EF3223	EF3224	EF3225	EF3226	EF3227	Hmpref 0346_1861	Hmpref 0346_1864	Hmpref 0346_1868	Junction hmpref0346_1861hmpref0346_1868
V583	USA	6	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-
E1828	ESP	6	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
442/05	POL	6	6	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
609/96	POL	6	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
368-42	NOR	6	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
372-56	NOR	6	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
MMH594	USA	6	6	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-
226B	NOR	6	6	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-
158B	NOR	6	6	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-
LMGT3303		6	6	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E1834	ESP	51	6	-	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
E4250	NED	183	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
E1841	ESP	9	9	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-
Vet179	NOR	9	9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E1807	ESP	17	9	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
OG1RF	USA	1	21	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
E1960	ESP	8	21	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2426/03	POL	21	21	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LMGT3406	DEN	22	21	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
111A	NOR	161	21	-	-	+	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
3339/04	POL	23	25	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
UC11/46	FIN	97	25	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
189	NOR	162	25	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Symbioflor 1	DEU	248	25	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
E1188	GRE	28	28	-	-	-	+	+	+	-	-	-	-	-	-	-	+	-	-	+	-	-	-
383/04	POL	87	28	-	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
85	NOR	30	30	-	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-
E1052	NED	30	30	-	-	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
597/96	POL	40	40	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
LMGT3209	GRE	40	40	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LMGT2333	ESP	40	40	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-
1645	DEN	220	40	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
29C	NOR	44	44	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
E2370	HUN	16	58	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-
105	NOR	16	58	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
LMGT3405	DEN	116	116	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	+	+	+
Vet138	NOR	164	119	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-
LMGT3407	DEN	34	121	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
LMGT3143	ESP	165	165	-	-	-	-	-	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-
82	NOR	65	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	+
62	NOR	66	S	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
266	NOR	163	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-
LMGT3208	GRE	166	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
84	NOR	249	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table S3: Enrichment analysis of CC6 non-V583 genes by Fisher's exact test.

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq1318_GID19_HMPREF0348_0424	2	0	0	0.01	0,325	hypothetical protein	HMPREF0346_1868	-
seq1319_GID19_HMPREF0348_0425	2	0	0	0.01	0,325	conserved hypothetical protein	HMPREF0346_1867	-
seq1320_GID19_HMPREF0348_0426	2	0	0	0.01	0,325	conserved hypothetical protein	HMPREF0346_1864 - HMPREF0346_1866	-
seq1323_GID19_HMPREF0348_0429	2	0	0	0.01	0,325	conserved hypothetical protein	HMPREF0346_1862	-
seq1324_GID19_HMPREF0348_0430	2	0	0	0.01	0,325	major facilitator superfamily permease	HMPREF0346_1861	-
seq1322_GID19_HMPREF0348_0428	2	1	0,035	0,029	0,325	mucin-binding domain protein	HMPREF0346_1863	-
seq1321_GID19_HMPREF0348_0427	2	2	0,063	0,057	0,325	mucin-binding domain protein	HMPREF0346_1863	-
seq1296_GID19_HMPREF0348_0402	2	3	0,093	0,091	0,325	conserved hypothetical protein	HMPREF0346_3112	-
seq416_GID9_HMPREF0346_0400	1	0	0	0.12	0,325	-	-	hypothetical protein
seq449_GID9_HMPREF0346_0432	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq471_GID9_HMPREF0346_0453	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq472_GID9_HMPREF0346_0454	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq2533_GID9_HMPREF0346_2970	1	0	0	0.12	0,325	-	-	hypothetical protein
seq2534_GID9_HMPREF0346_2971	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq2535_GID9_HMPREF0346_2972	1	0	0	0.12	0,325	-	-	ATP-binding protein
seq2536_GID9_HMPREF0346_2973	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq2538_GID9_HMPREF0346_2975	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq2539_GID9_HMPREF0346_2976	1	0	0	0.12	0,325	-	-	replication initiation protein
seq2542_GID9_HMPREF0346_2979	1	0	0	0.12	0,325	-	-	hypothetical protein
seq2543_GID9_HMPREF0346_2980	1	0	0	0.12	0,325	-	-	transcriptional regulator
seq2545_GID9_HMPREF0346_2982	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq2789_GID9_HMPREF0346_3163	1	0	0	0.12	0,325	-	-	transcriptional regulator PadR family protein
seq2790_GID9_HMPREF0346_3164	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq2799_GID9_HMPREF0346_3173	1	0	0	0.12	0,325	-	-	partitioning protein
seq2800_GID9_HMPREF0346_3174	1	0	0	0.12	0,325	-	-	replication initiator protein A
seq2801_GID9_HMPREF0346_3175	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq2802_GID9_HMPREF0346_3176	1	0	0	0.12	0,325	-	-	conserved hypothetical protein

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq2803_GID9_HMPREF0346_3177	1	0	0	0.12	0,325	-	-	nickase TraA
seq2804_GID9_HMPREF0346_3178	1	0	0	0.12	0,325	-	-	conserved hypothetical protein
seq2809_GID9_HMPREF0346_3183	1	0	0	0.12	0,325	-	-	possible beta-lactamase regulator BlaR
seq3068_GID9_HMPREF0346_1863	1	0	0	0.12	0,325	-	-	mucin-binding domain protein
seq795_GID19_HMPREF0348_2414	1	0	0	0.12	0,325	hypothetical protein	-	-
seq796_GID19_HMPREF0348_2415	1	0	0	0.12	0,325	hypothetical protein	-	-
seq970_GID19_HMPREF0348_2587	1	0	0	0.12	0,325	integrase family protein	-	-
seq971_GID19_HMPREF0348_2588	1	0	0	0.12	0,325	hypothetical protein	-	-
seq972_GID19_HMPREF0348_2589	1	0	0	0.12	0,325	hypothetical protein	-	-
seq973_GID19_HMPREF0348_2590	1	0	0	0.12	0,325	protein of hypothetical function DUF955	-	-
seq975_GID19_HMPREF0348_2592	1	0	0	0.12	0,325	hypothetical protein	-	-
seq976_GID19_HMPREF0348_2593	1	0	0	0.12	0,325	hypothetical protein	-	-
seq995_GID19_HMPREF0348_2612	1	0	0	0.12	0,325	SPP1 family phage portal protein	-	-
seq1002_GID19_HMPREF0348_2619	1	0	0	0.12	0,325	phage minor head protein	-	-
seq1003_GID19_HMPREF0348_2620	1	0	0	0.12	0,325	phage scaffold protein	-	-
seq1004_GID19_HMPREF0348_2621	1	0	0	0.12	0,325	phage scaffold protein	-	-
seq1005_GID19_HMPREF0348_2622	1	0	0	0.12	0,325	phage protein	-	-
seq1006_GID19_HMPREF0348_2623	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1007_GID19_HMPREF0348_2624	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1008_GID19_HMPREF0348_2625	1	0	0	0.12	0,325	phage protein	-	-
seq1009_GID19_HMPREF0348_2626	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1010_GID19_HMPREF0348_2627	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1011_GID19_HMPREF0348_2628	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1012_GID19_HMPREF0348_2629	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1013_GID19_HMPREF0348_2630	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1014_GID19_HMPREF0348_2631	1	0	0	0.12	0,325	tail protein	-	-
seq1015_GID19_HMPREF0348_2632	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1016_GID19_HMPREF0348_2633	1	0	0	0.12	0,325	possible reticulocyte binding protein	-	-

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq1017_GID19_HMPREF0348_2634	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1018_GID19_HMPREF0348_2635	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1020_GID19_HMPREF0348_2637	1	0	0	0.12	0,325	phi11 family holin	-	-
seq1021_GID19_HMPREF0348_2638	1	0	0	0.12	0,325	possible N-acetylmuramoyl-L-alanine amidase	-	-
seq1022_GID19_HMPREF0348_2639	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1024_GID19_HMPREF0348_2640	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1025_GID19_HMPREF0348_2641	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1297_GID19_HMPREF0348_0403	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1298_GID19_HMPREF0348_0404	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1348_GID19_HMPREF0348_0454	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1349_GID19_HMPREF0348_0455	1	0	0	0.12	0,325	transposase	-	-
seq1351_GID19_HMPREF0348_0457	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1358_GID19_HMPREF0348_0464	1	0	0	0.12	0,325	RNA-directed DNA polymerase	-	-
seq1359_GID19_HMPREF0348_0465	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1361_GID19_HMPREF0348_0467	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1364_GID19_HMPREF0348_0470	1	0	0	0.12	0,325	LtrC family protein	-	-
seq1365_GID19_HMPREF0348_0471	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1366_GID19_HMPREF0348_0472	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1367_GID19_HMPREF0348_0473	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1368_GID19_HMPREF0348_0474	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1370_GID19_HMPREF0348_0476	1	0	0	0.12	0,325	mobilization protein	-	-
seq1371_GID19_HMPREF0348_0477	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1372_GID19_HMPREF0348_0478	1	0	0	0.12	0,325	transposase	-	-
seq1373_GID19_HMPREF0348_0479	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1383_GID19_HMPREF0348_0489	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1384_GID19_HMPREF0348_0490	1	0	0	0.12	0,325	conserved hypothetical protein	-	-

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq1385_GID19_HMPREF0348_0491	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1386_GID19_HMPREF0348_0492	1	0	0	0.12	0,325	excisionase	-	-
seq1387_GID19_HMPREF0348_0493	1	0	0	0.12	0,325	integrase	-	-
seq1620_GID19_HMPREF0348_0725	1	0	0	0.12	0,325	positive regulatory protein Mga	-	-
seq1621_GID19_HMPREF0348_0726	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1622_GID19_HMPREF0348_0727	1	0	0	0.12	0,325	possible response regulator	-	-
seq1624_GID19_HMPREF0348_0729	1	0	0	0.12	0,325	WxL domain surface protein	-	-
seq1625_GID19_HMPREF0348_0730	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1858_GID19_HMPREF0348_0134	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1859_GID19_HMPREF0348_0135	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq1860_GID19_HMPREF0348_0136	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1886_GID19_HMPREF0348_0162	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1887_GID19_HMPREF0348_0163	1	0	0	0.12	0,325	hypothetical protein	-	-
seq1888_GID19_HMPREF0348_0164	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq2057_GID19_HMPREF0348_0333	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq2058_GID19_HMPREF0348_0334	1	0	0	0.12	0,325	ABC superfamily ATP binding cassette transporter permease protein	-	-
seq2060_GID19_HMPREF0348_0336	1	0	0	0.12	0,325	hypothetical protein	-	-
seq2081_GID19_HMPREF0348_0357	1	0	0	0.12	0,325	type I site-specific deoxyribonuclease specificity subunit	-	-
seq2084_GID19_HMPREF0348_0360	1	0	0	0.12	0,325	type I site-specific deoxyribonuclease specificity subunit	-	-
seq2114_GID19_HMPREF0348_0791	1	0	0	0.12	0,325	hypothetical protein	-	-
seq2115_GID19_HMPREF0348_0792	1	0	0	0.12	0,325	hypothetical protein	-	-
seq2285_GID19_HMPREF0348_0986	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq2578_GID19_HMPREF0348_2164	1	0	0	0.12	0,325	AraC family transcriptional regulator	-	-
seq2579_GID19_HMPREF0348_2165	1	0	0	0.12	0,325	conserved hypothetical protein	-	-

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq2580_GID19_HMPREF0348_2166	1	0	0	0.12	0,325	RADC family protein	-	-
seq2893_GID19_HMPREF0348_3128	1	0	0	0.12	0,325	hypothetical protein	-	-
seq3186_GID19_HMPREF0348_2913	1	0	0	0.12	0,325	trimethoprim resistant dihydrofolate reductase	-	-
seq3189_GID19_HMPREF0348_2916	1	0	0	0.12	0,325	conserved hypothetical protein	-	-
seq3313_GID19_HMPREF0348_2899	1	0	0	0.12	0,325	hypothetical protein	-	-
seq2612_GID19_HMPREF0348_1256	1	18	7,965	0,133	0,347	PemK family growth inhibitor	-	-
seq2613_GID19_HMPREF0348_1257	1	18	7,965	0,133	0,347	antitoxin MazE	-	-
seq2534_GID19_HMPREF0348_3050	2	4	0,126	0,133	0,347	TRAA protein	HMPREF0346_3129	-
seq2619_GID19_HMPREF0348_1263	2	4	0,126	0,133	0,347	conserved hypothetical protein	HMPREF0346_3165	-
seq2593_GID19_HMPREF0348_1237	2	5	0,162	0,180	0,436	possible bacitracin ABC ATP binding cassette transporter, membrane protein	HMPREF0346_1888	-
seq2594_GID19_HMPREF0348_1238	2	5	0,162	0,180	0,436	bacitracin ABC ATP binding cassette transporter, ABC protein	HMPREF0346_1889	-
seq2595_GID19_HMPREF0348_1239	2	5	0,162	0,180	0,436	transcriptional regulator	HMPREF0346_1890	-
seq2596_GID19_HMPREF0348_1240	2	5	0,162	0,180	0,436	transposase and inactivated derivative	HMPREF0346_1891	-
seq2597_GID19_HMPREF0348_1241	2	5	0,162	0,180	0,436	conserved hypothetical protein	HMPREF0346_1892	-
seq418_GID9_HMPREF0346_0402	1	1	0,114	0,230	0,436	-	-	methyltransferase
seq422_GID9_HMPREF0346_0406	1	1	0,114	0,230	0,436	-	-	conserved hypothetical protein
seq2643_GID9_HMPREF0346_3119	1	1	0,114	0,230	0,436	-	-	hypothetical protein
seq2667_GID9_HMPREF0346_2732	1	1	0,114	0,230	0,436	-	-	hypothetical protein
seq2691_GID9_HMPREF0346_2755	1	1	0,114	0,230	0,436	-	-	hypothetical protein
seq2805_GID9_HMPREF0346_3179	1	1	0,114	0,230	0,436	-	-	hypothetical protein
seq2806_GID9_HMPREF0346_3180	1	1	0,114	0,230	0,436	-	-	conserved hypothetical protein
seq2807_GID9_HMPREF0346_3181	1	1	0,114	0,230	0,436	-	-	conserved hypothetical protein
seq2808_GID9_HMPREF0346_3182	1	1	0,114	0,230	0,436	-	-	beta-lactamase
seq888_GID19_HMPREF0348_2507	1	1	0,114	0,230	0,436	conserved hypothetical protein	-	-
seq891_GID19_HMPREF0348_2510	1	1	0,114	0,230	0,436	hypothetical protein	-	-
seq911_GID19_HMPREF0348_2530	1	1	0,114	0,230	0,436	conserved hypothetical protein	-	-

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq912_GID19_HMPREF0348_2531	1	1	0,114	0,230	0,436	possible bacteriophage integrase	-	-
seq921_GID19_HMPREF0348_2539	1	1	0,114	0,230	0,436	phage-like protein	-	-
seq922_GID19_HMPREF0348_2540	1	1	0,114	0,230	0,436	terminase large subunit	-	-
seq925_GID19_HMPREF0348_2543	1	1	0,114	0,230	0,436	bacteriophage portal protein	-	-
seq926_GID19_HMPREF0348_2544	1	1	0,114	0,230	0,436	Clp protease	-	-
seq927_GID19_HMPREF0348_2545	1	1	0,114	0,230	0,436	major capsid protein	-	-
seq928_GID19_HMPREF0348_2546	1	1	0,114	0,230	0,436	conserved hypothetical protein	-	-
seq945_GID19_HMPREF0348_2563	1	1	0,114	0,230	0,436	prophage protein (ps3)	-	-
seq946_GID19_HMPREF0348_2564	1	1	0,114	0,230	0,436	conserved hypothetical protein	-	-
seq984_GID19_HMPREF0348_2601	1	1	0,114	0,230	0,436	hypothetical protein	-	-
seq993_GID19_HMPREF0348_2610	1	1	0,114	0,230	0,436	hypothetical protein	-	-
seq1144_GID19_HMPREF0348_2759	1	1	0,114	0,230	0,436	hypothetical protein	-	-
seq1166_GID19_HMPREF0348_2781	1	1	0,114	0,230	0,436	hypothetical protein	-	-
seq1929_GID19_HMPREF0348_0205	1	1	0,114	0,230	0,436	possible N(pi)-phosphohistidine--sugar phosphotransferase	-	-
seq1931_GID19_HMPREF0348_0207	1	1	0,114	0,230	0,436	PTS family lactose-N,N'-diacetylchitobiose-beta-glucoside (lac) porter component IIA	-	-
seq1985_GID19_HMPREF0348_0261	1	1	0,114	0,230	0,436	response regulator	-	-
seq1986_GID19_HMPREF0348_0262	1	1	0,114	0,230	0,436	hypothetical protein	-	-
seq1987_GID19_HMPREF0348_0263	1	1	0,114	0,230	0,436	ABC superfamily ATP binding cassette transporter, ABC protein	-	-
seq1988_GID19_HMPREF0348_0264	1	1	0,114	0,230	0,436	ABC superfamily ATP binding cassette transporter permease protein	-	-
seq2193_GID19_HMPREF0348_0870	1	1	0,114	0,230	0,436	conserved hypothetical protein	-	-
seq2194_GID19_HMPREF0348_0871	1	1	0,114	0,230	0,436	radical SAM domain protein protein	-	-
seq2195_GID19_HMPREF0348_0872	1	1	0,114	0,230	0,436	hypothetical protein	-	-
seq2575_GID19_HMPREF0348_2161	1	1	0,114	0,230	0,436	accessory protein family protein	-	-
seq2891_GID19_HMPREF0348_3126	1	1	0,114	0,230	0,436	hypothetical protein	-	-

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq988_GID19_HMPREF0348_2605	1	16	4,935	0,231	0,436	DNA binding protein	-	-
seq2531_GID19_HMPREF0348_3047	2	6	0,203	0,231	0,436	membrane-bound protease CAAX family protein	HMPREF0346_3127	-
seq2621_GID19_HMPREF0348_1265	2	6	0,203	0,231	0,436	possible type I topoisomerase	HMPREF0346_3167	-
seq2797_GID9_HMPREF0346_3171	1	2	0,221	0,330	0,547	-	-	epsilon-zeta postsegregational killing system toxin protein
seq896_GID19_HMPREF0348_2515	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq897_GID19_HMPREF0348_2516	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq919_GID19_HMPREF0348_2537	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq920_GID19_HMPREF0348_2538	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq924_GID19_HMPREF0348_2542	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq948_GID19_HMPREF0348_2565	1	2	0,221	0,330	0,547	domain of hypothetical function DUF1828	-	-
seq949_GID19_HMPREF0348_2566	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2063_GID19_HMPREF0348_0339	1	2	0,221	0,330	0,547	conserved hypothetical protein	-	-
seq2295_GID19_HMPREF0348_0996	1	2	0,221	0,330	0,547	conserved hypothetical protein	-	-
seq2296_GID19_HMPREF0348_0997	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2298_GID19_HMPREF0348_0999	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2299_GID19_HMPREF0348_1000	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2572_GID19_HMPREF0348_2158	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2573_GID19_HMPREF0348_2159	1	2	0,221	0,330	0,547	possible nisin resistance protein	-	-
seq2601_GID19_HMPREF0348_1245	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2602_GID19_HMPREF0348_1246	1	2	0,221	0,330	0,547	cell surface protein	-	-
seq2603_GID19_HMPREF0348_1247	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2604_GID19_HMPREF0348_1248	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2605_GID19_HMPREF0348_1249	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2607_GID19_HMPREF0348_1251	1	2	0,221	0,330	0,547	hypothetical protein	-	-
seq2617_GID19_HMPREF0348_1261	1	2	0,221	0,330	0,547	transposase	-	-
seq421_GID9_HMPREF0346_0405	1	3	0,336	0,422	0,648	-	-	hypothetical protein
seq2688_GID9_HMPREF0346_2752	1	3	0,336	0,422	0,648	-	-	possible transposase
seq2689_GID9_HMPREF0346_2753	1	3	0,336	0,422	0,648	-	-	possible transposase
seq2690_GID9_HMPREF0346_2754	1	3	0,336	0,422	0,648	-	-	transposase

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq893_GID19_HMPREF0348_2512	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq894_GID19_HMPREF0348_2513	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq898_GID19_HMPREF0348_2517	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq900_GID19_HMPREF0348_2519	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq916_GID19_HMPREF0348_2534	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq934_GID19_HMPREF0348_2552	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq1190_GID19_HMPREF0348_2805	1	3	0,336	0,422	0,648	glycerophosphodiester phosphodiesterase	-	-
seq1974_GID19_HMPREF0348_0250	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq2046_GID19_HMPREF0348_0322	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq2876_GID19_HMPREF0348_1153	1	3	0,336	0,422	0,648	hypothetical protein	-	-
seq2685_GID9_HMPREF0346_2749	1	4	0,462	0,504	0,680	-	-	ipoprotein
seq2686_GID9_HMPREF0346_2750	1	4	0,462	0,504	0,680	-	-	hypothetical protein
seq2687_GID9_HMPREF0346_2751	1	4	0,462	0,504	0,680	-	-	possible multidrug resistance protein 1
seq2693_GID9_HMPREF0346_2757	1	4	0,462	0,504	0,680	-	-	conserved hypothetical protein
seq2694_GID9_HMPREF0346_2758	1	4	0,462	0,504	0,680	-	-	hypothetical protein
seq887_GID19_HMPREF0348_2506	1	4	0,462	0,504	0,680	cassette chromosome recombinase B	-	-
seq892_GID19_HMPREF0348_2511	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq895_GID19_HMPREF0348_2514	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq899_GID19_HMPREF0348_2518	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq902_GID19_HMPREF0348_2521	1	4	0,462	0,504	0,680	conserved hypothetical protein	-	-
seq903_GID19_HMPREF0348_2522	1	4	0,462	0,504	0,680	phage protein	-	-
seq904_GID19_HMPREF0348_2523	1	4	0,462	0,504	0,680	phage protein	-	-
seq905_GID19_HMPREF0348_2524	1	4	0,462	0,504	0,680	conserved hypothetical protein	-	-
seq906_GID19_HMPREF0348_2525	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq907_GID19_HMPREF0348_2526	1	4	0,462	0,504	0,680	conserved hypothetical protein	-	-
seq908_GID19_HMPREF0348_2527	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq909_GID19_HMPREF0348_2528	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq910_GID19_HMPREF0348_2529	1	4	0,462	0,504	0,680	DNA binding protein	-	-
seq1522_GID19_HMPREF0348_0627	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq1523_GID19_HMPREF0348_0628	1	4	0,462	0,504	0,680	possible peptide-transporting ATPase	-	-

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq1524_GID19_HMPREF0348_0629	1	4	0,462	0,504	0,680	radical SAM domain protein	-	-
seq1525_GID19_HMPREF0348_0630	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq1526_GID19_HMPREF0348_0631	1	4	0,462	0,504	0,680	DNA repair exonuclease family protein	-	-
seq2581_GID19_HMPREF0348_2167	1	4	0,462	0,504	0,680	conserved hypothetical protein	-	-
seq2610_GID19_HMPREF0348_1254	1	4	0,462	0,504	0,680	cell division protein	-	-
seq2611_GID19_HMPREF0348_1255	1	4	0,462	0,504	0,680	hypothetical protein	-	-
seq2877_GID19_HMPREF0348_1154	1	4	0,462	0,504	0,680	conserved hypothetical protein	-	-
seq1954_GID19_HMPREF0348_0230	1	15	4,021	0,530	0,712	hypothetical protein	-	-
seq2568_GID19_HMPREF0348_2154	2	9	0,361	0,565	0,738	conserved hypothetical protein	HMPREF0346_3096	-
seq2569_GID19_HMPREF0348_2155	2	9	0,361	0,565	0,738	conserved hypothetical protein	HMPREF0346_3097	-
seq2570_GID19_HMPREF0348_2156	2	9	0,361	0,565	0,738	conserved hypothetical protein	HMPREF0346_3098	-
seq3174_GID9_HMPREF0346_1494	1	13	2,768	0,565	0,738	-	-	tetracycline resistance protein Tet (M)
seq787_GID19_HMPREF0348_2406	1	13	2,768	0,565	0,738	membrane protein	-	-
seq2083_GID19_HMPREF0348_0359	1	13	2,768	0,565	0,738	bacteriophage integrase	-	-
seq2794_GID9_HMPREF0346_3168	1	10	1,634	1	1,000	-	-	ATPase for chromosome partitioning
seq2796_GID9_HMPREF0346_3170	1	10	1,634	1	1,000	-	-	lon-zeta postsegregational killing system antidote protein
seq3177_GID9_HMPREF0346_1497	1	10	1,634	1	1,000	-	-	conserved hypothetical protein
seq3180_GID9_HMPREF0346_1500	1	10	1,634	1	1,000	-	-	hypothetical protein
seq3181_GID9_HMPREF0346_1501	1	10	1,634	1	1,000	-	-	Chain A, Excisionase (Xis) protein
seq3182_GID9_HMPREF0346_1502	1	10	1,634	1	1,000	-	-	phage integrase family site-specific recombinase
seq2191_GID19_HMPREF0348_0868	1	10	1,634	1	1,000	ABC superfamily ATP binding cassette transporter, ABC protein	-	-
seq2192_GID19_HMPREF0348_0869	1	10	1,634	1	1,000	possible membrane-embedded metalloprotease	-	-
seq2793_GID9_HMPREF0346_3167	1	5	0,602	1	1,000	-	-	possible DNA topoisomerase
seq423_GID9_HMPREF0346_0407	1	6	0,759	1	1,000	-	-	hypothetical protein
seq2695_GID9_HMPREF0346_2759	1	6	0,759	1	1,000	-	-	PcfW protein
seq2795_GID9_HMPREF0346_3169	1	11	1,947	1	1,000	-	-	transcriptional repressor

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq3076_GID9_HMPREF0346_1871	1	8	1,137	1	1,000	-	-	hypothetical protein
seq3077_GID9_HMPREF0346_1872	1	8	1,137	1	1,000	-	-	hypothetical protein
seq3120_GID9_HMPREF0346_3100	1	6	0,759	1	1,000	-	-	hypothetical protein
seq3175_GID9_HMPREF0346_1495	1	11	1,947	1	1,000	-	-	conserved hypothetical protein
seq3176_GID9_HMPREF0346_1496	1	11	1,947	1	1,000	-	-	Tn916, transcriptional regulator
seq3178_GID9_HMPREF0346_1498	1	11	1,947	1	1,000	-	-	conjugative transposon regulatory protein
seq3179_GID9_HMPREF0346_1499	1	11	1,947	1	1,000	-	-	jugative transposon protein
seq172_GID19_HMPREF0348_1453	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq930_GID19_HMPREF0348_2548	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2614_GID19_HMPREF0348_1258	1	5	0,602	1	1,000	cell division protein	-	-
seq2616_GID19_HMPREF0348_1260	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2622_GID19_HMPREF0348_1266	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2623_GID19_HMPREF0348_1267	1	5	0,602	1	1,000	possible DNA recombinase	-	-
seq2624_GID19_HMPREF0348_1268	1	5	0,602	1	1,000	possible DNA recombinase	-	-
seq2625_GID19_HMPREF0348_1269	1	5	0,602	1	1,000	recombinase	-	-
seq2626_GID19_HMPREF0348_1270	1	5	0,602	1	1,000	DNA recombinase	-	-
seq2664_GID19_HMPREF0348_2052	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2665_GID19_HMPREF0348_2053	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2868_GID19_HMPREF0348_1145	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2869_GID19_HMPREF0348_1146	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2870_GID19_HMPREF0348_1147	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2871_GID19_HMPREF0348_1148	1	5	0,602	1	1,000	conserved hypothetical protein	-	-
seq2872_GID19_HMPREF0348_1149	1	5	0,602	1	1,000	DNA nuclease	-	-
seq168_GID19_HMPREF0348_1449	1	6	0,759	1	1,000	WxL domain surface protein	-	-
seq169_GID19_HMPREF0348_1450	1	6	0,759	1	1,000	cell surface protein	-	-
seq170_GID19_HMPREF0348_1451	1	6	0,759	1	1,000	hypothetical protein	-	-
seq171_GID19_HMPREF0348_1452	1	6	0,759	1	1,000	conserved hypothetical protein	-	-

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq174_GID19_HMPREF0348_1455	1	6	0,759	1	1,000	hypothetical protein	-	-
seq917_GID19_HMPREF0348_2535	1	6	0,759	1	1,000	hypothetical protein	-	-
seq918_GID19_HMPREF0348_2536	1	6	0,759	1	1,000	endonuclease	-	-
seq923_GID19_HMPREF0348_2541	1	6	0,759	1	1,000	hypothetical protein	-	-
seq929_GID19_HMPREF0348_2547	1	6	0,759	1	1,000	gp8 family protein	-	-
seq931_GID19_HMPREF0348_2549	1	6	0,759	1	1,000	gp10 family protein	-	-
seq932_GID19_HMPREF0348_2550	1	6	0,759	1	1,000	major tail protein	-	-
seq935_GID19_HMPREF0348_2553	1	6	0,759	1	1,000	hypothetical protein	-	-
seq937_GID19_HMPREF0348_2555	1	6	0,759	1	1,000	tail protein	-	-
seq981_GID19_HMPREF0348_2598	1	8	1,137	1	1,000	hypothetical protein	-	-
seq985_GID19_HMPREF0348_2602	1	8	1,137	1	1,000	endonuclease	-	-
seq986_GID19_HMPREF0348_2603	1	8	1,137	1	1,000	recT protein	-	-
seq1857_GID19_HMPREF0348_0133	1	7	0,936	1	1,000	conserved hypothetical protein	-	-
seq2070_GID19_HMPREF0348_0346	1	7	0,936	1	1,000	mrr restriction system protein	-	-
seq2080_GID19_HMPREF0348_0356	1	7	0,936	1	1,000	possible site-specific DNA-methyltransferase (adenine-specific)	-	-
seq2082_GID19_HMPREF0348_0358	1	6	0,759	1	1,000	conserved hypothetical protein	-	-
seq2085_GID19_HMPREF0348_0361	1	7	0,936	1	1,000	type I site-specific deoxyribonuclease restriction subunit	-	-
seq2524_GID19_HMPREF0348_3040	1	6	0,759	1	1,000	transposase	-	-
seq2576_GID19_HMPREF0348_2162	2	14	0,880	1	1,000	transposase	HMPREF0346_2724	-
seq2577_GID19_HMPREF0348_2163	1	7	0,936	1	1,000	transposase	-	-
seq2582_GID19_HMPREF0348_2168	1	7	0,936	1	1,000	recombinase/integrase	-	-
seq2627_GID19_HMPREF0348_1271	1	6	0,759	1	1,000	conserved hypothetical protein	-	-
seq2628_GID19_HMPREF0348_1272	1	7	0,936	1	1,000	beta family like DNA polymerase	-	-
seq2629_GID19_HMPREF0348_1273	1	7	0,936	1	1,000	SAM-dependent methyltransferase	-	-
seq2631_GID19_HMPREF0348_1275	1	7	0,936	1	1,000	possible streptothricin acetyltransferase	-	-
seq2632_GID19_HMPREF0348_1276	1	7	0,936	1	1,000	conserved hypothetical protein	-	-
seq2633_GID19_HMPREF0348_1277	1	7	0,936	1	1,000	kanamycin kinase	-	-

Name	Non-V583 CC6-strains present (n = 3)	Non-CC6 strains present (n = 22)	Odds. ratio	P.value	*q*-value (FDR)	Product_TX0104	Tag_HH22	Product_HH22
seq2636_GID19_HMPREF0348_1280	1	7	0,936	1	1,000	recombinase	-	-
seq2637_GID19_HMPREF0348_1281	1	7	0,936	1	1,000	transposase	-	-
seq2873_GID19_HMPREF0348_1150	1	7	0,936	1	1,000	conserved hypothetical protein	-	-
seq2874_GID19_HMPREF0348_1151	1	8	1,137	1	1,000	conserved hypothetical protein	-	-

PAPER V

Transcriptomic analysis reveals that the enterococcal polysaccharide antigen (Epa) constitutes a major factor in *Enterococcus faecalis* intrinsic resistance to high level NaCl-induced osmotic stress.

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Abstract

The inherent robust physiology of *Enterococcus faecalis* facilitates tolerance to high level osmotic stress. We here report the global transcriptional profile of *E. faecalis* V583 upon NaCl-induced osmotic stress. Among the early responses observed was an immediate down-regulation of the mechanosensitive channel *mscL*, accompanied by a subsequent up-regulation of genes involved in uptake of extracellular potassium and accumulation of glycine betaine. An induction of the *ntp* operon (V-type ATPase) implied active extrusion of excess sodium ions. Notably, osmotic stress affected expression of several virulence factors, including strict repression of the *gelE-sprE* operon and impaired gelatinase and serine protease activities. Osmotic stress also induced increased chaperone expression and modulated changes in cell envelope related traits, such as type II fatty acid biosynthesis (FAS) and the enterococcal polysaccharide antigen (*epa*) locus. Reduced salt-tolerance phenotypes were observed for Epa deficient mutants. Complementation of an *epaB* mutant restored wild type salt tolerance. These functional genetic data demonstrated a role of Epa in the physiological robustness and stress management of *E. faecalis*. Furthermore, we demonstrate that Epa confers increased tolerance towards multiple cell envelope stress inducing agents including bile, sodium dodesyl sulphate and antimicrobial peptides. Consequently, these findings delineate a potential link between the robust nature of *E. faecalis* and its ability to perform as a human pathogen, and provide a new perspective concerning the mechanisms by which Epa contributes to virulence.

Introduction

Enterococcus faecalis constitutes part of the normal intestinal flora of humans, and only sporadic reports of enterococcal infections in immunocompromised patients existed until the 1980s (38). In recent years however, *E. faecalis* has emerged as a clinical important opportunistic pathogen. Enterococci now rank among the leading causes of nosocomial infections worldwide (50, 69). Medical treatment is difficult, as enterococci, favored by a high conjugation rate, have acquired or intrinsically evolved resistance mechanisms against the most commonly used antibiotics (3).

Generally, the *E. faecalis* species challenges the boundary between commensal and pathogen: while several genetic traits that contribute to the virulence of *E. faecalis* have been characterized (reviewed in (54)), none has appeared to be indispensible for its pathogenicity. A distinct trait in *E. faecalis* physiology, compared to other intestinal lactic acid bacteria, is its ability to persist and thrive in harsh environments, that include heat, acid, oxidative and hyperosmotic stress (26). It is thus conceivable that the intrinsic robustness of *E. faecalis* is significant to the pathogenic potential of this bacterium. In this context, acquiring in-depth knowledge of the basic physiology of *E. faecalis* as well as exploring the specific traits that enable this bacterium to persist is imperative in the quest to understand *E. faecalis* pathogenicity.

Elevated osmolarity is among the many stressful conditions encountered by this bacterium in its natural habitat, *e.g.* the salinity of the small intestines is equivalent to

0.3M NaCl. Interestingly, it was recently demonstrated that mechanisms involved in intrinsic resistance to osmotic stress were major constituents to multidrug resistance in *Acinetobacter baumannii*, and may thus contribute to the persistence of this emerging nosocomial pathogen in clinical settings (24). Previous reports suggest that enterococci control turgor by actively modulating the pool of osmotically active solutes in their cytoplasm, thereby allowing water content to be adjusted by osmosis (32, 35). As part of a continued effort to decipher the various physiological aspects contributing to the success of this versatile pathogen, we here describe the global transcriptional profile of *E. faecalis* V583 upon the encounter with high concentrations of NaCl.

Material and methods

Bacterial strain and growth conditions. Bacterial strains and plasmids used in this study are listed in Table 1. *Enterococcus faecalis* strains were grown as previously described (66). NaCl were solubilized in water to obtain 5M solution. Autoclaved stock solution was added to autoclaved medium. Antibiotic concentrations (per ml) were: 12.5 µg chloramphenicol and 150 µg spectinomycin for *Escherichia coli* and 500 µg spectinomycin for *E. faecalis*.

NaCl treatment. For broth assays, ON cultures were inoculated (50× dilution) into BHI, containing various concentrations of NaCl. Cell growth was measured spectrophotometrically and by viable cell counts as previously described (60). The added NaCl concentrations ranged between 1 - 8 % (inherent amounts of NaCl in BHI have not been counted in). All experiments were performed independently in triplicates.

Sample collection. ON cultures were diluted 50× and grown in BHI to an OD_{600} of ~ 0.2 and split into two. 5M NaCl was added to one of the cultures, to a final concentration of 6.5 % NaCl. An equal volume of sterile H_2O was added to the second culture (control culture), to neutralize the dilution factor. The two cultures were then further incubated, and 10 mL samples were collected immediately after addition of NaCl (t_5), and then after 30 (t_{30}) and 60min (t_{60}). Samples were centrifuged at 5000 rpm for 5 min in an Eppendorf 5804R tabletop centrifuge at 4 ºC, and pellets were flash frozen in N_2 (*l*) prior to RNA extraction.

RNA isolation, cDNA synthesis, fluorescent labeling, hybridization and data analysis. Total RNA was isolated by FastPrep (Bio 101/Savant) and RNeasy Mini kit (QIAGEN) as previously described (60). The concentrations of the RNA samples were measured by using the NanoDrop (NanoDrop Technologies), and the quality was assessed by using the RNA 600 Nano LabChip kit and the Bioanalyzer 2100 (Agilent Technologies). cDNA was synthesized and labeled with the Fairplay II Microarray labeling kit (Stratagene), with modifications as previously described (60). Labeled samples were then dried, prior to resuspension in 140 µl hybridization solution and hybridized as described by Vebø et al. (66). The microarray used in this work has also been described previously (59). Three replicate hybridizations were performed with three separate batches of RNA. The three batches of RNA were obtained in three separate growth experiments. The Cy3 and Cy5 dyes (Amersham) used during cDNA synthesis were swapped in one of the three replicate hybridizations. All samples were co-

hybridized with control samples collected at equal time points (*e.g.* t_{30} was hybridized along with t_{30}). Hybridized arrays were scanned at wavelengths of 532 nm (Cy3) and 635 nm (Cy5) with a Tecan scanner LS (Tecan). Fluorescent intensities and spot morphologies were analyzed using GenePix Pro 6.0 (Molecular Devices), and spots were excluded based on slide or morphology abnormalities. Downstream analysis was carried out using the LIMMA package (www.bioconductor.org) in the R computing environment (www.r-project.org) as previously described (66).

Microarray data accession number. The microarray data have been deposited in the ArrayExpress database with the series accession number E-TABM-904.

Validation of microarray data by real time qRT-PCR. Real time quantitative RT-PCR (QPCR) was used to validate the expression levels for the following genes as previously described (66): EF0282, EF1211 and EF2642 at t_{60}. *dnaB* was used as a reference. All genes were quantified in triplicate. The primers used are shown in Table 2.

Complementation of *E. faecalis* TX5179 insertion mutant. Plasmid DNA was extracted with the Qiaprep Spin Miniprep kit and the Qiagen Plasmid Midi kit (QIAGEN) according to the manufacture's protocol. A complementation construct of TX5179 was made in pAT28 (64). The *efaBCD* genes and their native promoter were first amplified from OG1RF with epaBpro-F/epaD-R and ligated blunt into the pCC1^{TM} vector (Epicentre). pCC1epaBCD was then digested with EcoRI and subcloned into pAT28, using the EcoRI restriction site. All constructs were propagated in *E. coli* EPI300

(Epicentre) and integrity confirmed by DNA-sequencing and, prior to transfer into *E. faecalis*. *E. faecalis* electrocompetent cells were prepared as described by Holo and Nes (22), with 3.5 to 6 % glycine in the growth medium. Primers used are listed in Table 2.

Validation of CGH microarray data by PCR. PCR was used to confirm a deletion in the *epa* cluster of *E. faecalis* INY3000. PCR was carried out in 20-µl reaction volumes containing 1× buffer, 250 µM of each deoxynucleotide triphosphate and 1 U DyNAZyme II polymerase (Finnzymes). Primers used are listed in Table 2.

Gelatinase assays. Gelatinase assays were performed on Todd Hewitt agar plates supplemented with 3 % gelatin, as previously described (59). To assess the effect of osmotic stress on gelatinase activity, various ionic and non-ionic osmolytes (NaCl, KCl, glycerol, sucrose, sorbitol) were added to a final concentration of 1.2 M (6.5 % NaCl ≈ 1.2.M NaCl). For induction assays the gelatinase biosynthesis-activating pheromone (GBAP) was purified by ammonium sulphate precipitation as previously described (41).

Determination of minimal inhibitory concentration. In order to identify phenotypes in which the enterococcal polysaccharide antigen (Epa) is involved, minimal inhibitory concentration (MIC) of various biologically relevant stressors were determined for wild type OG1RF and three different *epa* mutants (INY3000, TX5179 and TX5180) by plate assays as previously described (23). OD_{600} was determined after 4 h incubation and MIC was defined as the lowest concentration of the stressor that completely inhibited bacterial growth at the time of measurement.

Transmission electron microscopy. To assess phenotypic variations associated with osmotic stress, *E. faecalis* cells growth in BHI with or without the addition of 6.5 % NaCl were examined by transmission electron microscopy. Cells for microscopy were collected in mid exponential phase of growth (OD_{600} 0.3-0.4) and washed with PBS buffer. Samples were then prepared by mounting the cells onto a copper grid, followed by immersion in filtered 2% phosphotungstic acid (PTA; pH 7.0) and drying at room temperature.

Results and discussion.

The growth of *E. faecalis* V583 at high osmolarity. The growth of *E. faecalis* V583 at high osmolarity was investigated in BHI broth containing up to 8 % NaCl (Figure 1). Increasing concentrations of NaCl led to an extended lag phase, in addition to reduced growth rates and lower cell densities in the stationary phase of growth. The final OD_{600} of V583 challenged with 8 % NaCl was approximately half of the final cell density of untreated cultures (Figure 1). Viable cell counts of V583 treated with selected concentrations of NaCl at different time points during growth confirmed the results obtained by OD measurements (results not shown). In general, the NaCl-induced effects on growth reported here, were consistent with the effects of osmotic stress reported in other Gram-positive bacteria (1, 30).

Transcriptional response to osmotic stress. A genome-scale time course microarray experiment was carried out to characterize the acute transcriptional response of *E. faecalis* V583 to elevated osmolarity (6.5 % NaCl). By using a $\log_2$-ratio > 1 and FDR <

0.01, 515 genes were identified as differentially transcribed at one or more time points during the time course of the experiment (Table S1), of which seven genes showed differential expression at all time points (Figure 2). The alkyl hydroperoxide reductase gene *ahpC* (EF2739) was the only genes which was consistently up-regulated throughout the time course, and has previously been linked to osmotic stress responses in other bacteria (4, 37). Reduced transcription was observed for the EF0633 to -36 operon involved in tyramine production in *E. faecalis* (9). The production of various amines by decarboxylation of amino acids has also previously been reported to be inhibited by NaCl (16). In addition, three genes with unknown functions (EF2214, EF2547 and EF3287) and a formate/nitrite transporter family protein (EF0094) were consistently regulated at all time points. Both *ahpC* and EF0094 hold putative functions in oxidative stress response. The link between osmotic- and oxidative stress management in *E. faecalis* is discussed further below. The fluctuating expression patterns obtained for five of the seven genes may represent separate mechanisms involved in the acute response (t_5) and the more long-term adaptation (t_{30}- t_{60}) of *E. faecalis* to salt. The converse expression patterns between t_5 and t_{60} of an additional 24 genes further supported this notion. These 24 genes included among others the *pdh* operon (pyruvate dehydrogenase multienzyme complex; further discussed below), parts of the *malPBMR*/*bop* operon (25, 34) and two neighboring genes (EF0956 to -60) involved in *E. faecalis* maltose utilization and the two regulatory genes *pfoR* (EF0097) and *ctsR* (EF3283), both with putative implications in adaptation to atypical conditions (12, 43).

The numbers of differentially expressed genes, grouped by functional classification according to the TIGR comprehensive microbial resource; CMR (http://cmr.tigr.org/tigr-scripts/CMR/CmrHomePage.cgi), are shown in Figure 3. All functional groups were tested for significant enrichment among the differentially transcribed genes by Fisher's exact test ($P < 0.05$; data not shown). A total of four groups came out as significantly enriched: Purine/pyrimidine/nucleoside/nucleotide ($P = 4.0e^{-08}$), Fatty acid and phospholipid metabolism ($P = 1.1e^{-06}$), Protein synthesis ($P = 2.2e^{-05}$) and Energy metabolism ($P = 0.00056$). The enrichment of genes involved in protein synthesis most likely reflects the reduced growth rate induced by the presence of NaCl, and is consistent with the observations in osmotically challenged *Bacillus subtilis* (18). Log_2 ratios of differentially expressed genes in cells treated with 6.5 % NaCl are shown in Table S1.

Validation of microarray data. QPCR was used to validate our microarray analysis. The Pfaffl method (44) was used for relative quantification, and transcriptional data were obtained for the following genes: EF0282, EF1211 and EF2642 at t_{60}. *dnaB* was used as reference gene. The amplification efficiency varied from 61-102 %. The expression levels obtained by QPCR correlated well with the microarray data in terms of direction (Figure 4). The QPCR expression ratios for EF1211 and EF2642 were significantly greater than the microarray values. This may indicate that the change in expression exceeded the dynamic range of the microarray analysis. Indeed, EF1211 and EF2642 were the two genes with the highest positive change in expression at t_{60} in the microarray data set.

General stress response mechanisms were activated by osmotic stress. A partial stress proteome was previously characterized for *E. faecalis* under various stresses by Giard and co-workers (17). Approximately 200 different proteins were recognized as stress-responsive, of which 27 were identified by N-terminal sequencing (17). Five of the six general stress proteins (Gsp62-Gsp67; induced by at least six different stress conditions) responded to salt (17), of which only three showed differential expression during exposure to NaCl in the present study (EF0453, EF1308 and EF2633). Parts of the *dnaK* (EF1306- to 10) and *groE* (EF2633- to 34) operons were significantly induced at t_5-t_{30} and t_5, respectively. Interestingly, a general trend in our data set was an induction of heat shock determinants (*hslVU*, *dnaK* and *groE* operons), while genes involved in the *E. faecalis* cold shock response were repressed (EF0781, EF1367 and EF1991). Cold shock stress is associated with several changes in cellular physiology, including hampered protein synthesis (45). Many cold shock proteins thus hold important roles in stabilization of RNA, assembly of ribosomes and other vital aspects of translation (45). Down-regulation of these genes, may be related to the reduced growth rate of *E. faecalis* during treatment with NaCl. Heat shock proteins on the other hand mainly function as molecular chaperones, involved in protein (re)folding and prevention of unwanted protein aggregation induced by environmental stimuli such as heat. An up-regulation of genes encoding chaperones is in accordance with previous reports (18), and may be indicative of NaCl inducing aggregation and misfolding of proteins in an altered intracellular environment.

Gsp65 (EF0453) was previously shown to share homology with organic hydroperoxide resistance proteins from various bacteria (51). Moreover, phenotypic characterization of a *gsp65*-deficient mutant suggested that Gsp65 may be implicated in oxidative stress resistance in *E. faecalis* (51). Flahaut et al. (15) previously reported significant cross-protection between NaCl-induced osmotic stress and the hydrogen peroxide (H_2O_2) stress in *E. faecalis* (15) Indeed, a number of other oxidative stress protection genes were also affected by NaCl (Table S1), including *i.e. sodA* (EF0463), *npr* (EF1211), *trxB* (EF1338), *nox* (EF1586) and *katA* (EF1597). Many Dps-like proteins hold a potential role in protection of DNA during oxidative stress (19), however, no consistent differential expression indicative of NaCl-induced DNA damage was observed among genes involved in DNA repair in the present study. Analogous to *B. subtilis*, the V583 genome contains two genes encoding Dps family proteins (EF0606 and EF3233), of which only EF3233 appeared to be salt-responsive. In *B. subtilis* MrgA is induced by oxidative stress, while the expression of DpsA is modulated in response to various environmental stresses, including salt (19). The exact role of Dps-like proteins in osmoprotection still remains unclear.

The primary osmotic response phase processes: prevention of solute efflux and subsequent accumulation of potassium via the *kpd* system. Sensing of physical strain such as turgor pressure is primarily mediated by mechanosensitive ion channels in bacteria (8). The immediate regulation of the large conductance mechanosensitive channel *mscL* (EF3152) in response to NaCl was expected and in accordance with previous reports (18). The MscL type mechanosensitive channel proteins function as a

safety vault for release of cytoplasmic solutes in response to osmotic downshift (31). Significant repression of *mscL* at t_5 may thus represent a means by which *E. faecalis* prevents solute efflux in response to NaCl-induced hyperosmotic stress.

Interestingly, MscL has been reported as a regulator of the Kdp two-component system (TCS) in *E. coli* (52). According to previous reports, the response of nonhalophilic bacteria to hyperosmotic stress may be characterized by two phases, where the primary osmoresponse involves active potassium influx (11). The V583 genome contains several genes with putative functions in potassium transport, however, only parts of the *kpd* gene cluster (EF0568 and -69) showed differential expression in response to NaCl. Consistent with the observations of Kunin and Rudy (32), NaCl therefore seems to induce the uptake of extracellular K^+ in *E. faecalis*, however, our results suggest that recovery of turgor may be less K^+ dependent in *E. faecalis* than in Gram-negative bacteria. Indeed, Gram-positive bacteria have higher basal internal concentrations of potassium than Gram-negative bacteria (26). Reportedly, the expression of *kdpFABC* is under control of the KpdDE regulatory system (48), however, in line with our observations, the signal transduction cascade of this TCS is not sensitive to elevated osmolarity (20). On the other hand, adjustments in the membrane phospholipid composition towards higher anionic phospholipid content enhance the transcription of *kdpFABC*, as anionic phospholipids regulate the activation of KdpD (55). NaCl-induced potassium uptake in *E. faecalis* may thus be related to rearrangements of the membrane composition. Experimental evidence of a remodeling of the *E. faecalis* cell envelope upon osmotic upshift is discussed further below.

The accumulation of K^+ is known to induce uptake and synthesis of glutamate (11). Flahaut et al. (14) have previously reported glutamate to be a non-limiting factor in BHI broth, and proposed that this amino acid could play a major role in the osmoadaptation of *E. faecalis*. However, no changes in transcription were observed for either the *gln* operon (EF1117 to -20)) with inferred function in glutamine/glutamate transport in *E. faecalis* (33), or genes involved in glutamate biosynthesis (EF1415 and EF2560), suggesting that accumulation of glutamate is not a prominent part of the *E. faecalis* osmoresponse. Le Breton et al. (33) recently demonstrated that the *gln* operon is regulated by the *croRS* two-component system (TCS; EF3289 to -90) in *E. faecalis*. *croRS* was induced at t_{30} during treatment with NaCl. The induction of this *gln*-repressor further corroborates the notion that glutamate accumulation is not vital to counteract elevated osmolarity in *E. faecalis*. The basal concentrations of glutamate are generally 8- to 10-fold greater in Gram-positive than in Gram-negative bacteria (11). Combined with high basal intracellular K^+ concentrations, a large pool of free amino acids under non-stressed conditions may thus explain the modest transcriptional activation of the primary osmotic response by NaCl in *E. faecalis*. Indeed, elevated osmolarity only slightly affected intracellular glutamate concentrations in the Gram-positives *Bacillus*, *Streptomyces* and *Staphylococcus* sp. (2, 28, 29).

Secondary response phase: accumulation of compatible solutes. At high concentrations, monovalent ions such as K^+ can inhibit various enzymes. The secondary response phase is thus initiated when the intracellular potassium concentration reaches a

certain threshold. The second phase of osmoadaptation involves accumulation of compatible solutes, which can accumulate to high concentration to maintain turgor, without affecting cellular functionality (7, 28). Although some compatible solutes can accumulate by *de novo* synthesis, osmotic adaptation more often depend on the osmotic properties of the medium for uptake of exogenous osmolytes (14). NaCl-induced osmotic stress has been associated with an increase in intracellular glycine betaine (GB) in *E. faecalis* (32). BHI contains ~2 mM GB (58), and previous results indicated that GB accumulation depend on the activity of transport systems in *E. faecalis* (46). Two ABC transporters involved in the uptake of GB (EF0862 to -65 and EF2641 to -42) were induced at t_{30} and t_{60} in the present study. Interestingly, a peak in the expression of compatible solute transporters at t_{30} after onset of osmotic shock was also previously reported (18). Moreover, Pichereau et al. (46) recently showed that the addition of GB and its structural analogues to salt-stressed *E. faecalis* in a defined medium completely abolished the inhibitory effects of NaCl on bacterial growth, as opposed to proline, ectoine and pipecolate, which did not display any osmoprotective effects on *E. faecalis*.

Extrusion of excess salt ions. Sodium extrusion by bacteria is generally attributed to antiport of Na^+ for H^+ energized by a proton motive force (PMF). In *E. faecalis* however, the ATP-driven V-ATPase represents the primary system for sodium expulsion (21). Indeed, transcription of the V-ATPase (*ntp* operon; EF1492- to 1500) was significantly up-regulated at t_{30}-t_{60} in our experiments. The V583 genome also contains four putative Na^+/H^+ antiporters (EF0296, EF0402, EF0636 and EF1574), however, only one of these systems was differentially expressed in response to NaCl in the present study: EF0636

was induced at *t5*, while repressed at t_{30}-t_{60}. As the *E. faecalis* respiratory chain is impaired in the absence of exogenous heme, the PMF used to energize Na^+/H^+ antiporters is generated by proton expulsion via the F_0F_1 proton ATPase (F-ATPase). The F-ATPase (EF2607- to 14) was however, significantly down-regulated at t_{30} in response to NaCl. A diminished PMF may explain why EF0636 was repressed towards the end of the time course in V583 during treatment with NaCl. Furthermore, the transcription of genes encoding four different cation transporting systems was also activated at either t_{30} or t_{60} in the present study (EF0576, EF0859, EF0871 and EF1938). A potential role of these transporters in active extrusion of sodium ions during elevated osmolarity is conceivable. The induction of Na^+-translocating systems emphasizes the importance of retaining cytosolic ion homeostasis.

The pyruvate dehydrogenase multienzyme complex (PDHC; EF1353- to 56) was downregulated at t_5, while upregulated at t_{60} in V583 during elevated osmolarity. Vilhelmsson and Miller (68) have suggested that an increased pyruvate dehydrogenase activity during osmotic stress in *S. aureus*, provides the bacterium with a strategy for meeting the increased energy demands associated with sodium-induced uptake of compatible solutes. Such a rationale is consistent with the induction of several ATP-dependent transport systems during NaCl-induced osmotic stress in *E. faecalis* discussed above.

NaCl-induced osmotic stress interferes with the *fsr* autoregulatory circuit and represses *gelE-sprE* transcription. One of the most pronounced effects of osmotic stress

in *E. faecalis* was the down regulation of the gelatinase (*gelE*) and serine protease (*sprE*) at t_{60}, which was also manifested as a gelatinase-negative phenotype on Todd-Hewitt agar plates supplemented with 3 % gelatin and 6.5 % NaCl (Figure S1). Both GelE and SprE have been shown to play a role in mammalian and nematode models of enterococcal infection (13, 56, 63). Moreover, *gelE* and *sprE* appear to be co-transcribed and under positive regulation of the Fsr system, via the Fsr binding sequence (49). The observed down-regulation of *gelE-sprE* is thus suggestive of an interrupted FsrABCD phosphorelay, required for positive regulation of the Fsr-responsive genes.

The *fsr* system is the only autoregulatory two-component system in V583 where signal transduction is mediated by interaction between the histidine kinase FsrC and its cognate peptide pheromone GBAP (gelatinase biosynthesis-activating pheromone) (40). At the molecular level, hydrophobic and ionic interactions mediate pheromone-receptor binding (41). These interactions are susceptible to environmental conditions, such as temperature fluctuations, shifts in ionic strength and presence of organic solvents (41). Hence, we suspected that the down-regulation of *gelE* and *sprE* could be attributed to salt interfering with the receptor-pheromone interaction, rather than a response to osmotic stress. Preliminary observations indicate that in the presence of NaCl, externally supplemented GBAP does not augment gelatinase activity (data not shown). Moreover, gelatinase plate assays where NaCl was replaced with equal concentration of the non-ionic osmolyte glycerol demonstrated activity similar to the control (data not shown). On the other hand, the non-ionic osmolytes sucrose and sorbitol did not restore gelatinase activity (data not shown), indicating that the exact nature of the observed phenotype is yet to be uncovered.

Bourgogne et al. (6) previously identified a potential Fsr regulon consisting of > 450 genes; most of which are probably not directly regulated by Fsr, but whose regulation can be ascribed to indirect effects of the *fsrB* mutation on transcriptional activity. Indeed, the Fsr consensus sequence proposed by Qin et al. (49) was identified in the promoter region of three loci (EF0563, EF1818 and EF1821), whose expression is inferred to be dependent on the phosporylated FsrA response regulator. Of these putative Fsr-responsive loci, only the *gelE-sprE* operon was repressed in osmotically challenged *E. faecalis*. Transcription of *fsrBDC* was unaffected; an observation which is consistent with the proposed model by Qin et al. (49), who demonstrated that basal transcription of *fsrBDC*, is facilitated by read through from the *fsrA* promoter.

Osmotic stress influences genes involved in the cell envelope composition. The bacterial cell envelope provides essential protection from the external environment and confers strength and rigidity to counteract the effects of osmotic stress conditions on the cell. Furthermore, as suggested above, osmosensor activity is likely to be mediated through changes in membrane properties. Indeed, differential expression of several gene clusters with membrane/wall-associated functions reflects a major impact of NaCl on the cell envelope. Particularly, genes involved in fatty acid and lipid metabolism were strongly affected. Two gene clusters involved in type II fatty acid synthesis (FAS) (EF0282 to -84 and EF2875 to -86) were significantly repressed during elevated osmolarity. A similar observation was also made in osmotically challenged *Bacillus subtilis* (18). The Gram-positive cell envelope is characterized by a cytoplasmic

membrane with embedded proteins and lipoteichoic acids (LTA) and cell wall teichoic acids covered by a thick, multilayered peptidoglycan (10). In addition to peptidoglycan and teichoic acid, a rhamnose-containing polysaccharide has been shown to be the third main constituent of the *E. faecalis* cell wall (10). Four genes located in the *epa* (enterococcal polysaccharide antigen) gene cluster (EF2192 and EF2195- to 97), including genes that code for rhamnose biosynthesis and glycosyl transferases were up-regulated at t_{30} in V583 during treatment with NaCl. Additional genes in the same cluster were also significantly differentially expressed (FDR < 0.01), but with $\log_2$-values < 1. Moreover, an additional four glycosyl transferases and a penicillin-binding protein 2B (EF2857) also showed differential expression at one or more time points in the present study. Up-regulation of penicillin-binding protein expression is a common strategy in Gram-positive envelope stress responses (18, 27). Altogether, these results indicate that remodeling of the cell envelope constitute a vital mechanism by which *E. faecalis* cope with changes in the external osmolarity. This notion is consistent with osmotic stress induced cell envelope modifications in other Gram-positive bacteria (18, 47).

The cell wall rhamnose polysaccharide Epa confers osmotic stress protection. The *epa* gene cluster was originally characterized in *E. faecalis* OG1RF as an antigenic factor during infection in mice (70). A recent revision of the organization and annotation revealed that *epa* comprises a total of 18 ORFs (*epaA*-*R*) (62). The gene cluster consists of distinct modules responsible for the sequential steps of the polysaccharide biosynthesis process, *i.e.* synthesis of dTDP-rhamnose, glycosyltransferase activity, polymerization and peptidoglycan-linkage. The Epa polysaccharide has been investigated for its

implication in virulence in various animal infection models (57, 61), and has thus has been considered as a vital virulence trait of *E. faecalis*. The induction of the *epa* gene cluster during treatment with NaCl suggested that Epa may be involved in the osmotic stress response in *E. faecalis*. To further investigate this notion, a series of experiments providing unequivocal functional genetic evidence for the involvement of the *epa* locus in *E. faecalis* osmoprotection were designed using *epa* deficient mutants.

A previous comparative genomic analysis of INY3000 (72), a laboratory generated Tn*916* mutant of the OG1 strain, revealed a deletion of *epa D-M* (homologous to EF2182- to 84 and EF2189- to 95 in V583) in INY3000 compared to OG1RF (5). The deletion was confirmed by PCR (Figure 5A). Xu et al. (71) have previously constructed insertional mutants of OG1RF with disruptions in a glycosyl transferase (*epaB*/*orfde4*) and a glucose-1-phosphate thymidylyltransferase (*epaE*/*orfde6*; TX5179 and TX5180, respectively). Initially, the salt tolerance of OG1RF, INY3000, TX5179 and TX5180 was assessed by investigating their growth in BHI supplemented with 6.5 and 8 % NaCl. No significant effects of the mutations were observed in medium without any salt added (result not shown). A moderate but statistically significant reduction in growth rate for INY3000 and TX5180 was observed in the presence of 6.5 % NaCl, while the effect on TX5179 was more pronounced (Figure 5B). In the presence of 8 % NaCl, the impairment in growth of the mutants further increased compared to OG1RF (Figure 5C). Moreover, complementation of the Δ*epaB* mutant strain with the *epaBCD* genes cloned in vector pAT28 restored the wild type salt tolerance (results not shown). Unfortunately, despite exhaustive attempts, complementation of the TX5180 mutant by cloning of *epaEFGHIJ*

in different vectors systems was not achieved. Nevertheless, our results confirmed that the *epa* locus confers increased tolerance of *E. faecalis* to high level osmotic stress.

We hypothesized that Epa conferred osmoprotection by either of two mechanisms; *de novo* biosynthesis of rhamnose as a compatible solute, or alternatively that Epa itself, as part of the cell envelope, might act as a protective agent. In order to investigate whether *de novo* biosynthesis and subsequent accumulation of rhamnose serve as a mechanism of protection, we tested whether addition of rhamnose to the growth medium could alleviate the osmotically induced growth impairment of the different mutants; however, no obvious effect of rhamnose on growth was observed for neither the wild type nor the mutants (results not shown). This observation may be due to the cells not being able to efficiently import rhamnose from the medium under the experimental conditions used. However, if accumulated de novo synthsised rhamnose functioned as an osmoprotector, the salt tolerance of the Δ*epaB* mutant strain would be expected to resemble that of the parent strain. Our data thus indicate that the entire Epa biosynthesis pathway, and not only the genes responsible for rhamnose biosynthesis, must be intact in order to confer osmotic stress protection.

We suspect that genes encoded by the *epa* locus function in maintenance of cell envelope integrity, and that that the impaired virulence observed for *epa* mutants thus may result from a loss of cell envelope integrity. Trotter and Dunny (65) previously showed that the Tn*916*-induced mutations in INY3000 were associated with an increase in the amount of short chain (12 carbon) fatty acids of the LTA, compared to the parental strain. The

authors predicted these changes in the LTA composition to affect the fluidity of the cell envelope (65). Moreover, changes in membrane fluidity have been proposed as a signal for sensors of osmotic stress in other bacteria (36). It is therefore tempting to speculate that an induction of the *epa* gene cluster in the present study may be related to a NaCl-induced reduction in membrane fluidity in V583. However, transmission electron microscopy assessment of the cell envelope of *E. faecalis* did not reveal any obvious phenotypic changes in salt stressed cells compared to untreated cells (Figure 6). Further characterization of the effects of NaCl on *E. faecalis* membrane properties is in progress in our laboratory.

The role of Epa in *E. faecalis* stress responses. To evaluate whether the protective effect of Epa was specific to NaCl-induced osmotic stress, or if this cell wall polysaccharide also confers resistance to other types of stresses, OG1RF and the *epa* mutants were tested for their sensitivity to biologically relevant stressors (Table S2). The data revealed that Epa contributes to tolerance to the antimicrobial peptide leucocin C, ethanol, bile acids and the detergent SDS, in addition to hyperosmotic stress. Moreover, Epa did not significantly alter sensitivity to ampicillin, vancomycin or H_2O_2. These data indicate that Epa confers tolerance to stress that *E. faecalis* is likely to encounter in the human gastrointestinal tract, as well as during infection, thus providing novel clues to the mechanisms by which Epa contributes to enterococcal pathogenicity by rendering *E. faecalis* more stress resistant rather than acting as a classical virulence factor.

Conclusion.

In conclusion, the data presented here suggest that uptake of compatible solutes and alterations in cell envelope composition may be some of the ways by which *E. faecalis* responds to elevated osmolarity. Glycine betaine seems to be the predominant compatible solute taken up by V583 when grown in BHI. Growth experiments with *epa* deficient mutants confirmed a role of the enterococcal polysaccharide antigen in *E. faecalis* osmoprotection, and led to the elucidation of a more general function of Epa in the *E. faecalis* response to several biologically relevant stressors unveiling new insight onto the role of Epa in the ability of *E. faecalis* to cause infection.

Acknowledgements

This work was financially supported by the European Union 6th Framework Programme "Approaches to Control multi-resistant Enterococci: Studies on molecular ecology, horizontal gene transfer, fitness and prevention". TX5179 and TX5180 were kindly provided by Dr. Barbara E. Murray. Linda H. Godager is acknowledged for technical assistance with the QPCR. We also acknowledge Mari Christine Brekke and Hilde Raanaas Kolstad for technical assistance with the TEM and The Norwegian Microarray Consortium, Oslo, for printing of the microarray slides.

References

1. **Amezaga, M. R., I. Davidson, D. McLaggan, A. Verheul, T. Abee, and I. R. Booth.** 1995. The role of peptide metabolism in the growth of *Listeria monocytogenes* ATCC 23074 at high osmolarity. Microbiology **141 (Pt 1):**41-9.
2. **Anderson, C. B., and L. D. Witter.** 1982. Glutamine and proline accumulation by *Staphylococcus aureus* with reduction in water activity. Appl. Environ. Microbiol. **43:**1501-1503.
3. **Arias, C. A., and B. E. Murray.** 2008. Emergence and management of drug-resistant enterococcal infections. Expert Rev Anti Infect Ther **6:**637-55.
4. **Armstrong-Buisseret, L., M. B. Cole, and G. S. Stewart.** 1995. A homologue to the *Escherichia coli* alkyl hydroperoxide reductase AhpC is induced by osmotic upshock in *Staphylococcus aureus*. Microbiology **141 (Pt 7):**1655-61.
5. **Bourgogne, A., D. A. Garsin, X. Qin, K. V. Singh, J. Sillanpaa, S. Yerrapragada, Y. Ding, S. Dugan-Rocha, C. Buhay, H. Shen, G. Chen, G. Williams, D. Muzny, A. Maadani, K. A. Fox, J. Gioia, L. Chen, Y. Shang, C. A. Arias, S. R. Nallapareddy, M. Zhao, V. P. Prakash, S. Chowdhury, H. Jiang, R. A. Gibbs, B. E. Murray, S. K. Highlander, and G. M. Weinstock.** 2008. Large scale variation in *Enterococcus faecalis* illustrated by the genome analysis of strain OG1RF. Genome Biol **9:**R110.
6. **Bourgogne, A., S. G. Hilsenbeck, G. M. Dunny, and B. E. Murray.** 2006. Comparison of OG1RF and an isogenic *fsrB* deletion mutant by transcriptional analysis: the Fsr system of *Enterococcus faecalis* is more than the activator of gelatinase and serine protease. J Bacteriol **188:**2875-84.
7. **Bremer, E., and R. Krämer.** 2000. Coping with osmotic challenges: Osmoregulation through accumulation and release of compatible solutes in Bacteria. *In* G. Storz and R. Hengge-Aronis (ed.), Bacterial stress responses. ASM Press, Washington DC.
8. **Chang, G., R. H. Spencer, A. T. Lee, M. T. Barclay, and D. C. Rees.** 1998. Structure of the MscL homolog from *Mycobacterium tuberculosis*: a gated mechanosensitive ion channel. Science **282:**2220-6.
9. **Connil, N., Y. Le Breton, X. Dousset, Y. Auffray, A. Rince, and H. Prevost.** 2002. Identification of the *Enterococcus faecalis* tyrosine decarboxylase operon involved in tyramine production. Appl Environ Microbiol **68:**3537-44.
10. **Coyette, J., and L. E. Hancock.** 2002. Enterococcal cell wall. *In* M. S. Gilmore, D. B. Clewell, G. M. Dunny, B. E. Murray, L. B. Rice, and P. Courvalin (ed.), The Enterococci. Pathogenesis, Molecular biology and Antibiotic resistance. ASM Press, Washington DC.
11. **Csonka, L. N.** 1989. Physiological and genetic responses of bacteria to osmotic stress. Microbiol. Mol. Biol. Rev. **53:**121-147.
12. **Derre, I., G. Rapoport, and T. Msadek.** 1999. CtsR, a novel regulator of stress and heat shock response, controls clp and molecular chaperone gene expression in gram-positive bacteria. Mol Microbiol **31:**117-31.
13. **Engelbert, M., E. Mylonakis, F. M. Ausubel, S. B. Calderwood, and M. S. Gilmore.** 2004. Contribution of gelatinase, serine protease, and *fsr* to the

pathogenesis of *Enterococcus faecalis* endophthalmitis. Infect Immun **72:**3628-33.

14. **Flahaut, S., A. Benachour, J. C. Giard, P. Boutibonnes, and Y. Auffray.** 1996. Defense against lethal treatments and de novo protein synthesis induced by NaCl in *Enterococcus faecalis* ATCC 19433. Arch Microbiol **165:**317-24.
15. **Flahaut, S., J. M. Laplace, J. Frere, and Y. Auffray.** 1998. The oxidative stress response in *Enterococcus faecalis*: relationship between H2O2 tolerance and H2O2 stress proteins. Lett Appl Microbiol **26:**259-64.
16. **Gardini, F., M. Martuscelli, M. C. Caruso, F. Galgano, M. A. Crudele, F. Favati, M. E. Guerzoni, and G. Suzzi.** 2001. Effects of pH, temperature and NaCl concentration on the growth kinetics, proteolytic activity and biogenic amine production of *Enterococcus faecalis*. International Journal of Food Microbiology **64:**105-117.
17. **Giard, J. C., J. M. Laplace, A. Rince, V. Pichereau, A. Benachour, C. Leboeuf, S. Flahaut, Y. Auffray, and A. Hartke.** 2001. The stress proteome of *Enterococcus faecalis*. Electrophoresis **22:**2947-54.
18. **Hahne, H., U. Mader, A. Otto, F. Bonn, L. Steil, E. Bremer, M. Hecker, and D. Becher.** A comprehensive proteomics and transcriptomics analysis of *Bacillus subtilis* salt stress adaptation. J Bacteriol **192:**870-82.
19. **Haikarainen, T., and A. C. Papageorgiou.** Dps-like proteins: structural and functional insights into a versatile protein family. Cell Mol Life Sci **67:**341-51.
20. **Hamann, K., P. Zimmann, and K. Altendorf.** 2008. Reduction of turgor is not the stimulus for the sensor kinase KdpD of *Escherichia coli*. J Bacteriol **190:**2360-7.
21. **Heefner, D. L., and F. M. Harold.** 1982. ATP-driven sodium pump in *Streptococcus faecalis*. Proc Natl Acad Sci U S A **79:**2798-802.
22. **Holo, H., and I. F. Nes.** 1989. High-Frequency Transformation, by Electroporation, of *Lactococcus lactis* subsp. *cremoris* Grown with Glycine in Osmotically Stabilized Media. Appl Environ Microbiol **55:**3119-3123.
23. **Holo, H., O. Nilssen, and I. F. Nes.** 1991. Lactococcin A, a new bacteriocin from *Lactococcus lactis* subsp. *cremoris*: isolation and characterization of the protein and its gene. J Bacteriol **173:**3879-87.
24. **Hood, M. I., A. C. Jacobs, K. Sayood, P. M. Dunman, and E. P. Skaar.** *Acinetobacter baumannii* increases tolerance to antibiotics in response to monovalent cations. Antimicrob Agents Chemother **54:**1029-41.
25. **Hufnagel, M., S. Koch, R. Creti, L. Baldassarri, and J. Huebner.** 2004. A putative sugar-binding transcriptional regulator in a novel gene locus in *Enterococcus faecalis* contributes to production of biofilm and prolonged bacteremia in mice. J Infect Dis **189:**420-30.
26. **Huycke, M. M.** 2002. Physiology of enterococci. *In* M. S. Gilmore, D. B. Clewell, P. Courvalin, G. M. Dunny, B. E. Murray, and L. B. Rice (ed.), The Enterococci: Pathogenesis, molecular biology and antibiotic resistance. ASM Press, Washington DC.
27. **Jordan, S., M. I. Hutchings, and T. Mascher.** 2008. Cell envelope stress response in Gram-positive bacteria. Fems Microbiology Reviews **32:**107-146.

28. **Kempf, B., and E. Bremer.** 1998. Uptake and synthesis of compatible solutes as microbial stress responses to high-osmolality environments. Arch Microbiol **170:**319-30.
29. **Killham, K., and M. K. Firestone.** 1984. Salt Stress Control of Intracellular Solutes in *Streptomycetes* Indigenous to Saline Soils. Appl Environ Microbiol **47:**301-306.
30. **Kilstrup, M., S. Jacobsen, K. Hammer, and F. K. Vogensen.** 1997. Induction of heat shock proteins DnaK, GroEL, and GroES by salt stress in *Lactococcus lactis*. Appl Environ Microbiol **63:**1826-37.
31. **Kloda, A., E. Petrov, G. R. Meyer, T. Nguyen, A. C. Hurst, L. Hool, and B. Martinac.** 2008. Mechanosensitive channel of large conductance. Int J Biochem Cell Biol **40:**164-9.
32. **Kunin, C. M., and J. Rudy.** 1991. Effect of NaCl-induced osmotic stress on intracellular concentrations of glycine betaine and potassium in *Escherichia coli, Enterococcus faecalis,* and staphylococci. J Lab Clin Med **118:**217-24.
33. **Le Breton, Y., C. Muller, Y. Auffray, and A. Rince.** 2007. New Insights into the *Enterococcus faecalis* CroRS Two-Component System Obtained Using a Differential-Display Random Arbitrarily Primed PCR Approach. Appl. Environ. Microbiol. **73:**3738-3741.
34. **Le Breton, Y., V. Pichereau, N. Sauvageot, Y. Auffray, and A. Rince.** 2005. Maltose utilization in *Enterococcus faecalis*. J Appl Microbiol **98:**806-13.
35. **Measures, J. C.** 1975. Role of Amino-Acids in Osmoregulation of Non-Halophilic Bacteria. Nature **257:**398-400.
36. **Mikami, K., and N. Murata.** 2003. Membrane fluidity and the perception of environmental signals in cyanobacteria and plants. Prog Lipid Res **42:**527-43.
37. **Mishra, Y., N. Chaurasia, and L. C. Rai.** 2009. AhpC (alkyl hydroperoxide reductase) from *Anabaena* sp. PCC 7120 protects *Escherichia coli* from multiple abiotic stresses. Biochem Biophys Res Commun **381:**606-11.
38. **Murray, B. E.** 1990. The life and times of the *Enterococcus*. Clin Microbiol Rev **3:**46-65.
39. **Murray, B. E., K. V. Singh, R. P. Ross, J. D. Heath, G. M. Dunny, and G. M. Weinstock.** 1993. Generation of restriction map of *Enterococcus faecalis* OG1 and investigation of growth requirements and regions encoding biosynthetic function. J Bacteriol **175:**5216-23.
40. **Nakayama, J., S. Chen, N. Oyama, K. Nishiguchi, E. A. Azab, E. Tanaka, R. Kariyama, and K. Sonomoto.** 2006. Revised model for *Enterococcus faecalis fsr* quorum-sensing system: the small open reading frame *fsrD* encodes the gelatinase biosynthesis-activating pheromone propeptide corresponding to staphylococcal *agrD*. J Bacteriol **188:**8321-6.
41. **Nilsen, T., I. F. Nes, and H. Holo.** 1998. An exported inducer peptide regulates bacteriocin production in *Enterococcus faecium* CTC492. J Bacteriol **180:**1848-54.
42. **Opsata, M., I. F. Nes, and H. Holo.** Class IIa bacteriocin resistance in *Enterococcus faecalis* V583: The mannose PTS operon mediates global transcriptional responses. BMC Microbiol **10:**224.

43. **Paulsen, I. T., L. Banerjei, G. S. Myers, K. E. Nelson, R. Seshadri, T. D. Read, D. E. Fouts, J. A. Eisen, S. R. Gill, J. F. Heidelberg, H. Tettelin, R. J. Dodson, L. Umayam, L. Brinkac, M. Beanan, S. Daugherty, R. T. DeBoy, S. Durkin, J. Kolonay, R. Madupu, W. Nelson, J. Vamathevan, B. Tran, J. Upton, T. Hansen, J. Shetty, H. Khouri, T. Utterback, D. Radune, K. A. Ketchum, B. A. Dougherty, and C. M. Fraser.** 2003. Role of mobile DNA in the evolution of vancomycin-resistant *Enterococcus faecalis*. Science **299:**2071-4.
44. **Pfaffl, M. W.** 2001. A new mathematical model for relative quantification in real-time RT-PCR. Nucl. Acids Res. **29:**e45-.
45. **Phadtare, S.** 2004. Recent developments in bacterial cold-shock response. Curr Issues Mol Biol **6:**125-36.
46. **Pichereau, V., S. Bourot, S. Flahaut, C. Blanco, Y. Auffray, and T. Bernard.** 1999. The osmoprotectant glycine betaine inhibits salt-induced cross-tolerance towards lethal treatment in *Enterococcus faecalis*. Microbiology **145 (Pt 2):**427-35.
47. **Piuri, M., C. Sanchez-Rivas, and S. M. Ruzal.** 2005. Cell wall modifications during osmotic stress in *Lactobacillus casei*. J Appl Microbiol **98:**84-95.
48. **Polarek, J. W., G. Williams, and W. Epstein.** 1992. The products of the *kdpDE* operon are required for expression of the Kdp ATPase of *Escherichia coli*. J Bacteriol **174:**2145-51.
49. **Qin, X., K. V. Singh, G. M. Weinstock, and B. E. Murray.** 2001. Characterization of *fsr*, a regulator controlling expression of gelatinase and serine protease in *Enterococcus faecalis* OG1RF. J Bacteriol **183:**3372-82.
50. **Richards, M. J., J. R. Edwards, D. H. Culver, and R. P. Gaynes.** 2000. Nosocomial infections in combined medical-surgical intensive care units in the United States. Infect Control Hosp Epidemiol **21:**510-5.
51. **Rince, A., J. C. Giard, V. Pichereau, S. Flahaut, and Y. Auffray.** 2001. Identification and characterization of *gsp65*, an organic hydroperoxide resistance (*ohr*) gene encoding a general stress protein in *Enterococcus faecalis*. J Bacteriol **183:**1482-8.
52. **Roberts, M. F.** 2000. Osmoadaptation and osmoregulation in archaea. Frontiers in Bioscience **5:**D796-812.
53. **Sahm, D. F., J. Kissinger, M. S. Gilmore, P. R. Murray, R. Mulder, J. Solliday, and B. Clarke.** 1989. In vitro susceptibility studies of vancomycin-resistant *Enterococcus faecalis*. Antimicrob Agents Chemother **33:**1588-91.
54. **Sava, I. G., E. Heikens, and J. Huebner.** Pathogenesis and immunity in enterococcal infections. Clin Microbiol Infect **16:**533-40.
55. **Schniederberend, M., P. Zimmann, M. Bogdanov, W. Dowhan, and K. Altendorf.** Influence of K+-dependent membrane lipid composition on the expression of the *kdpFABC* operon in *Escherichia coli*. Biochim Biophys Acta **1798:**32-9.
56. **Sifri, C. D., E. Mylonakis, K. V. Singh, X. Qin, D. A. Garsin, B. E. Murray, F. M. Ausubel, and S. B. Calderwood.** 2002. Virulence effect of *Enterococcus faecalis* protease genes and the quorum-sensing locus *fsr* in *Caenorhabditis elegans* and mice. Infect Immun **70:**5647-50.

57. **Singh, K. V., R. J. Lewis, and B. E. Murray.** 2009. Importance of the *epa* locus of *Enterococcus faecalis* OG1RF in a mouse model of ascending urinary tract infection. J Infect Dis **200:**417-20.
58. **Smith, L. T.** 1996. Role of osmolytes in adaptation of osmotically stressed and chill-stressed *Listeria monocytogenes* grown in liquid media and on processed meat surfaces. Appl Environ Microbiol **62:**3088-93.
59. **Solheim, M., A. Aakra, L. G. Snipen, D. A. Brede, and I. F. Nes.** 2009. Comparative genomics of *Enterococcus faecalis* from healthy Norwegian infants. BMC Genomics **10:**194.
60. **Solheim, M., A. Aakra, H. Vebo, L. Snipen, and I. F. Nes.** 2007. Transcriptional responses of *Enterococcus faecalis* V583 to bovine bile and sodium dodecyl sulfate. Appl Environ Microbiol **73:**5767-74.
61. **Teng, F., K. D. Jacques-Palaz, G. M. Weinstock, and B. E. Murray.** 2002. Evidence that the enterococcal polysaccharide antigen gene (*epa*) cluster is widespread in *Enterococcus faecalis* and influences resistance to phagocytic killing of *E. faecalis*. Infect Immun **70:**2010-5.
62. **Teng, F., K. V. Singh, A. Bourgogne, J. Zeng, and B. E. Murray.** 2009. Further characterization of the *epa* gene cluster and Epa polysaccharides of *Enterococcus faecalis*. Infect Immun **77:**3759-67.
63. **Thurlow, L. R., V. C. Thomas, S. Narayanan, S. Olson, S. D. Fleming, and L. E. Hancock.** Gelatinase contributes to the pathogenesis of endocarditis caused by *Enterococcus faecalis*. Infect Immun.
64. **Trieu-Cuot, P., C. Carlier, C. Poyart-Salmeron, and P. Courvalin.** 1990. A pair of mobilizable shuttle vectors conferring resistance to spectinomycin for molecular cloning in *Escherichia coli* and in gram-positive bacteria. Nucleic Acids Res **18:**4296.
65. **Trotter, K. M., and G. M. Dunny.** 1990. Mutants of *Enterococcus faecalis* deficient as recipients in mating with donors carrying pheromone-inducible plasmids. Plasmid **24:**57-67.
66. **Vebo, H. C., M. Solheim, L. Snipen, I. F. Nes, and D. A. Brede.** Comparative genomic analysis of pathogenic and probiotic *Enterococcus faecalis* isolates, and their transcriptional responses to growth in human urine. PLoS One **5:**e12489.
67. **Verneuil, N., A. Rince, M. Sanguinetti, B. Posteraro, G. Fadda, Y. Auffray, A. Hartke, and J. C. Giard.** 2005. Contribution of a PerR-like regulator to the oxidative-stress response and virulence of *Enterococcus faecalis*. Microbiology **151:**3997-4004.
68. **Vilhelmsson, O., and K. J. Miller.** 2002. Synthesis of pyruvate dehydrogenase in *Staphylococcus aureus* is stimulated by osmotic stress. Appl Environ Microbiol **68:**2353-8.
69. **Wisplinghoff, H., T. Bischoff, S. M. Tallent, H. Seifert, R. P. Wenzel, and M. B. Edmond.** 2004. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis **39:**309-17.
70. **Xu, Y., B. E. Murray, and G. M. Weinstock.** 1998. A cluster of genes involved in polysaccharide biosynthesis from *Enterococcus faecalis* OG1RF. Infect Immun **66:**4313-23.

71. **Xu, Y., K. V. Singh, X. Qin, B. E. Murray, and G. M. Weinstock.** 2000. Analysis of a gene cluster of *Enterococcus faecalis* involved in polysaccharide biosynthesis. Infect Immun **68:**815-23.
72. **Aakra, A., O. L. Nyquist, L. Snipen, T. S. Reiersen, and I. F. Nes.** 2007. Survey of genomic diversity among *Enterococcus faecalis* strains by microarray-based comparative genomic hybridization. Appl Environ Microbiol **73:**2207-17.

Table 1. Bacterial strains and plasmids used in this study. Fus = fucidic acid, Km = kanamycin, r = resistance, Rif = rifampicin, Spe = spectinomycin, Str = streptomycin.

Strain or plasmid	Characteristic(s)	Reference
Strains		
E. faecalis		
V583		(53)
OG1RF	OG1 Rif^r Fus^r	(39)
TX5179	OG1RF *orfde4*::Km^r	(71)
TX5180	OG1RF *orfde6*::Km^r	(71)
INY3000	OG1 Str^r Spe^r::Tn916 (four copies)	(65)
Plasmids		
pCC1™		Epicentre
pAT28		(64)

Table 2. Primers used in this study.

Target gene/ primer name	Primer sequences (5' → 3')	Amplicon size (bp)	Application	Reference
ef0282	F. TGA TGG TTT CCT ATT AGC ACA AG R: GTT AGG AAT CGC ACG TTC GG	136	QPCR	This study
ef1211	F: AGT GAG CCG GAT GTA TTT GC R: TGT TTA CGA GCA TTC GTT GC	101	QPCR	(67)
ef2642	F: GTG CTG ATC GTG CTA TTA ACG R: AGT GGC ACA CCA ATG ATA ATG G	182	QPCR	This study
dnaB	F: TAG AAA TGG GGG CAG AAT CA R: ATT CGC ACG GGA CAA ACT AC	143	QPCR	(42)
ef2181	F:ACA CCA AAT CAG GCC AGA AG R: GGC GCT AAT TCA TCA TCG TT	499	PCR	This study
ef2182	F:AGG CGA GAT GAT TGG TTT TG R: TCA CAA AAA CGA CGA ATG GA	489	PCR	This study
ef2183	F: TAG GAA TTG TCT GGG CGT TT R:CAT TCC AGT TGG TTG CCA TA	497	PCR	This study
ef2184	F: TCT GTC TTC TGC TGG TCT GG R: TCA TAA TCA CAA TGC CGA CAA	305	PCR	This study
ef2189	F: CAA TAA TGT TTT AAT GCG ATT TTC GTG R: TGC TAC CAA CCG TGT TAT GG	302	PCR	This study
ef2190	F: TCG ACA GAT GGA ACC AAA CA R: CCA AGC CGT TCC ATC ATA TT	494	PCR	This study
ef2191	F: TGA TGC GGA TAG TAC GTT GG R: GGC GCT TTT TCT GCA ATA AC	498	PCR	This study
ef2192	F: TGC CGT AAA AAC AAT GTT CG R: TGC TCA TAG GCA TCA ACA GG	503	PCR	This study
ef2193	F: GGT GAT CAT CGT GGC TTT TT R: AAA CGG ATT TTC CGC TTC A	498	PCR	This study
ef2194	F: TGC CAA TTT ACG ACA AAC CA R: TCT GAC GGT TTG ATC CCT TT	496	PCR	This study
ef2195	F: ATT TTG CAT TTG CGC TTA CG R: CGT TGT TCC TTT AAA CGC TGA	502	PCR	This study
ef2196	F: TGG CTG ATA CGC CGA ATT AT R: TTC TTC CGA AAA TCC TTC CA	476	PCR	This study
ef2197	F: AAA GCC GAA CTG GGT ACT GA R: AAC CCA CCA ATT TCA ACG AA	509	PCR	This study
efaBpro-F *efaD-R*	F: GCA AGC ATT CTA AGA GAA AG R: GTA AAA GTT TAG CGT TGT TCC	2485[A]	Cloning	This study

[A] Product of efaBpro-F /efaD-R

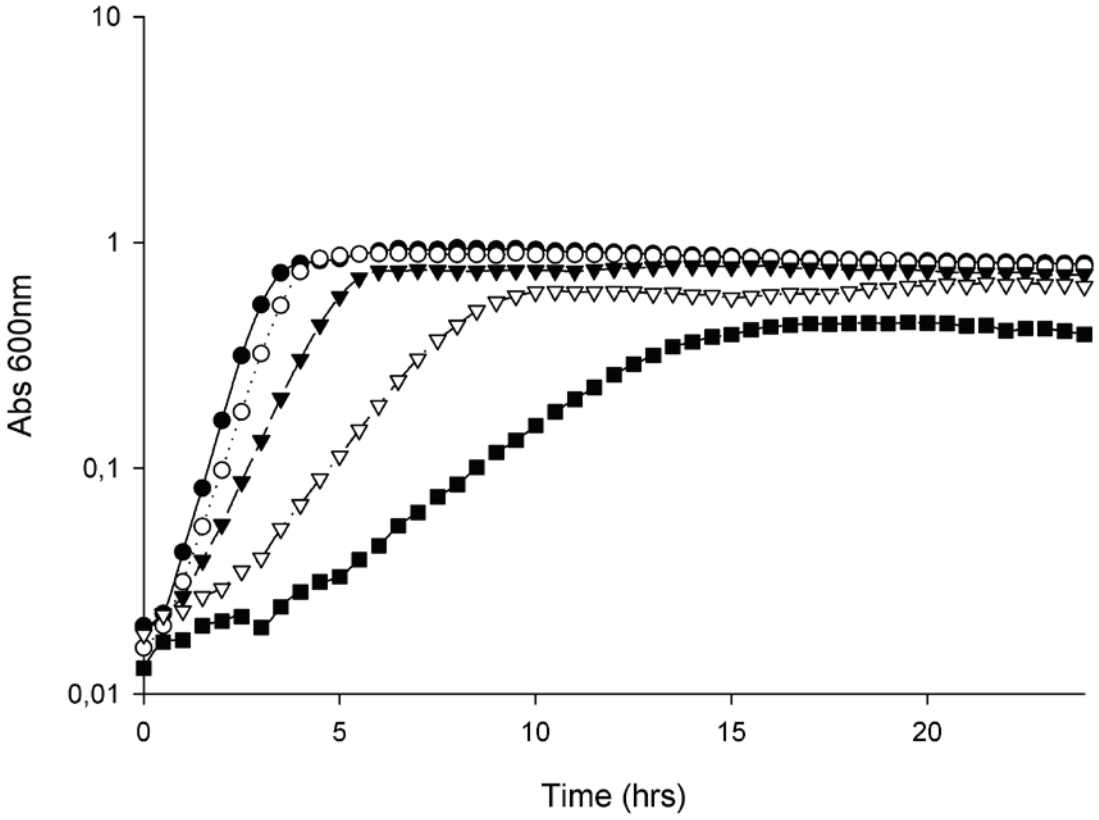


Figure 1. Growth of *E. faecalis* V583 treated with different concentrations of NaCl; untreated (●), 2 (○), 4 (▲), 6.5 (Δ) and 8 % (■).

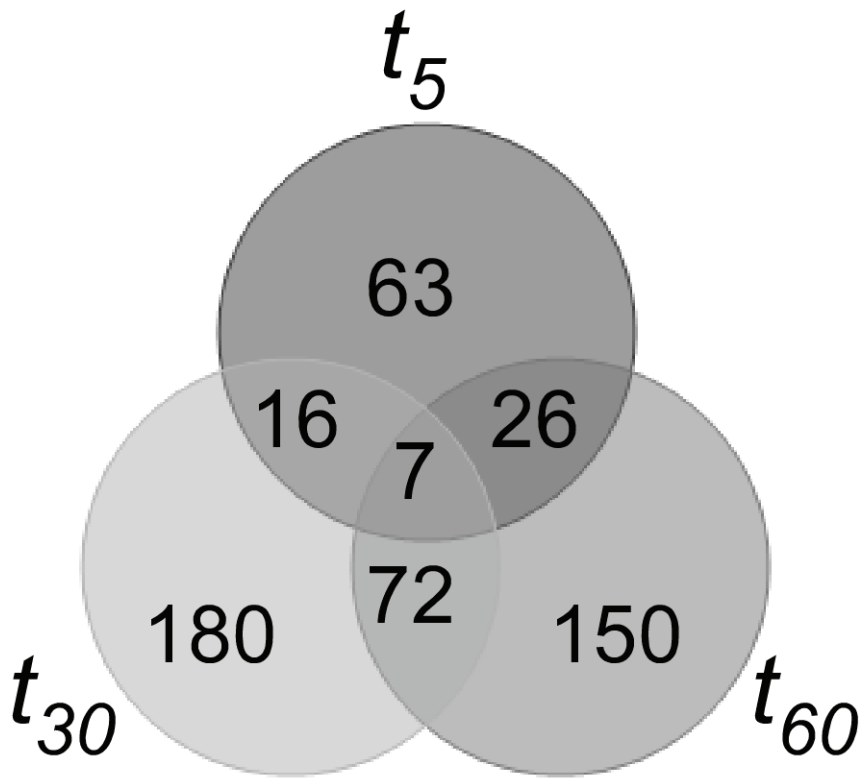


Figure 2. The distribution of differentially expressed genes in *E. faecalis* V583 during growth in NaCl. Venn diagram showing the number of unique and commonly regulated genes between the time points in the time course experiment.

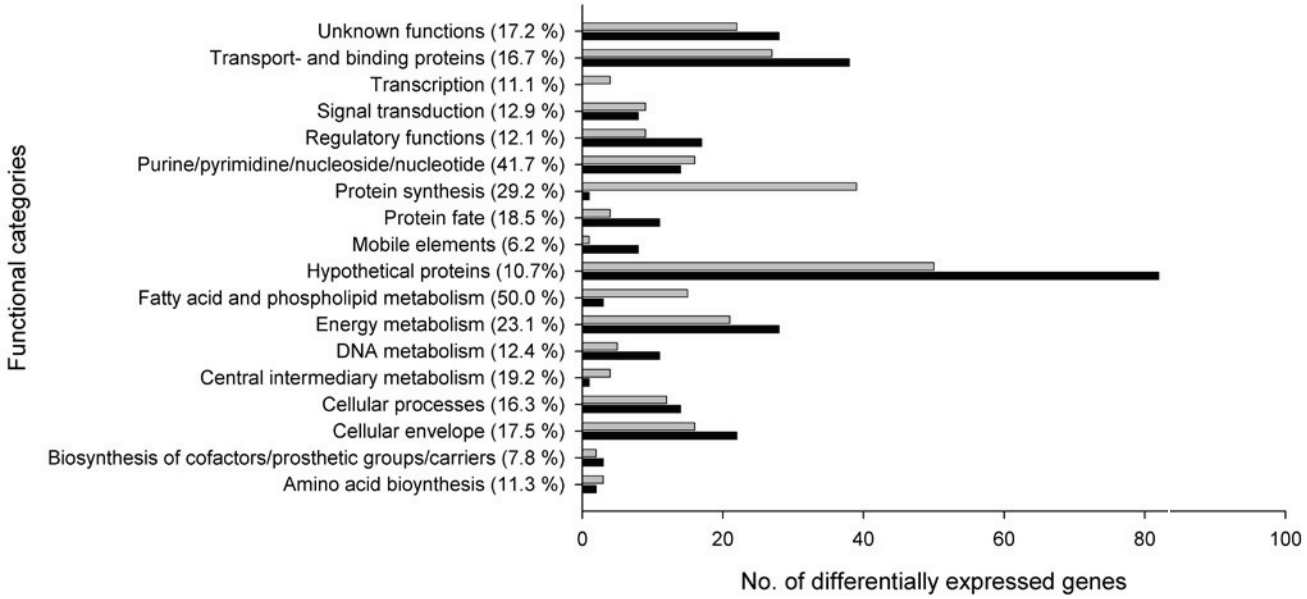


Figure 3. Differentially expressed genes in *E. faecalis* V583 during treatment with NaCl, grouped by functional classification according to the TIGR comprehensive microbial resource; CMR (http://cmr.tigr.org/tigr-scripts/CMR/CmrHomePage.cgi). Black bars refer to induced genes, and grey bars refer to repressed genes. Numbers in parenthesis represent the percentages of the total number of genes within each functional class in the genome. Genes that were both up- and down-regulated during the time course are counted twice.

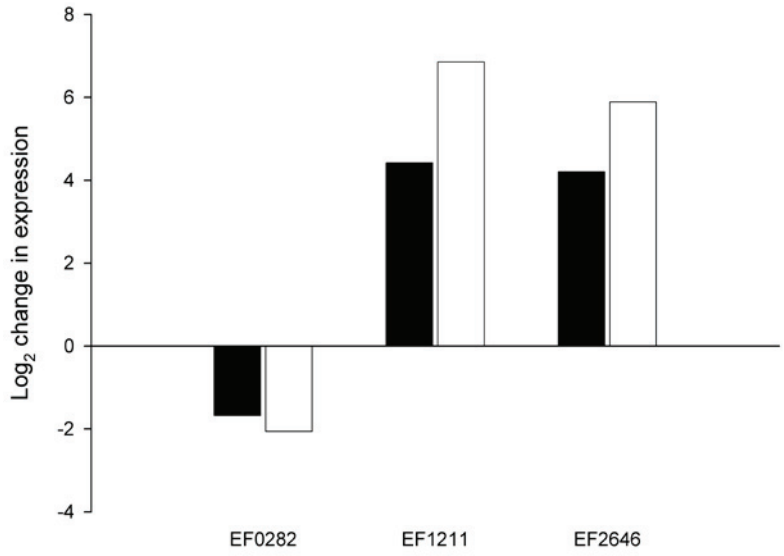


Figure 4. The effect of NaCl on the expression of EF0282, EF1211 and EF2642 as quantified by QPCR (□; Pfaffl method), and by microarray (■).

A

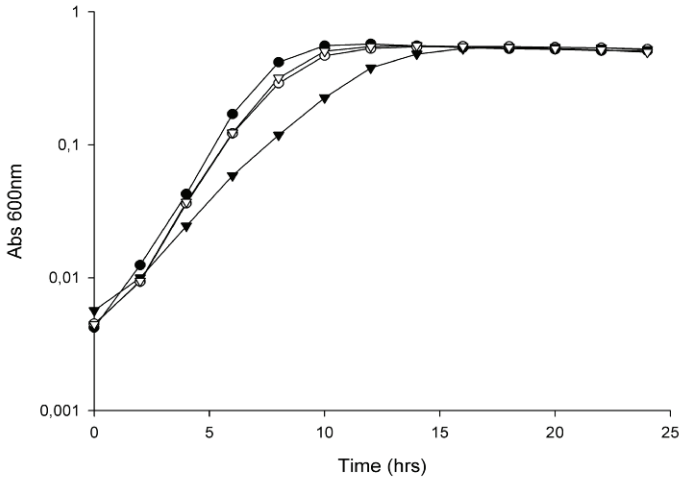
OG1RF

epaN epaM epaL epaK epaJ epaI epaH epaG epaF epaE epaD epaC epaB

INY3000

epaN epaM epaL epaK epaJ epaI epaH epaG epaF epaE epaD epaC epaB

B



C

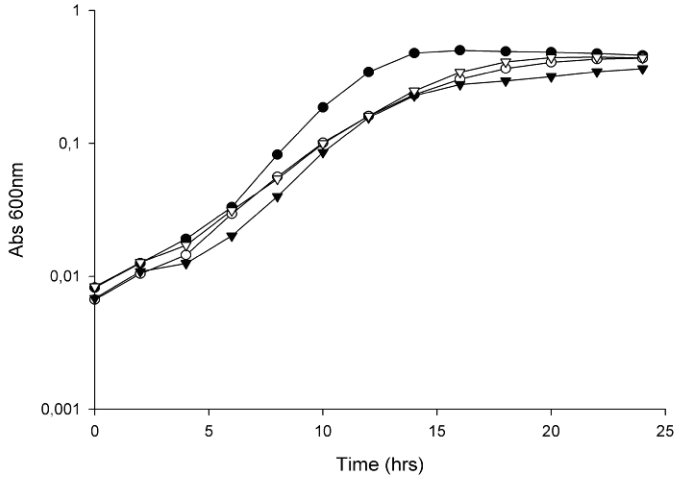


Figure 5. (A) PCR verification of the deletion of *orfde5_6-12* in *E. faecalis* INY3000 compared with *E. faecalis* OG1RF. (B) Growth of *E. faecalis* OG1RF (●), INY3000 (○), TX5179 (▲) and TX5180 (Δ) treated with 6.5 % NaCl. (C) Growth of *E. faecalis* OG1RF (●), INY3000 (○), TX5179 (▲) and TX5180 (Δ) treated with 8 % NaCl.

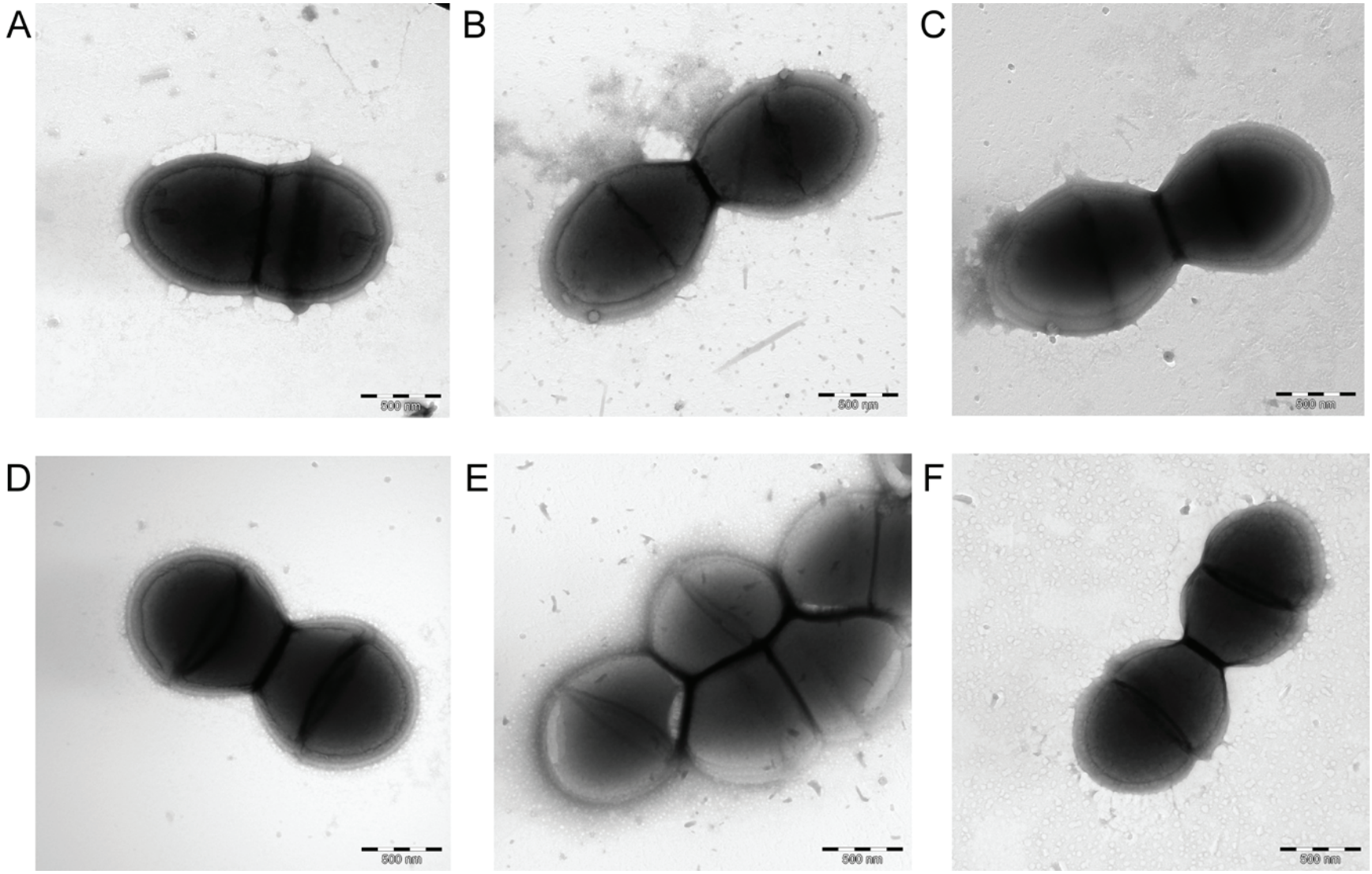

A
500 nm
B
500 nm
C
500 nm
D
500 nm
E
500 nm
F
500 nm

Figure 6: Transmission electron micrographs of *E. faecalis* strains V583 (A and D), OG1RF (B and E) and TX5179 (C and F) grown either in the absence (A-C) of in the presence (D-F) of 6.5 % NaCl.

Supplementary material

Table S1: Differentially expressed genes. Log_2 ratios of genes who were differentially expressed at one or more of the three time points at which the effect of NaCl treatment was studied, sorted by functional category (cellular role). Significant regulation is indicated in bold.

			Log_2-ratio at:		
Gene product	**Cellular role**	**ORF**	**T(0)**	**T(30)**	**T(60)**
Cystathionine gamma-synthase/cystathionine beta-lyase	Amino acid biosynthesis	EF0290	**0,90**	-0,21	0,85
Aspartate kinase	Amino acid biosynthesis	EF0368	0,81	**1,38**	0,27
Shikimate 5-dehydrogenase	Amino acid biosynthesis	EF1561	-0,02	-0,88	**-0,80**
Prephenate dehydrogenase	Amino acid biosynthesis	EF1565	0,42	**-1,34**	-0,55
Shikimate kinase	Amino acid biosynthesis	EF1567	0,31	**-1,29**	-0,21
Prephenate dehydratase	Amino acid biosynthesis	EF1568	0,12	**-1,22**	-0,38
Cysteine synthase A	Amino acid biosynthesis	EF1584	**-0,92**	-0,93	**1,43**
3-dehydroquinate dehydratase, type I	Amino acid biosynthesis	EF1731	-0,27	1,00	**0,95**
Serine hydroxymethyltransferase	Amino acid biosynthesis	EF2550	0,01	**-1,00**	0,00
4-diphosphocytidyl-2C-methyl-D-erythritol kinase	Biosynthesis of cofactors, prosthetic groups, and carriers	EF0051	0,72	**2,93**	0,05
Naphthoate synthase	Biosynthesis of cofactors, prosthetic groups, and carriers	EF0445	-0,45	-0,45	**1,09**
2-dehydropantoate 2-reductase, putative	Biosynthesis of cofactors, prosthetic groups, and carriers	EF0517	0,64	-0,73	**-0,97**
Hydroxymethylglutaryl-CoA synthase	Biosynthesis of cofactors, prosthetic groups, and carriers	EF1363	-0,25	-0,69	**-0,80**
Aspartate α-decarboxylase	Biosynthesis of cofactors, prosthetic groups, and carriers	EF1858	-0,11	-1,02	**-1,40**
Ferrochelatase	Biosynthesis of cofactors, prosthetic groups, and carriers	EF1989	0,38	0,77	**0,68**
HemK protein	Biosynthesis of cofactors, prosthetic groups, and carriers	EF2553	0,27	**-1,91**	-0,76
Cobyric acid synthase, putative	Biosynthesis of cofactors, prosthetic groups, and carriers	EF2586	-0,06	0,22	**0,68**
1,4-dihydroxy-2-naphthoate octaprenyltransferase, putative	Biosynthesis of cofactors, prosthetic groups, and carriers	EF3254	**1,38**	-0,34	-0,94
Membrane protein, putative	Cell envelope	EF0032	-0,13	**2,27**	**0,80**
Lipoprotein, putative	Cell envelope	EF0071	0,05	1,32	**1,45**
Basic membrane protein familiy	Cell envelope	EF0176	0,28	**-1,32**	-0,26
Basic membrane protein familiy	Cell envelope	EF0177	0,41	**-1,19**	-0,53
Membrane protein, putative	Cell envelope	EF0235	1,03	**1,11**	0,46
Lipoprotein, putative	Cell envelope	EF0304	0,23	-0,62	**-1,34**
Endolysin, putative	Cell envelope	EF0355	-0,52	-1,08	**-1,12**
Membrane protein, putative	Cell envelope	EF0516	0,59	**-1,58**	**-1,60**
Polysaccharide biosynthesis family protein	Cell envelope	EF0559	0,07	**2,15**	0,28
Membrane protein, putative	Cell envelope	EF0617	**1,12**	1,29	0,22
NAD-dependent epimerase/dehydratase family protein	Cell envelope	EF0646	0,59	**2,42**	0,21
Membrane protein, putative	Cell envelope	EF0673	-0,81	0,92	**1,16**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Membrane protein, putative	Cell envelope	EF0809	**-1,40**	0,87	**2,19**
Membrane protein, putative	Cell envelope	EF0860	0,24	**-2,45**	-0,68
Phospho-N-acetylmuramoyl-pentapeptide-transferase	Cell envelope	EF0992	**0,66**	0,19	-0,53
UDP-N-acetylmuramoyl-L-alanyl-D-glutamate synthetase	Cell envelope	EF0993	**1,05**	-0,05	-0,17
Lipoprotein, putative	Cell envelope	EF1677	-0,92	**1,87**	**2,84**
Lipoprotein, putative	Cell envelope	EF1796	**-1,00**	0,77	**1,77**
Coccolysin	Cell envelope	EF1818	-0,40	**-2,68**	**-4,55**
UDP-N-acetylmuramate--L-alanine ligase	Cell envelope	EF1908	0,14	**-1,61**	-0,13
Endocarditis specific antigen	Cell envelope	EF2076	-0,29	**2,54**	0,00
Lipoprotein, putative	Cell envelope	EF2144	-0,25	-0,82	**-0,79**
Membrane protein, putative	Cell envelope	EF2169	**0,80**	**-1,94**	-0,01
Membrane protein, putative	Cell envelope	EF2178	0,37	**-1,49**	-0,65
dTDP-glucose 4,6-dehydratase	Cell envelope	EF2192	0,42	**1,11**	0,37
Glucose-1-phosphate thymidylyltransferase	Cell envelope	EF2194	0,30	**0,98**	0,03
Glycosyl transferase, group 2 family protein	Cell envelope	EF2195	**0,69**	**1,60**	0,44
Glycosyl transferase, group 2 family protein	Cell envelope	EF2196	0,71	**1,72**	0,25
Glycosyl transferase, group 2 family protein	Cell envelope	EF2197	0,59	**1,90**	0,79
UDP-galactopyranose mutase	Cell envelope	EF2487	0,69	**-1,12**	**-1,30**
Glycosyl transferase, group 2 family protein	Cell envelope	EF2491	**1,27**	-0,54	**-1,14**
Glycosyl transferase, group 2 family protein	Cell envelope	EF2492	**0,78**	0,15	**-1,06**
Lipoprotein, putative	Cell envelope	EF2512	-0,57	**1,58**	0,06
FemAB family protein	Cell envelope	EF2658	0,28	-0,60	**-0,89**
Membrane protein, putative	Cell envelope	EF2708	**-1,43**	0,40	0,61
Cell wall surface anchor family protein	Cell envelope	EF2713	**-0,94**	0,16	-0,75
DltD protein	Cell envelope	EF2746	0,45	1,13	**-1,56**
Penicillin-binding protein 2B	Cell envelope	EF2857	**-1,01**	**1,89**	0,54
Glycosyl transferase, group 1 family protein	Cell envelope	EF2891	**1,08**	0,40	0,24
Glycosyl transferase, group 2 family protein	Cell envelope	EF2908	-0,41	**1,16**	0,50
Rod shape-determining protein MreD	Cell envelope	EF3061	-0,53	**1,45**	-0,01
Rod shape-determining protein MreC	Cell envelope	EF3062	**-0,68**	**0,94**	0,25
Lipoprotein, YaeC family	Cell envelope	EF3198	**-1,99**	**-1,56**	**0,98**
Thiamin biosynthesis lipoprotein ApbE, putative	Cell envelope	EF3255	**1,30**	-0,39	**-0,79**
Pheromone cAD1 precursor lipoprotein	Cell envelope	EF3256	**1,36**	0,00	**-1,28**
Gls24 protein	Cellular processes	EF0079	-1,02	-0,48	**1,91**
Gls24 protein	Cellular processes	EF0080	-0,92	-0,25	**3,21**
Regulatory protein pfoR, putative	Cellular processes	EF0097	**1,65**	0,07	**-1,76**
Superoxide dismutase, Mn	Cellular processes	EF0463	**-2,64**	0,22	1,17
Low temperature requirement C protein, putative	Cellular processes	EF0639	-0,70	0,59	**1,05**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Rhodanese family protein	Cellular processes	EF0748	**-1,78**	**-0,99**	0,30
Cold shock domain-contain protein	Cellular processes	EF0781	**-3,13**	**-1,33**	-0,20
Drug resistance transporter, EmrB/QacA family protein	Cellular processes	EF0785	**-0,94**	**-1,77**	-0,43
Drug resistance protein, putative	Cellular processes	EF1042	-0,82	0,16	**0,75**
Multidrug resistance protein, putative	Cellular processes	EF1078	0,68	-1,58	**-1,00**
Cold-shock domain-contain protein	Cellular processes	EF1367	-1,13	-0,79	**-1,67**
Catalase/peroxidase	Cellular processes	EF1597	**-1,16**	-0,82	0,67
ATP-dependent protease ATP-binding subunit	Cellular processes	EF1646	-0,07	0,65	**1,02**
Cell division ATP-binding protein FtsE	Cellular processes	EF1761	**0,39**	**1,08**	**0,72**
Cold shock protein CspC	Cellular processes	EF1991	**-3,46**	-0,55	-0,48
Multidrug resistance protein, putative	Cellular processes	EF2068	-0,84	**3,19**	0,28
Undecaprenyl pyrophosphate phosphatase	Cellular processes	EF2439	-0,32	-1,13	-0,75
Cell cycle protein FtsW	Cellular processes	EF2457	0,34	**1,57**	-0,19
Cell cycle protein FtsW	Cellular processes	EF2502	-0,52	**1,70**	-0,08
Adaptor protein	Cellular processes	EF2677	-0,53	0,10	**1,25**
Alkyl hydroperoxide reductase, C subunit	Cellular processes	EF2739	**1,08**	**1,29**	**1,03**
MarR family transcriptional regulator	Cellular processes	EF2886	-0,19	**-3,16**	**-2,06**
Large conductance mechanosensitive channel protein	Cellular processes	EF3152	**-1,03**	-0,63	0,96
Dps family protein	Cellular processes	EF3233	0,00	**2,96**	**1,96**
Abortive phage resistance protein, putative	Cellular processes	EF3241	0,64	**2,16**	0,58
Transcriptional regulator CtsR	Cellular processes	EF3283	**-1,30**	0,42	**1,42**
6-aminoglycoside N-acetyltransferase	Cellular processes	EFA0061	0,11	**-2,60**	**-2,13**
ParA family protein	Cellular processes	EFB0064	0,29	**1,59**	-0,23
Glucosamine-6-phosphate isomerase	Central intermediary metabolism	EF0466	-0,02	**1,14**	0,45
6-aminohexanoate-cyclic-dimer hydrolase, putative	Central intermediary metabolism	EF1033	**-1,18**	-0,10	0,37
Glyserol dehydrogenase, putative	Central intermediary metabolism	EF1358	**-1,11**	-0,43	**1,89**
Carbonic anhydrase, putative	Central intermediary metabolism	EF1711	**-1,32**	-0,83	0,84
D-fructose-6-phosphate amidotransferase	Central intermediary metabolism	EF2151	0,07	**-2,76**	**0,85**
Excinuclease ABC subunit B	DNA metabolism	EF0762	**-1,14**	-0,17	-0,04
DNA polymerase I	DNA metabolism	EF0878	**-0,88**	0,62	0,75
Uracil-DNA glycosylase	DNA metabolism	EF0948	0,65	0,85	**0,85**
DNA repair exonuclease family protein	DNA metabolism	EF0972	**-0,79**	**2,60**	-0,20
MutT/nudix family protein	DNA metabolism	EF1587	-0,25	**1,84**	0,17
Phage integrase family site specific recombinase	DNA metabolism	EF1648	-0,28	**1,27**	**1,10**
DNA topoisomerase I	DNA metabolism	EF1650	-0,20	**-2,35**	-0,21
Endonuclease IV	DNA metabolism	EF1736	**-0,85**	-0,87	**0,85**
Resolvase family site-specific recombinase	DNA metabolism	EF2283	0,24	**1,19**	**-0,98**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
TOPRIM domain-containing protein	DNA metabolism	EF2305	0,12	**1,72**	-0,27
Exonuclease SbcC	DNA metabolism	EF2689	0,25	**1,68**	0,46
Exonuclease SbcD	DNA metabolism	EF2690	0,00	**1,31**	0,32
A/G-specific adenine glycosylase	DNA metabolism	EF2704	-0,38	0,51	**0,87**
Phage integrase family site specific recombinase	DNA metabolism	EF2855	0,72	-1,84	**-1,91**
Competence/damage-inducible protein CinA	DNA metabolism	EF3172	**-1,10**	-0,05	**1,04**
ImpB/MucB/SamB family protein	DNA metabolism	EFA0078	NA	**2,67**	0,09
Single-strand binding protein	DNA metabolism	EFB0043	0,99	**2,00**	-0,45
Site-specific recombinase, resolvase family	DNA metabolism	EFC0009	**1,40**	**3,82**	0,26
L-serine dehydratase, iron-sulfur-dependent, beta subunit	Energy metabolism	EF0098	**1,90**	-0,56	**-1,78**
Arginine deiminase	Energy metabolism	EF0104	-0,07	0,78	**3,36**
NADH-dependent butanol dehydrogenase, putative	Energy metabolism	EF0194	-0,39	0,21	**2,31**
Ribose-5-phosphate isomerase A	Energy metabolism	EF0197	0,35	-0,10	**-1,08**
Maltose O-acetyltransferase, putative	Energy metabolism	EF0250	0,04	0,47	**0,81**
1-phosphofructokinase	Energy metabolism	EF0718	-0,23	**-1,06**	**0,99**
Methylglyoxal synthase	Energy metabolism	EF0939	**-1,47**	0,29	-0,03
Beta- phosphoglucomutase	Energy metabolism	EF0956	**-1,76**	-0,55	**2,16**
Glycosy hydrolase family protein	Energy metabolism	EF0957	-1,62	-0,75	**1,24**
Pyruvate kinase	Energy metabolism	EF1046	0,43	-1,15	**-0,81**
Iron-sulfur cluster binding protein	Energy metabolism	EF1109	0,60	1,16	**1,00**
Lactoylglutathione lyase	Energy metabolism	EF1140	**-1,64**	-1,29	**1,47**
NADH peroksidase	Energy metabolism	EF1211	-0,55	**2,39**	**4,42**
Alpha-acetolactate decarboxylase	Energy metabolism	EF1214	**-1,52**	**-1,78**	0,37
Glycosyl hydrolase family protein	Energy metabolism	EF1243	-0,20	-0,83	**0,94**
Thioredoxin reductase	Energy metabolism	EF1338	**-1,02**	**-1,74**	-0,18
Glucan 1,6-alpha-glucosidase, putative	Energy metabolism	EF1348	-0,88	-0,31	**2,28**
Glycosyl hydrolase family protein	Energy metabolism	EF1349	-1,14	-0,58	**2,42**
Pyruvate dehydrogenase complex E1 component, alpha subunit	Energy metabolism	EF1353	**-1,54**	-0,59	**1,44**
Pyruvate dehydrogenase complex E1 component, beta subunit	Energy metabolism	EF1354	**-1,44**	-0,67	**1,28**
Pyruvate dehydrogenase complex E2 component, dihydrolipoamide acetyltransferase	Energy metabolism	EF1355	**-1,55**	-1,03	**1,18**
Pyruvate dehydrogenase complex E3 component, dihydrolipoamide dehydrogenase	Energy metabolism	EF1356	**-1,67**	-0,82	**1,48**
V-type ATPase, subunit F	Energy metabolism	EF1492	-0,41	**2,83**	**1,33**
V-type ATPase, subunit I	Energy metabolism	EF1493	0,03	**2,85**	**1,64**
V-type ATPase, subunit K	Energy metabolism	EF1494	0,32	**3,14**	**1,74**
V-type ATPase, subunit C	Energy metabolism	EF1496	0,21	**3,21**	**2,05**
V-type ATPase, subunit G	Energy metabolism	EF1497	0,38	**2,83**	**1,79**
V-type ATPase, subunit A	Energy metabolism	EF1498	0,33	**3,10**	**1,76**
V-type ATPase, subunit B	Energy metabolism	EF1499	0,46	**3,35**	**2,52**
V-type ATPase, subunit D	Energy metabolism	EF1500	0,24	1,98	**1,53**
Ferredoxin	Energy metabolism	EF1543	**-0,96**	-0,54	0,33
NADH oxidase	Energy metabolism	EF1586	-1,81	**-2,05**	**1,66**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Pyruvate formate-lyase activating enzyme	Energy metabolism	EF1612	**1,09**	-0,47	-0,22
Glyserol-3-phosphate phosphate (NAD(P)+)	Energy metabolism	EF1747	0,11	**1,31**	0,44
Glyseraldehyde 3- phosphate dehydrogenases	Energy metabolism	EF1964	0,01	0,66	**1,13**
Cytochrome d ubiquinol oxidase, subunit I	Energy metabolism	EF2061	**-0,83**	-0,56	-0,47
Pyruvate carboxylase	Energy metabolism	EF2456	0,37	**1,51**	0,26
Fumarate reductase flavoprotein subunit precursor, putative	Energy metabolism	EF2556	0,65	**-1,40**	**-1,78**
ATP synthase F1, epsilon subunit	Energy metabolism	EF2607	0,19	**-1,56**	**-0,73**
ATP synthase F1, beta subunit	Energy metabolism	EF2608	0,34	**-1,21**	-0,34
ATP synthase F1, gamma subunit	Energy metabolism	EF2609	0,20	**-1,62**	-0,85
ATP synthase F1, alpha subunit	Energy metabolism	EF2610	0,27	**-1,66**	-0,60
ATP synthase F1, delta subunit	Energy metabolism	EF2611	0,33	**-1,55**	-0,43
ATP synthase F0, B subunit	Energy metabolism	EF2612	0,24	**-1,45**	-0,36
ATP synthase F0, C subunit	Energy metabolism	EF2613	0,46	**-1,54**	-0,29
ATP synthase F0, A subunit	Energy metabolism	EF2614	0,05	**-1,53**	-0,12
Sucrose-6-phosphate hydrolase	Energy metabolism	EFA0069	-0,06	0,38	**1,88**
Lipase/acylhydrolase	Fatty acid and phospholipid metabolism	EF0169	**-1,04**	0,73	1,20
Enoyl -(acyl-carrier-protein) reductase	Fatty acid and phospholipid metabolism	EF0282	-0,56	**-2,95**	**-1,67**
3-oxoacyl -(acyl-carrier-protein) reductase	Fatty acid and phospholipid metabolism	EF0283	-0,17	**-2,11**	**-2,44**
(3R)- -(acyl-carrier-protein) reductase	Fatty acid and phospholipid metabolism	EF0284	-0,23	**-1,99**	-1,93
Cardiolipin synthetase, putative	Fatty acid and phospholipid metabolism	EF0631	0,21	-0,28	**-0,91**
Short chain dehydrogenase	Fatty acid and phospholipid metabolism	EF1773	0,37	**1,47**	**1,02**
Glycerophosphoryl diester phosphodiesterase family protein	Fatty acid and phospholipid metabolism	EF1904	-0,43	**1,90**	-0,14
Acyl carrier protein, putative	Fatty acid and phospholipid metabolism	EF2601	0,16	-0,45	**-1,09**
Acetyl-CoA carboxylase, carboxyl transferase alpha subunit	Fatty acid and phospholipid metabolism	EF2875	0,04	**-2,24**	**-1,49**
Acetyl-CoA carboxylase, carboxyl transferase beta subunit	Fatty acid and phospholipid metabolism	EF2876	-0,03	**-2,58**	**-2,72**
Acetyl-CoA carboxylase, biotin carboxylase	Fatty acid and phospholipid metabolism	EF2877	-0,10	**-2,51**	**-2,34**
(3R)-hydroxymyristoyl-(acyl-carrier-protein) dehydratase	Fatty acid and phospholipid metabolism	EF2878	-0,18	**-2,31**	-1,97
Acetyl-CoA carboxylase, biotin carboxyl carrier protein	Fatty acid and phospholipid metabolism	EF2879	-0,28	-2,24	**-1,80**
3-oxoacyl-(acyl-carrier-protein) synthase II	Fatty acid and phospholipid metabolism	EF2880	0,31	**-1,94**	**-2,03**
Malonyl CoA-acyl carrier protein transacylase	Fatty acid and phospholipid metabolism	EF2882	0,21	**-2,47**	**-1,71**
Enoyl-(acyl-carrier-protein) reductase II	Fatty acid and phospholipid metabolism	EF2883	-0,08	**-3,35**	**-2,24**
Acyl-carrier-protein	Fatty acid and phospholipid metabolism	EF2884	-0,16	**-3,18**	**-2,84**
3-oxoacyl-(acyl-carrier-protein) synthase III	Fatty acid and phospholipid metabolism	EF2885	-0,39	**-3,68**	**-2,08**
Lipase, putative	Fatty acid and phospholipid	EF3191	**1,05**	0,64	0,35

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
	metabolism				
Hypothetical protein	Hypothetical protein	EF0083	-0,70	-0,81	**-1,73**
Hypothetical protein	Hypothetical protein	EF0183	0,69	**1,89**	0,65
Hypothetical protein	Hypothetical protein	EF0184	**1,05**	**2,45**	0,76
Hypothetical protein	Hypothetical protein	EF0248	0,18	-0,48	**-1,52**
Hypothetical protein	Hypothetical protein	EF0288	-0,59	**-1,30**	**-1,06**
Hypothetical protein	Hypothetical protein	EF0375	-0,13	**2,20**	**1,72**
Hypothetical protein	Hypothetical protein	EF0478	0,07	**-1,07**	-0,56
Hypothetical protein	Hypothetical protein	EF0610	**1,21**	0,23	-1,30
Hypothetical protein	Hypothetical protein	EF0637	**-0,92**	0,52	**1,42**
Hypothetical protein	Hypothetical protein	EF0652	NA	**1,76**	-0,01
Hypothetical protein	Hypothetical protein	EF0773	**-1,00**	**-0,89**	-0,48
Hypothetical protein	Hypothetical protein	EF0802	0,19	**3,94**	0,22
Hypothetical protein	Hypothetical protein	EF0925	**-0,88**	0,59	0,90
Hypothetical protein	Hypothetical protein	EF0953	**0,64**	0,32	-0,34
Hypothetical protein	Hypothetical protein	EF0959	**-1,47**	-0,42	**1,74**
Hypothetical protein	Hypothetical protein	EF0963	-0,20	0,61	**1,12**
Hypothetical protein	Hypothetical protein	EF1022	**-1,41**	-1,09	**1,22**
Hypothetical protein	Hypothetical protein	EF1107	0,62	**1,73**	**1,62**
Hypothetical protein	Hypothetical protein	EF1192	0,12	**-**0,89	**-1,43**
Hypothetical protein	Hypothetical protein	EF1248	**-1,61**	**-2,91**	**-0,89**
Hypothetical protein	Hypothetical protein	EF1258	0	**1,28**	0,18
Hypothetical protein	Hypothetical protein	EF1263	**0,82**	**1,89**	-0,33
Hypothetical protein	Hypothetical protein	EF1315	-0,08	-0,10	**-0,79**
Hypothetical protein	Hypothetical protein	EF1501	-0,03	1,32	**1,09**
Hypothetical protein	Hypothetical protein	EF1686	**-0,91**	0,93	-0,62
Hypothetical protein	Hypothetical protein	EF1734	-0,05	0,29	**- 1,03**
Hypothetical protein	Hypothetical protein	EF1735	**-1,10**	-0,33	0,64
Hypothetical protein	Hypothetical protein	EF1737	**-1,03**	-0,30	**1,24**
Hypothetical protein	Hypothetical protein	EF1853	0,1	**1,79**	0,86
Hypothetical protein	Hypothetical protein	EF1925	0,26	0,49	**-1,56**
Hypothetical protein	Hypothetical protein	EF1933	**-1,16**	0,35	**1,57**
Hypothetical protein	Hypothetical protein	EF1936	-0,56	**-1,45**	**-1,45**
Hypothetical protein	Hypothetical protein	EF1944	-1,07	0,09	**1,79**
Hypothetical protein	Hypothetical protein	EF2019	0,23	0,14	**-1,95**
Hypothetical protein	Hypothetical protein	EF2308	-0,22	**2,08**	0,66
Hypothetical protein	Hypothetical protein	EF2309	-0,32	**1,60**	0,34
Hypothetical protein	Hypothetical protein	EF2342	0,02	**1,67**	-0,14
Hypothetical protein	Hypothetical protein	EF2405	0,18	-0,79	**-0,71**
Hypothetical protein	Hypothetical protein	EF2427	-0,05	**1,38**	-0,05
Hypothetical protein	Hypothetical protein	EF2465	0,08	**2,66**	0,09
Hypothetical protein	Hypothetical protein	EF2547	**-1,42**	**3,11**	**1,17**
Hypothetical protein	Hypothetical protein	EF2615	-0,12	**-1,78**	**-1,21**
Hypothetical protein	Hypothetical protein	EF2702	**-1,36**	0,46	0,98
Hypothetical protein	Hypothetical protein	EF2796	0,60	**2,09**	**2,03**
Hypothetical protein	Hypothetical protein	EF2893	**-0,79**	1,10	-0,11
Hypothetical protein	Hypothetical protein	EF2896	-0,45	**1,86**	-0,01
Hypothetical protein	Hypothetical protein	EF2950	0,28	**1,89**	0,23
Hypothetical protein	Hypothetical protein	EF2952	0,20	**1,24**	-0,18
Hypothetical protein	Hypothetical protein	EF2953	0,16	**1,83**	0,36
Hypothetical protein	Hypothetical protein	EF3039	-0,22	0,94	**1,13**
Hypothetical protein	Hypothetical protein	EF3287	**-2,1**	**-1,51**	**-2,56**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Hypothetical protein	Hypothetical protein	EFA0017	-0,68	**1,37**	0,49
Hypothetical protein	Hypothetical protein	EFA0075	**1,07**	**4,08**	-0,36
Hypothetical protein	Hypothetical protein	EFC0012	0,82	**2,39**	0,17
Hypothetical protein	Hypothetical protein	EFC0014	NA	**2,40**	-0,47
Hypothetical protein	Hypothetical protein	EFC0016	0,14	0,73	-0,07
Hypothetical protein	Hypothetical protein	EFC0017	-0,13	**2,28**	-1,09
Conserved hypothetical protein	Hypothtical protein - conserved	EF0003	-0,45	**2,06**	0,58
Conserved hypothetical protein	Hypothtical protein - conserved	EF0024	-0,50	**-1,96**	-1,17
Conserved hypothetical protein	Hypothtical protein - conserved	EF0050	-0,68	**3,29**	-0,73
Conserved hypothetical protein	Hypothtical protein - conserved	EF0077	**-0,91**	0,17	**3,11**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0078	-0,80	0,36	**3,75**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0081	-0,74	0,23	**1,85**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0091	-0,56	-0,59	**0,91**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0127	**-0,59**	0,04	**-1,18**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0170	-0,36	1,10	**1,21**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0241	**-0,95**	0,24	**1,07**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0397	-0,38	0,99	**1,23**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0400	**0,73**	-1,49	-1,80
Conserved hypothetical protein	Hypothtical protein - conserved	EF0546	**0,95**	**-0,99**	**-0,51**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0667	**-1,25**	0,05	**1,07**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0766	-0,10	**1,10**	0,22
Conserved hypothetical protein	Hypothtical protein - conserved	EF0770	-0,74	0,09	**1,23**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0774	-0,28	**1,05**	0,39
Conserved hypothetical protein	Hypothtical protein - conserved	EF0819	NA	**2,80**	0,42
Conserved hypothetical protein	Hypothtical protein - conserved	EF0857	-0,22	-0,78	**-1,45**
Conserved hypothetical protein TIGR00244	Hypothtical protein - conserved	EF0881	-0,33	**1,12**	0,42
Conserved hypothetical protein	Hypothtical protein - conserved	EF0906	0,44	**2,03**	**1,67**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0908	0,43	**1,87**	0,64
Conserved hypothetical protein	Hypothtical protein - conserved	EF0937	0,83	**1,98**	0,77
Conserved hypothetical protein	Hypothtical protein - conserved	EF0940	0,03	**-1,03**	**-2,02**
Conserved hypothetical protein	Hypothtical protein - conserved	EF0971	**-1,00**	-0,51	-0,12
Conserved hypothetical protein	Hypothtical protein -	EF0988	-0,22	**1,35**	0,21

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
TIGR00242	conserved				
Conserved hypothetical protein	Hypothtical protein - conserved	EF1021	-0,48	1,29	**1,86**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1023	0,33	-0,40	**-1,19**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1047	-0,26	**-1,83**	-0,70
Conserved hypothetical protein	Hypothtical protein - conserved	EF1145	-0,60	**-1,08**	0,19
Conserved hypothetical protein	Hypothtical protein - conserved	EF1150	**-0,96**	0,80	**1,39**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1180	-1,26	0,82	**2,47**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1190	**-0,85**	**-1,79**	**-1,34**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1227	0,98	-0,62	**-1,08**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1247	**-2,65**	**-2,22**	-0,27
Conserved hypothetical protein	Hypothtical protein - conserved	EF1311	0,34	**1,24**	0,15
Conserved hypothetical protein	Hypothtical protein - conserved	EF1313	-0,36	-0,19	-0,40
Conserved hypothetical protein	Hypothtical protein - conserved	EF1368	-0,59	1,22	**2,54**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1371	-0,54	**1,17**	0,35
Conserved hypothetical protein	Hypothtical protein - conserved	EF1376	0,26	**-1,16**	0,24
Conserved hypothetical protein	Hypothtical protein - conserved	EF1419	0,27	**-1,23**	**-0,90**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1505	**-0,98**	-1,03	0,25
Conserved hypothetical protein	Hypothtical protein - conserved	EF1518	**-1,87**	0,61	0,45
Conserved hypothetical protein	Hypothetical protein - conserved	EF1609	**-0,98**	-0,49	0,52
Conserved hypothetical protein	Hypothtical protein - conserved	EF1664	-0,09	1,07	**1,10**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1702	-0,21	**2,15**	0,55
Conserved hypothetical protein	Hypothtical protein - conserved	EF1738	**-1,12**	-0,05	**2,41**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1745	-0,23	**1,24**	**0,84**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1792	0,14	**1,65**	0,76
Conserved hypothetical protein	Hypothtical protein - conserved	EF1794	-0,81	1,64	**2,40**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1797	0,21	0,70	**-0,97**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1903	**-1,16**	**2,19**	0,08
Conserved hypothetical protein	Hypothtical protein - conserved	EF1918	-0,25	0,84	**0,78**
Conserved hypothetical protein	Hypothtical protein - conserved	EF1926	0,42	0,75	**-1,22**
Conserved hypothetical protein	Hypothtical protein -	EF1949	**-2,03**	-0,69	0,30

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
	conserved				
Conserved hypothetical protein	Hypothtical protein - conserved	EF1968	**0,88**	-0,78	**-0,66**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2018	**1,46**	1,15	NA
Conserved domain protein	Hypothtical protein - conserved	EF2022	0,63	**1,62**	-0,23
Conserved hypothetical protein TIGR00048	Hypothtical protein - conserved	EF2048	**0,89**	-0,98	**-2,14**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2065	**-1,70**	-1,27	-0,56
Conserved hypothetical protein TIGR00481	Hypothtical protein - conserved	EF2067	NA	**4,72**	0,98
Conserved hypothetical protein	Hypothtical protein - conserved	EF2179	0,37	**-1,91**	-0,79
Conserved hypothetical protein	Hypothtical protein - conserved	EF2215	**-1,13**	0,89	**1,74**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2281	**0,99**	**1,88**	-0,29
Conserved hypothetical protein	Hypothtical protein - conserved	EF2303	0,13	**1,16**	-0,31
Conserved hypothetical protein	Hypothtical protein - conserved	EF2306	-0,01	**1,32**	-0,33
Conserved hypothetical protein	Hypothtical protein - conserved	EF2390	0,04	0,57	**0,85**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2454	0,49	**1,26**	-0,11
Conserved hypothetical protein	Hypothtical protein - conserved	EF2480	-0,03	0,28	**-1,15**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2490	**0,87**	**-0,94**	**-1,32**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2507	0,25	**2,33**	**1,10**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2588	0,46	0,01	**-1,16**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2602	-0,13	**1,90**	0,98
Conserved hypothetical protein	Hypothtical protein - conserved	EF2621	-0,11	1,13	**1,82**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2622	-0,31	0,81	**2,33**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2672	**-1,74**	-1,41	**1,16**
Conserved domain protein	Hypothtical protein - conserved	EF2673	**-1,83**	**-2,18**	1,05
Conserved hypothetical protein	Hypothtical protein - conserved	EF2678	-0,07	**0,96**	-0,67
Conserved domain protein	Hypothtical protein - conserved	EF2697	-0,44	**2,50**	0,35
Conserved hypothetical protein	Hypothtical protein - conserved	EF2742	**-0,98**	-0,57	0,63
Conserved hypothetical protein	Hypothtical protein - conserved	EF2771	-0,57	**1,89**	1,02
Conserved hypothetical protein	Hypothtical protein - conserved	EF2786	-0,32	**1,15**	**0,95**
Conserved hypothetical protein	Hypothtical protein - conserved	EF2793	-0,20	-1,03	**-1,31**
Conserved hypothetical protein	Hypothtical protein -	EF2909	**-1,11**	0,05	0,54

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
	conserved				
Conserved hypothetical protein	Hypothtical protein - conserved	EF2930	0,19	**1,49**	0,39
Conserved hypothetical protein	Hypothtical protein - conserved	EF3021	**-1,38**	-0,12	0,22
Conserved hypothetical protein	Hypothtical protein - conserved	EF3055	**-1,64**	-1,32	-0,73
Conserved hypothetical protein	Hypothtical protein - conserved	EF3151	**-0,90**	0,94	0,45
Conserved hypothetical protein	Hypothtical protein - conserved	EF3155	-0,03	**1,17**	-0,17
Conserved hypothetical protein	Hypothtical protein - conserved	EF3177	**-1,07**	-0,43	0,23
Conserved domain protein	Hypothtical protein - conserved	EF3259	**0,89**	-0,16	-0,42
Conserved domain	Hypothtical protein - conserved	EF3303	NA	1,87	**2,15**
Conserved domain protein	Hypothtical protein - conserved	EFA0074	0,97	**3,61**	0,08
Structural protein, putative	Mobile and extrachromosomal element functions	EF0351	-0,12	**-1,59**	-0,97
Transposase, putative	Mobile and extrachromosomal element functions	EF0913	0,81	**1,39**	0,33
Transposase, IS256 family	Mobile and extrachromosomal element functions	EF1855	**1,05**	0,77	-0,38
Terminase, large subunit, putative	Mobile and extrachromosomal element functions	EF2017	**1,25**	0,59	-0,17
Pheromone shutdown protein TraB	Mobile and extrachromosomal element functions	EFA0002	0,27	**1,06**	0,62
Replication protein	Mobile and extrachromosomal element functions	EFA0012	0,32	-0,56	**-0,94**
Transposase, IS6 family	Mobile and extrachromosomal element functions	EFA0016	0,45	**1,72**	0,21
PemK family protein	Mobile and extrachromosomal element functions	EFA0071	-0,87	**2,89**	-0,39
Replication-associated protein RepC	Mobile and extrachromosomal element functions	EFA0082	**1,43**	**1,48**	-0,24
Replication-associated protein RepB	Mobile and extrachromosomal element functions	EFA0083	**2,13**	**2,79**	0,10
Replication-associated protein RepB	Mobile and extrachromosomal element functions	EFC0018	-0,42	**1,67**	**-1,03**
RepS protein, putative	Mobile and extrachromosomal element functions	EFC0019	0,43	0,99	**0,86**
Ribosomal protein S6	Protein synthesis	EF0007	0,14	0,19	**-1,26**
Seryl-tRNA synthetase	Protein synthesis	EF0100	1,18	-1,14	**-1,27**
Ribosomal protein S12	Protein synthesis	EF0198	0,21	-0,35	**-1,53**
Ribosomal protein S7	Protein synthesis	EF0199	0,07	0,22	**-0,86**
Translation elongation factor G	Protein synthesis	EF0200	0,08	-0,60	**-1,48**
Ribosomal protein S10	Protein synthesis	EF0205	-0,16	**-1,83**	**-1,72**
Ribosomal protein L23	Protein synthesis	EF0208	0,42	-0,53	**-1,76**
Ribosomal protein L2	Protein synthesis	EF0209	-0,07	-0,39	**-0,84**
Ribosomal protein S19	Protein synthesis	EF0210	-0,02	-0,70	**-1,30**
Ribosomal protein L22	Protein synthesis	EF0211	-0,03	-0,23	**-0,91**
Ribosomal protein L16	Protein synthesis	EF0213	0,24	-0,54	**-1,27**
Ribosomal protein L29	Protein synthesis	EF0214	0,55	-0,25	**-2,05**
Ribosomal protein S17	Protein synthesis	EF0215	-0,06	-0,61	**-1,98**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Ribosomal protein L24	Protein synthesis	EF0217	-0,12	-0,15	**-1,48**
Ribosomal protein L5	Protein synthesis	EF0218	0,05	-0,32	**-1,56**
Ribosomal protein S8	Protein synthesis	EF0220	-0,02	-0,27	**-2,12**
Ribosomal protein L6	Protein synthesis	EF0221	-0,03	-0,28	**-1,03**
Ribosomal protein L18	Protein synthesis	EF0223	0,12	0,01	**-1,58**
Ribosomal protein S5	Protein synthesis	EF0224	0,15	-0,25	**-1,90**
Ribosomal protein L30	Protein synthesis	EF0225	-0,05	0,02	**-1,99**
Ribosomal protein L15	Protein synthesis	EF0226	0,12	0,07	**-1,97**
Translation initiation factor IF-1	Protein synthesis	EF0229	-0,20	**-0,66**	**-1,68**
Ribosomal protein L36	Protein synthesis	EF0230	0,00	**-1,21**	**-2,26**
Ribosomal protein	Protein synthesis	EF0231	0,02	-0,52	**-1,46**
Ribosomal protein S11	Protein synthesis	EF0232	-0,01	-0,40	**-0,84**
Ribosomal protein L17	Protein synthesis	EF0234	-0,18	**-0,99**	**-2,08**
Tyrosyl-tRNA synthetase	Protein synthesis	EF0633	**1,00**	-0,66	**-0,68**
Ribosomal protein L25	Protein synthesis	EF0820	-0,34	**3,12**	1,14
Translation initiation factor IF-3	Protein synthesis	EF0914	-0,11	0,25	**-1,60**
Ribosomal protein L35	Protein synthesis	EF0915	-0,03	0,46	**-2,62**
Ribosomal protein L20	Protein synthesis	EF0916	-0,09	0,33	**-2,84**
Ribosomal protein L27	Protein synthesis	EF0970	-0,14	-0,12	**-0,73**
Ribosomal protein L32	Protein synthesis	EF1048	-0,45	**-1,45**	-0,79
Phenylalanyl-tRNA synthetase, alpha subunit	Protein synthesis	EF1115	0,00	**-1,62**	-0,28
Ribosomal protein L31	Protein synthesis	EF1171	-0,05	-0,11	**-1,32**
Ribosomal protein S16	Protein synthesis	EF1694	-0,13	-0,68	**-2,39**
Ribosome recycling faktor	Protein synthesis	EF2395	0,19	-0,68	**-1,40**
Translation elongation factor Ts	Protein synthesis	EF2397	-0,35	-0,92	**-1,30**
Ribosomal protein S2	Protein synthesis	EF2398	-0,08	-0,87	**-1,03**
Ribosomal protein S20	Protein synthesis	EF2443	-0,53	**-1,83**	**-1,68**
Peptide chain release factor 1	Protein synthesis	EF2554	0,11	**-1,57**	**-1,00**
Ribosomal protein L7/L12	Protein synthesis	EF2715	-0,24	-0,27	**-2,29**
Ribosomal protein L10	Protein synthesis	EF2716	-0,04	-0,61	**-1,50**
Ribosomal protein L1	Protein synthesis	EF2718	0,27	0,03	**-1,00**
Ribosomal protein L11	Protein synthesis	EF2719	-0,21	-0,37	**-1,24**
Ribosomal protein L33	Protein synthesis	EF2731	**-1,05**	-0,86	-0,68
Ribosomal protein S4	Protein synthesis	EF3070	-0,27	-0,68	**-1,27**
Ribosomal protein L28	Protein synthesis	EF3116	-0,43	**-1,42**	**-1,56**
Ribosomal protein S9	Protein synthesis	EF3230	-0,13	-0,73	**-1,45**
Ribosomal protein L34	Protein synthesis	EF3333	-0,39	**-2,09**	**-1,54**
Chaperonin, 33 kDa	Protein fate	EF0266	-0,36	**-1,48**	0,25
Aminopeptidase C	Protein fate	EF0302	-0,03	0,27	**1,11**
Lipoate-protein ligase A	Protein fate	EF0650	**-1,07**	-0,18	0,07
ATP-dependent Clp protease, ATP-binding subunit ClpE	Protein fate	EF0706	-0,29	**1,31**	**1,76**
Trigger factor	Protein fate	EF0715	-0,33	**-0,85**	-0,66
Proline dipeptidase	Protein fate	EF0973	0,23	**1,55**	0,68
Lipoate-protein ligase A family protein, putativ	Protein fate	EF1144	**-0,93**	-0,10	0,07
Heat shock protein GrpE	Protein fate	EF1307	**1,21**	**1,89**	0,07
DnaK protein	Protein fate	EF1308	**1,34**	**2,30**	-0,07
DnaJ protein	Protein fate	EF1310	0,90	0,93	0,02
Heat shock protein HslV	Protein fate	EF1647	-0,09	1,83	**0,88**
Prolipoprotein diacylglyceryl transferase	Protein fate	EF1748	0,22	**1,44**	0,75

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Serine proteinase, V8 family	Protein fate	EF1817	-0,01	**-1,82**	**-4,43**
Chaperonin, 10 kDa	Protein fate	EF2634	**1,24**	1,05	0,93
Oligoendopeptidase F,plasmid	Protein fate	EF2674	0,29	0,32	**1,04**
Lipoate-protein ligase A	Protein fate	EF2741	**-0,93**	-0,80	**1,22**
Peptidyl-prolyl cis-trans isomerase, cyclophilin-type	Protein fate	EF2898	-0,20	0,20	**1,12**
Signal peptidase I	Protein fate	EF3073	0,52	**1,54**	1,03
Peptidase, M16 family	Protein fate	EF3150	-0,47	1,13	**0,81**
Peptidase, M20/M25/M40 family	Protein fate	EF3178	-0,26	0,84	**0,99**
Peptidase, U32 family	Protein fate	EF3279	**0,67**	-0,09	0,22
ATP-dependent Clp protease, ATP-binding subunit ClpC	Protein fate	EF3282	**-1,19**	-0,01	0,67
Adenylosuccinate synthetase	Purines, pyrimidines, nucleosides, and nucleotides	EF0014	0,15	**-2,35**	**-1,95**
Pur operon repressor PurR	Purines, pyrimidines, nucleosides, and nucleotides	EF0058	0,28	**-2,22**	**-2,11**
Adenosine deaminase	Purines, pyrimidines, nucleosides, and nucleotides	EF0171	0,33	**2,11**	**1,58**
Pyrimidin-nukleoside phosphorylase	Purines, pyrimidines, nucleosides, and nucleotides	EF0173	**1,19**	-0,04	-0,10
Cytidine deaminase	Purines, pyrimidines, nucleosides, and nucleotides	EF0175	**0,79**	-1,01	-0,50
Phosphopentomutase	Purines, pyrimidines, nucleosides, and nucleotides	EF0185	-0,22	**1,42**	1,13
Purine nucleoside phosphorylase	Purines, pyrimidines, nucleosides, and nucleotides	EF0186	-0,22	**0,91**	0,57
Adenylate kinase	Purines, pyrimidines, nucleosides, and nucleotides	EF0228	0,21	-0,52	**-1,82**
Hypoxanthine-guanine phosphoribosyltransferase	Purines, pyrimidines, nucleosides, and nucleotides	EF0264	0,17	0,77	**0,99**
Dihydroorotate dehydrogenase	Purines, pyrimidines, nucleosides, and nucleotides	EF0285	0,12	**-0,86**	-0,24
Ribonucleoside-diphosphate reductase 2, alpha subunit	Purines, pyrimidines, nucleosides, and nucleotides	EF0471	0,00	-0,04	**1,26**
nrdI protein	Purines, pyrimidines, nucleosides, and nucleotides	EF0472	0,00	-0,02	**1,17**
Nucleoside diphosphate kinase	Purines, pyrimidines, nucleosides, and nucleotides	EF1036	-0,03	0,55	**1,41**
CTP synthase	Purines, pyrimidines, nucleosides, and nucleotides	EF1147	0,10	**-2,07**	-0,63
Adenine phosphoribosyltransferase	Purines, pyrimidines, nucleosides, and nucleotides	EF1687	0,12	**-1,94**	**-1,39**
Orotate phosphoribosyltransferase	Purines, pyrimidines, nucleosides, and nucleotides	EF1712	0,04	-0,69	**-2,30**
Orotidine 5`- phosphate decarboxylase	Purines, pyrimidines, nucleosides, and nucleotides	EF1713	0,29	-1,07	**-2,53**
Dihydroorotate dehydrogenase	Purines, pyrimidines, nucleosides, and nucleotides	EF1714	0,43	**-0,81**	**-2,82**
Dihydroorotate dehydrogenase electron transfer subunit	Purines, pyrimidines, nucleosides, and nucleotides	EF1715	0,49	**-0,70**	**-3,30**
Carbamoyl-phosphate synthase, large subunit	Purines, pyrimidines, nucleosides, and nucleotides	EF1716	1,04	-0,10	**-2,27**
carbamoyl-phosphate synthase, small subunit	Purines, pyrimidines, nucleosides, and nucleotides	EF1717	**1,17**	0,42	**-2,62**
Dihydroorotase	Purines, pyrimidines, nucleosides, and nucleotides	EF1718	**1,20**	0,71	-1,56
Aspartate carbamoyltransferase	Purines, pyrimidines,	EF1719	**1,45**	0,91	**-2,23**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
	nucleosides, and nucleotides				
Pyrimidin operon regulatory protein PyrR	Purines, pyrimidines, nucleosides, and nucleotides	EF1721	**1,37**	1,04	**-3,23**
Phosphoribosylaminoimidazole-succinocarboxamide synthase	Purines, pyrimidines, nucleosides, and nucleotides	EF1785	0,50	-0,64	**-3,71**
Deoxyguanosinetriphosphate triphosphohydrolase, putative	Purines, pyrimidines, nucleosides, and nucleotides	EF1958	0,92	-0,54	**-4,22**
Phosphoribosylaminoimidazole carboxylase, ATPase subunit	Purines, pyrimidines, nucleosides, and nucleotides	EF2362	0,55	**1,20**	0,53
Uridylate kinase	Purines, pyrimidines, nucleosides, and nucleotides	EF2396	0,39	-0,44	**-1,18**
Inosine-uridine preferring nucleoside hydrolase	Purines, pyrimidines, nucleosides, and nucleotides	EF2587	0,23	-0,11	**-0,96**
Guanylate kinase	Purines, pyrimidines, nucleosides, and nucleotides	EF2595	-0,30	**1,59**	0,22
Anaerobic ribonucleoside-triphosphate reductase	Purines, pyrimidines, nucleosides, and nucleotides	EF2754	**1,05**	1,28	**1,23**
Anaerobic ribonucleoside-triphosphate reductase activating protein	Purines, pyrimidines, nucleosides, and nucleotides	EF2755	**1,21**	1,02	**1,62**
Transcriptional regulator, ArgR family	Regulatory functions	EF0103	-1,54	-0,07	**1,16**
Transcriptional regulator, Crp/Fnr family	Regulatory functions	EF0107	-0,35	0,39	**2,67**
Transcriptional repressor CopY	Regulatory functions	EF0297	-0,18	**1,85**	0,55
Transcriptional regulator, DeoR family	Regulatory functions	EF0719	-0,16	-1,18	**0,84**
DNA-binding response regulator	Regulatory functions	EF1050	-0,09	**-2,15**	**-0,87**
Sensory box histidine kinase VicK	Regulatory functions	EF1194	-0,27	**1,19**	**0,60**
Sugar-binding transcriptional regulator, LacI family	Regulatory functions	EF1240	0,40	**1,38**	0,69
Heat-inducible transcription repressor HrcA	Regulatory functions	EF1306	**1,24**	**2,07**	-0,08
Transcriptional regulator, Fur family	Regulatory functions	EF1585	-0,40	**-1,85**	0,08
Protease synthase and sporulation negative regulatory protein pai 1, putative	Regulatory functions	EF1590	-0,72	-1,34	**0,89**
Sucrose operon repressor ScrR	Regulatory functions	EF1604	-0,23	0,87	**0,94**
Transcriptional regulator CodY	Regulatory functions	EF1645	-0,13	0,50	**0,97**
Transcriptional regulator, GntR family	Regulatory functions	EF1676	0,22	**2,08**	0,55
Transcriptional regulator, LysR familie	Regulatory functions	EF1710	**-1,33**	-0,96	0,48
Catabolite control protein A	Regulatory functions	EF1741	0,34	-0,57	-1,33
Transcriptional regulator, SorC family	Regulatory functions	EF1965	0,33	**1,31**	**1,20**
Transcriptional regulator, GntR family	Regulatory functions	EF2051	**-0,80**	0,68	0,24
Transcriptional regulator, TetR family	Regulatory functions	EF2066	**0,90**	**1,55**	**-1,56**
tspO protein, putative	Regulatory functions	EF2202	-0,10	**1,44**	**1,77**
Transcriptional regulator, TetR family	Regulatory functions	EF2203	**-1,35**	0,51	0,66
Transcriptional regulator, Cro/CI family	Regulatory functions	EF2291	-0,20	0,31	**-1,90**
Transcriptional regulator, Cro/CI family	Regulatory functions	EF2304	0,32	**1,19**	0,22

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Transcriptional regulator, Cro/CI family	Regulatory functions	EF2508	0,16	**1,56**	0,17
Phosphotyrosine protein phosphatase	Regulatory functions	EF3058	0,31	**1,48**	0,15
Transcriptional regulator, TetR family	Regulatory functions	EF3059	0,34	**1,51**	-0,08
Transcriptional regulator, AbrB family	Regulatory functions	EF3261	**-1,01**	0,72	0,48
DNA-binding response regulator	Regulatory functions	EF3289	-0,77	**2,16**	0,28
Sucrose operon repressor ScrR	Regulatory functions	EFA0070	-0,15	-0,11	**2,02**
Transcriptional regulator, UvrC family	Regulatory functions	EFC0011	0,93	**3,44**	0,18
PTS system, IIB component	Signal transduction	EF0019	**-0,86**	**-2,01**	0,12
PTS system, mannose-specific IIAB components	Signal transduction	EF0020	-0,69	**-2,59**	-0,54
PTS system, mannose-specific IIC component	Signal transduction	EF0021	-0,46	**-2,54**	-0,18
PTS system, mannose-specific IID component	Signal transduction	EF0022	-0,27	**-2,24**	0,25
PTS system, fructose- specific family, IIABC components	Signal transduction	EF0717	-0,21	**-1,56**	**1,09**
PTS system, IIABC components	Signal transduction	EF0958	**-1,63**	-1,08	**2,25**
PTS system, IIB component	Signal transduction	EF1017	**-2,35**	-2,20	0,42
PTS system, IIC component	Signal transduction	EF1019	**-1,90**	-0,69	**3,00**
PTS system component, authentic frameshift	Signal transduction	EF1608	**-1,19**	-0,39	-0,06
Response regulator	Signal transduction	EF1822	-0,22	1,11	**1,00**
PTS system, IIBC components	Signal transduction	EF2213	-0,80	0,53	**2,00**
Sensor histidine kinase	Signal transduction	EF3290	-0,35	**2,05**	0,69
PTS system, IIABC components	Signal transduction	EFA0067	0,17	1,31	**1,12**
DNA-directed RNA polymerase, alpha subunit	Transcription	EF0233	0,08	-0,68	**-1,49**
ATP-dependent RNA helicase, DEAD/DEAH box family	Transcription	EF0846	-0,12	-0,88	**-1,17**
Polyribonucleotide nucleotidyltransferase	Transcription	EF3064	-0,12	**-1,24**	-0,02
DNA-directed RNA polymerase, alpha subunit, omega subunit	Transcription	EF3126	0,28	0,09	**-0,78**
DNA-directed RNA polymerase, beta-prime subunit	Transcription	EF3237	0,27	**-1,11**	**-0,91**
ABC transporter, ATP-binding protein	Transport and binding proteins	EF0017	-0,03	**-2,21**	**-0,99**
ABC transporter, permease protein	Transport and binding proteins	EF0057	0,04	**-1,94**	-0,20
Major facilitator family transporter	Transport and binding proteins	EF0082	-0,55	**-3,17**	**-4,45**
Formate/nitrite transporter family protein	Transport and binding proteins	EF0094	**1,35**	**-2,86**	**-3,46**
C4-dicarboxylate transporter, putative	Transport and binding proteins	EF0108	-0,12	0,60	**2,36**
ABC transporter, ATP-bindingprotein	Transport and binding proteins	EF0178	0,74	**-1,59**	**-0,93**
ABC transporter, permease protein	Transport and binding proteins	EF0179	0,55	**-2,53**	**-1,29**
ABC transporter, permease protein	Transport and binding proteins	EF0180	0,50	**-2,31**	**-1,24**
Amino acid ABC transporter, amino acid-binding/permease protein	Transport and binding proteins	EF0247	-0,18	**-1,21**	-0,39

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Potassium-transporting ATPase, subunit B	Transport and binding proteins	EF0568	0,28	0,66	**2,38**
Potassium-transporting ATPase, subunit C	Transport and binding proteins	EF0569	NA	-0,21	**1,20**
Cation ABC transporter, permease protein	Transport and binding proteins	EF0576	0,23	**1,55**	-0,46
Amino acid permease family protein	Transport and binding proteins	EF0635	**1,29**	**-4,13**	**-1,80**
Na+/H+ antiporter	Transport and binding proteins	EF0636	**1,63**	**-3,04**	**-1,18**
Mat efflux family protein	Transport and binding proteins	EF0660	0,61	**2,16**	**1,44**
Glycine betaine/carnitine/choline ABC transporter, ATP-binding protein	Transport and binding proteins	EF0674	**-1,44**	-0,51	0,60
Amino acid ABC transporter, ATP-binding protein	Transport and binding proteins	EF0760	-0,29	**-2,01**	-0,27
Cation efflux family protein	Transport and binding proteins	EF0859	0,24	0,79	**2,94**
Glycine betaine/carnitine/choline ABC transporter, permease protein	Transport and binding proteins	EF0862	-0,07	**1,11**	**1,23**
Glycine betaine/carnitine/choline ABC transporter, Glycine betaine/carnitine/choline -binding protein	Transport and binding proteins	EF0863	-0,11	**1,43**	**1,33**
Glycine betaine/carnitine/choline ABC transporter, permease protein	Transport and binding proteins	EF0864	-0,29	**1,37**	**1,34**
Glycine betaine/carnitine/choline transporter, ATP-binding protein	Transport and binding proteins	EF0865	-0,17	**1,38**	1,07
Cation-transporting ATPase, E1-E2 family	Transport and binding proteins	EF0871	-0,47	**2,03**	0,66
Amino acid ABC transporter, ATP-binding protein	Transport and binding proteins	EF0892	0,29	**-2,12**	-0,66
Peptide ABC transporter, peptide-binding protein	Transport and binding proteins	EF0907	-0,26	**2,51**	**0,75**
Amino acid permease family protein	Transport and binding proteins	EF0929	**0,83**	-0,23	-0,13
Aquaporin Z	Transport and binding proteins	EF1192	0,13	-0,89	**-1,43**
Permease domain protein	Transport and binding proteins	EF1321	0,00	0,70	**1,09**
ABC transporter, ATP-binding/permease protein	Transport and binding proteins	EF1341	0,33	**1,89**	0,79
Sugar ABC transporter, permease protein	Transport and binding proteins	EF1343	**-1,44**	0,22	**1,89**
Sugar ABC transporter, permease protein	Transport and binding proteins	EF1344	-1,45	-0,40	**2,15**
Sukker ABC transporter, sugar-binding protein	Transport and binding proteins	EF1345	**-1,37**	**-1,10**	**2,42**
ABC transporter, ATP-binding protein	Transport and binding proteins	EF1675	0,74	**1,95**	0,29
Phosphate-binding protein	Transport and binding proteins	EF1705	0,61	**1,70**	0,11
Uracil permease	Transport and binding proteins	EF1720	**1,32**	**1,00**	**-3,02**
Phosphate ABC transporter, ATP-binding protein	Transport and binding proteins	EF1756	**0,72**	**-1,03**	-0,26
Cation-transporting ATPase, E1-E2	Transport and binding	EF1938	-0,59	-0,59	**1,15**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
family	proteins				
Amino acid permease familie protein	Transport and binding proteins	EF2047	-0,14	**-1,65**	-0,62
ABC transporter, permease protein, putative	Transport and binding proteins	EF2049	0,12	**5,19**	0,20
ABC transporter, ATP-binding protein	Transport and binding proteins	EF2050	-0,69	**4,88**	-0,20
ABC transporter, ATP-binding protein	Transport and binding proteins	EF2074	-1,15	**2,20**	-0,04
ABC transporter, permease protein	Transport and binding proteins	EF2075	-0,65	**3,56**	-0,21
ABC transporter, permease protein	Transport and binding proteins	EF2081	0,94	-0,34	**-2,37**
ABC transporter, ATP-binding protein	Transport and binding proteins	EF2153	0,79	**-1,22**	-0,33
Xanthine permease	Transport and binding proteins	EF2364	**1,52**	0,51	-0,20
ABC transporter, ATP-binding protein	Transport and binding proteins	EF2394	0,13	**1,12**	0,63
ABC transporter, permease protein	Transport and binding proteins	EF2485	0,74	**-1,54**	**-2,32**
ABC transporter, ATP-binding protein	Transport and binding proteins	EF2486	0,73	-1,19	**-2,12**
Cadmium-translocating P-type ATPase	Transport and binding proteins	EF2623	0,06	**2,24**	**3,27**
Glycine betaine/L-proline ABC transporter, ATP-binding subunit	Transport and binding proteins	EF2641	-0,21	**3,42**	**2,92**
Glycine betaine/L-proline ABC transporter, glycine betaine/L-proline-binding/permease protein	Transport and binding proteins	EF2642	0,69	**4,99**	**4,21**
ABC transporter, ATP-binding protein	Transport and binding proteins	EF2720	-0,68	1,08	**1,17**
ABC transporter, ATP-binding/permease protein	Transport and binding proteins	EF2920	0,52	**1,46**	0,28
Xanthine/uracil permeases family protein	Transport and binding proteins	EF2935	-0,36	**-1,34**	-0,19
Ribose uptake protein, putative	Transport and binding proteins	EF2959	-0,27	1,29	**1,16**
ABC transporter, ATP-binding protein	Transport and binding proteins	EF2986	-0,16	**3,10**	-0,83
Sulfate transporter familiy/STAS domain protein	Transport and binding proteins	EF3004	1,03	-0,71	**-1,42**
Sodium:dicarboxylate symporter family protein	Transport and binding proteins	EF3022	**0,86**	-1,02	-1,01
Formate/nitrite transporter family protein	Transport and binding proteins	EF3069	0,55	**-1,66**	**-2,90**
Iron compound ABC transporter, permease protein	Transport and binding proteins	EF3085	0,08	**1,79**	0,08
ABC transporter, permease protein	Transport and binding proteins	EF3199	**-2,04**	-1,07	1,22
Oxidoreductase, short chain dehydrogenase/reductase family	Unknown function	EF0076	-0,84	0,49	**2,22**
Diacylglycerol kinase catalytic domain protein	Unknown function	EF0090	**-1,37**	-0,83	0,84
LysM domain protein	Unknown function	EF0443	-0,03	-0,76	**2,55**
AMP-binding family protein	Unknown function	EF0452	**1,26**	-0,34	**-1,36**
OsmC/Ohr family protein	Unknown function	EF0453	**-2,16**	0,47	**1,73**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
Decarboxylase, putative	Unknown function	EF0634	0,82	**-2,13**	**-1,65**
Glyoxalase family protein	Unknown function	EF0666	**-1,21**	-0,31	0,41
Acyltransferase, putative	Unknown function	EF0783	-0,67	**1,53**	0,70
Pentapeptide repeterende family protein	Unknown function	EF0905	0,38	**1,83**	**0,90**
Acetyltransferase, GNAT family	Unknown function	EF0945	**0,57**	**2,60**	**1,07**
Endonuclease/exonuclease/phosphatase family protein	Unknown function	EF0960	**-1,45**	-0,62	**2,32**
Oxidoreductase, Gfo/Idh/MocA family	Unknown function	EF1008	-0,36	0,00	**0,93**
Hydrolase, haloacid dehalogenase-like family	Unknown function	EF1039	-0,38	**1,57**	0,21
Hexapeptide-repeat containing-acetyltransferase	Unknown function	EF1066	**-0,84**	-0,18	**1,14**
Oxidoreductase, putative	Unknown function	EF1108	**0,62**	**1,57**	**1,32**
YkgG family protein	Unknown function	EF1110	0,26	0,43	**0,78**
Oxidoreductase, aldo/keto reductase family	Unknown function	EF1138	-0,87	-0,01	**1,09**
Glutamine amidotransferase, class I	Unknown function	EF1139	**-1,08**	**-1,74**	-0,09
DegV family protein	Unknown function	EF1191	-0,44	**-1,35**	**-0,96**
Oxidoreductase, putative	Unknown function	EF1226	**1,75**	-0,43	**-1,1**
S1 RNA binding domain protein	Unknown function	EF1312	-0,32	-0,01	0,05
BadF/BadG/BcrA/BcrD ATPase family protein	Unknown function	EF1327	**1,56**	-0,08	-0,29
Dihydroxyacetone kinase family protein	Unknown function	EF1361	**-1,26**	-0,55	1,08
LysM domain protein	Unknown function	EF1546	**-0,82**	0,22	**0,42**
GTPase, putative	Unknown function	EF1549	0,25	-0,76	**-0,75**
YitT family protein	Unknown function	EF1555	-0,59	-0,25	**0,67**
CoA-binding domain protein	Unknown function	EF1616	**-0,99**	-0,43	0,27
lacX protein, putative	Unknown function	EF1644	-0,22	0,62	**1,27**
Glucose-inhibited division protein	Unknown function	EF1649	-0,39	-2,44	**1,57**
Oxidoreductase, zinc-binding	Unknown function	EF1671	**-1,47**	-0,13	0,27
DegV family protein, putative	Unknown function	EF1684	**-0,71**	0,70	0,57
KH domain protein	Unknown function	EF1693	-0,22	-0,06	**-1,73**
Aminotransferase, class I	Unknown function	EF1706	0,41	**1,40**	0,37
GTP-binding protein	Unknown function	EF1916	**-0,84**	**-1,82**	0,80
Coenzyme F420 hydrogenase domain protein	Unknown function	EF2014	**-1,54**	0,74	0,35
Glyoxylase family protein	Unknown function	EF2214	**-1,22**	**1,20**	**1,83**
Aminotransferase, class V	Unknown function	EF2392	0,10	**1,02**	**0,67**
GTP-binding protein TypA	Unknown function	EF2460	-0,38	**-1,31**	-0,71
HD domene protein	Unknown function	EF2470	**-0,96**	0,37	**-0,72**
GcvH family protein	Unknown function	EF2500	0,03	**2,27**	0,23
Sua5/YciO/YrdC/YwlC family protein	Unknown function	EF2552	0,31	**-1,02**	**-0,46**
DNA-binding protein, putative	Unknown function	EF2638	**-2,16**	-0,58	0,77
Diacylglyserol kinase katalytisk domain protein	Unknown function	EF2644	**-1,00**	-1,05	0,82
Hydrolase, haloacid dehalogenase-like family	Unknown function	EF2681	**0,83**	0,38	-0,42
Oxidoreductase, Gfo/Idh/MocA family	Unknown function	EF2734	-0,09	**1,60**	**0,96**
ErfK/YbiS/YcfS/YnhG family protein, putative	Unknown function	EF2860	0,03	**2,00**	**1,42**

Gene product	Cellular role	ORF	Log_2-ratio at: T(0)	T(30)	T(60)
D-isomer specific 2-hydroxyacid dehydrogenase family protein	Unknown function	EF2901	**-1,37**	0,28	**1,85**
	Unknown function				
Hydrolase, haloacid dehalogenase-like family	Unknown function	EF2927	0,05	0,57	**1,07**
DNA-binding protein, putativ	Unknown function	EF2933	1,08	0,36	**-1,09**
Acetyltransferase, GNAT family	Unknown function	EF3079	0,42	-0,05	**1,00**
YitT family protein	Unknown function	EF3091	**0,85**	-0,59	**-0,87**
Glyoxalase family protein	Unknown function	EF3092	-0,30	-0,58	**0,90**
Thiamine pyrophosphokinase family protein	Unknown function	EF3117	**0,73**	0,86	0,22
Hydrolase, haloacid dehalogenase-like family	Unknown function	EF3158	0,01	0,49	**1,69**
LrgB family protein	Unknown function	EF3193	**1,57**	**0,78**	**-0,57**
Oxidoreductase, pyridine nucleotide-disulfide family	Unknown function	EF3257	**0,73**	**-2,56**	**-2,41**
PemI family protein	Unknown function	EFA0072	-0,64	**2,35**	-0,11

Table S2: Four-hour minimal inhibitory concentrations (MIC). MIC was determined at the lowest concentration of the stressor that resulted in complete inhibition of growth 4 hours after inoculation. Results show average of independent triplicate experiments, no variation was observed. AU = arbitrary units.

Stressor	**OG1RF**	**INY3000**	**TX5179**	**TX5180**
Ampicillin (µg/ml)	8	8	8	8
Vancomycin (µg/ml)	2	2	2	2
Leucocin C (AU*/ml)	> 2	1	1	1
Ethanol (%)	12.5	6.25	6.25	12.5
Sodim dodecyl sulphate (%)	0.04	0.02	0.02	0.04
Sodium taurodeoxycholate (%)	> 0.25	0.25	0.25	> 0.25
H_2O_2 (%)	0.12	0.12	0.12	0.12

*1 AU was defined as the bacteriocin concentration nessecary for complete inhibition of growth of *E. faecalis* TX5179 4 hours after inoculation.