博士論文
Doctoral Dissertation

Antibiotics shapes population-level diversity in the human gut microbiome

(抗生物質はヒト腸内細菌叢の集団レベルでの多様性を形成する)

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Abstract

The human gut microbiome has profound influences on the host's physiology through its interference with various intestinal functions. The development of next-generation sequencing (NGS) technologies enabled us to comprehensively explore ecological and functional features of the gut microbiomes. Recent studies using the NGS-based metagenomic approaches have suggested high ecological diversity of the microbiome across countries. However, little is known about the structure and feature of the Japanese gut microbiome, and the factor that shapes the population-level diversity in the human gut microbiome. In this thesis, to address the above questions regarding the human gut microbiome, I analyzed metagenomic data of fecal DNA samples from healthy Japanese individuals and compared the data with that from individuals in other countries.

I obtained approximately 350 Gb of metagenomic sequences of the gut microbiome of 106 Japanese individuals in this study. By comparing the metagenomic data with that of 757 individuals from other 11 countries, I found that the Japanese gut microbiome showed more abundant in the phylum Actinobacteria, in particular in the genus *Bifidobacterium*, than that of the other 11 nations. Regarding the microbial functions, those of carbohydrate metabolism were overrepresented with a concurrent decrease in those for replication and repair and cell motility in the Japanese gut microbiome. The remarkable low prevalence of genes for methanogenesis with a significant depletion of the archaeon *Methanobrevibacter smithii* and significant enrichment of acetogenesis genes in the Japanese gut microbiome as compared to others

suggested a difference in the hydrogen metabolism pathway in the gut between them. These data suggested considerable uniqueness in the taxonomy and function of the Japanese gut microbiome (Nishijima S. *et al*., DNA res., in press).

To explore the factors that contribute to differences in the human gut microbiomes across the 12 countries, I further conducted an association study of the epidemiological data on dietary intake and antibiotic usage with metagenomic data of the 861 human gut microbiomes from the 12 countries. I found that the gut microbiome structure is significantly diverse across the 12 countries, which was strongly correlated with antibiotics as well as diet. Notably, the abundance of the major species *Bacteroides* showed a significant correlation with both antibiotic usage in humans and farm animals but not with diet; whereas, the abundance of another major species *Prevotella* showed a significant correlation with diet but not with antibiotic usage. Thus, the trade-off relation between these two major species appears to be a consequence of respective independent effects from dietary and antibiotic factors. The proliferation of antibiotic resistant genes, including the efflux pump, may underlie the positive correlation between *Bacteroides* and antibiotic usage. Collectively, these results suggest that antibiotics may have had a striking impact on the shaping of the gut microbiome structure of modern human populations (Nishijima S. *et al*., in preparation).

Table of Contents

1. Introduction

1.1. Human gut microbiomes and study background

A large number of microbes colonize the human body, and they have a profound influence on the host's physiology[1, 2]. The total number of these microbes is estimated to be similar to or more than that of human cells (Fig. 1.1)[1, 3, 4]. The majority of them reside in the intestinal tract, and the gut microbiome (the collective genomes of the microbes) comprises a complex microbial community with more than 100 microbial species. Because of the importance of the gut microbiome for the host's health and disease, it is called the "second genome" or "forgotten organ"[2, 5]. Therefore, the humans can be considered as "superorganism" united with their symbiotic microbiome[6].

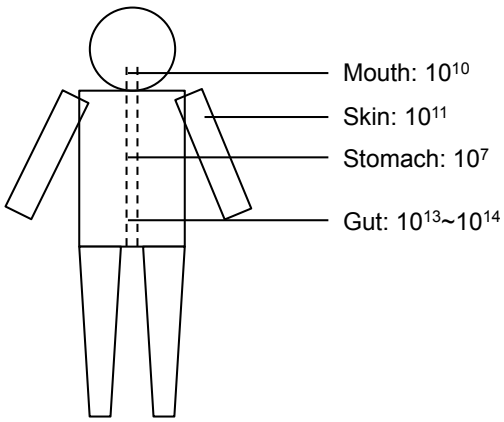


Fig. 1.1. The number of microbes on/in the human body. The number of microbial cells on/in whole human body. Data are from reference 1 and 3.

In the 17th century, Antonie van Leeuwenhoek observed indigenous microorganisms in feces using a microscope[7]. Thereafter, by the development of methods for culturing microorganisms, various commensal bacteria such as *Escherichia coli* and *Bifidobacterium* were isolated and identified from human feces around 1900,

which can be considered to be a starting point of the study of the human gut microbiome[7, 8]. In addition, *in vivo* analytical system using germ-free and gnotobiotic animals was established to evaluate the biological function of the microbes and revealed the indispensable association of the microbial community with the host's physiology[1, 9, 10]. Therefore, the culture-based method has been popularly used for investigating the gut microbial community structure. However, there were a large number of uncultivable species in the community[11]. As a result, knowledge about the gut microbial community obtained from the culture-based method has been limited and many unknown species have been left unanalyzed until recently.

1.2. Development of culture-independent method

To overcome the above mentioned problems encountered in the culture-based method, an alternative approach, a sequencing-based method was developed in 1980s, making it possible to directly acquire the DNA information of the collective genomes prepared from microbes in an environment[12-14]. Since a sequencing-based method did not require the culture step of microbes, these culture-independent methods enabled us to comprehensively elucidate the genomic and taxonomic information of the microbial community containing many uncultivable species.

There are two major culture-independent methods for the study of microbial communities (Fig. 1.2). One is a targeted sequencing of the ribosomal RNA (rRNA) gene in which the 16S rRNA gene regions are collectively amplified by PCR using the specific conserved primers and the amplified products are subsequently sequenced[14]. Variable regions in the 16S rRNA gene are useful for their taxonomic assignment and to know their phylogenetic relations. In the 16S rRNA gene analysis, the taxonomic assignment of microbes can be performed by similarity search of the 16S rRNA gene

sequences against the databases constructed from full-length 16S rRNA gene sequences of known individual microbes. Although this method can be applied only to taxonomic analysis of the microbial community, it can rapidly give us the information of an overview of the microbial content and abundance in the community with relatively low cost. In addition, the phylogenetic tree constructed from the 16S rRNA gene sequences can be used to quantitatively evaluate overall similarity or dissimilarity between different microbial communities[15].

Another is a metagenomic analysis, in which the collective genomes of microbes in an environment are randomly sequenced to collect whole genomic sequence data, from which both taxonomic and functional information can be obtained by employing several appropriate strategies. For example, mapping of the metagenomic reads to the reference genomes containing those of the isolated individual microbes can assign the reads to a particular taxonomy. The genes are computationally identified by using gene prediction softwares in the assembled data of the metagenomic reads or unassembled reads. The analysis of functional assignment of the genes identified in the metagenomic data can be performed by similarity search using KEGG and COG databases[12, 13].

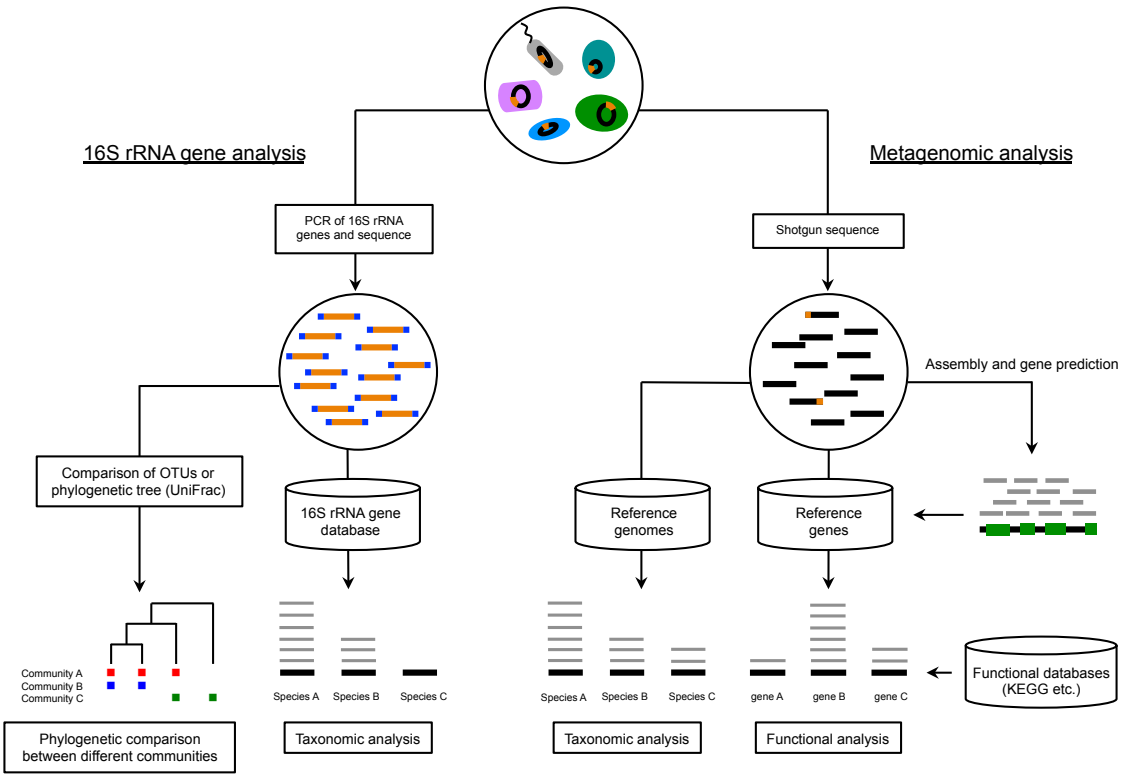


Fig. 1.2. Sequencing-based methods for the study of microbial communities.

1.3. International trends in the metagenomic study of the human microbiome

Up to date, many studies of human gut microbiomes using metagenomic and 16S rRNA gene analysis have been reported (Table 1.1). The first study of the human gut microbiome by metagenomic analysis was reported in 2006, in which the gut microbiomes of two Americans were sequenced[13], and the second study was published in 2007, in which the gut microbiomes of the 13 Japanese individuals were analyzed[16]. These two studies characterized the functional and microbial features of the community by analyzing the genes identified in the metagenomic data produced by the Sanger sequencing. After these two studies, in 2008, two large-scale international projects were

launched to study the human microbiome based on metagenomic analysis using next-generation sequencing (NGS) technologies. One is Metagenomics of the Human Intestinal Tract (Meta-HIT) project by the European Union and China. Another project is the Human Microbiome Project (HMP) by the United States. These two projects aimed to comprehensively analyze the human microbiome with a large dataset of microbiomes from numbers of individuals. In addition, the International Human Microbiome Consortium (IHMC) was also established by scientists from more than 10 countries including Japan, USA, several European countries and China to share technologies and exchange information about the human microbiome researches between the countries. Since then, many of the published projects have been carried out by metagenomic and 16S rRNA gene analysis using NGS.

The Meta-HIT and China groups conducted a large-scale metagenomic analysis of the human gut microbiome and identified 3.3 million (M) genes from the gut microbiomes of 124 European individuals[17], which was about five times more than that identified in the 13 Japanese individuals. The HMP aimed to collect microbiome data from the whole body including the gut, skin, and oral cavity[18, 19]. The HMP is also making an effort to construct the reference genome database comprising sequenced genomes of individual strains isolated from humans in collaboration with other IHMC members[20] and to develop bioinformatic tools and analytical pipelines for metagenomic data[21-23]. In addition to these large-scale projects, several studies targeting more than 100 individuals have been also conducted worldwide[16-18, 24-32].

Table 1.1. Metagenomic studies of human microbiomes.

Year	Sequencer	Research	Reference
2006	Sanger	Metagenomic and 16S rRNA gene analysis of 2 American gut microbiomes	13
2007	Sanger	Metagenomic analysis of 13 Japanese gut microbiomes (healthy and infant)	16
2009	454	Metagenomic and 16S rRNA gene analysis of 18 American gut microbiomes (twin and obesity)	24
2010	Illumina	Metagenomic analysis of 124 Danish and Spanish gut microbiomes (healthy and IBD)	17
2011	Sanger	Comparative metagenomics of 39 individuals and proposal of the concept of Enterotypes	25
2012	Illumina	Metagenomic analysis of 345 Chinese gut microbiomes (healthy and type II diabetes)	26
	Illumina	Metagenomic and 16S rRNA gene analysis of 139 American microbiomes	18
2013	SOLiD	Metagenomic analysis of 96 Russian gut microbiomes	28
	Illumina	Metagenomic analysis of 145 Swedish gut microbiomes (healthy and type II diabetes)	27
2014	Illumina	Metagenomic and 16S rRNA gene analysis of 196 French and German gut microbiomes (healthy and colorectal cancer)	33
	Illumina	Metagenomic analysis of 263 samples of American skin microbiomes	34
	Illumina	Metagenomic analysis of 237 Chinese gut microbiomes (healthy and liver cirrhosis)	29
2015	Illumina	Metagenomic analysis of 156 Austrian gut microbiomes (healthy and colorectal cancer)	30
	Illumina	Metagenomic analysis of 200 Swedish gut microbiomes (Mother and infant)	31
	Illumina	Metagenomic analysis of 212 Chinese oral and gut microbiomes (healthy and rheumatoid arthritis)	32

1.4. Structure of the human microbiome

Current studies based on a large-scale metagenomic and 16S rRNA gene analysis have more or less clarified details of the structure and function of the human microbiome. The human gut microbiome comprises mainly four phyla: Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria (Table 1.2)[14, 18]. Additionally, other phyla such as Euryarchaeota, Fusobacteria and Verrucomicrobia are also detected as minor phyla. At

the genus level, about 10 to 20 genera represent the majority of the microbial community (Table 1.2). The structure of the community in an individual is relatively stable over at least a few years despite dietary and life style variations in the individuals[35-37]. However, the relative abundances of each phylum, genus and species in the communities are significantly varied between individuals even for twins and within a family[18, 24]. In addition, microbiomes from the skin[34, 38-40], oral[18, 41], vaginal[42, 43], nasal[44], gastric[45], esophageal[46] and placental[47] have been also studied, which revealed significant variations and diversity in the microbial community structures among different body sites.

Table 1.2. Major phyla and genera comprising the human gut microbiome.

Phylum	Genus
Firmicutes	*Clostridium*
	Eubacterium
	Lactobacillus
	Ruminococcus
	Roseburia
	Blautia
	Dorea
	Enterococcus
	Faecalibacterium
	Streptococcus
	Dialister
	Anaerostipes
	Coprococcus
Bacteroidetes	*Bacteroides*
	Prevotella
	Parabacteroides
	Porphyromonas
	Alistipes
Actinobacteria	*Bifidobacterium*
	Eggerthella
	Collinsella
Proteobacteria	*Escherichia*
	Klebsiella
	Bilophila
Fusobacteria	*Fusobacterium*
Verrucomicrobia	*Akkermansia*
Euryarchaeotae	*Methanobrevibacter*

The human gut microbiome encodes an enormous number of and functionally diverse genes particularly involved in carbohydrate metabolism, which mainly metabolize dietary fibers that cannot be digested by the host[16, 48]. The over-representation of the genes is one of the characteristic features of the human gut microbiomes as compared with other environments[16]. Specifically, porphyranase, which degrades the cell walls of aquatic plants, was identified in many of Japanese gut microbiomes but not in those of Americans[49]. The prevalence of the porphyranase gene in the Japanese can be explained by the functional adaptation of the gut microbiome to the Japanese traditional dietary style. In contrast, genes for cell motility such as flagella and chemotaxis are relatively underrepresented in human gut microbiomes[16]. This feature may be due to the unnecessary movement of microbes in the gut because the stool content is stirred by peristalsis, and/or the host's immune system eliminating flagellated microbes that are highly immunogenic.

The formation of the gut microbiome begins after birth by colonizing environmental microbes mainly from mother's skin and the vaginal microbiome. The structure of the microbiome of newborn infants is largely influenced by several factors, such as ways of childbirth (natural childbirth or caesarean section), and breast or formula feeding[31, 50]. Also, the gut microbiome of infants is significantly different from that of children or adults[16, 51], but its structure becomes stable and similar to the adult gut microbiome around three years old[31, 51, 52]. The more long-term variation in the gut microbiome of individuals, such as from birth to old age, has not been studied yet.

The human gut microbiome structure is significantly different from those of microbial communities in other environments such as the sea and soil[53, 54]. Additionally, the gut microbiomes of various mammalians in the zoo and in the wild showed similarities in the taxonomic and functional components to that of humans, but those

possessed their own gut microbiome structure distinct from each other and humans[54-56], suggesting the influence of both host phylogeny and diet, and co-evolution between host and its microbiome while maintaining their symbiotic relation[57, 58].

1.5. Association with health and diseases

The human gut microbiome is profoundly associated with the host's health and diseases[59-61]. For example, the gut microbiome produces short chain fatty acids (SCFA) such as butyrate, acetate and propionate, which are known to be nutrients and have various biological activities to host cells[59, 60, 62]. In total, about 10% of the total calories are estimated to be derived from the gut microbiome in the form of these nutrients[63]. Butyrate induces colonic regulatory T cells, which play a central role in the suppression of autoimmune diseases[64, 65]. Acetate protects the host from infection by the pathogenic bacteria *Escherichia coli* O157:H7[66]. Furthermore, the gut microbiome produces several vitamins (vitamins B and K and others), some of which are essential for human health because the human genome lacks the biosynthesis genes of these vitamins[60, 62]. These bacterial metabolites are absorbed by epithelial cells and delivered throughout the body, which accounts for about 10% of total metabolites in the blood[67].

The aberrant structure of the gut microbiome is associated with various diseases such as obesity[24, 68], inflammatory bowel disease (IBD)[69, 70], colorectal cancer[30, 33, 71] and type 2 diabetes[26, 27] (Table 1.3). Typically, gut microbiomes in these patients commonly show an imbalance in the community (called dysbiosis) and a low microbial diversity[24, 68] (e.g., a lower number of species in samples with disease). A depletion of butyrate-producing species such as *Faecalibacterium* and other *Clostridiales* is often observed in the gut microbiomes of many of these patients[26, 72, 73]. In addition, several recent studies have indicated an association of the altered gut microbiomes with

neurologic diseases such as autism and multiple sclerosis[74-76], and normal gut microbiome with brain development and host's behavior, suggesting a tight interaction between the gut microbiome and the host's nervous system through the gut-brain axis[77, 78]. Thus, the human gut microbiome has a systemic impact on the host's physiological states (Fig. 1.3).

In 2013, van Nood *et al.* reported that fecal microbiota transplantation (FMT) showed an extremely higher therapeutic effect on recurrent *Clostridium difficile* infection than conventional antibiotic treatment alone[79]. FMT involves transplanting fecal microbiota from a healthy donor into the gut of a patient, suggesting the gut microbiome of healthy individuals has a strong biological activity for the host's physiologies. For therapeutics using FMT, many other studies have also been performed to better understand the recovery process of transplanted microbial community in patients[80], develop safer and more efficient FMT manipulations[81-83], and apply its use for other diseases associated with the gut microbiome such as inflammatory bowel disease[84, 85]. In addition, a variety of clinical applications using the gut microbiome have also been studied, which include exploration of beneficial microbes, development of drugs targeting or using the microbiome, and identification of microbial biomarkers specific to particular diseases[86].

Table 1.3. Diseases associated with the human gut microbiome.

Disease	Reference
Obesity	10, 24, 68
Inflammatory bowel disease	69, 70, 87
Colorectal cancer	30, 33, 71
Type II diabetes	26, 27
Type I diabetes	88, 89
Rheumatoid arthritis	32, 90
Atherosclerosis	91, 92
Irritable bowel syndrome	93, 94
Malnutrition	95, 96
Multiple sclerosis	72
Liver cirrhosis	29
Allergy	97
Eczema	98
Liver cancer	99
Autism	74-76

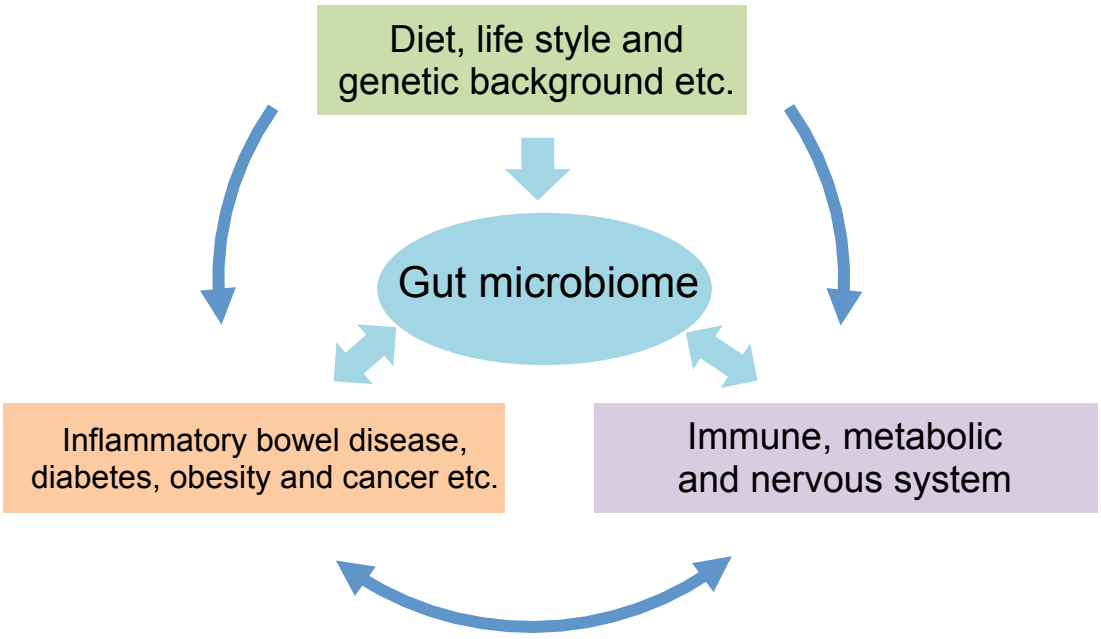


Fig. 1.3. Relationship between the host's physiology and the gut microbiome.

2. The gut microbiome of healthy Japanese and its microbial and functional uniqueness

2.1. Introduction

Various cohort studies of the human gut microbiome based on a metagenomic approach using NGS have been reported[17, 18, 24, 26-33]. These studies included patients with diseases such as obese[24], inflammatory bowel disease[17], type 2 diabetes[26, 27], colon cancer[30, 33], liver cirrhosis[29], and rheumatoid arthritis[32] patients, as well as numbers of healthy individuals in various countries including the United States, several European countries, and China. In addition, several studies have reported on gut microbiomes of Asian children and natives from rural areas[51, 100-103]. These studies suggested that the human gut microbiome is more or less affected by various factors such as diet and host's genetic background[104], and the altered microbiome is associated with diseases[105]. In addition, several comparative analyses have suggested a great diversity in human gut microbiomes at the population level[27, 28, 51, 100-103, 106], and even in those of patients with diseases[27, 107]. More basically, human gut microbiomes can be classified into 'enterotypes' on the basis of differences in the abundance of a few major species largely linked with dietary habits[25, 108].

Japanese have unique dietary culture and habits as compared with Western people, being reflected in the finding that their gut microbiomes have more genes for aquatic plant-derived polysaccharide-degrading enzymes with higher frequency than those of Americans[49]. In addition, Japanese exhibit the highest average life span and very low body mass index (BMI)[109]. A study on the gut microbiomes of 13 Japanese individuals has been previously published[16]. However, the dataset size was too small to allow comparison with other large datasets to precisely evaluate distinct features of the

Japanese gut microbiome (JPGM). Therefore, in this study, I collected and analyzed the metagenomic data from gut microbiomes of 106 Japanese individuals by sequencing of fecal DNA samples using NGS, and I further explored the unique microbial and functional features of the JPGM by comparing the microbiomes of a total of 861 healthy individuals selected from Japan and 11 other countries. The results of this study are shown in this chapter.

2.2. Methods

2.2.1. Subjects and fecal sample collection

One hundred and six healthy Japanese volunteers (age: 32 ± 11, BMI: 22 ± 2.7 [mean ± s.d.]; Appendix 1) were recruited by Azabu University (Japan). This study was approved by the Human Research Ethics Committee of Azabu University and the Research Ethics Committee of the University of Tokyo, and written consent was obtained from all subjects. No subjects were treated with antibiotics during fecal sample collection. Among them, fecal samples were longitudinally collected twice from 26 individuals every eight weeks and five times from nine individuals every two weeks, of which 16 individuals were shared with the previous study[110]. In total, 168 fecal samples were collected from the 106 individuals. The collected fresh feces were stored under anaerobic conditions using an AneroPack™ (Mitsubishi Gas Chemical Co. Inc., Tokyo, Japan) at 4 ºC. Within 36 hours after sampling, the feces were frozen in 20% glycerol (Wako Pure Chemical Industries, Osaka, Japan)/phosphate buffer saline (PBS) solution (Life Technologies, Tokyo, Japan) by liquid nitrogen and stored at −80 ºC until use.

2.2.2. Recovery of bacteria and archaea from fecal samples

Each frozen fecal sample (1.0 g) was thawed on ice and suspended vigorously in a 50 mL tube. The suspension was filtered with a 100 μm-mesh nylon filter (Becton Dickinson, Tokyo, Japan) to separate the bacterial cells from most of eukaryotic cells and other debris. When I compared microbial compositions at the genus level from seven samples with and without the filter, the Pearson's correlations between them were from 0.90 to 0.99, suggesting almost no significant difference in microbial compositions

between with and without filtration of feces. The debris on the filter was washed off twice using a glass or plastic bar with 10 mL PBS buffer. The filtrate was centrifuged at 5,000 X g for 10 min at 4 ºC. The bacterial pellet was rinsed twice with PBS, and finally with TE10 buffer (10 mM Tris-HCl, 10 mM EDTA, pH 8.0).

2.2.3. DNA isolation and purification

Each fecal DNA sample was isolated and purified according to the literature[110-112] with minor modifications. The bacterial pellet was suspended in 10 mL of TE10 buffer and incubated with 15 mg/mL lysozyme (Sigma-Aldrich Co. LCC., Tokyo, Japan) at 37 ºC for 1 h. Purified achromopeptidase (Wako) was added at a final concentration of 2,000 units/mL and further incubated at 37 ºC for 30 min. The suspension was treated with 1% (wt/vol) sodium dodecyl sulfate (SDS) and 1 mg/mL proteinase K (Merck, Tokyo, Japan), and incubated at 55 ºC for 1 h. The lysate was mixed with equal volumes of phenol/chloroform/isoamyl alcohol (Life Technologies) and centrifuged at 5,000 g for 10 min. DNA was precipitated by adding 1/10 volume of 3 M sodium acetate (pH 4.5) and 2 volumes of ethanol, and pelleted by centrifugation at 5,000 g at 4 ºC for 15 min. The DNA pellet was rinsed with 75% ethanol, dried and dissolved in TE. DNA samples were treated with 1 mg/mL RNase A (Wako) at 37 ºC for 30 min, precipitated by adding equal volumes of 20% PEG solution (PEG6000-2.5 M NaCl), and kept on ice for 10 min. DNA was pelleted by centrifugation at 20,000 g at 4 ºC for 10 min, rinsed twice with 75% ethanol and dissolved in TE buffer.

2.2.4. Metagenomic sequencing of fecal DNA

The sequencing of each fecal DNA sample was performed by the 454 (Roche), Ion PGM/Proton (Life Technologies) and MiSeq (Illumina) platforms according to the

suppliers' protocols, respectively. For 454, 5 μg of fecal DNA was sheared to obtain fragments ranging from 300 to 700 bp for the FLX Titanium platform and 500 to 1,000 bp for the FLX+ platform. The libraries were prepared using the GS FLX Titanium Rapid Library MID Adaptors Kit. For Ion PGM/Proton, 100 ng of fecal DNA was sheared to obtain fragments ranging from 350 to 470 bp and the library was prepared using the Ion Xpress Plus Fragment Library Kit. For the 454 and Ion PGM/Proton reads, artificially redundant reads were removed using a replicate filter if any sequences had ≥ 95% identity to other sequences with exactly the same starting point[113]. Reads that mapped to the human genome (HG19) with Newbler (version 2.7) were also removed. Finally, reads with an average Quality Value (QV) less than 20 or less than 75 bp in length were removed. For 150 bp paired-end sequencing of MiSeq, 20 ng of fecal DNA was sheared to obtain fragments ranging from 300 to 400 bp and the library was prepared using the TruSeq DNA Sample Prep Kit. For 300 bp paired-end sequencing by MiSeq, fecal DNA library was prepared using the Nextera DNA Sample Prep Kit. Any 5' end low quality (< 20 QV) bases in MiSeq reads were trimmed off. Reads having bases less than 20 QV for more than half of the read length and reads whose length was less than 50 bp, were also filtered out. These procedures were done using the FASTX-Tool kit (http://hannonlab.cshl.edu/fastx_toolkit/). The filter-passed reads were then mapped to the human and phiX genomes using Bowtie2[114] (version 2.2.1) and any mapped reads were removed. Sequencing statistics are summarized in Appendix 1.

2.2.5. Assembly and gene prediction for metagenomic sequences

For each individual sample, the filter-passed reads were assembled by Newbler assembler for 454 and Ion PGM/Proton, and MiSeq separately. The contigs (≥ 500bp)

generated from assembly of the reads of 454 and IonPGM/Proton, and MiSeq were further assembled with Minimus2[115] with default settings for each individual. Un-assembled reads (singletons) of all individuals were merged and re-assembled again for each sequencer. MetageneAnnotator[116] was employed to predict protein-coding genes (≥ 100 bp) in the contigs (≥ 500 bp) and singletons from 454 longer than 300 bp. The genes were clustered using CD-HIT[117] with a 95% identity and 90% length coverage thresholds, in which a longest gene in the cluster was selected as the representative gene.

2.2.6. Publically available metagenomic data

I collected publically available metagenomic data of individuals from Denmark (DK), Spain (ES), the United States (US), China (CN), Sweden (SE), Russia (RU), Venezuela (VE), Malawi (MW), Austria (AT), France (FR) and Peru (PE). Metagenomic reads from DK[17] and ES[17] were downloaded from http://public.genomics.org.cn. Filter-passed reads and non-redundant genes from US[18] were downloaded from the HMP DACC (http://www.hmpdacc.org). Raw reads from DK[68], ES[106], CN[26, 29], SE[27], RU[28], AT[30], FR[33], PE[102], Yanomami (VE)[118] and US[102] were also downloaded from public databases and quality control steps were conducted using the same methods described above. The SOLiD reads from RU were subjected to error correction using the SOLiD Accuracy Enhancement Tool (SAET), and the quality control steps were performed as described in the previous study[28]. Raw reads for Amerindian (VE)[51], MW[51] and US[51] were downloaded from MG-RAST (http://metagenomics.anl.gov) and reads mapped to the human genome were excluded.

2.2.7. Country-specific metagenomic datasets of healthy individuals

To construct metagenomic datasets consisting of healthy individuals from each country, the data for individuals with BMI ≥ 30, those with diseases such as inflammatory bowl disease, type 2 diabetes, liver cirrhosis or colorectal cancer, and infants age < 3 years old were excluded from the data collected from a total of 1,734 individuals. I then combined the data from remaining healthy individuals per each country to construct datasets for each country. Although I could not access the metadata for the individuals in US[18], I used all the data with an average BMI of 24 ± 4 (s.d.) for this cohort. In total, 861 individuals from the 12 countries were selected and used for the analysis (Table 3.2).

2.2.8. Construction of microbial reference genomes

For the microbial composition analysis, I used in-house reference genome database comprised of a total of 6,107 genomes representing 2,373 clusters at the species level of Bacteria and Archaea, which were selected from 2,788 complete and 22,317 draft genomes available in GenBank/DDBJ/EBI (as of July 2014), 20 genomes from the study published by Atarashi *et al.*[119] and two unpublished genomes in my laboratory. The reference genomes are listed in Appendix 2.

The reference genome database was constructed by the following procedures. First, genomes matching with either of the following criterion were selected as references; (i) genomes mapped with ≥ 10 metagenomic reads when 60 M metagenomic reads from six countries (Japan, China, Denmark, Spain, Sweden and the United States) were mapped to the 25,085 genomes in GenBank/DDBJ/EBI (BLASTN; 95% identity and 90% length coverage). (ii) genomes for which the 16S rRNA gene, identified with

RNAmmer[120], were mapped with ≥ 10 in-house 16S rRNA V1-V2 region sequences of human microbes, which comprised of about 600 thousand reads (BLASTN; 85% identity and 90% length coverage). Second, 25 typical known pathogenic species such as *Bacillus anthracis*, *Bordetella pertussis, Burkholderia pseudomallei, Campylobacter coli, Campylobacter jejuni, Clostridium botulinum*, *Clostridium chauvoei*, *Clostridium tetani, Corynebacterium diphtheria, Francisella tularensis, Leptospira interrogans, Listeria monocytogenes, Mycobacterium abscessus, Mycobacterium tuberculosis*, *Salmonella enterica, Shigella boydii, Shigella dysenteriae, Shigella flexneri, Shigella sonnei, Vibrio cholera, Vibrio vulnificus* and *Yersinia pestis*, and four genera including *Borrelia*, *Chlamydia*, *Mycoplasma*, and *Rickettsia* were excluded from the reference dataset. Third, to reduce complexity and excess load in computing, for the species with ≥ 50 sequenced genomes at the strain level, some of the genomes were excluded to the extent that the genomes still covered ≥ 99% of the total reads mapped to the species. Those included *Acinetobacter baumannii*, *Bacillus cereus*, *Bacteroides fragilis*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Helicobacter pylori*, *Klebsiella pneumonia*, *Peptoclostridium difficile*, *Propionibacterium acnes*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus agalactiae*, *Streptococcus mutans*, *Streptococcus pneumonia*, *Streptococcus pyogenes* and *Streptococcus suis*.

The reference genomes selected above were further clustered to reduce the complexity at the species level. The 16S rRNA genes of the reference genomes were clustered with a 98.8% identity cut-off, and the obtained clusters were defined as single species. Reads that mapped to the genomes in the same cluster were merged and assigned to the representative species of the cluster. For a few clusters that were composed of obviously different species, such as *Streptococcus salivarius* and

Streptococcus thermophiles, both of which have 16S rRNA genes of > 98.8% identity, I manually separated these clusters into different species. Of a few species, such as *Fusobacteroium nucleatum* and certain *E. coli* strains, that formed distinct clusters, even when the species' names were identical, the species/clusters were merged when a sufficient number of multi-hit reads were commonly shared among them. Several draft genomes lacking 16S rRNA genes were assigned to the most similar species or clusters when the species' names were related and multi-hit reads were commonly shared among the genomes.

2.2.9. Microbial composition by mapping of metagenomic reads to the reference genomes

One M metagenomic reads per individual were mapped to the reference genomes using Bowtie2 with a 95% identity threshold. For the SOLiD reads from RU, Bowtie[121] (version 0.12.7) was employed with the same threshold. For several samples of which the number of metagenomic reads was less than one M, all of the reads for the individual were mapped to the reference genomes. In the 861 individuals selected, the minimum number of reads per individual was about 60,000, but Pearson's correlation coefficients (PCCs) between microbial compositions obtained from the mapping of 1 M reads and 60,000 reads from several same Japanese individuals was 0.99996, indicating that the number of reads per individual between 60,000 and 1 M did not significantly affect the results obtained from the mapping analysis in this study. The number of multi-hit reads that mapped to several different genomes with equal scores were divided among those genomes in proportion to the number of reads uniquely mapped to each genome. A similar normalization was also used for the quantification of transcripts in the RNA-Seq analysis[122]. For genome g, I defined the abundance π_g as follows,

$$\pi_g = \frac{U_g + \sum_{r \in GtoR(g)} P_{r,g}}{l_g}$$

where U_g is the number of reads that are uniquely mapped to genome g, *GtoR(g)* is the set of reads that are equally mapped to several genomes including genome g, and l_g is the length of g. $P_{r,g}$ is the probability that a read r is assigned to genome g, and is calculated as follows,

$$P_{r,g} = \frac{U_g}{\sum_{g' \epsilon RtoG(r)} U_{g'}}$$

where *RtoG(r)* is a set of genomes to which a read *r* mapped. The relative abundance of each genome was calculated by normalizing the number of reads mapped to the genome by the total number of reads. NCBI taxonomy information was used for taxonomic assignment of genus and species for each genome. Genomes that could not be accurately assigned to a particular genus were assigned to their higher rank classification and designated as "Unclassified a higher rank".

2.2.10. Comparison of microbial compositions among the countries

A multi-dimensional scaling (MDS) plot was constructed using the Jensen-Shannon divergence between the microbial compositions at the genus level of the 861 individuals. Hierarchical clustering of the countries based on the average microbial composition at the genus level was performed using the Ward method and the Bray-Curtis distances. Construction of a predictive model for each country based on microbial composition at the genus level was performed using the randomforest package in R. Evaluation of the predictive power of the model was conducted by 10-fold cross-validation with 90% of the training data and 10% of the prediction data. The number of trees was set to 500 and

the sample size option was set to the minimum number of individuals among the countries. The receiver operating characteristic (ROC) and area under the ROC curves (AUCs) of the predictive model were calculated by a one vs. all approach and plotted with the smooth function using the ROCR and pROC packages. Pearson's correlation coefficients were calculated between individuals within and between countries and the statistical differences between them were evaluated by permutation test with 10,000 random samplings.

2.2.11. Assessment and comparison of different methodologies

To evaluate the effect of different methodologies on the metagenomic analysis, the same fecal samples were subjected to sequencing with different sequencers, different DNA extraction methods, and different fecal sample storage conditions (Table 3.3). The microbial compositions at the genus level were calculated with the method described above. Similarity of the microbial compositions was evaluated using Pearson's correlation coefficient. Permutation testing with 10,000 times randomization was conducted to test the statistical significance of the similarity between the data obtained by different methodologies and between individuals within and between countries.

2.2.12. PCR detection of *Methanobrevibacter smithii* in the Japanese individuals

M. smithii was detected by PCR using *M. smithii* 16S rRNA gene-specific primers 5′-ATGCACCTCCTCTCAGCTAGTC-3′ and 5′-AGAGGTACTCCCAGGGTAGAGG-3′, of which sequences were designed using Primer3[123]. PCR was conducted in 10.0 μL PCR solution containing 0.2 μL of template

DNA, 0.02 μL of each primer, 1.0 μL of 10 × PCR buffer, 1.0 μL of dNTP mixture, 0.04 μL of Ex Taq polymerase (Takara Bio Inc., Shiga, Japan) and 7.52 μL of ddH_2O using GeneAmp PCR System 9700 (Applied Biosystems, Tokyo, Japan) with 40 cycles of denaturation (30 sec at 96°C), annealing (20 sec at 60°C), and elongation (3 min at 70°C). The PCR products were separated on 1.5% of agarose gels with a positive control from genomic DNA of *M. smithii* JCM 30028^T. PCR without DNA was also performed as negative control. Genomic DNA of *M. smithii* JCM 30028^T was obtained from Japan Collection of Microorganisms, RIKEN BRC.

2.2.13. Generation of a merged reference gene set of Japanese and integrated gene catalog

I constructed the merged reference gene set by clustering the JP non-redundant genes (4.9 M) and the non-redundant genes (9.9 M) in the integrated gene catalogue (IGC)[106], which was constructed from metagenomic data of more than 1,000 individuals from DK, ES, US and CN using CD-HIT with a 95% nucleotide identity and 90% length coverage cut-off. The IGC genes were downloaded from http://meta.genomics.cn/metagene/meta/home.

2.2.14. Functional assignment of non-redundant genes

Functional assignment of the non-redundant genes was performed using BLASTP searches (e-value ≤ 1.0e-5) against the KEGG (Kyoto Encyclopedia of Genes and Genomes) database (release 63) to obtain the KEGG orthologies (KOs). The genes with a besthit to eukaryotic genes were excluded from further analysis. Additionally, The non-redundant genes were searched using BLASTP (e-value ≤ 1.0e-5) against the eggNOG database (version 4.5)[124] to assign them to non-supervised orthologous groups

(NOGs). The phylum-level taxonomic assignment of the genes assigned to NOGs was conducted by BLASTN searches to the reference genomes with a ≥ 65% identity and ≥ 85% length coverage cut-off.

2.2.15. Quantification of the annotated genes in human gut microbiomes

One M metagenomic reads per individual were mapped to the JP and IGC merged reference gene set using Bowtie2 with a 95% identity cut-off. To adjust the mapping conditions for long reads (*e.g.,* 454 FLX+ reads with an average read length of 730 bp) to the short reference genes with an average length of 620 bp, reads in the JP dataset > 100 bp were split into 100 bp fragments, which were used independently for similarity searches, while fragments < 50 bp were discarded. The number of reads that mapped equally to more than one gene was normalized by the number of reads uniquely mapped to the genes as was conducted for the reference genome mapping. The quantities of KOs were calculated from the number of reads mapped to them. I first compared the relative abundance of KOs between the 104 JP individuals and the 757 individuals in the other 11 countries using Student's *t*-test to enumerate the KOs enriched and depleted with statistical significance (FDR adjusted p-value < 0.01) in the JPGM. Of them, those having the highest and lowest relative abundance among the 12 countries were identified. P-values were adjusted for multiple testing using p.adjust(p, "BH") in R language, which is based on the Benjamini-Hogberg approach[125].

2.3. Results

2.3.1. Metagenomic sequencing of the Japanese gut microbiome

My colleagues collected 168 fecal samples from 106 healthy JP individuals (age: 32 ± 11, BMI: 22±2.7 (mean ± s.d.); Appendix 1), extracted DNA from them with enzymatic lysis method and sequenced those using 454, Ion PGM/Proton and MiSeq sequencers. After the quality filtering, in total, I obtained about 350 gigabases (Gb) of metagenomic reads with an average of 3.4 ± 1.9 Gb (mean ± s.d.) for each individual (Appendix 1).

I performed *de novo* assembly of the metagenomic reads of the JPGM using Newbler for each individual to generate 13 Gb of contigs (≥ 500 bp) and 0.6 Gb of singletons (≥ 300 bp) (Fig. 2.1). In the sequences, approximately 23 M genes (the length ≥ 100bp) were predicted with MetaGeneAnnotator. I further clustered them with CD-HIT with a 95% nucleotide identity and 90% length coverage cut off. This procedure excluded many redundant genes shared among the individuals. Finally, I obtained 4,854,719 non-redundant genes as the reference gene set of the JPGM (Fig. 2.1).

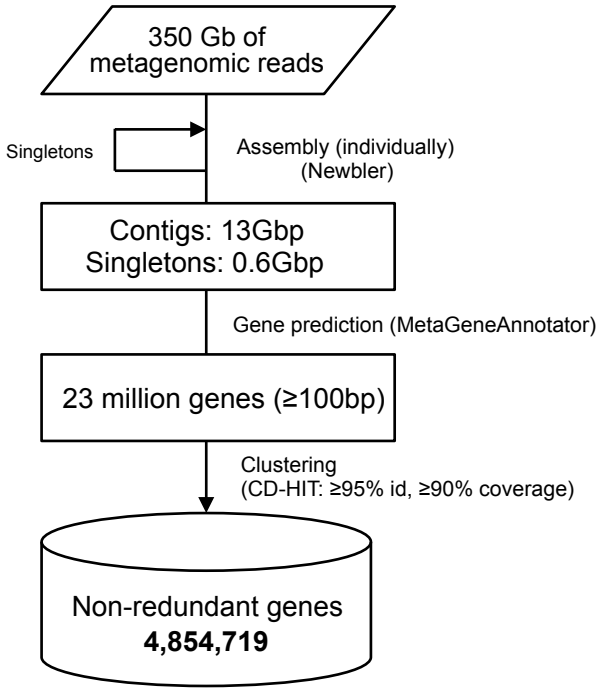


Fig. 2.1. Assembly and gene prediction of the metagenomic reads of the JPGM.

2.3.2. Analysis of the non-redundant genes of the Japanese gut microbiome

Rarefaction analysis of the number of non-redundant genes against the number of individuals sequenced showed that the genes shared by ≥ 1.9% (2/106) in the JP individuals were almost constant with approximately 100 individuals, while unique genes detected only in an individual were increased even beyond 100 individuals (Fig. 2.2a). The number of the genes shared by ≥ 1.9% in the JP individuals accounted for about 3.8 M genes, which covered 98.8% of the total mapped reads to the JP gene set. This result suggested that the reference gene set covers most of the genes encoded by the JPGM. The number of the genes shared by ≥ 50% in the JP individuals was

approximately 0.21 M, which accounted for about only 4% of the total JP gene set, indicating that only the small fraction constitutes the core gene set of the JPGM (Fig. 2.2b).

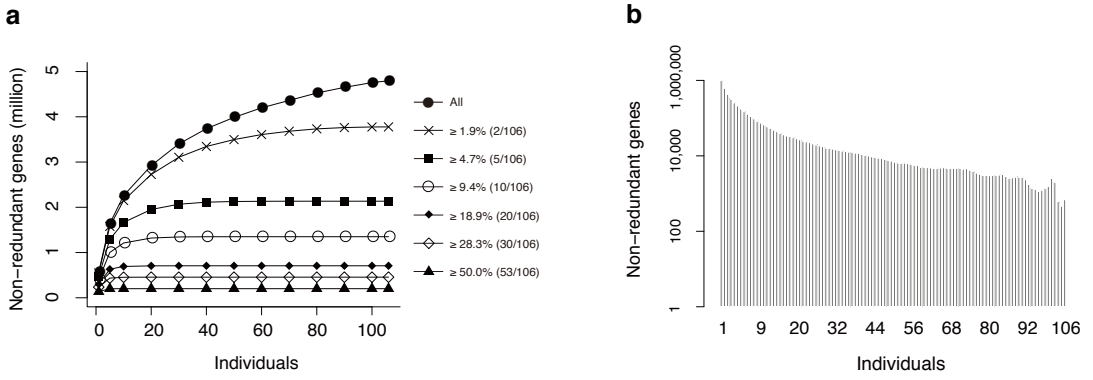


Fig. 2.2. Non-redundant genes in the JPGM. (a) The numbers of detected non-redundant genes plotted against the numbers of the JP individuals. Different symbols show the frequency of the genes in the JP individuals. (b) The number of the non-redundant genes shared by each number of the individuals plotted against the number of individuals.

Functional analysis of the non-redundant genes annotated with the KEGG database showed that the individual-specific genes contained significantly more functions involved in restriction-modification system such as type I restriction enzyme (K01154 and K03427), DNA methyltransferase (K00588) and site-specific DNA-methyltransferase (K00571) than the core genes shared by ≥ 50% in the JP individuals (Table 2.1a). Methyltransferases have the ability to frequently exchange their target recognition domains between them to increase the sequence diversity in these proteins[126], suggesting that restriction-modification system is a driving force for specifying individual gut microbiomes. On the other hand, the core genes were significantly rich in functions related to horizontal gene transfer (HGT) such as conjugal transfer ATP-binding protein TraC (K12063), site-specific DNA recombinase (K06400)

and integrase (K14059) in addition to many of essential genes such as ribosomal proteins (K02935, K02886, K02950 and K02967) as compared with individual-specific genes (Table 2.1b). From the finding that the genes involved in HGT are highly conserved, I hypothesize that HGT is crucial more than considered previously for functional adaptation of the gut microbial community to various ecological changes in the gut because novel or additional genes are acquired and spread in the microbial community by HGT. Similar results were also obtained in the analysis of gut microbiomes of China, Denmark, Spain and the United States[106], suggesting that the accelerated evolution of the individual-specific restriction-modification system and the highly conserved genes involved in HGT is a common feature of the human gut microbiome.

Table 2.1. Functions enriched in individual-specific genes (a) and core genes (b).

a

KEGG	Function	FDR adjusted p-value
K01154	type I restriction enzyme, S subunit [EC:3.1.21.3]	2.40E-180
K00754	not assigned	4.19E-97
K00558	DNA (cytosine-5-)-methyltransferase [EC:2.1.1.37]	1.80E-79
K01153	type I restriction enzyme, R subunit [EC:3.1.21.3]	8.75E-79
K00571	site-specific DNA-methyltransferase (adenine-specific) [EC:2.1.1.72]	8.66E-67
K03427	type I restriction enzyme M protein [EC:2.1.1.72]	2.10E-57
K07316	adenine-specific DNA-methyltransferase [EC:2.1.1.72]	5.36E-39
K00012	UDPglucose 6-dehydrogenase [EC:1.1.1.22]	3.08E-37
K07741	anti-repressor protein	4.10E-34
K01156	type III restriction enzyme [EC:3.1.21.5]	5.50E-32
K01791	UDP-N-acetylglucosamine 2-epimerase [EC:5.1.3.14]	4.61E-23
K08679	UDP-glucuronate 4-epimerase [EC:5.1.3.6]	3.19E-21
K06909	phage terminase large subunit	1.21E-19
K03328	polysaccharide transporter, PST family	4.22E-19
K06223	DNA adenine methylase [EC:2.1.1.72]	6.76E-19
K06915	not assigned	1.42E-18
K07474	phage terminase small subunit	5.60E-18
K01155	type II restriction enzyme [EC:3.1.21.4]	5.84E-18
K00786	not assigned	5.20E-16
K07459	putative ATP-dependent endonuclease of the OLD family	1.01E-15
K02334	DNA polymerase bacteriophage-type [EC:2.7.7.7]	1.56E-15
K02337	DNA polymerase III subunit alpha [EC:2.7.7.7]	1.71E-15
K06904	not assigned	4.79E-15
K15125	filamentous hemagglutinin	7.06E-15
K09952	hypothetical protein	2.29E-14
K01599	uroporphyrinogen decarboxylase [EC:4.1.1.37]	2.89E-14
K15914	N-acetyl-D-galactosamine transferase [EC:2.4.1.-]	1.24E-13
K03657	DNA helicase II / ATP-dependent DNA helicase PcrA [EC:3.6.4.12]	1.24E-13
K15342	CRISP-associated protein Cas1	1.58E-13
K06877	DEAD/DEAH box helicase domain-containing protein	2.88E-13

b

KEGG	Function	FDR adjusted p-value
K00936	not assigned	1.52E-69
K12063	conjugal transfer ATP-binding protein TraC	4.08E-67
K06400	site-specific DNA recombinase	1.05E-41
K00599	not assigned	6.44E-38
K03205	type IV secretion system protein VirD4	4.24E-37
K03088	RNA polymerase sigma-70 factor, ECF subfamily	7.01E-35
K07467	phage replication initiation protein	3.49E-33
K01144	exodeoxyribonuclease V [EC:3.1.11.5]	3.02E-21
K00689	dextransucrase [EC:2.4.1.5]	2.66E-19
K02574	ferredoxin-type protein NapH	2.66E-19
K02358	elongation factor Tu	4.17E-18
K07706	two-component system, AgrA family, sensor histidine kinase AgrC [EC:2.7.13.-]	3.05E-17
K01420	CRP/FNR family transcriptional regulator, anaerobic regulatory protein	1.56E-15
K14059	integrase	4.35E-13
K02855	AraC family transcriptional regulator, L-rhamnose operon regulatory protein RhaS	8.84E-13
K02982	small subunit ribosomal protein S3	1.34E-12
K07496	putative transposase	1.34E-12
K11527	two-component system, unclassified family, sensor histidine kinase and response regulator	3.16E-12
K07487	transposase	1.16E-11
K07814	putative two-component system response regulator	5.27E-11
K02935	large subunit ribosomal protein L7/L12	1.48E-10
K02886	large subunit ribosomal protein L2	1.55E-10
K02030	polar amino acid transport system substrate-binding protein	2.61E-10
K07052	not assigned	4.00E-10
K10117	multiple sugar transport system substrate-binding protein	6.43E-10
K02950	small subunit ribosomal protein S12	9.24E-10
K02967	small subunit ribosomal protein S2	1.28E-09
K02099	AraC family transcriptional regulator, arabinose operon regulatory protein	1.28E-09
K03327	multidrug resistance protein, MATE family	1.74E-09
K07775	two-component system, OmpR family, response regulator ResD	5.07E-09

P-values were calculated using the Fisher's exact test and adjusted for multiple testing.

2.3.3. Structure of the Japanese gut microbiomes

I analyzed the gut microbiomes from the 106 JP individuals by mapping the metagenomic reads to the reference genomes and genes. I identified 14 phyla and 178 genera of Bacteria and Archaea in the gut microbiomes of the 106 JP individuals (average relative abundance ≥ 0.001%). The obtained microbial compositions were mainly composed of four phyla such as Firmicutes (59.7 ± 14.7% (mean ± s.d.)), Actinobacteria (21.8 ± 16.3%), Bacteroidetes (16.7 ± 10.4%) and Proteobacteria (1.4 ± 1.6%) (Fig. 2.3a)[14, 18]. At the genus level, *Bifidobacteirum* (18 ± 15%), *Blautia* (17 ± 8.7%), *Bacteroides* (11 ± 8.5%), *Eubacterium* (6.5 ± 6.0%), *Faecalibacterium* (5.7 ± 4.7%) and *Ruminococcus* (5.6 ± 5.4%) dominated (mean relative abundance ≥ 5%) (Fig. 2.3b and 2.4), and at the species level, *Bifidobacterium adolescentis* (6.0 ± 8.9%), *Bifidobacterium pseudocatenulatum* (5.4 ± 7.5%), *Bifidobacterium longum* (4.6 ± 4.0%), *Blautia wexlerae* (4.3 ± 3.6%) and *Blautia* sp. CAG:37 (4.0 ± 5.1%) (mean relative abundance ≥ 3%) dominated in the JPGM (Fig. 2.3c and 2.4). Consistent with the previous studies, I observed high taxonomic diversity in the microbial compositions between individuals. The factors that determine the diversity in the microbial compositions of individuals have been poorly understood. On the other hand, the functional categories of the genes showed a relatively low diversity between individuals as compared with that in the microbial composition (Fig. 2.3). Similar results were also observed in the previous study of American gut microbiomes, implying the strong selective pressure for functions in shaping of the human gut microbiome[18, 24].

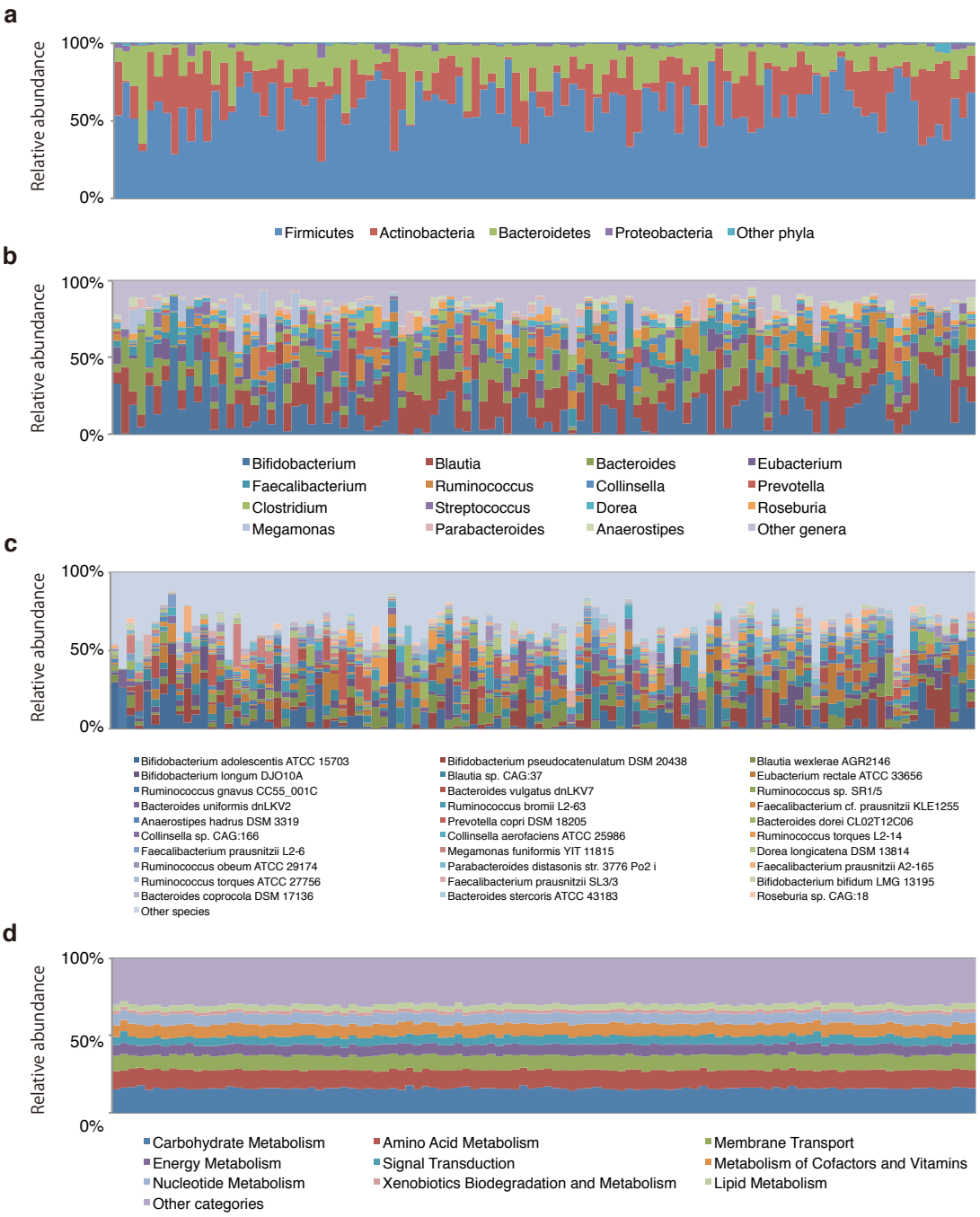


Fig. 2.3. Microbial and functional compositions of the 106 JP individuals. Metagenomic reads were analyzed with the pipeline and the microbial compositions at the phylum (a), the genus (b), the species level (c) and the functional profiles (d) were shown.

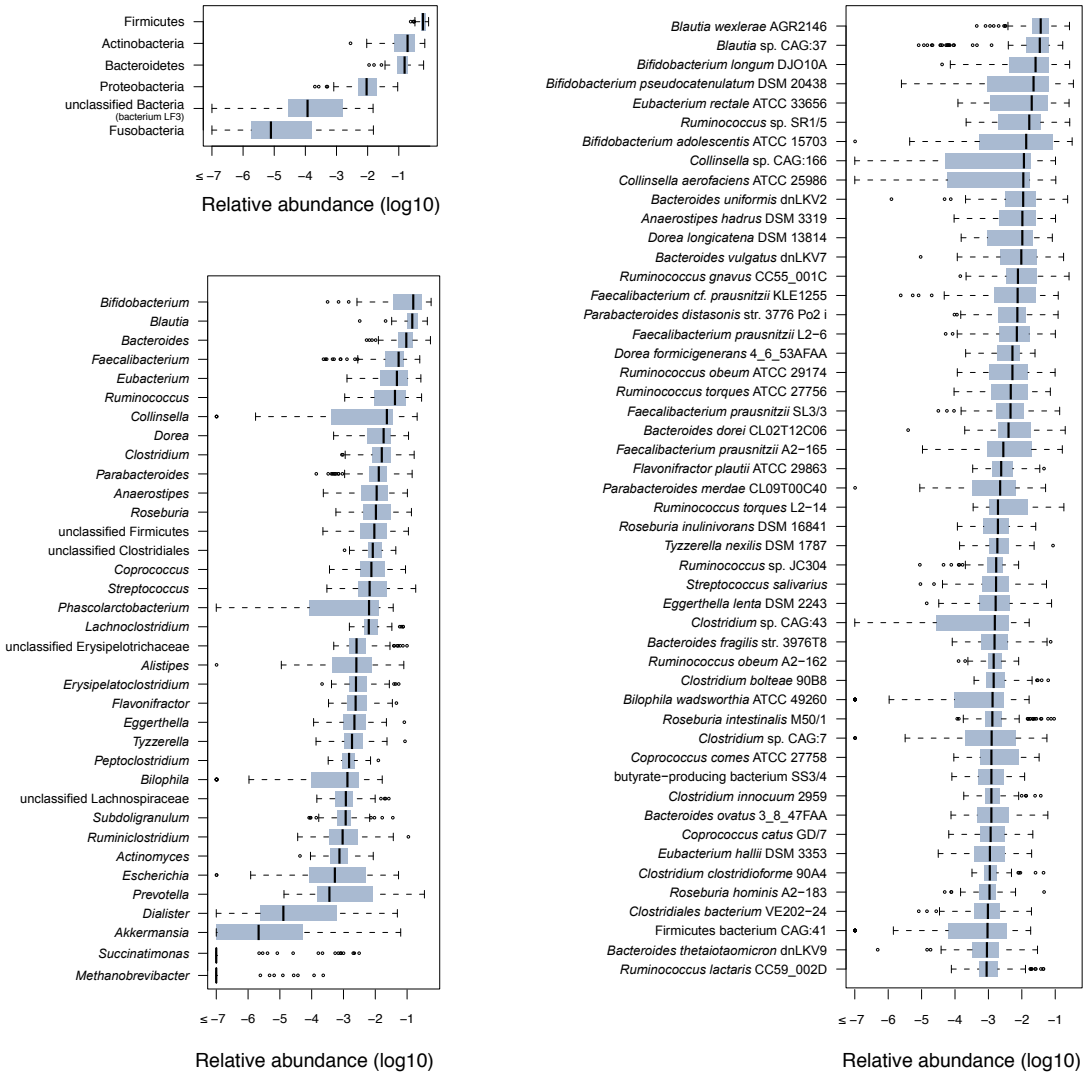


Fig. 2.4. Boxplot of the relative abundance of the taxonomy in the JPGM. Relative abundances of each genus (a) and species (b) in the 106 JP individuals were shown. Boxes represent the interquartile range (IQR) and the lines inside show the median. Whiskers denote the lowest and highest values within 1.5 times the IQR.

2.3.4. Population-level diversity in the human gut microbiome

In addition to metagenomic data of the JPGM, I collected metagenomic data of publically available samples from 11 other countries: i.e., Denmark (DK)[17, 68], Spain

(ES)[17, 106], the United States (US)[18, 51, 102], China (CN)[26, 29], Sweden (SE)[27], Russia (RU)[28], Venezuela (VE)[51, 118], Malawi (MW)[51], Austria (AT)[30], France (FR)[33] and Peru (PE)[102]. I combined the independent cohort data per country to construct country-specific metagenomic datasets, comprising a total of 861 healthy individuals in which the data for individuals with BMI ≥ 30, those designates with the following diseases based on the literature: IBD, type 2 diabetes, colorectal cancer, liver cirrhosis, and infants < 3 years old were excluded (Table. 2.2).

Table 2.2. The number of individuals from the 12 countries used in this study

Country	Total number of individuals in each country	The number of individuals used in this study*	Average age	Average BMI	References
Austria (AT)	156	41	66.6	26.0	30
China (CN)	382	187	39.1	22.0	25, 28
Denmark (DK)	290	121	55.2	24.2	5, 67
France (FR)	156	55	60.6	23.9	33
Japan (JP)	106	104	32.0	21.9	This study
Malawi (MW)	23	5	20.2	20.8	51
Peru (PE)	36	31	20.9	20.8	102
Russia (RU)	96	83	35.7	22.6	28
Spain (ES)	141	54	40.4	24.5	17, 106
Sweden (SE)	145	36	70.4	24.9	27
The United States (US)	174	126	26.5	23.6	17, 50, 100
Venezuela (VE)	29	18	20.2	20.8	50, 103
Total	1,734	861			

*: Patients with obesity (BMI ≥ 30), IBD, type 2 diabetes, colorectal cancer and liver cirrhosis and infants (< 3 years) were excluded (see text).

To investigate population-level variations in human gut microbiome structures among the 12 countries, I evaluated the microbial composition at the genus level by mapping the metagenomic reads to the reference genomes. The MDS plot of the microbial compositions showed that each country had a tendency to form distinct clusters (Fig. 2.5a). A permutation test confirmed significantly higher similarity of the microbial composition between individuals within a country than those between different countries (Fig. 2.5b). To test whether the microbial composition can predict an

individual's country of origin, I employed randomforest analysis[27, 51] to construct a predictive model for the 10 countries except VE and MW, for which sample numbers were too small to analyze. The results showed that AUCs ranged from 0.82 for US to near 1.00 for PE (Fig. 2.5c), demonstrating the high predictive accuracy of the model. Taken together, these results strongly suggested that the gut microbiome structure is significantly diverse across the 12 countries.

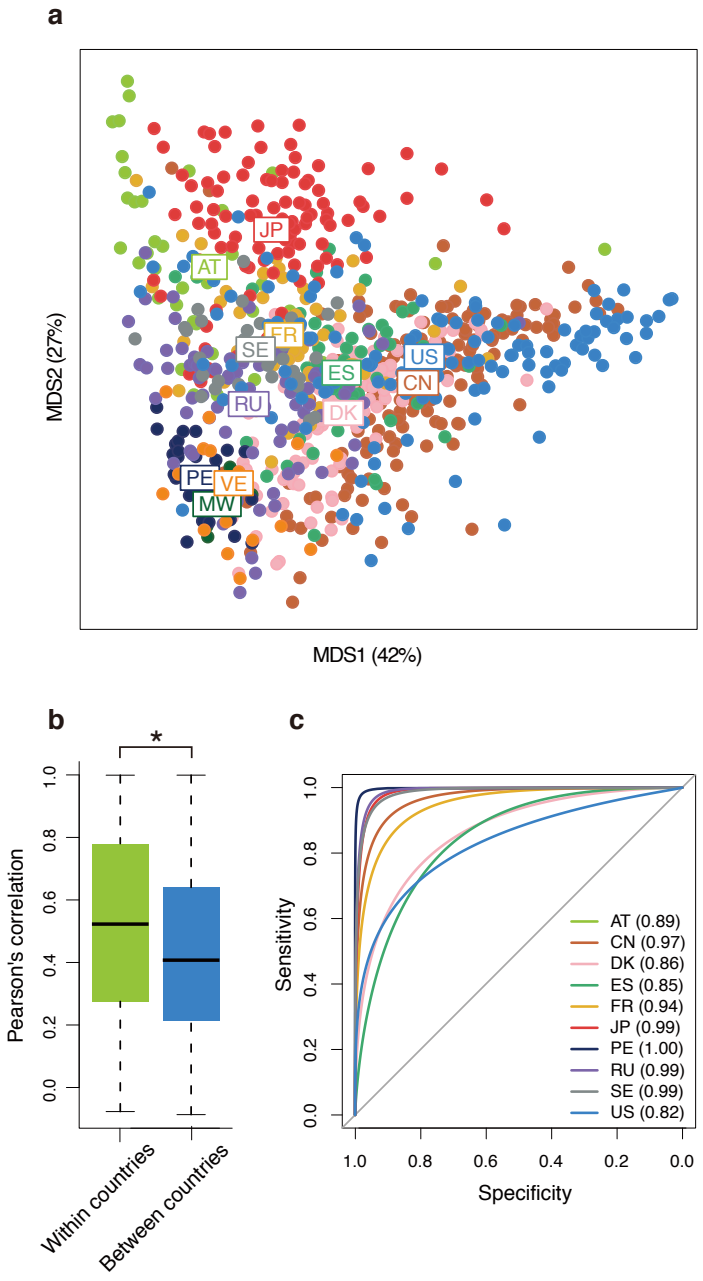


Fig. 2.5. Population-level diversity in human gut microbiomes from the 12 countries. a, MDS plot of microbial compositions at the genus level for the 861 individuals. Each circle represents an individual microbial composition and colors represent the country of origin. The position based on the average microbial composition for each country is displayed by abbreviations of the country name. b, Comparison of Pearson's correlation coefficients of microbial compositions in individuals within a country and those between different countries. Boxes represent the interquartile range (IQR) and the lines inside show the median. Whiskers denote the lowest and highest values within 1.5 times the IQR. Asterisk represents *P*-value < 0.05. c, ROC curves and AUC values from the randomforest model. The number in parenthesis represents the AUC values of the 10 countries.

To examine the effects of different protocols used in the present and other studies on the observed differences in the microbial composition at the genus level, I compared and assessed variations in the microbial composition estimated from three different NGS sequencers, four different DNA extraction methods including two enzymatic lysis methods and two commercially available kits based on mechanical disruption of cells, and four different fecal sample storage conditions (Table 2.3). For the fecal sample storage conditions, I focused on assessment of differences in the storage time from defecation until freezing of fecal samples because it was considered to be varied among the studies (Table 2.4). The results revealed that PCCs between the microbial compositions from different protocols were high (from 0.88 to 1.00) in any pair of comparisons between them (Fig. 2.6), and significantly higher than those observed for the individuals within and between countries (Fig. 2.7). Although several samples showed relatively low similarities in microbial composition between different DNA extraction methods, the lowered similarities observed were not caused by a particular protocol, rather due to differences in the individual samples used. These data suggested that the methodological differences had no significant effects on the observed variations among the human gut microbiomes.

Table 2.3. Methodologies and protocols used to assess their effects on microbial composition

Sequencer	Number of samples used
Roche 454	20
Ion PGM	20
Illumina MiSeq	20

DNA extraction method	Number of samples used
Enzymatic method with lysozyme and achromopeptidase	8
Enzymatic method with lysozyme only	8
FastDNA Spin Kit for soil (mechanical method)	8
PowerSoil DNA Isolation Kit (mechanical method)	8

Fecal sample storage conditions	Number of samples used
Stored for one day at room temperature under aerobic conditions (1d-air)	3
Stored for one day at room temperature under anaerobic conditions (1d-ane)	3
Stored for three days at room temperature under aerobic conditions (3d-air)	3
Stored for three days at room temperature under anaerobic conditions (3d-ane)	3

Table 2.4. Sequencers, DNA extraction methods and fecal sample storage conditions used in the present and the other studies.

Country	Sequencers	DNA extraction methods	Fecal sample storage conditions	References
Austria	Illumina	No information	Frozen at −20 ºC after defecation, then stored at −80 ºC within 48 hours	30
China	Illumina	Enzymatic lysis	Frozen at −20 ºC within one day after defecation, then stored at −80 ºC	26
China	Illumina	Mechanical lysis	Immediately transferred in an ice bag to laboratory after defecation, then stored at −80 ºC	29
Denmark	Illumina	Enzymatic lysis	Immediately frozen at −20 ºC after defecation, then stored at −80 ºC	17, 68
France	Illumina	GNOME DNA Isolation Kit (mechanical lysis)	Stored at −20 ºC within 4 hours after defecation	33
Japan	454, Illumina, Ion PGM/Proton	Enzymatic lysis	Transferred at 4 ºC to laboratory within 36 hours after defecation, then frozen in liquid nitrogen and stored at −80 ºC	This study
Malawi	454	No information	Stored at −80 ºC within 30 minites after defecation	51
Peru	Illumina	PowerSoil DNA Isolation Kit (mechanical lysis)	Stored on ice for at most 4 days after defecation, then frozen	102
Russia	SOLiD	Mechanical lysis	Immediately frozen at −20 ºC after defecation	28
Spain	Illumina	Enzymatic lysis	Immediately frozen at −20 ºC after defecation, then stored at −80 ºC	17, 106
Sweden	Illumina	Mechanical lysis	Stored at −80 ºC after defecation	
The United States	Illumina	PowerSoil DNA Isolation Kit (mechanical lysis)	Transferred to laboratory on ice within 24 hours after defecation, then stored at −80 ºC	18
The United States	454	No information	Stored at −80 ºC within 30 minites after defecation	51
The United States	Illumina	PowerMicrobiome RNA Isolation Kit (mechanical lysis)	Stored on ice after defecation, then frozen within 24 hours	102
Venezuela	454	No information	Stored at −80 ºC within 30 minites after defecation	51
Venezuela	Illumina	PowerSoil DNA Isolation Kit (mechanical lysis)	Immediately frozen in liquid nitrogen after defecation	118

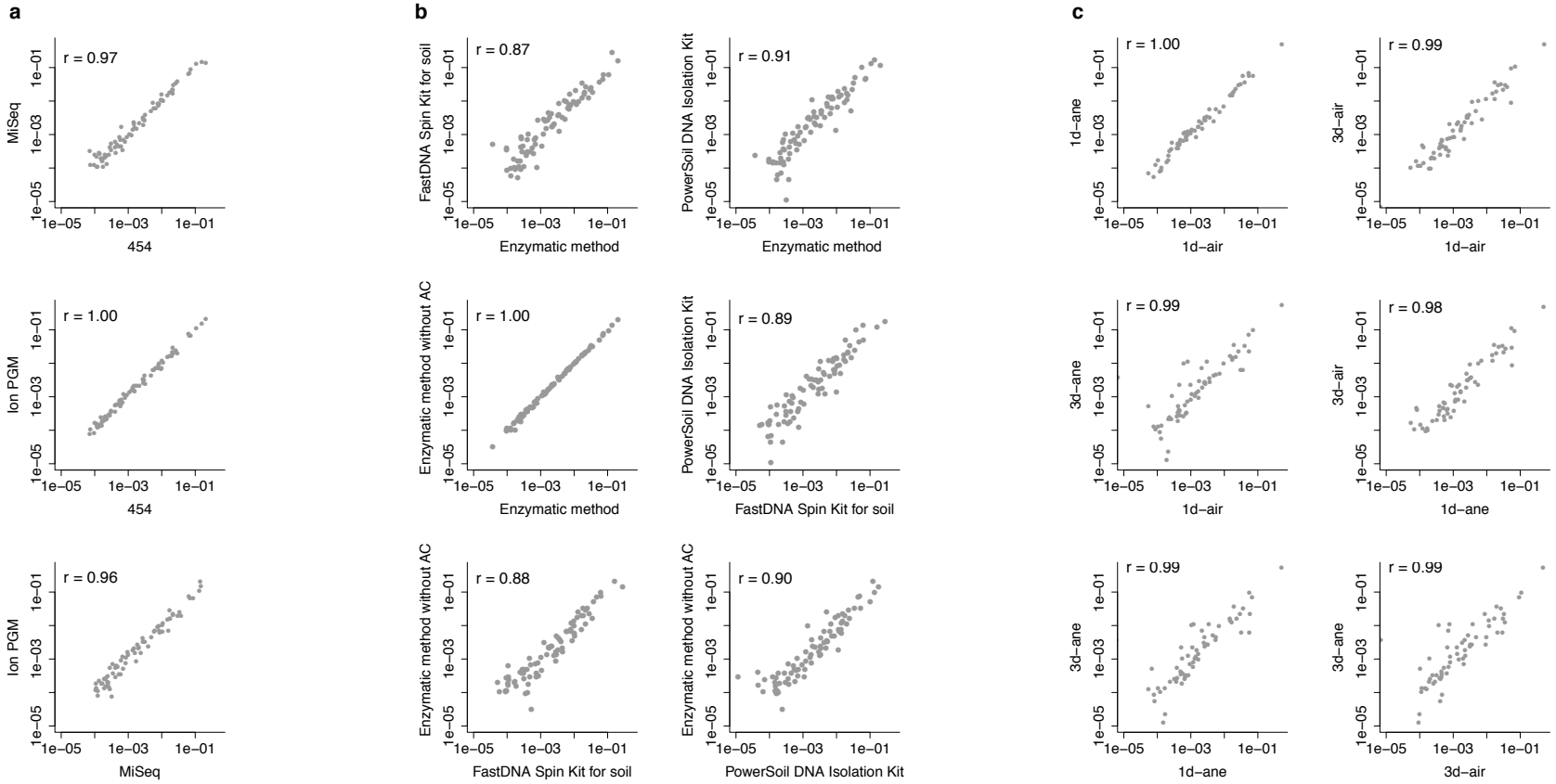


Fig. 2.6. **Comparison of PCCs of microbial compositions at the genus level among three different methodologies and those of individuals within a country and between different countries.** a, Twenty fecal DNA samples were subjected to sequencing with three different sequencers, Roche 454, Illumina MiSeq, and Ion PGM. b, Eight fecal samples were subjected to isolation of fecal DNA by five different DNA extraction methods. c, Three fecal samples were stored under four different storage conditions. Circles represent the genera with average relative abundance ≥ 0.01%. Vertical and horizontal axes indicate the average relative abundance of each genus. Abbreviations for fecal sample storage conditions are summarized in Table 3.3.

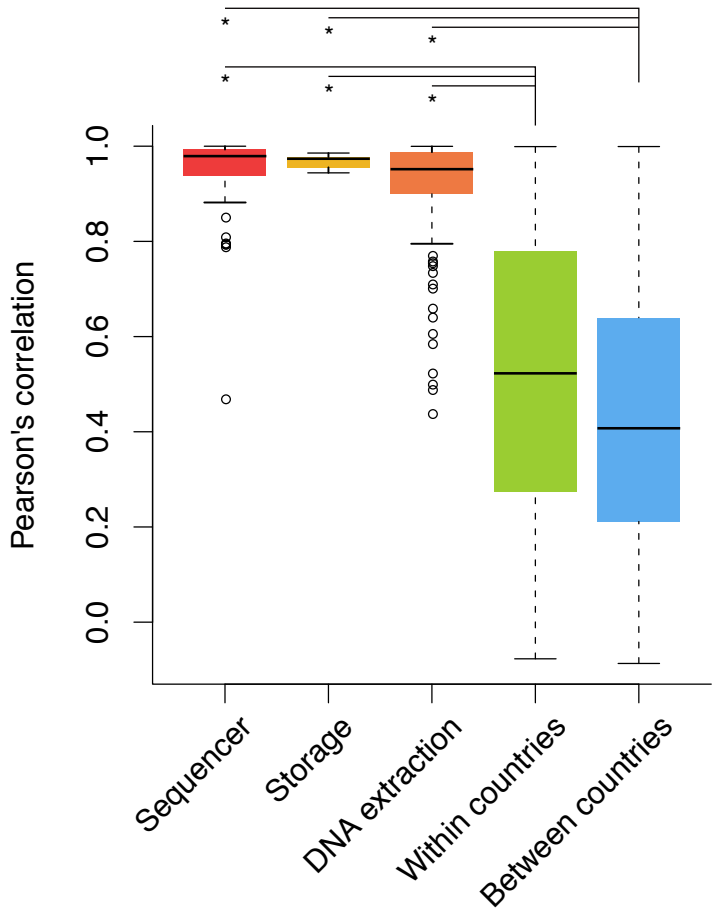


Fig. 2.7. Comparison of PCC obtained from different methodologies and individuals. PCCs of the microbial composition at the genus level in an individual obtained by different methodologies are shown in the left three boxes (red, yellow, and orange), and compared with those of individuals of within-country and between-countries shown in the right two boxes (green and blue). *P*-values were calculated by permutation tests with 10,000 random samplings. Asterisks represent *P*-values < 0.05.

Hierarchical clustering of the 12 countries based on the average microbial composition at the genus level showed that the JPGM was more similar to microbiomes of AT and SE than that of CN, while CN and US were most closely related, but far from the JP among the 12 countries (Fig. 2.8). These results strongly suggested that host ethnic and geographical closeness have no large influence on shaping of the overall

microbial composition of the human gut microbiome. We also assessed the contribution of variations in age and BMI to differences in the microbial abundance by using PERMANOVA. The coefficient of determination for the variation (R^2) in age and BMI was 0.16 (P-value = 0.07) and 0.2 (P-value = 0.14), suggesting that both factors had no significant influence on the observed results as well.

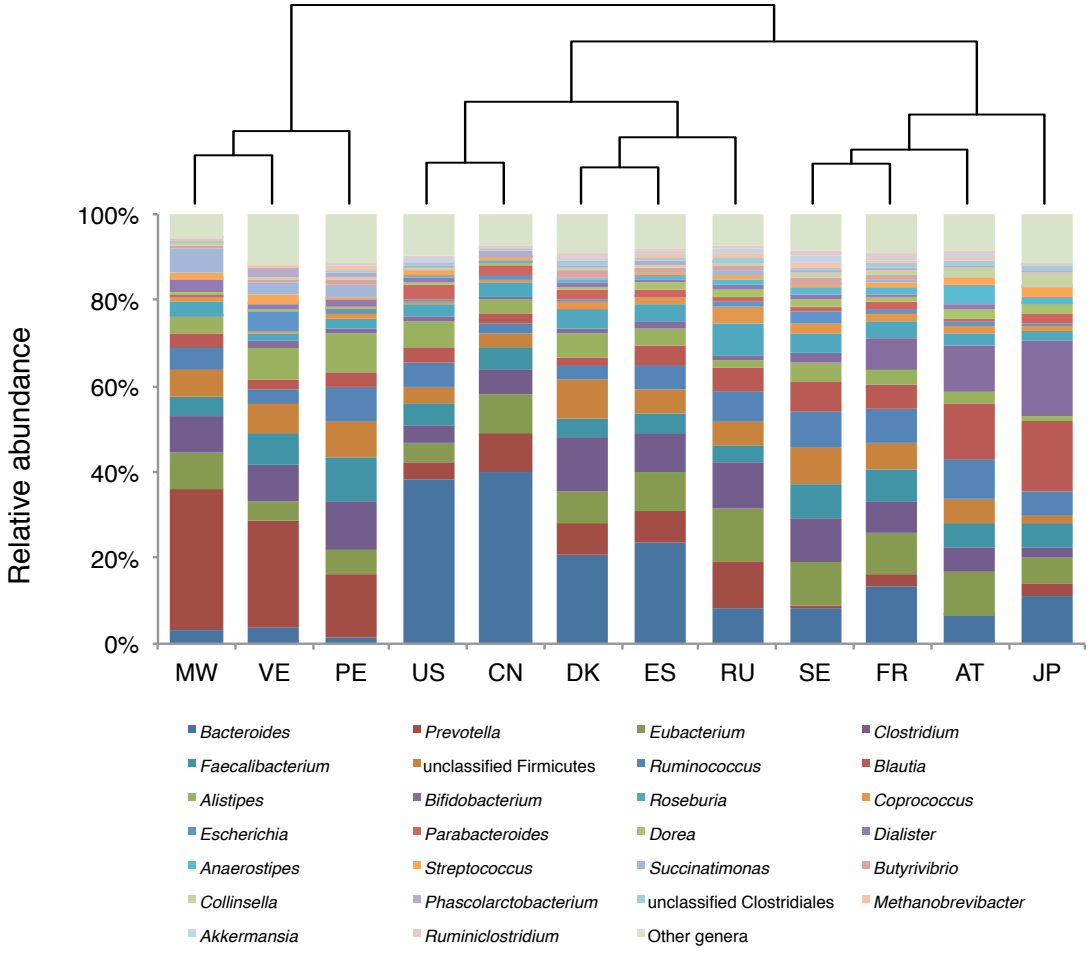


Fig. 2.8. **Hierarchical clustering of the 12 countries based on average microbial composition at the genus level.** Cluster dendrogram was generated with the Ward method using the Bray-Curtis distances. The top 26 genera with average relative abundance ≥ 0.5% are shown.

2.3.5. Characterization of the Japanese gut microbiome

When comparing the abundance of the bacterial phyla, the JPGM showed the highest abundance of Actinobacteria. In contrast, the abundance of Bacteroidetes and Proteobacteria in the JPGM was significantly lower than in the microbiomes of various other countries (Fig. 2.9a). Regarding the bacterial genera, the JPGM was characterized by the highest abundance of *Bidfidobacterium*, *Blautia*, *Collinsella*, *Streptococcus* and unclassified Clostridiales, but the lowest abundance of *Clostridium*, *Alistipes*, unclassified Firmicutes, *Dialister* and *Butyrivibrio* among the 12 countries (Fig. 2.9b).

Another characteristic feature of the JPGM was that it has the lowest frequency of *Methanobrevibacter smithii*, a methanogenic archaeon, among the 12 countries (Fig. 2.9c). Metagenomic mapping analysis showed that this species was detected only in eight (7.7%) JP individuals, while it was detected in a proportion of 39 – 100% of the individuals in other countries (relative abundance ≥ 0.0001%, Fig. 2.10a). The lowest prevalence of this archaeon in the JP cohort was also validated by PCR using species-specific 16S rRNA gene primers. The data showed that *M. smithii* was undetected in 97 (92%) of the 106 JP individuals both in the metagenomic mapping and PCR analysis, where five were positive in both analyses, three were positive only in the mapping analysis and one was positive only in the PCR analysis (Fig. 2.10b).

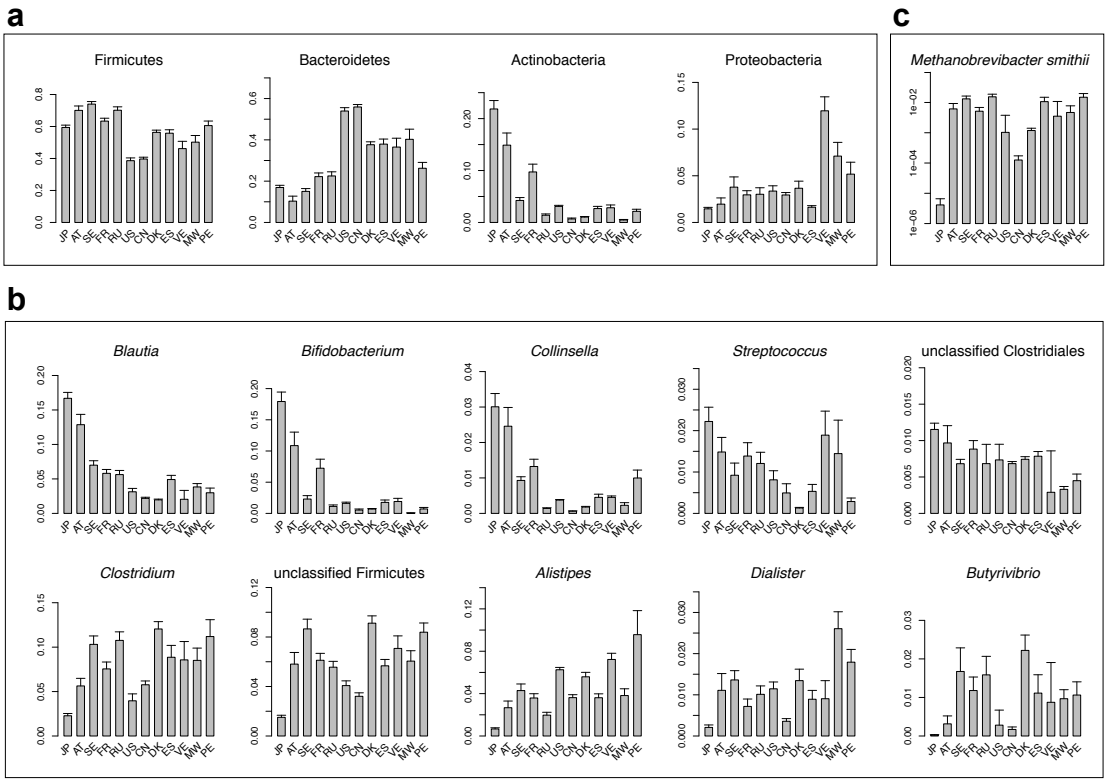


Fig. 2.9. **Taxonomic comparison of gut microbiomes of populations from the 12 countries.** Relative abundances of the four dominant phyla (a), the five genera with the highest and lowest abundance in the JPGM (b), and *M. smithii* (c) in the 12 countries are shown. Vertical axes represent the relative abundance of the species calculated from the number of mapped reads to the reference genomes.

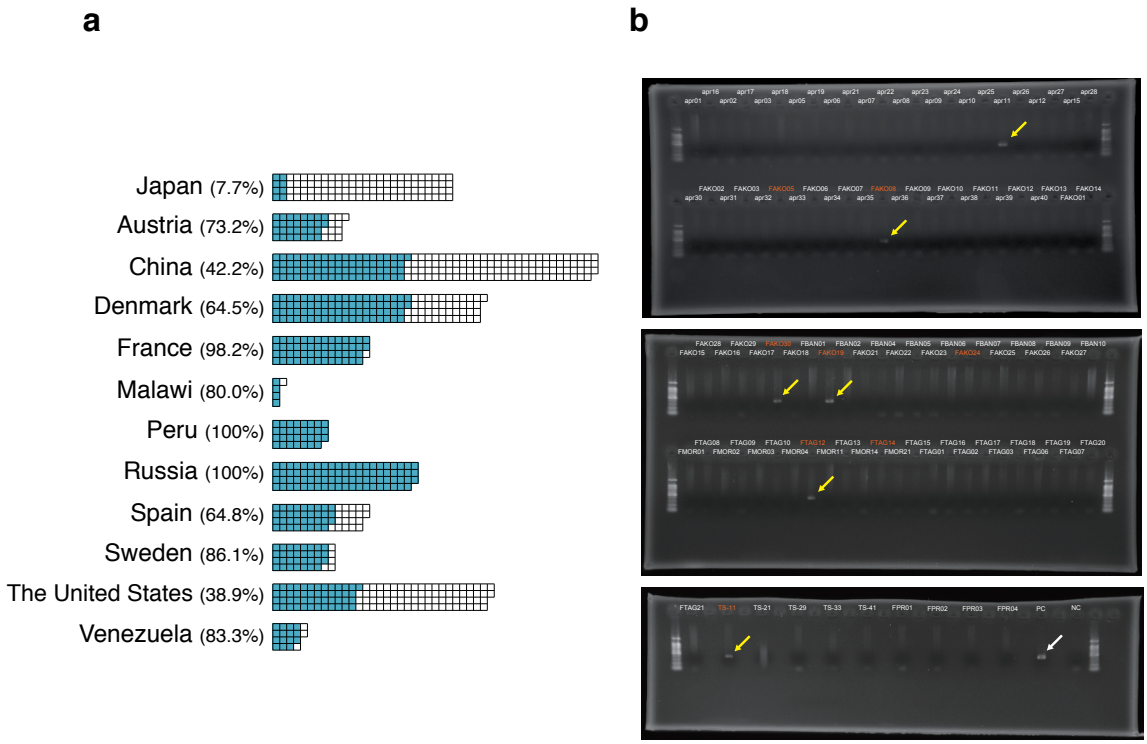


Fig. 2.10. **Detection of *M. smithii* in the human gut microbiome.** (a) Open and blue boxes indicate the individuals for which *M. smithii* was detected (relative abundance ≥ 0.0001%) and undetected, respectively, by mapping of metagenomic reads to the reference genomes. (b) PCR detection of *M. smithii* in the 106 JP individuals. Individual's IDs are represented at each lane, and the ones indicated in orange were *M. smithii*-positive in the mapping analysis. Yellow arrows indicate the bands for the PCR product of *M. smithii,* of which the positive control (PC) is shown by a white arrow. NC, negative control.

2.3.6. Functional comparison of the Japanese gut microbiome with the others

I compared the JP gene set with the IGC gene set[106]. The clustering of the JP (4.9 M) and the IGC genes (9.9 M) generated 11,929,034 non-redundant genes in total, of which about 2.0 M genes were shared by both gene sets, and 2.3 M and 7.7 M genes were unique to JP and IGC, respectively (Fig. 2.11a). This limited overlap between the JP and IGC gene sets was supported by the mapping analysis of metagenomic reads, in

which 45.6% of the JP metagenomic reads were mapped to the IGC gene set, while 80.0% were mapped to the JP gene set (Fig. 2.11b). In this clustering, 585,856 genes and 202,410 genes decreased from the original JP and IGC gene sets, respectively. This can be explained by the fact that these genes were fragmented and merged to longer authentic genes in either of the gene sets. As a result, the JP and IGC gene sets are composed of 4,268,863 and 9,676,237 non-redundant genes, respectively.

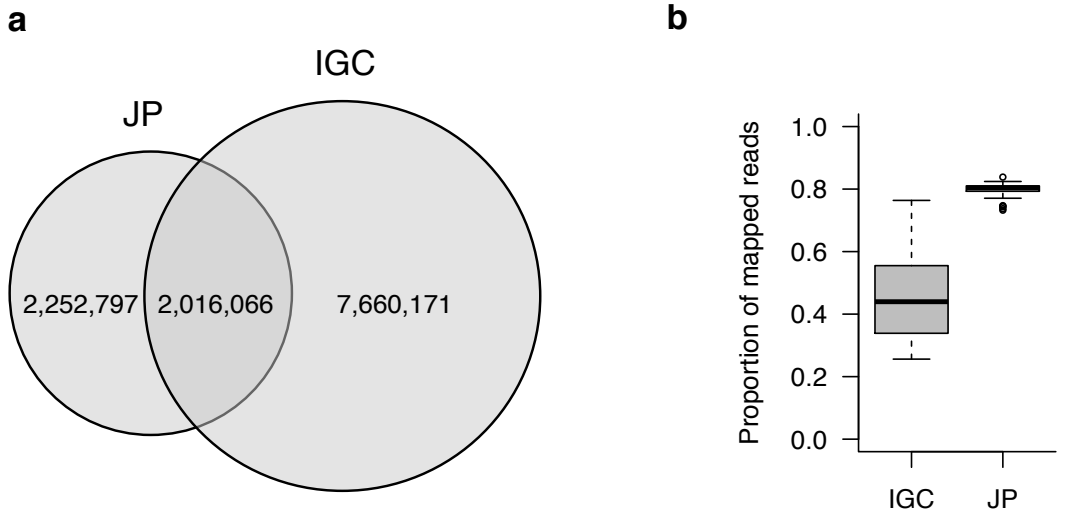


Fig. 2.11. **Comparison of JPGM and IGC non-redundant gene sets.** (a) Venn diagram of the number of genes in both gene sets. (b) Ratio of the mapped JP metagenomic reads to the JP and IGC gene sets.

Next, I annotated the gene sets with functions based the KEGG database. The analysis identified 5,789 KOs in the JPGM and a total of 6,205 KOs from both gene sets, in which 5,613 KOs (90%) were shared between both gene sets, demonstrating a significantly high similarity in functional profiles across the populations despite the small overlap in the gene sequences, which is concordant with the previous finding of a

high interindividual similarity of the functional profiles[24]. It was noted that the IGC-unique 416 KOs included multiple genes related to archaeal methane metabolism, while the JP-unique 176 KOs included more genes for spore formation than the IGC-unique KOs (Appendix 4 and 5).

To explore functions that are enriched or depleted in the JPGM as compared with microbiomes from the 11 other countries, I mapped the metagenomic reads of all individuals to the JP and IGC merged gene set. By comparing the numbers of mapped reads, we identified 563 and 521 KOs having the highest and lowest abundances in the JPGM among the 12 countries with statistical significance (Fig. 2.12, and Appendix 6 and7). The overrepresented KOs included functions for carbohydrate metabolism such as glucan 1,3-β-glucosidase (K01210), 6-phospho-β-galactosidase (K01220) and gluconokinase (K00851), and for membrane transport such as the phosphotransferase system of simple sugars including mannose, lactose, and *N*-acetylgalactosamine (K02796, K02787 and K02746). Thus, metabolic pathways for simple sugars such as mono- and oligosaccharides were significantly enriched in the JPGM as compared with the others. On the other hand, the depleted KOs included functions such as cell motility including chemotaxis protein CheX (K03409) and flagellar protein FliO/FilZ (K02418), replication and repair including DNA mismatch repair protein MutL (K03572) and DNA adenine methylase (K06223), suggesting a depletion of functions related to host immunity and DNA damage in the JPGM.

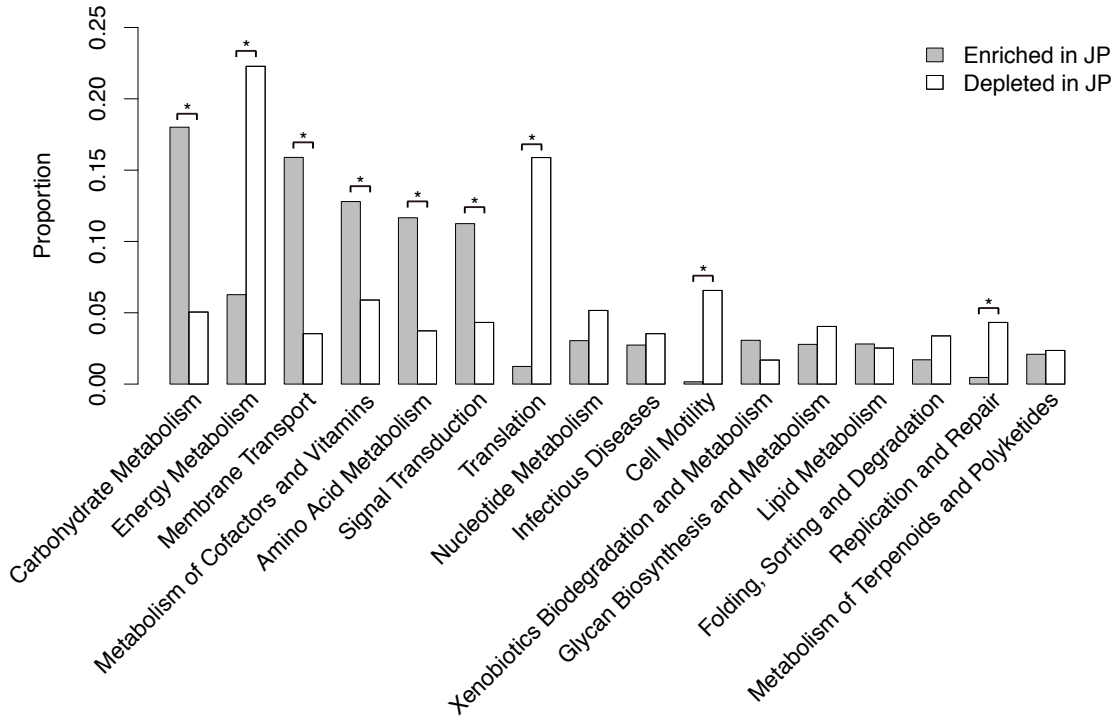


Fig. 2.12. **Enriched and depleted functions in the JP gut microbiome.** Functional categories of the KOs most enriched and depleted in the JPGM as compared with those of the other 11 countries are shown. The vertical axis represents the proportion of KOs assigned to the category. Asterisks indicate adjusted FDRs < 0.01 (Fisher's exact test).

In agreement with the lowest prevalence of *M. smithii* in the JP cohort, many of the KOs involved in methanogenesis were depleted in the JPGM. Of the 25 known KOs involved in methanogenesis, 18 were significantly depleted in the JPGM, with the lowest abundance among the 12 countries (Fig. 2.13 and 2.14). Conversely, I found a significant enrichment for multiple KOs involved in acetogenesis (the Wood–Ljungdahl pathway) in the JPGM. Of the 17 known KOs involved in acetogenesis, 13 were significantly enriched in the in the JPGM as compared with the other 11 countries, and five of them had the highest abundance among the 12 countries (Fig. 2.13 and 2.14). These two pathways utilize hydrogen to generate methane and acetate[127]. Furthermore the abundance of five known KOs involved in dissimilatory sulfate reduction (DSR),

which is the third pathway for hydrogen metabolism, was similar between the JP and other gut microbiomes (Fig. 2.13 and 2.14). These results indicated that the JPGM had a clear inverse pattern in the abundance of the KOs between both metabolic pathways as compared to all other microbiomes, suggesting a prominent difference in the pathways for hydrogen utilization in the gut between Japanese and other populations.

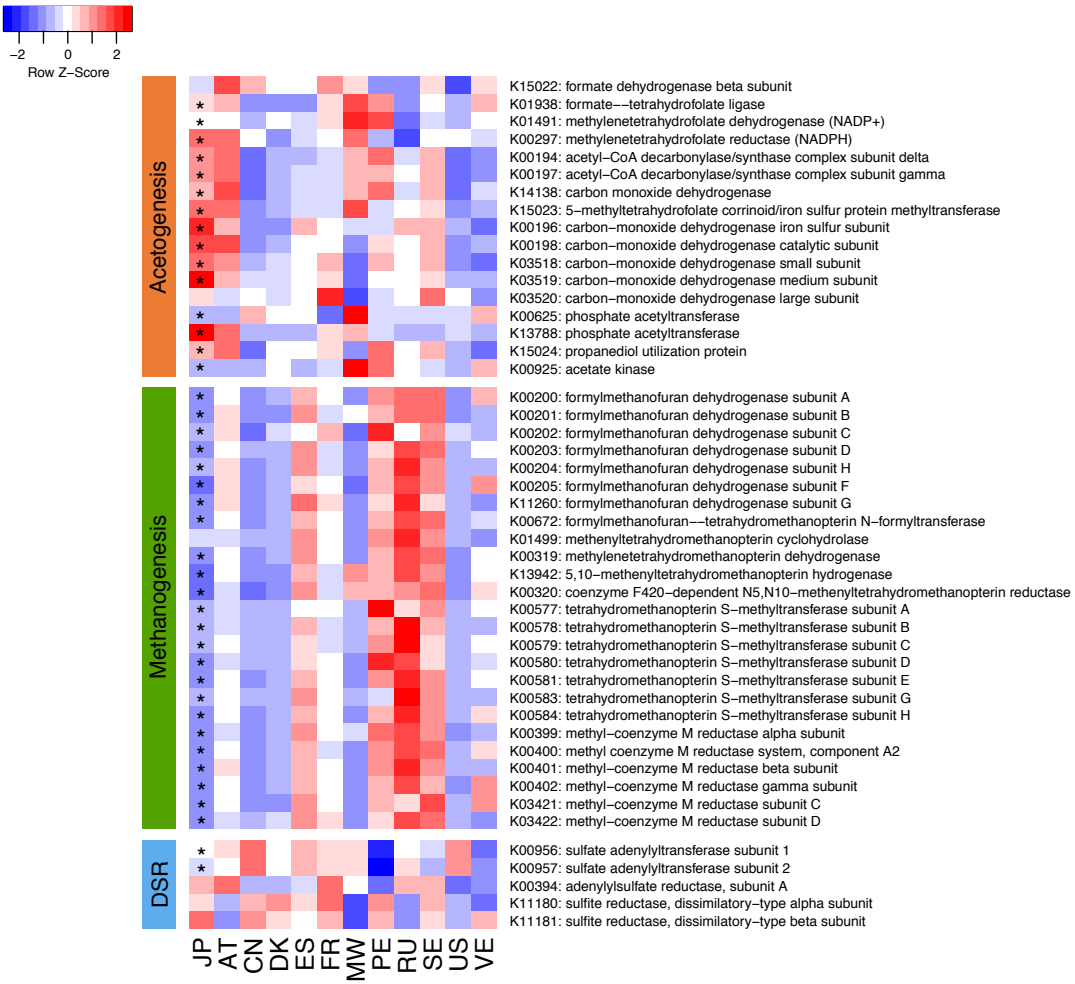


Fig. 2.13. **Enriched and depleted genes in the acetogenesis, methanogenesis, and dissimilatory sulfate reduction in the JPGM.** Relative abundances of KOs involved in the pathways for hydrogen metabolism in acetogenesis, methanogenesis and dissimilatory sulfate reduction among the 12 countries are shown. Red and blue boxes denote statistically high and low abundances as compared with the average abundance of the other 11 countries, respectively. Asterisks indicate adjusted FDRs < 0.01 (Student's *t*-test between the 104 JP individuals and the 757 individuals in the other countries).

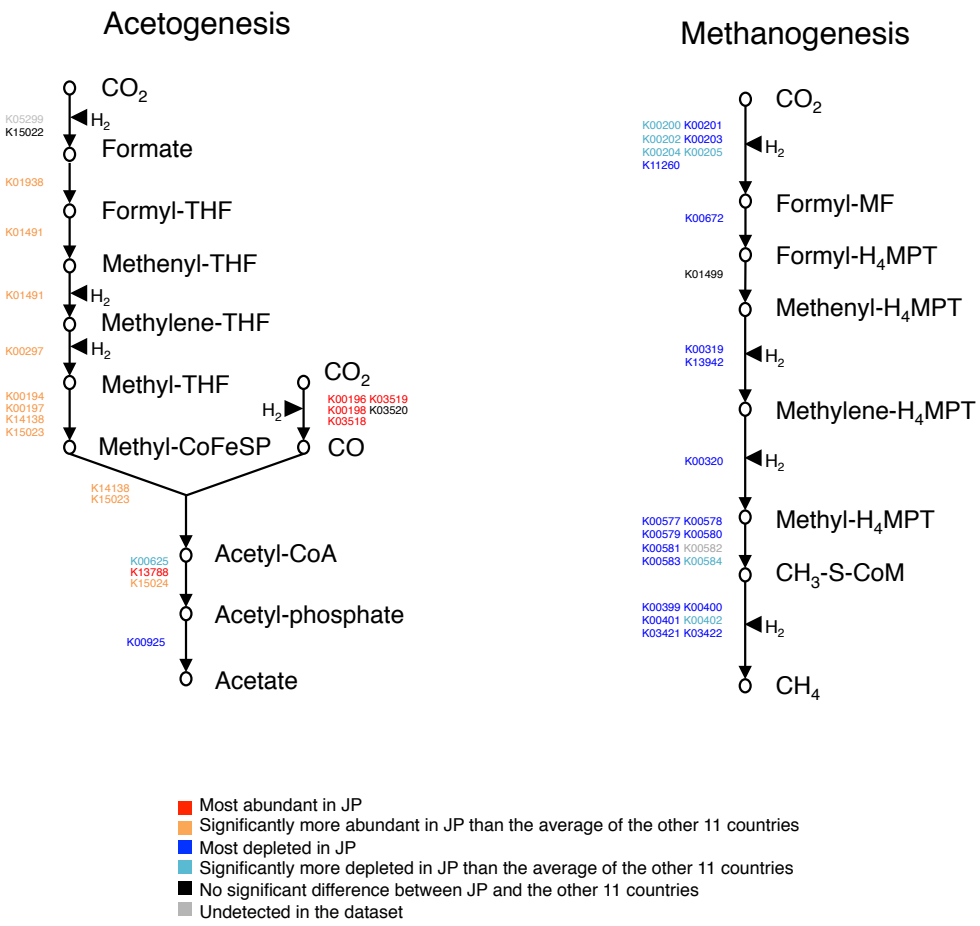


Fig. 2.14. **Metabolic pathways of acetogenesis and methanogenesis.** Metabolic pathways for acetogenesis and methanogenesis and KOs involved are shown. Colors indicate differences in the abundance of the KOs shown in the figure.

2.3.7. Gene families enriched in the Japanese population

I comprehensively surveyed gene families that are frequently present in the JP cohort by using the eggNOG database, which includes more compiled gene families than the KEGG database. The annotation of the merged JP and IGC non-redundant genes yielded 51,250 NOGs. In this analysis, I used 10 M metagenomic reads per individual

to detect a low content of NOGs, so that 60 individuals having < 10 M reads, including all individuals from MW and VE, were excluded from this analysis.

I mapped 10 M reads from the 801 individuals to the merged non-redundant genes to detect the NOGs present in the individual. For these NOGs, I compared the proportion of individuals possessing them in the JP cohort and with the average proportion of the individuals proportion in other the nine other countries, (Fig. 2.15). The results revealed 52 NOGs comprising a total of 1,114 genes that were detected in significantly higher proportions in the JP cohort than in the nine other countries using a threshold of a proportion of > 70% in JP, an average proportion of < 30% in other countries, and the a ratio of JP/others of ≥ 3. Of the 1,114 genes, 63% were taxonomically assigned to the known phyla. Among them, 30 (58%), eight (15%), and five (10%) NOGs were assigned to only Actinobacteria, Bacteroidetes, and Firmicutes, respectively, and nine other NOGs were distributed over more than two phyla (Fig. 2.16a). The high fraction of Actinobacteria may reflect the highest abundance of this phylum in the JP cohort among the 12 countries. Among the eight NOGs assigned to the Bacteroidetes, three NOGs (ENOG4108ZIS, ENOG4108MQB and ENOG4105WVE), that were detected in approximately 90% of the JP individuals cohort and in ~15% of other populations with the highest ratio of JP/others, were represented by the genes for aquatic plant-derived polysaccharide-degrading enzymes such as β-porphyranase (hydrolase family 16) and β-agarase published previously[49]. The functional distribution of the 52 NOGs revealed that 35% were of unknown function and no particular function was enriched (Fig. 2.16b).

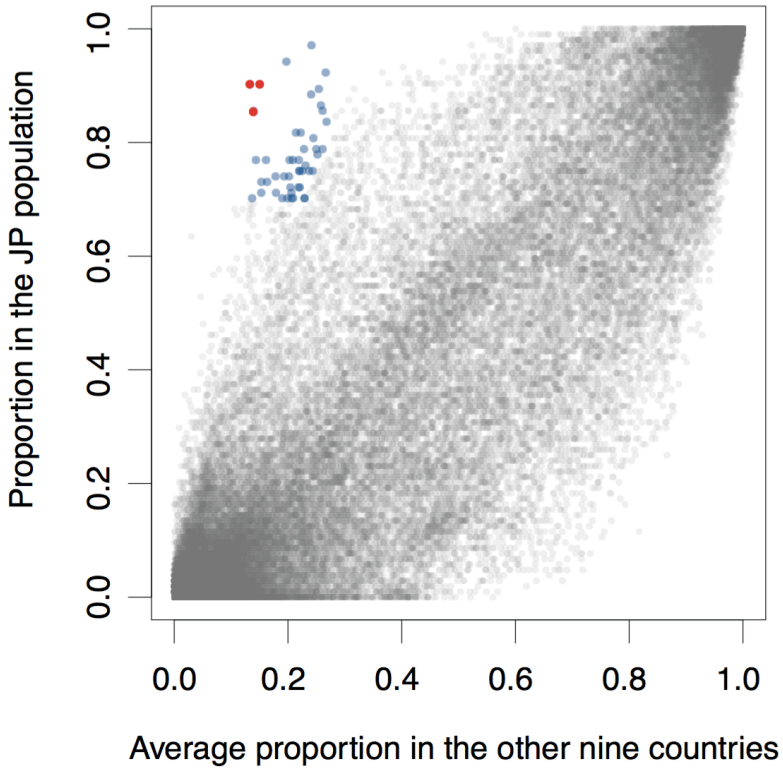


Fig. 2.15. Comparison of the prevalence of NOG gene families between the JP and the nine populations. The frequency of NOGs in the JP individuals plotted against those in the other nine countries. Each circle represents a NOG. The vertical axis represents the frequency of NOGs detected in the JP individuals. The horizontal axis represents the average frequency of NOGs detected in the individuals of the nine countries. Fifty-two NOGs significantly highly prevalent in the JP cohort as compared with the others (JP > 0.7 and the others < 0.3) are colored with blue. Three NOGs (ENOG4108MQB, ENOG4108ZIS, and ENOG4105WVE) were depicted in red.

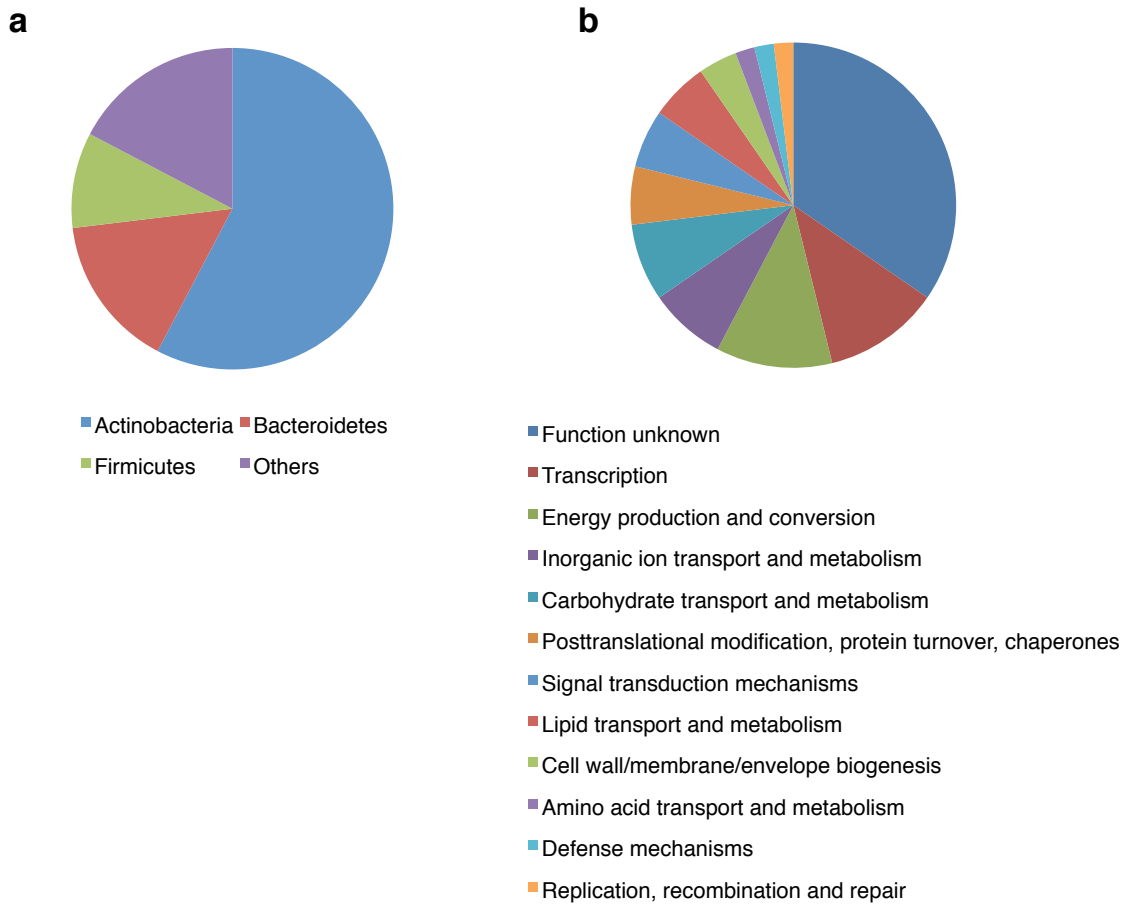


Fig. 2.16. Taxonomic and functional assignment of the 52 NOGs having a higher abundance in the JP cohort than in the other populations.
(a) Distribution of the 52 NOGs per phylum is shown. “Others” indicates more than two phyla.
(b) Distribution of the 52 NOGs per functions is shown.

2.1. Discussion

In this study, I conducted a metagenomic analysis of the JPGM from 106 individuals. By assembling the 350 Gb metagenomic sequences, predicting genes and clustering, I constructed a gene set of the JPGM comprising approximately 4.9 M non-redundant genes. The number of genes in this gene set is comparable to those (from 3.3 M to 6.0 M genes) reported in previous studies analyzing the gut microbiomes of individuals in other countries including DK, ES, CN, US and SE. The rarefaction analysis revealed that the JPGM gene set covered most of the genes shared by at least 1.9% in the JP individuals, indicating that the present gene set can be used as a reference for the genes in the JPGM.

The comparative analysis of the metagenomic datasets between the 104 JP individuals and the 757 individuals from other 11 other countries revealed a significant population-level diversity in the human gut microbiome across the 12 countries. The accuracy and reliability shown in this study is supported by the use of a larger dataset including more populations than that used in the previous studies. Additionally, the statistical assessment indicated no large effects of differences in experimental protocols such as DNA extraction method, fecal storage conditions and sequencer, BMI and age, on the observed results, which also supported the present findings. Thus, I provided the evidence for large variations in the structure and function of the human gut microbiomes of healthy adults at the population-level.

The present study also revealed various features specific to the JPGM. The JPGM showed the highest abundance of the phylum Actinobacteria among the microbiomes of the 12 countries, mainly because of the highest abundance of the genus *Bifidobacterium*. The high abundance of *Bifidobacterium* has also been observed in the gut microbiome

of Japanese children based on the 16S rRNA gene analysis[100], indicating that it is highly prevalent throughout the Japanese population. *Bifidobacterium* is thought to be a beneficial microbe having more glycoside hydrolases for degrading starch than other intestinal microbes[128]. Therefore, the high abundance of *Bifidobacterium* can be considered to be the consequence of the intake of various saccharides in traditional and unique Japanese foods. However, at present, it is unknown exactly which foods or nutrients unique to the Japanese diet contribute to the high abundance of *Bifidobacterium*.

Additionally, the JPGM is characterized by various unique functional features. For example, the high abundance of carbohydrate metabolism was observed in the JPGM, which leads to the production of high levels of short chain fatty acids and hydrogen as end products, both of which seems to be clinically beneficial[129, 130]. Concurrently, I found a depletion of deleterious functions such as cell motility, and replication and repair, suggesting a low abundance of the flagellated microbes leading to reduced proinflammatory responses by host cells and less DNA damage to be repaired in the gut of the Japanese individuals. Together, I suppose that such a gut ecosystem containing these beneficial functions might be globally associated with the highest average life span of Japanese in the world.

A remarkable depletion of the archaeon *M. smithii* is also characteristic of the JPGM, resulting in an overall depletion of genes for methanogenesis. In contrast, genes for acetogenesis, which are exclusively encoded by anaerobic acetogens such as the major species *Blautia*[131], were enriched in the JPGM as compared with other gut microbiomes. Both methanogenesis and acetogenesis are considered to be critical pathways for hydrogen consumption in the gut because these pathways are tightly linked with anaerobic fermentation of carbohydrates producing hydrogen[125]. My

findings suggest that acetogenesis is the preferable pathway for hydrogen metabolism in the JPGM, while methanogenesis is more actively utilized for hydrogen metabolism in many of the other gut microbiomes. Additionally, since the abundance of intestinal *M. smithii* is positively associated with the level of breath methane[132], the present data strongly suggest that *M. smithii* is the primary factor for ethnic differences in the level of methane in human breath reported previously[133, 134].

Many of microbial and functional uniqueness I found in the JPGM may be more or less influenced by various internal and external factors, contributing to the population-level diversity in the human gut microbiome. Therefore, to more deeply understand the diversity in human gut microbiomes, elucidation of such factors is further required.

3. Antibiotics shapes population level diversity in the human gut microbiome

3.1. Introduction

Human gut microbiome structure is affected by various factors such as diet[108, 135], antibiotics[136, 137], host's physiology[26, 29] and genetics[104]. For example, long-term dietary habit rich in protein and animal fat was correlated with a high abundance of *Bacteroides* in human gut, while that rich in carbohydrate was correlated with an enrichment of *Prevotella*[108]. Abundances of several taxonomies, particularly *Christensenellaceae*, were more largely associated between monozygotic twin pairs than between dizygotic twin pairs, suggesting the influence of host's genetic background[104]. In addition, antibiotic intake had a strong impact on the gut microbiome structure, resulting in an incomplete recovery of the structure to the initial state[138]. However, little is known about the factors and extent of their contribution to the population-level variability in the microbial abundance observed in chapter 1. To explore such factor, I conducted a large-scale association study of the epidemiological data of several external factors including dietary intake and antibiotic usage with metagenomic data of the 861 individuals from the 12 countries.

3.2. Methods

3.2.1. Collection of dietary intake data

Dietary intake information of 119 food items for the 12 countries was downloaded from the Food and Agriculture Organization Corporate Statistical database (FAOSTAT) (http://faostat3.fao.org/home/, as of June 2015). The averaged dietary intakes (g/capita/day) from 2002 to 2011 in the 12 countries were used for correlation analysis. According to the Standard Tables of Food Composition in Japan, 2010[139], three major nutrient compositions (carbohydrates, lipids and proteins) were calculated from the averaged dietary intakes of 119 food items, and the 119 food items were grouped into nine food categories based on their nutrient similarities. Nutrient quantities were transformed to z-scores before clustering, and dendrograms were generated using the Ward method and Spearman's correlation as dissimilarity. The amount of the nine food categories was normalized by the total dietary intake of each country.

3.2.2. Collection of antibiotic usage data

The data for antibiotic usage in humans, the defined daily dose (DDD) per 1,000 inhabitants, were collected from Hogberg LD *et al*[140], and the European Surveillance of Antimicrobial Consumption (ESAC) yearbook in 2009[141]. The data for China were obtained from Wang X *et al*[142]. The data of antibiotic usage in farm animals in kilograms were obtained from Van Boeckel TP *et al*[143]. The antibiotic usage in farm animals normalized by counting population number of the country was used for the correlation analysis. The details about the antibiotics are summarized in Tables 3.5 and 3.6.

3.2.3. Statistical analysis

Correlations between microbes and epidemiological factors (dietary and antibiotic usage data) were evaluated using Pearson's correlation coefficient (PCC) and Spearman's correlation coefficient (SCC). P-values were adjusted for multiple testing using p.adjust(p, "BH") in R language, which is based on the Benjamini-Hogberg approach[125]. Permutational Multivariate Analysis of Variance (PERMANOVA) was used to assess the association of these factors with variation of the overall gut microbiome structure using the adonis function in the Vegan package in R with Euclidian distances as dissimilarity.

3.2.4. Analysis of gut microbiomes of Asian children

The 16S rRNA gene sequence data of gut microbiomes of children from five Asian countries (Japan, China, Taiwan, Indonesia and Thailand)[100] were publically available and were obtained from GenBank/DDBJ/EMBL. Low quality bases (< 20 QV) at the 5′ ends were removed and reads with an average quality ≤ 25 were discarded. For each sample, up to 3,000 reads were used for similarity searches against the reference genomes using BLASTN with a 94% identity and a 90% length coverage cut-off. Antibiotic usage data of the five countries were obtained from the literature by Hogberg LD *et al*[144]. Correlations of between the relative abundance of *Bacteroides* and antibiotic usage were evaluated with PCC and SCC.

3.2.5. Antibiotic resistance genes analysis

To identify antibiotic resistance genes (ARs) in the gut microbiome, the Resfams database[144] was employed. The merged reference genes were searched against the Resfam database using the hmmscan function of HMMER3[145] with gathering thresholds.

The genes assigned to ‘transcriptional factor’ were excluded from further analysis. Up to one M metagenomic reads of each individual were mapped to the ARs using Bowtie2 with a 95% identity cut-off. The number of mapped reads to the ARs was normalized by the number of the total reads used to the mapping. One third of the genes assigned to ‘ABC transporter’ were used for the analysis since two thirds of them in this class were estimated to be false positives in the original paper[144].

ARs in the reference genomes were also examined by the same methods. For this analysis, we used 126 genomes of the species with > 0.05% abundance in average among the 12 countries. The genomes generated from assembly of only metagenomic reads[146] were not used in this analysis because they possessed significantly fewer ARs than the other genomes generated by sequencing of the cultured strains. For example, for *Bacteroides*, 8.2 ARs per genome were annotated for cultured strains, while 3.8 ARs per genome were found in the genomes generated from assembly only of the metagenomic reads. These data suggested the difficulty of sufficient reconstruction of genomes only from short metagenomic reads, particularly for the genomes containing ARs showing high sequence similarity due to horizontal gene transfer. Therefore, metagenomic reads containing ARs may not be efficiently incorporated into contigs in the assembly step to avoid misassembly, and contigs containing ARs may not be accurately assigned to particular species as well.

3.2.6. Analysis of the microbial composition in mice treated with beta-lactam antibiotics

The 16S rRNA gene sequence data of gut microbiomes of mice treated with and without beta-lactam antibiotics[119, 147] were obtained from GenBank/DDBJ/EMBL. For the data of reference 119, 16S rRNA gene sequence data were analyzed using the method

described previously[110]. In brief, the reads were quality-checked, and those lacking their PCR primer sequences at either sequence termini or the average quality value < 25 were discarded. The 3,000 filter-passed 16S reads for each sample were assigned to the genus using BLASTN with a 94% identity and a 90% length coverage cut off against the full-length 16S rRNA gene sequences database constructed from the Ribosomal Database Project[148]. The relative abundance of the top seven predominant genera was compared between untreated and treated mice (untreated: n=4, treated: n=5). Statistical differences were evaluated with Student's *t*-test. For the data of the reference 147, low quality bases (< 20 QV) at the 5' end were removed and the reads with an average quality ≤ 25 were discarded. For each sample, up to 3,000 reads were used to calculate microbial compositions at the genus level, which were compared between untreated and treated mice (untreated: n=36, treated: n=39) as described above.

3.3. Results

3.3.1. Dietary intake data of the 12 countries

I explored factors that are associated with population-level diversity in the gut microbiomes across the 12 countries. Since diet is considered to be a major factor influencing microbial composition[108, 135], I accessed the Food and Agriculture Organization Corporate Statistical Database (FAOSTAT) to collect the dietary intake data (g/capita/day) for 119 food items in the 12 countries. I calculated the average intakes of three main nutrients (carbohydrates, proteins and lipids) for the 10-year period from 2002 to 2011, and grouped the food items in nine food categories by clustering them by the compositional similarity of nutrients (Fig. 3.1). Cluster analysis based on these dietary data roughly segregated most of the Western countries from other countries in Asia, South America, and Africa (Fig. 3.2). This indicated that the FAOSTAT data properly represents the current diversity in dietary habits of the 12 countries, allowing for its use in the correlation analysis with the top 26 genera with an average abundance of > 0.5%, accounting for 91% of the total abundance (Table 3.1).

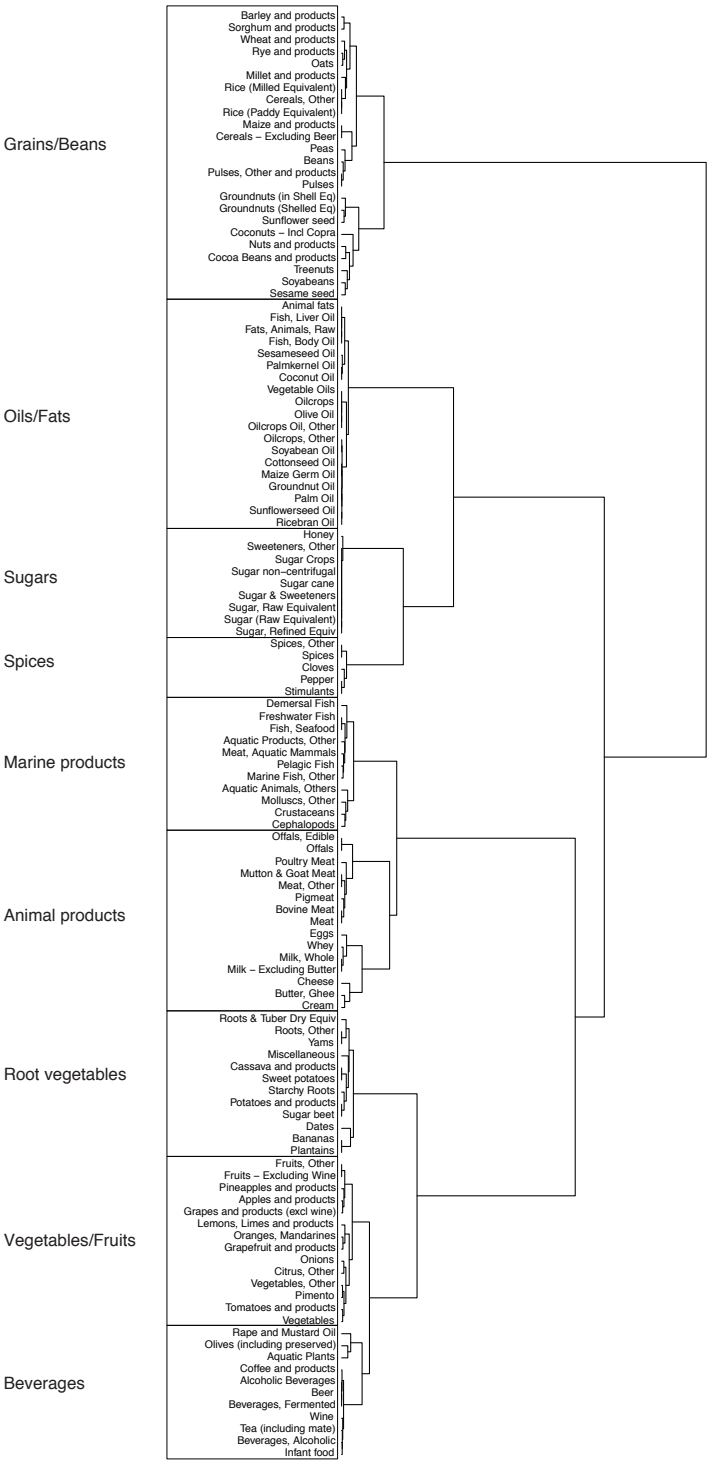


Fig. 3.1. Grouping of 119 food items into nine food categories. The 119 food items in the FAOSTAT database were clustered based on the compositional similarity of nutrients of which levels were calculated according to a book of the Standard Tables of Food Composition in Japan, 2010 (Methods). Quantity of the nutrients was transformed to z-scores before clustering and the dendrogram was generated using the Ward method and Spearman's correlation as dissimilarity.

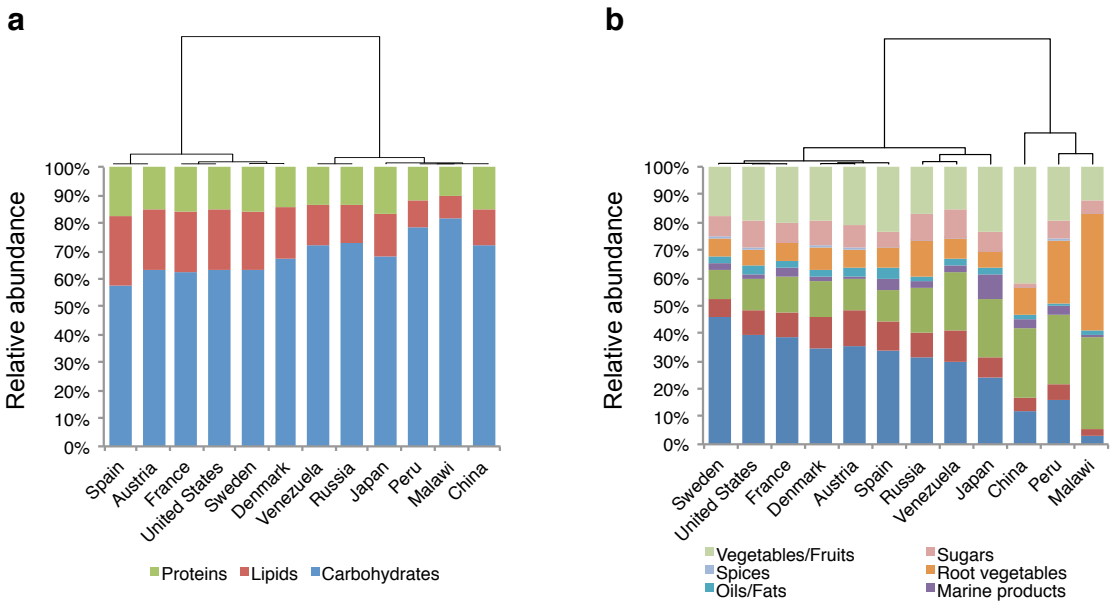


Fig. 3.2. Hierarchical clustering of the 12 countries based on average dietary intake data in the 10 years from 2002 to 2011. a, The dendrogarm of the 12 countries based on the ratio of three main nutrients (carbohydrates, proteins, and lipids) is shown. b, The dendrogarm of the 12 countries based on the ratio of nine food categories is shown. The dendrograms were generated using the Ward method and Pearson's correlation as dissimilarity.

Table 3.1. The average abundance of the top 26 genera used in this study

Genera	Average relative abundance
Bacteroides	14.89%
Prevotella	9.78%
Eubacterium	8.18%
Clostridium	7.95%
Faecalibacterium	5.96%
Unclassified Firmicutes	5.94%
Ruminococcus	5.86%
Blautia	5.75%
Alistipes	4.42%
Bifidobacterium	3.90%
Roseburia	3.61%
Coprococcus	1.53%
Escherichia	1.28%
Parabacteroides	1.27%
Dorea	1.24%
Dialister	1.12%
Anaerostipes	1.09%
Streptococcus	1.07%
Succinatimonas	1.05%
Butyrivibrio	0.96%
Collinsella	0.89%
Phascolarctobacterium	0.81%
Unclassified Clostridiales	0.70%
Methanobrevibacter	0.63%
Akkermansia	0.62%
Ruminiclostridium	0.53%
Total	91.02%

3.3.2. Correlation analysis of the microbiomes with dietary data

Correlation analysis with the three main nutrients revealed inverse relations between carbohydrate and protein/lipid levels for many of the genera tested (Fig. 3.3)[108]. Among them, the abundance of *Prevotella* and *Succinatimonas* positively correlated with carbohydrate and negatively with lipid and protein levels ($P < 0.05$ for all; Fig. 3.3a). At a finer level using nine food categories, the abundance of *Prevotella* and *Succinatimonas* positively correlated with "Grains/beans" and "Root vegetables", and negatively with "Animal products" ($P < 0.05$ for all; Fig. 3.3b). The abundance of *Ruminiclostridium* and *Akkermansia* showed inverse relations to those of *Prevotella* and

Succinatimonas (Fig. 3.3 and 3.4). The positive and negative associations of *Prevotella* with carbohydrate-rich and protein/lipid-rich diets respectively were also reported in several studies[51,101,108]. Unexpectedly, none of dietary factors showed a significant association with the major species *Bacteroides*, which is positively associated with Western diets rich in animal products and has a prominent trade-off relation with *Prevotella* in dietary association[51, 108, 135]

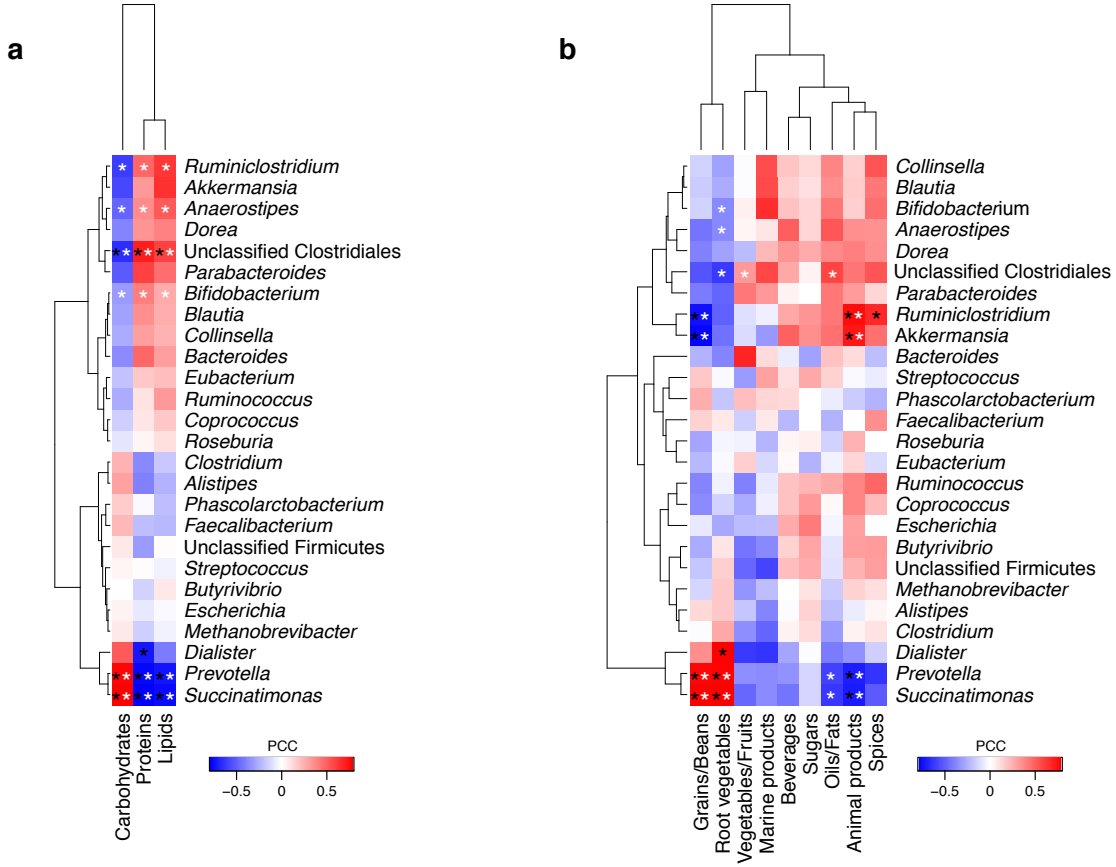


Fig. 3.3. Heat maps based on PCCs between the FAOSTAT dietary intake data and the abundance of the top 26 genera. Boxes depicted in red and blue indicate positive and negative correlations between microbial abundance and dietary intake data, for three main nutrients (a) and nine food categories (b). P-values were adjusted for multiple testing for each genus. Closed and open asterisks represent FDR adjusted p-values < 0.05 for PCC and SCC, respectively.

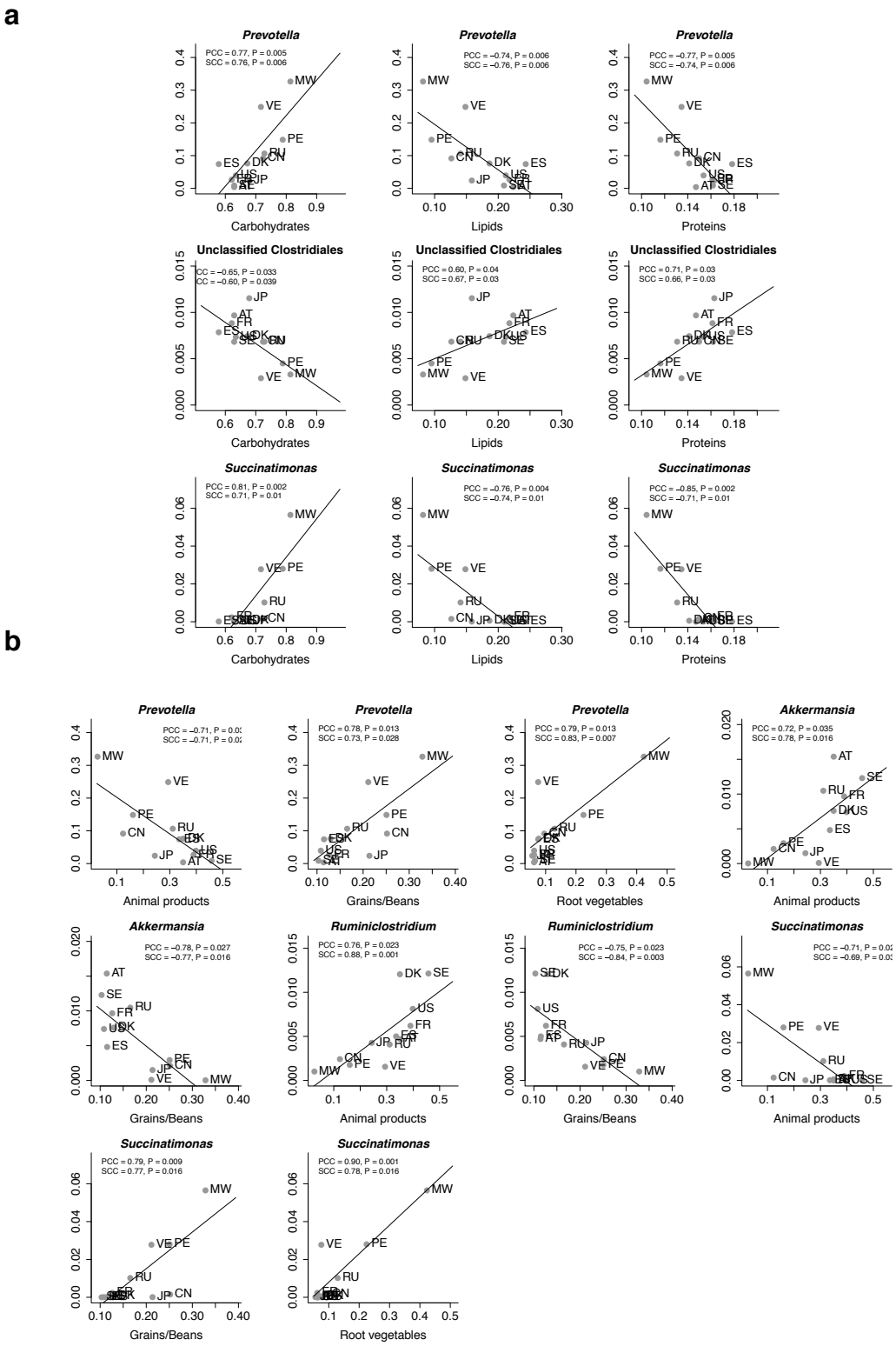


Fig. 3.4. Significant correlation between dietary data and genera. Correlations with statistical significance for both PCC and SCC between the abundance of genera and nutrients (a) and dietary categories (b) are shown**.**

3.3.3. Antibiotic usage in humans and farm animals in the countries

This shallow association between dietary intake and the abundance of *Bacteroides* suggested the existence of factors other than diet which might have a large influence on this major genus, as well as the population-level diversity in human gut microbiomes. In this context, I examined antibiotic usage because it can significantly alter the gut microbiome composition at the individual level[136-138]. Among the resources for antibiotic usage in humans, the collective data were available from two independent datasets: one mainly based on the IMS Health MIDAS database reported by Hogberg *et al*[140], and another based on the European Surveillance of Antimicrobial Consumption Network (ESAC)[141]. I found a significantly high correlation between the antibiotic usage of the countries common to both datasets (Fig. 3.5), suggesting the quantitative reliability and accuracy of both datasets. Since the Hogberg dataset included data for more countries than the ESAC dataset, I used the Hogberg dataset to collect the antibiotic usage information for 10 countries, since MW and CN were unavailable. The antibiotic usage for CN was obtained from other literature[142] (Tables 3.2). I also obtained the antibiotic usage in farm animals from a recent paper[143], for which data from seven countries were available (Table 3.3).

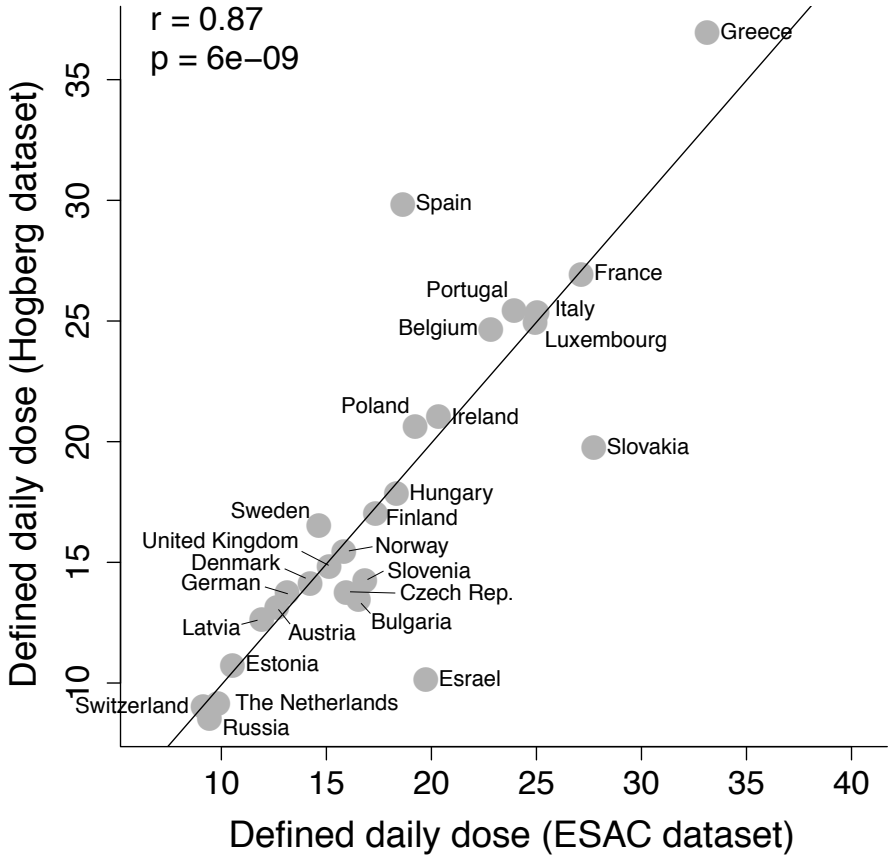


Fig. 3.5. Correlation between antibiotic usage data for countries common to both Hogberg and ESAC datasets. Two datasets of total antibiotic usages in humans, from the study by Hogberg *et al*[140] and the ESAC database[141], were used for the comparison. The antibiotic data of defined daily dose (DDD) in 2004 of the 26 countries common to both datasets were compared. PCCs and *P*-values are shown in the figure.

Table 3.2. Antibiotic usage in humans from 11 countries used in this study.

	AT (Austria)	CN (China)	DK (Denmark)	FR (France)	JP (Japan)	PE (Peru)	RU (Russia)	ES (Spain)	SE (Sweden)	US (The United States)	VE (Venezuela)
Beta-lactams	6.64	18.99	8.83	15.36	4.83	3.68	2.03	20.07	7.83	12.31	5.95
Macrolides/Liconsamides/Streptogramins	3.10	0.50	2.24	4.60	3.70	0.54	0.98	4.47	0.89	3.57	1.92
Quinolones	1.42	0.53	0.28	2.13	1.49	0.96	1.05	3.06	1.17	2.49	1.35
Tetracyclines	1.27	No data	1.17	3.50	0.71	0.42	1.29	1.19	3.65	4.65	0.55
Sufonamides/Trimethoprim	0.55	No data	0.77	0.43	0.03	0.59	2.01	0.54	0.79	1.34	1.13
Other antibiotics	0.16	No data	0.77	0.90	0.17	0.20	1.18	0.42	2.15	0.78	0.58
Total antibiotics	13.14	28.02	14.06	26.93	10.93	6.38	8.53	29.75	16.48	25.13	11.48

The antibiotic usage for all countries, except CN was obtained from Hogberg LD et al.

The antibiotic usage for CN was obtained from Wang X et al.

All the data was recorded in 2004.

Antibiotic usage was indicated by DDD (defined daily dose per 1,000 inhabitants).

No data for MW was available anywhere.

Table 3.2. Antibiotic usage in farm animals from seven countries used in this study

	AT (Austria)	DK (Denmark)	FR (France)	JP (Japan)	ES (Spain)	SE (Sweden)	US (The United States)
Total antibiotic usage	63,000	117,000	997,000	655,820	1,746,000	13,559	13,542,030
Total antibiotic usage per population	0.00739	0.0207	0.0154	0.00516	0.0371	0.00141	0.0420

The antibiotic usage was obtained from Boeckel TP et al.

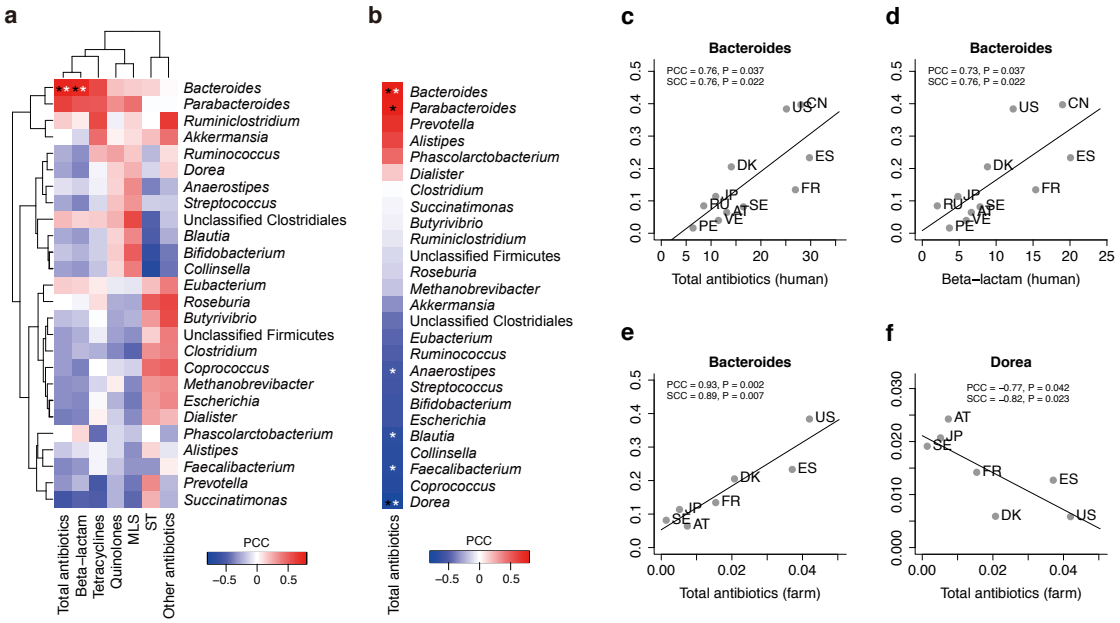
The population data was obtained from FAOSTAT.

All data was recorded in 2010, except for the US which was from 2011.

Antibiotic usage was indicated in kilograms

3.3.4. Correlation analysis of the microbiome with the antibiotic usage

Correlation analysis with the antibiotic usage data found significant positive correlations between the abundance of major species *Bacteroides* with both total antibiotic and beta-lactam usage in humans, and total antibiotic usage in farm animals ($P < 0.05$ for all; Fig. 3.6a-e). The abundance of minor genera, *Odoribacter*, *Parasutterella*, *Sutterella* and *Acetobacter,* also showed a significant positive correlation with total antibiotic usage in humans or farm animals ($P < 0.05$ for all; Fig. 3.7). In contrast, *Dorea* and *Eggerthella* showed significant negative correlation with total antibiotic usage in farm animals ($P < 0.05$ for both) and other five genera such as *Blautia, Collinsella, Coprococcus and Faecalibacterium* had the tendency of a high negative correlation with antibiotics (PCC and SCC < -0.60 for all; Fig. 3.6a and b). The strong association of antibiotics with the gut microbiome were further supported by PERMANOVA[108], where total antibiotic usage in humans and farm animals and beta-lactam usage in humans significantly contributed to the overall structure of the gut microbiome (coefficient of determination (R^2) = 0.34, 0.59 and 0.31 respectively) as well as plant-derived dietary factors such as “Root vegetables” and “Vegetables/Fruits” (R^2 = 0.26 and 0.26 respectively; Fig. 3.6g). These data are summarized in the correlation network of microbe-food-antibiotics (Fig. 3.8).



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	Factor	R^2	P-value
Food categories	Animal products	0.15	0.151
	Beverages	0.04	0.731
	Grains/beans	0.21	0.063
	Marine products	0.11	0.312
	Oils/Fats	0.14	0.184
	Root vegetables	**0.26**	**0.023**
	Spices	0.17	0.134
	Sugars	0.05	0.681
	Vegetables/Fruits	**0.26**	**0.014**
Antibiotics uses (Human)	**Beta-lactam**	**0.31**	**0.018**
	MLS	0.09	0.440
	Quinolones	0.15	0.244
	Tetracyclines	0.21	0.107
	ST	0.11	0.407
	Total antibiotics	**0.34**	**0.009**
Antibiotics uses (Farm)	**Total antibiotics**	**0.59**	**0.004**
Host data	Age	0.16	0.140
	BMI	0.20	0.072

Fig. 3.6. Correlations between the abundance of the top 26 genera and antibiotic usage. a, b, Heat maps based on PCCs between the abundance of the top 26 genera and antibiotic usage in humans and farm animals are shown. Closed and open asterisks represent FDR adjusted p-values < 0.05 for PCC and SCC, respectively. c-f, Significant correlations for both PCC and SCC of the abundance of *genera* with antibiotic usage are shown. Y-axes represent relative abundance of the genus. g, PERMANOVA for dietary and antibiotic factors to gut microbiome variation are shown. R^2 indicates the coefficient of determination. Factors with *P*-values < 0.05 are shown in bold letters.

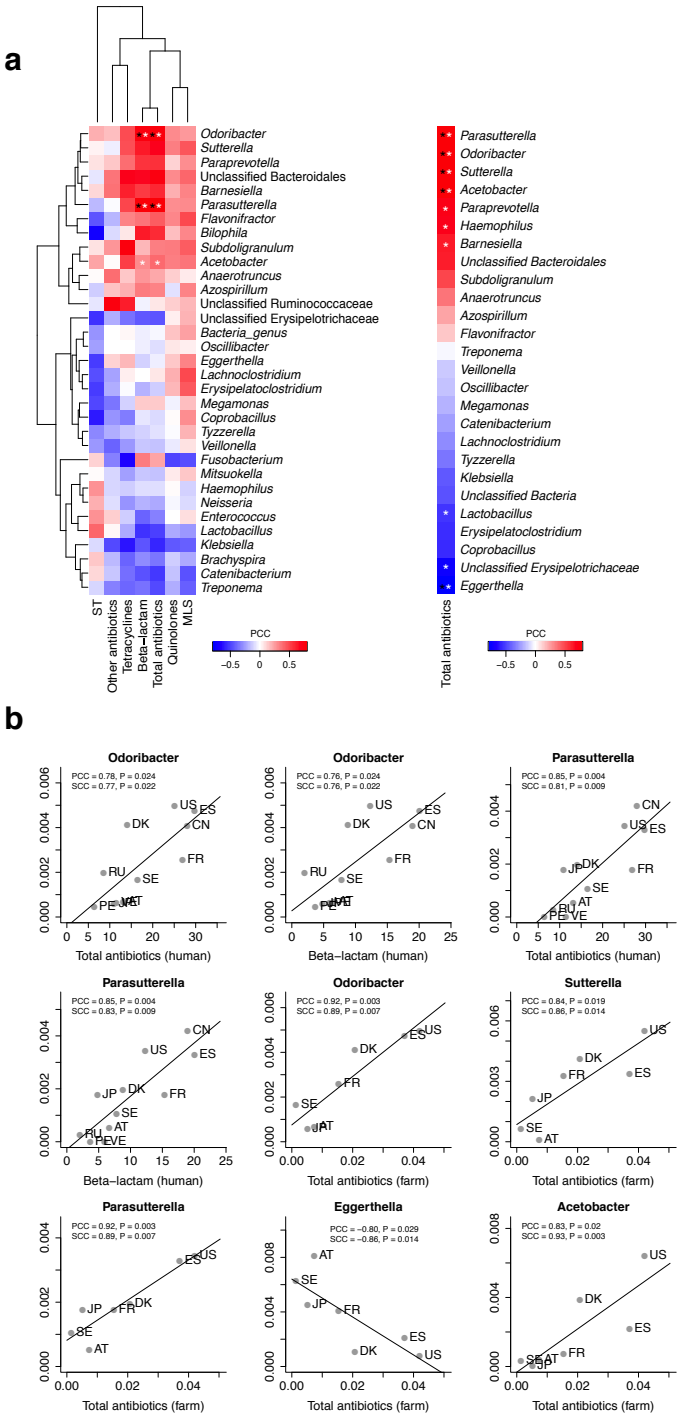

Fig. 3.7. Correlations between the abundance of minor genera and antibiotic usage. a, Heat maps based on PCCs that were calculated between 33 minor genera with the average abundance ≤ 0.05% and ≥ 0.01%, and antibiotic usage in humans and farm animals are shown. b, Significant correlations for both PCC and SCC of the abundance of the *genera* with antibiotic usage are shown. Y-axes represent relative abundance of the genus. P-values were adjusted for multiple testing for each genus. Closed and open asterisks represent FDR adjusted p-values < 0.05 for PCC and SCC, respectively. Significant correlations for both PCC and SCC of the abundance of several minor genera and antibiotic usage are shown in c.

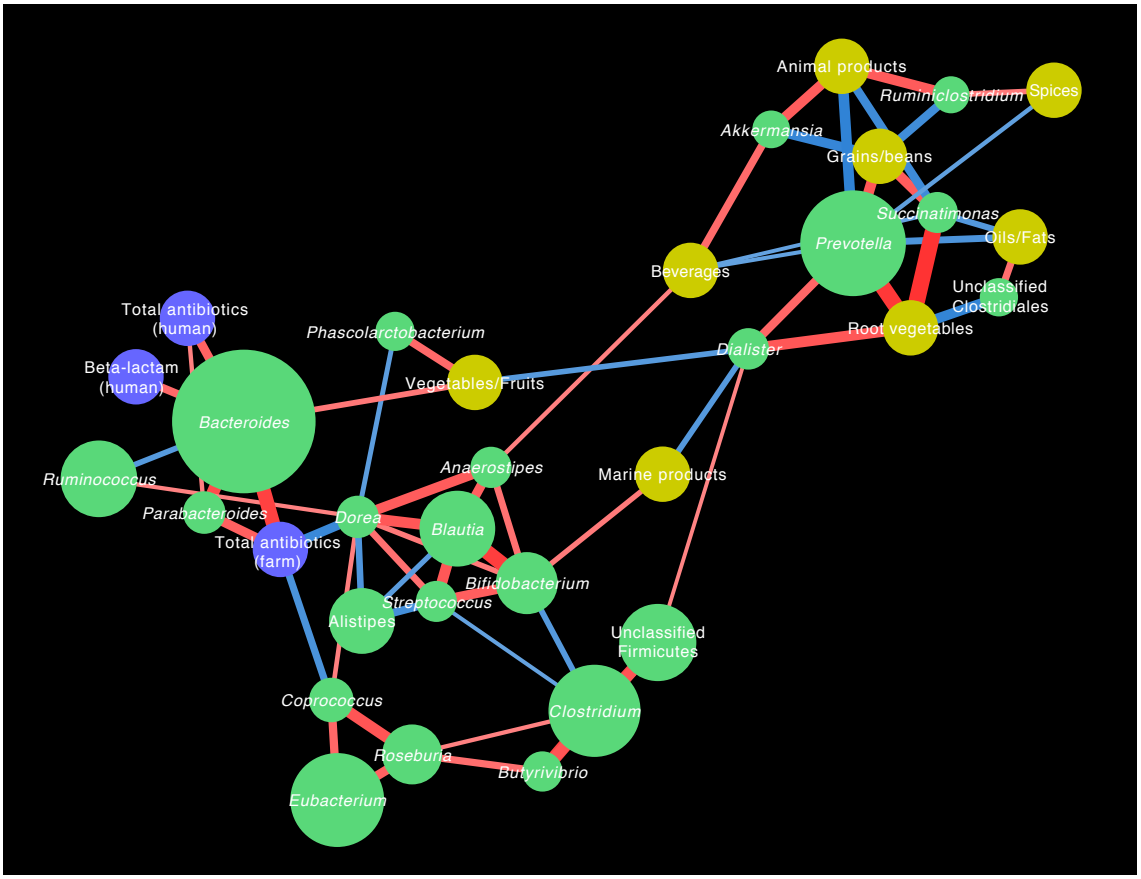

Fig. 3.8. Correlation network of microbes, antibiotics and diet. Circles in green, yellow and purple indicate microbes, dietary components, and antibiotics, respectively. Edges were drawn when the PCC is ≥ 0.6 or ≤ -0.6 between the abundance of microbes and dietary components, and antibiotic usage in humans, and when it is ≥ 0.7 or ≤ -0.7 between the abundance of microbes and antibiotic usage in farm animals. The red and blue colors of the edges indicate positive and negative correlations, respectively, and thickness indicates the degree of the PCC. The correlation network was drawn using Cytoscape 3.2.1.

Similarly, I also found the positive correlation between the abundance of *Bacteroides* and antibiotic usage in the gut microbiome of other independent cohort composed of 303 Asian children from five countries (China, Indonesia, Japan, Taiwan and Thailand)[97]. Since only 16S rRNA gene sequence data were used for the analysis of the microbial composition in this cohort, I used the 16S rRNA gene sequences publically available for estimation of the abundance of *Bacteroides* in the five countries.

Also, since the antibiotic usage data in humans for the five countries was available from the Hogberg dataset but that in farm animals for four countries was unavailable, I performed the correlation analysis between the abundance of *Bacteroides* and the antibiotic usage in humans among the five countries. The results showed the clear tendency of positive correlations between *Bacteroides* and antibiotic usage in humans in the five countries (Fig. 3.9). Thus, the positive correlation between *Bacteroides* and antibiotic usage seems to be also the case for the independent Asian's cohort although I did not statistically evaluate the correlation because of the number of countries was insufficient.

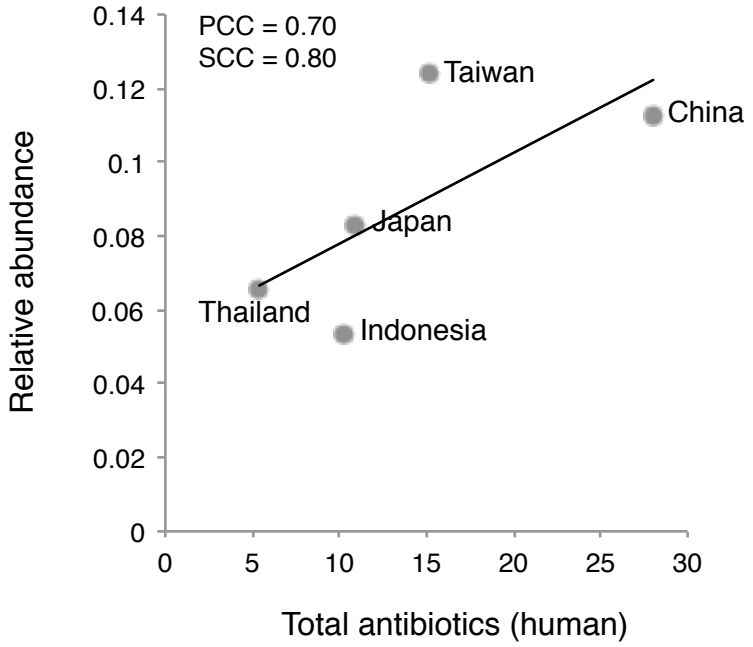

Fig. 3.9. Correlation between *Bacteroides* and antibiotic usage among the five Asian countries. Correlations between the average relative abundance of *Bacteroides* and the total antibiotic usage in humans are shown. PCC and SCC are indicated in the figure.

3.3.5. Antibiotic resistance genes

To explore the involvement of antibiotic resistance genes (ARs) in the association of antibiotics usage with gut microbiome structure, I compared the frequencies of ARs in the gut microbiome with antibiotic usage among the countries. The results showed that the total antibiotic usage and beta-lactam usage in humans showed a positive correlation with beta-lactam resistances, the resistance-nodulation-cell division (RND) efflux pump and total resistance genes ($P < 0.05$; Fig. 3.10a). Additionally, antibiotic usage in farm animals showed a positive correlation with RND efflux pomp among the countries (Fig. 3.10b). The positive correlations of the frequency of ARs in gut microbiomes with antibiotic usage in the country were also demonstrated previously[148, 149]. Collectively, these data suggested that the antibiotic usage tended to be associated with an increase of ARs in the individual gut microbiomes in the country.

To further investigate the contribution of ARs to association of the microbial abundance with antibiotic usage, I compared the frequencies of ARs annotated in genomes between *Bacteroides*, four minor genera positively associated with antibiotic usage, and other genera having little association with antibiotic usage. The results indicated that the positive-associated genera encoded more ARs than other genera, suggesting that the proliferation of ARs underlies the positive correlation between these genera and antibiotic usage (Fig. 3.11a). Among the ARs, RND efflux pump was significantly enriched in the positive-associated genera as compared with other genera (Fig. 3.11b).

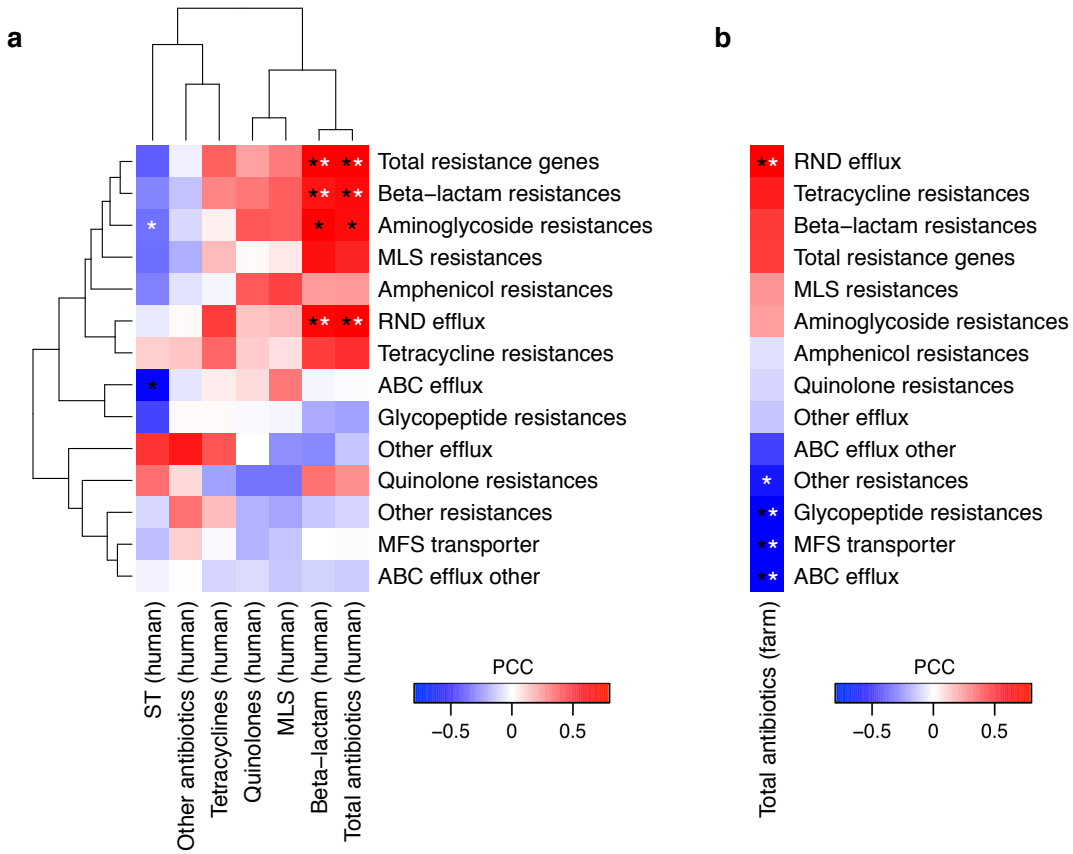

Fig. 3.10. Correlations between the abundance of ARs and antibiotic usage. Heat maps based on PCCs that were calculated between ARs and antibiotic usage in humans (a) and the total antibiotic usage in farm animals (b) are shown. P-values were adjusted for multiple testing for each AR. Closed and open asterisks represent FDR adjusted p-values < 0.05 for PCC and SCC, respectively.

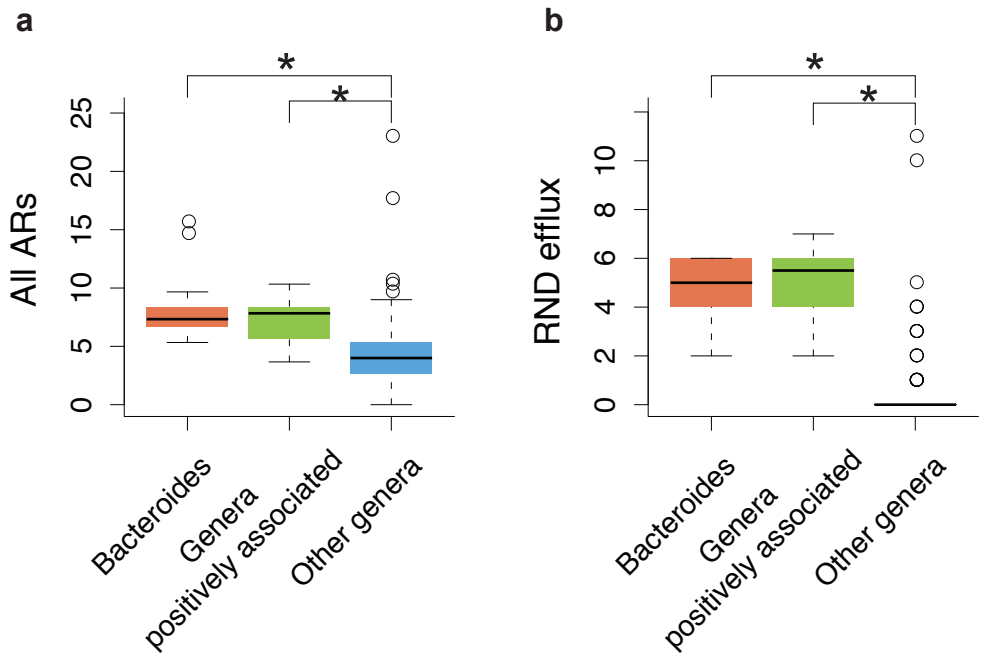

Fig. 3.11. Comparison of the frequency of ARs. a, b, The number of ARs annotated in genomes was compared among the genus *Bacteroides* (red) and four minor genera (*Parabacteroides*, *Parasutterella*, *Odoribacter* and *Sutterella*) having a significant positive correlation with antibiotic usage in humans or farm animals (green) and other genera having little association with antibiotic usage (blue). All ARs annotated and the RND efflux pump are shown in a and b, respectively. The vertical axis indicates the number of the corresponding ARs per genome. Asterisks represent *P*-values < 0.05 (Student's *t*-test).

3.3.6. Gut microbiomes of mice treated with antibiotics

I also experimentally validated the positive correlation between the abundance of *Bacteroides* and beta-lactam usage using mice treated and untreated with beta-lactam antibiotics. In two independent experiments[119, 147], the analysis of the 16S rRNA gene sequences of the gut microbiomes revealed that the antibiotic treatment increased the abundance of *Bacteroides* (Fig. 3.12). Similarly, the increase in *Bacteroides* abundance was also observed in a human intervention trial with beta-lactam[149].

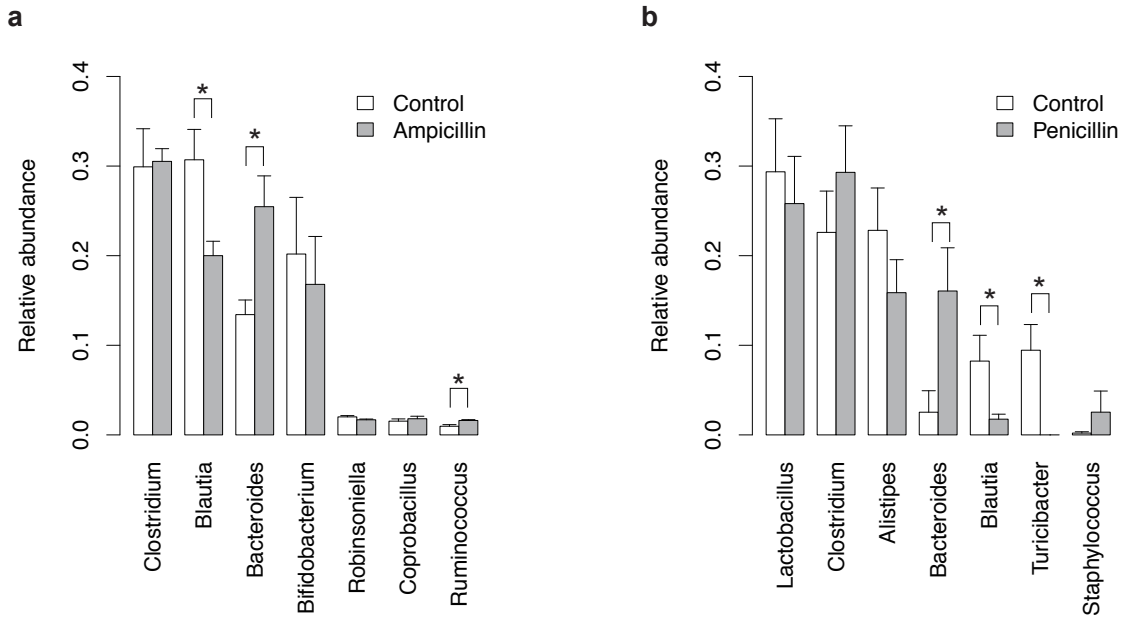

Fig. 3.12. Increase in the abundance of *Bacteroides* in mice treated with beta-lactams. a, b, The average microbial compositions at the genus level evaluated by the 16S rRNA gene sequences were compared between mice treated and untreated with beta-lactams. The results using the 16S rRNA sequenceing data obtained from reference 119 (control: n=4, ampicillin: n=5) and from reference 147 (control: n=36, penicillin: n=39) are shown in a and b, respectively. Top seven predominant genera including *Bacteroides* are shown in both analyses. Open and grey bars indicate control (untreated) and treated mice, respectively. Asterisks represent *P*-values < 0.05 (Student's *t*-test). Error bars indicate SEM.

3.4. Discussion

As presented here, a large-scale correlation analysis between gut microbes, diet and antibiotics provided evidence for the strong impact of antibiotics usage as well as diet on the gut microbiome structure. The present data also suggested that both antibiotics and diet more profoundly affect the microbial composition in the human gut microbiome than host's genetic and geographical closeness among the countries. Thus, both antibiotics and diet may be the primary factors that shape the human gut microbiome, resulting in the population-level diversity. It is also noted that antibiotics affects mainly *Bacteroides*, while diet affects mainly *Prevotella*, both of which are key species in determining the specificity and diversity in the human gut microbiome, such as enterotypes[25]. Therefore, the trade-off relation between these two major species, which was thought to be mainly due to differences in dietary habitat, may be a consequence of respective independent effects from dietary and antibiotic factors on the human gut microbiome. In addition, the present study also suggest that antibiotics has been involved in not only the emergence of the antibiotic resistance microbes[150, 151], but also in ecological changes to the human microbiome[152].

I showed that the RND efflux pomp is involved in the increase of the abundance of Bacteroides associated with antibiotic usage by conferring the antibiotic resistance property to this species. In addition, *Bacteroides* is also resistant to bile acids, which are excreted into the gut and act to form micelle with lipids in the diet. Interestingly, the RND efflux pump plays an important role in bacterial bile acid tolerance[150, 151]. Also, bile acid-tolerant species, including *Bacteroides*, were rapidly induced by animal-based dietary intervention[135]. Therefore, there may be a similar mechanism involving the RND efflux pump between the increase in *Bacteroides* due to antibiotic usage and that by short-term animal-based diets.

It has been demonstrated that antibiotics possess both rapid and long-term effects on the gut microbiome structure[136-138]. On the other hand, the dietary intervention studies for individuals indicated that diet-induced changes in the microbial abundance were smaller than inter-individual variations, and were restored rapidly when the intervention was eliminated[108, 135]. Thus, these observations support the present results showing that the association of antibiotics with gut microbiome structure is similar to or greater than that of the diet.

It should be also noted that antibiotics usage in farm animals showed a correlation with the human gut microbiome. Antibiotics usage in farm animals outnumbers that in humans in the United States[143]. As suggested for the high association between bacteria in the human gut and those in farm-associated environments[153, 154], it is also conceivable that the level of steady exposure of antibiotics from environments to humans may be stochastically greater than that of direct but occasional administration of antibiotics to humans[152]. The elucidation for plausible mechanisms proposed above remains as a future challenge.

Perturbations in the gut microbiome induced by antibiotic treatment have been proven to link to the etiology of several diseases in mice[147, 155, 156]. Additionally, for humans, several studies have suggested an association of antibiotic exposure with diseases such as IBD[157], obesity[158, 159] and asthma[160]. Thus, the present and other data imply a possible association of antibiotic usage with the prevalence of modern diseases in developed countries. However, further studies are required to address the influence of antibiotics on modern diseases through the gut microbiome.

4. Conclusion

In my study, I conducted a metagenomic analysis of fecal DNA samples from 106 JP individuals, compared the JP metagenomic data with those from other 11 countries, and performed an association study between 861 human gut microbiomes and the epidemiological data of dietary intake and antibiotic usage. Comparative analysis of the gut microbiomes among the 12 countries showed a great population-level diversity in the human gut microbiome. I found that the JPGM was characterized by a significant enrichment in the Actinobacteria phylum and *Bifidobacterium* genus and a remarkable depletion of the methanogenic archaeon, *Methanobrevibacter smithii*. These microbial differences in the abundance contributed to differences in functional features, such as the enrichment of carbohydrate metabolism genes with a concurrent depletion of genes involved in replication and repair. In addition, the high abundance of genes for acetogenesis in contrast to a depletion of genes for methanogenesis suggested a difference in hydrogen metabolism in the gut between the Japanese and other populations.

Additionally, I found that the population-level diversity in the human gut microbiome among the 12 countries was significantly associated with antibiotics usage in humans and farm animals as well as dietary intake. In particular, one of the major genus *Bacteroides* showed a strong positive correlation with total antibiotic usage in humans and farm animals and with beta-lactam antibiotic usage in humans. Another major genus *Prevotella* showed no association with antibiotic usages but a strong association with dietary intake. Comparative genome analysis revealed that the genera positively associated with antibiotics have more ARs than the genera that showed little association with antibiotics. Additionally, gut microbiomes of mice treated with a

beta-lactam antibiotic increased in the relative abundance of *Bacteroides*. These results suggested a strong contribution of antibiotics to the human gut microbiome.

Taken together, I revealed the characteristic features of the JPGM and found the strong association of antibiotics as well as diet with population-level diversity in the human gut microbiome. These results included many invaluable and novel findings, therefore, the present study provided new insights into the human gut microbiome research fields. In addition, I disclosed all resources which are of great use for metagenomics to public domains. I anticipate that these results will be helpful for future studies to promote human health and well-being.

5. References

1. Luckey, T.D. Introduction to intestinal microecology. *Am. J. Clin. Nultr.* **25**, 1292-1294 (1972).
2. Backhed, F., Ley, R.E., Sonnenburg, J.L., Peterson, D.A. & Gordon, J.I. Host-bacterial mutualism in the human intestine. *Science* **307**, 1915-20 (2005).
3. Sender, R., Fuchs, S. & Milo R. Revised estimates for the number of human and bacteria cells in the body. *bioRxiv* (2016).
4. Bianconi, E. et al. An estimation of the number of cells in the human body. *Ann. Hum. Biol.* **40**, 463-71 (2013).
5. O'Hara, A.M. & Shanahan, F. The gut flora as a forgotten organ. *EMBO reports* **7**, 688-93 (2006).
6. Lederberg, J. Infectious history. *Science* **288**, 287-293 (2000).
7. Tortora, G.J., Funke, B.R. & Case, C.L. *Microbiology: An Introduction, 11th edition*. (2012). San Fransisco: Benjamin Commings.
8. Leahy, S.C., Higgins, D.G., Fitzgerald, G.F. & van Sinderen, D. Getting better with bifidobacteria. *J. Appl. Microbiol.* **98**, 1303-15 (2005).
9. Hooper, L.V. & Gordon, J.I. Commensal host-bacterial relationships in the gut. *Science* **292**, 1115-1118 (2001).
10. Turnbaugh, P.J. et al. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* **444**, 1027-31 (2006).
11. Hayashi, H., Sakamoto, M. & Benno, Y. Phylogenetic analysis of human gut microbiota using 16S rDNA clone libraries and strictly anaerobic culture-based methods. *Microbial Immunol.* **46**, 535-548 (2002).
12. Venter, J.C. et al. Environmental genome shotgun sequencing of the Sargasso

Sea. *Science* **304**, 66-74 (2004).

13. Gill, S. et al. Metagenomic analysis of the human distal gut microbiome. *Science* **312**, 1355-9 (2006).
14. Eckburg, P.B. et al. Diversity of the human intestinal microbial flora. *Science* **308**, 1635-8 (2005).
15. Lozupone, C. & Knight, R. UniFrac: a new phylogenetic method for comparing microbial communities. *Appl. Environ. Microbiol.* **71**, 8228-35 (2005).
16. Kurokawa, K. et al. Comparative metagenomics revealed commonly enriched gene sets in human gut microbiomes. *DNA Res.* **14**, 169-81 (2007).
17. Qin, J. et al. A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* **464**, 59-65 (2010).
18. The Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. *Nature* **486**, 207-214 (2012).
19. The Human Microbiome Project Consortium. A framework for human microbiome research. *Nature* **486**, 215-21 (2012).
20. The Human Microbiome Jumpstart Reference Strains Consortium. A catalog of reference genomes from the human microbiome. *Science* **328**, 994-9 (2010).
21. Abubucker, S. et al. Metabolic reconstruction for metagenomic data and its application to the human microbiome. *PLoS Comput. Biol.* **8**, e1002358 (2012).
22. Langille, M.G. et al. Predictive functional profiling of microbial communities using 16S rRNA marker gene sequences. *Nat. Biotechnol.* **31**, 814-21 (2013).
23. Sunagawa, S. et al. Metagenomic species profiling using universal phylogenetic marker genes. *Nature methods* **10**, 1196-9 (2013).
24. Turnbaugh, P.J. et al. A core gut microbiome in obese and lean twins. *Nature* **457**, 480-4 (2009).

25. Arumugam, M. et al. Enterotypes of the human gut microbiome. *Nature* **473**, 174-180 (2011).

26. Qin, J. et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. *Nature* **490**, 55-60 (2012).

27. Karlsson, F.H. et al. Gut metagenome in European women with normal, impaired and diabetic glucose control. *Nature* **498**, 99-103 (2013).

28. Tyakht, A.V. et al. Human gut microbiota community structures in urban and rural populations in Russia. *Nat. Commun.* **4**, 2469 (2013).

29. Qin, N. et al. Alterations of the human gut microbiome in liver cirrhosis. *Nature* **513**, 59-64 (2014).

30. Feng, Q. et al. Gut microbiome development along the colorectal adenoma-carcinoma sequence. *Nat. Commun.* **6**, 6528 (2015).

31. Backhed, F. et al. Dynamics and tabilization of the human gut microbiome during the first year of life. *Cell host & microbe* **17**, 690-703 (2015).

32. Zhang, X. et al. The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment. *Nat. Med.* **21**, 895-905 (2015).

33. Zeller, G. et al. Potential of fecal microbiota for early-stage detection of colorectal cancer. *Mol. Syst. Biol.* **10**, 766 (2014).

34. Oh, J. et al. Biogeography and individuality shape function in the human skin metagenome. *Nature* **514**, 59-64 (2014).

35. Faith, J.J. et al. The long-term stability of the human gut microbiota. *Science* **341**, 1237439 (2013).

36. Schloissnig, S. et al. Genomic variation landscape of the human gut microbiome. *Nature* **493**, 45-50 (2013).

37. David, L.A. et al. Host lifestyle affects human microbiota on daily timescales.

Genome Biol. **15**, R89 (2014).

38. Gao, Z., Tseng, C.H., Pei, Z. & Blaser, M.J. Molecular analysis of human forearm superficial skin bacterial biota. *Proc. Natl. Acad. Sci. U. S. A.* **104**, 2927-32 (2007).

39. Fierer, N. et al. Forensic identification using skin bacterial communities. *Proc. Natl. Acad. Sci. U. S. A.* **107**, 6477-81 (2010).

40. Findley, K. et al. Topographic diversity of fungal and bacterial communities in human skin. *Nature* **498**, 367-70 (2013).

41. Dewhirst, F.E. et al. The human oral microbiome. *J. Bacteriol.* **192**, 5002-17 (2010).

42. Ravel, J. et al. Vaginal microbiome of reproductive-age women. *Proc. Natl. Acad. Sci. U.S.A.* **108**, 4680-4687 (2011).

43. Aagaard, K. et al. A metagenomic approach to characterization of the vaginal microbiome signature in pregnancy. *PLoS One* **7**, e36466 (2012).

44. Yan, M. et al. Nasal microenvironments and interspecific interactions influence nasal microbiota complexity and *S. aureus* carriage. *Cell host & microbe* **14**, 631-40 (2013).

45. Bik, E.M. et al. Molecular analysis of the bacterial microbiota in the human stomach. *Proc. Natl. Acad. Sci. U. S. A.* **103**, 732-7 (2006).

46. Pei, Z. et al. Bacterial biota in the human distal esophagus. *Proc. Natl. Acad. Sci. U. S. A.* **101**, 4250-5 (2004).

47. Aagaard, K. et al. The placenta harbors a unique microbiome. *Sci. Transl. Med.* **6**, 237ra65 (2014).

48. El Kaoutari, A., Armougom, F., Gordon, J.I., Raoult, D. & Henrissat, B. The abundance and variety of carbohydrate-active enzymes in the human gut

microbiota. *Nat. Rev. Microbiol.* **11**, 497-504 (2013).

49. Hehemann, J.H. et al. Transfer of carbohydrate-active enzymes from marine bacteria to Japanese gut microbiota. *Nature* **464**, 908-12 (2010).

50. Dominguez-Bello, M.G. et al. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proc. Natl. Acad. Sci. U. S. A.* **107**, 11971-5 (2010).

51. Yatsunenko, T. et al. Human gut microbiome viewed across age and geography. *Nature* **486**, 222-227 (2012).

52. Koenig, J.E. et al. Succession of microbial consortia in the developing infant gut microbiome. *Proc. Natl. Acad. Sci. U.S.A.* **108**, 4578-4585 (2011).

53. Dinsdale, E.A. et al. Functional metagenomic profiling of nine biomes. *Nature* **452**, 629-32 (2008).

54. Ley, R.E., Lozupone, C.A., Hamady, M., Knight, R. & Gordon, J.I. Worlds within worlds- evolution of the vertebrate gut microbiota. *Nat. Rev. Microbiol.* **6**, 776-788 (2008).

55. Ley, R.E. et al. Evolution of Mammals and Their Gut Microbes. *Science* **320**, 1647-1651 (2008).

56. Muegge, B.D. et al. Diet drives convergence in gut microbiome functions across mammalian phylogeny and within humans. *Science* **332**, 970-4 (2011).

57. Ley, R.E., Peterson, D.A. & Gordon, J.I. Ecological and evolutionary forces shaping microbial diversity in the human intestine. *Cell* **124**, 837-48 (2006).

58. Moeller, A.H. et al. Rapid changes in the gut microbiome during human evolution. *Proc. Natl. Acad. Sci. U. S. A.* **111**, 16431-5 (2014).

59. Kau, A.L., Ahern, P.P., Griffin, N.W., Goodman, A.L. & Gordon, J.I. Human nutrition, the gut microbiome and the immune system. *Nature* **474**, 327-36

(2011).

60. Cho, I. & Blaser, M.J. The human microbiome: at the interface of health and disease. *Nature reviews. Genetics* **13**, 260-70 (2012).

61. Lozupone, C.A., Stombaugh, J.I., Gordon, J.I., Jansson, J.K. & Knight, R. Diversity, stability and resilience of the human gut microbiota. *Nature* **489**, 220-30 (2012).

62. Nicholson, J.K. et al. Host-Gut microbiota metabolic interactions. *Science* **336**, 1262-1267 (2012).

63. Bergman, E.N. Energy contributions of volatile fatty acids from the gastrointestinal tract in various species. *Physiol. Rev.* **70**, 567-590 (1990).

64. Furusawa, Y. et al. Commensal microbe-derived butyrate induces the differentiation of colonic regulatory T cells. *Nature* **504**, 446-50 (2013).

65. Atarashi, K. et al. Treg induction by a rationally selected mixture of Clostridia strains from the human microbiota. *Nature* **500**, 232-6 (2013).

66. Fukuda, S. et al. Bifidobacteria can protect from enteropathogenic infection through production of acetate. *Nature* **469**, 543-7 (2011).

67. Wikoff, W.R. et al. Metabolomics analysis reveals large effects of gut microflora on mammalian blood metabolites. *Proc. Natl. Acad. Sci. U. S. A.* **106**, 3698-703 (2009).

68. Le Chatelier, E. et al. Richness of human gut microbiome correlates with metabolic markers. *Nature* **500**, 541-546 (2013).

69. Morgan, X.C. et al. Dysfunction of the intestinal microbiome in inflammatory bowel disease and treatment. *Genome Biol.* **13**, R79 (2012).

70. Gevers, D. et al. The treatment-naive microbiome in new-onset Crohn's disease. *Cell host & microbe* **15**, 382-92 (2014).

71. Zackular, J.P., Rogers, M.A., Ruffin, M.T.t. & Schloss, P.D. The human gut microbiome as a screening tool for colorectal cancer. *Cancer prevention research* **7**, 1112-1121 (2014).

72. Miyake, S. et al. Dysbiosis in the gut microbiota of patients with multiple sclerosis, with a striking depletion of species belonging to clostridia XIVa and IV clusters. *PLoS One* **10**, e0137429 (2015).

73. Sokol, H. et al. *Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc. Natl. Acad. Sci. U. S. A.* **105**, 16731-6 (2008).

74. Parracho, H.M., Bingham, M.O., Gibson, G.R. & McCartney, A.L. Differences between the gut microflora of children with autistic spectrum disorders and that of healthy children. *J. Med. Microbiol.* **54**, 987-91 (2005).

75. Kang, D.W. et al. Reduced incidence of *Prevotella* and other fermenters in intestinal microflora of autistic children. *PLoS One* **8**, e68322 (2013).

76. Diaz Heijtz, R. et al. Normal gut microbiota modulates brain development and behavior. *Proc. Natl. Acad. Sci. U. S. A.* **108**, 3047-52 (2011).

77. Cryan, J.F. & Dinan, T.G. Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. *Nat. Rev. Neurosci.* **13**, 701-12 (2012).

78. Hsiao, E.Y. et al. Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell* **155**, 1451-63 (2013).

79. van Nood, E. et al. Duodenal infusion of donor feces for recurrent *Clostridium difficile*. *N. Engl. J. Med.* **368**, 407-15 (2013).

80. Weingarden, A. et al. Dynamic changes in short- and long-term bacterial composition following fecal microbiota transplantation for recurrent *Clostridium*

difficile infection. *Microbiome* **3**, 10 (2015).

81. Youngster, I. et al. Oral, capsulized, frozen fecal microbiota transplantation for relapsing *Clostridium difficile* infection. *JAMA* **312**, 1772-8 (2014).

82. Hamilton, M.J., Weingarden, A.R., Unno, T., Khoruts, A. & Sadowsky, M.J. High-throughput DNA sequence analysis reveals stable engraftment of gut microbiota following transplantation of previously frozen fecal bacteria. *Gut microbes* **4**, 125-35 (2013).

83. Cammarota, G. et al. Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent *Clostridium difficile* infection. *Aliment. Pharmacol. Ther.* **41**, 835-43 (2015).

84. Angelberger, S. et al. Temporal bacterial community dynamics vary among ulcerative colitis patients after fecal microbiota transplantation. *Am. J. Gastroenterol.* **108**, 1620-30 (2013).

85. D., K., Hotte, N., Gillevet, P. & Madsen, K. Fecal microbiota transplantation inducing remission in Crohn's colitis and the associated changes in fecal microbiota profile. *J. Clin. Gastroenterol.* **48**, 625-628 (2014).

86. Olle, B. Medicines from microbiota. *Nat. Biotechnol.* **31**, 309-315 (2013).

87. Frank, D.N. et al. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc. Natl. Acad. Sci. U.S.A.* **104**, 13780-13785 (2007).

88. Giongo, A. et al. Toward defining the autoimmune microbiome for type 1 diabetes. *ISME J.* **5**, 82-91 (2011).

89. Wen, L. et al. Innate immunity and intestinal microbiota in the development of Type 1 diabetes. *Nature* **455**, 1109-13 (2008).

90. Scher, J.U. et al. Expansion of intestinal *Prevotella copri* correlates with

enhanced susceptibility to arthritis. *eLIFE*, e01202 (2013).

91. Koren, O. et al. Human oral, gut, and plaque microbiota in patients with atherosclerosis. *Proc. Natl. Acad. Sci. U.S.A.* **108**, 4592-4598 (2011).

92. Karlsson, F.H. et al. Symptomatic atherosclerosis is associated with an altered gut metagenome. *Nat. Commun.* **3**, 1245 (2012).

93. Saulnier, D.M. et al. Gastrointestinal microbiome signatures of pediatric patients with irritable bowel syndrome. *Gastroenterology* **141**, 1782-91 (2011).

94. Rigsbee, L. et al. Quantitative profiling of gut microbiota of children with diarrhea-predominant irritable bowel syndrome. *Am. J. Gastroenterol.* **107**, 1740-51 (2012).

95. Smith, M.I. et al. Gut microbiomes of Malawian twin pairs discordant for kwashiorkor. *Science* **339**, 548-54 (2013).

96. Subramanian, S. et al. Persistent gut microbiota immaturity in malnourished Bangladeshi children. *Nature* **510**, 417-21 (2014).

97. Bisgaard, H. et al. Reduced diversity of the intestinal microbiota during infancy is associated with increased risk of allergic disease at school age. *J. Allergy Clin. Immunol.* **128**, 646-52 e1-5 (2011).

98. Abrahamsson, T.R. et al. Low diversity of the gut microbiota in infants with atopic eczema. *J. Allergy Clin. Immunol.* **129**, 434-40, 440 e1-2 (2012).

99. Yoshimoto, S. et al. Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome. *Nature* **499**, 97-101 (2013).

100. Nakayama, J. et al. Diversity in gut bacterial community of school-age children in Asia. *Sci. Rep.* **5**, 8397 (2015).

101. De Filippo, C. et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. *Proc. Natl. Acad.*

Sci. U.S.A. **107**, 14691-14696 (2010).

102. Obregon-Tito, A.J. et al. Subsistence strategies in traditional societies distinguish gut microbiomes. *Nat. Commun.* **6**, 6505 (2015).

103. Martinez, I. et al. The gut microbiota of rural papua new guineans: composition, diversity patterns, and ecological processes. *Cell reports* **11**, 527-38 (2015).

104. Goodrich, J.K. et al. Human genetics shape the gut microbiome. *Cell* **159**, 789-99 (2014).

105. Clemente, J.C., Ursell, L.K., Parfrey, L.W. & Knight, R. The impact of the gut microbiota on human health: an integrative view. *Cell* **148**, 1258-70 (2012).

106. Li, J. et al. An integrated catalog of reference genes in the human gut microbiome. *Nat. Biotechnol.* **32**, 834-841 (2014).

107. Rehman, A. et al. Geographycal patterns of the standing and active human gut microbiome in health and IBD. *Gut* **65**, 238-248 (2015).

108. Wu, G.D. et al. Linking long-term dietary patterns with gut microbial enterotypes. *Science* **334**, 105-108 (2011).

109. World Health Organization. Global Health Observatory (GHO) data. (2015).

110. Kim, S.W. et al. Robustness of gut microbiota of healthy adults in response to probiotic intervention revealed by high-throughput pyrosequencing. *DNA Res.* **20**, 241-253 (2013).

111. Morita, H. et al. An improved DNA isolation method for metagenomic analysis of the microbial flora of the human intestine. *Microbes Environ.* **22**, 214-222 (2007).

112. Ueno, M. et al. Assessment and improvement of methods for microbial DNA preparation from fecal samples. *Handbook of Molecular Microbial Ecology, Volume II: Metagenomics in Different Habitats, First Edition*, 191-198 (2011).

New Jersey: Wiley-well.

113. Gomez-Alvarez, V., Teal, T.K. & Schmidt, T.M. Systematic artifacts in metagenomes from complex microbial communities. *ISME J.* **3**, 1314-1317 (2009).

114. Langmead, B. & Salzberg, S.L. Fast gapped-read alignment with Bowtie 2. *Nat. Methods* **9**, 357-359 (2012).

115. Treangen, T.J., Sommer, D.D., Angly, F.E., Koren, S. & Pop, M. Next generation sequence assembly with AMOS. *Curr Protoc Bioinformatics* **30**, 11.8-11.8.18 (2011).

116. Noguchi, H., Taniguchi, T. & Itoh, T. MetaGeneAnnotator: detecting species-specific patterns of ribosomal binding site for precise gene prediction in anonymous prokaryotic and phage genomes. *DNA Res.* **15**, 387-396 (2008).

117. Li, W. & Godzik, A. Cd-hit: a fast program for clustering and comparing large sets of protein or nucleotide sequences. *Bioinformatics* **22**, 1658-9 (2006).

118. Clemente, J.C. et al. The microbiome of uncontacted Amerindians. *Sci. Adv.* **1**, e1500183 (2015).

119. Atarashi, K. et al. Th17 cell induction by adhesion of microbes to intestinal epithelial cells. *Cell* **163**, 367-380 (2015).

120. Lagesen, K. et al. RNAmmer: consistent and rapid annotation of ribosomal RNA genes. *Nucleic Acids Res.* **35**, 3100-3108 (2007).

121. Langmead, B., Trapnell, C., Pop, M. & Salzberg, S.L. Ultrafast and memory-efficient alignment of short DNA sequences to the human genome. *Genome Biol.* **10**, R25 (2009).

122. Mortazave A., Williams B.A., McCue K., Schaeffer L. & Wold B. Mapping and quantifying mammlian transcriptomes by RNA-Seq. *Nat. Methods* **5**, 621-8

(2008).

123. Rosen, S. & Skaletsky, H. Primer3 on the WWW for general users and for biologist programmers. *Methods Mol. Biol.* **132**, 365-386 (2000).

124. Huerta-Cepas, J. et al. eggNOG 4.5: a hierarchical orthology framework with improved functional annotations for eukaryotic, prokaryotic and viral sequences. *Nucleic Acids Res.* **44**, D286-93 (2016).

125. Benjamini, Y. & Hochberg, Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J. R. Stat. Soc. Series B Stat. Methodol.* **75**, 305-322 (1995).

126. Furuta, Y. & Kobayashi, I. Movement of DNA sequence recognition domains between non-orthologous proteins. *Nucleic Acids Res.* **40**, 9218-32 (2012).

127. Nakamura, N., Lin, H.C., McSweeney, C.S., Mackie, R.I. & Gaskins, H.R. Mechanisms of microbial hydrogen disposal in the human colon and implications for health and disease. *Annual review of food science and technology* **1**, 363-95 (2010).

128. Liu, S. et al. Starch and starch hydrolysates are favorable carbon sources for bifidobacteria in the human gut. *BMC Microbiol.* **15**, 54 (2015).

129. Tedelind, S., Westberg, F., Kjerruf, M. & Vidal, A. Anti-inflammatory properties of the short-chain fatty acids acetate and propionate: A study with relevance to inflammatory bowel disease. *World J. Gastroenterol.* **28**, 2826-2832 (2007).

130. Ohsawa, I. et al. Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals. *Nat. Med.* **13**, 688-94 (2007).

131. Rey, F.E. et al. Dissecting the in vivo metabolic potential of two human gut acetogens. *J. Biol. Chem.* **285**, 22082-90 (2010).

132. Kim, G. et al. *Methanobrevibacter smithii* is the predominant methanogen in patients with constipation-predominant IBS and methane on breath. *Dig. Dis. Sci.* **57**, 3213-8 (2012).

133. Morii, H., Oda, K., Suenaga, Y. & Nakamura, T. Low Methane Concentration in the Breath of Japanese. *Journal of University of Occupational and Environmenatal Health* **25**, 397-407 (2003).

134. Levitt, M.D., Furne, J.K., Kuskowski, M. & Ruddy, J. Stability of human methanogenic flora over 35 years and a review of insights obtained from breath methane measurements. *Clin. Gastroenterol. Hepatol.* **4**, 123-9 (2006).

135. David, L.A. et al. Diet rapidly and reproducibly alters the human gut microbiome. *Nature* **505**, 559-563 (2014).

136. Dethlefsen, L., Huse, S., Sogin, M.L. & Relman, D.A. The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing. *PLoS Biol.* **6**, e280 (2008).

137. Jakobsson, H.E. et al. Short-term antibiotic treatment has differing long-term impacts on the human throat and gut microbiome. *PLoS One* **5**, e9836 (2010).

138. Dethlefsen, L. & Relman, D. Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation. *Proc. Natl. Acad. Sci. U.S.A.* **108**, 4554-4561 (2011).

139. Ministry of education, sports, science and technology: Japan. Standard Tables of Food Compositionin Japan: 2010. (2011). (in Japanese).

140. Högberg, L.D., Muller, A., Zorzet, A., Monnet, D.L. & Cars, O. Antibiotic use worldwide. *The Lancet Infectious Diseases* **14**, 1179-1180 (2014).

141. European Surveillance of Antimicrobial Consumption. ESAC Yearbook 2009. (2009).

142. Wang, X., Zeng, L. & Li, Z. Kang sheng su lin chuang ying yong ji he li xing ping jia (Antibiotic clinical application and rationality evaluation). *Ningxia Med. J.* **27**, 416 (2005). (in Chinese).

143. Van Boeckel, T.P. et al. Global trends in antimicrobial use in food animals. *Proc. Natl. Acad. Sci. U.S.A.* **112**, 5649-5654 (2015).

144. Gibson, M.K., Forsberg, K.J. & Dantas, G. Improved annotation of antibiotic resistance determinants reveals microbial resistomes cluster by ecology. *ISME J.* **9**, 207-216 (2015).

145. Finn, R.D., Clements, J. & Eddy, S.R. HMMER web server: interactive sequence similarity searching. *Nucleic Acids Res.* **39**, W29-37 (2011).

146. Nielsen, H.B. et al. Identification and assembly of genomes and genetic elements in complex metagenomic samples without using reference genomes. *Nat. Biotechnol.* **32**, 822-828 (2014).

147. Cox, L.M. et al. Altering the intestinal microbiota during a critical developmental window has lasting metabolic consequences. *Cell* **158**, 705-721 (2014).

148. Cole, J.R. et al. The Ribosomal Database Project: improved alignments and new tools for rRNA analysis. *Nucleic Acids Res.* **37**, D141-5 (2009).

149. Panda, S. et al. Short-term effect of antibiotics on human gut microbiota. *PLoS One* **9**, e95476 (2014).

150. Levy, S.B. & Marshall, B. Antibacterial resistance worldwide: causes, challenges and responses. *Nat. Med.* **10**, S122-9 (2004).

151. Goossens, H., Ferech, M., Vander Stichele, R. & Elseviers, M. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *The Lancet* **365**, 579-587 (2005).

152. Blaser, M.J. & Falkow, S. What are the consequences of the disappearing human microbiota? *Nat. Rev. Microbiol.* **7**, 887-894 (2009).

153. Smillie, C.S. et al. Ecology drives a global network of gene exchange connecting the human microbiome. *Nature* **480**, 241-244 (2011).

154. Harrison, E.M. et al. Whole genome sequencing identifies zoonotic transmission of MRSA isolates with the novel *mecA* homologue *mecC*. *EMBO Mol. Med.* **5**, 509-515 (2013).

155. Cho, I. et al. Antibiotics in early life alter the murine colonic microbiome and adiposity. *Nature* **488**, 621-626 (2012).

156. Hill, D.A. et al. Commensal bacteria-derived signals regulate basophil hematopoiesis and allergic inflammation. *Nat. Med.* **18**, 538-46 (2012).

157. Hviid, A., Svanstrom, H. & Frisch, M. Antibiotic use and inflammatory bowel diseases in childhood. *Gut* **60**, 49-54 (2011).

158. Trasande, L. et al. Infant antibiotic exposures and early-life body mass. *Int. J. Obes. (Lond.)* **37**, 16-23 (2013).

159. Saari, A., Virta, L.J., Sankilampi, U., Dunkel, L. & Saxen, H. Antibiotic exposure in infancy and risk of being overweight in the first 24 months of life. *Pediatrics* **135**, 617-26 (2015).

160. Kozyrskyj, A.L., Ernst, P. & Becker, A.B. Increased risk of childhood asthma from antibiotic use in early life. *Chest* **131**, 1753-9 (2007).

6. Appendix

Appendix 1. Metadata and sequencing statistics of the 106 JP individuals

Subject ID	Age	Sex	BMI	Roche 454		Ion PGM		Illumina MiSeq		Ion Proton		Total reads	Total base pairs
				Reads	Base pairs	Reads	Base pairs	Reads	Base pairs	Reads	Base pairs		
apr01	21	female	18.8	3,616,600	1,511,135,838	1,468,274	311,169,667	17,779,732	2,758,183,854	-	-	22,864,606	4,580,489,359
apr02	23	female	18.6	2,628,746	1,026,436,447	3,606,299	797,289,881	27,347,713	4,051,358,283	-	-	33,582,758	5,875,084,611
apr03	21	female	19.9	2,184,162	784,607,990	5,475,448	1,270,080,643	25,110,532	3,724,556,684	-	-	32,770,142	5,779,245,317
apr05	20	female	23.2	1,223,255	599,941,068	-	-	17,783,033	5,246,127,659	-	-	19,006,288	5,846,068,727
apr06	22	male	22.7	1,129,655	416,913,103	1,639,524	332,816,324	-	-	2,916,108	480,434,648	5,685,287	1,230,164,075
apr07	22	male	20.8	1,168,088	402,651,421	1,799,059	379,201,967	-	-	2,624,583	439,838,921	5,591,730	1,221,692,309
apr08	19	female	22.3	1,233,049	413,431,585	1,219,601	231,746,517	-	-	2,193,773	366,678,069	4,646,423	1,011,856,171
apr09	20	female	18.5	3,065,678	1,314,648,501	5,112,619	1,231,269,412	24,747,208	3,664,126,874	-	-	32,925,505	6,210,044,787
apr10	21	female	18.0	1,182,504	555,221,170	-	-	17,839,740	5,264,780,845	-	-	19,022,244	5,820,002,015
apr11	23	female	19.1	1,083,003	602,939,544	-	-	16,336,733	4,829,913,153	-	-	17,419,736	5,432,852,697
apr12	25	male	23.7	1,717,716	694,917,938	4,375,130	1,061,610,762	26,744,611	3,962,600,100	-	-	32,837,457	5,719,128,800
apr15	22	female	24.4	1,116,609	526,876,648	-	-	15,526,356	4,563,985,308	-	-	16,642,965	5,090,861,956
apr16	20	female	18.0	3,154,885	1,303,790,446	4,780,685	1,151,892,044	24,281,833	3,595,782,961	-	-	32,217,403	6,051,465,451
apr17	20	male	19.4	2,673,276	1,075,288,659	3,591,991	849,547,914	26,844,485	3,974,770,852	-	-	33,109,752	5,899,607,425
apr18	21	male	21.5	1,101,523	579,832,038	-	-	14,979,707	4,429,641,376	-	-	16,081,230	5,009,473,414
apr19	20	male	19.4	913,549	443,724,457	-	-	18,653,403	5,528,566,347	-	-	19,566,952	5,972,290,804
apr21	21	female	19.4	1,032,314	394,480,338	-	-	18,569,721	5,487,716,771	-	-	19,602,035	5,882,197,109
apr22	22	female	19.5	1,244,906	579,326,092	-	-	18,518,105	5,473,333,837	-	-	19,763,011	6,052,659,929
apr23	21	female	20.5	1,337,946	661,645,265	-	-	16,182,750	4,800,728,933	-	-	17,520,696	5,462,374,198
apr24	19	male	25.1	1,182,834	483,346,472	-	-	16,891,735	4,985,795,937	-	-	18,074,569	5,469,142,409
apr25	19	male	18.7	1,176,431	534,267,378	-	-	18,357,333	5,435,814,962	-	-	19,533,764	5,970,082,340
apr26	21	male	22.2	1,198,205	566,296,215	-	-	18,667,816	5,528,105,513	-	-	19,866,021	6,094,401,728
apr27	20	female	22.9	1,044,138	449,345,695	-	-	18,269,627	5,381,759,953	-	-	19,313,765	5,831,105,648
apr28	20	female	24.8	977,520	481,731,086	-	-	17,767,462	5,242,715,348	-	-	18,744,982	5,724,446,434
apr30	21	female	19.2	1,113,198	581,361,486	-	-	17,085,867	5,049,283,198	-	-	18,199,065	5,630,644,684
apr31	33	male	28.0	1,256,095	553,728,889	-	-	17,651,579	5,219,215,525	-	-	18,907,674	5,772,944,414
apr32	19	male	21.8	1,255,099	540,951,434	-	-	18,636,135	5,508,702,888	-	-	19,891,234	6,049,654,322
apr33	23	male	23.8	935,257	541,854,736	-	-	18,597,849	5,505,404,196	-	-	19,533,106	6,047,258,932
apr34	20	female	21.9	1,041,477	679,049,047	-	-	17,913,411	5,260,094,469	-	-	18,954,888	5,939,143,516
apr35	19	female	17.3	865,540	296,790,287	-	-	16,560,787	4,873,049,793	-	-	17,426,327	5,169,840,080
apr36	19	female	19.6	1,081,364	702,479,247	-	-	19,104,747	5,640,395,843	-	-	20,186,111	6,342,875,090
apr37	21	female	21.2	1,298,728	526,349,155	-	-	18,644,441	5,502,003,973	-	-	19,943,169	6,028,353,128
apr38	19	male	22.6	903,832	552,619,941	-	-	19,238,817	5,704,934,670	-	-	20,142,649	6,257,554,611
apr39	23	male	20.0	3,497,728	1,482,279,204	4,463,050	1,047,847,428	23,129,859	3,428,793,868	-	-	31,090,637	5,958,920,500
apr40	19	male	20.1	2,210,816	908,122,778	3,067,139	716,408,531	22,315,744	3,307,903,412	-	-	27,593,699	4,932,434,721
FAKO01	36	male	24.2	1,237,744	869,451,621	4,748,024	1,046,263,996	-	-	-	-	5,985,768	1,915,715,617
FAKO02	47	male	20.5	1,212,255	774,334,821	4,977,020	1,191,843,698	20,601,066	3,171,189,959	-	-	26,790,341	5,137,368,478

Subject ID	Age	Sex	BMI	Roche 454		Ion PGM		Illumina MiSeq		Ion Proton		Total reads	Total base pairs
				Reads	Base pairs	Reads	Base pairs	Reads	Base pairs	Reads	Base pairs		
FAKO03	50	male	21.3	813,005	474,528,076	3,060,941	722,273,852	23,416,757	3,635,198,059	-	-	27,290,703	4,831,999,987
FAKO05	50	male	25.2	1,013,519	772,877,228	4,135,434	983,799,832	18,049,491	2,806,997,676	-	-	23,198,444	4,563,674,736
FAKO06	35	male	25.1	896,724	691,460,477	3,663,174	867,073,373	-	-	-	-	4,559,898	1,558,533,850
FAKO07	37	male	21.8	1,067,246	843,542,653	4,994,918	1,222,374,117	-	-	-	-	6,062,164	2,065,916,770
FAKO08	42	female	21.2	1,278,699	1,004,402,889	3,226,732	815,214,279	23,173,959	3,582,193,756	-	-	27,679,390	5,401,810,924
FAKO09	38	male	21.7	1,230,727	653,861,422	4,357,923	1,067,163,963	-	-	-	-	5,588,650	1,721,025,385
FAKO10	28	female	20.9	1,283,259	961,493,654	4,584,414	1,120,482,459	-	-	-	-	5,867,673	2,081,976,113
FAKO11	39	male	24.2	1,289,524	1,020,526,742	5,142,605	1,147,275,552	-	-	-	-	6,432,129	2,167,802,294
FAKO12	42	male	25.3	1,157,631	977,103,944	3,003,363	700,304,286	-	-	-	-	4,160,994	1,677,408,230
FAKO13	41	male	22.2	1,165,486	962,790,091	5,772,999	1,378,317,392	-	-	-	-	6,938,485	2,341,107,483
FAKO14	39	male	23.6	1,128,975	884,274,843	5,539,788	1,295,742,281	-	-	-	-	6,668,763	2,180,017,124
FAKO15	48	female	19.5	1,216,894	905,201,847	2,694,894	624,040,817	23,536,367	3,631,105,909	-	-	27,448,155	5,160,348,573
FAKO16	40	male	22.1	1,070,336	864,313,128	5,251,067	1,246,229,222	-	-	-	-	6,321,403	2,110,542,350
FAKO17	39	female	22.6	991,117	775,552,908	5,475,359	1,294,615,850	-	-	-	-	6,466,476	2,070,168,758
FAKO18	33	female	17.7	1,204,743	875,237,342	4,193,796	998,072,479	-	-	-	-	5,398,539	1,873,309,821
FAKO19	48	female	21.4	1,122,447	543,290,354	4,373,108	1,042,114,670	20,386,865	3,154,605,955	-	-	25,882,420	4,740,010,979
FAKO21	42	male	21.1	1,177,223	941,278,809	4,444,365	1,151,398,095	-	-	-	-	5,621,588	2,092,676,904
FAKO22	50	male	25.5	976,949	790,243,385	2,877,561	678,295,459	16,251,627	2,498,181,407	-	-	20,106,137	3,966,720,251
FAKO23	45	male	21.9	1,220,750	1,012,362,085	4,739,884	1,204,939,249	21,753,613	3,343,822,908	-	-	27,714,247	5,561,124,242
FAKO24	35	male	25.0	973,738	798,939,235	2,286,503	536,921,141	-	-	-	-	3,260,241	1,335,860,376
FAKO25	41	male	22.0	1,144,317	915,839,466	3,484,222	841,216,134	-	-	-	-	4,628,539	1,757,055,600
FAKO26	34	male	23.3	1,103,457	800,679,479	3,562,065	869,101,657	-	-	-	-	4,665,522	1,669,781,136
FAKO27	50	male	20.9	1,116,983	876,718,876	6,178,406	1,358,286,547	25,430,117	3,958,248,462	-	-	32,725,506	6,193,253,885
FAKO28	35	male	23.0	1,178,034	842,873,775	4,749,838	1,192,897,406	-	-	-	-	5,927,872	2,035,771,181
FAKO29	46	male	30.1	989,403	559,118,324	3,663,125	887,626,961	25,101,385	3,907,335,310	-	-	29,753,913	5,354,080,595
FAKO30	31	male	23.1	1,110,845	825,752,152	4,614,918	998,457,552	-	-	-	-	5,725,763	1,824,209,704
FBAN01	41	male	22.0	878,733	717,225,682	4,512,715	1,156,400,900	-	-	-	-	5,391,448	1,873,626,582
FBAN02	36	male	25.6	1,270,826	809,732,938	4,752,649	1,186,547,726	-	-	6,767,151	1,161,937,321	12,790,626	3,158,217,985
FBAN04	31	male	20.5	572,667	462,253,834	4,587,752	1,048,495,854	-	-	-	-	5,160,419	1,510,749,688
FBAN05	38	male	21.5	843,706	633,605,730	4,474,844	999,852,346	-	-	-	-	5,318,550	1,633,458,076
FBAN06	33	male	24.2	1,263,073	964,216,429	4,519,180	1,151,424,172	-	-	-	-	5,782,253	2,115,640,601
FBAN07	31	male	24.6	979,165	760,821,899	3,592,110	899,974,202	-	-	6,584,827	1,085,930,759	11,156,102	2,746,726,860
FBAN08	29	male	22.2	1,001,583	441,929,434	4,419,297	1,084,654,590	-	-	-	-	5,420,880	1,526,584,024
FBAN09	28	male	26.5	896,341	724,591,809	4,711,730	1,150,786,567	-	-	-	-	5,608,071	1,875,378,376
FBAN10	28	male	21.4	1,122,997	816,962,343	4,378,734	1,126,727,661	-	-	-	-	5,501,731	1,943,690,004
FMOR01	23	female	20.7	1,039,730	776,147,874	4,234,927	1,028,449,248	-	-	-	-	5,274,657	1,804,597,122
FMOR02	22	female	21.5	1,280,287	1,053,221,731	4,392,453	1,127,834,787	-	-	-	-	5,672,740	2,181,056,518
FMOR03	23	male	21.4	1,003,142	818,978,759	3,190,182	752,074,790	-	-	-	-	4,193,324	1,571,053,549
FMOR04	22	male	20.5	639,688	528,052,776	4,056,646	977,374,544	-	-	-	-	4,696,334	1,505,427,320
FMOR11	22	female	17.7	1,297,180	972,570,359	4,789,473	1,178,775,252	-	-	6,705,707	1,137,599,554	12,792,360	3,288,945,165
FMOR14	22	male	20.5	1,199,711	939,575,474	4,644,847	1,150,837,494	-	-	-	-	5,844,558	2,090,412,968
FMOR21	49	male	21.0	1,049,399	806,315,831	3,799,519	874,085,087	-	-	-	-	4,848,918	1,680,400,918
FPR01	40	female	22.3	-	-	-	-	-	-	11,750,594	1,956,925,399	11,750,594	1,956,925,399

Subject ID	Age	Sex	BMI	Roche 454		Ion PGM		Illumina MiSeq		Ion Proton		Total reads	Total base pairs
				Reads	Base pairs	Reads	Base pairs	Reads	Base pairs	Reads	Base pairs		
FPR03	25	male	22.5	-	-	-	-	-	-	6,711,654	1,101,100,297	6,711,654	1,101,100,297
FPR04	35	male	19.7	-	-	-	-	-	-	7,276,806	1,069,850,871	7,276,806	1,069,850,871
FPR05	55	male	27.6	-	-	-	-	-	-	9,039,035	1,426,959,232	9,039,035	1,426,959,232
FTAG01	54	male	22.4	1,244,303	893,078,531	4,646,145	1,106,652,891	22,511,838	3,513,074,899	-	-	28,402,286	5,512,806,321
FTAG02	39	female	22.9	1,017,091	851,572,311	4,749,277	1,216,521,098	-	-	-	-	5,766,368	2,068,093,409
FTAG03	34	female	18.7	1,197,243	893,910,927	5,758,559	1,371,519,499	-	-	3,671,046	567,203,425	10,626,848	2,832,633,851
FTAG06	41	male	21.2	1,303,059	978,525,985	3,769,323	869,067,092	-	-	-	-	5,072,382	1,847,593,077
FTAG07	27	male	25.0	550,482	333,209,786	4,478,255	1,157,372,262	-	-	-	-	5,028,737	1,490,582,048
FTAG08	29	male	21.3	1,119,122	844,573,882	4,348,464	1,045,592,291	-	-	-	-	5,467,586	1,890,166,173
FTAG09	34	male	21.1	987,649	761,335,728	4,556,858	1,015,283,188	-	-	3,676,699	611,041,699	9,221,206	2,387,660,615
FTAG10	30	male	23.6	866,651	310,698,085	3,967,579	949,151,507	-	-	-	-	4,834,230	1,259,849,592
FTAG12	37	female	20.6	1,061,262	781,617,041	4,650,110	1,076,978,044	-	-	-	-	5,711,372	1,858,595,085
FTAG13	25	female	18.9	1,088,397	863,477,979	3,839,673	888,047,924	-	-	-	-	4,928,070	1,751,525,903
FTAG14	39	female	20.0	910,757	586,172,905	2,709,444	584,238,167	-	-	-	-	3,620,201	1,170,411,072
FTAG15	37	male	22.8	1,279,507	1,052,657,242	4,610,008	1,045,774,508	-	-	-	-	5,889,515	2,098,431,750
FTAG16	34	female	20.0	1,119,929	860,800,299	3,573,257	862,260,462	-	-	5,882,855	982,877,558	10,576,041	2,705,938,319
FTAG17	26	male	36.1	1,015,453	564,675,149	4,068,162	1,030,784,818	-	-	-	-	5,083,615	1,595,459,967
FTAG18	36	female	20.5	949,169	638,960,066	4,467,158	1,062,822,389	-	-	-	-	5,416,327	1,701,782,455
FTAG19	33	female	21.3	840,282	626,776,404	5,014,468	1,184,085,290	-	-	-	-	5,854,750	1,810,861,694
FTAG20	40	female	18.9	892,706	704,667,477	3,801,134	851,601,009	-	-	6,459,265	1,094,741,479	11,153,105	2,651,009,965
FTAG21	31	female	18.8	1,287,240	997,810,879	4,789,124	1,221,964,810	-	-	6,858,366	1,153,821,888	12,934,730	3,373,597,577
TS-11	60	male	24.8	-	-	-	-	-	-	8,836,531	1,549,259,449	8,836,531	1,549,259,449
TS-21	46	male	22.1	-	-	-	-	-	-	7,973,204	1,330,712,137	7,973,204	1,330,712,137
TS-29	48	female	18.7	-	-	-	-	-	-	7,752,836	1,374,864,110	7,752,836	1,374,864,110
TS-33	55	female	19.9	-	-	-	-	-	-	9,041,527	1,644,215,789	9,041,527	1,644,215,789
TS-41	48	male	23.0	-	-	-	-	-	-	7,996,333	1,396,681,648	7,996,333	1,396,681,648

Appendix 2. Reference genomes used in this study

a. Reference genomes collected from NCBI

Genome ID							
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AAVW00000000	AAWL00000000	AAXA00000000	AAXB00000000	AAXD00000000	AAXE00000000	AAXF00000000	AAXG00000000
AAXS00000000	AAXV00000000	AAXX00000000	AAYG00000000	AAYH00000000	AAYI00000000	AAYW00000000	AAZD00000000
AAZE00000000	AAZF00000000	AAZG00000000	AAZH00000000	AAZI00000000	AAZJ00000000	AAZP00000000	AAZZ00000000
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ACNJ00000000	ACNN00000000	ACNO00000000	ACNV00000000	ACOB00000000	ACOF00000000	ACOG00000000	ACOH00000000
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ACPS00000000	ACPT00000000	ACPV00000000	ACPW00000000	ACPZ00000000	ACQC00000000	ACQD00000000	ACQE00000000
ACQF00000000	ACQG00000000	ACQH00000000	ACQL00000000	ACQN00000000	ACQV00000000	ACRB00000000	ACRC00000000
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ACRM00000000	ACRN00000000	ACRO00000000	ACRP00000000	ACRQ00000000	ACRS00000000	ACRT00000000	ACRX00000000
ACRY00000000	ACSB00000000	ACSE00000000	ACSF00000000	ACSH00000000	ACSK00000000	ACSL00000000	ACSM00000000
ACTB00000000	ACTC00000000	ACTG00000000	ACTI00000000	ACTJ00000000	ACTK00000000	ACTL00000000	ACTM00000000
ACTN00000000	ACTO00000000	ACTP00000000	ACTR00000000	ACTS00000000	ACTT00000000	ACTV00000000	ACTW00000000
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ADCS00000000	ADCT00000000	ADCU00000000	ADCV00000000	ADCW00000000	ADCX00000000	ADCY00000000	ADCZ00000000
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b, Reference genomes collected from ref. 124

Genomes from reference 22
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Clostridiales bacterium 1E3
Clostridiales bacterium 2E3
Clostridiales bacterium 1E11
Clostridiales bacterium 1A9
Bifidobacterium pseudolongum 1B11
Clostridiales bacterium 1C12
Bifidobacterium breve 1C2
Clostridiales bacterium 1D10
Clostridiales bacterium 1D1
Clostridiales bacterium 1D2
Clostridiales bacterium 1D4
Clostridiales bacterium 1F7
Clostridiales bacterium 1F8
Clostridiales bacterium 2D9
Clostridiales bacterium 2F7
Bacteroides dorei 2G11
Clostridiales bacterium 2G4
Clostridiales bacterium 2H11
Clostridiales bacterium 2H6

c, reference genomes sequenced in my laboratory

Genomes sequenced in my laboratory
Slackia sp. 2F
Fusobacterium varium 70

Appendix 3. Details of deposited sequence files

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FAKO24.PGM.fastq	'FAKO24	-	Ion PGM	DRR042477
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FPR01.Proton.2.fastq	'FPR01	-	Ion Proton	DRR042550
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FTAG08.PGM.fastq	'FTAG08	-	Ion PGM	DRR042610
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FTAG09-m80c-QIA.Proton.fastq	'FTAG09	-	Ion Proton	DRR042617
FTAG09-m80c.Proton.fastq	'FTAG09	-	Ion Proton	DRR042616
FTAG09.454.fastq	'FTAG09	-	454	DRR042611
FTAG09.PGM.fastq	'FTAG09	-	Ion PGM	DRR042618
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FTAG10.PGM.fastq	'FTAG10	-	Ion PGM	DRR042620
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FTAG13.PGM.fastq	'FTAG13	-	Ion PGM	DRR042624
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FTAG14.PGM.fastq	'FTAG14	-	Ion PGM	DRR042626
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FTAG15.PGM.fastq	'FTAG15	-	Ion PGM	DRR042628
FTAG16-m80c-Fast.Proton.fastq	'FTAG16	-	Ion Proton	DRR042630
FTAG16-m80c-mAc.Proton.fastq	'FTAG16	-	Ion Proton	DRR042631
FTAG16-m80c-NF.Proton.fastq	'FTAG16	-	Ion Proton	DRR042632
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FTAG16-m80c-QIA.Proton.fastq	'FTAG16	-	Ion Proton	DRR042635
FTAG16-m80c.Proton.fastq	'FTAG16	-	Ion Proton	DRR042634
FTAG16.454.fastq	'FTAG16	-	454	DRR042629
FTAG16.PGM.fastq	'FTAG16	-	Ion PGM	DRR042636
FTAG17.454.fastq	'FTAG17	-	454	DRR042637
FTAG17.PGM.fastq	'FTAG17	-	Ion PGM	DRR042638
FTAG18.454.fastq	'FTAG18	-	454	DRR042639
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FTAG20-m80c.Proton.fastq	'FTAG20	-	Ion Proton	DRR042648
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TS-21.Proton.fastq	'TS-21	-	Ion Proton	DRR042660
TS-29.Proton.fastq	'TS-29	-	Ion Proton	DRR042661
TS-33.Proton.fastq	'TS-33	-	Ion Proton	DRR042662
TS-41.Proton.fastq	'TS-41	-	Ion Proton	DRR042663

Appendix 4. KOs unique to the JP gene set

KEGG orthology	Function
K00035	D-galactose 1-dehydrogenase [EC:1.1.1.48]
K00193	acetyl-CoA decarbonylase/synthase complex subunit beta [EC:2.3.1.-]
K00201	formylmethanofuran dehydrogenase subunit B [EC:1.2.99.5]
K00271	valine dehydrogenase [EC:1.4.1.8]
K00292	saccharopine dehydrogenase (NAD+, L-glutamate forming) [EC:1.5.1.9]
K00319	methylenetetrahydromethanopterin dehydrogenase [EC:1.5.99.9]
K00360	nitrate reductase (NADH) [EC:1.7.1.1]
K00401	methyl-coenzyme M reductase beta subunit [EC:2.8.4.1]
K00406	cytochrome c oxidase cbb3-type subunit III
K00407	cytochrome c oxidase cbb3-type subunit IV
K00410	ubiquinol-cytochrome c reductase cytochrome b/c1 subunit
K00413	ubiquinol-cytochrome c reductase cytochrome c1 subunit
K00440	coenzyme F420 hydrogenase alpha subunit [EC:1.12.98.1]
K00456	cysteine dioxygenase [EC:1.13.11.20]
K00496	alkane 1-monooxygenase [EC:1.14.15.3]
K00499	choline monooxygenase [EC:1.14.15.7]
K00507	stearoyl-CoA desaturase (delta-9 desaturase) [EC:1.14.19.1]
K00514	zeta-carotene desaturase [EC:1.3.5.6]
K00524	ribonucleotide reductase, class II [EC:1.17.4.1]
K00555	tRNA (guanine26-N2/guanine27-N2)-dimethyltransferase [EC:2.1.1.215 2.1.1.216]
K00577	tetrahydromethanopterin S-methyltransferase subunit A [EC:2.1.1.86]
K00578	tetrahydromethanopterin S-methyltransferase subunit B [EC:2.1.1.86]
K00579	tetrahydromethanopterin S-methyltransferase subunit C [EC:2.1.1.86]
K00580	tetrahydromethanopterin S-methyltransferase subunit D [EC:2.1.1.86]
K00582	tetrahydromethanopterin S-methyltransferase subunit F [EC:2.1.1.86]
K00583	tetrahydromethanopterin S-methyltransferase subunit G [EC:2.1.1.86]
K00586	diphthine synthase [EC:2.1.1.98]
K00624	carnitine O-acetyltransferase [EC:2.3.1.7]
K00635	diacylglycerol O-acyltransferase [EC:2.3.1.20]
K00862	erythritol kinase [EC:2.7.1.27]
K00887	undecaprenol kinase [EC:2.7.1.66]
K00988	ATP adenylyltransferase [EC:2.7.7.53]
K01001	UDP-N-acetylglucosamine--dolichyl-phosphate N-acetylglucosaminephosphotransferase [EC:2.7.8.15]
K01084	glucose-6-phosphatase [EC:3.1.3.9]
K01117	sphingomyelin phosphodiesterase [EC:3.1.4.12]
K01158	deoxyribonuclease II [EC:3.1.22.1]
K01170	tRNA-intron endonuclease, archaea type [EC:3.1.27.9]
K01172	NA
K01230	mannosyl-oligosaccharide alpha-1,2-mannosidase [EC:3.2.1.113]
K01280	tripeptidyl-peptidase II [EC:3.4.14.10]
K01385	thermopsin [EC:3.4.23.42]
K01504	glucosamine-6-phosphate isomerase [EC:3.5.99.6]
K01510	apyrase [EC:3.6.1.5]
K01594	sulfinoalanine decarboxylase [EC:4.1.1.29]
K01622	fructose 1,6-bisphosphate aldolase/phosphatase [EC:4.1.2.13 3.1.3.11]
K01663	glutamine amidotransferase / cyclase [EC:2.4.2.- 4.1.3.-]
K01769	guanylate cyclase, other [EC:4.6.1.2]
K01969	3-methylcrotonyl-CoA carboxylase beta subunit [EC:6.4.1.4]
K02201	pantetheine-phosphate adenylyltransferase [EC:2.7.7.3]
K02288	phycocyanobilin lyase alpha subunit [EC:4.-.-.-]
K02289	phycocyanobilin lyase beta subunit
K02322	DNA polymerase II large subunit [EC:2.7.7.7]
K02497	HemX protein
K02571	periplasmic nitrate reductase NapE
K02595	nitrogenase-stabilizing/protective protein
K02659	twitching motility protein PilI
K02665	type IV pilus assembly protein PilP
K02672	type IV pilus assembly protein PilW
K02676	type IV pilus assembly protein PilZ
K02683	DNA primase [EC:2.7.7.-]
K02685	DNA primase large subunit [EC:2.7.7.-]
K02691	photosystem I subunit VII
K02717	photosystem II oxygen-evolving enhancer protein 2
K02866	large subunit ribosomal protein L10e
K02869	large subunit ribosomal protein L12
K02877	large subunit ribosomal protein L15e
K02883	large subunit ribosomal protein L18e
K02885	large subunit ribosomal protein L19e

KEGG orthology	Function
K02889	large subunit ribosomal protein L21e
K02896	large subunit ribosomal protein L24e
K02910	large subunit ribosomal protein L31e
K02912	large subunit ribosomal protein L32e
K02915	large subunit ribosomal protein L34e
K02921	large subunit ribosomal protein L37Ae
K02922	large subunit ribosomal protein L37e
K02924	large subunit ribosomal protein L39e
K02927	large subunit ribosomal protein L40e
K02929	large subunit ribosomal protein L44e
K02930	large subunit ribosomal protein L4e
K02944	large subunit ribosomal protein LX
K02966	small subunit ribosomal protein S19e
K02974	small subunit ribosomal protein S24e
K02978	small subunit ribosomal protein S27e
K02979	small subunit ribosomal protein S28e
K02984	small subunit ribosomal protein S3Ae
K02987	small subunit ribosomal protein S4e
K02991	small subunit ribosomal protein S6e
K02995	small subunit ribosomal protein S8e
K03044	DNA-directed RNA polymerase subunit B' [EC:2.7.7.6]
K03045	DNA-directed RNA polymerase subunit B" [EC:2.7.7.6]
K03049	DNA-directed RNA polymerase subunit E' [EC:2.7.7.6]
K03050	DNA-directed RNA polymerase subunit E" [EC:2.7.7.6]
K03051	DNA-directed RNA polymerase subunit F [EC:2.7.7.6]
K03053	DNA-directed RNA polymerase subunit H [EC:2.7.7.6]
K03055	DNA-directed RNA polymerase subunit K [EC:2.7.7.6]
K03057	transcription elongation factor
K03058	DNA-directed RNA polymerase subunit N [EC:2.7.7.6]
K03059	DNA-directed RNA polymerase subunit P [EC:2.7.7.6]
K03105	signal recognition particle subunit SRP19
K03120	transcription initiation factor TFIID TATA-box-binding protein
K03136	transcription initiation factor TFIIE subunit alpha
K03166	DNA topoisomerase VI subunit A [EC:5.99.1.3]
K03167	DNA topoisomerase VI subunit B [EC:5.99.1.3]
K03232	elongation factor 1-beta
K03236	translation initiation factor 1A
K03237	translation initiation factor 2 subunit 1
K03239	translation initiation factor eIF-2B subunit alpha
K03242	translation initiation factor 2 subunit 3
K03243	translation initiation factor 5B
K03264	translation initiation factor 6
K03268	benzene 1,2-dioxygenase [EC:1.14.12.3]
K03395	gentamicin 3'-N-acetyltransferase [EC:2.3.1.60]
K03538	ribonuclease P protein subunit POP4 [EC:3.1.26.5]
K03539	ribonuclease P/MRP protein subunit RPP1 [EC:3.1.26.5]
K03540	ribonuclease P protein subunit RPR2 [EC:3.1.26.5]
K03622	archaea-specific DNA-binding protein
K03626	nascent polypeptide-associated complex subunit alpha
K04071	6-pyruvoyltetrahydropterin 2'-reductase [EC:1.1.1.220]
K04090	indolepyruvate ferredoxin oxidoreductase [EC:1.2.7.8]
K04097	glutathione S-transferase [EC:2.5.1.18]
K04340	scyllo-inosamine-4-phosphate amidinotransferase 1 [EC:2.1.4.2]
K04341	dTDP-dihydrostreptose-streptidine-6-phosphate dihydrostreptosyltransferase [EC:2.4.2.27]
K04484	DNA repair protein RadB
K04496	C-terminal binding protein
K04791	mycobactin polyketide synthetase MbtD
K04795	fibrillarin-like pre-rRNA processing protein
K04796	small nuclear ribonucleoprotein
K04797	prefoldin alpha subunit
K04798	prefoldin beta subunit
K04801	replication factor C small subunit
K04802	proliferating cell nuclear antigen
K05301	sulfite dehydrogenase [EC:1.8.2.1]
K05383	CpeT protein
K05551	act minimal PKS ketosynthase (KS/KS alpha) [EC:2.3.1.-]
K05552	act minimal PKS chain-length factor (CLF/KS beta) [EC:2.3.1.-]
K05553	act minimal PKS acyl carrier protein
K05559	multicomponent K+:H+ antiporter subunit A
K05560	multicomponent K+:H+ antiporter subunit C

KEGG orthology	Function
K05561	multicomponent K+:H+ antiporter subunit D
K05562	multicomponent K+:H+ antiporter subunit E
K05563	multicomponent K+:H+ antiporter subunit F
K05564	multicomponent K+:H+ antiporter subunit G
K05573	NAD(P)H-quinone oxidoreductase subunit 2 [EC:1.6.5.3]
K05574	NAD(P)H-quinone oxidoreductase subunit 3 [EC:1.6.5.3]
K05575	NAD(P)H-quinone oxidoreductase subunit 4 [EC:1.6.5.3]
K05576	NAD(P)H-quinone oxidoreductase subunit 4L [EC:1.6.5.3]
K05597	glutamin-(asparagin-)ase [EC:3.5.1.38]
K05716	cyclic 2,3-diphosphoglycerate synthetase [EC:4.6.1.-]
K05797	4-cresol dehydrogenase (hydroxylating) [EC:1.17.99.1]
K05889	polyvinyl alcohol dehydrogenase (cytochrome) [EC:1.1.2.6]
K05908	NA
K05927	quinone-reactive Ni/Fe-hydrogenase small subunit [EC:1.12.5.1]
K05973	poly(3-hydroxybutyrate) depolymerase [EC:3.1.1.75]
K05986	NA
K05994	bacterial leucyl aminopeptidase [EC:3.4.11.10]
K05998	pseudomonalisin [EC:3.4.21.100]
K06034	sulfopyruvate decarboxylase subunit alpha [EC:4.1.1.79]
K06154	Lrp/AsnC family transcriptional regulator, involved in the regulation of lysine biosynthesis
K06237	collagen, type IV, alpha
K06363	response regulator aspartate phosphatase E [EC:3.1.-.-]
K06364	response regulator aspartate phosphatase F [EC:3.1.-.-]
K06377	sporulation-control protein
K06434	small acid-soluble spore protein (thioredoxin-like protein)
K06596	chemosensory pili system protein ChpA (sensor histidine kinase/response regulator)
K06601	flagellar protein FlbT
K06602	flagellar protein FlaF
K06718	L-2,4-diaminobutyric acid acetyltransferase [EC:2.3.1.178]
K06862	energy-converting hydrogenase B subunit Q
K06863	5-formaminoimidazole-4-carboxamide-1-(beta)-D-ribofuranosyl 5'-monophosphate synthetase [EC:6.3.4.-]
K06868	Sep-tRNA:Cys-tRNA synthetase [EC:2.5.1.73]
K06869	uncharacterized protein
K06873	NA
K06874	zinc finger protein
K06875	programmed cell death protein 5
K06914	NA
K06930	NA
K06931	NA
K06943	nucleolar GTP-binding protein
K06953	NA
K06961	ribosomal RNA assembly protein
K06963	tRNA acetyltransferase TAN1
K06964	NA
K06982	pantoate kinase [EC:2.7.1.169]
K06984	NA
K07049	TatD-related deoxyribonuclease
K07055	tRNA wybutosine-synthesizing protein 2 [EC:2.1.1.-]
K07060	UPF0271 protein
K07061	NA
K07073	NA
K07086	NA
K07092	NA
K07103	NA
K07108	NA
K07123	NA
K07131	NA
K07135	NA
K07144	NA
K07155	quercetin 2,3-dioxygenase [EC:1.13.11.24]
K07157	NA
K07158	NA
K07159	NA
K07178	RIO kinase 1 [EC:2.7.11.1]
K07179	RIO kinase 2 [EC:2.7.11.1]
K07244	mgtE-like transporter
K07254	tRNA (cytidine56-2'-O)-methyltransferase [EC:2.1.1.206]
K07288	uncharacterized membrane protein
K07333	archaeal flagellar protein FlaJ
K07338	hypothetical protein

KEGG orthology	Function
K07342	protein transport protein SEC61 subunit gamma and related proteins
K07394	SM-20-related protein
K07477	translin
K07544	benzylsuccinate CoA-transferase BbsF subunit [EC:2.8.3.15]
K07558	tRNA nucleotidyltransferase (CCA-adding enzyme) [EC:2.7.7.72]
K07562	nonsense-mediated mRNA decay protein 3
K07569	RNA-binding protein
K07572	putative nucleotide binding protein
K07575	PUA domain protein
K07580	hypothetical protein
K07581	hypothetical protein
K07585	hypothetical protein
K07732	riboflavin kinase, archaea type [EC:2.7.1.161]
K07823	3-oxoadipyl-CoA thiolase [EC:2.3.1.174]
K08076	astacin [EC:3.4.24.21]
K08085	type IV fimbrial biogenesis protein FimU
K08096	GTP cyclohydrolase IIa [EC:3.5.4.29]
K08176	MFS transporter, PHS family, inorganic phosphate transporter
K08477	outer membrane protease E [EC:3.4.21.-]
K08598	YopJ protease family
K08604	vibriolysin [EC:3.4.24.25]
K08645	anthrax lethal toxin endopeptidase [EC:3.4.24.83]
K08698	carbon dioxide concentrating mechanism protein CcmM
K08713	potassium channel LctB
K08953	chlorosome envelope protein J
K08971	putative membrane protein
K08973	putative membrane protein
K08975	putative membrane protein
K08979	putative membrane protein
K08983	putative membrane protein
K09119	hypothetical protein
K09139	hypothetical protein
K09140	pre-rRNA-processing protein TSR3
K09148	hypothetical protein
K09152	hypothetical protein
K09154	hypothetical protein
K09713	hypothetical protein
K09721	hypothetical protein
K09722	4-phosphopantoate---beta-alanine ligase [EC:6.3.2.36]
K09723	hypothetical protein
K09724	hypothetical protein
K09725	hypothetical protein
K09727	hypothetical protein
K09732	hypothetical protein
K09735	hypothetical protein
K09736	hypothetical protein
K09737	hypothetical protein
K09738	hypothetical protein
K09739	hypothetical protein
K09741	hypothetical protein
K09744	hypothetical protein
K09746	hypothetical protein
K09796	hypothetical protein
K09845	1-hydroxycarotenoid 3,4-desaturase [EC:1.3.99.27]
K09846	demethylspheroidene O-methyltransferase [EC:2.1.1.210]
K09879	isorenieratene synthase
K09919	hypothetical protein
K09941	hypothetical protein
K09943	hypothetical protein
K09947	hypothetical protein
K09950	hypothetical protein
K09959	hypothetical protein
K09965	hypothetical protein
K09966	hypothetical protein
K09983	hypothetical protein
K10023	arginine/ornithine transport system permease protein
K10024	arginine/ornithine transport system permease protein
K10025	arginine/ornithine transport system ATP-binding protein [EC:3.6.3.-]
K10123	putative ferrous iron transport protein C
K10216	2-hydroxymuconate-semialdehyde hydrolase [EC:3.7.1.9]

KEGG orthology	Function
K10221	2-pyrone-4,6-dicarboxylate lactonase [EC:3.1.1.57]
K10222	2,6-dioxo-6-phenylhexa-3-enoate hydrolase [EC:3.7.1.8]
K10233	alpha-glucoside transport system permease protein
K10623	HOMODA hydrolase [EC:3.7.1.-]
K10725	archaeal cell division control protein 6
K10764	O-succinylhomoserine sulfhydrylase [EC:2.5.1.-]
K10829	iron-chelate-transporting ATPase [EC:3.6.3.34]
K10873	DNA repair and recombination protein RAD52
K10911	two-component system, phosphorelay protein LuxU
K10923	AraC family transcriptional regulator, TCP pilus virulence regulatory protein
K10925	MSHA pilin protein MshB
K10926	MSHA pilin protein MshC
K10929	cholera enterotoxin subunit B
K10930	toxin co-regulated pilin
K10932	toxin co-regulated pilus biosynthesis outer membrane protein C
K10938	accessory colonization factor AcfC
K10966	toxin co-regulated pilus biosynthesis protein J [EC:3.4.23.43 2.1.1.-]
K11006	shiga toxin subunit A
K11007	shiga toxin subunit B
K11014	cytolethal distending toxin subunit B
K11015	cytolethal distending toxin subunit C
K11016	hemolysin
K11023	pertussis toxin subunit 1 [EC:2.4.2.-]
K11028	vacuolating cytotoxin
K11057	beta2-toxin
K11058	enterotoxin Cpe
K11212	LPPG:FO 2-phospho-L-lactate transferase [EC:2.7.8.28]
K11260	formylmethanofuran dehydrogenase subunit G [EC:1.2.99.5]
K11395	2-keto-3-deoxy-gluconate aldolase [EC:4.1.2.-]
K11434	protein arginine N-methyltransferase 1 [EC:2.1.1.-]
K11526	two-component system, chemotaxis family, sensor histidine kinase and response regulator PixL
K11600	exosome complex component RRP41
K11638	two-component system, CitB family, response regulator CitT
K11780	FO synthase subunit 1 [EC:2.5.1.77]
K11814	multidrug resistance protein EbrA
K11913	type VI secretion system protein
K12048	ComB10 competence protein
K12049	ComB9 competence protein
K12054	lytic transglycosylase AtlA
K12080	type IV secretion system protein PtlC
K12247	alpha-2,3 sialyltransferase [EC:2.4.99.-]
K12430	polyketide synthase 1/15
K12513	tight adherence protein E
K12514	tight adherence protein F
K12515	tight adherence protein G
K12534	membrane fusion protein RsaE
K12589	exosome complex component RRP42
K12673	N2-(2-carboxyethyl)arginine synthase [EC:2.5.1.66]
K12786	LEE-encoded effector EspF
K12789	Tir-cytoskeleton coupling protein
K12809	T3SS secreted effector EspG-like protein
K12953	cation-transporting ATPase F [EC:3.6.3.-]
K12978	lipid A 4'-phosphatase [EC:3.1.3.-]
K13008	O-antigen polymerase
K13039	sulfopyruvate decarboxylase subunit beta [EC:4.1.1.79]
K13060	acyl homoserine lactone synthase [EC:2.3.1.184]
K13284	invasin A
K13286	invasin C
K13317	NDP-4-keto-2,6-dideoxyhexose 3-C-methyltransferase
K13450	phosphothreonine lyase [EC:4.2.3.-]
K13455	avirulence protein
K13488	chemotaxis-related protein WspB
K13489	chemotaxis-related protein WspD
K13503	anthranilate synthase [EC:4.1.3.27]
K13520	outer membrane protease [EC:3.4.23.-]
K13583	GcrA cell cycle regulator
K13659	2-beta-glucuronyltransferase [EC:2.4.1.264]
K13661	GumC protein
K13740	secreted effector protein SptP
K13742	protein IpgB1

KEGG orthology	Function
K13790	virulence protein IcsB
K13793	secreted effector OspE
K13797	DNA-directed RNA polymerase subunit beta-beta' [EC:2.7.7.6]
K13798	DNA-directed RNA polymerase subunit B [EC:2.7.7.6]
K13875	L-arabonate dehydrase [EC:4.2.1.25]
K13941	2-amino-4-hydroxy-6-hydroxymethyldihydropteridine diphosphokinase / dihydropteroate synthase [EC:2.7.6.3 2.5.1.15]
K14092	energy-converting hydrogenase A subunit A
K14093	energy-converting hydrogenase A subunit B
K14094	energy-converting hydrogenase A subunit C
K14095	energy-converting hydrogenase A subunit D
K14096	energy-converting hydrogenase A subunit E
K14097	energy-converting hydrogenase A subunit F
K14098	energy-converting hydrogenase A subunit G
K14100	energy-converting hydrogenase A subunit I
K14102	energy-converting hydrogenase A subunit K
K14103	energy-converting hydrogenase A subunit L
K14104	energy-converting hydrogenase A subunit M
K14105	energy-converting hydrogenase A subunit N
K14109	energy-converting hydrogenase A subunit R
K14110	energy-converting hydrogenase B subunit A
K14111	energy-converting hydrogenase B subunit B
K14113	energy-converting hydrogenase B subunit D
K14114	energy-converting hydrogenase B subunit E
K14115	energy-converting hydrogenase B subunit F
K14116	energy-converting hydrogenase B subunit G
K14117	energy-converting hydrogenase B subunit H
K14118	energy-converting hydrogenase B subunit I
K14119	energy-converting hydrogenase B subunit J
K14122	energy-converting hydrogenase B subunit M
K14123	energy-converting hydrogenase B subunit N
K14124	energy-converting hydrogenase B subunit O
K14125	energy-converting hydrogenase B subunit P
K14165	dual specificity phosphatase [EC:3.1.3.16 3.1.3.48]
K14166	copper transport protein
K14201	clumping factor A
K14269	glutarate semialdehyde dehydrogenase [EC:1.2.1.20]
K14451	(3S)-malyl-CoA thioesterase
K14465	succinate semialdehyde reductase (NADPH) [EC:1.1.1.-]
K14468	malonyl-CoA reductase / 3-hydroxypropionate dehydrogenase (NADP+) [EC:1.2.1.75 1.1.1.298]
K14561	U3 small nucleolar ribonucleoprotein protein IMP4
K14564	nucleolar protein 56
K14568	essential for mitotic growth 1
K14598	chlorobactene lauroyltransferase
K14628	enoyl reductase
K14653	2-amino-5-formylamino-6-ribosylaminopyrimidin-4(3H)-one 5'-monophosphate deformylase [EC:3.5.1.102]
K14661	nodulation protein F [EC:2.3.1.-]
K14683	solute carrier family 34 (sodium-dependent phosphate cotransporter)
K14974	6-hydroxynicotinate 3-monooxygenase [EC:1.14.13.114]
K14998	surfeit locus 1 family protein
K15226	arogenate dehydrogenase (NADP+) [EC:1.3.1.78]
K15327	polyketide biosynthesis malonyl-CoA-[acyl-carrier-protein] transacylase
K15355	NA
K15366	salmonella plasmid virulence protein B
K15468	cytochrome P450 PksS
K15645	coronafacic acid polyketide synthase Cfa7
K15650	non-haem Fe2+, alpha-ketoglutarate-dependent halogenase
K15676	rhizoxin biosynthesis, polyketide synthase RhiC
K15681	aminotransferase MxcL
K15784	N-alpha-acetyl-L-2,4-diaminobutyrate deacetylase [EC:3.5.1.-]
K15845	outer membrane protein HopZ
K15853	acyl transferase [EC:2.3.1.-]
K15900	tRNA threonylcarbamoyladenosine biosynthesis protein
K15904	bifunctional tRNA threonylcarbamoyladenosine biosynthesis protein [EC:2.7.11.1]
K15918	D-glycerate 3-kinase [EC:2.7.1.31]
K16081	alginate production protein
K16149	1,4-alpha-glucan branching enzyme [EC:2.4.1.18]
K16152	heme acquisition protein HasR
K16190	glucuronokinase [EC:2.7.1.43]

NA indicates not assigned

Appendix 5. KOs unique to the IGC gene set

KEGG orthology	Function
K00035	D-galactose 1-dehydrogenase [EC:1.1.1.48]
K00193	acetyl-CoA decarbonylase/synthase complex subunit beta [EC:2.3.1.-]
K00201	formylmethanofuran dehydrogenase subunit B [EC:1.2.99.5]
K00271	valine dehydrogenase [EC:1.4.1.8]
K00292	saccharopine dehydrogenase (NAD+, L-glutamate forming) [EC:1.5.1.9]
K00319	methylenetetrahydromethanopterin dehydrogenase [EC:1.5.99.9]
K00360	nitrate reductase (NADH) [EC:1.7.1.1]
K00401	methyl-coenzyme M reductase beta subunit [EC:2.8.4.1]
K00406	cytochrome c oxidase cbb3-type subunit III
K00407	cytochrome c oxidase cbb3-type subunit IV
K00410	ubiquinol-cytochrome c reductase cytochrome b/c1 subunit
K00413	ubiquinol-cytochrome c reductase cytochrome c1 subunit
K00440	coenzyme F420 hydrogenase alpha subunit [EC:1.12.98.1]
K00456	cysteine dioxygenase [EC:1.13.11.20]
K00496	alkane 1-monooxygenase [EC:1.14.15.3]
K00499	choline monooxygenase [EC:1.14.15.7]
K00507	stearoyl-CoA desaturase (delta-9 desaturase) [EC:1.14.19.1]
K00514	zeta-carotene desaturase [EC:1.3.5.6]
K00524	ribonucleotide reductase, class II [EC:1.17.4.1]
K00555	tRNA (guanine26-N2/guanine27-N2)-dimethyltransferase [EC:2.1.1.215 2.1.1.216]
K00577	tetrahydromethanopterin S-methyltransferase subunit A [EC:2.1.1.86]
K00578	tetrahydromethanopterin S-methyltransferase subunit B [EC:2.1.1.86]
K00579	tetrahydromethanopterin S-methyltransferase subunit C [EC:2.1.1.86]
K00580	tetrahydromethanopterin S-methyltransferase subunit D [EC:2.1.1.86]
K00582	tetrahydromethanopterin S-methyltransferase subunit F [EC:2.1.1.86]
K00583	tetrahydromethanopterin S-methyltransferase subunit G [EC:2.1.1.86]
K00586	diphthine synthase [EC:2.1.1.98]
K00624	carnitine O-acetyltransferase [EC:2.3.1.7]
K00635	diacylglycerol O-acyltransferase [EC:2.3.1.20]
K00862	erythritol kinase [EC:2.7.1.27]
K00887	undecaprenol kinase [EC:2.7.1.66]
K00988	ATP adenylyltransferase [EC:2.7.7.53]
K01001	UDP-N-acetylglucosamine--dolichyl-phosphate N-acetylglucosaminephosphotransferase [EC:2.7.8.15]
K01084	glucose-6-phosphatase [EC:3.1.3.9]
K01117	sphingomyelin phosphodiesterase [EC:3.1.4.12]
K01158	deoxyribonuclease II [EC:3.1.22.1]
K01170	tRNA-intron endonuclease, archaea type [EC:3.1.27.9]
K01172	NA
K01230	mannosyl-oligosaccharide alpha-1,2-mannosidase [EC:3.2.1.113]
K01280	tripeptidyl-peptidase II [EC:3.4.14.10]
K01385	thermopsin [EC:3.4.23.42]
K01504	glucosamine-6-phosphate isomerase [EC:3.5.99.6]
K01510	apyrase [EC:3.6.1.5]
K01594	sulfinoalanine decarboxylase [EC:4.1.1.29]
K01622	fructose 1,6-bisphosphate aldolase/phosphatase [EC:4.1.2.13 3.1.3.11]
K01663	glutamine amidotransferase / cyclase [EC:2.4.2.- 4.1.3.-]
K01769	guanylate cyclase, other [EC:4.6.1.2]
K01969	3-methylcrotonyl-CoA carboxylase beta subunit [EC:6.4.1.4]
K02201	pantetheine-phosphate adenylyltransferase [EC:2.7.7.3]
K02288	phycocyanobilin lyase alpha subunit [EC:4.-.-.-]
K02289	phycocyanobilin lyase beta subunit
K02322	DNA polymerase II large subunit [EC:2.7.7.7]
K02497	HemX protein
K02571	periplasmic nitrate reductase NapE
K02595	nitrogenase-stabilizing/protective protein
K02659	twitching motility protein PilI
K02665	type IV pilus assembly protein PilP
K02672	type IV pilus assembly protein PilW
K02676	type IV pilus assembly protein PilZ
K02683	DNA primase [EC:2.7.7.-]
K02685	DNA primase large subunit [EC:2.7.7.-]
K02691	photosystem I subunit VII
K02717	photosystem II oxygen-evolving enhancer protein 2
K02866	large subunit ribosomal protein L10e
K02869	large subunit ribosomal protein L12
K02877	large subunit ribosomal protein L15e
K02883	large subunit ribosomal protein L18e
K02885	large subunit ribosomal protein L19e

KEGG orthology	Function
K02889	large subunit ribosomal protein L21e
K02896	large subunit ribosomal protein L24e
K02910	large subunit ribosomal protein L31e
K02912	large subunit ribosomal protein L32e
K02915	large subunit ribosomal protein L34e
K02921	large subunit ribosomal protein L37Ae
K02922	large subunit ribosomal protein L37e
K02924	large subunit ribosomal protein L39e
K02927	large subunit ribosomal protein L40e
K02929	large subunit ribosomal protein L44e
K02930	large subunit ribosomal protein L4e
K02944	large subunit ribosomal protein LX
K02966	small subunit ribosomal protein S19e
K02974	small subunit ribosomal protein S24e
K02978	small subunit ribosomal protein S27e
K02979	small subunit ribosomal protein S28e
K02984	small subunit ribosomal protein S3Ae
K02987	small subunit ribosomal protein S4e
K02991	small subunit ribosomal protein S6e
K02995	small subunit ribosomal protein S8e
K03044	DNA-directed RNA polymerase subunit B' [EC:2.7.7.6]
K03045	DNA-directed RNA polymerase subunit B" [EC:2.7.7.6]
K03049	DNA-directed RNA polymerase subunit E' [EC:2.7.7.6]
K03050	DNA-directed RNA polymerase subunit E" [EC:2.7.7.6]
K03051	DNA-directed RNA polymerase subunit F [EC:2.7.7.6]
K03053	DNA-directed RNA polymerase subunit H [EC:2.7.7.6]
K03055	DNA-directed RNA polymerase subunit K [EC:2.7.7.6]
K03057	transcription elongation factor
K03058	DNA-directed RNA polymerase subunit N [EC:2.7.7.6]
K03059	DNA-directed RNA polymerase subunit P [EC:2.7.7.6]
K03105	signal recognition particle subunit SRP19
K03120	transcription initiation factor TFIID TATA-box-binding protein
K03136	transcription initiation factor TFIIE subunit alpha
K03166	DNA topoisomerase VI subunit A [EC:5.99.1.3]
K03167	DNA topoisomerase VI subunit B [EC:5.99.1.3]
K03232	elongation factor 1-beta
K03236	translation initiation factor 1A
K03237	translation initiation factor 2 subunit 1
K03239	translation initiation factor eIF-2B subunit alpha
K03242	translation initiation factor 2 subunit 3
K03243	translation initiation factor 5B
K03264	translation initiation factor 6
K03268	benzene 1,2-dioxygenase [EC:1.14.12.3]
K03395	gentamicin 3'-N-acetyltransferase [EC:2.3.1.60]
K03538	ribonuclease P protein subunit POP4 [EC:3.1.26.5]
K03539	ribonuclease P/MRP protein subunit RPP1 [EC:3.1.26.5]
K03540	ribonuclease P protein subunit RPR2 [EC:3.1.26.5]
K03622	archaea-specific DNA-binding protein
K03626	nascent polypeptide-associated complex subunit alpha
K04071	6-pyruvoyltetrahydropterin 2'-reductase [EC:1.1.1.220]
K04090	indolepyruvate ferredoxin oxidoreductase [EC:1.2.7.8]
K04097	glutathione S-transferase [EC:2.5.1.18]
K04340	scyllo-inosamine-4-phosphate amidinotransferase 1 [EC:2.1.4.2]
K04341	dTDP-dihydrostreptose-streptidine-6-phosphate dihydrostreptosyltransferase [EC:2.4.2.27]
K04484	DNA repair protein RadB
K04496	C-terminal binding protein
K04791	mycobactin polyketide synthetase MbtD
K04795	fibrillarin-like pre-rRNA processing protein
K04796	small nuclear ribonucleoprotein
K04797	prefoldin alpha subunit
K04798	prefoldin beta subunit
K04801	replication factor C small subunit
K04802	proliferating cell nuclear antigen
K05301	sulfite dehydrogenase [EC:1.8.2.1]
K05383	CpeT protein
K05551	act minimal PKS ketosynthase (KS/KS alpha) [EC:2.3.1.-]
K05552	act minimal PKS chain-length factor (CLF/KS beta) [EC:2.3.1.-]
K05553	act minimal PKS acyl carrier protein
K05559	multicomponent K+:H+ antiporter subunit A
K05560	multicomponent K+:H+ antiporter subunit C

KEGG orthology	Function
K05561	multicomponent K+:H+ antiporter subunit D
K05562	multicomponent K+:H+ antiporter subunit E
K05563	multicomponent K+:H+ antiporter subunit F
K05564	multicomponent K+:H+ antiporter subunit G
K05573	NAD(P)H-quinone oxidoreductase subunit 2 [EC:1.6.5.3]
K05574	NAD(P)H-quinone oxidoreductase subunit 3 [EC:1.6.5.3]
K05575	NAD(P)H-quinone oxidoreductase subunit 4 [EC:1.6.5.3]
K05576	NAD(P)H-quinone oxidoreductase subunit 4L [EC:1.6.5.3]
K05597	glutamin-(asparagin-)ase [EC:3.5.1.38]
K05716	cyclic 2,3-diphosphoglycerate synthetase [EC:4.6.1.-]
K05797	4-cresol dehydrogenase (hydroxylating) [EC:1.17.99.1]
K05889	polyvinyl alcohol dehydrogenase (cytochrome) [EC:1.1.2.6]
K05908	NA
K05927	quinone-reactive Ni/Fe-hydrogenase small subunit [EC:1.12.5.1]
K05973	poly(3-hydroxybutyrate) depolymerase [EC:3.1.1.75]
K05986	NA
K05994	bacterial leucyl aminopeptidase [EC:3.4.11.10]
K05998	pseudomonalisin [EC:3.4.21.100]
K06034	sulfopyruvate decarboxylase subunit alpha [EC:4.1.1.79]
K06154	Lrp/AsnC family transcriptional regulator, involved in the regulation of lysine biosynthesis
K06237	collagen, type IV, alpha
K06363	response regulator aspartate phosphatase E [EC:3.1.-.-]
K06364	response regulator aspartate phosphatase F [EC:3.1.-.-]
K06377	sporulation-control protein
K06434	small acid-soluble spore protein (thioredoxin-like protein)
K06596	chemosensory pili system protein ChpA (sensor histidine kinase/response regulator)
K06601	flagellar protein FlbT
K06602	flagellar protein FlaF
K06718	L-2,4-diaminobutyric acid acetyltransferase [EC:2.3.1.178]
K06862	energy-converting hydrogenase B subunit Q
K06863	5-formaminoimidazole-4-carboxamide-1-(beta)-D-ribofuranosyl 5'-monophosphate synthetase [EC:6.3.4.-]
K06868	Sep-tRNA:Cys-tRNA synthetase [EC:2.5.1.73]
K06869	uncharacterized protein
K06873	NA
K06874	zinc finger protein
K06875	programmed cell death protein 5
K06914	NA
K06930	NA
K06931	NA
K06943	nucleolar GTP-binding protein
K06953	NA
K06961	ribosomal RNA assembly protein
K06963	tRNA acetyltransferase TAN1
K06964	NA
K06982	pantoate kinase [EC:2.7.1.169]
K06984	NA
K07049	TatD-related deoxyribonuclease
K07055	tRNA wybutosine-synthesizing protein 2 [EC:2.1.1.-]
K07060	UPF0271 protein
K07061	NA
K07073	NA
K07086	NA
K07092	NA
K07103	NA
K07108	NA
K07123	NA
K07131	NA
K07135	NA
K07144	NA
K07155	quercetin 2,3-dioxygenase [EC:1.13.11.24]
K07157	NA
K07158	NA
K07159	NA
K07178	RIO kinase 1 [EC:2.7.11.1]
K07179	RIO kinase 2 [EC:2.7.11.1]
K07244	mgtE-like transporter
K07254	tRNA (cytidine56-2'-O)-methyltransferase [EC:2.1.1.206]
K07288	uncharacterized membrane protein
K07333	archaeal flagellar protein FlaJ
K07338	hypothetical protein

KEGG orthology	Function
K07342	protein transport protein SEC61 subunit gamma and related proteins
K07394	SM-20-related protein
K07477	translin
K07544	benzylsuccinate CoA-transferase BbsF subunit [EC:2.8.3.15]
K07558	tRNA nucleotidyltransferase (CCA-adding enzyme) [EC:2.7.7.72]
K07562	nonsense-mediated mRNA decay protein 3
K07569	RNA-binding protein
K07572	putative nucleotide binding protein
K07575	PUA domain protein
K07580	hypothetical protein
K07581	hypothetical protein
K07585	hypothetical protein
K07732	riboflavin kinase, archaea type [EC:2.7.1.161]
K07823	3-oxoadipyl-CoA thiolase [EC:2.3.1.174]
K08076	astacin [EC:3.4.24.21]
K08085	type IV fimbrial biogenesis protein FimU
K08096	GTP cyclohydrolase IIa [EC:3.5.4.29]
K08176	MFS transporter, PHS family, inorganic phosphate transporter
K08477	outer membrane protease E [EC:3.4.21.-]
K08598	YopJ protease family
K08604	vibriolysin [EC:3.4.24.25]
K08645	anthrax lethal toxin endopeptidase [EC:3.4.24.83]
K08698	carbon dioxide concentrating mechanism protein CcmM
K08713	potassium channel LctB
K08953	chlorosome envelope protein J
K08971	putative membrane protein
K08973	putative membrane protein
K08975	putative membrane protein
K08979	putative membrane protein
K08983	putative membrane protein
K09119	hypothetical protein
K09139	hypothetical protein
K09140	pre-rRNA-processing protein TSR3
K09148	hypothetical protein
K09152	hypothetical protein
K09154	hypothetical protein
K09713	hypothetical protein
K09721	hypothetical protein
K09722	4-phosphopantoate---beta-alanine ligase [EC:6.3.2.36]
K09723	hypothetical protein
K09724	hypothetical protein
K09725	hypothetical protein
K09727	hypothetical protein
K09732	hypothetical protein
K09735	hypothetical protein
K09736	hypothetical protein
K09737	hypothetical protein
K09738	hypothetical protein
K09739	hypothetical protein
K09741	hypothetical protein
K09744	hypothetical protein
K09746	hypothetical protein
K09796	hypothetical protein
K09845	1-hydroxycarotenoid 3,4-desaturase [EC:1.3.99.27]
K09846	demethylspheroidene O-methyltransferase [EC:2.1.1.210]
K09879	isorenieratene synthase
K09919	hypothetical protein
K09941	hypothetical protein
K09943	hypothetical protein
K09947	hypothetical protein
K09950	hypothetical protein
K09959	hypothetical protein
K09965	hypothetical protein
K09966	hypothetical protein
K09983	hypothetical protein
K10023	arginine/ornithine transport system permease protein
K10024	arginine/ornithine transport system permease protein
K10025	arginine/ornithine transport system ATP-binding protein [EC:3.6.3.-]
K10123	putative ferrous iron transport protein C
K10216	2-hydroxymuconate-semialdehyde hydrolase [EC:3.7.1.9]

KEGG orthology	Function
K10221	2-pyrone-4,6-dicarboxylate lactonase [EC:3.1.1.57]
K10222	2,6-dioxo-6-phenylhexa-3-enoate hydrolase [EC:3.7.1.8]
K10233	alpha-glucoside transport system permease protein
K10623	HOMODA hydrolase [EC:3.7.1.-]
K10725	archaeal cell division control protein 6
K10764	O-succinylhomoserine sulfhydrylase [EC:2.5.1.-]
K10829	iron-chelate-transporting ATPase [EC:3.6.3.34]
K10873	DNA repair and recombination protein RAD52
K10911	two-component system, phosphorelay protein LuxU
K10923	AraC family transcriptional regulator, TCP pilus virulence regulatory protein
K10925	MSHA pilin protein MshB
K10926	MSHA pilin protein MshC
K10929	cholera enterotoxin subunit B
K10930	toxin co-regulated pilin
K10932	toxin co-regulated pilus biosynthesis outer membrane protein C
K10938	accessory colonization factor AcfC
K10966	toxin co-regulated pilus biosynthesis protein J [EC:3.4.23.43 2.1.1.-]
K11006	shiga toxin subunit A
K11007	shiga toxin subunit B
K11014	cytolethal distending toxin subunit B
K11015	cytolethal distending toxin subunit C
K11016	hemolysin
K11023	pertussis toxin subunit 1 [EC:2.4.2.-]
K11028	vacuolating cytotoxin
K11057	beta2-toxin
K11058	enterotoxin Cpe
K11212	LPPG:FO 2-phospho-L-lactate transferase [EC:2.7.8.28]
K11260	formylmethanofuran dehydrogenase subunit G [EC:1.2.99.5]
K11395	2-keto-3-deoxy-gluconate aldolase [EC:4.1.2.-]
K11434	protein arginine N-methyltransferase 1 [EC:2.1.1.-]
K11526	two-component system, chemotaxis family, sensor histidine kinase and response regulator PixL
K11600	exosome complex component RRP41
K11638	two-component system, CitB family, response regulator CitT
K11780	FO synthase subunit 1 [EC:2.5.1.77]
K11814	multidrug resistance protein EbrA
K11913	type VI secretion system protein
K12048	ComB10 competence protein
K12049	ComB9 competence protein
K12054	lytic transglycosylase AtlA
K12080	type IV secretion system protein PtlC
K12247	alpha-2,3 sialyltransferase [EC:2.4.99.-]
K12430	polyketide synthase 1/15
K12513	tight adherence protein E
K12514	tight adherence protein F
K12515	tight adherence protein G
K12534	membrane fusion protein RsaE
K12589	exosome complex component RRP42
K12673	N2-(2-carboxyethyl)arginine synthase [EC:2.5.1.66]
K12786	LEE-encoded effector EspF
K12789	Tir-cytoskeleton coupling protein
K12809	T3SS secreted effector EspG-like protein
K12953	cation-transporting ATPase F [EC:3.6.3.-]
K12978	lipid A 4'-phosphatase [EC:3.1.3.-]
K13008	O-antigen polymerase
K13039	sulfopyruvate decarboxylase subunit beta [EC:4.1.1.79]
K13060	acyl homoserine lactone synthase [EC:2.3.1.184]
K13284	invasin A
K13286	invasin C
K13317	NDP-4-keto-2,6-dideoxyhexose 3-C-methyltransferase
K13450	phosphothreonine lyase [EC:4.2.3.-]
K13455	avirulence protein
K13488	chemotaxis-related protein WspB
K13489	chemotaxis-related protein WspD
K13503	anthranilate synthase [EC:4.1.3.27]
K13520	outer membrane protease [EC:3.4.23.-]
K13583	GcrA cell cycle regulator
K13659	2-beta-glucuronyltransferase [EC:2.4.1.264]
K13661	GumC protein
K13740	secreted effector protein SptP
K13742	protein IpgB1

KEGG orthology	Function
K13790	virulence protein IcsB
K13793	secreted effector OspE
K13797	DNA-directed RNA polymerase subunit beta-beta' [EC:2.7.7.6]
K13798	DNA-directed RNA polymerase subunit B [EC:2.7.7.6]
K13875	L-arabonate dehydrase [EC:4.2.1.25]
K13941	2-amino-4-hydroxy-6-hydroxymethyldihydropteridine diphosphokinase / dihydropteroate synthase [EC:2.7.6.3 2.5.1.15]
K14092	energy-converting hydrogenase A subunit A
K14093	energy-converting hydrogenase A subunit B
K14094	energy-converting hydrogenase A subunit C
K14095	energy-converting hydrogenase A subunit D
K14096	energy-converting hydrogenase A subunit E
K14097	energy-converting hydrogenase A subunit F
K14098	energy-converting hydrogenase A subunit G
K14100	energy-converting hydrogenase A subunit I
K14102	energy-converting hydrogenase A subunit K
K14103	energy-converting hydrogenase A subunit L
K14104	energy-converting hydrogenase A subunit M
K14105	energy-converting hydrogenase A subunit N
K14109	energy-converting hydrogenase A subunit R
K14110	energy-converting hydrogenase B subunit A
K14111	energy-converting hydrogenase B subunit B
K14113	energy-converting hydrogenase B subunit D
K14114	energy-converting hydrogenase B subunit E
K14115	energy-converting hydrogenase B subunit F
K14116	energy-converting hydrogenase B subunit G
K14117	energy-converting hydrogenase B subunit H
K14118	energy-converting hydrogenase B subunit I
K14119	energy-converting hydrogenase B subunit J
K14122	energy-converting hydrogenase B subunit M
K14123	energy-converting hydrogenase B subunit N
K14124	energy-converting hydrogenase B subunit O
K14125	energy-converting hydrogenase B subunit P
K14165	dual specificity phosphatase [EC:3.1.3.16 3.1.3.48]
K14166	copper transport protein
K14201	clumping factor A
K14269	glutarate semialdehyde dehydrogenase [EC:1.2.1.20]
K14451	(3S)-malyl-CoA thioesterase
K14465	succinate semialdehyde reductase (NADPH) [EC:1.1.1.-]
K14468	malonyl-CoA reductase / 3-hydroxypropionate dehydrogenase (NADP+) [EC:1.2.1.75 1.1.1.298]
K14561	U3 small nucleolar ribonucleoprotein protein IMP4
K14564	nucleolar protein 56
K14568	essential for mitotic growth 1
K14598	chlorobactene lauroyltransferase
K14628	enoyl reductase
K14653	2-amino-5-formylamino-6-ribosylaminopyrimidin-4(3H)-one 5'-monophosphate deformylase [EC:3.5.1.102]
K14661	nodulation protein F [EC:2.3.1.-]
K14683	solute carrier family 34 (sodium-dependent phosphate cotransporter)
K14974	6-hydroxynicotinate 3-monooxygenase [EC:1.14.13.114]
K14998	surfeit locus 1 family protein
K15226	arogenate dehydrogenase (NADP+) [EC:1.3.1.78]
K15327	polyketide biosynthesis malonyl-CoA-[acyl-carrier-protein] transacylase
K15355	NA
K15366	salmonella plasmid virulence protein B
K15468	cytochrome P450 PksS
K15645	coronafacic acid polyketide synthase Cfa7
K15650	non-haem Fe2+, alpha-ketoglutarate-dependent halogenase
K15676	rhizoxin biosynthesis, polyketide synthase RhiC
K15681	aminotransferase MxcL
K15784	N-alpha-acetyl-L-2,4-diaminobutyrate deacetylase [EC:3.5.1.-]
K15845	outer membrane protein HopZ
K15853	acyl transferase [EC:2.3.1.-]
K15900	tRNA threonylcarbamoyladenosine biosynthesis protein
K15904	bifunctional tRNA threonylcarbamoyladenosine biosynthesis protein [EC:2.7.11.1]
K15918	D-glycerate 3-kinase [EC:2.7.1.31]
K16081	alginate production protein
K16149	1,4-alpha-glucan branching enzyme [EC:2.4.1.18]
K16152	heme acquisition protein HasR
K16190	glucuronokinase [EC:2.7.1.43]

NA indicates not assigned

Appendix 6. KOs having the highest abundance in the JP cohort among the 12 countries

KEGG orthology	Function
K00005	glycerol dehydrogenase [EC:1.1.1.6]
K00016	L-lactate dehydrogenase [EC:1.1.1.27]
K00020	3-hydroxyisobutyrate dehydrogenase [EC:1.1.1.31]
K00033	6-phosphogluconate dehydrogenase [EC:1.1.1.44]
K00042	2-hydroxy-3-oxopropionate reductase [EC:1.1.1.60]
K00044	estradiol 17beta-dehydrogenase [EC:1.1.1.62]
K00048	lactaldehyde reductase [EC:1.1.1.77]
K00052	3-isopropylmalate dehydrogenase [EC:1.1.1.85]
K00053	ketol-acid reductoisomerase [EC:1.1.1.86]
K00058	D-3-phosphoglycerate dehydrogenase [EC:1.1.1.95]
K00065	2-deoxy-D-gluconate 3-dehydrogenase [EC:1.1.1.125]
K00076	7-alpha-hydroxysteroid dehydrogenase [EC:1.1.1.159]
K00100	NA
K00128	aldehyde dehydrogenase (NAD+) [EC:1.2.1.3]
K00129	aldehyde dehydrogenase (NAD(P)+) [EC:1.2.1.5]
K00131	glyceraldehyde-3-phosphate dehydrogenase (NADP) [EC:1.2.1.9]
K00171	pyruvate ferredoxin oxidoreductase, delta subunit [EC:1.2.7.1]
K00196	carbon-monoxide dehydrogenase iron sulfur subunit
K00198	carbon-monoxide dehydrogenase catalytic subunit [EC:1.2.99.2]
K00215	dihydrodipicolinate reductase [EC:1.3.1.26]
K00324	NAD(P) transhydrogenase subunit alpha [EC:1.6.1.2]
K00325	NAD(P) transhydrogenase subunit beta [EC:1.6.1.2]
K00354	NADPH2 dehydrogenase [EC:1.6.99.1]
K00359	NADH oxidase [EC:1.6.-.-]
K00384	thioredoxin reductase (NADPH) [EC:1.8.1.9]
K00386	NA
K00459	nitronate monooxygenase [EC:1.13.12.16]
K00492	NA
K00564	16S rRNA (guanine1207-N2)-methyltransferase [EC:2.1.1.172]
K00588	caffeoyl-CoA O-methyltransferase [EC:2.1.1.104]
K00595	precorrin-6Y C5,15-methyltransferase / precorrin-8W decarboxylase [EC:2.1.1.132 1.-.-.-]
K00614	NA
K00616	transaldolase [EC:2.2.1.2]
K00620	glutamate N-acetyltransferase / amino-acid N-acetyltransferase [EC:2.3.1.35 2.3.1.1]
K00651	homoserine O-succinyltransferase [EC:2.3.1.46]
K00674	2,3,4,5-tetrahydropyridine-2-carboxylate N-succinyltransferase [EC:2.3.1.117]
K00687	penicillin-binding protein 2B [EC:2.3.2.-]
K00689	dextransucrase [EC:2.4.1.5]
K00690	sucrose phosphorylase [EC:2.4.1.7]
K00762	orotate phosphoribosyltransferase [EC:2.4.2.10]
K00777	NA
K00797	spermidine synthase [EC:2.5.1.16]
K00798	cob(I)alamin adenosyltransferase [EC:2.5.1.17]
K00842	aminotransferase [EC:2.6.1.-]
K00851	gluconokinase [EC:2.7.1.12]
K00852	ribokinase [EC:2.7.1.15]
K00854	xylulokinase [EC:2.7.1.17]
K00864	glycerol kinase [EC:2.7.1.30]
K00868	pyridoxine kinase [EC:2.7.1.35]
K00872	homoserine kinase [EC:2.7.1.39]
K00878	hydroxyethylthiazole kinase [EC:2.7.1.50]
K00886	polyphosphate glucokinase [EC:2.7.1.63]
K00917	tagatose 6-phosphate kinase [EC:2.7.1.144]
K00926	carbamate kinase [EC:2.7.2.2]
K00928	aspartate kinase [EC:2.7.2.4]
K00938	phosphomevalonate kinase [EC:2.7.4.2]
K00942	guanylate kinase [EC:2.7.4.8]
K00949	thiamine pyrophosphokinase [EC:2.7.6.2]
K00960	DNA-directed RNA polymerase [EC:2.7.7.6]
K00965	UDPglucose--hexose-1-phosphate uridylyltransferase [EC:2.7.7.12]
K00982	glutamate-ammonia-ligase adenylyltransferase [EC:2.7.7.42]
K00989	ribonuclease PH [EC:2.7.7.56]
K00997	holo-[acyl-carrier protein] synthase [EC:2.7.8.7]
K01012	biotin synthetase [EC:2.8.1.6]
K01026	propionate CoA-transferase [EC:2.8.3.1]

KEGG orthology	Function
K01055	3-oxoadipate enol-lactonase [EC:3.1.1.24]
K01104	protein-tyrosine phosphatase [EC:3.1.3.48]
K01121	2',3'-cyclic-nucleotide 3'-phosphodiesterase [EC:3.1.4.37]
K01182	oligo-1,6-glucosidase [EC:3.2.1.10]
K01191	alpha-mannosidase [EC:3.2.1.24]
K01193	beta-fructofuranosidase [EC:3.2.1.26]
K01210	glucan 1,3-beta-glucosidase [EC:3.2.1.58]
K01215	glucan 1,6-alpha-glucosidase [EC:3.2.1.70]
K01220	6-phospho-beta-galactosidase [EC:3.2.1.85]
K01223	6-phospho-beta-glucosidase [EC:3.2.1.86]
K01232	maltose-6'-phosphate glucosidase [EC:3.2.1.122]
K01239	purine nucleosidase [EC:3.2.2.1]
K01256	aminopeptidase N [EC:3.4.11.2]
K01261	glutamyl aminopeptidase [EC:3.4.11.7]
K01266	D-aminopeptidase [EC:3.4.11.19]
K01274	D-alanyl-D-alanine dipeptidase [EC:3.4.13.-]
K01305	beta-aspartyl-dipeptidase (metallo-type) [EC:3.4.19.-]
K01322	prolyl oligopeptidase [EC:3.4.21.26]
K01354	oligopeptidase B [EC:3.4.21.83]
K01400	bacillolysin [EC:3.4.24.28]
K01420	CRP/FNR family transcriptional regulator, anaerobic regulatory protein
K01421	putative membrane protein
K01444	N4-(beta-N-acetylglucosaminyl)-L-asparaginase [EC:3.5.1.26]
K01446	N-acetylmuramoyl-L-alanine amidase [EC:3.5.1.28]
K01459	NA
K01462	peptide deformylase [EC:3.5.1.88]
K01466	allantoinase [EC:3.5.2.5]
K01470	creatinine amidohydrolase [EC:3.5.2.10]
K01473	N-methylhydantoinase A [EC:3.5.2.14]
K01478	arginine deiminase [EC:3.5.3.6]
K01488	adenosine deaminase [EC:3.5.4.4]
K01494	dCTP deaminase [EC:3.5.4.13]
K01496	phosphoribosyl-AMP cyclohydrolase [EC:3.5.4.19]
K01515	ADP-ribose pyrophosphatase [EC:3.6.1.13]
K01523	phosphoribosyl-ATP pyrophosphohydrolase [EC:3.6.1.31]
K01567	NA
K01577	oxalyl-CoA decarboxylase [EC:4.1.1.8]
K01589	5-(carboxyamino)imidazole ribonucleotide synthase [EC:6.3.4.18]
K01593	aromatic-L-amino-acid decarboxylase [EC:4.1.1.28]
K01595	phosphoenolpyruvate carboxylase [EC:4.1.1.31]
K01597	diphosphomevalonate decarboxylase [EC:4.1.1.33]
K01599	uroporphyrinogen decarboxylase [EC:4.1.1.37]
K01620	threonine aldolase [EC:4.1.2.5]
K01626	3-deoxy-7-phosphoheptulonate synthase [EC:2.5.1.54]
K01632	fructose-6-phosphate phosphoketolase [EC:4.1.2.22]
K01653	acetolactate synthase I/III small subunit [EC:2.2.1.6]
K01658	anthranilate synthase component II [EC:4.1.3.27]
K01664	para-aminobenzoate synthetase component II [EC:2.6.1.85]
K01697	cystathionine beta-synthase [EC:4.2.1.22]
K01699	propanediol dehydratase large subunit [EC:4.2.1.28]
K01704	3-isopropylmalate/(R)-2-methylmalate dehydratase small subunit [EC:4.2.1.33 4.2.1.35]
K01706	glucarate dehydratase [EC:4.2.1.40]
K01708	galactarate dehydratase [EC:4.2.1.42]
K01739	cystathionine gamma-synthase [EC:2.5.1.48]
K01749	hydroxymethylbilane synthase [EC:2.5.1.61]
K01751	diaminopropionate ammonia-lyase [EC:4.3.1.15]
K01754	threonine dehydratase [EC:4.3.1.19]
K01759	lactoylglutathione lyase [EC:4.4.1.5]
K01760	cystathionine beta-lyase [EC:4.4.1.8]
K01777	proline racemase [EC:5.1.1.4]
K01781	mandelate racemase [EC:5.1.2.2]
K01788	N-acylglucosamine-6-phosphate 2-epimerase [EC:5.1.3.9]
K01792	glucose-6-phosphate 1-epimerase [EC:5.1.3.15]
K01807	ribose 5-phosphate isomerase A [EC:5.3.1.6]
K01814	phosphoribosylformimino-5-aminoimidazole carboxamide ribotide isomerase [EC:5.3.1.16]
K01817	phosphoribosylanthranilate isomerase [EC:5.3.1.24]
K01819	galactose-6-phosphate isomerase [EC:5.3.1.26]
K01820	NA
K01823	isopentenyl-diphosphate delta-isomerase [EC:5.3.3.2]
K01826	5-carboxymethyl-2-hydroxymuconate isomerase [EC:5.3.3.10]

KEGG orthology	Function
K01839	phosphopentomutase [EC:5.4.2.7]
K01854	UDP-galactopyranose mutase [EC:5.4.99.9]
K01903	succinyl-CoA synthetase beta subunit [EC:6.2.1.5]
K01906	6-carboxyhexanoate--CoA ligase [EC:6.2.1.14]
K01951	GMP synthase (glutamine-hydrolysing) [EC:6.3.5.2]
K01961	acetyl-CoA carboxylase, biotin carboxylase subunit [EC:6.4.1.2 6.3.4.14]
K02004	putative ABC transport system permease protein
K02007	cobalt/nickel transport system permease protein
K02018	molybdate transport system permease protein
K02020	molybdate transport system substrate-binding protein
K02025	multiple sugar transport system permease protein
K02026	multiple sugar transport system permease protein
K02027	multiple sugar transport system substrate-binding protein
K02030	polar amino acid transport system substrate-binding protein
K02032	peptide/nickel transport system ATP-binding protein
K02033	peptide/nickel transport system permease protein
K02035	peptide/nickel transport system substrate-binding protein
K02036	phosphate transport system ATP-binding protein [EC:3.6.3.27]
K02039	phosphate transport system protein
K02054	putative spermidine/putrescine transport system permease protein
K02055	putative spermidine/putrescine transport system substrate-binding protein
K02068	putative ABC transport system ATP-binding protein
K02074	zinc/manganese transport system ATP-binding protein
K02077	zinc/manganese transport system substrate-binding protein
K02081	DeoR family transcriptional regulator, aga operon transcriptional repressor
K02082	tagatose-6-phosphate ketose/aldose isomerase [EC:5.-.-.-]
K02083	allantoate deiminase [EC:3.5.3.9]
K02100	MFS transporter, SP family, arabinose:H+ symporter
K02103	GntR family transcriptional regulator, arabinose operon transcriptional repressor
K02113	F-type H+-transporting ATPase subunit delta [EC:3.6.3.14]
K02122	V-type H+-transporting ATPase subunit F [EC:3.6.3.14]
K02188	cobalt-precorrin-5B (C1)-methyltransferase [EC:2.1.1.195]
K02189	cobalt-precorrin 5A hydrolase [EC:3.7.1.12]
K02190	sirohydrochlorin cobaltochelatase [EC:4.99.1.3]
K02191	cobalt-precorrin-7 (C15)-methyltransferase [EC:2.1.1.196]
K02224	cobyrinic acid a,c-diamide synthase [EC:6.3.5.9 6.3.5.11]
K02231	adenosylcobinamide kinase / adenosylcobinamide-phosphate guanylyltransferase [EC:2.7.1.156 2.7.7.62]
K02232	adenosylcobyric acid synthase [EC:6.3.5.10]
K02237	competence protein ComEA
K02243	competence protein ComGA
K02246	competence protein ComGD
K02304	precorrin-2 dehydrogenase / sirohydrochlorin ferrochelatase [EC:1.3.1.76 4.99.1.4]
K02424	cystine transport system substrate-binding protein
K02438	glycogen operon protein [EC:3.2.1.-]
K02440	glycerol uptake facilitator protein
K02443	glycerol uptake operon antiterminator
K02444	DeoR family transcriptional regulator, glycerol-3-phosphate regulon repressor
K02501	glutamine amidotransferase [EC:2.4.2.-]
K02525	LacI family transcriptional regulator, kdg operon repressor
K02526	2-keto-3-deoxygluconate permease
K02529	LacI family transcriptional regulator
K02530	DeoR family transcriptional regulator, lactose phosphotransferase system repressor
K02531	transcriptional antiterminator
K02532	MFS transporter, OHS family, lactose permease
K02565	N-acetylglucosamine repressor
K02575	MFS transporter, NNP family, nitrate/nitrite transporter
K02598	nitrite transporter NirC
K02624	IclR family transcriptional regulator, pca regulon regulatory protein
K02647	carbohydrate diacid regulator
K02671	type IV pilus assembly protein PilV
K02688	transcriptional regulator, propionate catabolism operon regulatory protein
K02744	PTS system, N-acetylgalactosamine-specific IIA component [EC:2.7.1.69]
K02745	PTS system, N-acetylgalactosamine-specific IIB component [EC:2.7.1.69]
K02746	PTS system, N-acetylgalactosamine-specific IIC component
K02747	PTS system, N-acetylgalactosamine-specific IID component
K02749	PTS system, arbutin-like IIB component [EC:2.7.1.69]
K02755	PTS system, beta-glucosides-specific IIA component [EC:2.7.1.69]
K02756	PTS system, beta-glucosides-specific IIB component [EC:2.7.1.69]
K02757	PTS system, beta-glucosides-specific IIC component
K02759	PTS system, cellobiose-specific IIA component [EC:2.7.1.69]

KEGG orthology	Function
K02760	PTS system, cellobiose-specific IIB component [EC:2.7.1.69]
K02761	PTS system, cellobiose-specific IIC component
K02763	PTS system, D-glucosamine-specific IIA component [EC:2.7.1.69]
K02764	PTS system, D-glucosamine-specific IIB component [EC:2.7.1.69]
K02765	PTS system, D-glucosamine-specific IIC component
K02771	PTS system, fructose-specific IID component
K02773	PTS system, galactitol-specific IIA component [EC:2.7.1.69]
K02774	PTS system, galactitol-specific IIB component [EC:2.7.1.69]
K02777	PTS system, glucose-specific IIA component [EC:2.7.1.69]
K02786	PTS system, lactose-specific IIA component [EC:2.7.1.69]
K02787	PTS system, lactose-specific IIB component [EC:2.7.1.69]
K02793	PTS system, mannose-specific IIA component [EC:2.7.1.69]
K02794	PTS system, mannose-specific IIB component [EC:2.7.1.69]
K02795	PTS system, mannose-specific IIC component
K02796	PTS system, mannose-specific IID component
K02803	PTS system, N-acetylglucosamine-specific IIB component [EC:2.7.1.69]
K02808	PTS system, sucrose-specific IIA component [EC:2.7.1.69]
K02809	PTS system, sucrose-specific IIB component [EC:2.7.1.69]
K02810	PTS system, sucrose-specific IIC component
K02817	PTS system, trehalose-specific IIA component [EC:2.7.1.69]
K02819	PTS system, trehalose-specific IIC component
K02855	AraC family transcriptional regulator, L-rhamnose operon regulatory protein RhaS
K03147	thiamine biosynthesis protein ThiC
K03148	sulfur carrier protein ThiS adenylyltransferase [EC:2.7.7.73]
K03149	thiamine biosynthesis ThiG
K03182	3-octaprenyl-4-hydroxybenzoate carboxy-lyase UbiD [EC:4.1.1.-]
K03186	3-octaprenyl-4-hydroxybenzoate carboxy-lyase UbiX [EC:4.1.1.-]
K03216	tRNA (cytidine/uridine-2'-O-)-methyltransferase [EC:2.1.1.207]
K03293	amino acid transporter, AAT family
K03294	basic amino acid/polyamine antiporter, APA family
K03295	cation efflux system protein, CDF family
K03299	gluconate:H+ symporter, GntP family
K03322	manganese transport protein
K03332	fructan beta-fructosidase [EC:3.2.1.80]
K03342	para-aminobenzoate synthetase / 4-amino-4-deoxychorismate lyase [EC:2.6.1.85 4.1.3.38]
K03394	precorrin-2/cobalt-factor-2 C20-methyltransferase [EC:2.1.1.130 2.1.1.151]
K03400	long-chain-fatty-acyl-CoA reductase [EC:1.2.1.50]
K03426	NAD+ diphosphatase [EC:3.6.1.22]
K03439	tRNA (guanine-N7-)-methyltransferase [EC:2.1.1.33]
K03446	MFS transporter, DHA2 family, multidrug resistance protein B
K03458	nucleobase:cation symporter-2, NCS2 family
K03475	PTS system, ascorbate-specific IIC component
K03480	transcriptional antiterminator
K03481	RpiR family transcriptional regulator, glv operon transcriptional regulator
K03484	LacI family transcriptional regulator, sucrose operon repressor
K03486	GntR family transcriptional regulator, trehalose operon transcriptional repressor
K03488	beta-glucoside operon transcriptional antiterminator
K03491	lichenan operon transcriptional antiterminator
K03492	GntR family transcriptional regulator
K03518	carbon-monoxide dehydrogenase small subunit [EC:1.2.99.2]
K03519	carbon-monoxide dehydrogenase medium subunit [EC:1.2.99.2]
K03547	exonuclease SbcD
K03604	LacI family transcriptional regulator, purine nucleotide synthesis repressor
K03635	molybdopterin synthase catalytic subunit [EC:2.-.-.-]
K03637	molybdenum cofactor biosynthesis protein C
K03646	colicin import membrane protein
K03647	protein involved in ribonucleotide reduction
K03676	glutaredoxin 3
K03680	translation initiation factor eIF-2B subunit delta
K03684	ribonuclease D [EC:3.1.13.5]
K03688	ubiquinone biosynthesis protein
K03693	penicillin-binding protein
K03707	thiaminase (transcriptional activator TenA) [EC:3.5.99.2]
K03710	GntR family transcriptional regulator
K03721	transcriptional regulator of aroF, aroG, tyrA and aromatic amino acid transport
K03724	ATP-dependent helicase Lhr and Lhr-like helicase [EC:3.6.4.-]
K03727	ATP-dependent RNA helicase HelY [EC:3.6.4.-]
K03743	NA
K03750	molybdopterin molybdotransferase [EC:2.10.1.1]
K03753	molybdopterin-guanine dinucleotide biosynthesis protein B

KEGG orthology	Function
K03767	peptidyl-prolyl cis-trans isomerase A (cyclophilin A) [EC:5.2.1.8]
K03785	3-dehydroquinate dehydratase I [EC:4.2.1.10]
K03790	ribosomal-protein-alanine N-acetyltransferase [EC:2.3.1.128]
K03799	heat shock protein HtpX [EC:3.4.24.-]
K03823	phosphinothricin acetyltransferase [EC:2.3.1.183]
K03831	molybdopterin adenylyltransferase [EC:2.7.7.75]
K03833	selenocysteine-specific elongation factor
K03851	taurine-pyruvate aminotransferase [EC:2.6.1.77]
K03975	membrane-associated protein
K03980	virulence factor
K04023	ethanolamine transporter
K04034	anaerobic magnesium-protoporphyrin IX monomethyl ester cyclase [EC:4.-.-.-]
K04069	pyruvate formate lyase activating enzyme [EC:1.97.1.4]
K04085	tRNA 2-thiouridine synthesizing protein A [EC:2.8.1.-]
K04086	ATP-dependent Clp protease ATP-binding subunit ClpL
K04092	chorismate mutase [EC:5.4.99.5]
K04477	putative hydrolase
K04565	Cu/Zn superoxide dismutase [EC:1.15.1.1]
K04653	hydrogenase expression/formation protein HypC
K04654	hydrogenase expression/formation protein HypD
K04655	hydrogenase expression/formation protein HypE
K04720	threonine-phosphate decarboxylase [EC:4.1.1.81]
K04748	nitric oxide reductase NorQ protein
K04757	anti-sigma B factor [EC:2.7.11.1]
K04761	LysR family transcriptional regulator, hydrogen peroxide-inducible genes activator
K04767	acetoin utilization protein AcuB
K04783	yersiniabactin salicyl-AMP ligase [EC:6.3.2.-]
K04940	opine dehydrogenase [EC:1.5.1.28]
K05020	glycine betaine transporter
K05275	pyridoxine 4-dehydrogenase [EC:1.1.1.65]
K05303	O-methyltransferase [EC:2.1.1.-]
K05339	holin-like protein LrgB
K05341	amylosucrase [EC:2.4.1.4]
K05350	beta-glucosidase [EC:3.2.1.21]
K05351	D-xylulose reductase [EC:1.1.1.9]
K05362	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate-L-lysine ligase [EC:6.3.2.7]
K05499	LacI family transcriptional regulator, repressor for deo operon, udp, cdd, tsx, nupC, and nupG
K05541	tRNA-dihydrouridine synthase C [EC:1.-.-.-]
K05783	1,6-dihydroxycyclohexa-2,4-diene-1-carboxylate dehydrogenase [EC:1.3.1.25]
K05786	chloramphenicol-sensitive protein RarD
K05823	N-acetyldiaminopimelate deacetylase [EC:3.5.1.47]
K05836	GntR family transcriptional regulator, histidine utilization repressor
K05838	putative thioredoxin
K05845	osmoprotectant transport system substrate-binding protein
K05903	NADH dehydrogenase (quinone) [EC:1.6.99.5]
K05936	precorrin-4 C11-methyltransferase [EC:2.1.1.133]
K05937	hypothetical protein
K06016	N-carbamoyl-L-amino-acid hydrolase [EC:3.5.1.87]
K06019	pyrophosphatase PpaX [EC:3.6.1.1]
K06042	precorrin-8X methylmutase [EC:5.4.1.2]
K06046	long-chain-fatty-acid---luciferin-component ligase [EC:6.2.1.19]
K06155	Gnt-I system high-affinity gluconate transporter
K06187	recombination protein RecR
K06189	magnesium and cobalt transporter
K06191	glutaredoxin-like protein NrdH
K06199	CrcB protein
K06201	copper homeostasis protein
K06221	2,5-diketo-D-gluconate reductase A [EC:1.1.1.274]
K06317	inhibitor of the pro-sigma K processing machinery
K06330	spore coat protein H
K06331	spore coat protein I
K06403	stage V sporulation protein AA
K06606	inosose isomerase [EC:5.3.99.-]
K06610	MFS transporter, SP family, inositol transporter
K06864	uncharacterized protein
K06898	NA
K06902	MFS transporter, UMF1 family
K06910	NA
K06924	NA
K06940	NA

KEGG orthology	Function
K06951	NA
K06962	NA
K06971	NA
K06972	NA
K06999	phospholipase/carboxylesterase
K07006	NA
K07008	glutamine amidotransferase
K07013	NA
K07023	putative hydrolases of HD superfamily
K07024	NA
K07038	inner membrane protein
K07046	NA
K07047	NA
K07067	DNA integrity scanning protein
K07104	NA
K07105	NA
K07138	NA
K07173	S-ribosylhomocysteine lyase [EC:4.4.1.21]
K07177	PDZ domain-containing protein
K07230	NA
K07243	high-affinity iron transporter
K07393	putative glutathione S-transferase
K07396	putative protein-disulfide isomerase
K07402	xanthine dehydrogenase accessory factor
K07442	tRNA (adenine57-N1/adenine58-N1)-methyltransferase [EC:2.1.1.219 2.1.1.220]
K07443	methylated-DNA-protein-cysteine methyltransferase related protein
K07457	endonuclease III related protein
K07461	putative endonuclease
K07467	phage replication initiation protein
K07503	hypothetical protein
K07646	two-component system, OmpR family, sensor histidine kinase KdpD [EC:2.7.13.3]
K07649	two-component system, OmpR family, sensor histidine kinase TctE [EC:2.7.13.3]
K07654	two-component system, OmpR family, sensor histidine kinase MtrB [EC:2.7.13.3]
K07664	two-component system, OmpR family, response regulator BaeR
K07680	two-component system, NarL family, sensor histidine kinase ComP [EC:2.7.13.3]
K07685	two-component system, NarL family, nitrate/nitrite response regulator NarP
K07688	two-component system, NarL family, response regulator, fimbrial Z protein, FimZ
K07690	two-component system, NarL family, response regulator EvgA
K07692	two-component system, NarL family, response regulator DegU
K07693	two-component system, NarL family, response regulator DesR
K07710	two-component system, NtrC family, sensor histidine kinase AtoS [EC:2.7.13.3]
K07718	two-component system, sensor histidine kinase YesM [EC:2.7.13.3]
K07719	two-component system, response regulator YcbB
K07720	two-component system, response regulator YesN
K07722	CopG family transcriptional regulator, nickel-responsive regulator
K07739	elongator complex protein 3 [EC:2.3.1.48]
K07749	formyl-CoA transferase [EC:2.8.3.16]
K07768	two-component system, OmpR family, sensor histidine kinase SenX3 [EC:2.7.13.3]
K07770	two-component system, OmpR family, response regulator CssR
K07794	putative tricarboxylic transport membrane protein
K08092	3-dehydro-L-gulonate 2-dehydrogenase [EC:1.1.1.130]
K08094	6-phospho-3-hexuloisomerase [EC:5.3.1.27]
K08139	MFS transporter, SP family, sugar:H+ symporter
K08152	MFS transporter, DHA1 family, multidrug resistance protein B
K08156	MFS transporter, DHA1 family, arabinose polymer transporter
K08164	MFS transporter, DHA1 family, chloramphenicol resistance protein
K08168	MFS transporter, DHA2 family, metal-tetracycline-proton antiporter
K08174	MFS transporter, FHS family, glucose/mannose:H+ symporter
K08177	MFS transporter, OFA family, oxalate/formate antiporter
K08282	non-specific serine/threonine protein kinase [EC:2.7.11.1]
K08296	phosphohistidine phosphatase [EC:3.1.3.-]
K08300	ribonuclease E [EC:3.1.26.12]
K08302	tagatose 1,6-diphosphate aldolase [EC:4.1.2.40]
K08313	fructose-6-phosphate aldolase 1 [EC:4.1.2.-]
K08369	MFS transporter, putative metabolite:H+ symporter
K08372	putative serine protease PepD [EC:3.4.21.-]
K08483	phosphotransferase system, enzyme I, PtsI [EC:2.7.3.9]
K08643	zinc metalloprotease ZmpB [EC:3.4.24.-]
K08700	carbon dioxide concentrating mechanism protein CcmO
K08969	aminotransferase [EC:2.6.1.-]

KEGG orthology	Function
K08972	putative membrane protein
K08987	putative membrane protein
K09004	hypothetical protein
K09009	hypothetical protein
K09017	TetR/AcrR family transcriptional regulator
K09117	hypothetical protein
K09118	hypothetical protein
K09121	hypothetical protein
K09133	hypothetical protein
K09155	hypothetical protein
K09681	LysR family transcriptional regulator, transcription activator of glutamate synthase operon
K09684	purine catabolism regulatory protein
K09694	lipooligosaccharide transport system permease protein
K09696	sodium transport system permease protein
K09698	nondiscriminating glutamyl-tRNA synthetase [EC:6.1.1.24]
K09729	hypothetical protein
K09759	nondiscriminating aspartyl-tRNA synthetase [EC:6.1.1.23]
K09767	hypothetical protein
K09773	hypothetical protein
K09925	hypothetical protein
K09931	hypothetical protein
K09936	hypothetical protein
K09962	hypothetical protein
K09963	hypothetical protein
K10005	glutamate transport system substrate-binding protein
K10006	glutamate transport system permease protein
K10007	glutamate transport system permease protein
K10008	glutamate transport system ATP-binding protein [EC:3.6.3.-]
K10041	putative glutamine transport system ATP-binding protein [EC:3.6.3.-]
K10117	multiple sugar transport system substrate-binding protein
K10118	multiple sugar transport system permease protein
K10119	multiple sugar transport system permease protein
K10121	putative sugar transport system permease protein
K10122	putative sugar transport system permease protein
K10189	lactose/L-arabinose transport system permease protein
K10190	lactose/L-arabinose transport system permease protein
K10200	N-acetylglucosamine transport system substrate-binding protein
K10243	cellobiose transport system ATP-binding protein
K10439	ribose transport system substrate-binding protein
K10441	ribose transport system ATP-binding protein [EC:3.6.3.17]
K10546	putative multiple sugar transport system substrate-binding protein
K10561	rhamnose transport system permease protein
K10670	glycine reductase [EC:1.21.4.2]
K10671	sarcosine reductase [EC:1.21.4.3]
K10672	betaine reductase [EC:1.21.4.4]
K10682	two-component system, OmpR family, response regulator SaeR
K10708	fructoselysine 6-phosphate deglycase [EC:3.5.-.-]
K10709	protein FrlC
K10710	fructoselysine 6-kinase [EC:2.7.1.-]
K10711	GntR family transcriptional regulator, frlABCD operon transcriptional regulator
K10793	D-proline reductase (dithiol) PrdA [EC:1.21.4.1]
K10795	D-proline reductase (dithiol) PrdD [EC:1.21.4.1]
K10796	D-proline reductase (dithiol) PrdE [EC:1.21.4.1]
K10805	acyl-CoA thioesterase II [EC:3.1.2.-]
K10823	oligopeptide transport system ATP-binding protein
K10844	DNA excision repair protein ERCC-2 [EC:3.6.4.12]
K10917	PadR family transcriptional regulator, regulatory protein AphA
K11003	hemolysin D
K11041	exfoliative toxin A/B
K11063	toxin A/B
K11068	hemolysin III
K11261	formylmethanofuran dehydrogenase subunit E [EC:1.2.99.5]
K11263	acetyl-/propionyl-CoA carboxylase, biotin carboxylase, biotin carboxyl carrier protein [EC:6.3.4.14]
K11358	aspartate aminotransferase [EC:2.6.1.1]
K11384	two-component system, NtrC family, response regulator AlgB
K11521	two-component system, OmpR family, manganese sensing response regulator
K11533	fatty acid synthase, bacteria type [EC:2.3.1.-]
K11616	malate:Na+ symporter
K11617	two-component system, NarL family, sensor histidine kinase LiaS [EC:2.7.13.3]
K11618	two-component system, NarL family, response regulator LiaR

KEGG orthology	Function
K11622	lia operon protein LiaF
K11631	bacitracin transport system ATP-binding protein
K11636	putative ABC transport system permease protein
K11686	chromosome-anchoring protein RacA
K11688	C4-dicarboxylate-binding protein DctP
K11689	C4-dicarboxylate transporter, DctQ subunit
K11690	C4-dicarboxylate transporter, DctM subunit
K11692	two-component system, CitB family, response regulator DctR
K11923	MerR family transcriptional regulator, copper efflux regulator
K12112	evolved beta-galactosidase subunit beta
K12143	hydrogenase-4 component H
K12283	MSHA biogenesis protein MshM
K12296	competence protein ComX
K12297	23S rRNA (guanine2445-N2)-methyltransferase [EC:2.1.1.173]
K12510	tight adherence protein B
K12554	alanine adding enzyme [EC:2.3.2.-]
K12555	penicillin-binding protein 2A [EC:2.4.1.129 2.3.2.-]
K12556	penicillin-binding protein 2X [EC:2.3.2.-]
K12992	rhamnosyltransferase [EC:2.4.1.-]
K13051	beta-aspartyl-peptidase (threonine type) [EC:3.4.19.5]
K13059	N-acetylhexosamine 1-kinase [EC:2.7.1.162]
K13252	putrescine carbamoyltransferase [EC:2.1.3.6]
K13275	major intracellular serine protease [EC:3.4.21.-]
K13288	oligoribonuclease [EC:3.1.-.-]
K13419	serine/threonine-protein kinase PknK [EC:2.7.11.1]
K13527	proteasome-associated ATPase
K13530	AraC family transcriptional regulator, regulatory protein of adaptative response / methylphosphotriester-DNA alkyltransferase methyltransferase [EC:2.1.1.-]
K13541	cobalt-precorrin 5A hydrolase / precorrin-3B C17-methyltransferase [EC:3.7.1.12 2.1.1.131]
K13570	prokaryotic ubiquitin-like protein Pup
K13571	proteasome accessory factor A [EC:6.3.2.-]
K13631	AraC family transcriptional regulator, transcriptional activator of the superoxide response regulon
K13639	MerR family transcriptional regulator, redox-sensitive transcriptional activator SoxR
K13640	MerR family transcriptional regulator, heat shock protein HspR
K13641	IclR family transcriptional regulator, acetate operon repressor
K13771	Rrf2 family transcriptional regulator, nitric oxide-sensitive transcriptional repressor
K13786	cob(II)yrinic acid a,c-diamide reductase [EC:1.16.8.1]
K13787	geranylgeranyl diphosphate synthase, type I [EC:2.5.1.1 2.5.1.10 2.5.1.29]
K13788	phosphate acetyltransferase [EC:2.3.1.8]
K13818	molybdopterin-guanine dinucleotide biosynthesis protein
K13829	shikimate kinase / 3-dehydroquinate synthase [EC:2.7.1.71 4.2.3.4]
K13889	glutathione transport system substrate-binding protein
K13891	glutathione transport system permease protein
K13920	propanediol dehydratase small subunit [EC:4.2.1.28]
K13921	1-propanol dehydrogenase
K13923	phosphotransacylase
K13927	holo-ACP synthase / triphosphoribosyl-dephospho-CoA synthase [EC:2.7.7.61 2.7.8.25]
K13940	dihydroneopterin aldolase / 2-amino-4-hydroxy-6-hydroxymethyldihydropteridine diphosphokinase [EC:4.1.2.25 2.7.6.3]
K13955	zinc-binding alcohol dehydrogenase/oxidoreductase
K14082	[methyl-Co(III) methylamine-specific corrinoid protein]:coenzyme M methyltransferase [EC:2.1.1.247]
K14083	trimethylamine---corrinoid protein Co-methyltransferase [EC:2.1.1.250]
K14088	ech hydrogenase subunit C
K14089	ech hydrogenase subunit D
K14090	ech hydrogenase subunit E
K14153	hydroxymethylpyrimidine kinase / phosphomethylpyrimidine kinase / thiamine-phosphate diphosphorylase [EC:2.7.1.49 2.7.4.7 2.5.1.3]
K14205	phosphatidylglycerol lysyltransferase [EC:2.3.2.3]
K14475	inhibitor of cysteine peptidase
K14956	6 kDa early secretory antigenic target
K15066	vanillate/3-O-methylgallate O-demethylase
K15330	phosphoglycerate kinase / triosephosphate isomerase [EC:2.7.2.3 5.3.1.1]
K15545	transcriptional regulator of PTS gene
K15598	putative hydroxymethylpyrimidine transport system substrate-binding protein
K15599	putative hydroxymethylpyrimidine transport system permease protein
K15634	probable phosphoglycerate mutase [EC:5.4.2.1]
K15653	nonribosomal peptide synthetase MxcG
K15835	RpiR family transcriptional regulator, murPQ operon repressor
K15866	2-(1,2-epoxy-1,2-dihydrophenyl)acetyl-CoA isomerase [EC:5.3.3.18]
K15922	alpha-glucosidase [EC:3.2.1.20]

KEGG orthology	Function
K15973	MarR family transcriptional regulator, 2-MHQ and catechol-resistance regulon repressor
K15984	16S rRNA (guanine1516-N2)-methyltransferase [EC:2.1.1.242]
K16012	ATP-binding cassette, subfamily C, bacterial CydC
K16013	ATP-binding cassette, subfamily C, bacterial CydD
K16048	3-hydroxy-9,10-secoandrosta-1,3,5(10)-triene-9,17-dione monooxygenase subunit HsaB (Flavin:NADH reductase)
K16137	TetR/AcrR family transcriptional regulator, transcriptional repressor for nem operon
K16147	starch synthase (maltosyl-transferring) [EC:2.4.99.16]
K16148	starch synthase [EC:2.4.1.21]
K16169	xanthine permease
K16179	dimethylamine corrinoid protein
K16202	dipeptide transport system ATP-binding protein

NA indicates not assigned

Appendix 7. KOs having the lowest abundance in the JP cohort among the 12 countries

KEGG orthology	Function
K00021	hydroxymethylglutaryl-CoA reductase (NADPH) [EC:1.1.1.34]
K00060	threonine 3-dehydrogenase [EC:1.1.1.103]
K00091	dihydroflavonol-4-reductase [EC:1.1.1.219]
K00113	glycerol-3-phosphate dehydrogenase subunit C [EC:1.1.5.3]
K00134	glyceraldehyde 3-phosphate dehydrogenase [EC:1.2.1.12]
K00179	indolepyruvate ferredoxin oxidoreductase, alpha subunit [EC:1.2.7.8]
K00186	2-oxoisovalerate ferredoxin oxidoreductase, alpha subunit [EC:1.2.7.7]
K00187	2-oxoisovalerate ferredoxin oxidoreductase, beta subunit [EC:1.2.7.7]
K00201	formylmethanofuran dehydrogenase subunit B [EC:1.2.99.5]
K00203	formylmethanofuran dehydrogenase subunit D [EC:1.2.99.5]
K00273	D-amino-acid oxidase [EC:1.4.3.3]
K00311	electron-transferring-flavoprotein dehydrogenase [EC:1.5.5.1]
K00319	methylenetetrahydromethanopterin dehydrogenase [EC:1.5.99.9]
K00320	coenzyme F420-dependent N5,N10-methenyltetrahydromethanopterin reductase [EC:1.5.99.11]
K00350	Na+-transporting NADH:ubiquinone oxidoreductase subunit E [EC:1.6.5.-]
K00390	phosphoadenosine phosphosulfate reductase [EC:1.8.4.8]
K00399	methyl-coenzyme M reductase alpha subunit [EC:2.8.4.1]
K00400	methyl coenzyme M reductase system, component A2
K00401	methyl-coenzyme M reductase beta subunit [EC:2.8.4.1]
K00440	coenzyme F420 hydrogenase alpha subunit [EC:1.12.98.1]
K00442	coenzyme F420 hydrogenase delta subunit
K00443	coenzyme F420 hydrogenase gamma subunit [EC:1.12.98.1]
K00555	tRNA (guanine26-N2/guanine27-N2)-dimethyltransferase [EC:2.1.1.215 2.1.1.216]
K00558	DNA (cytosine-5-)-methyltransferase [EC:2.1.1.37]
K00571	site-specific DNA-methyltransferase (adenine-specific) [EC:2.1.1.72]
K00575	chemotaxis protein methyltransferase CheR [EC:2.1.1.80]
K00577	tetrahydromethanopterin S-methyltransferase subunit A [EC:2.1.1.86]
K00578	tetrahydromethanopterin S-methyltransferase subunit B [EC:2.1.1.86]
K00579	tetrahydromethanopterin S-methyltransferase subunit C [EC:2.1.1.86]
K00580	tetrahydromethanopterin S-methyltransferase subunit D [EC:2.1.1.86]
K00581	tetrahydromethanopterin S-methyltransferase subunit E [EC:2.1.1.86]
K00583	tetrahydromethanopterin S-methyltransferase subunit G [EC:2.1.1.86]
K00586	diphthine synthase [EC:2.1.1.98]
K00590	site-specific DNA-methyltransferase (cytosine-N4-specific) [EC:2.1.1.113]
K00640	serine O-acetyltransferase [EC:2.3.1.30]
K00641	homoserine O-acetyltransferase [EC:2.3.1.31]
K00672	formylmethanofuran--tetrahydromethanopterin N-formyltransferase [EC:2.3.1.101]
K00683	glutaminyl-peptide cyclotransferase [EC:2.3.2.5]
K00703	starch synthase [EC:2.4.1.21]
K00721	dolichol-phosphate mannosyltransferase [EC:2.4.1.83]
K00737	beta-1,4-mannosyl-glycoprotein beta-1,4-N-acetylglucosaminyltransferase [EC:2.4.1.144]
K00769	xanthine phosphoribosyltransferase [EC:2.4.2.22]
K00801	farnesyl-diphosphate farnesyltransferase [EC:2.5.1.21]
K00809	deoxyhypusine synthase [EC:2.5.1.46]
K00876	uridine kinase [EC:2.7.1.48]
K00908	Ca2+/calmodulin-dependent protein kinase [EC:2.7.11.17]
K00925	acetate kinase [EC:2.7.2.1]
K00929	butyrate kinase [EC:2.7.2.7]
K00962	polyribonucleotide nucleotidyltransferase [EC:2.7.7.8]
K00972	UDP-N-acetylglucosamine pyrophosphorylase [EC:2.7.7.23]
K00981	phosphatidate cytidylyltransferase [EC:2.7.7.41]
K01001	UDP-N-acetylglucosamine--dolichyl-phosphate N-acetylglucosaminephosphotransferase [EC:2.7.8.15]
K01006	pyruvate,orthophosphate dikinase [EC:2.7.9.1]
K01062	1-alkyl-2-acetylglycerophosphocholine esterase [EC:3.1.1.47]
K01067	acetyl-CoA hydrolase [EC:3.1.2.1]
K01068	palmitoyl-CoA hydrolase [EC:3.1.2.2]
K01112	NA
K01126	glycerophosphoryl diester phosphodiesterase [EC:3.1.4.46]
K01139	guanosine-3',5'-bis(diphosphate) 3'-pyrophosphohydrolase [EC:3.1.7.2]
K01147	exoribonuclease II [EC:3.1.13.1]
K01150	deoxyribonuclease I [EC:3.1.21.1]
K01153	type I restriction enzyme, R subunit [EC:3.1.21.3]
K01156	type III restriction enzyme [EC:3.1.21.5]
K01157	NA
K01167	ribonuclease T1 [EC:3.1.27.3]

KEGG orthology	Function
K01170	tRNA-intron endonuclease, archaea type [EC:3.1.27.9]
K01174	micrococcal nuclease [EC:3.1.31.1]
K01179	endoglucanase [EC:3.2.1.4]
K01225	cellulose 1,4-beta-cellobiosidase [EC:3.2.1.91]
K01387	microbial collagenase [EC:3.4.24.3]
K01417	NA
K01553	myosin ATPase [EC:3.6.4.1]
K01572	oxaloacetate decarboxylase, beta subunit [EC:4.1.1.3]
K01610	phosphoenolpyruvate carboxykinase (ATP) [EC:4.1.1.49]
K01622	fructose 1,6-bisphosphate aldolase/phosphatase [EC:4.1.2.13 3.1.3.11]
K01667	tryptophanase [EC:4.1.99.1]
K01738	cysteine synthase A [EC:2.5.1.47]
K01791	UDP-N-acetylglucosamine 2-epimerase [EC:5.1.3.14]
K01841	phosphoenolpyruvate phosphomutase [EC:5.4.2.9]
K01844	beta-lysine 5,6-aminomutase [EC:5.4.3.3]
K01866	tyrosyl-tRNA synthetase [EC:6.1.1.1]
K01869	leucyl-tRNA synthetase [EC:6.1.1.4]
K01880	glycyl-tRNA synthetase [EC:6.1.1.14]
K01886	glutaminyl-tRNA synthetase [EC:6.1.1.18]
K01894	glutamyl-Q tRNA(Asp) synthetase [EC:6.1.1.-]
K01895	acetyl-CoA synthetase [EC:6.2.1.1]
K01916	NAD+ synthase [EC:6.3.1.5]
K02042	phosphonate transport system permease protein
K02044	phosphonate transport system substrate-binding protein
K02102	arabinose operon protein AraM
K02201	pantetheine-phosphate adenylyltransferase [EC:2.7.7.3]
K02288	phycocyanobilin lyase alpha subunit [EC:4.-.-.-]
K02314	replicative DNA helicase [EC:3.6.4.12]
K02319	DNA polymerase I [EC:2.7.7.7]
K02322	DNA polymerase II large subunit [EC:2.7.7.7]
K02323	DNA polymerase II small subunit [EC:2.7.7.7]
K02335	DNA polymerase I [EC:2.7.7.7]
K02356	elongation factor P
K02358	elongation factor Tu
K02377	GDP-L-fucose synthase [EC:1.1.1.271]
K02386	flagella basal body P-ring formation protein FlgA
K02387	flagellar basal-body rod protein FlgB
K02388	flagellar basal-body rod protein FlgC
K02389	flagellar basal-body rod modification protein FlgD
K02390	flagellar hook protein FlgE
K02391	flagellar basal-body rod protein FlgF
K02400	flagellar biosynthesis protein FlhA
K02401	flagellar biosynthetic protein FlhB
K02404	flagellar biosynthesis protein FlhF
K02409	flagellar M-ring protein FliF
K02410	flagellar motor switch protein FliG
K02411	flagellar assembly protein FliH
K02412	flagellum-specific ATP synthase [EC:3.6.3.14]
K02414	flagellar hook-length control protein FliK
K02418	flagellar protein FliO/FliZ
K02421	flagellar biosynthetic protein FliR
K02427	23S rRNA (uridine2552-2'-O)-methyltransferase [EC:2.1.1.166]
K02441	GlpG protein
K02445	MFS transporter, OPA family, glycerol-3-phosphate transporter
K02453	general secretion pathway protein D
K02455	general secretion pathway protein F
K02482	two-component system, NtrC family, sensor kinase [EC:2.7.13.3]
K02496	uroporphyrin-III C-methyltransferase [EC:2.1.1.107]
K02549	O-succinylbenzoate synthase [EC:4.2.1.113]
K02556	chemotaxis protein MotA
K02557	chemotaxis protein MotB
K02650	type IV pilus assembly protein PilA
K02655	type IV pilus assembly protein PilE
K02664	type IV pilus assembly protein PilO
K02674	type IV pilus assembly protein PilY1
K02683	DNA primase [EC:2.7.7.-]
K02685	DNA primase large subunit [EC:2.7.7.-]
K02844	UDP-glucose:(heptosyl)LPS alpha-1,3-glucosyltransferase [EC:2.4.1.-]
K02852	UDP-N-acetyl-D-mannosaminuronic acid transferase [EC:2.4.1.-]
K02866	large subunit ribosomal protein L10e

KEGG orthology	Function
K02869	large subunit ribosomal protein L12
K02875	large subunit ribosomal protein L14e
K02877	large subunit ribosomal protein L15e
K02883	large subunit ribosomal protein L18e
K02885	large subunit ribosomal protein L19e
K02889	large subunit ribosomal protein L21e
K02896	large subunit ribosomal protein L24e
K02910	large subunit ribosomal protein L31e
K02912	large subunit ribosomal protein L32e
K02921	large subunit ribosomal protein L37Ae
K02924	large subunit ribosomal protein L39e
K02929	large subunit ribosomal protein L44e
K02930	large subunit ribosomal protein L4e
K02944	large subunit ribosomal protein LX
K02966	small subunit ribosomal protein S19e
K02974	small subunit ribosomal protein S24e
K02978	small subunit ribosomal protein S27e
K02979	small subunit ribosomal protein S28e
K02984	small subunit ribosomal protein S3Ae
K02986	small subunit ribosomal protein S4
K02987	small subunit ribosomal protein S4e
K02991	small subunit ribosomal protein S6e
K02995	small subunit ribosomal protein S8e
K03041	DNA-directed RNA polymerase subunit A' [EC:2.7.7.6]
K03042	DNA-directed RNA polymerase subunit A" [EC:2.7.7.6]
K03044	DNA-directed RNA polymerase subunit B' [EC:2.7.7.6]
K03045	DNA-directed RNA polymerase subunit B" [EC:2.7.7.6]
K03049	DNA-directed RNA polymerase subunit E' [EC:2.7.7.6]
K03050	DNA-directed RNA polymerase subunit E" [EC:2.7.7.6]
K03051	DNA-directed RNA polymerase subunit F [EC:2.7.7.6]
K03053	DNA-directed RNA polymerase subunit H [EC:2.7.7.6]
K03056	DNA-directed RNA polymerase subunit L [EC:2.7.7.6]
K03057	transcription elongation factor
K03087	RNA polymerase nonessential primary-like sigma factor
K03089	RNA polymerase sigma-32 factor
K03105	signal recognition particle subunit SRP19
K03120	transcription initiation factor TFIID TATA-box-binding protein
K03124	transcription initiation factor TFIIB
K03136	transcription initiation factor TFIIE subunit alpha
K03166	DNA topoisomerase VI subunit A [EC:5.99.1.3]
K03167	DNA topoisomerase VI subunit B [EC:5.99.1.3]
K03183	ubiquinone/menaquinone biosynthesis methyltransferase [EC:2.1.1.163 2.1.1.201]
K03203	type IV secretion system protein VirB8
K03231	elongation factor 1-alpha
K03232	elongation factor 1-beta
K03236	translation initiation factor 1A
K03237	translation initiation factor 2 subunit 1
K03238	translation initiation factor 2 subunit 2
K03242	translation initiation factor 2 subunit 3
K03243	translation initiation factor 5B
K03263	translation initiation factor 5A
K03264	translation initiation factor 6
K03271	D-sedoheptulose 7-phosphate isomerase [EC:5.3.1.28]
K03273	D-glycero-D-manno-heptose 1,7-bisphosphate phosphatase [EC:3.1.3.82 3.1.3.83]
K03275	UDP-glucose:(glucosyl)LPS alpha-1,3-glucosyltransferase [EC:2.4.1.-]
K03324	phosphate:Na+ symporter
K03329	hypothetical protein
K03403	magnesium chelatase subunit H [EC:6.6.1.1]
K03405	magnesium chelatase subunit I [EC:6.6.1.1]
K03406	methyl-accepting chemotaxis protein
K03408	purine-binding chemotaxis protein CheW
K03409	chemotaxis protein CheX
K03412	two-component system, chemotaxis family, response regulator CheB [EC:3.1.1.61]
K03420	proteasome regulatory subunit
K03421	methyl-coenzyme M reductase subunit C
K03422	methyl-coenzyme M reductase subunit D
K03427	type I restriction enzyme M protein [EC:2.1.1.72]
K03432	proteasome alpha subunit [EC:3.4.25.1]
K03465	thymidylate synthase (FAD) [EC:2.1.1.148]
K03495	tRNA uridine 5-carboxymethylaminomethyl modification enzyme

KEGG orthology	Function
K03503	DNA polymerase V [EC:3.4.21.-]
K03521	electron transfer flavoprotein beta subunit
K03537	ribonuclease P/MRP protein subunit POP5 [EC:3.1.26.5]
K03538	ribonuclease P protein subunit POP4 [EC:3.1.26.5]
K03539	ribonuclease P/MRP protein subunit RPP1 [EC:3.1.26.5]
K03540	ribonuclease P protein subunit RPR2 [EC:3.1.26.5]
K03546	exonuclease SbcC
K03548	putative permease
K03553	recombination protein RecA
K03555	DNA mismatch repair protein MutS
K03560	biopolymer transport protein TolR
K03562	biopolymer transport protein TolQ
K03567	glycine cleavage system transcriptional repressor
K03570	rod shape-determining protein MreC
K03572	DNA mismatch repair protein MutL
K03583	exodeoxyribonuclease V gamma subunit [EC:3.1.11.5]
K03584	DNA repair protein RecO (recombination protein O)
K03595	GTP-binding protein Era
K03596	GTP-binding protein LepA
K03612	electron transport complex protein RnfG
K03613	electron transport complex protein RnfE
K03614	electron transport complex protein RnfD
K03622	archaea-specific DNA-binding protein
K03625	N utilization substance protein B
K03626	nascent polypeptide-associated complex subunit alpha
K03643	LPS-assembly lipoprotein
K03650	tRNA modification GTPase [EC:3.6.-.-]
K03673	thiol:disulfide interchange protein DsbA
K03679	exosome complex component RRP4
K03726	helicase [EC:3.6.4.-]
K03737	putative pyruvate-flavodoxin oxidoreductase [EC:1.2.7.-]
K03748	SanA protein
K03756	putrescine:ornithine antiporter
K03772	FKBP-type peptidyl-prolyl cis-trans isomerase FkpA [EC:5.2.1.8]
K03796	Bax protein
K03810	virulence factor
K03820	apolipoprotein N-acyltransferase [EC:2.3.1.-]
K03893	arsenical pump membrane protein
K03924	MoxR-like ATPase [EC:3.6.3.-]
K03932	polyhydroxybutyrate depolymerase
K03969	phage shock protein A
K03977	GTP-binding protein
K04067	primosomal replication protein N''
K04071	6-pyruvoyltetrahydropterin 2'-reductase [EC:1.1.1.220]
K04076	Lon-like ATP-dependent protease [EC:3.4.21.-]
K04079	molecular chaperone HtpG
K04084	thiol:disulfide interchange protein DsbD [EC:1.8.1.8]
K04095	cell filamentation protein
K04109	4-hydroxybenzoyl-CoA reductase subunit beta [EC:1.3.7.9]
K04112	benzoyl-CoA reductase subunit [EC:1.3.7.8]
K04484	DNA repair protein RadB
K04754	lipoprotein
K04760	transcription elongation factor GreB
K04795	fibrillarin-like pre-rRNA processing protein
K04797	prefoldin alpha subunit
K04798	prefoldin beta subunit
K04801	replication factor C small subunit
K04802	proliferating cell nuclear antigen
K05365	penicillin-binding protein 1B [EC:2.4.1.129 3.4.-.-]
K05367	penicillin-binding protein 1C [EC:2.4.1.-]
K05384	bilin biosynthesis protein
K05515	penicillin-binding protein 2
K05566	multicomponent Na+:H+ antiporter subunit B
K05569	multicomponent Na+:H+ antiporter subunit E
K05716	cyclic 2,3-diphosphoglycerate synthetase [EC:4.6.1.-]
K05802	potassium efflux system protein KefA
K05837	rod shape determining protein RodA
K05844	ribosomal protein S6 modification protein
K05851	adenylate cyclase, class 1 [EC:4.6.1.1]
K05929	phosphoethanolamine N-methyltransferase [EC:2.1.1.103]

KEGG orthology	Function
K05939	acyl-[acyl-carrier-protein]-phospholipid O-acyltransferase / long-chain-fatty-acid--[acyl-carrier-protein] ligase [EC:2.3.1.40 6.2.1.20]
K06001	tryptophan synthase beta chain [EC:4.2.1.20]
K06027	vesicle-fusing ATPase [EC:3.6.4.6]
K06034	sulfopyruvate decarboxylase subunit alpha [EC:4.1.1.79]
K06190	intracellular septation protein
K06192	paraquat-inducible protein B
K06203	CysZ protein
K06223	DNA adenine methylase [EC:2.1.1.72]
K06296	spore germination protein KB
K06313	spore germination protein
K06343	spore coat protein Y
K06370	morphogenetic protein associated with SpoVID
K06384	stage II sporulation protein M
K06401	stage IV sporulation protein FA
K06402	stage IV sporulation protein FB [EC:3.4.24.-]
K06601	flagellar protein FlbT
K06862	energy-converting hydrogenase B subunit Q
K06863	5-formaminoimidazole-4-carboxamide-1-(beta)-D-ribofuranosyl 5'-monophosphate synthetase [EC:6.3.4.-]
K06872	uncharacterized protein
K06874	zinc finger protein
K06875	programmed cell death protein 5
K06877	DEAD/DEAH box helicase domain-containing protein
K06881	phosphoesterase RecJ domain-containing protein
K06883	NA
K06909	phage terminase large subunit
K06914	NA
K06915	NA
K06927	NA
K06932	NA
K06943	nucleolar GTP-binding protein
K06961	ribosomal RNA assembly protein
K06965	protein pelota
K06982	pantoate kinase [EC:2.7.1.169]
K06984	NA
K06985	aspartyl protease family protein
K07022	NA
K07041	NA
K07055	tRNA wybutosine-synthesizing protein 2 [EC:2.1.1.-]
K07058	membrane protein
K07060	UPF0271 protein
K07072	NA
K07082	UPF0755 protein
K07102	NA
K07103	NA
K07108	NA
K07121	NA
K07123	NA
K07135	NA
K07144	NA
K07158	NA
K07159	NA
K07164	NA
K07174	Mn2+-dependent serine/threonine protein kinase [EC:2.7.1.-]
K07178	RIO kinase 1 [EC:2.7.11.1]
K07244	mgtE-like transporter
K07273	lysozyme
K07316	adenine-specific DNA-methyltransferase [EC:2.1.1.72]
K07318	adenine-specific DNA-methyltransferase [EC:2.1.1.72]
K07332	archaeal flagellar protein FlaI
K07333	archaeal flagellar protein FlaJ
K07388	hydrogenase expression/formation protein
K07444	putative N6-adenine-specific DNA methylase [EC:2.1.1.-]
K07459	putative ATP-dependent endonuclease of the OLD family
K07462	single-stranded-DNA-specific exonuclease [EC:3.1.-.-]
K07463	archaea-specific RecJ-like exonuclease
K07466	replication factor A1
K07487	transposase
K07507	putative Mg2+ transporter-C (MgtC) family protein
K07557	archaeosine tRNA-ribosyltransferase [EC:2.4.2.-]

KEGG orthology	Function
K07558	tRNA nucleotidyltransferase (CCA-adding enzyme) [EC:2.7.7.72]
K07562	nonsense-mediated mRNA decay protein 3
K07569	RNA-binding protein
K07572	putative nucleotide binding protein
K07573	exosome complex component CSL4
K07575	PUA domain protein
K07581	hypothetical protein
K07583	tRNA pseudouridine synthase 10 [EC:5.4.99.-]
K07585	hypothetical protein
K07645	two-component system, OmpR family, sensor histidine kinase QseC [EC:2.7.13.3]
K07666	two-component system, OmpR family, response regulator QseB
K07687	two-component system, NarL family, captular synthesis response regulator RcsB
K07732	riboflavin kinase, archaea type [EC:2.7.1.161]
K07769	two-component system, OmpR family, sensor histidine kinase NblS [EC:2.7.13.3]
K07783	MFS transporter, OPA family, sugar phosphate sensor protein UhpC
K07790	putative membrane protein PagO
K08096	GTP cyclohydrolase IIa [EC:3.5.4.29]
K08097	phosphosulfolactate synthase [EC:4.4.1.19]
K08137	MFS transporter, SP family, galactose:H+ symporter
K08259	lysostaphin [EC:3.4.24.75]
K08264	heterodisulfide reductase subunit D [EC:1.8.98.1]
K08309	soluble lytic murein transglycosylase [EC:3.2.1.-]
K08310	dATP pyrophosphohydrolase [EC:3.6.1.-]
K08311	putative (di)nucleoside polyphosphate hydrolase [EC:3.6.1.-]
K08484	phosphotransferase system, enzyme I, PtsP [EC:2.7.3.9]
K08587	clostripain [EC:3.4.22.8]
K08589	gingipain R [EC:3.4.22.37]
K08590	carbon-nitrogen hydrolase family protein
K08641	D-alanyl-D-alanine dipeptidase [EC:3.4.13.22]
K08722	5'-nucleotidase [EC:3.1.3.5]
K08971	putative membrane protein
K08974	putative membrane protein
K08978	putative membrane protein
K08979	putative membrane protein
K09003	hypothetical protein
K09119	hypothetical protein
K09139	hypothetical protein
K09140	pre-rRNA-processing protein TSR3
K09144	hypothetical protein
K09152	hypothetical protein
K09154	hypothetical protein
K09482	glutamyl-tRNA(Gln) amidotransferase subunit D [EC:6.3.5.7]
K09713	hypothetical protein
K09720	hypothetical protein
K09721	hypothetical protein
K09722	4-phosphopantoate---beta-alanine ligase [EC:6.3.2.36]
K09723	hypothetical protein
K09724	hypothetical protein
K09727	hypothetical protein
K09728	hypothetical protein
K09730	hypothetical protein
K09733	hypothetical protein
K09735	hypothetical protein
K09738	hypothetical protein
K09739	hypothetical protein
K09766	hypothetical protein
K09807	hypothetical protein
K09826	Fur family transcriptional regulator, iron response regulator
K09859	hypothetical protein
K09882	cobaltochelatase CobS [EC:6.6.1.2]
K09914	putative lipoprotein
K09942	hypothetical protein
K09968	hypothetical protein
K09973	hypothetical protein
K09987	hypothetical protein
K09989	hypothetical protein
K10212	glycosyl-4,4'-diaponeurosporenoate acyltransferase [EC:2.3.1.-]
K10219	2-hydroxy-4-carboxymuconate semialdehyde hemiacetal dehydrogenase [EC:1.1.1.312]
K10679	nitroreductase / dihydropteridine reductase [EC:1.-.-.- 1.5.1.34]
K10697	two-component system, OmpR family, response regulator RpaA

KEGG orthology	Function
K10702	2-hydroxy-6-oxohepta-2,4-dienoate hydroxylase [EC:3.7.1.-]
K10725	archaeal cell division control protein 6
K10747	DNA ligase 1 [EC:6.5.1.1]
K10806	acyl-CoA thioesterase YciA [EC:3.1.2.-]
K10857	exodeoxyribonuclease X [EC:3.1.11.-]
K10960	geranylgeranyl reductase [EC:1.3.1.83]
K11004	ATP-binding cassette, subfamily B, bacterial HlyB/CyaB
K11005	hemolysin A
K11021	insecticidal toxin complex protein TccC
K11070	spermidine/putrescine transport system permease protein
K11130	H/ACA ribonucleoprotein complex subunit 3
K11131	H/ACA ribonucleoprotein complex subunit 4 [EC:5.4.99.-]
K11212	LPPG:FO 2-phospho-L-lactate transferase [EC:2.7.8.28]
K11260	formylmethanofuran dehydrogenase subunit G [EC:1.2.99.5]
K11434	protein arginine N-methyltransferase 1 [EC:2.1.1.-]
K11600	exosome complex component RRP41
K11693	peptidoglycan pentaglycine glycine transferase (the first glycine) [EC:2.3.2.16]
K11749	regulator of sigma E protease [EC:3.4.24.-]
K11780	FO synthase subunit 1 [EC:2.5.1.77]
K11915	serine/threonine protein phosphatase Stp1 [EC:3.1.3.16]
K11941	glucans biosynthesis protein C [EC:2.1.-.-]
K12071	conjugal transfer pilus assembly protein TraD
K12152	phosphatase NudJ [EC:3.6.1.-]
K12164	ubiquitin-like modifier-activating enzyme 5
K12234	coenzyme F420-0:L-glutamate ligase / coenzyme F420-1:gamma-L-glutamate ligase [EC:6.3.2.31 6.3.2.34]
K12278	MSHA biogenesis protein MshG
K12287	MSHA biogenesis protein MshQ
K12294	two-component system, AgrA family, sensor histidine kinase ComD [EC:2.7.13.-]
K12516	putative surface-exposed virulence protein
K12543	outer membrane protein LapE
K12573	ribonuclease R [EC:3.1.-.-]
K12589	exosome complex component RRP42
K12682	tracheal colonization factor
K12686	outer membrane lipase/esterase
K12975	phosphoethanolamine transferase
K12988	alpha-1,3-rhamnosyltransferase [EC:2.4.1.-]
K13010	perosamine synthetase
K13039	sulfopyruvate decarboxylase subunit beta [EC:4.1.1.79]
K13243	c-di-GMP-specific phosphodiesterase [EC:3.1.4.52]
K13282	cyanophycinase [EC:3.4.15.6]
K13500	chondroitin synthase [EC:2.4.1.175 2.4.1.226]
K13522	bifunctional NMN adenylyltransferase/nudix hydrolase [EC:2.7.7.1 3.6.1.-]
K13583	GcrA cell cycle regulator
K13588	histidine phosphotransferase ChpT
K13730	internalin A
K13735	adhesin/invasin
K13789	geranylgeranyl diphosphate synthase, type II [EC:2.5.1.1 2.5.1.10 2.5.1.29]
K13812	bifunctional enzyme Fae/Hps [EC:4.3.-.- 4.1.2.43]
K13896	microcin C transport system ATP-binding protein
K13929	malonate decarboxylase alpha subunit [EC:2.3.1.187]
K13942	5,10-methenyltetrahydromethanopterin hydrogenase [EC:1.12.98.2]
K14058	tRNA 2-thiocytidine biosynthesis protein TtcA
K14092	energy-converting hydrogenase A subunit A
K14093	energy-converting hydrogenase A subunit B
K14094	energy-converting hydrogenase A subunit C
K14095	energy-converting hydrogenase A subunit D
K14096	energy-converting hydrogenase A subunit E
K14097	energy-converting hydrogenase A subunit F
K14098	energy-converting hydrogenase A subunit G
K14101	energy-converting hydrogenase A subunit J
K14102	energy-converting hydrogenase A subunit K
K14103	energy-converting hydrogenase A subunit L
K14104	energy-converting hydrogenase A subunit M
K14105	energy-converting hydrogenase A subunit N
K14109	energy-converting hydrogenase A subunit R
K14110	energy-converting hydrogenase B subunit A
K14111	energy-converting hydrogenase B subunit B
K14112	energy-converting hydrogenase B subunit C
K14113	energy-converting hydrogenase B subunit D

KEGG orthology	Function
K14115	energy-converting hydrogenase B subunit F
K14116	energy-converting hydrogenase B subunit G
K14117	energy-converting hydrogenase B subunit H
K14118	energy-converting hydrogenase B subunit I
K14119	energy-converting hydrogenase B subunit J
K14121	energy-converting hydrogenase B subunit L
K14122	energy-converting hydrogenase B subunit M
K14123	energy-converting hydrogenase B subunit N
K14124	energy-converting hydrogenase B subunit O
K14125	energy-converting hydrogenase B subunit P
K14126	F420-non-reducing hydrogenase subunit A [EC:1.12.99.-]
K14196	immunoglobulin G-binding protein A
K14415	tRNA-splicing ligase RtcB [EC:6.5.1.3]
K14441	ribosomal protein S12 methylthiotransferase [EC:2.-.-.-]
K14561	U3 small nucleolar ribonucleoprotein protein IMP4
K14564	nucleolar protein 56
K14574	ribosome maturation protein SDO1
K14598	chlorobactene lauroyltransferase
K14623	DNA-damage-inducible protein D
K14653	2-amino-5-formylamino-6-ribosylaminopyrimidin-4(3H)-one 5'-monophosphate deformylase [EC:3.5.1.102]
K14680	RNA ligase [EC:6.5.1.3]
K14682	amino-acid N-acetyltransferase [EC:2.3.1.1]
K15125	filamentous hemagglutinin
K15353	E3 ubiquitin-protein ligase SspH2 [EC:6.3.2.19]
K15359	6-hydroxy-3-succinoylpyridine hydroxylase [EC:3.7.1.-]
K15429	tRNA (guanine37-N1)-methyltransferase [EC:2.1.1.228]
K15525	N-acetyl-1-D-myo-inositol-2-amino-2-deoxy-alpha-D-glucopyranoside deacetylase [EC:3.5.1.103]
K15527	cysteate synthase [EC:2.5.1.76]
K15633	2,3-bisphosphoglycerate-independent phosphoglycerate mutase [EC:5.4.2.1]
K15640	uncharacterized phosphatase
K15665	fengycin family lipopeptide synthetase B
K15770	putative arabinogalactan oligomer transport system substrate-binding protein
K15778	phosphomannomutase / phosphoglucomutase [EC:5.4.2.8 5.4.2.2]
K15888	tritrans,polycis-undecaprenyl-diphosphate synthase [geranylgeranyl-diphosphate specific] [EC:2.5.1.89]
K15904	bifunctional tRNA threonylcarbamoyladenosine biosynthesis protein [EC:2.7.11.1]
K16091	Fe(3+) dicitrate transport protein
K16150	glycogen(starch) synthase [EC:2.4.1.11]
K16183	methylamine methyltransferase corrinoid activation protein

NA indicates not assigned