

Supplementary Materials

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Contents

S1 Previous Works	3
S2 Dataset Creation Process	4
S2.1 Labeling Method	4
S2.2 Manual Inspection of the WSPC Test Set Genomes	5
S2.3 Manual Verification of the BacPaCS Test Set Genomes	6
S3 Methods	7
S3.1 Evaluation Metrics	7
S3.2 Feature Selection of the WSPC Classifier - Parameter Tuning	8
S3.3 Mean Decrease Impurity Measure Computation for Feature Importance	9
S4 Classification Performance Comparison on Benchmark Test 1	9
S5 Biological Interpretation	9
S5.1 A Detailed Description of Each of the Top HP PGFams	9
S5.2 Top NHP Features	12
S6 BacPaCS Test Genomes	14
S7 WSPC Test Genomes	16

List of Figures

S1 Selecting the most discriminative features and removing highly correlated features	8
S2 Classification performance comparison between WSPC and extant classifiers on 94 out of 100 genomes of the original BacPaCS test set	9

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List of Tables

S1	Top NHP PGFams of the WSPC classifier	13
S2	A list of genomes included in the BacPaCS test set	16
S3	A list of genomes included in the WSPC test set	23

S1 Previous Works

In this section, we review previous computational methods for pathogenicity classification. The methods can be divided into two main categories: Read-based methods and protein-content-based methods.

Read-based Methods. Read-based classification approaches use short genomic reads as raw input, and hence do not depend on assembled genomes or on coding sequences. Several tools were proposed for the detection of pathogens in metagenomic reads based on mapping the reads to a species, genus, or phylum of reference genomes, and/or based on their sequence composition homology [1]. However, these methods were mainly designed for taxonomic assignment using known species that are present in a reference database, rather than for pathogenicity predictions. In addition to the taxonomy-dependent methods, several taxonomy-agnostic read-based methods were designed specifically for pathogenicity predictions [2, 3]. In 2017, Deneke *et al.* published PaPrBaG [2], an RF approach that uses classification features of two types: k -mer occurrence-based features and peptide features. PaPrBaG assigns pathogenicity prediction to each read in a genome sample, and computes the final prediction of the genome by averaging over all of its read-based prediction probabilities. A more recent read-based taxonomy-agnostic classification tool is DeePaC [3], which applies reverse-complement convolutional and recurrent neural networks to the classification task.

Protein-content-based Methods. Protein-content-based methods are classification approaches that require the availability of assembled and annotated genomes as they characterize a bacterial genome by the presence or absence of protein family members [4, 5, 6, 7].

Iraola *et al.* [5] constructed an SVM-based model to classify a bacteria, based on its genome, as a human pathogen or a non-pathogen using protein families annotated as virulence genes. Thus, their method has the disadvantage of not taking into account other protein families that could be associated with either HP or NHP phenotypes. Other protein-content-based tools constructed new protein families instead of relying on existing ones [4, 6, 7]. Andreatta *et al.* [4] developed a method to predict human pathogenicity in γ -Proteobacteria. They clustered new protein families using BLAST, and identified protein families that distinguish between the two phenotypes by their enrichment in either pathogens or non-pathogens. The pathogenicity of a new bacterium was determined by the presence or absence of proteins that belong to these distinguishing protein families in its genome. Building on the former method, Cosentino *et al.* [6] developed PathogenFinder, a similar method extended to handle a variety of bacterial taxonomic groups. In order to reduce the method’s runtime, CD-HIT was used instead of BLAST in the protein family clustering step of the algorithm, which took four weeks for a dataset of 885 genomes.

Recently, Barash *et al.* [7] developed BacPaCS, a sparse-SVM-based method for bacterial pathogenicity classification. Barash *et al.* also used CD-HIT for the construction of protein families, but in order to reduce the runtime of the clustering phase and to scale up the method to larger training data, only the top 10% of the longest gene sequences in the training set were used for the construction of protein families. Although this selection reduced the estimated runtime from 8 months to 12 days (for 21,155 genomes), the clustering step still remained the most computationally expensive step of the

training in all the aforementioned methods. Furthermore, when examining the top-scoring features of the BacPaCS classifier, as reported in the paper, it is evident that many of the top-ranking features appear in only a few genomes, which may hamper the classifier’s ability to contribute to the general understanding of pathogenic lifestyle, or to predict the pathogenicity of novel bacterial species.

The number of available sequenced strains per bacterial species varies greatly, mainly due to a bias towards pathogen studies [2]. Thus, the distribution of strains per species in a given database may not represent their distribution in the real world or in future applications. Consequently, this may result in a training dataset and a classifier that are biased towards specific species. Existing read-based methods addressed this issue by selecting one strain per species for their training sets [2, 3]. However, previous protein-content-based methods [4, 6, 7] did not properly address this normalization issue, and thus their generality may be at fault.

S2 Dataset Creation Process

S2.1 Labeling Method

To identify the HP and NHP bacteria in our dataset, we initially followed Barash *et al.* [7] annotation-based pathogenicity classification method, as described below:

1. Genomes are labeled as HP if they satisfy any of the following criteria:
 - (a) The ‘Disease’ field is not empty, and does not contain a commensal term, as defined below.
 - (b) One of the fields ‘Isolation Source’, ‘Host Health’, or ‘Comments’ includes an HP term. In addition, the same fields cannot include any of the NHP terms (the terms used for HP and NHP are presented below).
 - (c) A genome was manually verified as HP, by reviewing it in the literature.
2. Excluding the generated HP list, genomes are labeled as NHP if they satisfy any of the following criteria:
 - (a) One of the fields ‘Isolation Source’, ‘Host Health’, or ‘Comments’ includes an NHP term.
 - (b) One of the fields ‘Isolation Source’, ‘Host Health’, or ‘Comments’ includes a weaker NHP term.
3. The following term lists were used for the criteria above:
 - HP terms: virulence, disease, superbug, patient, diarrhea, waterborne, foodborne, toxin, clinical, intensive, outbreak, infection, pathogen, water borne, food borne.
 - NHP terms: healthy, probiotic, commensal.
 - Weaker NHP terms: ‘comparative’, ‘reference’.
 - Commensal terms: ‘healthy’, ‘Healthy’, ‘Commensal’, ‘Commensal (plant)’, ‘Periodontally healthy’.

A manual examination of a random sample from the training set revealed that some of the genomes were mislabeled. These labeling mistakes were caused by using keywords that can both describe HP and NHP genomes. In addition, a manual examination of a random sample from the group of genomes that were labeled as inconclusive revealed that some genomes could be labeled by utilizing additional keywords and fields. Therefore, the following modifications to the annotation process were made:

- ‘Other Clinical’ and ‘Isolation Comments’ were added to the list of relevant fields in 1(b) and 2(a).
- The word ‘intensive’ was removed from the HP terms.
- The words ‘microbiome’ and ‘microbiota’ were added to the NHP terms.
- All the weaker NHP terms were removed.

This rule-based labeling process correctly identifies HP genomes due to the pathogenic sample collection process. First, the PATRIC database utilizes information from standard medical practice in which clinical samples are taken from diseased individuals based on the illness symptoms. Thus, the decision of which sample to take (e.g., stool, urine, blood, nasal swab, sputum swab) is illness-related. Second, the samples are processed based on the suspected pathogens, i.e., cultured using specific conditions that will allow the growth of the suspected pathogen. Therefore, in the case of an identification of a bacterial strain, it can be medically referred to as the infectious agent.

S2.2 Manual Inspection of the WSPC Test Set Genomes

We manually inspected all the genomes in the WSPC test set (Section 2.1.3, main text) to ensure that their labels are correct by reviewing the associated PATRIC metadata. We verified a genome as HP if the isolation source is a diseased individual, and as NHP if the isolation source is a healthy individual or a probiotic supplement. Additionally, we performed a literature search to confirm the corresponding label.

The following strains could not be verified as HP or NHP:

1. The PATRIC metadata of a strain belonging to the species *Escherichia marmotae* (Genome ID: 1499973.23) indicated that it was collected as part of a study that sequenced metagenomes from urinary tract patients as well as from a control group. There was no indication to which of the two groups this strain belonged, and it was thus removed from the test set.
2. The PATRIC metadata of a strain belonging to an unclassified species of the genus *Starkeya* (Genome ID: 2666134.3) indicated that the host health status is diseased. However, this genus includes soil bacteria [8], and we were not able to find a study suggesting that *Starkeya* species could be pathogenic. Therefore, this genome was removed from the test set.

In addition, two strains were mislabeled by the automatic annotation. A strain of the species *Bacillus clausii* was labeled HP because of the keyword “disease” in the “Comments” field. The full sentence “Genome analysis of *Bacillus clausii* B619/R for evaluation of its health promoting and disease

preventing properties” indicates that it is a commensal probiotic bacterium, which is also supported by the literature [9]. Therefore, its label was corrected to NHP. A strain of the unclassified species *Clostridium sp. C5-48* was labeled as HP because of the keyword ”patient” in the isolation source field. However, this strain was collected from the feces of an alcoholic patient to study his metagenomic population in the colon, and a different database indicates that this strain is commensal [10]. Therefore, its label was corrected to NHP.

S2.3 Manual Verification of the BacPaCS Test Set Genomes

We manually curated the 100 genomes included in the BacPaCS test set using the metadata associated with each genome and the literature. We verified a genome label as HP if it was isolated from a diseased host (based on the PARTIC database entry), and if there was also evidence in the literature that the corresponding species or strain is pathogenic. We verified a genome label as NHP if it was isolated from a healthy host, and if the corresponding species or strain was also described in the literature as commensal or probiotic.

A list of all the genomes included in the original BacPaCS test set along with their verified labels, references to relevant studies, as well as an indication of whether each genome was included in Benchmark Test 2, is given in Table S2. In what follows, we summarize the modifications we made following the verification process.

1. A total of 18 strains belonging to the species *Pseudomonas aeruginosa*, *Acinetobacter nosocomialis*, *Streptococcus sp. NPS 3089*, *Acinetobacter baumannii*, *Escherichia coli*, and *Enterococcus faecium* were originally labeled as NHP, but were verified by us as HP as these strains were isolated from clinical samples or described in the literature as well-known pathogenic strains. This may explain the discrepancy between the pathogenicity annotations detected by Bartosezewitch *et al.* [3].
2. The labels of another six strains belonging to the species *Fusobacterium nucleatum*, *Fusobacterium periodonticum* and *Rothia aeria*, could not be verified by us as neither HP nor NHP:
 - The species *Fusobacterium nucleatum* included one strain that was collected from subgingival dental plaque (which may be an initiating factor in periodontal diseases [11]) and the species *Fusobacterium periodonticum* included four strains that were collected from the tongue or from dental plaque. For these genomes there was no indication in the corresponding metadata whether the hosts carried a periodontal disease. The species *Fusobacterium nucleatum* and *Fusobacterium periodonticum* are associated with a wide spectrum of human periodontal diseases [12, 13]. Therefore, these strains could not be reliably labeled and were removed from the test set.
 - The species *Rothia aeria* included one strain, which was isolated from an air sample of the living environment in the Mir space station [14]. *Rothia aeria* is described as an opportunistic periodontal pathogen that causes infections of immunocompromised patients and neonates, but its virulent features remain uncertain [14]. As it was collected from the

environment, it is not clear whether this specific strain can cause disease, and therefore it was removed from the test set.

S3 Methods

S3.1 Evaluation Metrics

Some of the test sets used in this paper consist of more HP than NHP labeled genomes. Using a regular accuracy metric (the proportion of correct predictions in the test set) may result in misleading classification evaluation due to the imbalance between the two classes. Therefore, we used Sensitivity (true positive rate), Specificity (true negative rate), and Balanced Accuracy (BACC), which denotes the mean of sensitivity and specificity [15]. In addition, for ranking evaluation of WSPC, we used the areas under the precision recall (AUPR) [16], and the receiver operation characteristic (AUROC) [17] curves. Since AUROC considers the ranking of all predictions while accuracy only considers a single prediction threshold (i.e., 0.5) [18], we used AUROC for the feature selection parameter tuning (Section S3.2 and Section 2.4.3 in the main text). Note that in the case of a highly imbalanced dataset, AUPR is more informative than AUROC [19]. However, since there is only a slight imbalance between the classes of the validation set (ratio of 2:1 HP to NHP), and as AUROC is more commonly used than AUPR in the general case, we opted to use AUROC for the purpose of parameter tuning.

S3.2 Feature Selection of the WSPC Classifier - Parameter Tuning

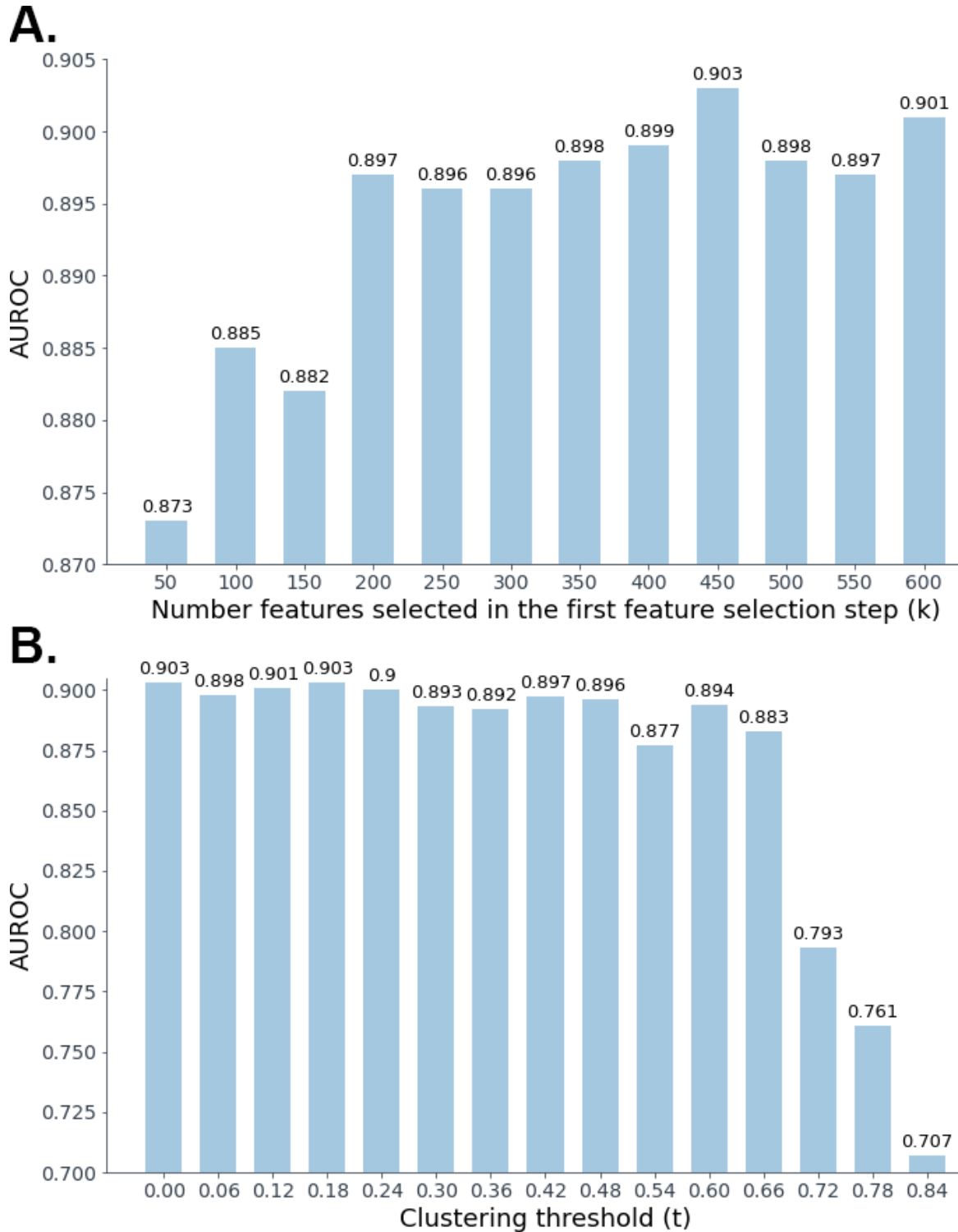


Figure S1: Performance evaluation of the RF classifier using different values for the k and t parameters of the two-step feature selection process (Section 2.4.3, main text). We trained on the training set, and evaluated on the validation set. **A.** AUROC values achieved by the classifier, as a function of k - the number of features selected in the first feature selection step (based on their χ^2 scores, without correlation reduction). The maximum value was obtained for $k = 450$. **B.** AUROC values achieved by the classifier using different subsets of the 450 features selected in the first feature selection step, as a function of t - the clustering threshold. The maximum value was obtained for $t = 0.18$ resulting in a subset of 244 features, and is equal to the AUROC score value obtained before removing correlated features ($t = 0$).

S3.3 Mean Decrease Impurity Measure Computation for Feature Importance

The Mean Decrease Impurity (MDI) importance measure [20, 21] of a feature of interest is computed by the Scikit-learn python package [22] as follows:

1. For each tree in the forest, the total decrease in Gini impurity in all the splits that use this feature, weighted by the proportion of samples reaching that split, is computed.
2. The resulting value in each tree is averaged over all trees in the forest

Consequently, the MDI values for all features sum to one. Thus, an “important” feature is often selected for tree splits and yields a high decrease of Gini impurity, leading to a high MDI. To evaluate the feature importance of each PGFam feature in the final set of features, we computed its average MDI value using 100 RF classifiers with different random seeds (seeds 0-99) trained on the combined training and validation sets.

S4 Classification Performance Comparison on Benchmark Test 1

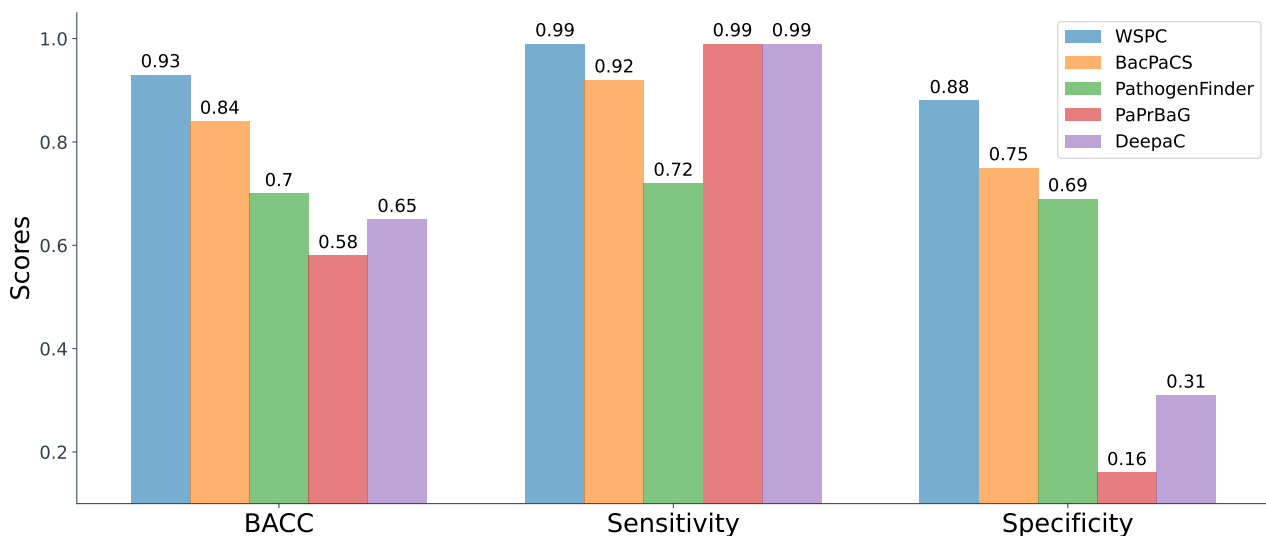


Figure S2: Classification performance comparison between WSPC and extant classifiers on 94 out of 100 genomes of the original BacPaCS test set with manually verified labels (Benchmark Test 1, Section 2.2 in the main text).

S5 Biological Interpretation

S5.1 A Detailed Description of Each of the Top HP PGFams

As a part of the feature selection process, we performed clustering based on a correlation measure between all pairs of features (i.e., genes), and then selected a PGFam representative from each cluster. Interestingly, 14 out of the 15 PGFams that yielded highest MDI scores in the HP category (Table 1 in the main text), each belong to a “singleton” cluster that contains a single member.

In what follows, we describe the biological function of each of the 15 PGFams in Table 1 from the main text. In addition, we provide a list of PGFams that belong to the same cluster as the PGFam ranked seventh (tRNA-modifying protein YgfZ).

1. Uroporphyrinogen III decarboxylase (EC 4.1.1.37) is an enzyme that catalyzes the fifth step in heme biosynthesis [23]. Heme is essential to the function of hemoproteins, which are involved in processes such as energy generation by the electron transport chain and detoxification of host immune effectors. Both heme acquisition and synthesis are important for pathogenesis [24]. Uroporphyrinogen decarboxylase was found to be important for the survival of *Actinobacillus pleuropneumoniae*, a pathogen swine, during infection [25].

Other PGFams in the corresponding cluster: None.

2. Dihydrolipoamide acetyltransferase (EC 2.3.1.12) is an enzyme component of the multienzyme pyruvate dehydrogenase complex, which has an important role in aerobic respiration pathways [26]. It has been shown that Dihydrolipoamide acyltransferase is critical for *Mycobacterium tuberculosis* pathogenesis [27], and for the colonization of *Vibrio cholerae* [28].

Other PGFams in the corresponding cluster: None.

3. Cytosol aminopeptidase PepA (EC 3.4.11.1). Aminopeptidases are enzymes that catalyze the cleavage of amino acids and are active in several essential cellular processes [29]. PepA transcriptionally regulates the *carB* gene, which plays multiple roles in the pathogenicity of *Xanthomonas citri* [30]. In addition, PepA mediates pH regulation of virulence genes in *Vibrio cholerae* [31].

Other PGFams in the corresponding cluster: None.

4. Protoheme IX farnesyltransferase is an enzyme involved in catalysing the conversion of heme B to heme O, encoded by the gene *ctaB*. Heme O is incorporated into the electron transport chain as an electron acceptor, facilitating aerobic respiration and energy production [32]. The deletion of *ctaB* was observed to cause attenuated growth and virulence of *Staphylococcus aureus* [33], and it was also observed that this gene plays a critical role in the ability of *S. aureus* to secrete cytolytic toxins [34].

Other PGFams in the corresponding cluster: None.

5. Molybdopterin synthase catalytic subunit MoeA (EC 2.8.1.12), is involved in the molybdenum cofactor (MoCo) biosynthetic pathway [35]. Bacteria possess MoCo-dependent enzymes that catalyze redox reactions associated with bacterial respiration and energy conversion processes. These enzymes have been linked to virulence in a variety of bacteria [36]. The prevalence of MoCo-dependent enzymes in key bacterial pathogens, paired with the mounting evidence of their central roles in bacterial fitness during infection, suggest that they could be important future drug targets [37].

Other PGFams in the corresponding cluster: None.

6. Class 2 dihydroorotate dehydrogenase (DHODase) participates in the pyrimidine de novo biosynthesis pathway. The pyrimidine synthetic pathway plays essential roles in the pathogenesis and antibiotic resistance of *P. aeruginosa* and *E. coli*, and in the survival of the pathogen *H. pylori*. Other PGFams in the corresponding cluster: None.
7. Uncharacterized tRNA-modifying protein YgfZ, participates in the synthesis and repair of iron-sulfur (Fe-S) clusters. A mutation in YgfZ causes growth defects in *Escherichia coli*, particularly under oxidative stress, and lowers the activities several Fe-S enzymes [38].
Other PGFams in the corresponding cluster:
PGF_00024322 NAD(P) transhydrogenase subunit beta (EC 1.6.1.2)
PGF_00045982 Pyruvate dehydrogenase E1 component (EC 1.2.4.1)
PGF_00416576 3'-to-5' oligoribonuclease (orn)
PGF_01053024 Glutamine synthetase adenylyl-L-tyrosine phosphorylase (EC 2.7.7.89) / Glutamate-ammonia-ligase adenylyltransferase (EC 2.7.7.42)
PGF_03000099 Ribonuclease Y
PGF_04792416 LSU ribosomal protein L32p @ LSU ribosomal protein L32p, zinc-independent
PGF_05562713 [Protein-PII] uridylyltransferase (EC 2.7.7.59) / [Protein-PII]-UMP uridylyl-removing enzyme
PGF_10461681 Ribonuclease E (EC 3.1.26.12)
PGF_10525969 Magnesium and cobalt efflux protein CorC
8. 23S rRNA (uracil(1939)-C(5))-methyltransferase (EC 2.1.1.190). Methylation of 23S rRNA was found to provide a significant advantage for bacteria at osmotic and oxidative stress [39].
Other PGFams in the corresponding cluster: None.
9. YpfJ protein, zinc metalloprotease superfamily, is a protein that cleaves other proteins and uses zinc as a metal cofactor. Metalloproteases play multiple roles in virulence including the disruption of physiologically important host processes, release of nutrients such as metals from host metalloproteins, cleavage of host immune components, and interference with host immune signaling cascades [40].
Other PGFams in the corresponding cluster: None.
10. Threonine dehydratase biosynthetic (EC 4.3.1.19). Threonine dehydratase mediated isoleucine biosynthesis is an important step in maintaining the metabolic pool of isoleucine, a branch chain amino acid. It has been shown that down-regulation of threonine dehydratase in the pathogen *Mycobacterium tuberculosis* increases its susceptibility to oxidative stress [41]. It also has been suggested that the genes for threonine biosynthesis are critical factors for the multiplication of *Staphylococcus aureus* in the blood [42]. Although *S. aureus* is usually commensal in the skin and the mucosa, its presence in the blood can lead to a bloodstream infection with a high fatality rate [43]. The enzymes belonging to the branch chain amino acid biosynthetic pathway

in bacteria are promising drug targets due to the lack of a similar pathway in mammals, which would reduce related toxicity [44].

Other PGFams in the corresponding cluster: None.

11. The enzyme glutathione reductase (EC 1.8.1.7) is part of the antioxidant glutathione system. Glutathione is an abundant antioxidant in bacteria, where it serves a key function in protecting the cell from the action of low pH, chlorine compounds, osmotic stresses, and reactive oxygen species (ROS) [45]. Glutathione reductase is one of the main enzymes involved in glutathione metabolism [45]. Recent studies suggested that generation of ROS acts as a common mechanism of antibiotics-induced bacterial death, thus inhibiting antioxidant systems such as the glutathione system may limit antibiotic resistance [46].

Other PGFams in the corresponding cluster: None.

12. Cell division integral membrane protein, YggT and half-length relatives. This is an unknown gene with the predicted function of a cell division integral membrane protein, and its gene symbol is YggT. YggT seems to play a role in osmotic stress tolerance in *Escherichia coli* [47]. It has been suggested that osmotic stress responsive systems contribute to the virulence potential of a number of pathogenic bacteria [48].

Other PGFams in the corresponding cluster: None.

13. Superoxide dismutase [Cu-Zn] precursor (EC 1.15.1.1) enzyme. As part of the innate immune response, macrophages and neutrophils attack invading microbes with toxic superoxide [49]. To counteract this attack, some microbial pathogens express Cu, Zn superoxide dismutase enzymes [50]. This enzyme was shown to induce protection against oxidative stress and enhance the pathogenicity of *Bacillus anthracis* [51]. In addition, it was shown to contribute to the resistance of *Mycobacterium tuberculosis* against oxidative burst products generated by macrophages [52].

Other PGFams in the corresponding cluster: None.

14. Sulfur carrier protein FdhD. FdhD is required for formate dehydrogenase to be functional. Formate dehydrogenase was suggested to be involved in oxidative stress tolerance in *E. coli* [53].

Other PGFams in the corresponding cluster: None.

15. Deoxyribodipyrimidine photolyase. Photolyases are enzymes that repair UV-induced DNA lesions by using light energy. Interestingly, many human and plant pathogens contain photolyases [54].

Other PGFams in the corresponding cluster: None.

S5.2 Top NHP Features

	PGFam	Function	MDI (SD ¹)	HPs	NHPs	P-Ratio ²	# Genera ³
1	PGF_03029062	Dihydroorotate dehydrogenase (NAD(+)), catalytic subunit (EC 1.3.1.14)	0.034 (0.01)	70	182	5.17	98
2	PGF_01667671	Cytidylate kinase (EC 2.7.4.25)	0.031 (0.009)	7	125	31.57	60
3	PGF_02930287	Reverse rubrerythrin	0.027 (0.01)	11	125	21.05	57
4	PGF_08946513	Flavodoxin	0.021 (0.007)	67	170	5.04	94
5	PGF_01469197	RNA methyltransferase, TrmA family	0.021 (0.009)	76	180	4.71	100
6	PGF_01333294	Activator of (R)-2-hydroxyglutaryl-CoA dehydratase	0.019 (0.007)	25	128	9.95	77
7	PGF_01284176	Rubrerythrin	0.018 (0.009)	35	142	7.96	81
8	PGF_00006245	Formate-tetrahydrofolate ligase (EC 6.3.4.3)	0.016 (0.007)	138	201	2.91	122
9	PGF_00033940	Phosphoribosyl-aminoimidazole-carboxamide formyltransferase (EC 2.1.2.3)	0.016 (0.006)	6	106	30.64	53
10	PGF_10332317	Electron transport complex protein RnfB	0.014 (0.006)	18	123	13.08	62
11	PGF_08126536	Flavoprotein	0.013 (0.006)	13	114	16.47	58
12	PGF_00401757	no significant homology.	0.013 (0.006)	8	106	23.83	44
13	PGF_00016404	LSU ribosomal protein L32p @ LSU ribosomal protein L32p, zinc-dependent	0.012 (0.005)	88	173	3.92	100
14	PGF_00075770	FIG00519347: Ribonucleotide reductase-like protein	0.012 (0.003)	51	135	5.24	76
15	PGF_00003251	Macrolide export ATP-binding/permease protein	0.01 (0.002)	16	69	8.25	40

Table S1: The top NHP PGFams that serve as features of the WSPC classifier according to their average Mean Decrease Impurity (MDI) rank, along with the number of HP and NHP genomes in the training set that contain the respective PGFams. The average MDI rank of a PGFam is the average value of the feature’s MDI values computed using 100 random forest classifiers with different random seeds trained on the training set. ¹Standard Deviation. ²The ratio between the proportion of NHPs with the corresponding PGFam and the proportion of HPs with the corresponding PGFam. To avoid zero division, add-one smoothing was performed. ³ The number of different genera to which the genomes that contain the respective PGFams belong.

S6 BacPaCS Test Genomes

	Genome ID	Genome Name	BacPaCS Label ¹	Validated Label ²	References ³	OPP ⁴	Balanced Test ⁵
1	470.3353	Acinetobacter baumannii strain HWBA8	NHP	HP	Clinical isolate [55]	[56]	Yes
2	106654.48	Acinetobacter nosocomialis strain SSA3	NHP	HP	Clinical isolate [55]	[56]	Yes
3	520.659	Bordetella pertussis strain B227	HP	HP	[57]		Yes
4	28450.385	Burkholderia pseudomallei strain MSHR5864	HP	HP	[58]	[59]	Yes
5	83554.74	Chlamydia psittaci strain 2005:CpsCP1	HP	HP	[60]		Yes
6	813.141	Chlamydia trachomatis strain SQ12	HP	HP	[61]		Yes
7	545.38	Citrobacter koseri strain FDAAR-GOS.287	HP	HP	[62, 63]	[63]	Yes
8	777.186	Coxiella burnetii strain Heizberg	HP	HP	[64]		Yes
9	1352.1760	Enterococcus faecium strain Ef_aus00233	NHP	HP	Hospital outbreak isolate [65]	[66]	Yes
10	562.22306	Escherichia coli strain FDAAR-GOS.433 strain Not applicable	HP	HP	[67]		Yes
11	210.2912	Helicobacter pylori strain F20	HP	HP	[68]		Yes
12	573.16474	Klebsiella pneumoniae strain KP9	HP	HP	[69, 70]	[70]	Yes
13	1639.2624	Listeria monocytogenes strain H34	HP	HP	[71]	[71]	Yes
14	1041522.28	Mycobacterium colombiense strain CECT 3035	HP	HP	[72]	[72]	Yes
15	722731.3	Mycobacterium shigaense strain UN-152	HP	HP	[73]	[74]	Yes
16	1773.8714	Mycobacterium tuberculosis strain MDRMA2441	HP	HP	[75]		Yes
17	2104.190	Mycoplasma pneumoniae strain KCH-405	HP	HP	[76]		Yes
18	37326.9	Nocardia brasiliensis strain FDAARGOS.352	HP	HP	[77, 78]		Yes
19	28131.10	Prevotella intermedia strain OMA14	HP	HP	[79]	[80]	Yes
20	287.4623	Pseudomonas aeruginosa strain PB350	HP	HP	[81]	[82]	Yes
21	1280.11681	Staphylococcus aureus strain USA300-SUR15	HP	HP	[83]	[84]	Yes
22	1302.83	Streptococcus gordonii strain FDAARGOS_257	HP	HP	[85, 86]	[86]	Yes
23	1338.30	Streptococcus intermedius strain FDAARGOS_233	HP	HP	[87]	[87]	Yes
24	1902136.3	Streptococcus sp. NPS 308	NHP	HP	Clinical isolate [88]	[88]	Yes
25	730.54	[Haemophilus] ducreyi strain FDAARGOS_297	HP	HP	[89, 90]		Yes
26	28025.19	Bifidobacterium animalis strain BL3	NHP	NHP	[91]		Yes
27	1496.1556	Clostridioides difficile strain BR81	NHP	NHP	[92, 93]	[93]	Yes
28	74426.49	Collinsella aerofaciens strain indica	NHP	NHP	[94]	[95]	Yes
29	853.172	Faecalibacterium prausnitzii strain Indica	NHP	NHP	[96]		Yes
30	1841863.3	Gordonibacter sp. Marseille-P2775 strain Marseille-P2775	NHP	NHP	[97]		Yes
31	1582.99	Lactobacillus casei strain LC5	NHP	NHP	[98]		Yes
32	1613.133	Lactobacillus fermentum strain FTDC 8312	NHP	NHP	[99]		Yes
33	1590.548	Lactobacillus plantarum strain LP3	NHP	NHP	[100]		Yes
34	47715.277	Lactobacillus rhamnosus strain Pen	NHP	NHP	[101]		Yes

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	Genome ID	Genome Name	BacPaCS Label ¹	Validated Label ²	References ³	OPP ⁴	Balanced Test ⁵
35	487.1231	<i>Neisseria meningitidis</i> strain 38277	NHP	NHP	[102]		Yes
36	1944646.3	<i>Phoenicibacter massiliensis</i> strain Marseille-P3241	NHP	NHP	[103]		Yes
37	1849491.6	Staphylococcaceae bacterium S31 strain S31	NHP	NHP	[104]		Yes
38	1308.247	<i>Streptococcus thermophilus</i> strain ST3	NHP	NHP	[105]		Yes
39	137591.34	<i>Weissella cibaria</i> strain CMS3	NHP	NHP	[106]		Yes
40	515619.32	[<i>Eubacterium rectale</i>] ATCC 33656	NHP	NHP	[107]		Yes
41	470.3349	<i>Acinetobacter baumannii</i> strain 15A34	NHP	HP	Clinical isolate [55]		No
42	470.3350	<i>Acinetobacter baumannii</i> strain 15A5	NHP	HP	Clinical isolate [55]		No
43	470.3348	<i>Acinetobacter baumannii</i> strain CBA7	NHP	HP	Clinical isolate [55]		No
44	470.3347	<i>Acinetobacter baumannii</i> strain JBA13	NHP	HP	Clinical isolate [55]		No
45	470.3356	<i>Acinetobacter baumannii</i> strain SAA14	NHP	HP	Clinical isolate [55]		No
46	470.3357	<i>Acinetobacter baumannii</i> strain SSA12	NHP	HP	Clinical isolate [55]		No
47	470.3352	<i>Acinetobacter baumannii</i> strain SSA6	NHP	HP	Clinical isolate [55]		No
48	470.3358	<i>Acinetobacter baumannii</i> strain SSMA17	NHP	HP	Clinical isolate [55]		No
49	470.3355	<i>Acinetobacter baumannii</i> strain USA15	NHP	HP	Clinical isolate [55]		No
50	470.3351	<i>Acinetobacter baumannii</i> strain USA2	NHP	HP	Clinical isolate [55]		No
51	470.3354	<i>Acinetobacter baumannii</i> strain WKA02	NHP	HP	Clinical isolate [55]		No
52	520.747	<i>Bordetella pertussis</i> strain C934	HP	HP	[57]		No
53	520.694	<i>Bordetella pertussis</i> strain H361	HP	HP	[57]		No
54	520.667	<i>Bordetella pertussis</i> strain H698	HP	HP	[57]		No
55	520.529	<i>Bordetella pertussis</i> strain H754	HP	HP	[57]		No
56	520.670	<i>Bordetella pertussis</i> strain H771	HP	HP	[57]		No
57	520.535	<i>Bordetella pertussis</i> strain H812	HP	HP	[57]		No
58	520.698	<i>Bordetella pertussis</i> strain H876	HP	HP	[57]		No
59	520.699	<i>Bordetella pertussis</i> strain I093	HP	HP	[57]		No
60	520.572	<i>Bordetella pertussis</i> strain I112	HP	HP	[57]		No
61	520.537	<i>Bordetella pertussis</i> strain I238	HP	HP	[57]		No
62	520.629	<i>Bordetella pertussis</i> strain I461	HP	HP	[57]		No
63	520.543	<i>Bordetella pertussis</i> strain I763	HP	HP	[57]		No
64	520.574	<i>Bordetella pertussis</i> strain I998	HP	HP	[57]		No
65	520.546	<i>Bordetella pertussis</i> strain J018	HP	HP	[57]		No
66	520.650	<i>Bordetella pertussis</i> strain J073	HP	HP	[57]		No
67	520.737	<i>Bordetella pertussis</i> strain J078	HP	HP	[57]		No
68	520.708	<i>Bordetella pertussis</i> strain J122	HP	HP	[57]		No
69	520.671	<i>Bordetella pertussis</i> strain J178	HP	HP	[57]		No
70	520.672	<i>Bordetella pertussis</i> strain J179	HP	HP	[57]		No
71	520.678	<i>Bordetella pertussis</i> strain J194	HP	HP	[57]		No
72	520.680	<i>Bordetella pertussis</i> strain J296	HP	HP	[57]		No
73	28450.655	<i>Burkholderia pseudomallei</i> strain 2010007509	HP	HP	[108, 59]	[59]	No
74	813.142	<i>Chlamydia trachomatis</i> strain SQ14	HP	HP	[61]		No
75	168807.6	<i>Escherichia coli</i> O127:H6 strain EPEC1	NHP	HP	Pathogenic <i>E. coli</i> strain [109]		No
76	562.16466	<i>Escherichia coli</i> strain 5CRE51	HP	HP	[110]		No
77	562.22333	<i>Escherichia coli</i> strain ATCC 43896	HP	HP	[111]		No

Continued on next page

	Genome ID	Genome Name	BacPaCS Label ¹	Validated Label ²	References ³	OPP ⁴	Balanced Test ⁵
78	562.15193	Escherichia coli strain Ecol.276	HP	HP	[112]		No
79	562.22323	Escherichia coli strain FDAAR-GOS.434 strain Not applicable	HP	HP	[113]		No
80	562.22307	Escherichia coli strain FDAAR-GOS.448 strain Not applicable	HP	HP	[114]		No
81	562.16428	Escherichia coli strain G199	NHP	HP	Pathogenic <i>E. coli</i> strain [115]		No
82	562.22326	Escherichia coli strain UFU_EC98	HP	HP	[116]		No
83	573.16440	Klebsiella pneumoniae strain 459	HP	HP	[117]	[70]	No
84	573.15319	Klebsiella pneumoniae strain FDAARGOS_436 strain Not applicable	HP	HP	[118]	[70]	No
85	1196172.3	Listeria monocytogenes serotype 4b str. 02-1289 strain 02-1289	HP	HP	[119, 71]	[71]	No
86	1196162.3	Listeria monocytogenes serotype 4b str. 10-0809 strain 10-0809	HP	HP	[120, 71]	[71]	No
87	1773.8686	Mycobacterium tuberculosis strain LE13	HP	HP	[75]		No
88	1773.8719	Mycobacterium tuberculosis strain TBDM2489	HP	HP	[75]		No
89	2104.189	Mycoplasma pneumoniae strain KCH-402	HP	HP	[76]		No
90	487.1548	Neisseria meningitidis strain M26417	HP	HP	[121]	[102]	No
91	287.3868	Pseudomonas aeruginosa strain RIVM-EMC2982	NHP	HP	Clinical isolate [122]	[82]	No
92	1280.12234	Staphylococcus aureus strain JE2	HP	HP	[123, 84]	[84]	No
93	1280.11677	Staphylococcus aureus strain USA300-SUR11	HP	HP	[124, 84]	[84]	No
94	76857.43	Fusobacterium nucleatum subsp. polymorphum strain KCOM 1275	NHP	INC	[12]		No
95	172042.4	Rothia aeria strain JCM 11412	NHP	INC		[14]	No
96	860.11	Fusobacterium periodonticum strain KCOM 1261	NHP	INC	[125]		No
97	860.17	Fusobacterium periodonticum strain KCOM 1262	NHP	INC	[125]		No
98	860.16	Fusobacterium periodonticum strain KCOM 2555	NHP	INC	[125]		No
99	860.18	Fusobacterium periodonticum strain KCOM 2653	NHP	INC	[125]		No
100	47715.310	Lactobacillus rhamnosus strain LR5	NHP	NHP	[126]		No

Table S2: A list of genomes included in the BacPaCS test set. ¹The original label given to each genome by Barash *et al.* [7]. ^{2,3}Manually validated label according to the PATRIC metadata entry and according to the literature, along with the respective reference. INC stands for an inconclusive label, see text. ⁴A reference is provided if the corresponding species is known to cause opportunistic infections. ⁵Whether the genome is part of the balanced version of the BacPaCS test, which includes one genomes per species.

S7 WSPC Test Genomes

	Genome ID	Genome Name	Label	HP/NHP ¹	Species	References ²	OPP ³
1	163603.4	Actinomadura latina strain ATCC BAA-277	HP	1/0	Actinomadura latina	[127]	No
2	648.157	Aeromonas caviae strain ScAc2001	HP	9/0	Aeromonas caviae	[128]	No
3	565.15	Atlantibacter hermannii strain 3608	HP	1/0	Atlantibacter hermannii	[129]	No

Continued on next page

	Genome ID	Genome Name	Label	HP/NHP ¹	Species	References ²	OPP. ³
4	29459.655	<i>Brucella melitensis</i> strain HN20190002	HP	13/0	<i>Brucella melitensis</i>	[130]	No
5	87883.284	<i>Burkholderia multivorans</i> strain C1576	HP	107/0	<i>Burkholderia multivorans</i>	[131]	No
6	195.2778	<i>Campylobacter coli</i> strain 202823	HP	95/0	<i>Campylobacter coli</i>	[132, 133]	No
7	201.69	<i>Campylobacter lari</i> strain 503734	HP	3/0	<i>Campylobacter lari</i>	[134, 135]	No
8	2572066.4	<i>Campylobacter</i> sp. CFSAN093243	HP	194/0	<i>Campylobacter jejuni</i>	[134, 136, 137]	No
9	1491.1756	<i>Clostridium botulinum</i> strain ZBS3_16-240-01	HP	7/0	<i>Clostridium botulinum</i>	[138]	No
10	65058.433	<i>Corynebacterium ulcerans</i> strain 02-13	HP	8/0	<i>Corynebacterium ulcerans</i>	[139]	No
11	208962.153	<i>Escherichia albertii</i> strain 13S38	HP	34/0	<i>Escherichia albertii</i>	[140]	No
12	562.55247	<i>Escherichia coli</i> strain 4374	HP	4352/396	<i>Escherichia coli</i>	[141]	No
13	210.6620	<i>Helicobacter pylori</i> strain MHP47	HP	526/0	<i>Helicobacter pylori</i>	[142]	No
14	104628.50	<i>Helicobacter suis</i> strain NHP19-4022	HP	2/0	<i>Helicobacter suis</i>	[143]	No
15	44275.61	<i>Leptospira interrogans</i> serovar Copenhageni strain CLEP00179	HP	6/0	<i>Leptospira interrogans</i>	[144]	No
16	1639.7756	<i>Listeria monocytogenes</i> strain SCPM-O-B-7909	HP	197/0	<i>Listeria monocytogenes</i>	[145]	No
17	78331.108	<i>Mycobacterium canettii</i> strain NLA000701671	HP	1/0	<i>Mycobacterium canettii</i>	[146]	No
18	1768.199	<i>Mycobacterium kansasii</i> strain JALMAMYKAN-1	HP	34/0	<i>Mycobacterium kansasii</i>	[147]	No
19	2664891.3	<i>Mycobacterium tuberculosis</i> complex sp. AY1MRC	HP	1/0	<i>Mycobacterium tuberculosis</i> complex sp. AY1MRC	[148]	No
20	1773.20690	<i>Mycobacterium tuberculosis</i> strain <i>Mycobacterium tuberculosis</i> 79499	HP	3445/2	<i>Mycobacterium tuberculosis</i>	[149]	No
21	485.8128	<i>Neisseria gonorrhoeae</i> strain 5671 strain not applicable	HP	289/0	<i>Neisseria gonorrhoeae</i>	[150]	No
22	90370.3046	<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Typhi strain 343077_206161	HP	1480/2	<i>Salmonella enterica</i>	[151]	No
23	624.2242	<i>Shigella sonnei</i> strain 7109.28	HP	850/0	<i>Shigella sonnei</i>	[152]	No
24	686.65	<i>Vibrio cholerae</i> O1 biovar El Tor strain NALMLE37	HP	344/0	<i>Vibrio cholerae</i>	[153]	No
25	150053.31	<i>Yersinia enterocolitica</i> subsp. <i>palaearctica</i> strain Ye9N	HP	5/0	<i>Yersinia enterocolitica</i>	[154]	No
26	85698.208	<i>Achromobacter xylosoxidans</i> strain DN2019	HP	16/0	<i>Achromobacter xylosoxidans</i>	[155]	Yes
27	470.9648	<i>Acinetobacter baumannii</i> strain KT_2016_39	HP	2281/0	<i>Acinetobacter baumannii</i>	[156]	Yes
28	29430.96	<i>Acinetobacter haemolyticus</i> strain 11654	HP	25/0	<i>Acinetobacter haemolyticus</i>	[157]	Yes
29	28090.110	<i>Acinetobacter lwoffii</i> strain FDAARGOS_620 strain Not applicable	HP	2/0	<i>Acinetobacter lwoffii</i>	[158]	Yes
30	48296.376	<i>Acinetobacter pittii</i> strain VNMU 150	HP	43/2	<i>Acinetobacter pittii</i>	[159]	Yes
31	2026190.21	<i>Bacillus mobilis</i> strain 1428.155	HP	1/0	<i>Bacillus mobilis</i>	[160, 161]	Yes
32	2026186.33	<i>Bacillus paranthracis</i> strain ELWA-3-3298	HP	1/1	<i>Bacillus paranthracis</i>	[162]	Yes
33	817.1653	<i>Bacteroides fragilis</i> strain PP971	HP	61/45	<i>Bacteroides fragilis</i>	[163]	Yes

Continued on next page

	Genome ID	Genome Name	Label	HP/NHP ¹	Species	References ²	OPP. ³
34	95486.460	Burkholderia cenocepacia strain MS-2140	HP	206/0	Burkholderia cenocepacia	[164]	Yes
35	292.237	Burkholderia cepacia strain IST612	HP	3/0	Burkholderia cepacia	[165]	Yes
36	28450.2018	Burkholderia pseudomallei strain haikou8	HP	168/0	Burkholderia pseudomallei	[59]	Yes
37	1507806.57	Campylobacter fetus subsp. testudinum strain wqj4	HP	14/0	Campylobacter fetus	[166]	Yes
38	57706.80	Citrobacter braakii strain CB00017	HP	1/0	Citrobacter braakii	[167]	Yes
39	67824.24	Citrobacter farmeri strain YDC697-2	HP	1/0	Citrobacter farmeri	[63, 168]	Yes
40	546.797	Citrobacter freundii strain YDC638-3	HP	34/1	Citrobacter freundii	[63]	Yes
41	545.121	Citrobacter koseri strain AS012499	HP	7/1	Citrobacter koseri	[63]	Yes
42	67827.42	Citrobacter werkmanii strain YDC667-1	HP	4/0	Citrobacter werkmanii	[63]	Yes
43	133448.15	Citrobacter youngae strain AS012330	HP	1/0	Citrobacter youngae	[63]	Yes
44	1496.5104	Clostridioides difficile strain TMD0138	HP	601/39	Clostridioides difficile	[93, 169]	Yes
45	413503.68	Cronobacter malonaticus strain BJ15	HP	8/0	Cronobacter malonaticus	[170]	Yes
46	413501.15	Cronobacter muytjensii strain Cr150	HP	1/0	Cronobacter muytjensii	[170]	Yes
47	28141.803	Cronobacter sakazakii strain SD45	HP	47/0	Cronobacter sakazakii	[170]	Yes
48	413502.35	Cronobacter turicensis strain SH11	HP	2/0	Cronobacter turicensis	[170]	Yes
49	539.170	Eikenella corrodens strain EL_09	HP	8/0	Eikenella corrodens	[171, 172]	Yes
50	2528037.4	Eikenella exigua strain EL_02	HP	1/0	Eikenella exigua	[171, 173]	Yes
51	1117645.412	Elizabethkingia anophelis strain PHOL-515	HP	11/0	Elizabethkingia anophelis	[174]	Yes
52	238.101	Elizabethkingia meningoseptica strain GX196	HP	6/0	Elizabethkingia meningoseptica	[174]	Yes
53	61645.317	Enterobacter asburiae strain TUM17941	HP	20/0	Enterobacter asburiae	[175]	Yes
54	2494701.5	Enterobacter chengduensis strain C2-143-1	HP	2/0	Enterobacter chengduensis	[176]	Yes
55	550.2644	Enterobacter cloacae strain AS012445	HP	119/1	Enterobacter cloacae	[176]	Yes
56	299767.100	Enterobacter ludwigii strain AS012471	HP	6/0	Enterobacter ludwigii	[175]	Yes
57	1812935.59	Enterobacter roggenkampii strain AS012293	HP	12/0	Enterobacter roggenkampii	[177]	Yes
58	1351.3480	Enterococcus faecalis strain VNMU281	HP	98/13	Enterococcus faecalis	[178, 179]	Yes
59	1353.134	Enterococcus gallinarum strain EGR748	HP	2/1	Enterococcus gallinarum	[180, 181]	Yes
60	727.2505	Haemophilus influenzae strain AS012767	HP	409/0	Haemophilus influenzae	[182]	Yes
61	729.1932	Haemophilus parainfluenzae strain COPD-014-E1 O	HP	3/0	Haemophilus parainfluenzae	[183]	Yes
62	548.678	Klebsiella aerogenes strain AS012329	HP	96/0	Klebsiella aerogenes	[184]	Yes
63	1134687.181	Klebsiella michiganensis strain AS012446	HP	13/0	Klebsiella michiganensis	[185]	Yes
64	571.798	Klebsiella oxytoca strain AS012479	HP	28/0	Klebsiella oxytoca	[186]	Yes
65	573.29103	Klebsiella pneumoniae strain ST974-OXA48	HP	3859/8	Klebsiella pneumoniae	[186]	Yes

Continued on next page

	Genome ID	Genome Name	Label	HP/NHP ¹	Species	References ²	OPP. ³
66	1463165.235	Klebsiella quasipneumoniae strain M36	HP	67/0	Klebsiella quasipneumoniae	[187]	Yes
67	244366.462	Klebsiella variicola strain AS012291	HP	129/0	Klebsiella variicola	[187]	Yes
68	109328.8	Leptotrichia trevisanii strain JMUB3870	HP	1/0	Leptotrichia trevisanii	[188]	Yes
69	480.450	Moraxella catarrhalis strain AS012766	HP	64/0	Moraxella catarrhalis	[189]	Yes
70	582.399	Morganella morganii strain AS012332	HP	18/0	Morganella morganii	[190]	Yes
71	1809.19	Mycobacterium ulcerans strain CSURQ0185	HP	3/0	Mycobacterium ulcerans	[191]	Yes
72	36809.633	Mycobacteroides abscessus strain 1322-S0	HP	682/0	Mycobacteroides abscessus	[192]	Yes
73	948102.18	Mycobacteroides franklinii strain 9917	HP	1/0	Mycobacteroides franklinii	[193]	Yes
74	487.3238	Neisseria meningitidis strain N186_00	HP	278/43	Neisseria meningitidis	[102]	Yes
75	455432.12	Nocardia terpenica strain IFM 0706	HP	1/0	Nocardia terpenica	[194, 195]	Yes
76	419475.21	Ochrobactrum pseudogrignonense strain SHIN	HP	1/0	Ochrobactrum pseudogrignonense	[196, 197]	Yes
77	1202713.3	Paenaltcaligenes suwonensis strain 191B	HP	1/0	Paenaltcaligenes suwonensis	[198]	Yes
78	44250.11	Paenibacillus alvei strain bk032014	HP	1/0	Paenibacillus alvei	[199]	Yes
79	753.7	Pasteurella canis strain QBSD	HP	1/0	Pasteurella canis	[200]	Yes
80	584.1255	Proteus mirabilis strain L76	HP	68/2	Proteus mirabilis	[201]	Yes
81	585.92	Proteus vulgaris strain AS012427	HP	2/0	Proteus vulgaris	[202]	Yes
82	588.149	Providencia stuartii strain AS012498	HP	7/0	Providencia stuartii	[203]	Yes
83	287.11178	Pseudomonas aeruginosa strain PASP309	HP	1957/0	Pseudomonas aeruginosa	[204]	Yes
84	46680.55	Pseudomonas nitroreducens strain SC-1148-IPA-05	HP	1/0	Pseudomonas nitroreducens	[204, 205]	Yes
85	2681497.3	Pseudomonas sp. AU8050	HP	32/0	unclassified Pseudomonas	[206, 207]	Yes
86	190721.31	Ralstonia insidiosa strain 5047 strain not applicable	HP	1/0	Ralstonia insidiosa	[208]	Yes
87	54291.261	Raoultella ornithinolytica strain Z&Z370	HP	10/0	Raoultella ornithinolytica	[209]	Yes
88	575.68	Raoultella planticola strain AS012264	HP	5/0	Raoultella planticola	[210]	Yes
89	648995.31	Rhizobium pusense strain FDAAR-GOS.618 strain Not applicable	HP	3/0	Rhizobium pusense	[211]	Yes
90	615.1093	Serratia marcescens strain C3	HP	137/0	Serratia marcescens	[212]	Yes
91	29378.48	Staphylococcus arlettae strain N283	HP	2/0	Staphylococcus arlettae	[213]	Yes
92	1280.23630	Staphylococcus aureus strain SA15KEN strain not applicable	HP	2605/61	Staphylococcus aureus	[214, 215]	Yes
93	29388.243	Staphylococcus capitis strain 12-400	HP	29/1	Staphylococcus capitis	[216]	Yes
94	1283.793	Staphylococcus haemolyticus strain 166 strain not applicable	HP	131/0	Staphylococcus haemolyticus	[217]	Yes
95	2045451.27	Stenotrophomonas indicatrix strain AS012656	HP	1/0	Stenotrophomonas indicatrix	[218, 219]	Yes
96	40324.1544	Stenotrophomonas maltophilia strain AS012600	HP	216/1	Stenotrophomonas maltophilia	[220]	Yes
97	119602.327	Streptococcus dysgalactiae subsp. equisimilis strain KNZ15	HP	15/0	Streptococcus dysgalactiae	[221]	Yes
98	254785.37	Streptococcus halichoeri strain CCUG67100	HP	1/0	Streptococcus halichoeri	[222]	Yes

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	Genome ID	Genome Name		Label	HP/NHP ¹	Species	References ²	OPP. ³
99	1313.20171	Streptococcus pneumoniae strain GPSC334		HP	4748/235	Streptococcus pneumoniae	[223, 224]	Yes
100	257758.659	Streptococcus pseudopneumoniae strain CCUG 72018		HP	40/0	Streptococcus pseudopneumoniae	[225]	Yes
101	1343.51	Streptococcus vestibularis strain AS012761		HP	1/1	Streptococcus vestibularis	[226, 227]	Yes
102	40545.1254	Sutterella wadsworthensis strain 809h		HP	20/0	Sutterella wadsworthensis	[228, 229]	Yes
103	1648923.136	Bacillus paralicheniformis strain 6-1		NHP	0/2	Bacillus paralicheniformis	[230, 231]	No
104	1423.1028	Bacillus subtilis strain 8-1		NHP	0/3	Bacillus subtilis	[232, 233]	No
105	492670.508	Bacillus velezensis strain Marseille-Q1230		NHP	0/1	Bacillus velezensis	[234, 235]	No
106	28116.1355	Bacteroides ovatus strain F11		NHP	2/28	Bacteroides ovatus	[236, 237]	No
107	820.4961	Bacteroides uniformis strain A23		NHP	2/46	Bacteroides uniformis	[238, 239]	No
108	371601.509	Bacteroides xylanisolvens strain BIOML-A67		NHP	0/11	Bacteroides xylanisolvens	[240, 241]	No
109	1680.1978	Bifidobacterium adolescentis strain BIO5485		NHP	0/24	Bifidobacterium adolescentis	[242]	No
110	28025.139	Bifidobacterium animalis strain BIOML-A2		NHP	0/6	Bifidobacterium animalis	[240, 243]	No
111	1681.836	Bifidobacterium bifidum strain BIOML-A20		NHP	0/33	Bifidobacterium bifidum	[240, 244]	No
112	1689.110	Bifidobacterium dentium strain UT_Austin_Bifido_FMT_C1		NHP	0/4	Bifidobacterium dentium	[245]	No
113	1679.240	Bifidobacterium longum subsp. longum strain BIO6283		NHP	0/60	Bifidobacterium longum	[246]	No
114	1720313.7	Bittarella massiliensis strain BIOML-A2		NHP	0/2	Bittarella massiliensis	[240, 247]	No
115	1737424.51	Blautia massiliensis strain BIOML-A2		NHP	0/4	Blautia massiliensis	[240, 248]	No
116	40520.1620	Blautia obeum strain BIOML-A1		NHP	0/28	Blautia obeum	[240, 249]	No
117	2584624.3	Blautia sp. BIOML-A1		NHP	0/40	unclassified Blautia	[240, 250]	No
118	418240.274	Blautia wexlerae strain BIOML-A15		NHP	0/17	Blautia wexlerae	[240, 251]	No
119	2584625.3	Butyricoccus sp. BIOML-A1		NHP	0/18	unclassified Butyricoccus	[240, 252]	No
120	2584626.3	Catenibacterium sp. BIOML-A1		NHP	0/4	unclassified Catenibacterium	[240, 253]	No
121	1520.337	Clostridium beijerinckii strain BIOML-A8		NHP	0/11	Clostridium beijerinckii	[240, 254]	No
122	2547410.3	Clostridium sp. C5-48		NHP	1/88	unclassified Clostridium	[10]	No
123	2584634.3	Coprobacillus sp. BIOML-A1		NHP	0/39	unclassified Coprobacillus	[240, 255]	No
124	410072.542	Coprococcus comes strain F22		NHP	0/6	Coprococcus comes	[256]	No
125	2584635.3	Coprococcus sp. BIOML-A1		NHP	0/17	unclassified Coprococcus	[240, 257]	No
126	88431.891	Dorea longicatena strain BIOML-A2		NHP	0/14	Dorea longicatena	[240, 258]	No
127	2584637.3	Dorea sp. BIOML-A1		NHP	0/9	unclassified Dorea	[240, 259]	No
128	39490.144	Eubacterium ramulus strain BIOML-A2		NHP	0/4	Eubacterium ramulus	[240, 260]	No

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	Genome ID	Genome Name	Label	HP/NHP ¹	Species	References ²	OPP. ³
129	2584644.3	Eubacterium sp. BIOML-A2	NHP	0/29	unclassified Eubacterium	[240, 261]	No
130	853.7356	Faecalibacterium prausnitzii strain BIOML-B10	NHP	0/39	Faecalibacterium prausnitzii	[240, 262]	No
131	2584645.3	Faecalibacterium sp. BIOML-A1	NHP	0/11	unclassified Faecalibacterium	[240, 263]	No
132	292800.500	Flavonifractor plautii strain BIOML-A3	NHP	0/3	Flavonifractor plautii	[240, 264]	No
133	1335613.28	Gordonibacter urolithinfaciens strain BIOML-A1	NHP	0/1	Gordonibacter urolithinfaciens	[240, 265]	No
134	2686092.3	Halobacillus sp. Marseille-Q1234	NHP	0/1	unclassified Halobacillus	[266]	No
135	1468449.9	Holdemania massiliensis strain BIOML-A4	NHP	0/5	Holdemania massiliensis	[240, 267]	No
136	1613.506	Lactobacillus fermentum strain CVM-347	NHP	1/11	Lactobacillus fermentum	[268]	No
137	1587.365	Lactobacillus helveticus strain DLBSA201	NHP	0/3	Lactobacillus helveticus	[269]	No
138	1597.462	Lactobacillus paracasei strain BIOML-A2	NHP	0/19	Lactobacillus paracasei	[240, 270]	No
139	47715.653	Lactobacillus rhamnosus strain BIOML-A3	NHP	2/20	Lactobacillus rhamnosus	[240, 271]	No
140	1623.232	Lactobacillus ruminis strain BIOML-A15	NHP	0/31	Lactobacillus ruminis	[240, 272]	No
141	2584658.3	Lactonifactor sp. BIOML-A5	NHP	0/7	unclassified Lactonifactor	[240, 273]	No
142	2584661.3	Megasphaera sp. BIOML-A1	NHP	0/4	unclassified Megasphaera	[240, 274]	No
143	28118.1621	Odoribacter splanchnicus strain BIOML-A4	NHP	0/16	Odoribacter splanchnicus	[240, 275]	No
144	823.3208	Parabacteroides distasonis strain BIOML-A11	NHP	5/66	Parabacteroides distasonis	[240, 276]	No
145	328812.119	Parabacteroides goldsteinii strain BIOML-A2	NHP	1/11	Parabacteroides goldsteinii	[240, 277]	No
146	46503.1849	Parabacteroides merdae strain BIOML-A28	NHP	0/43	Parabacteroides merdae	[240, 278]	No
147	487175.63	Parasutterella excrementihominis strain BIOML-A4	NHP	0/15	Parasutterella excrementihominis	[240, 279]	No
148	33025.448	Phascolarctobacterium faecium strain BIOML-A6	NHP	0/17	Phascolarctobacterium faecium	[240, 280]	No
149	2049039.16	Phascolarctobacterium sp. P2A-2	NHP	0/2	unclassified Phascolarctobacterium	[280]	No
150	571933.10	Piscibacillus halophilus strain Marseille-Q1613	NHP	0/1	Piscibacillus halophilus	[281]	No
151	2584670.3	Pseudoflavonifractor sp. BIOML-A8	NHP	0/17	unclassified Pseudoflavonifractor	[240, 282]	No
152	301302.2226	Roseburia faecis strain BIOML-A1	NHP	0/2	Roseburia faecis	[240, 283]	No
153	166486.885	Roseburia intestinalis strain BIOML-A1	NHP	0/6	Roseburia intestinalis	[240, 284]	No
154	40518.2573	Ruminococcus bromii strain BIOML-A2	NHP	3/12	Ruminococcus bromii	[240, 285]	No
155	592978.29	Ruminococcus faecis strain BIOML-A1	NHP	0/1	[Ruminococcus] faecis	[240, 286]	No
156	1550024.413	Ruthenibacterium lactatiformans strain BIOML-A15	NHP	0/13	Ruthenibacterium lactatiformans	[240, 287]	No
157	2681551.3	Staphylococcus sp. 170179	NHP	3/2	unclassified Staphylococcus	[288]	No

Continued on next page

	Genome ID	Genome Name	Label	HP/NHP ¹	Species	References ²	OPP. ³
158	1304.1361	Streptococcus salivarius strain BIOML-A17	NHP	2/43	Streptococcus salivarius	[240, 289]	No
159	2053618.40	Subdoligranulum sp. strain P1-4	NHP	0/6	unclassified Subdoligranulum	[290]	No
160	2093855.3	Veillonellaceae bacterium M2-8	NHP	0/3	unclassified Veillonellaceae	[291, 292]	No
161	39485.1649	[Eubacterium] eligens strain BIOML-A1	NHP	0/13	Lachnospira eligens	[240, 293]	No
162	39491.2484	[Eubacterium] rectale strain BIOML-A5	NHP	6/70	unclassified Lachnospiraceae	[240, 294]	No
163	33039.1028	[Ruminococcus] torques strain BIOML-A5	NHP	0/9	[Ruminococcus] torques	[240, 295]	No
164	1872444.542	Alistipes sp. strain P1-1	NHP	0/5	unclassified Alistipes	[296]	Yes
165	1396.2563	Bacillus cereus strain 2-1	NHP	16/7	Bacillus cereus	[297, 298]	Yes
166	79880.75	Bacillus clausii strain B619/R	NHP	5/0	Bacillus clausii	[299]	Yes
167	818.1282	Bacteroides thetaiotaomicron strain F9-2	NHP	2/15	Bacteroides thetaiotaomicron	[300, 301]	Yes
168	821.3918	Bacteroides vulgatus strain H23	NHP	3/70	Bacteroides vulgatus	[302]	Yes
169	2044936.47	Bacteroidia bacterium strain T-B-M_MAG_00007	NHP	0/3	unclassified Bacteroidia	[303]	Yes
170	2044595.31	Candidatus Gracilibacteria bacterium strain P-C-F_MAG_00005	NHP	0/2	unclassified Candidatus Gracilibacteria	[304]	Yes
171	2026720.132	Candidatus Saccharibacteria bacterium strain T-D-F_MAG_00008	NHP	0/20	unclassified Saccharibacteria	[303]	Yes
172	44737.7	Capnocytophaga sp. strain P-B-M_MAG_00008	NHP	0/1	unclassified Capnocytophaga	[305]	Yes
173	35703.89	Citrobacter amalonaticus strain BIOML-A5	NHP	1/13	Citrobacter amalonaticus	[240, 306]	Yes
174	1898207.3769	Clostridiales bacterium strain T-D-F_MAG_00006	NHP	0/9	unclassified Clostridiales	[303]	Yes
175	1492.181	Clostridium butyricum strain BIOML-A2	NHP	0/2	Clostridium butyricum	[240, 307]	Yes
176	74426.1601	Collinsella aerofaciens strain BIOML-A15	NHP	0/20	Collinsella aerofaciens	[240, 95]	Yes
177	2584631.3	Collinsella sp. BIOML-A4	NHP	0/82	unclassified Collinsella	[240, 95]	Yes
178	218538.1051	Dialister invisus strain P2A-1	NHP	0/1	Dialister invisus	[308]	Yes
179	2584641.3	Eggerthella sp. BIOML-A4	NHP	0/5	unclassified Eggerthella	[240, 309]	Yes
180	158836.472	Enterobacter hormaechei strain BIOML-A4	NHP	305/6	Enterobacter hormaechei	[240, 310]	Yes
181	33945.49	Enterococcus avium strain BIOML-A3	NHP	4/5	Enterococcus avium	[240, 311]	Yes
182	53345.154	Enterococcus durans strain BIOML-A46	NHP	0/67	Enterococcus durans	[240, 312]	Yes
183	1352.8997	Enterococcus faecium strain C59	NHP	666/7	Enterococcus faecium	[66]	Yes
184	1354.275	Enterococcus hirae strain BIOML-A52	NHP	0/87	Enterococcus hirae	[240, 313]	Yes
185	53346.66	Enterococcus mundtii strain BIOML-A5	NHP	1/14	Enterococcus mundtii	[240, 314]	Yes
186	71452.14	Enterococcus raffinosus strain BIOML-A1	NHP	0/1	Enterococcus raffinosus	[240, 315]	Yes
187	1260.144	Finegoldia magna strain BIOML-A2	NHP	10/2	Finegoldia magna	[240, 316]	Yes
188	2584653.3	Finegoldia sp. BIOML-A5	NHP	0/5	unclassified Finegoldia	[240, 317]	Yes
189	1871037.250	Flavobacteriaceae bacterium strain P-A-M_MAG_00002	NHP	1/3	unclassified Flavobacteriaceae	[318]	Yes

Continued on next page

	Genome ID	Genome Name		Label	HP/NHP ¹	Species		References ²	OPP. ³
190	471189.25	Gordonibacter pamelaee strain BIOML-A2		NHP	0/1	Gordonibacter pamelaee		[240, 319]	Yes
191	104608.5	Leptotrichia sp. strain T-B-M_MAG_00008		NHP	0/1	unclassified Leptotrichia		[303]	Yes
192	1246.49	Leuconostoc lactis strain BIOML-A1		NHP	0/2	Leuconostoc lactis		[240, 320]	Yes
193	2049035.5	Mogibacterium sp. strain T-C-M_MAG_00002		NHP	0/3	unclassified Mogibacterium		[303]	Yes
194	1505.72	Paeniclostridium sordellii strain BIOML-A6		NHP	4/2	Paeniclostridium sordellii		[240, 321]	Yes
195	165179.2440	Prevotella copri strain P2B-2		NHP	0/21	Prevotella copri		[322]	Yes
196	59823.699	Prevotella sp. strain P-A-F_MAG_00002		NHP	1/7	unclassified Prevotella		[323, 324, 325]	Yes
197	1282.3805	Staphylococcus epidermidis strain JH		NHP	85/69	Staphylococcus epidermidis		[326, 327]	Yes
198	1311.2752	Streptococcus agalactiae strain M134		NHP	236/5	Streptococcus agalactiae		[328]	Yes
199	1318.781	Streptococcus parasanguinis strain BIOML-A16		NHP	3/25	Streptococcus parasanguinis		[240, 329]	Yes
200	2584682.3	Streptococcus sp. BIOML-A1		NHP	4/5	unclassified Streptococcus		[240, 330]	Yes
201	39778.876	Veillonella dispar strain BIOML-A2		NHP	0/3	Veillonella dispar		[240, 331]	Yes
202	29466.1006	Veillonella parvula strain BIOML-A1		NHP	1/4	Veillonella parvula		[240, 332]	Yes
203	1522.125	[Clostridium] innocuum strain BIOML-A2		NHP	0/15	[Clostridium] innocuum		[240, 333]	Yes
204	2044938.12	candidate division SR1 bacterium strain P-B-M_MAG_00018		NHP	0/19	unclassified Bacteria		[303]	Yes

Table S3: A list of genomes included in the WSPC test set. ¹HP to NHP ratio among the labeled genomes of the corresponding species (before choosing a representative from each species). ²References to literature or a database entry asserting the label and the "group" annotations the corresponding genome belongs to. ³OPP: opportunistic.

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