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Comparative Genomic Analyses of Copper Transporters and Cuproproteomes Reveal Evolutionary Dynamics of Copper Utilization and Its Link to Oxygen

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Copper is an essential trace element in many organisms and is utilized in all domains of life. It is often used as a cofactor of redox proteins, but is also a toxic metal ion. Intracellular copper must be carefully handled to prevent the formation of reactive oxygen species which pose a threat to DNA, lipids, and proteins. In this work, we examined patterns of copper utilization in prokaryotes by analyzing the occurrence of copper transporters and copper-containing proteins. Many organisms, including those that lack copper-dependent proteins, had copper exporters, likely to protect against copper ions that inadvertently enter the cell. We found that copper use is widespread among prokaryotes, but also identified several phyla that lack cuproproteins. This is in contrast to the use of other trace elements, such as selenium, which shows more scattered and reduced usage, yet larger selenoproteomes. Copper transporters had different patterns of occurrence than cuproproteins, suggesting that the pathways of copper utilization and copper detoxification are independent of each other. We present evidence that organisms living in oxygen-rich environments utilize copper, whereas the majority of anaerobic organisms do not. In addition, among copper users, cuproproteomes of aerobic organisms were larger than those of anaerobic organisms. Prokaryotic cuproproteomes were small and dominated by a single protein, cytochrome c oxidase. The data are consistent with the idea that proteins evolved to utilize copper following the oxygenation of the Earth.

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INTRODUCTION

All organisms are thought to require metal ion cofactors (i.e., Fe, Zn, Mg, Mn, Co, Ni and Cu) which are involved in a wide variety of cellular processes. Additionally, certain non-metal trace elements, such as selenium (Se), and iodine (I) may be utilized. Most of these elements are necessary for redox catalysis and other enzymatic reactions, for sensing and signaling, and some serve structural roles in proteins. Defects in their homeostasis have been linked to a variety of diseases [1–4].

Metals are particularly important for life and may have been utilized by organisms since the time life originated on Earth. For example, before the advent of oxygenic photosynthesis, the most active ecosystems were probably driven by the cycling of H_2 and Fe^{2+} through primary production conducted by anoxygenic phototrophs [5]. Additionally, it is thought that a substrate-level phosphorylation cycle may have been an early form of metabolism – one which required both iron and molybdenum [6].

Biological metal utilization has been driven, at least in part, by availability. As the Earth has evolved its chemical environment has significantly changed, which altered availability of certain metal ions [7,8]. For example, as environmental oxygen increased, various metal ions, such as Cu, Co, Ni, Zn, Cd, and Mo were released from their sulfide forms and became more soluble [8], making them more readily available for biological utilization. Oxygenation of the Earth also changed the redox state of some metal ions, such as Fe (Fe^{2+} to Fe^{3+}), which reduced its availability [8]. Accordingly, organisms became less dependent on the metal ions that were scarce and adapted to use the available metal ions [7].

Studying metal use in organisms can provide various insights. In this study, we use the term metalloproteome, which is a subset of the proteins from a particular proteome, which bind metal ions. Improved understanding of the composition and functions of metalloproteomes in prokaryotes, combined with our knowledge of the chemical evolution of the earth, can help decipher the evolutionary relationships among organisms and improve understanding of the roles metals play in biology. Analyses of evolutionary trends in trace element utilization have been performed for several trace elements, such as Fe and Mn [9], Se [10,11], and Ni and Co [12].

One of the widely used trace elements is copper. This metal ion is known to be a cofactor in a number of proteins. Copper is redox-active (in biological systems it can exist as either Cu^{2+} or Cu^{+} and is more reactive in its reduced state [13]) and consequently, is a highly toxic element. The challenge, then, for copper-dependent organisms is to obtain sufficient levels of this metal ion to meet their needs, while tightly controlling intracellular copper to avoid toxicity. It is likely that little free copper exists in the cytoplasm (the same is not necessarily true for the periplasm [14]), both because of its toxicity, and because it exists at such low concentrations in the cytoplasm that it is unlikely to encounter its target proteins in a reasonable amount of time without assistance [15]. Thus, it is likely that copper is delivered to target proteins by metallochaperones.

To date, 10 Cu-containing proteins (cuproproteins) have been characterized in prokaryotes, including cytochrome c oxidase (COX), NADH dehydrogenase-2 (ND2), Cu,Zn-superoxide dis-

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mutase (SOD1), nitrosocyanin, plastocyanin, Cu-containing nitrite reductase, Cu amine oxidase, particulate methane monooxygenase (pMMO), CotA, and tyrosinase. Each of these proteins is unable to substitute other metal ions for copper. Biosynthesis of cuproproteins is dependent on high-affinity uptake of the copper ion from natural environments, regulatory proteins, and other auxiliary proteins.

In prokaryotes, two chaperones [14,16,17] and 9 Cu-specific transporters have been reported and only one of these transporters, CtaA, has a clearly defined role as an importer [14,18–20]. CtaA imports copper from the periplasm rather than extracellular space [13,18,19]. Another transporter, PacS, transports copper from the cytoplasm to the thylakoid and assists in copper homeostasis [18,19]. PacS is a class of CopA [21], another transporter. CopA presents a unique challenge as multiple different copper transporters (and cuproproteins) have been named CopA. In *Escherichia coli*, CopA is an exporter, in *Enterococcus hirae* an importer (homologous to CtaA), and in *Pseudomonas* and *Xanthomonas* a multicopper oxidase [22]. Regarding CopA transporters, there were two protein subgroups: a CopA1 subfamily containing ATPases with documented Cu^+ influx activity, and CopA2 proteins that are more ancient and include both influx and efflux transporters spanning the entire bacterial domain [21].

In recent years, the complete genomes of numerous prokaryotic organisms have become available. Using this resource, it is possible to examine the occurrence and evolution of numerous biological pathways that organisms utilize. In this study we performed a comprehensive genome-wide investigation of both copper transport systems and cuproproteins. We analyzed 450 bacterial and 35 archaeal organisms for copper utilization. Our data revealed that copper is used by most prokaryotes and that cuproproteomes are larger in organisms living in oxygen-rich environments. Our results suggest that copper use increased as the atmosphere became more oxygenic.

Table 1. List of cuproproteins and copper transporters, chaperones, and regulators examined in the study.

#	Protein	Protein category [reference]
1	Cytochrome C Oxidase Family	Enzyme [18]
2	NADH dehydrogenase-2	Enzyme [23,24]
3	Superoxide dismutase	Enzyme [25]
4	Nitrosocyanin Family	Enzyme [26]
5	Plastocyanin Family	Enzyme [18]
6	Cu-containing nitrite reductase	Enzyme [27]
7	Cu amine oxidase	Enzyme [28]
8	Particulate methane monooxygenase (pMMO)	Enzyme [29]
9	CotA	Enzyme [30]
10	Tyrosinase (melc2)	Enzyme [31]
11	PacS, CopA (*E. coli*), CopB (*E. hirae*)	Efflux system [13,15,16,18,19,32]
12	CutC	Efflux system [17,33,34]
13	CopB	Efflux system [13,34]
14	PcoA (multicopper oxidase)	Efflux system [13,32]
15	CueO (multicopper oxidase)	Efflux system [13,32,34]
16	PcoC	Efflux system [2,4]
17	CusCFBA	Efflux system [2,4,14]
18	PcoE	Efflux system [2,4]
19	CtaA, CopA (*E. hirae*)	Importer [13,16,19,20]
20	CopZ, Atx1 (*Synechocystis* PCC 6803)	Chaperone [16,17]
21	CopC	Chaperone, possibly efflux [14,17,35]
22	CopD	Not clear, possibly importer [17,35,36]

The numbers in the first column are the numbers used in Figures 1–3 to identify the cuproproteins.

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RESULTS

Identification of Cu-utilizing prokaryotes

We examined 450 sequenced bacterial genomes and 35 sequenced archaeal genomes for copper utilization by searching for occurrence of cuproproteins (see Table 1 for a list of reference proteins). A majority of bacteria (326 of the 450 analyzed, or 72%) were found to be copper-utilizing or users (i.e., organisms that had at least one copper-dependent protein), while the remaining 124 bacteria (28%), appeared to be nonusers (i.e., organisms in which we were unable to identify even a single cuproprotein). In contrast, among archaea, most organisms appeared to be nonusers (24 archaea, or 69%), whereas 11 archaea, or 31%, were users. Overall, copper utilization was widely distributed in prokaryotes, with more than 2/3 of all organisms being dependent on this metal. Detailed distribution of copper utilization among prokaryotes is reported in Table S1.

Of 22 examined bacterial phyla represented by at least 4 completely sequenced genomes, 7 (enterobacteriales, vibrionaceae, pseudomonadaceae, xanthomonadaceae, burkholderiaceae, rhizobiaceae and cyanobacteria) consisted of bacteria that were all users. In addition, almost all bacteria from an additional 5 phyla (pasteurellaceae, rickettsiales, chloroflexi, actinobacteria, and bacillales) were users (Figure 1).

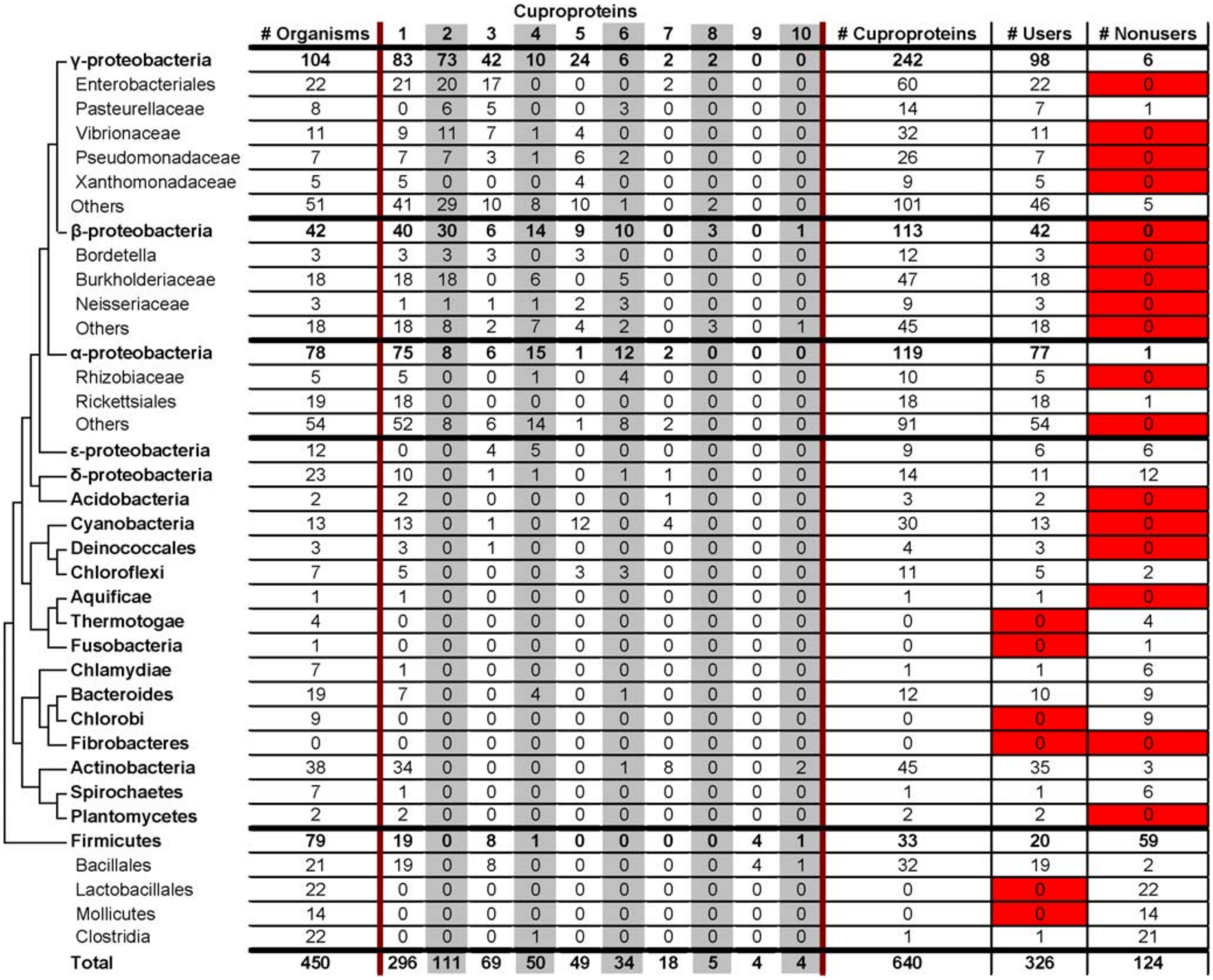
Only a few bacterial phyla (thermotogae, chlorobi, lactobacillales, and mollicutes) consisted exclusively of apparent nonusers. In addition, all but one bacterium from each of an additional three phyla (chlamydiae, spirochaetes, and clostridia) appeared to be nonusers. The phyla with the highest number of apparent nonusers were subphyla of firmicutes, which are among the most ancient organisms. Interestingly, even though we found no connection between genome size and copper use in the bacterial domain, for firmicutes, users had an average genome size of 3.93 Mb while the genome size of nonusers was only 2.27 Mb.

In archaea, the trend was somewhat reversed. There were 5 phyla with 4 or more representative organisms and only 2 of these, sulfobales and halobacteriales, consisted of exclusively users. Archaea from sulfobales prefer a harsh environment (temperature of 74°C or higher and pH of 3 or lower). In contrast, halobacteriales prefer a mild environment (temperature of 25°C and neutral pH).

Lastly, archaea from two additional phyla (methanosarcinales and thermococcales) all appeared to be nonusers, and all but one archaeon (*Picrophilus torridus* is the exception) from the final remaining phylum, thermoplasmales, were classified as nonusers (Figure 2).

Distribution of Cu transporter systems

Table 1 also shows all of the Cu importers/exporters analyzed in our study. CtaA (CopA in *Enterococcus hirae* [16]), the only identified Cu-specific importer, was only present in cyanobacteria. 13 different cyanobacteria were included in this study and all but one had CtaA (Figure 3). No archaea that utilize CtaA were identified (Figure 2). Each of the organisms that utilize CtaA also utilizes at least one cuproprotein.



		Cuproproteins												
	# Organisms	1	2	3	4	5	6	7	8	9	10	# Cuproproteins	# Users	# Nonusers
γ-proteobacteria	**104**	**83**	**73**	**42**	**10**	**24**	**6**	**2**	**2**	**0**	**0**	**242**	**98**	**6**
Enterobacteriales	22	21	20	17	0	0	0	2	0	0	0	60	22	0
Pasteurellaceae	8	0	6	5	0	0	3	0	0	0	0	14	7	1
Vibrionaceae	11	9	11	7	1	4	0	0	0	0	0	32	11	0
Pseudomonadaceae	7	7	7	3	1	6	2	0	0	0	0	26	7	0
Xanthomonadaceae	5	5	0	0	0	4	0	0	0	0	0	9	5	0
Others	51	41	29	10	8	10	1	0	2	0	0	101	46	5
β-proteobacteria	**42**	**40**	**30**	**6**	**14**	**9**	**10**	**0**	**3**	**0**	**1**	**113**	**42**	**0**
Bordetella	3	3	3	3	0	3	0	0	0	0	0	12	3	0
Burkholderiaceae	18	18	18	0	6	0	5	0	0	0	0	47	18	0
Neisseriaceae	3	1	1	1	1	2	3	0	0	0	0	9	3	0
Others	18	18	8	2	7	4	2	0	3	0	1	45	18	0
α-proteobacteria	**78**	**75**	**8**	**6**	**15**	**1**	**12**	**2**	**0**	**0**	**0**	**119**	**77**	**1**
Rhizobiaceae	5	5	0	0	1	0	4	0	0	0	0	10	5	0
Rickettsiales	19	18	0	0	0	0	0	0	0	0	0	18	18	1
Others	54	52	8	6	14	1	8	2	0	0	0	91	54	0
ε-proteobacteria	12	0	0	4	5	0	0	0	0	0	0	9	6	6
δ-proteobacteria	23	10	0	1	1	0	1	1	0	0	0	14	11	12
Acidobacteria	2	2	0	0	0	0	0	1	0	0	0	3	2	0
Cyanobacteria	13	13	0	1	0	12	0	4	0	0	0	30	13	0
Deinococcales	3	3	0	1	0	0	0	0	0	0	0	4	3	0
Chloroflexi	7	5	0	0	0	3	3	0	0	0	0	11	5	2
Aquificae	1	1	0	0	0	0	0	0	0	0	0	1	1	0
Thermotogae	4	0	0	0	0	0	0	0	0	0	0	0	0	4
Fusobacteria	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Chlamydiae	7	1	0	0	0	0	0	0	0	0	0	1	1	6
Bacteroides	19	7	0	0	4	0	1	0	0	0	0	12	10	9
Chlorobi	9	0	0	0	0	0	0	0	0	0	0	0	0	9
Fibrobacteres	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Actinobacteria	38	34	0	0	0	0	1	8	0	0	2	45	35	3
Spirochaetes	7	1	0	0	0	0	0	0	0	0	0	1	1	6
Plantomycetes	2	2	0	0	0	0	0	0	0	0	0	2	2	0
Firmicutes	**79**	**19**	**0**	**8**	**1**	**0**	**0**	**0**	**0**	**4**	**1**	**33**	**20**	**59**
Bacillales	21	19	0	8	0	0	0	0	0	4	1	32	19	2
Lactobacillales	22	0	0	0	0	0	0	0	0	0	0	0	0	22
Mollicutes	14	0	0	0	0	0	0	0	0	0	0	0	0	14
Clostridia	22	0	0	0	1	0	0	0	0	0	0	1	1	21
Total	**450**	**296**	**111**	**69**	**50**	**49**	**34**	**18**	**5**	**4**	**4**	**640**	**326**	**124**

Figure 1. Occurrence of cuproproteins in bacteria. Phylogenetic tree was adapted from [37]. Reported is the total number of bacteria for each phylum and the numbers of bacteria that utilize a given cuproprotein. Numbers across the top refer to the cuproproteins in Table 1. The last two columns (Users and Nonusers) refer to the number of organisms in the specific phylum that are users and nonusers, respectively. Fields colored in red represent phyla where all bacteria belonging to that phylum were classified as either users or nonusers. The "# Cuproproteins" column shows the total number of cuproproteins utilized by all bacteria belonging to a particular phylum.

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In bacteria, PacS (CopA in *Escherichia coli* [32] or CopB in *Enterococcus hirae* [16]) was the most widespread copper exporter. PacS was identified in 355 of 450 bacteria and was present in 29 of 32 phyla (absent in mollicutes, thermotogae, and rickettsiales). In archaea, CopA (PacS) was the only transporter identified (Figure 2). It was present in 6 of 13 phyla (archaeoglobales, halobacteriales, methanobacteriales, methanomicrobiales, methanosarcinales, and thermococcales).

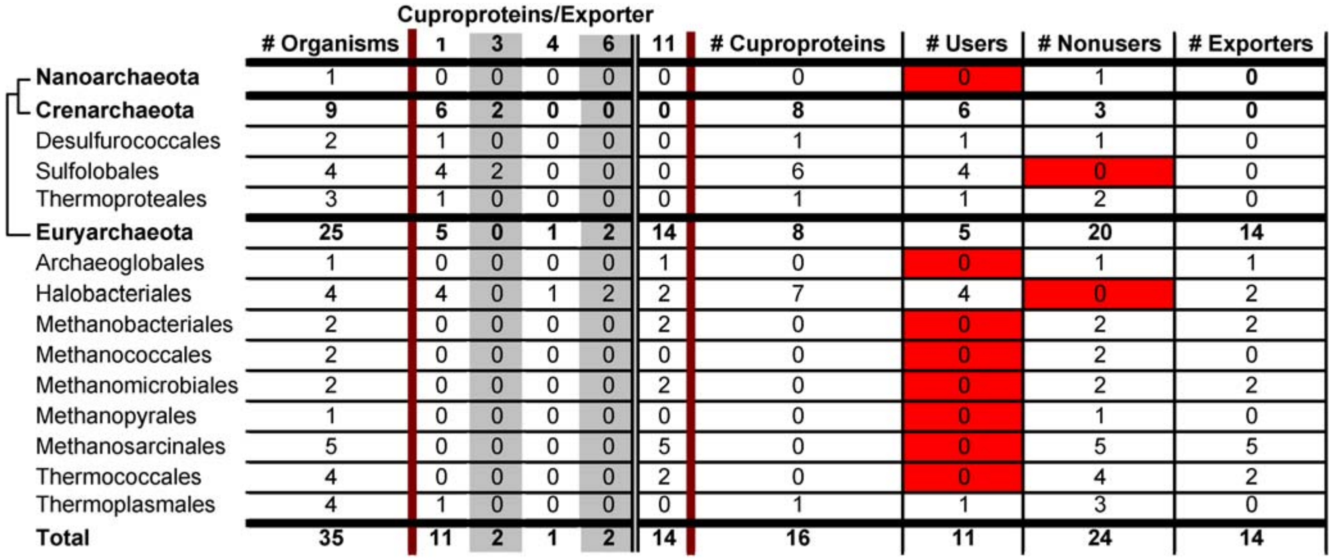
These two transporters, CtaA and PacS, have complimentary roles. CtaA is responsible for copper import from the periplasm to the cytoplasm and PacS is responsible for copper transport to the thylakoid [13,18,19]. Consistent with this, all of the examined organisms that appeared to utilize CtaA also utilize PacS.

We also examined the genomes for the other 7 copper exporters and observed some interesting features. Most organisms had copper exporters, even if they appeared to be nonusers. Nearly 50% of nonusers had copper exporters while about 25% of users appeared to lack these proteins. It is interesting to note that more than half of the bacteria that did not have exporters (79 of 142, or 56%) were parasites (overall, only 29% of the examined bacteria were parasites). Regarding the occurrence of exporters in archaea, we again observed a reversal of the trend compared to bacteria. Only 2 users (18%) had exporters while exactly half the nonusers had these proteins.

There did not appear to be any trend of importers and exporters co-occurring except for CtaA and PacS; however, PacS is nearly ubiquitous while CtaA is utilized by only a few organisms. CtaA and PacS as well as other importers and exporters are likely differentially regulated.

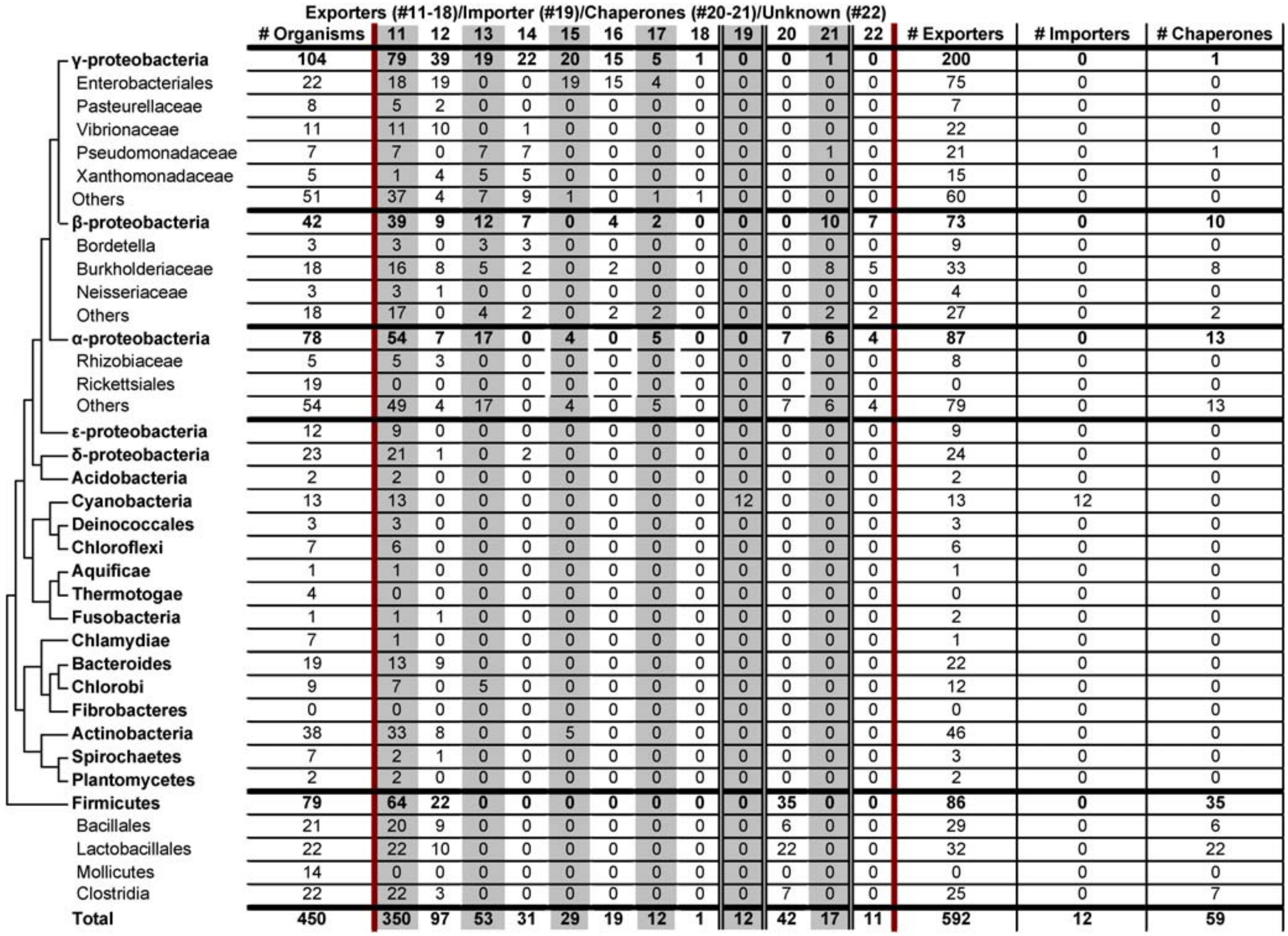
Composition of cuproproteomes

For further discussion, we introduce and define the term cuproproteome. The cuproproteome of an organism is the set of proteins from its proteome which require a copper ion for their biological function (typically catalysis). Transporters, chaperones, and storage proteins constitute cellular Cu transport and maintenance machinery and are not part of the cuproproteome.



	# Organisms	Cuproproteins/Exporter 1	3	4	6	11	# Cuproproteins	# Users	# Nonusers	# Exporters
Nanoarchaeota	1	0	0	0	0	0	0	0	1	**0**
Crenarchaeota	**9**	**6**	**2**	**0**	**0**	**0**	**8**	**6**	**3**	**0**
Desulfurococcales	2	1	0	0	0	0	1	1	1	0
Sulfolobales	4	4	2	0	0	0	6	4	0	0
Thermoproteales	3	1	0	0	0	0	1	1	2	0
Euryarchaeota	**25**	**5**	**0**	**1**	**2**	**14**	**8**	**5**	**20**	**14**
Archaeoglobales	1	0	0	0	0	1	0	0	1	1
Halobacteriales	4	4	0	1	2	2	7	4	0	2
Methanobacteriales	2	0	0	0	0	2	0	0	2	2
Methanococcales	2	0	0	0	0	0	0	0	2	0
Methanomicrobiales	2	0	0	0	0	2	0	0	2	2
Methanopyrales	1	0	0	0	0	0	0	0	1	0
Methanosarcinales	5	0	0	0	0	5	0	0	5	5
Thermococcales	4	0	0	0	0	2	0	0	4	2
Thermoplasmales	4	1	0	0	0	0	1	1	3	0
Total	**35**	**11**	**2**	**1**	**2**	**14**	**16**	**11**	**24**	**14**

Figure 2. Occurrence of cuproproteins in Archaea. Reported is the occurrence (by phylum) of cuproproteins and Cu exporters in archaea. No importers, repressors, or chaperones were identified in archaea. See legend to Figure 1 for further details.
doi:10.1371/journal.pone.0001378.g002



	# Organisms	Exporters (#11-18)/Importer (#19)/Chaperones (#20-21)/Unknown (#22) 11	12	13	14	15	16	17	18	19	20	21	22	# Exporters	# Importers	# Chaperones
γ-proteobacteria	**104**	**79**	**39**	**19**	**22**	**20**	**15**	**5**	**1**	**0**	**0**	**1**	**0**	**200**	**0**	**1**
Enterobacteriales	22	18	19	0	0	19	15	4	0	0	0	0	0	75	0	0
Pasteurellaceae	8	5	2	0	0	0	0	0	0	0	0	0	0	7	0	0
Vibrionaceae	11	11	10	0	1	0	0	0	0	0	0	0	0	22	0	0
Pseudomonadaceae	7	7	0	7	7	0	0	0	0	0	0	1	0	21	0	1
Xanthomonadaceae	5	1	4	5	5	0	0	0	0	0	0	0	0	15	0	0
Others	51	37	4	7	9	1	0	1	1	0	0	0	0	60	0	0
β-proteobacteria	**42**	**39**	**9**	**12**	**7**	**0**	**4**	**2**	**0**	**0**	**0**	**10**	**7**	**73**	**0**	**10**
Bordetella	3	3	0	3	3	0	0	0	0	0	0	0	0	9	0	0
Burkholderiaceae	18	16	8	5	2	0	2	0	0	0	0	8	5	33	0	8
Neisseriaceae	3	3	1	0	0	0	0	0	0	0	0	0	0	4	0	0
Others	18	17	0	4	2	0	2	2	0	0	0	2	2	27	0	2
α-proteobacteria	**78**	**54**	**7**	**17**	**0**	**4**	**0**	**5**	**0**	**0**	**7**	**6**	**4**	**87**	**0**	**13**
Rhizobiaceae	5	5	3	0	0	0	0	0	0	0	0	0	0	8	0	0
Rickettsiales	19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Others	54	49	4	17	0	4	0	5	0	0	7	6	4	79	0	13
ε-proteobacteria	12	9	0	0	0	0	0	0	0	0	0	0	0	9	0	0
δ-proteobacteria	23	21	1	0	2	0	0	0	0	0	0	0	0	24	0	0
Acidobacteria	2	2	0	0	0	0	0	0	0	0	0	0	0	2	0	0
Cyanobacteria	13	13	0	0	0	0	0	0	0	12	0	0	0	13	12	0
Deinococcales	3	3	0	0	0	0	0	0	0	0	0	0	0	3	0	0
Chloroflexi	7	6	0	0	0	0	0	0	0	0	0	0	0	6	0	0
Aquificae	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Thermotogae	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Fusobacteria	1	1	1	0	0	0	0	0	0	0	0	0	0	2	0	0
Chlamydiae	7	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Bacteroides	19	13	9	0	0	0	0	0	0	0	0	0	0	22	0	0
Chlorobi	9	7	0	5	0	0	0	0	0	0	0	0	0	12	0	0
Fibrobacteres	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Actinobacteria	38	33	8	0	0	5	0	0	0	0	0	0	0	46	0	0
Spirochaetes	7	2	1	0	0	0	0	0	0	0	0	0	0	3	0	0
Plantomycetes	2	2	0	0	0	0	0	0	0	0	0	0	0	2	0	0
Firmicutes	**79**	**64**	**22**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**35**	**0**	**0**	**86**	**0**	**35**
Bacillales	21	20	9	0	0	0	0	0	0	0	6	0	0	29	0	6
Lactobacillales	22	22	10	0	0	0	0	0	0	0	22	0	0	32	0	22
Mollicutes	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Clostridia	22	22	3	0	0	0	0	0	0	0	7	0	0	25	0	7
Total	**450**	**350**	**97**	**53**	**31**	**29**	**19**	**12**	**1**	**12**	**42**	**17**	**11**	**592**	**12**	**59**

Figure 3. Occurrence of transporters, repressors and chaperones in bacteria. Phylogenetic tree was adapted from [37]. Reported are the number of bacteria (by phylum) which utilized a given transporter, repressor, or chaperone. Numbers across the top refer to specific transporters or chaperones (see Table 1 for protein names). Columns 10–17 are exporters, column 18 is the sole importer, columns 19–20 are chaperones, and column 21 is a transporter whose exact function has not been characterized. The last four columns report the number of exporters, importers, and chaperones present in each phyla.
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Analysis of cuproproteomes revealed that organisms having cuproproteomes of identical size do not necessarily have the same set of cuproproteins. The biological function of copper is maintained by cuproproteomes, whereas the Cu transport and maintenance machinery serves an intermediate role and is not preserved during evolution when an organism lacks cuproproteins.

Distribution of cuproproteins is reported in Figures 1 and 2 for bacteria and archaea, respectively. In bacteria, the most frequently utilized cuproprotein was cytochrome c oxidase (COX). COX was identified in 296 bacteria, or 91% of the users. Moreover, among those that appeared to utilize a single cuproprotein, about 70% (94 out of 136 organisms) only utilized COX. The same was true for archaea. COX was utilized by all 11 of the archaeal users. 7 of the 11 (64%) archaeal users only utilized COX.

No other cuproproteins were nearly as widespread in bacteria. The second most frequently utilized cuproprotein was NADH dehydrogenase-2 (ND2) – utilized by 111 bacteria, or 34% of the users. Superoxide dismutase 1 (SOD1) was the only other cuproprotein utilized by more than 20% of the users (utilized by 21%), and was found predominantly in gram-negative bacteria. The remaining cuproproteins were utilized by 15% or less of the users and their frequencies were as follows:

- nitrosocyanin, 15%
- plastocyanin, 15%
- Cu-containing nitrite reductase, 10%
- Cu-amine oxidase, 6%
- pMMO, 2%
- CotA, 1%
- tyrosinase, 1%

Only four cuproproteins were identified in archaea: COX, SOD1, nitrosocyanin, and Cu-containing nitrite reductase. As previously mentioned, COX was utilized by 11 archaea (all of the users) and SOD1, Cu-containing nitrite reductase, and nitrosocyanin, were only utilized by 2 (14% of the users), 2 (14% of the users), and 1 (7% of the users) archaea, respectively.

Although 9 cuproproteins are known, none of the examined organisms utilized all of them. In fact, cuproproteomes of most bacteria were quite small, with the largest identified bacterial cuproproteome having only 5 cuproproteins. Only a single bacterium (*Acidovorax avenae*), less than 1% of all the bacteria included in the study, had a cuproproteome consisting of 5 cuproproteins. More common, although still infrequent, were bacteria having cuproproteomes of 4 cuproproteins; 29 bacteria or 6% had 4 cuproproteins in their cuproproteomes. The most common cuproproteomes had only one cuproprotein (128, or 28%, of all bacteria). It is interesting to note that the second most common cuproproteome size was 0 cuproproteins (124, or 28% of bacteria). So, while copper use was widespread in bacteria, most copper-dependent organisms utilized few cuproproteins (Figure 4).

Archaeal cuproproteomes appeared to be even smaller. The largest identified cuproproteome had only 3 cuproproteins (found only in *Haloarcula marismortui*). 3 archaea (*Sulfolobus acidocaldarius*, *Sulfolobus solfataricus*, and *Natronomonas pharaonis*), or 9%, had cuproproteomes consisting of two cuproproteins. Most archaea (~70%) appeared to utilize no cuproproteins (Figures 2 and 5).

Copper utilization in relation to environmental factors and organism features

We analyzed the following environmental factors and organism features to determine their effect on copper utilization:

- Habitat
- Oxygen requirement
- Genome size
- GC % in genome
- Gram strain (bacteria)
- Methanogen (archaea)
- Optimal temperature
- Optimal pH

One feature that showed a clear association was oxygen requirement. In our study, 82 (18%) bacteria were anaerobic, 205 (46%) aerobic, 140 (31%) facultative, and 23 (5%) microaerophilic. Most anaerobic bacteria (62 of 85, or 73%) were nonusers, while most aerobic bacteria (192 of 205, or 94%) were users. 99 of 140 facultative bacteria (71%) and 15 of 23 microaerophilic bacteria (65%) were users (Figure 6). Excluding facultative organisms, a Chi-square test showed a statistically significant difference in Cu utilization between aerobic (including microaerophilic) and anaerobic organisms (P-value$<$0.01).

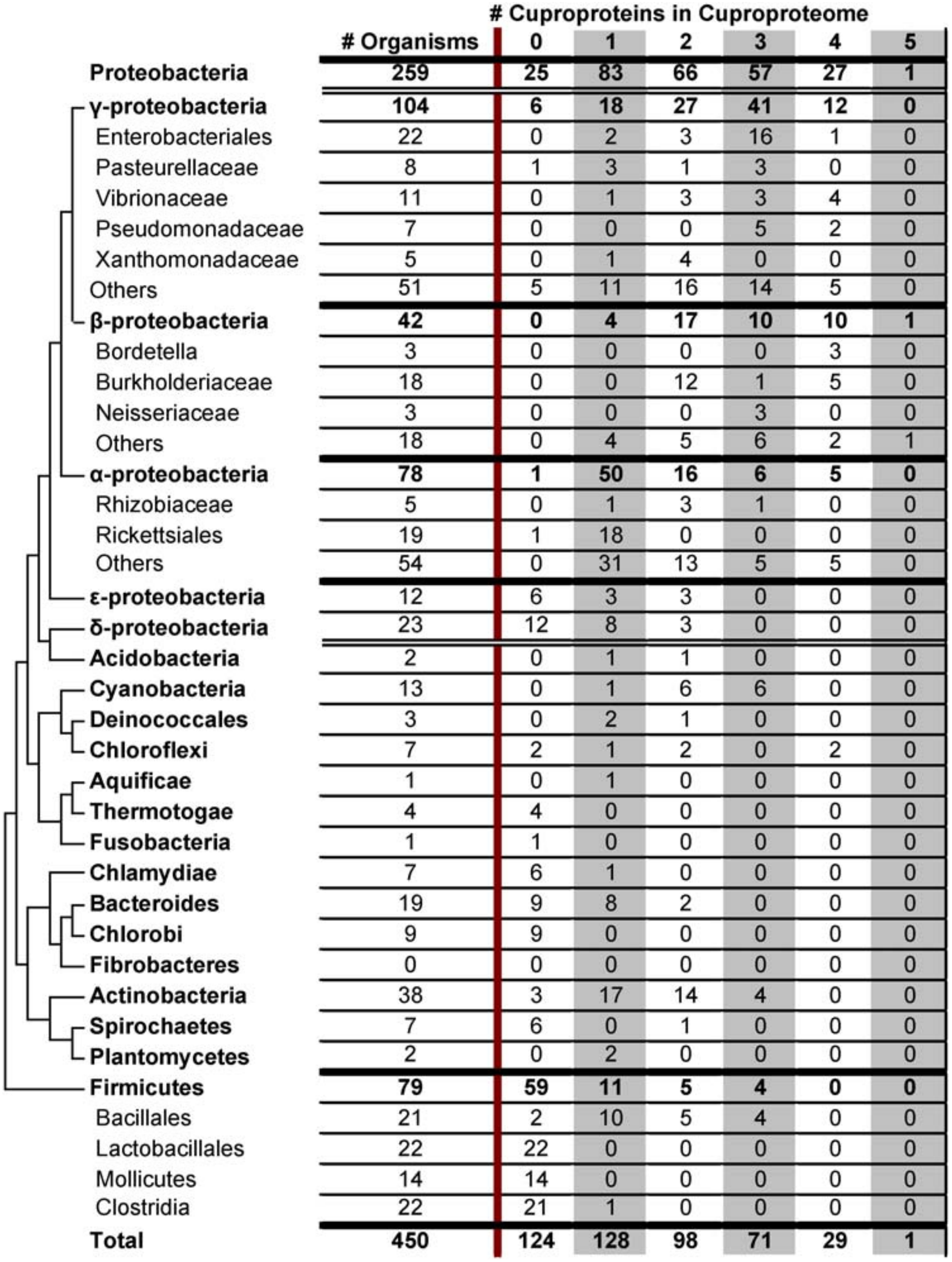
This trend was even more pronounced in archaea (Figure 7). We examined 21 anaerobic, 9 aerobic, and 5 facultative archaea. All 21 anaerobic archaea were nonusers and all 9 aerobic archaea were users. Similarly, a Chi-square test suggested a significant difference in Cu utilization between aerobic and anaerobic species (P-value$<$0.01). Thus, such a striking preference for the use of copper in aerobic organisms is present in both kingdoms of prokaryotes.

Not surprising, based on these results, aerobic bacteria had the largest average cuproproteomes with an average size of 1.8 cuproproteins, compared to anaerobic bacteria which had the smallest average cuproproteomes (0.4 cuproproteins). Surprising, however, is that among users, facultative and microaerophilic bacteria had larger average cuproproteomes (2.26 cuproproteins) than aerobic users which had an average cuproproteome of 1.93 cuproproteins. In archaea, where all the aerobic organisms are users and all the anaerobic organisms are nonusers, aerobic organisms clearly have the larger average cuproproteomes.

DISCUSSION

Oxygen levels are thought to have been quite low until 2.45 billion years ago, but by 2.32 billion years ago had sharply risen [38]. Oxygen levels rose following the origin of oxygenic photosynthetic organisms [39]. At the same time, levels of bioavailable copper increased [40]. Prior to ocean oxygenation, copper likely existed as a sulfide and was insoluble in aqueous solutions. It was suggested [41] that copper was largely unavailable for cellular life; however, upon the rise of oxygen in the atmosphere, copper was converted, at least in part to Cu^{2+}, and as such, became more soluble and more readily available for biological use [41]. It is possible that at least some bacteria evolved near hydrothermal vents in waters replete with heavy metal ions, where sulfides would likely have been more soluble. However, the large-scale evolution of cuproproteins likely occurred in oxygen-rich environments where copper was plentiful. Our analyses of copper utilizing prokaryotes clearly support this idea. We found that in most prokaryotes that require oxygen are copper users, while most anaerobic prokaryotes are nonusers.

Prior to the evolution of cuproproteins, organisms may have already utilized copper exporters [16], but with the increase in soluble copper, this function became even more important as a means of removal of this metal ion. The presence of copper exporters in nonusers and the sheer number of known copper exporters suggest that copper can be taken up accidentally and these organisms need a defense mechanism against copper ions that inadvertently enter the cell.



	# Organisms	# Cuproproteins in Cuproproteome					
		0	1	2	3	4	5
Proteobacteria	**259**	**25**	**83**	**66**	**57**	**27**	**1**
γ-proteobacteria	**104**	**6**	**18**	**27**	**41**	**12**	**0**
Enterobacteriales	22	0	2	3	16	1	0
Pasteurellaceae	8	1	3	1	3	0	0
Vibrionaceae	11	0	1	3	3	4	0
Pseudomonadaceae	7	0	0	0	5	2	0
Xanthomonadaceae	5	0	1	4	0	0	0
Others	51	5	11	16	14	5	0
β-proteobacteria	**42**	**0**	**4**	**17**	**10**	**10**	**1**
Bordetella	3	0	0	0	0	3	0
Burkholderiaceae	18	0	0	12	1	5	0
Neisseriaceae	3	0	0	0	3	0	0
Others	18	0	4	5	6	2	1
α-proteobacteria	**78**	**1**	**50**	**16**	**6**	**5**	**0**
Rhizobiaceae	5	0	1	3	1	0	0
Rickettsiales	19	1	18	0	0	0	0
Others	54	0	31	13	5	5	0
ε-proteobacteria	12	6	3	3	0	0	0
δ-proteobacteria	23	12	8	3	0	0	0
Acidobacteria	2	0	1	1	0	0	0
Cyanobacteria	13	0	1	6	6	0	0
Deinococcales	3	0	2	1	0	0	0
Chloroflexi	7	2	1	2	0	2	0
Aquificae	1	0	1	0	0	0	0
Thermotogae	4	4	0	0	0	0	0
Fusobacteria	1	1	0	0	0	0	0
Chlamydiae	7	6	1	0	0	0	0
Bacteroides	19	9	8	2	0	0	0
Chlorobi	9	9	0	0	0	0	0
Fibrobacteres	0	0	0	0	0	0	0
Actinobacteria	38	3	17	14	4	0	0
Spirochaetes	7	6	0	1	0	0	0
Plantomycetes	2	0	2	0	0	0	0
Firmicutes	**79**	**59**	**11**	**5**	**4**	**0**	**0**
Bacillales	21	2	10	5	4	0	0
Lactobacillales	22	22	0	0	0	0	0
Mollicutes	14	14	0	0	0	0	0
Clostridia	22	21	1	0	0	0	0
Total	**450**	**124**	**128**	**98**	**71**	**29**	**1**

Figure 4. Bacterial cuproproteomes. Phylogenetic tree adapted from [37]. Numbers across the top (1–5) show the size of cuproproteomes (i.e., the number of cuproproteins in a phylum or organism). Displayed is the number of organisms from each phylum with the cuproproteome of the particular size.
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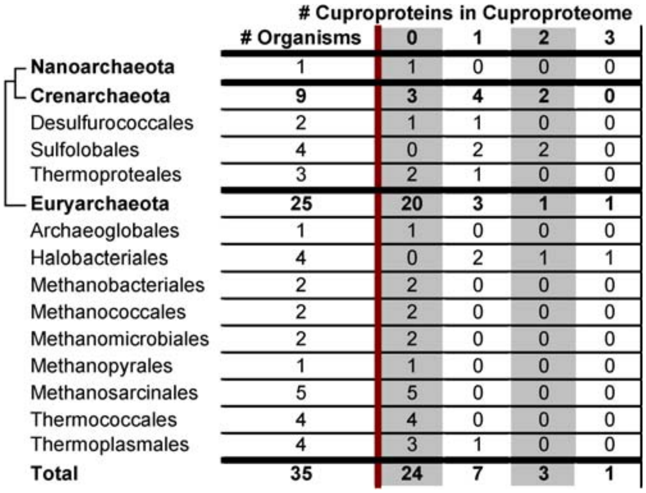
Although exporters have been readily identified, importers have almost completely eluded researchers. As pointed out above, only one copper-dependent importer has been identified in prokaryotes. However, it is noteworthy that at least one example of an ABC transporter has been reported which has broad specificity for a number of metal ions, including copper, and this could potentially explain copper uptake by prokaryotes [42].

Additionally, while there are examples of cuproproteins that obtain copper from the cytoplasm (for example, plastocyanin gets copper from PacS, which exports copper from the cytoplasm to the thylakoid [18,19]) most cuproproteins are periplasmic or membrane proteins and therefore it is possible that little cytoplasmic copper is needed for these proteins, which could help explain the lack of copper-specific importers.

In this study we only included proteins that are unable to function without copper. While no reports of prokaryotic enzymes evolving by changing the catalytic copper to other metals exist, it is a possibility, although unlikely, that some of the proteins we have identified as cuproproteins actually utilize a different metal ion.

Various cuproproteins have been identified by researchers over the years. The two most widespread cuproproteins are COX and ND2, both of which are involved in the electron transport chain. The redox properties of copper make this metal ion a prime candidate for use in the active sites of oxidoreductases involved in energy generation. In fact, in bacteria, 84% of the cuproproteins, including COX and ND2, are involved in energy producing pathways, and in archaea 86% of the cuproproteins are involved in ATP production. These data suggest that ATP generation via



	# Organisms	0	1	2	3
Nanoarchaeota	1	1	0	0	0
Crenarchaeota	**9**	**3**	**4**	**2**	**0**
Desulfurococcales	2	1	1	0	0
Sulfolobales	4	0	2	2	0
Thermoproteales	3	2	1	0	0
Euryarchaeota	**25**	**20**	**3**	**1**	**1**
Archaeoglobales	1	1	0	0	0
Halobacteriales	4	0	2	1	1
Methanobacteriales	2	2	0	0	0
Methanococcales	2	2	0	0	0
Methanomicrobiales	2	2	0	0	0
Methanopyrales	1	1	0	0	0
Methanosarcinales	5	5	0	0	0
Thermococcales	4	4	0	0	0
Thermoplasmales	4	3	1	0	0
Total	**35**	**24**	**7**	**3**	**1**

Figure 5. Archaeal cuproproteomes. See the legend to Figure 4.
doi:10.1371/journal.pone.0001378.g005

oxygen-dependent respiration is the major use of copper in biology. Being readily available in the environment and with such wide use in oxygenic organisms, it is a paradox that the utilization of this metal is restricted to only a few enzymes in prokaryotes.

Copper use in organisms does have its associated dangers though, and organisms which have evolved to use this metal have to have ways to deal with copper toxicity. Copper toxicity comes from its ability to produce reactive oxygen species (ROS). Thus, copper is intimately involved in the cellular control of redox homeostasis. SODs are important proteins which protect the cell against ROS by removing superoxide anions. Each of the known SODs requires at least one metal cofactor. Among these is a cuproprotein, SOD1, which utilizes both copper and zinc. Other SODs are known to use iron, manganese, or nickel [25,43]. Interestingly, copper is used in both respiration and the associated removal of ROS, which are by-products of oxygen-dependent respiration.

Another interesting cuproprotein is a multicopper oxidase, CotA, which is a spore coat protein. Only four bacteria (and no archaea) were found to utilize CotA, all of which were Bacillales. It appears that CotA is a recently evolved cuproprotein. Other multicopper oxidases studied (CueO and PcoA) are components of efflux systems.

Cuproproteomes appear to be quite small in prokaryotes. In both bacteria and archaea, the most common cuproproteome size for users was one, and frequently this single cuproprotein was COX. Interestingly, organisms with cuproproteomes of the same size do not necessarily utilize the same cuproproteins, and most cuproproteins are used in a limited number of organisms.

The use of copper can be compared (or rather contrasted) with that of another trace element, selenium. The size of prokaryotic selenoproteomes is highly variable, from 0 to 56 [10,44]. However, approximately 80% of prokaryotes do not have selenoproteins. Thus, whereas prokaryotic selenium use shows a mosaic pattern and most selenoprotein-rich organisms are anaerobic, copper is utilized by a limited number of processes (essentially restricted to respiration), but in many aerobic organisms.

Our study was based on the premise that most cuproproteins are already known. The striking occurrence of these proteins in aerobic organisms suggests that we could reliably identify most users. The possibility cannot be excluded, however, that additional, unknown Cu-dependent proteins are present in some prokaryotes. Nevertheless, while additional cuproproteins would increase the size of cuproproteomes, it is unlikely that this would lead to identification of many additional users.

It would be interesting to expand this work to the third superkingdom, eukaryotes. By definition, these organisms evolved in oxygenated environments, but whether copper utilization remained widespread during evolution of eukaryotes is not known. There is some overlap between eukaryotes and prokaryotes on which a study of this nature could be based; for example, both prokaryotes and eukaryotes have COX and SOD1.

Finally, we have pointed out that some very important enzymes require a copper cofactor, and while many of them are periplasmic and membrane-bound, some are intracellular. In the future, it would be interesting to examine the means by which prokaryotes bring

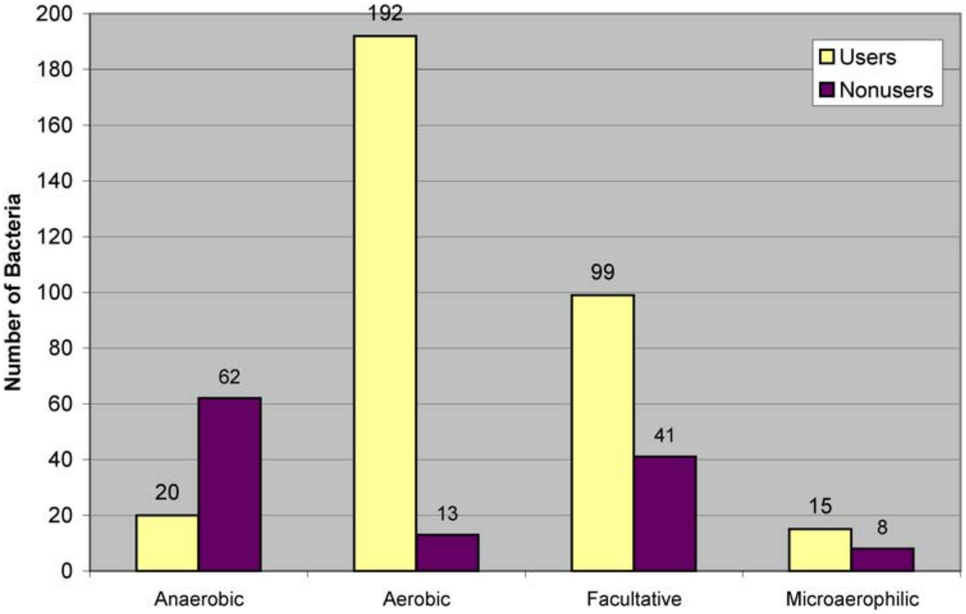


Figure 6. Occurrence of Cu users and nonusers among bacteria differing in their dependence on oxygen. Bacteria were divided based on their oxygen requirement into anaerobic, aerobic, facultative, and microaerophilic. Shown are the numbers of users/nonusers for each of these groups of organisms.
doi:10.1371/journal.pone.0001378.g006

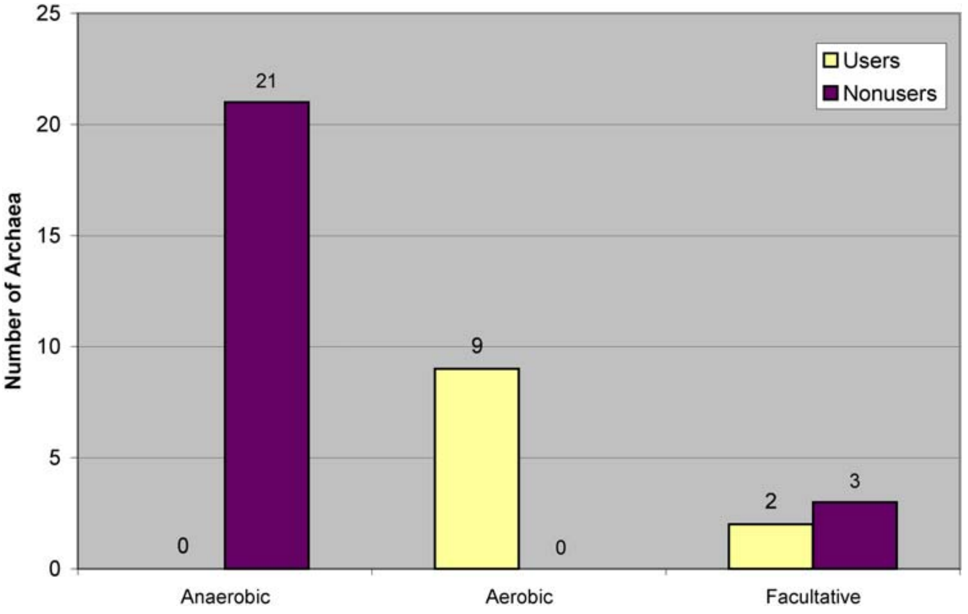


Figure 7. Occurrence of Cu users and nonusers among archaea differing in their dependence on oxygen. Archaea were divided based on their oxygen requirement into anaerobic, aerobic, facultative, and microaerophilic. Shown are the numbers of users/nonusers for each of these groups of organisms.
doi:10.1371/journal.pone.0001378.g007

copper into the cell under conditions of deficiency in this trace element. Very little is known about copper import in prokaryotes; in many cases unspecific import systems would likely be sufficient, but whether this is the major route for copper use is not known.

MATERIALS AND METHODS

Genomic sequence resources

In our study, we examined fully sequenced prokaryotic genomes (450 unique bacterial and 35 unique archaeal genomes were available as of January 31, 2007). Only a single strain of each species was included in this research. A list of fully sequenced prokaryotic genomes, both those used in this research and those completed since we began our research, can be found on the NCBI website at: http://www.ncbi.nlm.nih.gov/sutils/genom_table.cgi.

Identification of Cu-utilizing organisms, Cu-specific transporters, and cuproproteins

Initially, primary literature was used to identify Cu-dependent proteins, and Cu importers, exporters, and regulators. Cuproproteins were included in the set if their close homologs were experimentally demonstrated to be specific for copper. Copper transporters were included if they were previously reported to be copper-specific or if they had a much higher affinity for copper than other metal ions. A complete list of identified proteins, importers, exporters, and regulators is shown in Table 1.

Organisms that had at least one copper-dependent protein were considered copper-dependent, or users. If we were unable to find at least one cuproprotein in an organism it was designated as copper-independent or a nonuser. Determining if a specific organism had cuproproteins was accomplished in the following steps:

- Using primary literature, organisms were identified that had a particular cuproprotein;
- TBlastn [45] search with default parameters was performed against all organisms in the study using the protein sequences from the step above;
- The organism from each phylum having a proteome containing the examined cuproprotein and having the highest homology to the query sequence was identified;
- A new Blast search was performed using the protein sequence from the previous step as query sequence and only searching the genomes from that particular phylum. In the case that no organism from the phylum had the original protein, this additional search was not performed;
- Manual analysis of the resulting sequences to determine which organisms had the cuproprotein in question.

Other analysis tools

Inferred phylogenies were used to verify similarity to putative cuproprotein sequences. Multiple sequence alignments of proteins and inferred phylogenies were created using ClustalW [46] with default parameters. Manual analysis of the inferred phylogeny was performed to identify which candidate sequences clustered around the putative cuproprotein.

Identification of environmental and other factors for each organism

To examine trends of copper utilization we collected information for various environmental factors (e.g., habitat, oxygen requirement, optimal temperature and optimal pH), and other factors and properties (e.g., genome size, GC content and Gram strain) which were retrieved from the NCBI prokaryotic genome project database (http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=File&db=genomeprj) for all examined archaeal and bacterial species.

SUPPORTING INFORMATION

Table S1

Found at: doi:10.1371/journal.pone.0001378.s001 (0.18 MB XLS)

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Author Contributions

Conceived and designed the experiments: VG YZ PR. Performed the experiments: PR. Analyzed the data: VG YZ PR. Wrote the paper: VG PR.

REFERENCES

1. Forbes JR, His G, Cox DW (1999) Role of the copper-binding domain in the copper transport function of ATP7B, the P-type ATPase defective in Wilson's Disease. J Bio Chem 274: 12408–12413.
2. Andrews NC (2002) Metal transporters and disease. Curr Opin Chem Biol 6: 181–186.
3. Talbot K (2002) Motor neuron disease. Postgrad Med J 78: 513–519.
4. Sayre LM, Smith MA, Perry G (2001) Chemistry and biochemistry of oxidative stress in neurodegenerative disease. Current Medicinal Chemistry 8: 721–738.
5. Canfield DE, Rosing MT, Bjerrum C (2006) Early anaerobic metabolisms. Philosophical Transactions of The Royal Society B 361: 1819–1836.
6. Ferry JG, House CH (2006) The stepwise evolution of early life driven by energy conservation. Molecular Biology and Evolution 23: 1286–1292.
7. Saito MA, Sigman DM, Morel FMM (2003) The bioinorganic chemistry of the ancient ocean: the co-evolution of cyanobacterial metal requirements and biogeochemical cycles at the archean-proterozoic boundary? Inorganica Chimica Acta 356: 308–318.
8. Williams RJP, Fraústo da Silva JJR (2006) The Chemistry of Evolution: The Development of our Ecosystem. The Netherlands: Elsevier BV. pp 253–262.
9. Rodionov DA, Gelfand MS, Todd JD, Curson ARJ, Johnston AWB (2006) Computational reconstruction of iron- and manganese-responsive transcriptional networks in α-proteobacteria. PLoS Computational Biology 2: 1568–1585.
10. Zhang Y, Romero H, Salinas G, Gladyshev VN (2006) Dynamic evolution of selenocysteine utilization in bacteria: a balance between selenoprotein loss and evolution of selenocysteine from redox-active cysteine residues. Genome Biology 7: R94.
11. Lobanov AV, Fomenko DE, Zhang Y, Sengupta A, Hatfield DL, et al. (2007) Evolutionary dynamics of eukaryotic selenoproteomes: large selenoproteomes may associate with aquatic and small with terrestrial life. Genome Biol 8: R198.
12. Rodionov DA, Hebbeln P, Gelfand MS, Eitinger T (2006) Comparative and functional genomic analysis of prokaryotic nickel and cobalt uptake transporters: evidence for a novel group of ATP-binding cassette transporters. J Bacteriol 188: 317–327.
13. Silver S, Phung LT (2005) A bacterial view of the periodic table: genes and proteins for toxic inorganic ions. J Ind Microbiol Biotechnol 32: 587–605.
14. Vulpe CD, Packman S (1995) Cellular copper transport. Annu Rev Nutr 15: 293–322.
15. Finney LA, O'Halloran TV (2003) Transition metal speciation in the cell: insights from the chemistry of metal ion receptors. Science 300: 931–936.
16. Solioz M, Stoyanov JV (2003) Copper homeostasis in *Enterococcus hirae*. FEMS Microbiol Rev 27: 183–195.
17. Banci L, Bertini I, Ciofi-Baffoni S, Su X, Borrelly GPM, et al. (2004) Solution structures of a cyanobacterial metallchaperone: insight into an atypical copper-binding motif. J Biol Chem 279: 27502–27510.
18. Cavet JS, Borrelly GPM, Robinson NJ (2003) Zn, Cu and Co in cyanobacteria: selective control of metal availability. FEMS Microbiol Rev 27: 165–181.
19. Tottey S, Rich PR, Rondet SAM, Robinson NJ (2001) Two Menkes-type ATPases supply copper for photosynthesis in *Synechocystis* PCC 6803. J Biol Chem 276: 19999–20004.
20. Shcolnick S, Keren N (2006) Metal homeostasis in cyanobacteria and chloroplasts. Balancing benefits and risks to the photosynthetic apparatus. Plant Physiology 141: 805–810.
21. Coombs JM, Barkay T (2005) New findings on evolution of metal homeostasis genes: evidence from comparative genome analysis of bacteria and archaea. Appl Environ Microbiol 71: 7083–7091.
22. Voloudakis AE, Reignier TM, Cooksey DA (2005) Regulation of resistance to copper in Xanthomonas axonopodis pv. vesicatoria. Applied and Environmental Microbiology 71: 782–789.
23. Rodríguez-Montelongo L, Volentini SI, Farias RN, Massa EM, Rapisarda VA (2006) The Cu(II)-reductase NADH dehydrogenase-2 of *Escherichia coli* improves the bacterial growth in extreme copper concentrations and increases the resistance to the damage caused by copper and hydroperoxide. Archives of Biochemistry and Biophysics 451: 1–7.
24. Rapisarda VA, Chehin RN, De Las Rivas J, Rodriguez-Montelongo L, Farias RN, et al. (2002) Evidence for Cu(I)-thiolate ligation and prediction of a putative copper-binding site in the Escherichia coli NADH dehydrogenase-2. Arch Biochem Biophysics 405: 87–97.
25. Zelko IN, Marianl TJ, Folz RJ (2002) Superoxide dismutase multigene family: a comparison of the CuZn-SOD (SOD1), Mn-SOD (SOD2), and EC-SOD (SOD3) gene structures, evolution, and expression. Free Radical Biology and Medicine 33: 337–349.
26. Arciero DM, Pierce BS, Hendrich MP, Hooper AB (2002) Nitrosocyanin, a red cupredoxin-like protein from *Nitrosomonas europaea*. Biochemistry 41: 1703–1709.
27. Ellis MJ, Grossman JG, Eady RR, Hasnain SS (2007) Genomic analysis reveals widespread occurrence of new classes of copper nitrite reductases. J Biol Inorg Chem. In press.
28. Wilmot CM (2003) Oxygen activation in a copper-containing amine oxidase. Biochem Soc Trans 31: 493–496.
29. Chan SI, Chen KH-C, Yu SS-F, Chen C-L, Kuo SS-J (2004) Toward delineating the structure and function of the particulate methane monooxygenase from methanotropic bacteria. Biochemistry 43: 4421–4430.
30. Hullo MF, Moszer I, Danchin A, Martin-Verstraete I (2001) CotA of *Bacillus subtilis* is a copper-dependent laccase. J Bacteriol 183: 5426–5430.
31. Berks B, Sargent F, Palmer T (2000) The tat protein export pathway. Molecular Microbiology 35: 260–274.
32. Rensing C, Grass G (2003) *Escherichia coli* mechanisms of copper homeostasis in a changing environment. FEMS Microbiol Rev 27: 197–213.
33. Gupta SD, Lee BT, Camakaris J, Wu HC (1995) Identification of cutC and cutF (nlpE) genes involved in copper tolerance in *Escherichia Coli*. J Bacteriol 177: 4207–4215.
34. Grass G, Rensing C (2001) Genes involved in copper homeostasis in *Escherichia coli*. J Bacteriol 183: 2145–2147.
35. Arnesano F, Banci L, Bertini I, Mangani S, Thompsett AR (2003) A redox switch in CopC: an intriguing copper trafficking protein than binds copper(I) and copper(II) at different sites. Proceedings of the National Academy of the Sciences 100: 3814–3819.
36. Cha J, Cooksey DA (1993) Copper hypersensitivity and uptake in *Pseudomonas syringae* containing cloned components of the copper resistance operon. Appl Environ Microbiol 59: 1671–1674.
37. Ciccarelli FD, Doerks T, von Mering C, Creevey CJ, Snel B, et al. (2006) Toward automatic reconstruction of a highly resolved tree of life. Science 311: 1283–1287.
38. Bekker A, Holland HD, Wang P-L, Rumble D III, Stein HJ, et al. (2004) Dating the rise of atmospheric oxygen. Nature 427: 117–120.
39. Decker H, Terwilliger N (2000) Cops and robbers: putative evolution of copper oxygen-binding proteins. The Journal of Experimental Biology 203: 1777–1782.
40. Saito MA, Signman DM, Morel FMM (2003) The bioinorganic chemistry of the ancient ocean: the co-evolution of cyanobacterial metal requirements and biogeochemical cycles at the Archean-Proterozic boundary? Inorganica Chimica Acta 356: 308–318.
41. Ochiai E (1983) Copper and the biological evolution. BioSystems 16: 81–86.
42. Janulczyk R, Pallon J, Bjorck L (1999) Identification and characterization of a *Streptococcus pyogenes* ABC transporter with multiple specificity for metal cations. Molecular Microbiology 34: 596–606.
43. Culotta VC, Yang M, O'Halloran TV (2006) Activation of superoxide dismutases: putting the metal to the petal. Biochimica et Biophysica Acta 1763: 747–758.
44. Zhang Y, Gladyshev V N (2007) High content of proteins containing 21st and 22nd amino acids, selenocysteine and pyrrolysine, in a symbiotic deltaproteobacterium of gutless worm Olavius algarvensis. Nucleic Acids Res. In Press.
45. Altschul SF, Madden TL, Schaffer AA, Zhang J, Zhang Z, et al. (1997) Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res 25: 3389–3402.
46. Chenna R, Sugawara H, Koike T, Lopez R, Gibson TJ, et al. (2003) Multiple sequence alignment with the Clustal series of programs. Nucleic Acids Res 31: 3497–3500.

Bacteria	**Oxygen Req**	**Habitat**	**Gram Strain**		**Cuproproteins**	**Importers**	**Chaperones**	**Exporters**	**Cuproproteins➔**
Acidothermus cellulolyticus 11B	Aerobic	Aquatic	+		1	0	0	1	
Arthrobacter aurescens TC1	Aerobic	Terrestrial	+		1	0	0	0	
Arthrobacter sp. FB24	Aerobic	Terrestrial	+		2	0	0	2	
Bifidobacterium adolescentis	Anaerobic	Host	+		0	0	0	1	
Bifidobacterium longum DJO10A	Anaerobic	Host	+		0	0	0	0	
Brevibacterium linens BL2	Aerobic	Multiple	+		2	0	0	1	
Collinsella aerofaciens ATCC 25986	Anaerobic	Host	+		0	0	0	1	
Corynebacterium diphtheriae NCTC 13129	Aerobic	Multiple	+		1	0	0	1	
Corynebacterium efficiens YS-314	Facultative	Multiple	+		1	0	0	2	
Corynebacterium glutamicum ATCC 13032	Facultative	Multiple	+		1	0	0	2	
Corynebacterium jeikeium K411	Facultative	Multiple	+		1	0	0	0	
Frankia alni ACN14a	Aerobic	Host	+		2	0	0	0	
Frankia sp. EAN1pec	Aerobic	Multiple	+		4	0	0	2	
Janibacter sp. HTCC2649	Microaerophilic	Aquatic	+		2	0	0	2	
Kineococcus radiotolerans SRS30216	Aerobic	Multiple	+		1	0	0	1	
Leifsonia xyli subsp. xyli str. CTCB07	Aerobic	Host	+		2	0	0	2	
Mycobacterium avium subsp. paratuberculosis K-10	Aerobic	Multiple	+		2	0	0	1	
Mycobacterium bovis AF2122/97	Aerobic	Multiple	+		2	0	0	1	
Mycobacterium flavescens PYR-GCK	Aerobic	Multiple	+		2	0	0	1	
Mycobacterium leprae TN	Aerobic	Multiple	+		1	0	0	1	
Mycobacterium smegmatis str. MC2 155	Aerobic	Host	+		1	0	0	0	
Mycobacterium sp. KMS	Aerobic	Multiple	+		2	0	0	1	
Mycobacterium tuberculosis C	Aerobic	Host	+		1	0	0	1	
Mycobacterium ulcerans Agy99	Aerobic	Host	+		1	0	0	0	
Mycobacterium vanbaalenii PYR-1	Aerobic	Multiple	+		3	0	0	1	
Nocardia farcinica IFM 10152	Aerobic	Multiple	+		3	0	0	1	
Nocardioides sp. JS614	Aerobic	Terrestrial	+		2	0	0	2	
Propionibacterium acnes KPA171202	Anaerobic	Host	+		2	0	0	1	
Rhodococcus sp. RHA1	Aerobic	Terrestrial	+		3	0	0	1	
Rubrobacter xylanophilus DSM 9941	Aerobic	Multiple	+		2	0	0	1	
Salinispora arenicola CNS205	Aerobic	Aquatic	+		1	0	0	0	
Salinispora tropica CNB-440	Aerobic	Multiple	+		2	0	0	2	
Streptomyces avermitilis MA-4680	Aerobic	Multiple	+		2	0	0	3	
Streptomyces coelicolor A3(2)	Aerobic	Multiple	+		1	0	0	2	
Symbiobacterium thermophilum IAM 14863	Microaerophilic	Terrestrial	+		2	0	0	1	
Thermobifida fusca YX	Aerobic	Multiple	+		1	0	0	1	
Tropheryma whipplei TW08/27	Aerobic	Host	+		1	0	0	1	
marine actinobacterium PHSC20C1	Aerobic	Aquatic	+		1	0	0	2	
Bacteroidetes/Chlorobi									
Bacteroides caccae ATCC 43185	Anaerobic	Host	-		0	0	0	0	
Bacteroides fragilis YCH46	Anaerobic	Host	-		0	0	0	2	
Bacteroides thetaiotaomicron VPI-5482	Anaerobic	Host	+		0	0	0	2	
Candidatus Sulcia muelleri str. Hc (Homalodisca coagu	Anaerobic	Host	-		0	0	0	0	
Cellulophaga sp. MED134	Aerobic	Aquatic	-		1	0	0	1	
Chlorobium chlorochromatii CaD3	Anaerobic	Multiple	-		0	0	0	1	
Chlorobium ferrooxidans DSM 13031	Anaerobic	Aquatic	-		0	0	0	1	
Chlorobium limicola DSM 245	Anaerobic	Aquatic	-		0	0	0	1	
Chlorobium phaeobacteroides BS1	Facultative	Aquatic	-		0	0	0	1	
Chlorobium tepidum TLS	Anaerobic	Aquatic	-		0	0	0	1	
Croceibacter atlanticus HTCC2559	Aerobic	Aquatic	-		1	0	0	1	
Cytophaga hutchinsonii ATCC 33406	Aerobic	Multiple	-		0	0	0	1	
Flavobacteria bacterium BBFL7	Aerobic	Aquatic	-		1	0	0	1	
Flavobacteriales bacterium HTCC2170	Aerobic	Aquatic	-		1	0	0	1	
Flavobacterium johnsoniae UW101	Aerobic	Multiple	-		0	0	0	2	
Gramella forsetii KT0803	Aerobic	Multiple	-		0	0	0	0	
Leeuwenhoekiella blandensis MED217	Aerobic	Aquatic	-		1	0	0	2	
Microscilla marina ATCC 23134	Aerobic	Aquatic	-		0	0	0	0	

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Pelodictyon luteolum DSM 273	Anaerobic	Multiple	-		0	0	0	1	
Pelodictyon phaeoclathratiforme BU-1	Anaerobic	Multiple	-		0	0	0	1	
Polaribacter irgensii 23-P	Aerobic	Aquatic	-		1	0	0	0	
Porphyromonas gingivalis W83	Anaerobic	Host	-		0	0	0	2	
Prosthecochloris aestuarii DSM 271	Anaerobic	Aquatic	-		0	0	0	0	
Prosthecochloris vibrioformis DSM 265	Facultative	Aquatic	-		0	0	0	0	
Psychroflexus torquis ATCC 700755	Aerobic	Aquatic	-		2	0	0	0	
Robiginitalea biformata HTCC2501	Aerobic	Aquatic	-		2	0	0	2	
Salinibacter ruber DSM 13855	Aerobic	Aquatic	-		1	0	0	1	
Tenacibaculum sp. MED152	Aerobic	Aquatic	-		0	0	0	1	
Chlamydiae									
Candidatus Protochlamydia amoebophila UWE25	Anaerobic	Host	-		2	0	0	0	
Chlamydia muridarum Nigg	Anaerobic	Host	-		0	0	0	0	
Chlamydia trachomatis A/HAR-13	Anaerobic	Host	-		0	0	0	0	
Chlamydophila abortus S26/3	Anaerobic	Host	-		0	0	0	0	
Chlamydophila caviae GPIC	Anaerobic	Host	-		0	0	0	0	
Chlamydophila felis Fe/C-56	Anaerobic	Host	-		0	0	0	0	
Chlamydophila pneumoniae AR39	Anaerobic	Host	-		0	0	0	0	
Cyanobacteria									
Anabaena variabilis ATCC 29413	Aerobic	Multiple	-		3	1	0	1	
Crocosphaera watsonii WH 8501	Aerobic	Aquatic	-		2	1	0	1	
Gloeobacter violaceus PCC 7421	Aerobic	Terrestrial	-		2	0	0	1	
Lyngbya sp. PCC 8106	Aerobic	Aquatic	-		2	1	0	1	
Nodularia spumigena CCY9414	Aerobic	Aquatic	-		2	1	0	0	
Nostoc punctiforme PCC 73102	Aerobic	Multiple	-		3	1	0	1	
Nostoc sp. PCC 7120	Aerobic	Multiple	-		3	1	0	1	
Prochlorococcus marinus str. MIT 9312	Microaerophilic	Aquatic	-		2	1	0	1	
Synechococcus elongatus PCC 6301	Microaerophilic	Aquatic	-		2	1	0	1	
Synechococcus sp. CC9311	Microaerophilic	Aquatic	-		3	1	0	1	
Synechocystis sp. PCC 6803	Microaerophilic	Aquatic	-		3	1	0	0	
Thermosynechococcus elongatus BP-1	Aerobic	Aquatic	-		1	1	0	1	
Trichodesmium erythraeum IMS101	Aerobic	Aquatic	-		3	1	0	1	
Firmicutes									
Bacillales									
Bacillus anthracis str. Ames	Facultative	Multiple	+		2	0	2	2	
Bacillus cereus ATCC 10987	Aerobic	Multiple	+		3	0	2	2	
Bacillus clausii KSM-K16	Aerobic	Terrestrial	+		2	0	2	1	
Bacillus halodurans C-125	Facultative	Multiple	+		1	0	1	1	
Bacillus licheniformis ATCC 14580	Facultative	Terrestrial	+		3	0	2	1	
Bacillus sp. NRRL B-14911	Facultative	Aquatic	+		1	0	1	1	
Bacillus subtilis subsp. subtilis str. 168	Facultative	Terrestrial	+		3	0	1	1	
Bacillus thuringiensis serovar konkukian str. 97-27	Facultative	Multiple	+		2	0	1	2	
Bacillus weihenstephanensis KBAB4	Aerobic	Terrestrial	+		2	0	1	2	
Exiguobacterium sibiricum 255-15	Facultative	Terrestrial	+		1	0	0	2	
Geobacillus kaustophilus HTA426	Aerobic	Aquatic	+		2	0	1	1	
Listeria innocua Clip112624	Facultative	Multiple	+		1	0	1	2	
Listeria monocytogenes EGD-e	Facultative	Multiple	+		1	0	1	2	
Listeria welshimeri serovar 6b str. SLCC5334	Facultative	Multiple	+		0	0	1	0	
Oceanobacillus iheyensis HTE831	Aerobic	Aquatic	+		3	0	1	2	
Paenibacillus larvae subsp. larvae BRL-230010	Facultative	Terrestrial	+		1	0	1	2	
Pasteuria nishizawae str. North American	Facultative	Host	+		0	0	0	0	
Staphylococcus aureus RF122	Facultative	Host	+		1	0	1	1	
Staphylococcus epidermidis ATCC 12228	Facultative	Host	+		1	0	2	1	
Staphylococcus haemolyticus JCSC1435	Facultative	Host	+		1	0	2	1	
Staphylococcus saprophyticus subsp. saprophyticus A	Aerobic	Host	+		1	0	1	1	
Clostridia									
Alkaliphilus metalliredigenes QYMF	Anaerobic	Aquatic	+		0	0	1	1	

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Caldicellulosiruptor saccharolyticus DSM 8903	Anaerobic	Aquatic	+		0	0	2	1	
Carboxydothermus hydrogenoformans Z-2901	Anaerobic	Aquatic	+		0	0	1	1	
Clostridium acetobutylicum ATCC 824	Anaerobic	Multiple	+		0	0	2	1	
Clostridium beijerincki NCIMB 8052	Anaerobic	Multiple	+		0	0	2	2	
Clostridium cellulolyticum H10	Anaerobic	Terrestrial	+		0	0	1	1	
Clostridium difficile QCD-32g58	Anaerobic	Multiple	+		0	0	2	1	
Clostridium novyi NT	Anaerobic	Terrestrial	+		0	0	0	1	
Clostridium perfringens ATCC 13124	Anaerobic	Multiple	+		0	0	1	2	
Clostridium phytofermentans ISDg	Anaerobic	Terrestrial	+		0	0	1	2	
Clostridium sp. OhILAs	Anaerobic	Aquatic	+		0	0	1	1	
Clostridium tetani E88	Anaerobic	Multiple	+		0	0	1	1	
Clostridium thermocellum ATCC 27405	Anaerobic	Multiple	+		0	0	2	1	
Desulfitobacterium hafniense DCB-2	Anaerobic	Multiple	-		1	0	2	1	
Desulfotomaculum reducens MI-1	Anaerobic	Aquatic	+		0	0	1	1	
Eubacterium ventriosum ATCC 27560	Anaerobic	Host	+		0	0	0	0	
Halothermothrix orenii H 168	Anaerobic	Aquatic	-		0	0	1	1	
Moorella thermoacetica ATCC 39073	Anaerobic	Aquatic	+		0	0	1	1	
Syntrophomonas wolfei subsp. wolfei str. Goettingen	Anaerobic	Multiple	-		0	0	1	1	
Thermoanaerobacter ethanolicus ATCC 33223	Anaerobic	Aquatic	+		0	0	1	1	
Thermoanaerobacter tengcongensis MB4	Anaerobic	Aquatic	-		0	0	2	1	
Thermosinus carboxydivorans Nor1	Anaerobic	Aquatic	-		0	0	1	1	
Lactobacillales									
Enterococcus faecalis V583	Facultative	Multiple	+		0	0	1	2	
Enterococcus faecium DO	Facultative	Multiple	+		0	0	1	1	
Lactobacillus acidophilus NCFM	Facultative	Multiple	+		0	0	2	1	
Lactobacillus brevis ATCC 367	Facultative	Multiple	+		0	0	1	0	
Lactobacillus casei ATCC 334	Facultative	Multiple	+		0	0	2	2	
Lactobacillus delbrueckii subsp. bulgaricus ATCC 1184	Facultative	Multiple	+		0	0	2	1	
Lactobacillus gasseri ATCC 33323	Facultative	Host	+		0	0	2	2	
Lactobacillus johnsonii NCC 533	Facultative	Host	+		0	0	2	1	
Lactobacillus plantarum WCFS1	Facultative	Host	+		0	0	2	2	
Lactobacillus reuteri 100-23	Facultative	Host	+		0	0	2	1	
Lactobacillus sakei subsp. sakei 23K	Facultative	Multiple	+		0	0	2	1	
Lactobacillus salivarius subsp. salivarius UCC118	Facultative	Host	+		0	0	1	0	
Lactococcus lactis subsp. lactis Il1403	Facultative	Multiple	+		0	0	2	2	
Leuconostoc mesenteroides subsp. mesenteroides AT	Facultative	Multiple	+		0	0	2	2	
Oenococcus oeni PSU-1	Facultative	Multiple	+		0	0	2	1	
Pediococcus pentosaceus ATCC 25745	Facultative	Multiple	+		0	0	2	2	
Streptococcus agalactiae 2603V/R	Facultative	Host	+		0	0	1	2	
Streptococcus mutans UA159	Facultative	Host	+		0	0	1	1	
Streptococcus pneumoniae R6	Facultative	Multiple	+		0	0	1	1	
Streptococcus pyogenes M1 GAS	Facultative	Host	+		0	0	1	2	
Streptococcus suis 89/1591	Facultative	Multiple	+		0	0	1	2	
Streptococcus thermophilus CNRZ1066	Anaerobic	Multiple	+		0	0	1	1	
Mollicutes									
Aster yellows witches1-broom phytoplasma AYWB	Aerobic	Host	-		0	0	0	0	
Mesoplasma florum L1	Facultative	Host	-		0	0	0	0	
Mycoplasma capricolum subsp. capricolum ATCC 2734	Facultative	Host	-		0	0	0	0	
Mycoplasma gallisepticum R	Facultative	Host	-		0	0	0	0	
Mycoplasma genitalium G37	Facultative	Host	-		0	0	0	0	
Mycoplasma hyopneumoniae 232	Facultative	Host	-		0	0	0	0	
Mycoplasma mobile 163K	Facultative	Host	-		0	0	0	0	
Mycoplasma mycoides subsp. mycoides SC str. PG1	Facultative	Host	-		0	0	0	0	
Mycoplasma penetrans HF-2	Facultative	Host	-		0	0	0	0	
Mycoplasma pneumoniae M129	Facultative	Host	-		0	0	0	0	
Mycoplasma pulmonis UAB CTIP	Facultative	Host	-		0	0	0	0	
Mycoplasma synoviae 53	Facultative	Host	-		0	0	0	0	

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Onion yellows phytoplasma OY-M	Facultative	Host	-		0	0	0	0	
Ureaplasma parvum serovar 3 str. ATCC 700970	Facultative	Host	-		0	0	0	0	
Others									
Acidobacteria bacterium Ellin345	Aerobic	Terrestrial	-		1	0	0	1	
Aquifex aeolicus VF5	Aerobic	Aquatic	-		1	0	1	1	
Blastopirellula marina DSM 3645	Aerobic	Aquatic	-		2	0	0	1	
Chloroflexus aggregans DSM 9485	Facultative	Aquatic	-		2	0	0	0	
Chloroflexus aurantiacus J-10-fl	Anaerobic	Aquatic	-		2	0	0	1	
Dehalococcoides ethenogenes 195	Anaerobic	Multiple	+		0	0	0	1	
Dehalococcoides sp. CBDB1	Anaerobic	Multiple	+		0	0	0	0	
Deinococcus geothermalis DSM 11300	Aerobic	Aquatic	+		1	0	0	1	
Deinococcus radiodurans R1	Aerobic	Terrestrial	+		2	0	0	1	
Fervidobacterium nodosum Rt17-B1	Anaerobic	Aquatic	-		0	0	0	0	
Fusobacterium nucleatum subsp. nucleatum ATCC 255	Anaerobic	Host	-		0	0	0	2	
Herpetosiphon aurantiacus ATCC 23779	Aerobic	Multiple	-		1	0	0	1	
Rhodopirellula baltica SH 1	Aerobic	Aquatic	-		1	0	0	1	
Roseiflexus castenholzii DSM 13941	Facultative	Aquatic	-		1	0	0	0	
Roseiflexus sp. RS-1	Facultative	Aquatic	-		3	0	0	1	
Solibacter usitatus Ellin6076	Aerobic	Terrestrial	-		3	0	0	1	
Thermosipho melanesiensis BI429	Anaerobic	Aquatic	-		0	0	0	0	
Thermotoga maritima MSB8	Anaerobic	Aquatic	-		0	0	0	0	
Thermotoga petrophila RKU-1	Anaerobic	Aquatic	-		0	0	0	0	
Thermus thermophilus HB27	Aerobic	Aquatic	-		3	0	0	1	
Proteobacteria									
Others									
Magnetococcus sp. MC-1	Facultative	Aquatic	-		0	0	0	1	
Mariprofundus ferrooxydans PV-1	Anaerobic	Aquatic	-		0	0	0	1	
alpha subdivision									
Others									
Acidiphilium cryptum JF-5	Aerobic	Multiple	-		2	0	0	1	
Aurantimonas sp. SI85-9A1	Aerobic	Aquatic	-		2	0	0	1	
Bartonella bacilliformis KC583	Aerobic	Host	-		2	0	0	0	
Bartonella henselae str. Houston-1	Aerobic	Host	-		3	0	0	0	
Bartonella quintana str. Toulouse	Aerobic	Host	-		2	0	0	0	
Bradyrhizobium japonicum USDA 110	Aerobic	Host	-		4	0	0	1	
Bradyrhizobium sp. BTAi1	Aerobic	Host	-		4	0	0	2	
Brucella abortus biovar 1 str. 9-941	Facultative	Host	-		4	0	1	2	
Brucella melitensis 16M	Aerobic	Host	-		4	0	0	2	
Brucella suis 1330	Aerobic	Host	-		4	0	0	2	
Caulobacter crescentus CB15	Aerobic	Aquatic	-		2	0	1	3	
Caulobacter sp. K31	Aerobic	Multiple	-		2	1	2	3	
Dinoroseobacter shibae DFL 12	Aerobic	Aquatic	-		2	0	0	0	
Erythrobacter litoralis HTCC2594	Aerobic	Aquatic	-		1	0	1	2	
Erythrobacter sp. NAP1	Aerobic	Aquatic	-		2	0	1	2	
Fulvimarina pelagi HTCC2506	Aerobic	Aquatic	-		2	0	0	1	
Gluconobacter oxydans 621H	Aerobic	Multiple	-		2	0	0	2	
Granulobacter bethesdensis CGDNIH1	Aerobic	Multiple	-		2	0	0	2	
Hyphomonas neptunium ATCC 15444	Aerobic	Aquatic	-		1	0	1	3	
Jannaschia sp. CCS1	Aerobic	Aquatic	-		1	0	0	1	
Loktanella vestfoldensis SKA53	Aerobic	Aquatic	-		1	0	0	1	
Magnetospirillum magneticum AMB-1	Microaerophilic	Aquatic	-		3	0	0	1	
Magnetospirillum magnetotacticum MS-1	Microaerophilic	Aquatic	-		3	0	0	0	
Maricaulis maris MCS10	Facultative	Multiple	-		1	0	0	2	
Mesorhizobium loti MAFF303099	Aerobic	Multiple	-		3	0	0	2	
Mesorhizobium sp. BNC1	Aerobic	Multiple	-		2	0	0	1	
Nitrobacter hamburgensis X14	Aerobic	Terrestrial	-		1	0	0	2	
Nitrobacter sp. Nb-311A	Facultative	Aquatic	-		1	0	0	1	

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Nitrobacter winogradskyi Nb-255	Facultative	Terrestrial	-		1	0	0	1	
Novosphingobium aromaticivorans DSM 12444	Aerobic	Multiple	-		1	1	1	3	
Oceanicaulis alexandrii HTCC2633	Aerobic	Multiple	-		1	0	0	2	
Oceanicola batsensis HTCC2597	Aerobic	Aquatic	-		1	0	0	2	
Oceanicola granulosus HTCC2516	Aerobic	Aquatic	-		1	0	0	2	
Paracoccus denitrificans PD1222	Facultative	Multiple	-		4	0	0	1	
Parvibaculum lavamentivorans DS-1	Aerobic	Multiple	-		1	0	0	0	
Parvularcula bermudensis HTCC2503	Aerobic	Aquatic	-		1	0	0	2	
Rhodobacter sphaeroides 2.4.1	Facultative	Multiple	-		1	0	0	1	
Rhodobacterales bacterium HTCC2654	Aerobic	Aquatic	-		2	0	0	1	
Rhodopseudomonas palustris BisA53	Facultative	Multiple	-		3	0	0	1	
Rhodospirillum rubrum ATCC 11170	Facultative	Multiple	-		1	0	0	1	
Roseobacter denitrificans OCh 114	Aerobic	Multiple	-		2	0	0	1	
Roseobacter sp. MED193	Aerobic	Aquatic	-		1	0	0	1	
Roseovarius nubinhibens ISM	Aerobic	Aquatic	-		1	0	0	2	
Roseovarius sp. 217	Aerobic	Aquatic	-		2	0	0	1	
Silicibacter pomeroyi DSS-3	Aerobic	Aquatic	-		2	0	0	2	
Silicibacter sp. TM1040	Aerobic	Multiple	-		2	0	0	1	
Sphingomonas sp. SKA58	Aerobic	Aquatic	-		2	1	2	3	
Sphingomonas wittichii RW1	Aerobic	Aquatic	-		1	0	1	0	
Sphingopyxis alaskensis RB2256	Aerobic	Aquatic	-		2	1	2	3	
Stappia aggregata IAM 12614	Facultative	Multiple	-		2	0	0	0	
Sulfitobacter sp. EE-36	Aerobic	Aquatic	-		1	0	0	1	
Xanthobacter autotrophicus Py2	Facultative	Multiple	-		1	0	0	2	
Zymomonas mobilis subsp. mobilis ZM4	Anaerobic	Multiple	-		1	0	0	1	
alpha proteobacterium HTCC2255	Aerobic	Aquatic	-		1	0	0	0	
Rhizobiaceae									
Agrobacterium tumefaciens str. C58	Aerobic	Multiple	-		2	0	0	2	
Rhizobium etli CFN 42	Aerobic	Host	-		2	0	0	2	
Rhizobium leguminosarum bv. viciae 3841	Aerobic	Multiple	-		1	0	0	0	
Sinorhizobium medicae WSM419	Aerobic	Multiple	-		2	0	0	2	
Sinorhizobium meliloti 1021	Aerobic	Multiple	-		3	0	0	1	
Rickettsiales									
Anaplasma marginale str. St. Maries	Aerobic	Host	-		1	0	0	0	
Anaplasma phagocytophilum HZ	Aerobic	Host	-		1	0	0	0	
Candidatus Pelagibacter ubique HTCC1062	Aerobic	Aquatic	-		1	0	0	0	
Ehrlichia canis str. Jake	Aerobic	Host	-		1	0	0	0	
Ehrlichia chaffeensis str. Arkansas	Aerobic	Host	-		1	0	0	0	
Ehrlichia ruminantium str. Gardel	Aerobic	Host	-		1	0	0	0	
Neorickettsia sennetsu str. Miyayama	Aerobic	Host	-		1	0	0	0	
Rickettsia africae ESF-5	Aerobic	Host	-		1	0	0	0	
Rickettsia akari str. Hartford	Aerobic	Host	-		1	0	0	0	
Rickettsia bellii RML369-C	Aerobic	Host	-		1	0	0	0	
Rickettsia canadensis str. McKiel	Aerobic	Host	-		1	0	0	0	
Rickettsia conorii str. Malish 7	Aerobic	Host	-		1	0	0	0	
Rickettsia felis URRWXCal2	Aerobic	Host	-		1	0	0	0	
Rickettsia massiliae MTU5	Aerobic	Host	-		1	0	0	0	
Rickettsia prowazekii str. Madrid E	Aerobic	Host	-		1	0	0	0	
Rickettsia rickettsii	Aerobic	Host	-		1	0	0	0	
Rickettsia sibirica 246	Aerobic	Host	-		1	0	0	0	
Rickettsia typhi str. Wilmington	Aerobic	Host	-		0	0	0	0	
Wolbachia endosymbiont of Drosophila melanogaster	Aerobic	Host	-		1	0	0	0	
beta subdivision									
Bordetella									
Bordetella bronchiseptica RB50	Aerobic	Host	-		5	0	0	2	
Bordetella parapertussis 12822	Aerobic	Host	-		5	0	0	2	
Bordetella pertussis Tohama I	Aerobic	Host	-		5	0	0	2	

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Burkholderiaceae									
Burkholderia ambifaria MC40-6	Aerobic	Multiple	-		2	0	0	1	
Burkholderia cenocepacia AU 1054	Facultative	Multiple	-		3	0	0	2	
Burkholderia cepacia AMMD	Facultative	Multiple	-		3	0	0	2	
Burkholderia dolosa AUO158	Facultative	Multiple	-		3	0	0	1	
Burkholderia mallei ATCC 23344	Aerobic	Host	-		4	0	1	2	
Burkholderia multivorans ATCC 17616	Aerobic	Host	-		3	1	1	4	
Burkholderia phymatum STM815	Aerobic	Host	-		2	0	0	0	
Burkholderia phytofirmans PsJN	Aerobic	Terrestrial	-		2	0	0	0	
Burkholderia pseudomallei 1710b	Aerobic	Terrestrial	-		4	0	1	2	
Burkholderia sp. 383	Facultative	Multiple	-		3	0	0	2	
Burkholderia thailandensis E264	Aerobic	Terrestrial	-		4	0	1	2	
Burkholderia vietnamiensis G4	Facultative	Multiple	-		3	0	0	2	
Burkholderia xenovorans LB400	Aerobic	Multiple	-		3	0	0	2	
Polynucleobacter sp. QLW-P1DMWA-1	Anaerobic	Aquatic	-		2	0	0	0	
Ralstonia eutropha JMP134	Facultative	Multiple	-		3	1	1	2	
Ralstonia metallidurans CH34	Facultative	Multiple	-		4	1	1	2	
Ralstonia pickettii 12J	Aerobic	Multiple	-		4	1	1	3	
Ralstonia solanacearum GMI1000	Aerobic	Multiple	-		4	1	1	2	
Neisseriaceae									
Chromobacterium violaceum ATCC 12472	Facultative	Multiple	-		3	0	0	2	
Neisseria gonorrhoeae FA 1090	Aerobic	Host	-		2	0	0	1	
Neisseria meningitidis MC58	Aerobic	Host	-		2	0	0	1	
Others									
Acidovorax avenae subsp. citrulli AAC00-1	Aerobic	Multiple	-		5	0	0	1	
Acidovorax sp. JS42	Aerobic	Terrestrial	-		4	0	0	2	
Azoarcus sp. EbN1	Facultative	Terrestrial	-		3	0	0	1	
Comamonas testosteroni KF-1	Aerobic	Multiple	-		2	1	1	2	
Dechloromonas aromatica RCB	Facultative	Multiple	-		1	0	0	1	
Delftia acidovorans SPH-1	Aerobic	Multiple	-		2	1	1	2	
Methylibium petroleiphilum PM1					1	0	0	0	
Methylobacillus flagellatus KT	Aerobic	Multiple	-		4	0	0	1	
Methylophilales bacterium HTCC2181	Aerobic	Aquatic	-		2	0	0	0	
Nitrosomonas europaea ATCC 19718	Aerobic	Multiple	-		3	0	0	2	
Nitrosomonas eutropha C71	Aerobic	Multiple	-		4	0	0	2	
Nitrosospira multiformis ATCC 25196	Aerobic	Terrestrial	-		4	0	0	1	
Polaromonas naphthalenivorans CJ2	Aerobic	Aquatic	-		2	0	0	1	
Polaromonas sp. JS666	Aerobic	Multiple	-		2	0	0	1	
Rhodoferax ferrireducens T118	Facultative	Multiple	-		2	0	0	1	
Rubrivivax gelatinosus PM1	Facultative	Aquatic	-		2	0	0	2	
Thiobacillus denitrificans ATCC 25259	Facultative	Multiple	-		4	0	0	3	
Verminephrobacter eiseniae EF01-2	Anaerobic	Host	-		1	0	0	1	
delta subdivision									
Anaeromyxobacter dehalogenans 2CP-C	Anaerobic	Terrestrial	-		2	0	0	1	
Anaeromyxobacter sp. Fw109-5	Anaerobic	Terrestrial	-		0	0	0	1	
Bdellovibrio bacteriovorus HD100	Aerobic	Multiple	-		1	0	0	1	
Candidatus Desulfococcus oleovorans Hxd3	Anaerobic	Aquatic	-		0	0	0	0	
Desulfotalea psychrophila LSv54	Anaerobic	Aquatic	-		0	0	0	0	
Desulfovibrio desulfuricans G20	Anaerobic	Multiple	-		1	0	0	1	
Desulfovibrio vulgaris subsp. vulgaris str. Hildenboroug	Anaerobic	Multiple	-		1	0	0	0	
Desulfuromonas acetoxidans DSM 684	Anaerobic	Aquatic	-		0	0	0	1	
Geobacter lovleyi SZ	Anaerobic	Multiple	-		0	0	0	1	
Geobacter metallireducens GS-15	Anaerobic	Aquatic	-		1	0	0	1	
Geobacter sp. FRC-32	Anaerobic	Multiple	-		0	0	0	1	
Geobacter sulfurreducens PCA	Anaerobic	Multiple	-		1	0	0	1	
Geobacter uraniumreducens Rf4	Anaerobic	Multiple	-		1	0	0	1	
Lawsonia intracellularis PHE/MN1-00	Facultative	Host	-		1	0	0	0	

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Myxococcus xanthus DK 1622	Aerobic	Terrestrial	-		1	0	0	1	
Pelobacter carbinolicus DSM 2380	Anaerobic	Aquatic	-		1	0	0	1	
Pelobacter propionicus DSM 2379	Anaerobic	Multiple	-		0	0	0	1	
Stigmatella aurantiaca DW4/3-1	Aerobic	Terrestrial	-		2	0	0	2	
Syntrophobacter fumaroxidans MPOB	Anaerobic	Aquatic	-		0	0	0	1	
Syntrophus aciditrophicus SB	Anaerobic	Multiple	-		0	0	0	1	
delta proteobacterium MLMS-1	Microaerophilic	Aquatic	-		0	0	0	0	
epsilon subdivision									
Campylobacter coli RM2228	Microaerophilic	Multiple	-		0	0	0	0	
Campylobacter concisus 13826	Microaerophilic	Host	-		2	0	0	0	
Campylobacter curvus 525.92	Microaerophilic	Host	-		2	0	0	0	
Campylobacter fetus subsp. fetus 82-40	Microaerophilic	Host	-		2	0	0	0	
Campylobacter jejuni RM1221	Microaerophilic	Multiple	-		0	0	0	0	
Campylobacter lari RM2100	Microaerophilic	Multiple	-		1	0	0	0	
Campylobacter upsaliensis RM3195	Microaerophilic	Multiple	-		0	0	0	0	
Helicobacter acinonychis str. Sheeba	Microaerophilic	Host	-		0	0	0	0	
Helicobacter hepaticus ATCC 51449	Microaerophilic	Host	-		0	0	0	0	
Helicobacter pylori 26695	Aerobic	Host	-		0	0	0	0	
Thiomicrospira denitrificans ATCC 33889	Anaerobic	Multiple	-		1	0	0	0	
Wolinella succinogenes DSM 1740	Microaerophilic	Host	-		1	0	0	0	
gamma subdivision									
Enterobacteriales									
Buchnera aphidicola str. APS (Acyrthosiphon pisum)	Facultative	Host	-		2	0	0	0	
Candidatus Blochmannia floridanus	Facultative	Host	-		2	0	0	0	
Enterobacter sp. 638	Facultative	Multiple	-		3	0	0	3	
Erwinia carotovora subsp. atroseptica SCRI1043	Facultative	Multiple	-		4	0	0	4	
Escherichia coli 536	Facultative	Host	-		5	0	0	5	
Photorhabdus luminescens subsp. laumondii TTO1	Facultative	Host	-		3	0	0	4	
Salmonella enterica subsp. enterica serovar Choleraes	Facultative	Host	-		4	0	0	4	
Salmonella typhimurium LT2	Facultative	Host	-		4	0	0	4	
Serratia proteamaculans 568	Facultative	Multiple	-		3	0	0	2	
Shigella boydii Sb227	Facultative	Host	-		4	0	0	4	
Shigella dysenteriae Sd197	Facultative	Host	-		3	0	0	4	
Shigella flexneri 2a str. 2457T	Facultative	Host	-		4	0	0	5	
Shigella sonnei Ss046	Facultative	Host	-		4	0	0	5	
Sodalis glossinidius str. 'morsitans'	Microaerophilic	Host	-		3	0	0	3	
Wigglesworthia glossinidia endosymbiont of Glossina b	Microaerophilic	Host	-		3	0	0	0	
Yersinia bercovieri ATCC 43970	Facultative	Multiple	-		4	0	0	4	
Yersinia enterocolitica subsp. enterocolitica 8081	Facultative	Multiple	-		3	0	0	3	
Yersinia frederiksenii ATCC 33641	Facultative	Multiple	-		4	0	0	4	
Yersinia intermedia ATCC 29909	Facultative	Multiple	-		4	0	0	4	
Yersinia mollaretii ATCC 43969	Facultative	Multiple	-		4	0	0	4	
Yersinia pestis Antiqua	Facultative	Multiple	-		4	0	0	4	
Yersinia pseudotuberculosis IP 32953	Facultative	Multiple	-		4	0	0	4	
Others									
Acinetobacter sp. ADP1	Aerobic	Multiple	-		2	0	0	1	
Aeromonas hydrophila subsp. hydrophila ATCC 7966	Facultative	Multiple	-		3	0	0	1	
Alcanivorax borkumensis SK2	Aerobic	Aquatic	-		3	0	1	3	
Alkalilimnicola ehrlichei MLHE-1	Facultative	Aquatic	-		2	0	0	0	
Alteromonadales bacterium TW-7	Aerobic	Aquatic	-		2	0	0	0	
Alteromonas macleodii 'Deep ecotype'	Aerobic	Aquatic	-		5	0	0	1	
Baumannia cicadellinicola str. Hc (Homalodisca coagul	Facultative	Host	-		2	0	0	0	
Candidatus Carsonella ruddii PV	Facultative	Host	-		0	0	0	0	
Candidatus Ruthia magnifica str. Cm (Calyptogena mag	Facultative	Host	-		0	0	0	0	
Chromohalobacter salexigens DSM 3043	Aerobic	Multiple	-		4	0	0	0	
Colwellia psychrerythraea 34H	Facultative	Aquatic	-		2	0	0	1	
Congregibacter litoralis KT71	Aerobic	Aquatic	-		0	0	0	0	

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Coxiella burnetii RSA 493	Facultative	Multiple	-		3	0	0	0	
Endoriftia persephone 'Hot96_1+Hot96_2'	Aerobic	Host	-		0	0	0	0	
Francisella tularensis subsp. holarctica	Aerobic	Host	-		3	0	0	1	
Hahella chejuensis KCTC 2396	Facultative	Aquatic	-		3	0	0	1	
Halorhodospira halophila SL1	Facultative	Multiple	-		0	0	0	0	
Idiomarina baltica OS145	Aerobic	Aquatic	-		3	0	1	1	
Idiomarina loihiensis L2TR	Aerobic	Aquatic	-		3	0	1	2	
Legionella pneumophila str. Lens	Aerobic	Host	-		2	0	0	0	
Marinobacter aquaeolei VT8	Facultative	Aquatic	-		4	0	1	1	
Marinomonas sp. MED121	Aerobic	Aquatic	-		2	0	0	0	
Methylococcus capsulatus str. Bath	Aerobic	Multiple	-		3	0	0	1	
Nitrococcus mobilis Nb-231	Aerobic	Aquatic	-		2	0	0	0	
Nitrosococcus oceani ATCC 19707	Aerobic	Aquatic	-		3	0	1	0	
Oceanobacter sp. RED65	Aerobic	Aquatic	-		2	0	0	0	
Oceanospirillum sp. MED92	Aerobic	Aquatic	-		2	0	0	0	
Pseudoalteromonas atlantica T6c	Aerobic	Aquatic	-		4	0	0	1	
Pseudoalteromonas haloplanktis TAC125	Aerobic	Aquatic	-		3	0	0	2	
Pseudoalteromonas tunicata D2	Facultative	Aquatic	-		2	0	0	0	
Psychrobacter arcticus 273-4	Aerobic	Aquatic	-		1	0	1	1	
Psychrobacter cryohalolentis K5	Aerobic	Multiple	-		1	0	1	1	
Psychrobacter sp. PRwf-1	Aerobic	Multiple	-		1	0	1	1	
Psychromonas ingrahamii 37	Anaerobic	Aquatic	-		3	0	1	1	
Psychromonas sp. CNPT3	Facultative	Aquatic	-		1	0	0	1	
Reinekea sp. MED297	Aerobic	Aquatic	-		3	0	1	0	
Rickettsiella grylli	Facultative	Host	-		1	0	0	0	
Saccharophagus degradans 2-40	Aerobic	Aquatic	-		1	0	0	2	
Shewanella amazonensis SB2B	Facultative	Multiple	-		2	0	0	2	
Shewanella baltica OS155	Facultative	Aquatic	-		3	0	0	0	
Shewanella denitrificans OS217	Facultative	Aquatic	-		4	0	0	3	
Shewanella frigidimarina NCIMB 400	Facultative	Multiple	-		3	0	0	2	
Shewanella oneidensis MR-1	Facultative	Multiple	-		3	0	0	0	
Shewanella pealeana ATCC 700345	Facultative	Multiple	-		2	0	0	0	
Shewanella putrefaciens CN-32	Facultative	Multiple	-		5	0	0	3	
Shewanella sp. MR-4	Facultative	Multiple	-		5	0	0	0	
Shewanella woodyi ATCC 51908	Facultative	Multiple	-		4	0	0	0	
Thiomicrospira crunogena XCL-2	Anaerobic	Aquatic	-		1	0	0	3	
marine gamma proteobacterium HTCC2080	Aerobic	Aquatic	-		1	0	0	0	
marine gamma proteobacterium HTCC2143	Aerobic	Aquatic	-		1	0	0	0	
marine gamma proteobacterium HTCC2207	Aerobic	Aquatic	-		1	0	0	0	
Pasteurellaceae									
Actinobacillus pleuropneumoniae serovar 1 str. 4074	Facultative	Host	-		2	0	0	0	
Actinobacillus succinogenes 130Z	Anaerobic	Host	-		2	0	0	0	
Haemophilus ducreyi 35000HP	Anaerobic	Host	-		2	0	0	0	
Haemophilus influenzae 86-028NP	Facultative	Host	-		1	0	1	2	
Haemophilus somnus 129PT	Facultative	Host	-		0	0	0	1	
Mannheimia haemolytica PHL213	Facultative	Multiple	-		1	0	1	1	
Mannheimia succiniciproducens MBEL55E	Anaerobic	Host	-		2	0	0	0	
Pasteurella multocida subsp. multocida str. Pm70	Facultative	Host	-		1	0	1	3	
Pseudomonadaceae									
Azotobacter vinelandii AvOP	Aerobic	Multiple	-		3	0	0	2	
Pseudomonas aeruginosa PAO1	Aerobic	Multiple	-		4	0	0	2	
Pseudomonas entomophila L48	Aerobic	Multiple	-		3	0	0	2	
Pseudomonas fluorescens Pf-5	Aerobic	Multiple	-		3	0	1	2	
Pseudomonas mendocina ymp	Aerobic	Multiple	-		4	0	0	2	
Pseudomonas putida KT2440	Aerobic	Multiple	-		4	0	0	2	
Pseudomonas syringae pv. phaseolicola 1448A	Aerobic	Multiple	-		5	0	0	2	
Vibrionaceae									

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Photobacterium profundum SS9	Facultative	Multiple	-		4	0	0	2	
Photobacterium sp. SKA34	Facultative	Multiple	-		3	0	0	1	
Vibrio alginolyticus 12G01	Facultative	Multiple	-		5	0	0	1	
Vibrio angustum S14	Facultative	Aquatic	-		3	0	0	1	
Vibrio cholerae O1 biovar eltor str. N16961	Facultative	Aquatic	-		2	0	0	1	
Vibrio fischeri ES114	Facultative	Aquatic	-		1	0	0	1	
Vibrio harveyi HY01	Facultative	Aquatic	-		5	0	0	0	
Vibrio parahaemolyticus RIMD 2210633	Facultative	Aquatic	-		5	0	0	1	
Vibrio sp. Ex25	Facultative	Aquatic	-		5	0	0	1	
Vibrio splendidus 12B01	Facultative	Aquatic	-		4	0	0	1	
Vibrio vulnificus CMCP6	Facultative	Aquatic	-		3	0	0	1	
Xanthomonadaceae									
Stenotrophomonas maltophilia R551-3	Aerobic	Multiple	-		2	0	0	2	
Xanthomonas axonopodis pv. citri str. 306	Aerobic	Host	-		3	0	0	3	
Xanthomonas campestris pv. campestris str. 8004	Aerobic	Host	-		3	0	0	3	
Xanthomonas oryzae pv. oryzae KACC10331	Aerobic	Host	-		3	0	0	3	
Xylella fastidiosa 9a5c	Aerobic	Host	-		3	0	0	3	
Spirochaetales					6			6	
Borrelia afzelii PKo	Aerobic	Host	-		0	0	0	0	
Borrelia burgdorferi B31	Microaerophilic	Host	-		0	0	0	0	
Borrelia garinii PBi	Microaerophilic	Host	-		0	0	0	0	
Leptospira borgpetersenii serovar Hardjo-bovis JB197	Aerobic	Host	-		0	0	0	0	
Leptospira interrogans serovar Copenhageni str. Fiocru	Aerobic	Host	-		2	0	0	0	
Treponema denticola ATCC 35405	Anaerobic	Host	-		0	0	0	1	
Treponema pallidum subsp. pallidum str. Nichols	Anaerobic	Host	-		0	0	0	0	
Archaea									
Crenarchaeota									
Desulfurococcales									
Aeropyrum pernix K1	Aerobic	Terrestrial			1	0	0	0	
Hyperthermus butylicus DSM 5456	Anaerobic	Aquatic			0	0	0	0	
Sulfolobales									
Metallosphaera sedula DSM 5348	Aerobic	Aquatic			1	0	0	0	
Sulfolobus acidocaldarius DSM 639	Aerobic	Aquatic			2	0	0	0	
Sulfolobus solfataricus P2	Aerobic	Aquatic			2	0	0	0	
Sulfolobus tokodaii str. 7	Aerobic	Aquatic			1	0	0	0	
Thermoproteales									
Pyrobaculum aerophilum str. IM2	Facultative	Aquatic			1	0	0	0	
Pyrobaculum islandicum DSM 4184	Anaerobic	Aquatic			0	0	0	0	
Thermofilum pendens Hrk 5	Anaerobic	Aquatic			0	0	0	0	
Euryarchaeota									
Archaeoglobales									
Archaeoglobus fulgidus DSM 4304	Anaerobic	Aquatic			0	0	0	1	
Halobacteriales									
Haloarcula marismortui ATCC 43049	Aerobic	Aquatic			2	0	0	1	
Halobacterium sp. NRC-1	Aerobic	Aquatic			1	0	0	0	
Haloquadratum walsbyi DSM 16790	Aerobic	Aquatic			1	0	0	0	
Natronomonas pharaonis DSM 2160	Aerobic	Aquatic			1	0	0	1	
Methanobacteriales									
Methanosphaera stadtmanae DSM 3091	Anaerobic	Host			0	0	0	1	
Methanothermobacter thermautotrophicus str. Delta H	Anaerobic	Aquatic			0	0	0	1	
Methanococcales									
Methanocaldococcus jannaschii DSM 2661	Anaerobic	Aquatic			0	0	0	0	
Methanococcus maripaludis S2	Anaerobic	Aquatic			0	0	0	0	
Methanomicrobiales									
Methanoculleus marisnigri JR1	Anaerobic	Aquatic			0	0	0	1	
Methanospirillum hungatei JF-1	Anaerobic	Multiple			0	0	0	1	

Bacteria	Oxygen Req	Habitat	Gram Strain		Cuproproteins	Importers	Chaperones	Exporters	Cuproproteins➔
Methanopyrales									
Methanopyrus kandleri AV19	Anaerobic	Aquatic			**0**	**0**	**0**	**0**	
Methanosarcinales									
Methanococcoides burtonii DSM 6242	Anaerobic	Aquatic			**0**	**0**	**0**	**1**	
Methanosaeta thermophila PT	Anaerobic	Aquatic			**0**	**0**	**0**	**1**	
Methanosarcina acetivorans C2A	Anaerobic	Aquatic			**0**	**0**	**0**	**1**	
Methanosarcina barkeri str. Fusaro	Anaerobic	Aquatic			**0**	**0**	**0**	**1**	
Methanosarcina mazei Go1	Anaerobic	Aquatic			**0**	**0**	**0**	**1**	
Thermococcales									
Pyrococcus abyssi GE5	Anaerobic	Aquatic			**0**	**0**	**0**	**0**	
Pyrococcus furiosus DSM 3638	Anaerobic	Aquatic			**0**	**0**	**0**	**1**	
Pyrococcus horikoshii OT3	Anaerobic	Aquatic			**0**	**0**	**0**	**0**	
Thermococcus kodakarensis KOD1	Anaerobic	Aquatic			**0**	**0**	**0**	**1**	
Thermoplasmales									
Ferroplasma acidarmanus Fer1	Facultative	Terrestrial			**0**	**0**	**0**	**0**	
Picrophilus torridus DSM 9790	Facultative	Terrestrial			**1**	**0**	**0**	**0**	
Thermoplasma acidophilum DSM 1728	Facultative	Aquatic			**0**	**0**	**0**	**0**	
Thermoplasma volcanium GSS1	Facultative	Aquatic			**0**	**0**	**0**	**0**	
Nanoarchaeota									
Nanoarchaeum equitans Kin4-M	Anaerobic	Aquatic			**0**	**0**	**0**	**0**	

Bacteria	COX	ND2	SOD1	Nitrosocyanin	Plastocyanin	Cu-containing Nitrite Reductase	Cu amine oxidase	pMMO
Acidothermus cellulolyticus 11B	+							
Arthrobacter aurescens TC1	+							
Arthrobacter sp. FB24	+						+	
Bifidobacterium adolescentis								
Bifidobacterium longum DJO10A								
Brevibacterium linens BL2	+						+	
Collinsella aerofaciens ATCC 25986								
Corynebacterium diphtheriae NCTC 13129	+							
Corynebacterium efficiens YS-314	+							
Corynebacterium glutamicum ATCC 13032	+							
Corynebacterium jeikeium K411	+							
Frankia alni ACN14a	+							
Frankia sp. EAN1pec	+						+	
Janibacter sp. HTCC2649	+							
Kineococcus radiotolerans SRS30216	+							
Leifsonia xyli subsp. xyli str. CTCB07	+							
Mycobacterium avium subsp. paratuberculosis K-10	+							
Mycobacterium bovis AF2122/97	+							
Mycobacterium flavescens PYR-GCK	+						+	
Mycobacterium leprae TN	+							
Mycobacterium smegmatis str. MC2 155	+							
Mycobacterium sp. KMS	+						+	
Mycobacterium tuberculosis C	+							
Mycobacterium ulcerans Agy99	+							
Mycobacterium vanbaalenii PYR-1	+						+	
Nocardia farcinica IFM 10152	+						+	
Nocardioides sp. JS614	+							
Propionibacterium acnes KPA171202	+							
Rhodococcus sp. RHA1	+						+	
Rubrobacter xylanophilus DSM 9941								
Salinispora arenicola CNS205	+							
Salinispora tropica CNB-440	+							
Streptomyces avermitilis MA-4680	+							
Streptomyces coelicolor A3(2)	+							
Symbiobacterium thermophilum IAM 14863	+					+		
Thermobifida fusca YX	+							
Tropheryma whipplei TW08/27	+							
marine actinobacterium PHSC20C1	+							
Bacteroidetes/Chlorobi								
Bacteroides caccae ATCC 43185								
Bacteroides fragilis YCH46								
Bacteroides thetaiotaomicron VPI-5482								
Candidatus Sulcia muelleri str. Hc (Homalodisca coagu								
Cellulophaga sp. MED134	+							
Chlorobium chlorochromatii CaD3								
Chlorobium ferrooxidans DSM 13031								
Chlorobium limicola DSM 245								
Chlorobium phaeobacteroides BS1								
Chlorobium tepidum TLS								
Croceibacter atlanticus HTCC2559	+							
Cytophaga hutchinsonii ATCC 33406								
Flavobacteria bacterium BBFL7	+							
Flavobacteriales bacterium HTCC2170				+				
Flavobacterium johnsoniae UW101						+		
Gramella forsetii KT0803								
Leeuwenhoekiella blandensis MED217	+							
Microscilla marina ATCC 23134								

Bacteria	**COX**	**ND2**	**SOD1**	**Nitrosocyanin**	**Plastocyanin**	**Cu-containing Nitrite Reductase**	**Cu amine oxidase**	**pMMO**
Pelodictyon luteolum DSM 273								
Pelodictyon phaeoclathratiforme BU-1								
Polaribacter irgensii 23-P	+							
Porphyromonas gingivalis W83								
Prosthecochloris aestuarii DSM 271								
Prosthecochloris vibrioformis DSM 265								
Psychroflexus torquis ATCC 700755	+			+				
Robiginitalea biformata HTCC2501	+			+				
Salinibacter ruber DSM 13855				+				
Tenacibaculum sp. MED152								
Chlamydiae								
Candidatus Protochlamydia amoebophila UWE25	+							
Chlamydia muridarum Nigg								
Chlamydia trachomatis A/HAR-13								
Chlamydophila abortus S26/3								
Chlamydophila caviae GPIC								
Chlamydophila felis Fe/C-56								
Chlamydophila pneumoniae AR39								
Cyanobacteria								
Anabaena variabilis ATCC 29413	+				+		+	
Crocosphaera watsonii WH 8501	+				+			
Gloeobacter violaceus PCC 7421	+				+			
Lyngbya sp. PCC 8106	+				+			
Nodularia spumigena CCY9414	+				+			
Nostoc punctiforme PCC 73102	+				+		+	
Nostoc sp. PCC 7120	+				+		+	
Prochlorococcus marinus str. MIT 9312	+				+			
Synechococcus elongatus PCC 6301	+				+			
Synechococcus sp. CC9311	+		+		+			
Synechocystis sp. PCC 6803	+				+			
Thermosynechococcus elongatus BP-1	+							
Trichodesmium erythraeum IMS101	+				+		+	
Firmicutes								
Bacillales								
Bacillus anthracis str. Ames	+		+					
Bacillus cereus ATCC 10987	+		+					
Bacillus clausii KSM-K16	+							
Bacillus halodurans C-125	+							
Bacillus licheniformis ATCC 14580	+		+					
Bacillus sp. NRRL B-14911	+							
Bacillus subtilis subsp. subtilis str. 168	+		+					
Bacillus thuringiensis serovar konkukian str. 97-27	+		+					
Bacillus weihenstephanensis KBAB4	+		+					
Exiguobacterium sibiricum 255-15	+							
Geobacillus kaustophilus HTA426	+		+					
Listeria innocua Clip112624	+							
Listeria monocytogenes EGD-e	+							
Listeria welshimeri serovar 6b str. SLCC5334								
Oceanobacillus iheyensis HTE831	+		+					
Paenibacillus larvae subsp. larvae BRL-230010	+							
Pasteuria nishizawae str. North American								
Staphylococcus aureus RF122	+							
Staphylococcus epidermidis ATCC 12228	+							
Staphylococcus haemolyticus JCSC1435	+							
Staphylococcus saprophyticus subsp. saprophyticus A	+							
Clostridia								
Alkaliphilus metalliredigenes QYMF								

Bacteria	**COX**	**ND2**	**SOD1**	**Nitrosocyanin**	**Plastocyanin**	**Cu-containing Nitrite Reductase**	**Cu amine oxidase**	**pMMO**
Caldicellulosiruptor saccharolyticus DSM 8903								
Carboxydothermus hydrogenoformans Z-2901								
Clostridium acetobutylicum ATCC 824								
Clostridium beijerincki NCIMB 8052								
Clostridium cellulolyticum H10								
Clostridium difficile QCD-32g58								
Clostridium novyi NT								
Clostridium perfringens ATCC 13124								
Clostridium phytofermentans ISDg								
Clostridium sp. OhILAs								
Clostridium tetani E88								
Clostridium thermocellum ATCC 27405								
Desulfitobacterium hafniense DCB-2								
Desulfotomaculum reducens MI-1								
Eubacterium ventriosum ATCC 27560								
Halothermothrix orenii H 168								
Moorella thermoacetica ATCC 39073								
Syntrophomonas wolfei subsp. wolfei str. Goettingen								
Thermoanaerobacter ethanolicus ATCC 33223								
Thermoanaerobacter tengcongensis MB4								
Thermosinus carboxydivorans Nor1								
Lactobacillales								
Enterococcus faecalis V583								
Enterococcus faecium DO								
Lactobacillus acidophilus NCFM								
Lactobacillus brevis ATCC 367								
Lactobacillus casei ATCC 334								
Lactobacillus delbrueckii subsp. bulgaricus ATCC 1184								
Lactobacillus gasseri ATCC 33323								
Lactobacillus johnsonii NCC 533								
Lactobacillus plantarum WCFS1								
Lactobacillus reuteri 100-23								
Lactobacillus sakei subsp. sakei 23K								
Lactobacillus salivarius subsp. salivarius UCC118								
Lactococcus lactis subsp. lactis Il1403								
Leuconostoc mesenteroides subsp. mesenteroides AT								
Oenococcus oeni PSU-1								
Pediococcus pentosaceus ATCC 25745								
Streptococcus agalactiae 2603V/R								
Streptococcus mutans UA159								
Streptococcus pneumoniae R6								
Streptococcus pyogenes M1 GAS								
Streptococcus suis 89/1591								
Streptococcus thermophilus CNRZ1066								
Mollicutes								
Aster yellows witches1-broom phytoplasma AYWB								
Mesoplasma florum L1								
Mycoplasma capricolum subsp. capricolum ATCC 2734								
Mycoplasma gallisepticum R								
Mycoplasma genitalium G37								
Mycoplasma hyopneumoniae 232								
Mycoplasma mobile 163K								
Mycoplasma mycoides subsp. mycoides SC str. PG1								
Mycoplasma penetrans HF-2								
Mycoplasma pneumoniae M129								
Mycoplasma pulmonis UAB CTIP								
Mycoplasma synoviae 53								

Bacteria	**COX**	**ND2**	**SOD1**	**Nitrosocyanin**	**Plastocyanin**	**Cu-containing Nitrite Reductase**	**Cu amine oxidase**	**pMMO**
Onion yellows phytoplasma OY-M								
Ureaplasma parvum serovar 3 str. ATCC 700970								
Others								
Acidobacteria bacterium Ellin345	+							
Aquifex aeolicus VF5	+							
Blastopirellula marina DSM 3645	+							
Chloroflexus aggregans DSM 9485	+				+	+		
Chloroflexus aurantiacus J-10-fl	+				+	+		
Dehalococcoides ethenogenes 195								
Dehalococcoides sp. CBDB1								
Deinococcus geothermalis DSM 11300	+							
Deinococcus radiodurans R1	+							
Fervidobacterium nodosum Rt17-B1								
Fusobacterium nucleatum subsp. nucleatum ATCC 255								
Herpetosiphon aurantiacus ATCC 23779	+					+		
Rhodopirellula baltica SH 1	+							
Roseiflexus castenholzii DSM 13941	+							
Roseiflexus sp. RS-1	+				+			
Solibacter usitatus Ellin6076	+						+	
Thermosipho melanesiensis BI429								
Thermotoga maritima MSB8								
Thermotoga petrophila RKU-1								
Thermus thermophilus HB27	+		+					
Proteobacteria								
Others								
Magnetococcus sp. MC-1								
Mariprofundus ferrooxydans PV-1								
alpha subdivision								
Others								
Acidiphilium cryptum JF-5	+							
Aurantimonas sp. SI85-9A1	+	+						
Bartonella bacilliformis KC583	+							
Bartonella henselae str. Houston-1	+		+					
Bartonella quintana str. Toulouse	+							
Bradyrhizobium japonicum USDA 110	+	+		+				
Bradyrhizobium sp. BTAi1	+			+		+	+	
Brucella abortus biovar 1 str. 9-941	+		+	+		+		
Brucella melitensis 16M	+		+	+		+		
Brucella suis 1330	+		+	+		+		
Caulobacter crescentus CB15	+							
Caulobacter sp. K31	+	+						
Dinoroseobacter shibae DFL 12	+			+				
Erythrobacter litoralis HTCC2594	+							
Erythrobacter sp. NAP1	+	+						
Fulvimarina pelagi HTCC2506	+							
Gluconobacter oxydans 621H	+							
Granulobacter bethesdensis CGDNIH1	+	+						
Hyphomonas neptunium ATCC 15444	+							
Jannaschia sp. CCS1	+							
Loktanella vestfoldensis SKA53	+							
Magnetospirillum magneticum AMB-1	+		+	+				
Magnetospirillum magnetotacticum MS-1	+	+	+					
Maricaulis maris MCS10	+							
Mesorhizobium loti MAFF303099	+						+	
Mesorhizobium sp. BNC1	+					+		
Nitrobacter hamburgensis X14	+							
Nitrobacter sp. Nb-311A	+							

Bacteria	COX	ND2	SOD1	Nitrosocyanin	Plastocyanin	Cu-containing Nitrite Reductase	Cu amine oxidase	pMMO
Nitrobacter winogradskyi Nb-255	+							
Novosphingobium aromaticivorans DSM 12444	+							
Oceanicaulis alexandrii HTCC2633	+							
Oceanicola batsensis HTCC2597	+							
Oceanicola granulosus HTCC2516	+							
Paracoccus denitrificans PD1222	+			+	+			
Parvibaculum lavamentivorans DS-1	+					+		
Parvularcula bermudensis HTCC2503	+							
Rhodobacter sphaeroides 2.4.1	+							
Rhodobacterales bacterium HTCC2654	+			+		+		
Rhodopseudomonas palustris BisA53	+	+		+		+		
Rhodospirillum rubrum ATCC 11170								
Roseobacter denitrificans OCh 114	+			+				
Roseobacter sp. MED193	+							
Roseovarius nubinhibens ISM	+							
Roseovarius sp. 217	+			+				
Silicibacter pomeroyi DSS-3	+			+				
Silicibacter sp. TM1040	+							
Sphingomonas sp. SKA58	+							
Sphingomonas wittichii RW1	+							
Sphingopyxis alaskensis RB2256	+							
Stappia aggregata IAM 12614	+			+				
Sulfitobacter sp. EE-36	+							
Xanthobacter autotrophicus Py2	+							
Zymomonas mobilis subsp. mobilis ZM4		+						
alpha proteobacterium HTCC2255	+							
Rhizobiaceae								
Agrobacterium tumefaciens str. C58	+					+		
Rhizobium etli CFN 42	+					+		
Rhizobium leguminosarum bv. viciae 3841	+							
Sinorhizobium medicae WSM419	+					+		
Sinorhizobium meliloti 1021	+			+		+		
Rickettsiales								
Anaplasma marginale str. St. Maries	+							
Anaplasma phagocytophilum HZ	+							
Candidatus Pelagibacter ubique HTCC1062	+							
Ehrlichia canis str. Jake	+							
Ehrlichia chaffeensis str. Arkansas	+							
Ehrlichia ruminantium str. Gardel	+							
Neorickettsia sennetsu str. Miyayama	+							
Rickettsia africae ESF-5	+							
Rickettsia akari str. Hartford	+							
Rickettsia bellii RML369-C	+							
Rickettsia canadensis str. McKiel	+							
Rickettsia conorii str. Malish 7	+							
Rickettsia felis URRWXCal2	+							
Rickettsia massiliae MTU5	+							
Rickettsia prowazekii str. Madrid E	+							
Rickettsia rickettsii	+							
Rickettsia sibirica 246	+							
Rickettsia typhi str. Wilmington								
Wolbachia endosymbiont of Drosophila melanogaster	+							
beta subdivision								
Bordetella								
Bordetella bronchiseptica RB50	+	+	+		+			
Bordetella parapertussis 12822	+	+	+		+			
Bordetella pertussis Tohama I	+	+	+		+			

Bacteria	COX	ND2	SOD1	Nitrosocyanin	Plastocyanin	Cu-containing Nitrite Reductase	Cu amine oxidase	pMMO
Burkholderiaceae								
Burkholderia ambifaria MC40-6	+	+						
Burkholderia cenocepacia AU 1054	+	+						
Burkholderia cepacia AMMD	+	+						
Burkholderia dolosa AUO158	+	+						
Burkholderia mallei ATCC 23344	+	+		+		+		
Burkholderia multivorans ATCC 17616	+	+						
Burkholderia phymatum STM815	+	+						
Burkholderia phytofirmans PsJN	+	+						
Burkholderia pseudomallei 1710b	+	+		+		+		
Burkholderia sp. 383	+	+						
Burkholderia thailandensis E264	+	+		+		+		
Burkholderia vietnamiensis G4	+	+						
Burkholderia xenovorans LB400	+	+						
Polynucleobacter sp. QLW-P1DMWA-1	+	+						
Ralstonia eutropha JMP134	+	+						
Ralstonia metallidurans CH34	+	+		+				
Ralstonia pickettii 12J	+	+		+		+		
Ralstonia solanacearum GMI1000	+	+		+		+		
Neisseriaceae								
Chromobacterium violaceum ATCC 12472	+	+				+		
Neisseria gonorrhoeae FA 1090				+	+	+		
Neisseria meningitidis MC58			+		+	+		
Others								
Acidovorax avenae subsp. citrulli AAC00-1	+	+	+		+			
Acidovorax sp. JS42	+	+		+				
Azoarcus sp. EbN1	+	+		+				
Comamonas testosteroni KF-1	+				+			
Dechloromonas aromatica RCB	+							
Delftia acidovorans SPH-1	+				+			
Methylibium petroleiphilum PM1	+							
Methylobacillus flagellatus KT	+	+			+			
Methylophilales bacterium HTCC2181	+	+						
Nitrosomonas europaea ATCC 19718	+			+				+
Nitrosomonas eutropha C71	+			+				+
Nitrosospira multiformis ATCC 25196	+			+		+		+
Polaromonas naphthalenivorans CJ2	+	+				+		
Polaromonas sp. JS666	+	+						
Rhodoferax ferrireducens T118	+			+				
Rubrivivax gelatinosus PM1	+							
Thiobacillus denitrificans ATCC 25259	+	+	+	+				
Verminephrobacter eiseniae EF01-2	+							
delta subdivision								
Anaeromyxobacter dehalogenans 2CP-C	+			+				
Anaeromyxobacter sp. Fw109-5								
Bdellovibrio bacteriovorus HD100	+					+		
Candidatus Desulfococcus oleovorans Hxd3								
Desulfotalea psychrophila LSv54								
Desulfovibrio desulfuricans G20	+							
Desulfovibrio vulgaris subsp. vulgaris str. Hildenboroug	+							
Desulfuromonas acetoxidans DSM 684								
Geobacter lovleyi SZ								
Geobacter metallireducens GS-15	+							
Geobacter sp. FRC-32								
Geobacter sulfurreducens PCA	+							
Geobacter uraniumreducens Rf4	+							
Lawsonia intracellularis PHE/MN1-00			+					

Bacteria	**COX**	**ND2**	**SOD1**	**Nitrosocyanin**	**Plastocyanin**	**Cu-containing Nitrite Reductase**	**Cu amine oxidase**	**pMMO**
Myxococcus xanthus DK 1622	+							
Pelobacter carbinolicus DSM 2380	+							
Pelobacter propionicus DSM 2379								
Stigmatella aurantiaca DW4/3-1	+						+	
Syntrophobacter fumaroxidans MPOB								
Syntrophus aciditrophicus SB								
delta proteobacterium MLMS-1								
epsilon subdivision								
Campylobacter coli RM2228								
Campylobacter concisus 13826			+	+				
Campylobacter curvus 525.92			+	+				
Campylobacter fetus subsp. fetus 82-40			+	+				
Campylobacter jejuni RM1221								
Campylobacter lari RM2100			+					
Campylobacter upsaliensis RM3195								
Helicobacter acinonychis str. Sheeba								
Helicobacter hepaticus ATCC 51449								
Helicobacter pylori 26695								
Thiomicrospira denitrificans ATCC 33889				+				
Wolinella succinogenes DSM 1740				+				
gamma subdivision								
Enterobacteriales								
Buchnera aphidicola str. APS (Acyrthosiphon pisum)	+							
Candidatus Blochmannia floridanus	+							
Enterobacter sp. 638	+	+	+					
Erwinia carotovora subsp. atroseptica SCRI1043	+	+	+					
Escherichia coli 536	+	+	+				+	
Photorhabdus luminescens subsp. laumondii TTO1	+	+						
Salmonella enterica subsp. enterica serovar Choleraes	+	+	+					
Salmonella typhimurium LT2	+	+	+					
Serratia proteamaculans 568	+	+	+					
Shigella boydii Sb227	+	+	+					
Shigella dysenteriae Sd197		+	+				+	
Shigella flexneri 2a str. 2457T	+	+	+					
Shigella sonnei Ss046	+	+	+					
Sodalis glossinidius str. 'morsitans'	+	+						
Wigglesworthia glossinidia endosymbiont of Glossina b	+	+						
Yersinia bercovieri ATCC 43970	+	+	+					
Yersinia enterocolitica subsp. enterocolitica 8081	+	+	+					
Yersinia frederiksenii ATCC 33641	+	+	+					
Yersinia intermedia ATCC 29909	+	+	+					
Yersinia mollaretii ATCC 43969	+	+	+					
Yersinia pestis Antiqua	+	+	+					
Yersinia pseudotuberculosis IP 32953	+	+	+					
Others								
Acinetobacter sp. ADP1	+	+						
Aeromonas hydrophila subsp. hydrophila ATCC 7966	+	+			+			
Alcanivorax borkumensis SK2	+	+						
Alkalilimnicola ehrlichei MLHE-1	+			+				
Alteromonadales bacterium TW-7	+	+						
Alteromonas macleodii 'Deep ecotype'	+	+	+		+			
Baumannia cicadellinicola str. Hc (Homalodisca coagul	+							
Candidatus Carsonella ruddii PV								
Candidatus Ruthia magnifica str. Cm (Calyptogena mag								
Chromohalobacter salexigens DSM 3043	+	+	+					
Colwellia psychrerythraea 34H	+			+				
Congregibacter litoralis KT71								

Bacteria	**COX**	**ND2**	**SOD1**	**Nitrosocyanin**	**Plastocyanin**	**Cu-containing Nitrite Reductase**	**Cu amine oxidase**	**pMMO**
Coxiella burnetii RSA 493	+		+					
Endoriftia persephone 'Hot96_1+Hot96_2'								
Francisella tularensis subsp. holarctica	+		+					
Hahella chejuensis KCTC 2396	+	+		+				
Halorhodospira halophila SL1								
Idiomarina baltica OS145	+	+			+			
Idiomarina loihiensis L2TR	+	+			+			
Legionella pneumophila str. Lens	+		+					
Marinobacter aquaeolei VT8	+	+	+	+				
Marinomonas sp. MED121	+	+						
Methylococcus capsulatus str. Bath	+	+						+
Nitrococcus mobilis Nb-231	+		+					
Nitrosococcus oceani ATCC 19707	+			+				+
Oceanobacter sp. RED65	+	+						
Oceanospirillum sp. MED92	+	+						
Pseudoalteromonas atlantica T6c	+	+	+					
Pseudoalteromonas haloplanktis TAC125	+	+				+		
Pseudoalteromonas tunicata D2	+	+						
Psychrobacter arcticus 273-4								
Psychrobacter cryohalolentis K5								
Psychrobacter sp. PRwf-1								
Psychromonas ingrahamii 37	+	+		+				
Psychromonas sp. CNPT3		+						
Reinekea sp. MED297	+	+		+				
Rickettsiella grylli	+							
Saccharophagus degradans 2-40	+							
Shewanella amazonensis SB2B	+	+						
Shewanella baltica OS155	+	+			+			
Shewanella denitrificans OS217	+	+		+	+			
Shewanella frigidimarina NCIMB 400	+	+						
Shewanella oneidensis MR-1	+	+			+			
Shewanella pealeana ATCC 700345	+	+						
Shewanella putrefaciens CN-32	+	+	+		+			
Shewanella sp. MR-4	+	+	+		+			
Shewanella woodyi ATCC 51908	+	+			+			
Thiomicrospira crunogena XCL-2								
marine gamma proteobacterium HTCC2080	+							
marine gamma proteobacterium HTCC2143	+							
marine gamma proteobacterium HTCC2207	+							
Pasteurellaceae								
Actinobacillus pleuropneumoniae serovar 1 str. 4074		+	+			+		
Actinobacillus succinogenes 130Z		+	+			+		
Haemophilus ducreyi 35000HP		+	+					
Haemophilus influenzae 86-028NP		+						
Haemophilus somnus 129PT								
Mannheimia haemolytica PHL213		+						
Mannheimia succiniciproducens MBEL55E		+	+			+		
Pasteurella multocida subsp. multocida str. Pm70			+					
Pseudomonadaceae								
Azotobacter vinelandii AvOP	+	+	+					
Pseudomonas aeruginosa PAO1	+	+		+	+			
Pseudomonas entomophila L48	+	+			+	+		
Pseudomonas fluorescens Pf-5	+	+			+	+		
Pseudomonas mendocina ymp	+	+	+		+			
Pseudomonas putida KT2440	+	+			+			
Pseudomonas syringae pv. phaseolicola 1448A	+	+	+		+			
Vibrionaceae								

Bacteria	**COX**	**ND2**	**SOD1**	**Nitrosocyanin**	**Plastocyanin**	**Cu-containing Nitrite Reductase**	**Cu amine oxidase**	**pMMO**
Photobacterium profundum SS9	+	+		+				
Photobacterium sp. SKA34	+	+						
Vibrio alginolyticus 12G01	+	+	+		+			
Vibrio angustum S14	+	+						
Vibrio cholerae O1 biovar eltor str. N16961		+	+					
Vibrio fischeri ES114		+						
Vibrio harveyi HY01	+	+	+		+			
Vibrio parahaemolyticus RIMD 2210633	+	+	+		+			
Vibrio sp. Ex25	+	+	+		+			
Vibrio splendidus 12B01	+	+	+					
Vibrio vulnificus CMCP6	+	+	+					
Xanthomonadaceae								
Stenotrophomonas maltophilia R551-3	+							
Xanthomonas axonopodis pv. citri str. 306	+				+			
Xanthomonas campestris pv. campestris str. 8004	+				+			
Xanthomonas oryzae pv. oryzae KACC10331	+				+			
Xylella fastidiosa 9a5c	+				+			
Spirochaetales								
Borrelia afzelii PKo								
Borrelia burgdorferi B31								
Borrelia garinii PBi								
Leptospira borgpetersenii serovar Hardjo-bovis JB197								
Leptospira interrogans serovar Copenhageni str. Fiocru	+							
Treponema denticola ATCC 35405								
Treponema pallidum subsp. pallidum str. Nichols								
Archaea								
Crenarchaeota								
Desulfurococcales								
Aeropyrum pernix K1	+							
Hyperthermus butylicus DSM 5456								
Sulfolobales								
Metallosphaera sedula DSM 5348	+							
Sulfolobus acidocaldarius DSM 639	+						+	
Sulfolobus solfataricus P2	+						+	
Sulfolobus tokodaii str. 7	+							
Thermoproteales								
Pyrobaculum aerophilum str. IM2	+							
Pyrobaculum islandicum DSM 4184								
Thermofilum pendens Hrk 5								
Euryarchaeota								
Archaeoglobales								
Archaeoglobus fulgidus DSM 4304								
Halobacteriales								
Haloarcula marismortui ATCC 43049	+			+		+		
Halobacterium sp. NRC-1	+							
Haloquadratum walsbyi DSM 16790	+							
Natronomonas pharaonis DSM 2160	+					+		
Methanobacteriales								
Methanosphaera stadtmanae DSM 3091								
Methanothermobacter thermautotrophicus str. Delta H								
Methanococcales								
Methanocaldococcus jannaschii DSM 2661								
Methanococcus maripaludis S2								
Methanomicrobiales								
Methanoculleus marisnigri JR1								
Methanospirillum hungatei JF-1								

Bacteria	COX	ND2	SOD1	Nitrosocyanin	Plastocyanin	Cu-containing Nitrite Reductase	Cu amine oxidase	pMMO
Methanopyrales								
Methanopyrus kandleri AV19								
Methanosarcinales								
Methanococcoides burtonii DSM 6242								
Methanosaeta thermophila PT								
Methanosarcina acetivorans C2A								
Methanosarcina barkeri str. Fusaro								
Methanosarcina mazei Go1								
Thermococcales								
Pyrococcus abyssi GE5								
Pyrococcus furiosus DSM 3638								
Pyrococcus horikoshii OT3								
Thermococcus kodakarensis KOD1								
Thermoplasmales								
Ferroplasma acidarmanus Fer1								
Picrophilus torridus DSM 9790	+							
Thermoplasma acidophilum DSM 1728								
Thermoplasma volcanium GSS1								
Nanoarchaeota								
Nanoarchaeum equitans Kin4-M								

Bacteria	CotA	Tyrosinase	Exporters➔	PacS/CopA	CutC	CopB	PcoA	CueO	PcoC	CusCFBA
Acidothermus cellulolyticus 11B				+						
Arthrobacter aurescens TC1				+						
Arthrobacter sp. FB24				+	+					
Bifidobacterium adolescentis				+						
Bifidobacterium longum DJO10A										
Brevibacterium linens BL2				+						
Collinsella aerofaciens ATCC 25986				+						
Corynebacterium diphtheriae NCTC 13129				+						
Corynebacterium efficiens YS-314				+				+		
Corynebacterium glutamicum ATCC 13032				+				+		
Corynebacterium jeikeium K411										
Frankia alni ACN14a										
Frankia sp. EAN1pec				+				+		
Janibacter sp. HTCC2649				+				+		
Kineococcus radiotolerans SRS30216					+					
Leifsonia xyli subsp. xyli str. CTCB07				+	+					
Mycobacterium avium subsp. paratuberculosis K-10				+						
Mycobacterium bovis AF2122/97				+						
Mycobacterium flavescens PYR-GCK				+						
Mycobacterium leprae TN				+						
Mycobacterium smegmatis str. MC2 155				+						
Mycobacterium sp. KMS				+						
Mycobacterium tuberculosis C				+						
Mycobacterium ulcerans Agy99				+						
Mycobacterium vanbaalenii PYR-1				+						
Nocardia farcinica IFM 10152				+						
Nocardioides sp. JS614				+	+					
Propionibacterium acnes KPA171202				+						
Rhodococcus sp. RHA1				+						
Rubrobacter xylanophilus DSM 9941		+		+						
Salinispora arenicola CNS205				+						
Salinispora tropica CNB-440				+	+					
Streptomyces avermitilis MA-4680		+		+	+			+		
Streptomyces coelicolor A3(2)				+	+					
Symbiobacterium thermophilum IAM 14863				+						
Thermobifida fusca YX				+						
Tropheryma whipplei TW08/27				+						
marine actinobacterium PHSC20C1				+	+					
Bacteroidetes/Chlorobi										
Bacteroides caccae ATCC 43185				+						
Bacteroides fragilis YCH46				+	+					
Bacteroides thetaiotaomicron VPI-5482				+	+					
Candidatus Sulcia muelleri str. Hc (Homalodisca coagu										
Cellulophaga sp. MED134					+					
Chlorobium chlorochromatii CaD3				+						
Chlorobium ferrooxidans DSM 13031				+						
Chlorobium limicola DSM 245				+						
Chlorobium phaeobacteroides BS1				+						
Chlorobium tepidum TLS				+						
Croceibacter atlanticus HTCC2559				+						
Cytophaga hutchinsonii ATCC 33406				+						
Flavobacteria bacterium BBFL7					+					
Flavobacteriales bacterium HTCC2170					+					
Flavobacterium johnsoniae UW101				+	+					
Gramella forsetii KT0803				+						
Leeuwenhoekiella blandensis MED217				+	+					
Microscilla marina ATCC 23134				+						

Bacteria	CotA	Tyrosinase	Exporters➔	PacS/CopA	CutC	CopB	PcoA	CueO	PcoC	CusCFBA
Pelodictyon luteolum DSM 273				+						
Pelodictyon phaeoclathratiforme BU-1				+						
Polaribacter irgensii 23-P										
Porphyromonas gingivalis W83				+	+					
Prosthecochloris aestuarii DSM 271										
Prosthecochloris vibrioformis DSM 265										
Psychroflexus torquis ATCC 700755										
Robiginitalea biformata HTCC2501				+	+					
Salinibacter ruber DSM 13855				+						
Tenacibaculum sp. MED152				+						
Chlamydiae										
Candidatus Protochlamydia amoebophila UWE25				+						
Chlamydia muridarum Nigg										
Chlamydia trachomatis A/HAR-13										
Chlamydophila abortus S26/3										
Chlamydophila caviae GPIC										
Chlamydophila felis Fe/C-56										
Chlamydophila pneumoniae AR39										
Cyanobacteria										
Anabaena variabilis ATCC 29413				+						
Crocosphaera watsonii WH 8501				+						
Gloeobacter violaceus PCC 7421				+						
Lyngbya sp. PCC 8106				+						
Nodularia spumigena CCY9414				+						
Nostoc punctiforme PCC 73102				+						
Nostoc sp. PCC 7120				+						
Prochlorococcus marinus str. MIT 9312				+						
Synechococcus elongatus PCC 6301				+						
Synechococcus sp. CC9311				+						
Synechocystis sp. PCC 6803				+						
Thermosynechococcus elongatus BP-1				+						
Trichodesmium erythraeum IMS101				+						
Firmicutes										
Bacillales										
Bacillus anthracis str. Ames				+	+					
Bacillus cereus ATCC 10987		+		+	+					
Bacillus clausii KSM-K16	+			+						
Bacillus halodurans C-125				+						
Bacillus licheniformis ATCC 14580	+			+						
Bacillus sp. NRRL B-14911				+						
Bacillus subtilis subsp. subtilis str. 168	+			+						
Bacillus thuringiensis serovar konkukian str. 97-27				+	+					
Bacillus weihenstephanensis KBAB4				+	+					
Exiguobacterium sibiricum 255-15				+	+					
Geobacillus kaustophilus HTA426				+						
Listeria innocua Clip112624				+	+					
Listeria monocytogenes EGD-e				+	+					
Listeria welshimeri serovar 6b str. SLCC5334				+						
Oceanobacillus iheyensis HTE831	+			+	+					
Paenibacillus larvae subsp. larvae BRL-230010				+	+					
Pasteuria nishizawae str. North American										
Staphylococcus aureus RF122				+						
Staphylococcus epidermidis ATCC 12228				+						
Staphylococcus haemolyticus JCSC1435				+						
Staphylococcus saprophyticus subsp. saprophyticus A				+						
Clostridia										
Alkaliphilus metalliredigenes QYMF				+						

Bacteria	CotA	Tyrosinase	Exporters➔	PacS/CopA	CutC	CopB	PcoA	CueO	PcoC	CusCFBA
Caldicellulosiruptor saccharolyticus DSM 8903				+						
Carboxydothermus hydrogenoformans Z-2901				+						
Clostridium acetobutylicum ATCC 824				+						
Clostridium beijerincki NCIMB 8052				+	+					
Clostridium cellulolyticum H10				+						
Clostridium difficile QCD-32g58				+						
Clostridium novyi NT				+						
Clostridium perfringens ATCC 13124				+	+					
Clostridium phytofermentans ISDg				+	+					
Clostridium sp. OhILAs				+						
Clostridium tetani E88				+						
Clostridium thermocellum ATCC 27405				+						
Desulfitobacterium hafniense DCB-2				+						
Desulfotomaculum reducens MI-1				+						
Eubacterium ventriosum ATCC 27560				+						
Halothermothrix orenii H 168				+						
Moorella thermoacetica ATCC 39073				+						
Syntrophomonas wolfei subsp. wolfei str. Goettingen				+						
Thermoanaerobacter ethanolicus ATCC 33223				+						
Thermoanaerobacter tengcongensis MB4				+						
Thermosinus carboxydivorans Nor1				+						
Lactobacillales										
Enterococcus faecalis V583				+	+					
Enterococcus faecium DO				+						
Lactobacillus acidophilus NCFM				+						
Lactobacillus brevis ATCC 367				+						
Lactobacillus casei ATCC 334				+	+					
Lactobacillus delbrueckii subsp. bulgaricus ATCC 1184				+						
Lactobacillus gasseri ATCC 33323				+	+					
Lactobacillus johnsonii NCC 533				+						
Lactobacillus plantarum WCFS1				+	+					
Lactobacillus reuteri 100-23				+						
Lactobacillus sakei subsp. sakei 23K				+						
Lactobacillus salivarius subsp. salivarius UCC118				+						
Lactococcus lactis subsp. lactis Il1403				+	+					
Leuconostoc mesenteroides subsp. mesenteroides AT				+	+					
Oenococcus oeni PSU-1				+						
Pediococcus pentosaceus ATCC 25745				+	+					
Streptococcus agalactiae 2603V/R				+	+					
Streptococcus mutans UA159				+						
Streptococcus pneumoniae R6				+						
Streptococcus pyogenes M1 GAS				+	+					
Streptococcus suis 89/1591				+	+					
Streptococcus thermophilus CNRZ1066				+						
Mollicutes										
Aster yellows witches1-broom phytoplasma AYWB										
Mesoplasma florum L1										
Mycoplasma capricolum subsp. capricolum ATCC 2734										
Mycoplasma gallisepticum R										
Mycoplasma genitalium G37										
Mycoplasma hyopneumoniae 232										
Mycoplasma mobile 163K										
Mycoplasma mycoides subsp. mycoides SC str. PG1										
Mycoplasma penetrans HF-2										
Mycoplasma pneumoniae M129										
Mycoplasma pulmonis UAB CTIP										
Mycoplasma synoviae 53										

Bacteria	**CotA**	**Tyrosinase**	**Exporters➔**	**PacS/CopA**	**CutC**	**CopB**	**PcoA**	**CueO**	**PcoC**	**CusCFBA**
Onion yellows phytoplasma OY-M										
Ureaplasma parvum serovar 3 str. ATCC 700970										
Others										
Acidobacteria bacterium Ellin345				+						
Aquifex aeolicus VF5				+						
Blastopirellula marina DSM 3645				+						
Chloroflexus aggregans DSM 9485				+						
Chloroflexus aurantiacus J-10-fl				+						
Dehalococcoides ethenogenes 195				+						
Dehalococcoides sp. CBDB1				+						
Deinococcus geothermalis DSM 11300				+						
Deinococcus radiodurans R1				+						
Fervidobacterium nodosum Rt17-B1										
Fusobacterium nucleatum subsp. nucleatum ATCC 255				+	+					
Herpetosiphon aurantiacus ATCC 23779				+						
Rhodopirellula baltica SH 1				+						
Roseiflexus castenholzii DSM 13941										
Roseiflexus sp. RS-1				+						
Solibacter usitatus Ellin6076				+						
Thermosipho melanesiensis BI429										
Thermotoga maritima MSB8										
Thermotoga petrophila RKU-1										
Thermus thermophilus HB27				+						
Proteobacteria										
Others										
Magnetococcus sp. MC-1				+						
Mariprofundus ferrooxydans PV-1				+						
alpha subdivision										
Others										
Acidiphilium cryptum JF-5				+						
Aurantimonas sp. SI85-9A1				+						
Bartonella bacilliformis KC583										
Bartonella henselae str. Houston-1										
Bartonella quintana str. Toulouse										
Bradyrhizobium japonicum USDA 110				+						
Bradyrhizobium sp. BTAi1				+		+				
Brucella abortus biovar 1 str. 9-941				+				+		
Brucella melitensis 16M				+				+		
Brucella suis 1330				+				+		
Caulobacter crescentus CB15				+	+	+				
Caulobacter sp. K31				+		+				+
Dinoroseobacter shibae DFL 12				+						
Erythrobacter litoralis HTCC2594				+		+				
Erythrobacter sp. NAP1				+		+				
Fulvimarina pelagi HTCC2506				+						
Gluconobacter oxydans 621H				+		+				
Granulobacter bethesdensis CGDNIH1				+		+				
Hyphomonas neptunium ATCC 15444				+		+				+
Jannaschia sp. CCS1				+						
Loktanella vestfoldensis SKA53				+						
Magnetospirillum magneticum AMB-1				+						
Magnetospirillum magnetotacticum MS-1				+						
Maricaulis maris MCS10				+		+				
Mesorhizobium loti MAFF303099				+	+					
Mesorhizobium sp. BNC1				+						
Nitrobacter hamburgensis X14				+						+
Nitrobacter sp. Nb-311A				+						

Bacteria	**CotA**	**Tyrosinase**	**Exporters➔**	**PacS/CopA**	**CutC**	**CopB**	**PcoA**	**CueO**	**PcoC**	**CusCFBA**
Nitrobacter winogradskyi Nb-255				+						
Novosphingobium aromaticivorans DSM 12444				+	+	+				
Oceanicaulis alexandrii HTCC2633				+		+				
Oceanicola batsensis HTCC2597				+		+				
Oceanicola granulosus HTCC2516				+	+					
Paracoccus denitrificans PD1222				+						
Parvibaculum lavamentivorans DS-1				+						
Parvularcula bermudensis HTCC2503				+		+				
Rhodobacter sphaeroides 2.4.1				+						
Rhodobacterales bacterium HTCC2654				+						
Rhodopseudomonas palustris BisA53				+						
Rhodospirillum rubrum ATCC 11170				+						
Roseobacter denitrificans OCh 114				+						
Roseobacter sp. MED193				+						
Roseovarius nubinhibens ISM				+		+				
Roseovarius sp. 217				+						
Silicibacter pomeroyi DSS-3				+		+				
Silicibacter sp. TM1040				+						
Sphingomonas sp. SKA58				+		+				+
Sphingomonas wittichii RW1										
Sphingopyxis alaskensis RB2256				+		+				+
Stappia aggregata IAM 12614				+						
Sulfitobacter sp. EE-36				+						
Xanthobacter autotrophicus Py2				+				+		
Zymomonas mobilis subsp. mobilis ZM4				+						
alpha proteobacterium HTCC2255										
Rhizobiaceae										
Agrobacterium tumefaciens str. C58				+	+					
Rhizobium etli CFN 42				+	+					
Rhizobium leguminosarum bv. viciae 3841				+						
Sinorhizobium medicae WSM419				+	+					
Sinorhizobium meliloti 1021				+						
Rickettsiales										
Anaplasma marginale str. St. Maries										
Anaplasma phagocytophilum HZ										
Candidatus Pelagibacter ubique HTCC1062										
Ehrlichia canis str. Jake										
Ehrlichia chaffeensis str. Arkansas										
Ehrlichia ruminantium str. Gardel										
Neorickettsia sennetsu str. Miyayama										
Rickettsia africae ESF-5										
Rickettsia akari str. Hartford										
Rickettsia bellii RML369-C										
Rickettsia canadensis str. McKiel										
Rickettsia conorii str. Malish 7										
Rickettsia felis URRWXCal2										
Rickettsia massiliae MTU5										
Rickettsia prowazekii str. Madrid E										
Rickettsia rickettsii										
Rickettsia sibirica 246										
Rickettsia typhi str. Wilmington										
Wolbachia endosymbiont of Drosophila melanogaster										
beta subdivision										
Bordetella										
Bordetella bronchiseptica RB50				+		+	+			
Bordetella parapertussis 12822				+		+	+			
Bordetella pertussis Tohama I				+		+	+			

Bacteria	CotA	Tyrosinase	Exporters➔	PacS/CopA	CutC	CopB	PcoA	CueO	PcoC	CusCFBA
Burkholderiaceae										
Burkholderia ambifaria MC40-6				+						
Burkholderia cenocepacia AU 1054				+	+					
Burkholderia cepacia AMMD				+	+					
Burkholderia dolosa AUO158				+						
Burkholderia mallei ATCC 23344				+	+					
Burkholderia multivorans ATCC 17616				+		+	+		+	
Burkholderia phymatum STM815				+						
Burkholderia phytofirmans PsJN										
Burkholderia pseudomallei 1710b				+	+					
Burkholderia sp. 383				+	+					
Burkholderia thailandensis E264				+	+					
Burkholderia vietnamiensis G4				+	+					
Burkholderia xenovorans LB400				+	+					
Polynucleobacter sp. QLW-P1DMWA-1										
Ralstonia eutropha JMP134				+		+				
Ralstonia metallidurans CH34				+		+				
Ralstonia pickettii 12J				+		+	+		+	
Ralstonia solanacearum GMI1000				+		+				
Neisseriaceae										
Chromobacterium violaceum ATCC 12472				+	+					
Neisseria gonorrhoeae FA 1090				+						
Neisseria meningitidis MC58				+						
Others										
Acidovorax avenae subsp. citrulli AAC00-1				+						
Acidovorax sp. JS42				+		+				
Azoarcus sp. EbN1				+						
Comamonas testosteroni KF-1				+			+		+	
Dechloromonas aromatica RCB				+						
Delftia acidovorans SPH-1				+			+		+	
Methylibium petroleiphilum PM1				+						
Methylobacillus flagellatus KT				+						
Methylophilales bacterium HTCC2181										
Nitrosomonas europaea ATCC 19718				+		+				
Nitrosomonas eutropha C71				+		+				
Nitrosospira multiformis ATCC 25196		+		+						
Polaromonas naphthalenivorans CJ2				+						
Polaromonas sp. JS666				+						
Rhodoferax ferrireducens T118				+						
Rubrivivax gelatinosus PM1				+						+
Thiobacillus denitrificans ATCC 25259				+		+				+
Verminephrobacter eiseniae EF01-2				+						
delta subdivision										
Anaeromyxobacter dehalogenans 2CP-C				+						
Anaeromyxobacter sp. Fw109-5				+			+			
Bdellovibrio bacteriovorus HD100				+						
Candidatus Desulfococcus oleovorans Hxd3				+						
Desulfotalea psychrophila LSv54				+						
Desulfovibrio desulfuricans G20				+						
Desulfovibrio vulgaris subsp. vulgaris str. Hildenboroug										
Desulfuromonas acetoxidans DSM 684				+						
Geobacter lovleyi SZ							+			
Geobacter metallireducens GS-15				+						
Geobacter sp. FRC-32				+						
Geobacter sulfurreducens PCA				+						
Geobacter uraniumreducens Rf4				+						
Lawsonia intracellularis PHE/MN1-00				+						

Bacteria	CotA	Tyrosinase	Exporters➔	PacS/CopA	CutC	CopB	PcoA	CueO	PcoC	CusCFBA
Myxococcus xanthus DK 1622				+						
Pelobacter carbinolicus DSM 2380				+						
Pelobacter propionicus DSM 2379				+						
Stigmatella aurantiaca DW4/3-1				+	+					
Syntrophobacter fumaroxidans MPOB				+						
Syntrophus aciditrophicus SB				+						
delta proteobacterium MLMS-1				+						
epsilon subdivision										
Campylobacter coli RM2228										
Campylobacter concisus 13826				+						
Campylobacter curvus 525.92				+						
Campylobacter fetus subsp. fetus 82-40				+						
Campylobacter jejuni RM1221				+						
Campylobacter lari RM2100				+						
Campylobacter upsaliensis RM3195										
Helicobacter acinonychis str. Sheeba				+						
Helicobacter hepaticus ATCC 51449										
Helicobacter pylori 26695				+						
Thiomicrospira denitrificans ATCC 33889				+						
Wolinella succinogenes DSM 1740				+						
gamma subdivision										
Enterobacteriales										
Buchnera aphidicola str. APS (Acyrthosiphon pisum)										
Candidatus Blochmannia floridanus										
Enterobacter sp. 638				+	+			+		
Erwinia carotovora subsp. atroseptica SCRI1043				+	+			+		+
Escherichia coli 536				+	+			+	+	+
Photorhabdus luminescens subsp. laumondii TTO1				+	+			+	+	
Salmonella enterica subsp. enterica serovar Choleraes				+	+			+	+	
Salmonella typhimurium LT2				+	+			+	+	
Serratia proteamaculans 568				+	+			+		
Shigella boydii Sb227				+	+			+	+	
Shigella dysenteriae Sd197				+	+			+	+	
Shigella flexneri 2a str. 2457T				+	+			+	+	+
Shigella sonnei Ss046				+	+			+	+	+
Sodalis glossinidius str. 'morsitans'					+			+	+	
Wigglesworthia glossinidia endosymbiont of Glossina b										
Yersinia bercovieri ATCC 43970				+	+			+	+	
Yersinia enterocolitica subsp. enterocolitica 8081				+	+			+		
Yersinia frederiksenii ATCC 33641				+	+			+	+	
Yersinia intermedia ATCC 29909				+	+			+	+	
Yersinia mollaretii ATCC 43969				+	+			+	+	
Yersinia pestis Antiqua				+	+			+	+	
Yersinia pseudotuberculosis IP 32953				+	+			+	+	
Others										
Acinetobacter sp. ADP1				+						
Aeromonas hydrophila subsp. hydrophila ATCC 7966				+				+		
Alcanivorax borkumensis SK2				+		+	+			
Alkalilimnicola ehrlichei MLHE-1				+						
Alteromonadales bacterium TW-7										
Alteromonas macleodii 'Deep ecotype'				+			+			
Baumannia cicadellinicola str. Hc (Homalodisca coagul										
Candidatus Carsonella ruddii PV										
Candidatus Ruthia magnifica str. Cm (Calyptogena mag										
Chromohalobacter salexigens DSM 3043				+						
Colwellia psychrerythraea 34H				+						
Congregibacter litoralis KT71										

Bacteria	**CotA**	**Tyrosinase**	**Exporters➔**	**PacS/CopA**	**CutC**	**CopB**	**PcoA**	**CueO**	**PcoC**	**CusCFBA**
Coxiella burnetii RSA 493				+						
Endoriftia persephone 'Hot96_1+Hot96_2'										
Francisella tularensis subsp. holarctica					+					
Hahella chejuensis KCTC 2396				+						
Halorhodospira halophila SL1										
Idiomarina baltica OS145				+			+			
Idiomarina loihiensis L2TR				+			+			
Legionella pneumophila str. Lens				+						
Marinobacter aquaeolei VT8				+			+			
Marinomonas sp. MED121				+						
Methylococcus capsulatus str. Bath				+						
Nitrococcus mobilis Nb-231				+						
Nitrosococcus oceani ATCC 19707				+						
Oceanobacter sp. RED65										
Oceanospirillum sp. MED92				+						
Pseudoalteromonas atlantica T6c				+	+					
Pseudoalteromonas haloplanktis TAC125				+		+	+			
Pseudoalteromonas tunicata D2										
Psychrobacter arcticus 273-4				+						
Psychrobacter cryohalolentis K5				+						
Psychrobacter sp. PRwf-1				+						
Psychromonas ingrahamii 37				+						
Psychromonas sp. CNPT3				+	+					
Reinekea sp. MED297										
Rickettsiella grylli				+						
Saccharophagus degradans 2-40				+		+	+			
Shewanella amazonensis SB2B				+	+					
Shewanella baltica OS155				+						
Shewanella denitrificans OS217				+		+	+			
Shewanella frigidimarina NCIMB 400				+		+	+			
Shewanella oneidensis MR-1				+						
Shewanella pealeana ATCC 700345				+						
Shewanella putrefaciens CN-32				+		+	+			+
Shewanella sp. MR-4				+						
Shewanella woodyi ATCC 51908				+						
Thiomicrospira crunogena XCL-2				+		+	+			
marine gamma proteobacterium HTCC2080										
marine gamma proteobacterium HTCC2143										
marine gamma proteobacterium HTCC2207										
Pasteurellaceae										
Actinobacillus pleuropneumoniae serovar 1 str. 4074				+						
Actinobacillus succinogenes 130Z				+						
Haemophilus ducreyi 35000HP										
Haemophilus influenzae 86-028NP				+						
Haemophilus somnus 129PT					+					
Mannheimia haemolytica PHL213				+						
Mannheimia succiniciproducens MBEL55E				+						
Pasteurella multocida subsp. multocida str. Pm70					+					
Pseudomonadaceae										
Azotobacter vinelandii AvOP				+		+	+			
Pseudomonas aeruginosa PAO1				+		+	+			
Pseudomonas entomophila L48				+		+	+			
Pseudomonas fluorescens Pf-5				+		+	+			
Pseudomonas mendocina ymp				+		+	+			
Pseudomonas putida KT2440				+		+	+			
Pseudomonas syringae pv. phaseolicola 1448A				+		+	+			
Vibrionaceae										

Bacteria	**CotA**	**Tyrosinase**	**Exporters➔**	**PacS/CopA**	**CutC**	**CopB**	**PcoA**	**CueO**	**PcoC**	**CusCFBA**
Photobacterium profundum SS9				+	+		+			
Photobacterium sp. SKA34				+	+					
Vibrio alginolyticus 12G01				+	+					
Vibrio angustum S14				+	+					
Vibrio cholerae O1 biovar eltor str. N16961				+	+					
Vibrio fischeri ES114				+	+					
Vibrio harveyi HY01				+						
Vibrio parahaemolyticus RIMD 2210633				+	+					
Vibrio sp. Ex25				+	+					
Vibrio splendidus 12B01				+	+					
Vibrio vulnificus CMCP6				+	+					
Xanthomonadaceae										
Stenotrophomonas maltophilia R551-3				+		+	+			
Xanthomonas axonopodis pv. citri str. 306					+	+	+			
Xanthomonas campestris pv. campestris str. 8004					+	+	+			
Xanthomonas oryzae pv. oryzae KACC10331					+	+	+			
Xylella fastidiosa 9a5c					+	+	+			
Spirochaetales										
Borrelia afzelii PKo										
Borrelia burgdorferi B31										
Borrelia garinii PBi										
Leptospira borgpetersenii serovar Hardjo-bovis JB197				+						
Leptospira interrogans serovar Copenhageni str. Fiocru				+						
Treponema denticola ATCC 35405					+					
Treponema pallidum subsp. pallidum str. Nichols										
Archaea										
Crenarchaeota										
Desulfurococcales										
Aeropyrum pernix K1										
Hyperthermus butylicus DSM 5456										
Sulfolobales										
Metallosphaera sedula DSM 5348										
Sulfolobus acidocaldarius DSM 639										
Sulfolobus solfataricus P2										
Sulfolobus tokodaii str. 7										
Thermoproteales										
Pyrobaculum aerophilum str. IM2										
Pyrobaculum islandicum DSM 4184				+						
Thermofilum pendens Hrk 5										
Euryarchaeota										
Archaeoglobales										
Archaeoglobus fulgidus DSM 4304				+						
Halobacteriales										
Haloarcula marismortui ATCC 43049				+						
Halobacterium sp. NRC-1				+						
Haloquadratum walsbyi DSM 16790										
Natronomonas pharaonis DSM 2160				+						
Methanobacteriales										
Methanosphaera stadtmanae DSM 3091				+						
Methanothermobacter thermautotrophicus str. Delta H				+						
Methanococcales										
Methanocaldococcus jannaschii DSM 2661										
Methanococcus maripaludis S2										
Methanomicrobiales										
Methanoculleus marisnigri JR1				+						
Methanospirillum hungatei JF-1				+						

Bacteria	**CotA**	**Tyrosinase**	**Exporters➔**	**PacS/CopA**	**CutC**	**CopB**	**PcoA**	**CueO**	**PcoC**	**CusCFBA**
Methanopyrales										
Methanopyrus kandleri AV19										
Methanosarcinales										
Methanococcoides burtonii DSM 6242				+						
Methanosaeta thermophila PT				+						
Methanosarcina acetivorans C2A				+						
Methanosarcina barkeri str. Fusaro				+						
Methanosarcina mazei Go1				+						
Thermococcales										
Pyrococcus abyssi GE5										
Pyrococcus furiosus DSM 3638				+						
Pyrococcus horikoshii OT3										
Thermococcus kodakarensis KOD1				+						
Thermoplasmales										
Ferroplasma acidarmanus Fer1										
Picrophilus torridus DSM 9790										
Thermoplasma acidophilum DSM 1728										
Thermoplasma volcanium GSS1										
Nanoarchaeota										
Nanoarchaeum equitans Kin4-M										

Bacteria	**PcoE**	**Importer➔**	**CtaA**	**Repressor➔**	**CopY**	**Chaperones➔**	**CopZ**	**CopC**	**Unclearn Function➔**	**CopD**
Acidothermus cellulolyticus 11B										
Arthrobacter aurescens TC1										
Arthrobacter sp. FB24										
Bifidobacterium adolescentis										
Bifidobacterium longum DJO10A										
Brevibacterium linens BL2										
Collinsella aerofaciens ATCC 25986										
Corynebacterium diphtheriae NCTC 13129										
Corynebacterium efficiens YS-314										
Corynebacterium glutamicum ATCC 13032										
Corynebacterium jeikeium K411										
Frankia alni ACN14a										
Frankia sp. EAN1pec										
Janibacter sp. HTCC2649										
Kineococcus radiotolerans SRS30216										
Leifsonia xyli subsp. xyli str. CTCB07										
Mycobacterium avium subsp. paratuberculosis K-10										
Mycobacterium bovis AF2122/97										
Mycobacterium flavescens PYR-GCK										
Mycobacterium leprae TN										
Mycobacterium smegmatis str. MC2 155										
Mycobacterium sp. KMS										
Mycobacterium tuberculosis C										
Mycobacterium ulcerans Agy99										
Mycobacterium vanbaalenii PYR-1										
Nocardia farcinica IFM 10152										
Nocardioides sp. JS614										
Propionibacterium acnes KPA171202										
Rhodococcus sp. RHA1										
Rubrobacter xylanophilus DSM 9941										
Salinispora arenicola CNS205										
Salinispora tropica CNB-440										
Streptomyces avermitilis MA-4680										
Streptomyces coelicolor A3(2)										
Symbiobacterium thermophilum IAM 14863										
Thermobifida fusca YX										
Tropheryma whipplei TW08/27										
marine actinobacterium PHSC20C1										
Bacteroidetes/Chlorobi										
Bacteroides caccae ATCC 43185										
Bacteroides fragilis YCH46										
Bacteroides thetaiotaomicron VPI-5482										
Candidatus Sulcia muelleri str. Hc (Homalodisca coagu										
Cellulophaga sp. MED134										
Chlorobium chlorochromatii CaD3										
Chlorobium ferrooxidans DSM 13031										
Chlorobium limicola DSM 245										
Chlorobium phaeobacteroides BS1										
Chlorobium tepidum TLS										
Croceibacter atlanticus HTCC2559										
Cytophaga hutchinsonii ATCC 33406										
Flavobacteria bacterium BBFL7										
Flavobacteriales bacterium HTCC2170										
Flavobacterium johnsoniae UW101										
Gramella forsetii KT0803										
Leeuwenhoekiella blandensis MED217										
Microscilla marina ATCC 23134										

Bacteria	PcoE	Importer➔	CtaA	Repressor➔	CopY	Chaperones➔	CopZ	CopC	Unclearn Function➔	CopD
Pelodictyon luteolum DSM 273										
Pelodictyon phaeoclathratiforme BU-1										
Polaribacter irgensii 23-P										
Porphyromonas gingivalis W83										
Prosthecochloris aestuarii DSM 271										
Prosthecochloris vibrioformis DSM 265										
Psychroflexus torquis ATCC 700755										
Robiginitalea biformata HTCC2501										
Salinibacter ruber DSM 13855										
Tenacibaculum sp. MED152										
Chlamydiae										
Candidatus Protochlamydia amoebophila UWE25										
Chlamydia muridarum Nigg										
Chlamydia trachomatis A/HAR-13										
Chlamydophila abortus S26/3										
Chlamydophila caviae GPIC										
Chlamydophila felis Fe/C-56										
Chlamydophila pneumoniae AR39										
Cyanobacteria										
Anabaena variabilis ATCC 29413			+							
Crocosphaera watsonii WH 8501			+							
Gloeobacter violaceus PCC 7421										
Lyngbya sp. PCC 8106			+							
Nodularia spumigena CCY9414			+							
Nostoc punctiforme PCC 73102			+							
Nostoc sp. PCC 7120			+							
Prochlorococcus marinus str. MIT 9312			+							
Synechococcus elongatus PCC 6301			+							
Synechococcus sp. CC9311			+							
Synechocystis sp. PCC 6803			+							
Thermosynechococcus elongatus BP-1			+							
Trichodesmium erythraeum IMS101			+							
Firmicutes										
Bacillales										
Bacillus anthracis str. Ames					+		+			
Bacillus cereus ATCC 10987					+		+			
Bacillus clausii KSM-K16					+		+			
Bacillus halodurans C-125							+			
Bacillus licheniformis ATCC 14580					+		+			
Bacillus sp. NRRL B-14911							+			
Bacillus subtilis subsp. subtilis str. 168							+			
Bacillus thuringiensis serovar konkukian str. 97-27							+			
Bacillus weihenstephanensis KBAB4							+			
Exiguobacterium sibiricum 255-15										
Geobacillus kaustophilus HTA426							+			
Listeria innocua Clip112624							+			
Listeria monocytogenes EGD-e							+			
Listeria welshimeri serovar 6b str. SLCC5334							+			
Oceanobacillus iheyensis HTE831							+			
Paenibacillus larvae subsp. larvae BRL-230010							+			
Pasteuria nishizawae str. North American										
Staphylococcus aureus RF122							+			
Staphylococcus epidermidis ATCC 12228					+		+			
Staphylococcus haemolyticus JCSC1435					+		+			
Staphylococcus saprophyticus subsp. saprophyticus A							+			
Clostridia										
Alkaliphilus metalliredigenes QYMF							+			

Bacteria	**PcoE**	**Importer→**	**CtaA**	**Repressor→**	**CopY**	**Chaperones→**	**CopZ**	**CopC**	**Unclearn Function→**	**CopD**
Caldicellulosiruptor saccharolyticus DSM 8903					+		+			
Carboxydothermus hydrogenoformans Z-2901							+			
Clostridium acetobutylicum ATCC 824					+		+			
Clostridium beijerincki NCIMB 8052					+		+			
Clostridium cellulolyticum H10							+			
Clostridium difficile QCD-32g58					+		+			
Clostridium novyi NT										
Clostridium perfringens ATCC 13124							+			
Clostridium phytofermentans ISDg							+			
Clostridium sp. OhILAs							+			
Clostridium tetani E88							+			
Clostridium thermocellum ATCC 27405					+		+			
Desulfitobacterium hafniense DCB-2					+		+			
Desulfotomaculum reducens MI-1							+			
Eubacterium ventriosum ATCC 27560										
Halothermothrix orenii H 168							+			
Moorella thermoacetica ATCC 39073							+			
Syntrophomonas wolfei subsp. wolfei str. Goettingen							+			
Thermoanaerobacter ethanolicus ATCC 33223							+			
Thermoanaerobacter tengcongensis MB4					+		+			
Thermosinus carboxydivorans Nor1							+			
Lactobacillales										
Enterococcus faecalis V583					+					
Enterococcus faecium DO					+					
Lactobacillus acidophilus NCFM					+		+			
Lactobacillus brevis ATCC 367					+					
Lactobacillus casei ATCC 334					+		+			
Lactobacillus delbrueckii subsp. bulgaricus ATCC 1184					+		+			
Lactobacillus gasseri ATCC 33323					+		+			
Lactobacillus johnsonii NCC 533					+		+			
Lactobacillus plantarum WCFS1					+		+			
Lactobacillus reuteri 100-23					+		+			
Lactobacillus sakei subsp. sakei 23K					+		+			
Lactobacillus salivarius subsp. salivarius UCC118					+					
Lactococcus lactis subsp. lactis Il1403					+		+			
Leuconostoc mesenteroides subsp. mesenteroides AT					+		+			
Oenococcus oeni PSU-1					+		+			
Pediococcus pentosaceus ATCC 25745					+		+			
Streptococcus agalactiae 2603V/R					+					
Streptococcus mutans UA159					+					
Streptococcus pneumoniae R6					+					
Streptococcus pyogenes M1 GAS					+					
Streptococcus suis 89/1591					+					
Streptococcus thermophilus CNRZ1066					+					
Mollicutes										
Aster yellows witches1-broom phytoplasma AYWB										
Mesoplasma florum L1										
Mycoplasma capricolum subsp. capricolum ATCC 2734										
Mycoplasma gallisepticum R										
Mycoplasma genitalium G37										
Mycoplasma hyopneumoniae 232										
Mycoplasma mobile 163K										
Mycoplasma mycoides subsp. mycoides SC str. PG1										
Mycoplasma penetrans HF-2										
Mycoplasma pneumoniae M129										
Mycoplasma pulmonis UAB CTIP										
Mycoplasma synoviae 53										

Bacteria	**PcoE**	**Importer→**	**CtaA**	**Repressor→**	**CopY**	**Chaperones→**	**CopZ**	**CopC**	**Unclearn Function→**	**CopD**
Onion yellows phytoplasma OY-M										
Ureaplasma parvum serovar 3 str. ATCC 700970										
Others										
Acidobacteria bacterium Ellin345										
Aquifex aeolicus VF5							+			
Blastopirellula marina DSM 3645										
Chloroflexus aggregans DSM 9485										
Chloroflexus aurantiacus J-10-fl										
Dehalococcoides ethenogenes 195										
Dehalococcoides sp. CBDB1										
Deinococcus geothermalis DSM 11300										
Deinococcus radiodurans R1										
Fervidobacterium nodosum Rt17-B1										
Fusobacterium nucleatum subsp. nucleatum ATCC 255										
Herpetosiphon aurantiacus ATCC 23779										
Rhodopirellula baltica SH 1										
Roseiflexus castenholzii DSM 13941										
Roseiflexus sp. RS-1										
Solibacter usitatus Ellin6076										
Thermosipho melanesiensis BI429										
Thermotoga maritima MSB8										
Thermotoga petrophila RKU-1										
Thermus thermophilus HB27										
Proteobacteria										
Others										
Magnetococcus sp. MC-1										
Mariprofundus ferrooxydans PV-1										
alpha subdivision										
Others										
Acidiphilium cryptum JF-5										
Aurantimonas sp. SI85-9A1										
Bartonella bacilliformis KC583										
Bartonella henselae str. Houston-1										
Bartonella quintana str. Toulouse										
Bradyrhizobium japonicum USDA 110										
Bradyrhizobium sp. BTAi1										
Brucella abortus biovar 1 str. 9-941								+		
Brucella melitensis 16M										
Brucella suis 1330										
Caulobacter crescentus CB15					+					
Caulobacter sp. K31					+			+		+
Dinoroseobacter shibae DFL 12										
Erythrobacter litoralis HTCC2594					+					
Erythrobacter sp. NAP1					+					
Fulvimarina pelagi HTCC2506										
Gluconobacter oxydans 621H										
Granulobacter bethesdensis CGDNIH1										
Hyphomonas neptunium ATCC 15444					+					
Jannaschia sp. CCS1										
Loktanella vestfoldensis SKA53										
Magnetospirillum magneticum AMB-1										
Magnetospirillum magnetotacticum MS-1										
Maricaulis maris MCS10										
Mesorhizobium loti MAFF303099										
Mesorhizobium sp. BNC1										
Nitrobacter hamburgensis X14										
Nitrobacter sp. Nb-311A										

Bacteria	**PcoE**	**Importer→**	**CtaA**	**Repressor→**	**CopY**	**Chaperones→**	**CopZ**	**CopC**	**Unclearn Function→**	**CopD**
Nitrobacter winogradskyi Nb-255										
Novosphingobium aromaticivorans DSM 12444								+		+
Oceanicaulis alexandrii HTCC2633										
Oceanicola batsensis HTCC2597										
Oceanicola granulosus HTCC2516										
Paracoccus denitrificans PD1222										
Parvibaculum lavamentivorans DS-1										
Parvularcula bermudensis HTCC2503										
Rhodobacter sphaeroides 2.4.1										
Rhodobacterales bacterium HTCC2654										
Rhodopseudomonas palustris BisA53										
Rhodospirillum rubrum ATCC 11170										
Roseobacter denitrificans OCh 114										
Roseobacter sp. MED193										
Roseovarius nubinhibens ISM										
Roseovarius sp. 217										
Silicibacter pomeroyi DSS-3										
Silicibacter sp. TM1040										
Sphingomonas sp. SKA58					+			+		+
Sphingomonas wittichii RW1								+		
Sphingopyxis alaskensis RB2256					+			+		+
Stappia aggregata IAM 12614										
Sulfitobacter sp. EE-36										
Xanthobacter autotrophicus Py2										
Zymomonas mobilis subsp. mobilis ZM4										
alpha proteobacterium HTCC2255										
Rhizobiaceae										
Agrobacterium tumefaciens str. C58										
Rhizobium etli CFN 42										
Rhizobium leguminosarum bv. viciae 3841										
Sinorhizobium medicae WSM419										
Sinorhizobium meliloti 1021										
Rickettsiales										
Anaplasma marginale str. St. Maries										
Anaplasma phagocytophilum HZ										
Candidatus Pelagibacter ubique HTCC1062										
Ehrlichia canis str. Jake										
Ehrlichia chaffeensis str. Arkansas										
Ehrlichia ruminantium str. Gardel										
Neorickettsia sennetsu str. Miyayama										
Rickettsia africae ESF-5										
Rickettsia akari str. Hartford										
Rickettsia bellii RML369-C										
Rickettsia canadensis str. McKiel										
Rickettsia conorii str. Malish 7										
Rickettsia felis URRWXCal2										
Rickettsia massiliae MTU5										
Rickettsia prowazekii str. Madrid E										
Rickettsia rickettsii										
Rickettsia sibirica 246										
Rickettsia typhi str. Wilmington										
Wolbachia endosymbiont of Drosophila melanogaster										
beta subdivision										
Bordetella										
Bordetella bronchiseptica RB50										
Bordetella parapertussis 12822										
Bordetella pertussis Tohama I										

Bacteria	**PcoE**	**Importer→**	**CtaA**	**Repressor→**	**CopY**	**Chaperones→**	**CopZ**	**CopC**	**Unclearn Function→**	**CopD**
Burkholderiaceae										
Burkholderia ambifaria MC40-6										
Burkholderia cenocepacia AU 1054										
Burkholderia cepacia AMMD										
Burkholderia dolosa AUO158										
Burkholderia mallei ATCC 23344								+		
Burkholderia multivorans ATCC 17616								+		+
Burkholderia phymatum STM815										
Burkholderia phytofirmans PsJN										
Burkholderia pseudomallei 1710b								+		
Burkholderia sp. 383										
Burkholderia thailandensis E264								+		
Burkholderia vietnamiensis G4										
Burkholderia xenovorans LB400										
Polynucleobacter sp. QLW-P1DMWA-1										
Ralstonia eutropha JMP134								+		+
Ralstonia metallidurans CH34								+		+
Ralstonia pickettii 12J								+		+
Ralstonia solanacearum GMI1000								+		+
Neisseriaceae										
Chromobacterium violaceum ATCC 12472										
Neisseria gonorrhoeae FA 1090										
Neisseria meningitidis MC58										
Others										
Acidovorax avenae subsp. citrulli AAC00-1										
Acidovorax sp. JS42										
Azoarcus sp. EbN1										
Comamonas testosteroni KF-1								+		+
Dechloromonas aromatica RCB										
Delftia acidovorans SPH-1								+		+
Methylibium petroleiphilum PM1										
Methylobacillus flagellatus KT										
Methylophilales bacterium HTCC2181										
Nitrosomonas europaea ATCC 19718										
Nitrosomonas eutropha C71										
Nitrosospira multiformis ATCC 25196										
Polaromonas naphthalenivorans CJ2										
Polaromonas sp. JS666										
Rhodoferax ferrireducens T118										
Rubrivivax gelatinosus PM1										
Thiobacillus denitrificans ATCC 25259										
Verminephrobacter eiseniae EF01-2										
delta subdivision										
Anaeromyxobacter dehalogenans 2CP-C										
Anaeromyxobacter sp. Fw109-5										
Bdellovibrio bacteriovorus HD100										
Candidatus Desulfococcus oleovorans Hxd3										
Desulfotalea psychrophila LSv54										
Desulfovibrio desulfuricans G20										
Desulfovibrio vulgaris subsp. vulgaris str. Hildenboroug										
Desulfuromonas acetoxidans DSM 684										
Geobacter lovleyi SZ										
Geobacter metallireducens GS-15										
Geobacter sp. FRC-32										
Geobacter sulfurreducens PCA										
Geobacter uraniumreducens Rf4										
Lawsonia intracellularis PHE/MN1-00										

Bacteria	**PcoE**	**Importer➔**	**CtaA**	**Repressor➔**	**CopY**	**Chaperones➔**	**CopZ**	**CopC**	**Unclearn Function➔**	**CopD**
Myxococcus xanthus DK 1622										
Pelobacter carbinolicus DSM 2380										
Pelobacter propionicus DSM 2379										
Stigmatella aurantiaca DW4/3-1										
Syntrophobacter fumaroxidans MPOB										
Syntrophus aciditrophicus SB										
delta proteobacterium MLMS-1										
epsilon subdivision										
Campylobacter coli RM2228										
Campylobacter concisus 13826										
Campylobacter curvus 525.92										
Campylobacter fetus subsp. fetus 82-40										
Campylobacter jejuni RM1221										
Campylobacter lari RM2100										
Campylobacter upsaliensis RM3195										
Helicobacter acinonychis str. Sheeba										
Helicobacter hepaticus ATCC 51449										
Helicobacter pylori 26695										
Thiomicrospira denitrificans ATCC 33889										
Wolinella succinogenes DSM 1740										
gamma subdivision										
Enterobacteriales										
Buchnera aphidicola str. APS (Acyrthosiphon pisum)										
Candidatus Blochmannia floridanus										
Enterobacter sp. 638										
Erwinia carotovora subsp. atroseptica SCRI1043										
Escherichia coli 536										
Photorhabdus luminescens subsp. laumondii TTO1										
Salmonella enterica subsp. enterica serovar Choleraes										
Salmonella typhimurium LT2										
Serratia proteamaculans 568										
Shigella boydii Sb227										
Shigella dysenteriae Sd197										
Shigella flexneri 2a str. 2457T										
Shigella sonnei Ss046										
Sodalis glossinidius str. 'morsitans'										
Wigglesworthia glossinidia endosymbiont of Glossina b										
Yersinia bercovieri ATCC 43970										
Yersinia enterocolitica subsp. enterocolitica 8081										
Yersinia frederiksenii ATCC 33641										
Yersinia intermedia ATCC 29909										
Yersinia mollaretii ATCC 43969										
Yersinia pestis Antiqua										
Yersinia pseudotuberculosis IP 32953										
Others										
Acinetobacter sp. ADP1										
Aeromonas hydrophila subsp. hydrophila ATCC 7966										
Alcanivorax borkumensis SK2							+			
Alkalilimnicola ehrlichei MLHE-1										
Alteromonadales bacterium TW-7										
Alteromonas macleodii 'Deep ecotype'										
Baumannia cicadellinicola str. Hc (Homalodisca coagul										
Candidatus Carsonella ruddii PV										
Candidatus Ruthia magnifica str. Cm (Calyptogena mag										
Chromohalobacter salexigens DSM 3043										
Colwellia psychrerythraea 34H										
Congregibacter litoralis KT71										

Bacteria	**PcoE**	**Importer➔**	**CtaA**	**Repressor➔**	**CopY**	**Chaperones➔**	**CopZ**	**CopC**	**Unclearn Function➔**	**CopD**
Coxiella burnetii RSA 493										
Endoriftia persephone 'Hot96_1+Hot96_2'										
Francisella tularensis subsp. holarctica										
Hahella chejuensis KCTC 2396										
Halorhodospira halophila SL1										
Idiomarina baltica OS145							+			
Idiomarina loihiensis L2TR							+			
Legionella pneumophila str. Lens										
Marinobacter aquaeolei VT8							+			
Marinomonas sp. MED121										
Methylococcus capsulatus str. Bath										
Nitrococcus mobilis Nb-231										
Nitrosococcus oceani ATCC 19707							+			
Oceanobacter sp. RED65										
Oceanospirillum sp. MED92										
Pseudoalteromonas atlantica T6c										
Pseudoalteromonas haloplanktis TAC125										
Pseudoalteromonas tunicata D2										
Psychrobacter arcticus 273-4							+			
Psychrobacter cryohalolentis K5							+			
Psychrobacter sp. PRwf-1							+			
Psychromonas ingrahamii 37							+			
Psychromonas sp. CNPT3										
Reinekea sp. MED297							+			
Rickettsiella grylli										
Saccharophagus degradans 2-40										
Shewanella amazonensis SB2B										
Shewanella baltica OS155										
Shewanella denitrificans OS217										
Shewanella frigidimarina NCIMB 400										
Shewanella oneidensis MR-1										
Shewanella pealeana ATCC 700345										
Shewanella putrefaciens CN-32	+									
Shewanella sp. MR-4										
Shewanella woodyi ATCC 51908										
Thiomicrospira crunogena XCL-2										
marine gamma proteobacterium HTCC2080										
marine gamma proteobacterium HTCC2143										
marine gamma proteobacterium HTCC2207										
Pasteurellaceae										
Actinobacillus pleuropneumoniae serovar 1 str. 4074										
Actinobacillus succinogenes 130Z										
Haemophilus ducreyi 35000HP										
Haemophilus influenzae 86-028NP							+			
Haemophilus somnus 129PT										
Mannheimia haemolytica PHL213							+			
Mannheimia succiniciproducens MBEL55E										
Pasteurella multocida subsp. multocida str. Pm70							+			
Pseudomonadaceae										
Azotobacter vinelandii AvOP										
Pseudomonas aeruginosa PAO1										
Pseudomonas entomophila L48										
Pseudomonas fluorescens Pf-5								+		
Pseudomonas mendocina ymp										
Pseudomonas putida KT2440										
Pseudomonas syringae pv. phaseolicola 1448A										
Vibrionaceae										

Bacteria	**PcoE**	**Importer➔**	**CtaA**	**Repressor➔**	**CopY**	**Chaperones➔**	**CopZ**	**CopC**	**Unclearn Function➔**	**CopD**
Photobacterium profundum SS9										
Photobacterium sp. SKA34										
Vibrio alginolyticus 12G01										
Vibrio angustum S14										
Vibrio cholerae O1 biovar eltor str. N16961										
Vibrio fischeri ES114										
Vibrio harveyi HY01										
Vibrio parahaemolyticus RIMD 2210633										
Vibrio sp. Ex25										
Vibrio splendidus 12B01										
Vibrio vulnificus CMCP6										
Xanthomonadaceae										
Stenotrophomonas maltophilia R551-3										
Xanthomonas axonopodis pv. citri str. 306										
Xanthomonas campestris pv. campestris str. 8004										
Xanthomonas oryzae pv. oryzae KACC10331										
Xylella fastidiosa 9a5c										
Spirochaetales										
Borrelia afzelii PKo										
Borrelia burgdorferi B31										
Borrelia garinii PBi										
Leptospira borgpetersenii serovar Hardjo-bovis JB197										
Leptospira interrogans serovar Copenhageni str. Fiocru										
Treponema denticola ATCC 35405										
Treponema pallidum subsp. pallidum str. Nichols										
Archaea										
Crenarchaeota										
Desulfurococcales										
Aeropyrum pernix K1										
Hyperthermus butylicus DSM 5456										
Sulfolobales										
Metallosphaera sedula DSM 5348										
Sulfolobus acidocaldarius DSM 639										
Sulfolobus solfataricus P2										
Sulfolobus tokodaii str. 7										
Thermoproteales										
Pyrobaculum aerophilum str. IM2										
Pyrobaculum islandicum DSM 4184										
Thermofilum pendens Hrk 5										
Euryarchaeota										
Archaeoglobales										
Archaeoglobus fulgidus DSM 4304										
Halobacteriales										
Haloarcula marismortui ATCC 43049										
Halobacterium sp. NRC-1										
Haloquadratum walsbyi DSM 16790										
Natronomonas pharaonis DSM 2160										
Methanobacteriales										
Methanosphaera stadtmanae DSM 3091										
Methanothermobacter thermautotrophicus str. Delta H										
Methanococcales										
Methanocaldococcus jannaschii DSM 2661										
Methanococcus maripaludis S2										
Methanomicrobiales										
Methanoculleus marisnigri JR1										
Methanospirillum hungatei JF-1										

Bacteria	**PcoE**	**Importer→**	**CtaA**	**Repressor→**	**CopY**	**Chaperones→**	**CopZ**	**CopC**	**Unclearn Function→**	**CopD**
Methanopyrales										
Methanopyrus kandleri AV19										
Methanosarcinales										
Methanococcoides burtonii DSM 6242										
Methanosaeta thermophila PT										
Methanosarcina acetivorans C2A										
Methanosarcina barkeri str. Fusaro										
Methanosarcina mazei Go1										
Thermococcales										
Pyrococcus abyssi GE5										
Pyrococcus furiosus DSM 3638										
Pyrococcus horikoshii OT3										
Thermococcus kodakarensis KOD1										
Thermoplasmales										
Ferroplasma acidarmanus Fer1										
Picrophilus torridus DSM 9790										
Thermoplasma acidophilum DSM 1728										
Thermoplasma volcanium GSS1										
Nanoarchaeota										
Nanoarchaeum equitans Kin4-M										