

# Microbial Genomics

## Comparative genomics and evolution of transcriptional regulons in Proteobacteria --Manuscript Draft--

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<b>Abstract:</b>	<p>Comparative genomics approaches are broadly used for analysis of transcriptional regulation in bacterial genomes. In this work, we identified binding sites and reconstructed regulons for 33 orthologous groups of transcription factors (TFs) in 196 reference genomes from 21 taxonomic groups of Proteobacteria. Overall, we predict over 10,600 TF binding sites and identified more than 15,600 target genes for 1,896 TFs constituting the studied orthologous groups of regulators. These include a set of orthologs for 21 metabolism-associated TFs from <i>Escherichia coli</i> and/or <i>Shewanella</i> that are conserved in five or more taxonomic groups and several additional TFs that represent non-orthologous substitutions of the metabolic regulators in some lineages of Proteobacteria. By comparing gene contents of the reconstructed regulons, we identified the core, taxonomy-specific and genome-specific TF regulon members and classified them by their metabolic functions. The detailed analysis of ArgR, TyrR, TrpR, HutC, HypR and other amino acid-specific regulons demonstrated remarkable differences in regulatory strategies used by various lineages of Proteobacteria. The obtained genomic collection of in silico reconstructed TF regulons contains a large number of new regulatory interactions that awaits future experimental validation. It provides a framework for future evolutionary studies of transcriptional regulatory networks in Bacteria. It can be also used for functional annotation of putative metabolic transporters and enzymes that are abundant in the reconstructed regulons.</p>

# MICROBIAL GENOMICS

Research paper template

## Comparative genomics and evolution of transcriptional regulons in Proteobacteria.

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### ABSTRACT

Comparative genomics approaches are broadly used for analysis of transcriptional regulation in bacterial genomes. In this work, we identified binding sites and reconstructed regulons for 33 orthologous groups of transcription factors (TFs) in 196 reference genomes from 21 taxonomic groups of Proteobacteria. Overall, we predict over 10,600 TF binding sites and identified more than 15,600 target genes for 1,896 TFs constituting the studied orthologous groups of regulators. These include a set of orthologs for 21 metabolism-associated TFs from *Escherichia coli* and/or *Shewanella* that are conserved in five or more taxonomic groups and several additional TFs that represent non-orthologous substitutions of the metabolic regulators in some lineages of Proteobacteria. By comparing gene contents of the reconstructed regulons, we identified the core, taxonomy-specific and genome-specific TF regulon members and classified them by their metabolic functions. The detailed analysis of ArgR, TyrR, TrpR, HutC, HypR and other amino acid-specific regulons demonstrated remarkable differences in regulatory strategies used by various lineages of Proteobacteria. The obtained genomic collection of *in silico* reconstructed TF regulons contains a large number of new regulatory interactions that awaits future experimental validation. It provides a framework for future evolutionary studies of transcriptional regulatory networks in Bacteria. It can be also used for functional annotation of putative metabolic transporters and enzymes that are abundant in the reconstructed regulons.

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### DATA SUMMARY

34 Inferred transcription factor binding sites and reconstructed regulons have been deposited in the  
35 RegPrecise database (URL – [http://regprecise.lbl.gov/RegPrecise/project\\_proteobacteria.jsp](http://regprecise.lbl.gov/RegPrecise/project_proteobacteria.jsp)).

36

37 **We confirm all supporting data, code and protocols have been provided within the article or**  
38 **through supplementary data files.**

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## 41 **IMPACT STATEMENT**

42 Bacteria in most ecological niches are constantly exposed to variations in many factors  
43 including nutrient availability. Changes in gene expression using transcription factors allow  
44 bacteria to adapt to these variations. Knowledge of transcriptional regulatory networks is  
45 essential for understanding cellular processes. Comparative genomics is the analysis and  
46 comparison of genomes from different species. Thousands of sequenced bacterial genomes  
47 open an opportunity to reconstruct transcriptional regulatory networks using the  
48 comparative genomics. Despite the importance of transcriptional regulation of the central  
49 metabolism for systems-level metabolic modelling of Bacteria, our understanding of the  
50 respective transcription factor regulons is limited for the majority of sequenced bacteria. In  
51 this study, the researches have applied the comparative genomics approach to describe  
52 regulatory networks of genes involved in the central metabolism in four major classes of  
53 Proteobacteria. The reconstructed regulatory networks involve 33 groups of orthologous  
54 transcription factors with different DNA recognition motifs. Large-scale phylogenomic  
55 analysis of the reconstructed TF regulons reveals and classifies various evolutionary  
56 processes that shape regulatory networks in Bacteria. The reconstructed regulon contents  
57 suggest numerous novel functional associations between both known and uncharacterized  
58 genes encoding enzymes and transporters thus providing testable hypotheses for future  
59 experimental studies. This study demonstrates the power of comparative genomics for the  
60 reconstruction of transcription factor regulons in bacteria.

## 61 INTRODUCTION

62 Regulation of gene expression is an important mechanism for fast adaptation of prokaryotic  
63 metabolism to changing environmental conditions. Transcription factors (TFs) repress or activate  
64 gene transcription via specific binding to TF binding sites (TFBSs) in regulatory gene regions. Binding  
65 ability of many bacterial TFs depends on the presence or absence of an effector such as intracellular  
66 metabolites, inorganic chemicals or physical stimuli (Browning and Busby 2004). A set of genes  
67 directly controlled by a single TF is called a regulon. Global TF regulons in bacteria contain large sets  
68 of genes (operons) that share similar TFBSs in their promoter regions, while local TFs control one or  
69 several operons that are often co-localized with a TF gene (Rodionov 2007).

70 Experimental studies built a foundation for understanding mechanisms laying behind  
71 transcription regulation (Minchin and Busby 2009). However even with high throughput  
72 technologies as ChIP-Seq or RNA-Seq, these approaches still consume a lot of time and resources  
73 and therefore are restricted by few model organisms (Grainger, et al. 2009). At this point  
74 comparative genomics studies of growing number of sequenced bacterial genomes provide a  
75 successful approach to extend our knowledge of known TF regulons to wide range of bacterial  
76 lineages, as well as to perform *ab initio* prediction of novel TF regulons (Rodionov 2007).  
77 Comparative genomics-based regulon reconstruction combines identification of conserved *cis*-acting  
78 TFBSs, their genomic and metabolic context analysis in a set of closely-related genomes. Finally, it  
79 results in determination of a regulog that is a set of genes/operons co-regulated by orthologous TFs  
80 in closely related organisms. Implementation of this approach in the RegPredict web tool  
81 (Novichkov, et al. 2010) produced numerous computational reconstructions of TF regulogs across a  
82 wide range of bacterial taxa (Ravcheev, et al. 2011; Rodionov, et al. 2011; Leyn, et al. 2013;  
83 Ravcheev, et al. 2013; Rodionov, et al. 2013). This substantial amount of data on regulon  
84 reconstructions captured in the RegPrecise database (Novichkov, et al. 2013) provides the basis for  
85 description of most common types of events associated with evolution of TF regulons in bacteria  
86 such as duplications and losses of TFs and their TFBSs that result in expansions, shrinkages, mergers  
87 and split-ups of regulons (Gelfand 2006; Rodionov, et al. 2006; Ravcheev, et al. 2014). New non-  
88 orthologous TFs could be introduced to control equivalent pathways or, vice versa, orthologous TFs  
89 could control distinct pathways in related taxonomic groups of bacteria (Yang, et al. 2006; Rodionov,  
90 et al. 2008; Kazakov, et al. 2009; Leyn, et al. 2014).

91 We recently conducted a comprehensive comparative genomics analysis of regulatory systems  
92 for methionine metabolism in near 200 representative genomes from 22 taxonomic groups from the  
93 phylum Proteobacteria (Leyn, et al. 2014). In  $\gamma$ -proteobacteria, two TFs, MetJ and MetR, are  
94 implicated in the control of methionine metabolism, whereas this function is taken by other TFs  
95 (SahR and SamR) or RNA regulatory systems (e.g., SAH and SAM riboswitches) in other lineages of  
96 Proteobacteria. The core of MetJ regulons includes a large numbers of genes that are highly  
97 conserved in most lineages of  $\gamma$ -proteobacteria. In contrast, the core of MetR regulons includes only  
98 two genes, *metE* and *metR*, whereas regulatory interactions between MetR and other target genes  
99 are mostly lineage-specific. Regulatory system replacement and lineage-specific regulon expansions in  
100 Proteobacteria were also observed in the comparative genomics analyses of TF regulons involved in  
101 fatty acid degradation (FadR, PsaA, FadP), branched-chain amino acid utilization (LiuR, LiuQ), N-  
102 acetylglucosamine utilization (NagC, NagR, NagQ) (Yang, et al. 2006; Kazakov, et al. 2009), biotin  
103 biosynthesis (BirA, BioR) (Rodionov and Gelfand 2006) and central carbohydrate metabolism (HexR)  
104 (Leyn, et al. 2011).

105 Here, we extended these observations toward large-scale regulon reconstructions for 21 known  
106 TFs that have orthologs in a wide phylogenetic range of Proteobacteria. By comparing the metabolic  
107 context of the reconstructed TF regulons, we identified the core, taxonomy-specific and genome-  
108 specific members of regulons, and proposed evolutionary scenarios for regulation of several  
109 pathways involved in metabolism of amino and fatty acids, nucleotides and co-factors in  
110 Proteobacteria. Additionally, we predicted novel regulators of aromatic amino acid metabolism  
111 replacing the TyrR/PhrR and HmgR regulons in Alteromonadales and Pseudomonadales (named  
112 HmgS and HmgQ), and a novel regulator of NAD metabolism in  $\beta$ - and  $\alpha$ -proteobacteria, named  
113 NadQ. The obtained regulatory reconstructions for both known and new TF regulons across 196  
114 reference genomes of Proteobacteria will be useful for development of theoretical models for the  
115 evolution of microbial regulatory networks.

116

## 117 METHODS

118 For regulon reconstruction, we selected 196 reference genomes of  $\alpha$ -,  $\beta$ -,  $\gamma$ - and  $\delta$ -  
119 proteobacteria and subdivided them into 21 sets of evolutionary related genomes (Table S1). Closely  
120 related strains and species were excluded from the analysis because they skew the TFBS training set  
121 and thus decrease the sensitivity of the TFBS recognition rule. Genomes and the phylogenetic  
122 species tree were downloaded from MicrobesOnline database (Dehal, et al. 2010). Each taxonomic  
123 group includes 4 to 16 genomes of bacteria. Orthologs of TFs in the selected genomes were  
124 identified as bidirectional best hits using protein BLAST search (Altschul, et al. 1997) and were  
125 additionally confirmed via phylogenetic trees using precomputed protein trees in MicrobesOnline.  
126 The genomes of  $\epsilon$ -proteobacteria were not analyzed because of the absence of orthologs for target  
127 TFs.  $\zeta$ -proteobacteria, which is represented by a single genome in the MicrobesOnline database, was  
128 not suitable for the comparative genomic analysis.

129 Genes in the reconstructed regulons were considered orthologs if they were classified as specific  
130 tree-based orthologs in MicrobesOnline. Conservancy of the genomic context through related  
131 genomes was considered as an additional support for gene orthology. Comparative analysis of  
132 conserved gene neighborhoods was conducted in MicrobesOnline. Biological functions of genes  
133 were predicted by BLAST search against the SwissProt/Uniprot database (UniProt 2014), domain  
134 architecture analysis in the Pfam database (Finn, et al. 2014), and by using gene function  
135 assignments in the PubSEED database (Overbeek, et al. 2005). Known metabolic pathways were  
136 taken from KEGG (Kanehisa and Goto 2000) and EcoCyc (Karp, et al. 2014). Sequence logos for TF  
137 binding sites were drawn using the WebLogo package (Crooks, et al. 2004).

138 For regulon reconstruction we used an established comparative genomics approach implemented  
139 in the RegPredict interactive tool (Novichkov, et al. 2010). This approach is based on construction of  
140 positional weight matrices (PWMs) for TFBS motifs, and further genomic searches for additional  
141 regulon members on the basis of predicted TFBSs in upstream gene regions (Rodionov 2007).  
142 Bioinformatics workflow used for regulon reconstruction is described in Figure S1. Two main  
143 workflows were applied for regulon reconstructions: (i) propagation and expansion of known TF  
144 regulons that were previously experimentally studied in model organisms (Table S2) and/or  
145 computationally reconstructed in *Shewanella* spp. (Rodionov, et al. 2011); and (ii) *ab initio* prediction  
146 of novel TF regulons for sets of potential target genes involved in the same metabolic pathway. To  
147 find conserved TFBS motifs for the known TFs in each taxonomic group where their orthologs are  
148 present, we used initial training sets of genes that are orthologous to previously established regulon

149 members in model species, and then updated each set by potential regulon members confirmed by  
150 the comparative genomics checks. For novel TF regulons, the original training sets included genes  
151 from the respective metabolic pathways and/or conservative chromosomal gene neighborhoods  
152 around analyzed TFs.

153 A simple iterative procedure implemented in the Discover Profile tool in RegPredict was used for  
154 identification of conserved palindromic DNA motifs and construction of PWMs. For most of the  
155 analyzed TFs, their DNA motifs have palindromic structure and length between 15 and 25 nt,  
156 whereas the TFBS motifs of NagQ and BirA represent tandem and inverted repeats, respectively. The  
157 obtained PMWs (both known and *ab initio* predicted) were further used for identification of  
158 additional candidate sites in upstream gene regions as previously described (Leyn, et al. 2014;  
159 Ravcheev, et al. 2014). Each predicted regulatory interaction was analyzed for conservation within  
160 the analyzed groups of genomes using the Clusters of co-Regulated Orthologous operoNs (CRONs)  
161 approach in RegPredict. Further analysis of functional and genomic context and curation of each  
162 CRON resulted in the final TF regulon model. All reconstructed TF regulons including TFBS motifs and  
163 sets of TF-regulated genes/operons with their functional annotations are accessible in the latest  
164 release of the RegPrecise database (Novichkov, et al. 2013) (Data Citation 1). Each TF regulon in  
165 RegPrecise belong to two types of regulon collections classified by either taxonomy of studied  
166 bacteria, or by the name of TFs.

167

## 168 RESULTS AND DISCUSSION

### 169 Statistics of reconstructed regulons and regulogs

170 A set of 196 representative genomes of  $\gamma$ -,  $\beta$ -,  $\alpha$ -, and  $\delta$ -proteobacteria selected from the  
171 MicrobesOnline database was classified into 21 taxonomic groups by analyzing the phylogenetic  
172 species tree (Table S1). For the analysis of evolution of transcriptional regulation, we selected a set  
173 of 21 transcriptional regulators of the central metabolism that are present either in *E. coli* and/or  
174 *Shewanella* spp. and that are conserved in five or more taxonomic groups of Proteobacteria (Table 1;  
175 Figure S1). The selected TFs include the previously known regulators that control  
176 biosynthesis/utilization of amino acids (ArgR, HutC, HypR, LiuR, MetJ, MetR, TrpR, TyrR), fatty acids  
177 (FabR, FadR, PsrA), nucleotides (NrdR, RutR), and vitamins (BirA, NrtR), as well as nitrogen and  
178 carbon metabolism (HexR, GlcC, LldR, NagC, NtrC, PdhR). Sixteen of these TFs are present in *E. coli*,  
179 of them twelve regulators are also shared by *Shewanella* spp., whereas the remaining five TFs (LiuR,  
180 HutC, HypR, NrtR, PsrA) are unique for *Shewanella* spp. We also studied 12 additional TFs that  
181 appear to substitute some of the above TFs in the control of specific metabolic pathways, and thus  
182 can be assumed as non-orthologous TF replacements. These include known and predicted regulators  
183 that control metabolism of amino acids (HmgQ, HmgR, HmgS, LiuQ, SahR, SamR) and fatty acids  
184 (FadP), vitamin biosynthesis (BioR, NadR, NadQ), and N-acetyl-glucosamine metabolism (NagQ,  
185 NagR) (marked with asterisk in Table 1).

186 Application of the comparative genomics procedure to 33 analyzed groups of orthologous TFs  
187 resulted in reconstruction of 283 regulogs containing 1896 regulons that are unevenly distributed  
188 across 21 taxonomic groups of Proteobacteria (Figure S2). Each regulon includes a set of target  
189 genes/operons that are co-regulated by the same TF in a particular genome. A regulog represents a  
190 set of regulons under control of orthologous TFs in a specific taxonomic group of Proteobacteria. The  
191 most widespread orthologous groups of analyzed TFs are NrdR (186 regulons, 20 regulogs), NtrC

192 (169 regulons, 19 regulogs), MetR (117 regulons, 14 regulogs), HutC (113 regulons, 18 regulogs), LiuR  
193 (104 regulons, 16 regulogs), HexR (95 regulons, 13 regulogs), and BirA (94 regulons, 11 regulogs).

194 The taxonomical distribution of analyzed TF regulogs across four subdivisions from the  
195 Proteobacteria phylum is summarized in Figure 1. Overall, 30 out of 33 analyzed TFs are present in  $\gamma$ -  
196 proteobacteria, and 14 of these regulators do not have orthologs in other classes of Proteobacteria.  
197  $\alpha$ -proteobacteria totally possess 15 studied TFs, including one regulator (BioR), which is unique for  
198 this class. Among 17 studied TFs in  $\beta$ -proteobacteria, two regulators (LiuQ, FadP) are unique for this  
199 class.  $\delta$ -proteobacteria that represent the most taxonomically diverged subdivision of Proteobacteria  
200 have orthologs for only five studied TFs. Several TFs (such as LldR, GlcC, RutR) that are present in  
201 several classes of Proteobacteria show a mosaic distribution across the analyzed genomes and taxa,  
202 while other TFs (such as ArgR, FabR, FadR, MetJ, TrpR, TyrR) are highly conserved in many taxonomic  
203 groups of  $\gamma$ -proteobacteria but are absent in other classes. The diverse distribution of TFs suggests  
204 different evolutionary pathways for the studied metabolic regulons.

205 The detailed descriptions of reconstructed regulons and regulogs are captured in the RegPrecise  
206 database (Data Citation 1), whereas the complete list of regulatory interactions between the studied  
207 TFs and their target genes is provided in Table S3. Overall, the obtained regulons included 10,663  
208 candidate TFBSs and 15,690 target genes (Table 1). The largest average number of target genes per  
209 genome (more than 10 genes per genome) was observed for regulators of amino acid metabolism  
210 (ArgR, LiuR, MetJ, TyrR), the fatty acid degradation regulators FadP and PsrA, the carbohydrate  
211 metabolism regulators HexR, NagC and NagR, and the pyrimidine utilization regulator RutR.

212 For most of the studied TFs, their cognate DNA binding motifs are generally conserved across the  
213 analyzed taxonomic groups (see the RegPrecise database for detailed lists of taxonomy-specific TFBS  
214 motifs, Data Citation 1). However, for several TFs including FabR, HypR, NrtR, RutR, SahR and TrpR,  
215 we observed taxon-specific substitutions in their cognate DNA motifs, whereas the GlcC-binding DNA  
216 motifs in  $\alpha$ - and  $\beta$ -/ $\gamma$ -subdivisions of Proteobacteria are characterized by different length of the  
217 spacer between the conserved palindromic half-sites (Figure 2). Finally, the HexR and NagQ motifs in  
218 several taxonomic groups of  $\gamma$ -proteobacteria have different consensus sequences and structures  
219 (Yang, et al. 2006; Leyn, et al. 2011).

220

## 221 Conservation of reconstructed regulons

222 To analyze conservation of regulatory interactions in the reconstructed regulogs, we calculated  
223 the conservation score as a number of gene occurrence in a regulog divided by a number of regulons  
224 in a regulog. Average of these taxonomy-specific conservation scores was calculated for all  
225 orthologous groups of target genes across analyzed lineages of Proteobacteria. For each group of  
226 orthologous TFs, we plotted the average conservation score of a target gene against the number of  
227 taxonomic groups, in which this gene is regulated. The obtained plots visualize average conservation  
228 of regulatory interactions and thus help to determine the core, taxonomy-specific and genome-  
229 specific target genes within the reconstructed TF regulons (Figure S3).

230 The core regulon members determined by this approach represent regulatory interactions with  
231 high average conservation scores that are conserved in more than half of reconstructed TF regulogs.  
232 The core members of most of the analyzed regulons are consistent with major biological functions  
233 and molecular effectors of their cognate TFs (Table S4). For instance, the arginine repressor regulon  
234 ArgR in  $\gamma$ -proteobacteria has a conserved core that includes genes involved in arginine biosynthesis  
235 (*argABCEFGH*, *carAB*), transport (*artPIQM*), and degradation (*astAD*), as well as the *argR* gene itself



236 (Figure 3). The cores of most other reconstructed TF regulons include their cognate TF genes.  
237 Exceptions from this observation include the FabR, FadR and NadQ regulons that include their  
238 cognate TF genes only in some taxonomic groups of Proteobacteria; the biotin repressor BirA, which  
239 is autoregulated only in *Desulfovibrionales*, and the deoxyribonucleotide reductase regulator NrdR,  
240 which was never found under autoregulation. Negative autoregulation of a TF gene is a common  
241 feature of bacterial regulatory networks. Here, we demonstrate that this type of regulatory  
242 interaction is highly conserved in the evolution of regulatory networks of Proteobacteria.

243 The remaining members of reconstructed regulons were classified into the taxon- and genome-  
244 specific groups depending on their average conservation scores. The taxonomy-specific regulon  
245 members are characterized by strong conservation of regulatory interactions restricted to a half or  
246 less taxonomic groups containing an orthologous TF. At that the **taxon-specific regulon members**  
247 were defined as genes that **are regulated in more than 65% of genomes in at least one taxonomic**  
248 **group**. In contrast, the genome-specific regulon members are characterized by low conservation of  
249 regulatory interactions, when in each taxonomic group conservation of a regulatory interaction is  
250 less than 65%. The groups of taxonomy- and genome-specific TF regulon members with assigned  
251 metabolic pathways are often involved in the same major biological process as the core regulon  
252 members (Table S4). However, in some TF regulons these categories also involve genes that  
253 participate in other metabolic pathways or biological processes. For example, the taxon-specific  
254 members of ArgR regulons include genes involved in arginine biosynthesis (*argD*) and transport (*artJ*,  
255 *argW*, *omp*), arginine degradation (*astBC*), as well as genes from glutamate (*gltBD*) and branched-  
256 chain amino acid (*ilvMGDA*) biosynthesis, putrescine transport (*potFGHI*), and pyruvate metabolism  
257 (*oadABG*) (Figure 3). The genome-specific ArgR regulon members include arginine degradation genes  
258 (*arcABCD*, *astE*), proline (*proVWX*) and histidine (*hisJMPQ*) transporters and putrescine metabolism  
259 genes (*speF*, *potE*). Likewise, in our previous analysis of the methionine-specific regulons MetJ, MetR  
260 and SahR in Proteobacteria, we identified the core-, taxonomy- and genome-specific members of  
261 regulons and demonstrated their involvement in different aspects of the methionine metabolism.  
262 Other amino acid-specific TF regulons analyzed in the current work are described in more detail in  
263 the following sections.

#### 264 **TrpR, TyrR and other TF regulons for aromatic amino acid metabolism**

265 The aromatic amino acids tryptophan, tyrosine and phenylalanine are synthesized in  
266 Proteobacteria by the common pathway leading from erythrose 4-phosphate through 2-dehydro-3-  
267 deoxy-D-arabinoheptonate-7-phosphate (DAHP), and shikimate to chorismate (Figure 4). After  
268 chorismate, the pathway divides into the three terminal biosynthetic pathways that are specific for  
269 each aromatic amino acid. *E. coli* has three DAHP synthase isoenzymes, AroF, AroG, and AroH, which  
270 are feedback inhibited by tyrosine, phenylalanine and tryptophan, respectively. The biosynthesis of  
271 aromatic amino acids is regulated at both the DNA and RNA levels. The DNA-binding transcription  
272 factors TyrR and TrpR jointly control the expression of genes involved in the aromatic amino acid  
273 metabolism in *E. coli* (Pittard and Yang 2008). At the RNA level, the *trpEDCBA* operon encoding the  
274 tryptophan biosynthesis enzymes and the phenylalanine biosynthesis gene *pheA* are regulated by  
275 translational attenuation in *E. coli* and other  $\gamma$ -proteobacteria (Panina, et al. 2001). The tryptophan-  
276 responsive regulator TrpR in *E. coli* acts as a repressor of the *trpEDCBA* operon, the tryptophan  
277 transporter gene *mtr*, and the regulatory gene *trpR* (Czernik, et al. 1994; Jeeves, et al. 1999). In  
278 addition, TrpR negatively regulates the expression of the shikimate kinase *aroL* and the DAHP  
279 synthase *aroH* that are involved in the chorismate biosynthesis. The tyrosine-responsive regulator  
280 TyrR in *E. coli* negatively controls the tyrosine biosynthesis genes *tyrB*, *aroF-tyrA*, *aroLM*, the  
281 aromatic amino acid transporter *aroP* and the *tyrR* gene itself. In addition, TyrR activates the

282 tyrosine- and tryptophan-specific transporters *tyrP* and *mtr* and the folate biosynthesis gene *folA* in  
283 the presence of tyrosine or phenylalanine (Yang, et al. 2004; Pittard, et al. 2005). The TyrR regulon  
284 was also partially studied in two other Enterobacteria. In *Citrobacter freundii*, it activates the  
285 tyrosine degradation gene *tpl* (Smith and Somerville 1997). In *Enterobacter cloacae*, TyrR activates  
286 the *ipdC* gene involved in the synthesis of indole acetate from tryptophan and represses a  
287 divergently transcribed gene, *akr*, encoding a putative aldo-keto reductase (Coulson and Patten  
288 2015). An ortholog of TyrR in *Pseudomonas putida*, known as PhhR, is responsible for the activation  
289 of genes essential for phenylalanine degradation and phenylalanine homeostasis (Herrera, et al.  
290 2010). In *Pseudomonas aeruginosa*, PhhR directly controls the *phhABC*, *hpd*, and *dhcA* transcriptional  
291 units involved in the phenylalanine and tyrosine catabolism (Palmer, et al. 2010).

292 The comparative genomics approach was applied to analyze regulons controlled by transcription  
293 factors homologous to TrpR and TyrR/PhhR and to predict novel regulons for aromatic amino acid  
294 metabolism (Table S5). The TrpR-family regulons reconstructed in eight lineages of  $\gamma$ -proteobacteria  
295 control genes for the tryptophan biosynthesis, uptake and catabolism (Figure 4). In most of the  
296 analyzed taxonomic groups, TrpR regulates the *trpR* and *trpE* genes that form the conserved regulon  
297 core, whereas other genes from tryptophan biosynthesis pathway and the *mtr* transporter were  
298 classified as taxon-specific members of the regulon. Two other known targets of TrpR in *E. coli*, the  
299 chorismate biosynthesis genes *aroLM* and *aroH*, represent regulatory interactions that are  
300 conserved in a small number of closely-related *Enterobacteriales* genomes but not in other lineages.  
301 New predicted members of the TrpR regulons include various aromatic amino acid biosynthesis  
302 genes such as *aroG* in *Pasteurellales*, *aroF-tyrA* in *Shewanellaceae*, *aroF2* and *aroA* in *Vibrionales*, as  
303 well as the tryptophan degradation genes *tnaAB* and a predicted tryptophan transporter from the  
304 COG0733 family in *Vibrionales*. Interestingly, the TrpR regulon in *Shewanella* spp. does not include  
305 the tryptophan biosynthesis operon, which is regulated by a translational attenuator at the RNA  
306 level (Panina, et al. 2001).

307 The content of reconstructed TyrR (PhhR) regulons is highly variable across the analyzed 6  
308 lineages of  $\gamma$ -proteobacteria (Table S5). The most conserved members of these regulons are the *tyrR*  
309 gene itself, the tyrosine biosynthesis and transport genes *aroF-tyrA* and *tyrP*, as well as the  
310 phenylalanine and tyrosine degradation genes *phhAB*, *hmgABC* and *hpd* (Figure 4). The aromatic  
311 amino acid transporters *mtr* and *aroP*, as well as the chorismate biosynthesis genes *aroLM*, which  
312 were previously known as TyrR-regulated genes in *E. coli*, belong to the TyrR regulons only in  
313 *Enterobacteriales*. The *folA* gene represents another previously known member of the TyrR regulon  
314 in *E. coli*, however we were unable to find conserved TyrR-binding sites upstream of *folA* orthologs in  
315 other *Enterobacteriales*.

316 A novel predicted tyrosine transporter from the COG2814 family was found under TyrR  
317 regulation in seven genomes of *Enterobacteriales*. The reconstructed TyrR regulons in *Vibrionales*  
318 are extended to include a predicted novel tyrosine transporter from the COG0733 family and the  
319 *aroG* gene. The most significant shifts in the regulon content were identified in *Shewanellaceae*,  
320 where TyrR controls the degradation pathways for various amino acids including phenylalanine  
321 (*phhAB*), tyrosine (*hmgCB*), tryptophan (*tdo-kyn*), branched chain amino acids (*ldh*, *brnQ*, *liu*, *ivd*, and  
322 *bkd* operons), proline (*putA*), methionine (*mdeA*), and oligopeptides (various peptidase genes). In  
323 addition, the conserved part of the TyrR regulons in *Shewanellaceae* includes the  
324 tyrosine/phenylalanine biosynthesis genes *aroA* and *tyrB*, as well as the *aceBA* and *acsA* genes from  
325 the central carbon metabolism. Finally, the *tpl* gene encoding an alternative pathway of tyrosine  
326 degradation belongs to the TyrR regulons in *Citrobacter koseri* and two *Pasteurellales*, whereas the

327 indole acetate synthesis gene *ipdC* is regulated by TyrR in some *Enterobacteriales* and  
328 *Shewanellaceae* genomes.

329 The homogentisate pathway of the tyrosine degradation encoded by the *hmgABC* operon in *P.*  
330 *putida* is regulated by the IclR-family repressor HmgR and homogentisate as anitirepressor (Arias-  
331 Barrau, et al. 2004). Similar HmgR regulons were reconstructed in four other *Pseudomonas* species,  
332 whereas the *hmgABC* genes in two other *Pseudomonas* spp. belong to the TyrR-family PhrR regulons  
333 (Table S5). In a closely-related bacterium from the *Pseudomonadaceae* family, *Azotobacter*  
334 *vinelandii*, which lack both PhrR and HmgR regulons, we identified a novel LysR-family regulon for  
335 the homogentisate pathway genes, which we termed HmgQ. Orthologous HmgQ regulators in the  
336 *Shewanellaceae* family are predicted to control the *hmgA-hpd* genes, whereas the *hmgCB* genes of  
337 the homogentisate pathway belong to the extended TyrR regulon in *Shewanella* spp.. Another novel  
338 regulator from the MarR family (termed HmgS), was identified in several *Alteromonadales* and  
339 *Pseudoalteromonadales* species, where it is predicted to control the *hmgAB* genes.

340 In conclusion, the transcriptional regulation of aromatic amino acid metabolism is highly  
341 variable among major lineages of  $\gamma$ -proteobacteria (Table S5). The TyrR-family regulators control the  
342 aromatic amino acid biosynthesis, uptake and/or catabolic pathways in most of the analyzed taxa. In  
343 contrast, the reconstructed regulons in the *Shewanellaceae* family predict a global regulatory role of  
344 TyrR for genes that are involved in catabolism of various amino acids and in central carbon  
345 metabolism. The mode of TyrR action on its predicted novel targets in *Shewanella* is to be  
346 determined experimentally. Preliminary comparative analysis of positions of the TyrR-binding sites in  
347 the promoter gene regions suggest that TyrR probably acts as an activator for most of the amino  
348 acid degradation operons in *Shewanella* spp. (data not shown). The homogentisate pathway in  $\gamma$ -  
349 proteobacteria is controlled by either TyrR/PhhR, or by non-orthologous local regulators from the  
350 IclR, LysR, and MarR protein families. We also observed interchangeability between the TyrR and  
351 TrpR regulons: the *aroF-tyrA* genes are controlled by TyrR in most of the analyzed lineages, whereas  
352 in the *Shewanellaceae* family, this operon is predicted to be controlled by TrpR. Overall, the major  
353 biological role of TyrR in *Enterobacteriales* and *Pasteurellales* is the regulation of aromatic amino  
354 acid biosynthesis and transport genes, however in *Pseudomonas* and *Shewanella* it mostly controls  
355 the amino acid degradation pathways, whereas in other *Alteromonadales* species, as well as in  
356 *Vibrionales* and *Aeromonadales*, it is implicated in the control of both biosynthetic and catabolic  
357 pathways.

358

359

### 360 **HypR regulon for proline and 4-hydroxyproline utilization**

361 L-proline, the only proteinogenic imino acid, is used by many bacteria as a source of energy  
362 and a precursor for other amino acid synthesis. 4-hydroxy-L-proline, which can be synthesized post-  
363 translationally from L-proline, is also a rich source of carbon and nitrogen for many microorganisms.  
364 In *Sinorhizobium meliloti*, the hydroxyproline transport and utilization genes (*hyp*) are negatively  
365 regulated by the GntR-family regulator HypR, with 4-hydroxy-L-proline as an inducer (White, et al.  
366 2012). Orthologs of HypR were identified in 13 taxonomic groups that mostly belong to  $\gamma$ -  
367 proteobacteria but also include three  $\alpha$ -proteobacterial and two  $\beta$ -proteobacterial taxa (Figure S2).  
368 The core of reconstructed HypR regulons includes *hypR*, which is autoregulated in 32 out of 46  
369 studied genomes, and *hypE*, *hypO*, *hypD*, and *hypH* encoding enzymes involved in the conversion of  
370 hydroxyproline into  $\alpha$ -ketoglutarate (Figure 5). Operon organization of the *hyp* genes varies among

371 the studied bacteria. Taxonomy-specific regulon members include an alternative 4-hydroxyproline  
372 epimerase (*hypY*) and two putative enzymes from the TCA cycle, malate dehydrogenase (*hypS*) and  
373 citrate isomerase (*hypX*), that are potentially involved in  $\alpha$ -ketoglutarate utilization (Figure 5). PutA,  
374 the main enzyme of the proline catabolic pathway that provides proline oxidation into 1-pyrroline-5-  
375 carboxylate, is the taxonomy-specific member of the HypR regulons in the *Shewanellaceae* and  
376 *Aeromonas* spp. Ornithine can be converted into proline via ornithine cyclodeaminase (COG2423),  
377 which is predicted to be a part of HypR regulon in *Vibrio parahaemolyticus*, *Paracoccus denitrificans*  
378 and several *Shewanella* spp. Thus, HypR function probably expands onto ornithine degradation.

379 In *S. meliloti*, hydroxyproline is imported into the cell via the ABC-family transporter  
380 HypMNPQ, which is predicted to be a part of HypR regulons only in three other genomes and thus  
381 was classified as a taxonomy-specific regulon member. Two other predicted hydroxyproline  
382 transporters, namely HypT from the MFS family and HypABC from the TRAP family, were identified  
383 as genome-specific members of the HypR regulons. Furthermore, HypR-regulated genes encoding a  
384 putative TonB-dependent outer membrane transporter in several *Alteromonadales* and a COG531-  
385 family permease in *Erwinia amylovora* can be also involved in hydroxyproline/proline transport.

386 The large amounts of proline and hydroxyproline are found in the abundant protein collagen  
387 (Phang, et al. 2015). We identified a number of secreted collagenases (*colA1*, *colA2* and *colA3*) within  
388 the reconstructed HypR regulons in the *Alteromonadales* (mostly in *Shewanella* spp.), suggesting the  
389 HypR regulons evolved in these species to include the upstream metabolic steps in the  
390 proline/hydroxyproline utilization pathway (Figure 5). Moreover, the reconstructed HypR regulons in  
391 the *Alteromonadales* and *Aeromonas* taxa of  $\gamma$ -proteobacteria include various proline (di)peptidases  
392 (PrdP, AmpP, and YpdF) and proline dipeptide/tripeptide permease (PdtP), suggesting these species  
393 utilize another upstream source of proline for the catabolic pathway (Figure 5).

394

### 395 **HutC regulon for histidine utilization**

396 Histidine is a well-known source of carbon, nitrogen and energy for many bacteria. The  
397 histidine degradation pathway was studied in *Klebsiella aerogenes* and *Salmonella typhimurium* and  
398 involves four reactions catalyzed by HutH, HutU, HutI and HutG (re-named HutG2 in this work,  
399 belongs to the COG0010 family), whereas in *Pseudomonas* spp. the pathway involves an alternative  
400 HutG enzyme from the COG3741 family, as well as an additional reaction catalyzed by HutF (Figure  
401 6) (Goldberg and Magasanik 1975; Zhang and Rainey 2007). The histidine utilization genes are  
402 regulated by orthologous HutC repressors in the above three  $\gamma$ -proteobacteria. Orthologs of HutC  
403 were identified in 113 genomes from all studied taxa of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -proteobacteria except the  
404 *Pasteurellales* (Figure S2). The core of reconstructed HutC regulons includes all known histidine  
405 catabolic enzymes including both alternative HutG enzymes, as well as the HutD protein, which has  
406 yet unknown function in the pathway. At that the HutC regulons in the *Pseudomonadaceae*,  
407 *Enterobacteriales*, *Burkholderiales*, *Rhizobiales* and *Vibrionales* taxa often include multiple paralogs  
408 of the histidine ammonia-lyase HutH. In addition to the *hut* genes, HutC was predicted to co-regulate  
409 the histidine biosynthesis operon in *Colwellia psychrerythraea* and *Idiomarina loihiensis* (Figure 6).

410 The taxonomy- and genome-specific members of the reconstructed HutC regulons are  
411 represented by a number of known or putative transporters involved in histidine uptake (Figure 6).  
412 These include three known histidine uptake systems: the HisT permease in the *Burkholderiales*,  
413 *Moraxellaceae* and *Pseudomonadaceae*, and two distinct ABC-family transporters, HisJMPQ in  
414 *Burkholderia* and HutXYZ in *Pseudomonadas* and some *Rhizobiales*. A novel histidine transporter

415 from the ABC family (named HisXYZ) was predicted in the *Comamonadaceae*, *Ralstonia* and  
416 *Rhizobiales*. Moreover, the reconstructed regulons include a novel TonB-dependent outer  
417 membrane transporter in the *Caulobacteriales* and *Sphingomonadales*, a COG2814-family permease  
418 in *Ralstonia* spp. and a COG3314-family transmembrane protein in *Aeromonas*, *Psychromonas* and  
419 *Marinomonas* spp. that are potentially involved in histidine uptake. Additional putative transporter  
420 from the COG1457 family was identified in the HutC regulons of *Burkholderia*, *Pseudomonas*,  
421 *Klebsiella* and *Acinetobacter* spp., however all these species already possess the HisT permease.  
422 Therefore, there is not enough information to support assignment of histidine specificity to these  
423 novel COG1457-family transporters that are homologous to purine and allantoine transporters.

424

#### 425 **Taxonomy-specific regulon expansion/shrinking**

426 In addition to the above described five amino acid-specific regulons and also the previously  
427 described methionine regulons (Leyn, et al. 2014), we observed many variations in reconstructed  
428 regulons for orthologous TFs in different lineages of Proteobacteria including regulon expansion and  
429 contraction and many cases of recruiting non-orthologous TFs to control equivalent pathways. The  
430 most interesting and novel examples of the observed evolutionary changes in the reconstructed TF  
431 regulons are briefly described below.

432 The FabR repressor, which was previously known to control the fatty acid biosynthesis genes  
433 *fabAB* in *E. coli* and other *Enterobacteriales*, co-regulates the unsaturated fatty acid biosynthesis  
434 genes *desABC* in several lineages of  $\gamma$ -proteobacteria. In addition, the FabR regulon in six *Shewanella*  
435 species is expanded by the *pfaRABCD* operon encoding polyunsaturated fatty acid synthase. The  
436 fatty acid degradation pathway in *Shewanellaceae* and other  $\gamma$ -proteobacteria is regulated by PsrA,  
437 whereas in *Enterobacteriales* the analogous pathway is regulated by FadR. The FadR regulon in  
438 *Shewanellaceae* is contracted and retains only two operons shared with the orthologous regulon in  
439 *Enterobacteriales* and *Vibrionales* (*fadIJ* and *fadL*). The PsrA regulon in *Shewanellaceae* is expanded  
440 by several operons involved in the tricarboxylic acid cycle (*aceBA*, *sdh*, *gltA*). The biological role of  
441 PsrA regulons in two lineages of  $\beta$ -proteobacteria, *Ralstonia* and *Burkholderia*, is shifted to control  
442 the fatty acid biosynthesis genes, whereas the fatty acid degradation genes are predicted to be co-  
443 regulated by a novel regulator TetR-family regulator, termed FadP, in the above two lineages, as well  
444 in *Comamonadaceae*, which lack PsrA or FadR regulons (Kazakov, et al. 2009).

445 HexR in *Enterobacteriales* is a local regulator of glucose-6-phosphate dehydrogenase (*zwf*),  
446 whereas in other lineages of  $\gamma$ -proteobacteria it co-regulates *zwf-pgl* with genes from the Entner-  
447 Doudoroff pathway (*edd*, *eda*), glucokinase (*glk*) and pyruvate kinase (*pykA*). The HexR regulons in  
448 *Shewanellaceae* and *Vibrionales* are significantly expanded to include various other genes from the  
449 central glycolytic and fermentation pathways, glucose transport, mannitol utilization, nucleoside  
450 metabolism, glutamate biosynthesis, and the glycine cleavage system (Leyn, et al. 2011). The  
451 pyruvate-responsive regulator PdhR, which solely control the pyruvate dehydrogenase operon  
452 *aceEF-lpdA* in *Enterobacteriales*, *Vibrionales* and several other lineages, undergoes radical expansion  
453 to include genes involved in the tricarboxylic acid cycle (*sdhCDAB*, *gltA*, *aceAB*, *oadGAB*) and  
454 fermentation (*pflBA*, *focA*, *lldP-dld*) in *Shewanellaceae*.

455 NtrC protein is a regulator of nitrogen assimilation described in *E. coli* and *Rhodobacter*  
456 *capsulatus* (Reitzer 2003; Masepohl and Hallenbeck 2010). Orthologs of the NtrC protein were found  
457 in 19 analyzed taxa. A core part of the regulon contains genes for glutamine synthetase (*glnA*),  
458 ammonium transporter (*amtB*) and nitrogen assimilation regulatory genes (*glnBK* and *ntrB*, *ntrC*). On

459 the other hand, the NtrC regulon demonstrates taxon-specific expansions to other nitrogen  
460 metabolism genes. NtrC-dependent regulation of glutamate dehydrogenase (*gdhA*) is a specific  
461 feature of the *Moraxellaceae*, *Rhodobacterales* and  $\delta$ -proteobacteria. Genes encoding glutamate  
462 synthase (*gltBD*) are regulated by NtrC in the *Moraxellaceae* and *Shewanellaceae*, as well as in some  
463  $\beta$ -,  $\alpha$ - and  $\delta$ -proteobacteria. In a number of taxa, the NtrC regulon is expanded to the genes  
464 encoding hydrogenases that act on carbon-nitrogen bonds. Thus, allophanate hydrolase (*atzF*) and  
465 agmatinase (*speB*) are regulated in the *Rhizobiales* and  $\beta$ -proteobacteria, respectively, whereas  
466 urease (*ureABC*) and urea ABC transporters (*uctABC* and *urtABCDEF*) are regulated in the  
467 *Alteromonadales*, *Oceanospirillales*, *Rhizobiales* and *Rhodobacterales*. In  $\alpha$ - and  $\beta$ -proteobacteria,  
468 the NtrC regulon is expanded to genes involved in nitrogen oxide uptake and reduction, such as  
469 assimilatory reductases of nitrate (*nasAB*) and nitrite (*nasDE* and *nirA*), nitrate-nitrite antiporter  
470 (*nark*) and nitrate ABC transporter (*nrtABC*). Together, the core of the NtrC regulon includes genes  
471 necessary to inclusion of ammonia into organic compounds through glutamine synthesis, whereas  
472 the taxon-specific regulon members are necessary for generation of ammonia via metabolism of  
473 various nitrogen compounds.

474

#### 475 **Non-orthologous TFs for N-acetylglucosamine utilization pathway**

476 Three different TFs were previously found in Proteobacteria to control the N-  
477 acetylglucosamine catabolic pathway, namely NagC, NagQ and NagR (Yang, et al. 2006). All three  
478 regulons have similar cores consisting of two central enzymes from the N-acetylglucosamine  
479 pathway (*nagA* and *nagB*) and a PTS-family transporter that is involved in uptake and  
480 phosphorylation of N-acetylglucosamine. Taxonomic distribution of these three regulatory systems is  
481 not uniform: NagC and NagR were found in  $\gamma$ -proteobacteria, whereas NagQ was identified in  $\alpha$ - and  
482  $\beta$ -proteobacteria, as well as in some lineages of and  $\gamma$ -proteobacteria. Interestingly, *Reinekea* sp. has  
483 two distinct regulators, where the NagQ regulon contains genes involved in the sugar catabolic  
484 pathway (*nagKAB*) and chitin degradation (*cdxA*, *chiA*), whereas NagC controls genes encoding an N-  
485 acetylglucosamine-specific PTS transporter and chemotaxis proteins. Furthermore, in two  
486 *Xanthomonas* spp. we found both NagQ and NagR, where NagQ regulates the N-acetylglucosamine  
487 catabolic and transport genes (*nagAB* and *nagP*), while NagR regulons include the N-  
488 acetylglucosamine kinase and TonB-dependent outer membrane receptors that might be involved in  
489 sugar transport across the outer memberane. Overall, all three N-acetylglucosamine-specific TF  
490 regulons are expanded in many genomes to include various chitin utilization genes. Also, a  
491 significant expansion of the NagC regulon was observed in the *Vibrionales*, where it includes the  
492 central glycolytic (*gapA*, *gapB*, *fbaA*, *pgk*, *eno*) and glycogen biosynthesis (*glgAC*) genes.

493

#### 494 **Two distinct TF regulons for biotin biosynthesis pathway**

495 Two distinct TFs, BirA and BioQ, control the biotin/vitamin B7 biosynthesis pathway in  
496 Proteobacteria. BirA was previously studied in many details in *E. coli* (Beckett 2005). It is a  
497 bifunctional protein that functions both as a transcriptional repressor and a biotin-protein ligase,  
498 which covalently links biotin to biotin-dependent enzymes. BirA enzymes are ubiquitous in  
499 microorganisms, while the N-terminal DNA-binding domain can be only found in a subset of BirA  
500 proteins from a broad number of Proteobacteria, Firmicutes and several other lineages of Bacteria  
501 and Archaea. Among the studied Proteobacteria, BirA repressors and regulons were found in the  $\gamma$ -  
502 and  $\delta$ -subdivisions. The most conserved part of BirA regulons consists of the biotin biosynthesis

503 genes (*bioABCDF*). The BirA regulons in *Desulfovibrionales* are expanded to include the fatty acid  
504 biosynthesis genes (*fabF*, *fabH*, *acpP*), that are involved in the same pathway with the biotin-  
505 dependent acetyl-CoA carboxylase. The BirA proteins from  $\beta$ - and  $\alpha$ -subdivisions of Proteobacteria  
506 have lost their DNA-binding domains, and apparently the BirA regulons do not exist in these species.

507 The previous comparative genomics analysis of biotin pathway genes has identified a novel  
508 GntR-family TF in  $\alpha$ -proteobacteria from the *Rhizobiales* and *Rhodobacteriales* lineages, termed  
509 BioR, which was predicted to control the biotin metabolism genes (Rodionov and Gelfand 2006). The  
510 reconstructed BioR regulons include the biotin biosynthesis genes (*bioABDF*, *bioCG*, *bioZ*), as well as  
511 a novel ECF-family transporter for biotin (*bioYMN*) (Hebbeln, et al. 2007). The BioR regulon was later  
512 experimentally validated in *Brucella melitensis* and *Paracoccus denitrificans* (Feng, et al. 2013; Feng,  
513 et al. 2015).

514

### 515 Identification of a novel TF regulon involved in NAD biosynthesis

516 In the *Enterobacteriales*, the NAD cofactor metabolism genes are controlled by NadR  
517 regulator, which is absent in all other lineages of Proteobacteria. The most conserved part of NadR  
518 regulon is the *nadA-pnuC* operon that encodes a *de novo* NAD biosynthesis enzymes and a ribosyl  
519 nicotinamide transporter. In several enterobacterial genomes, NadR controls additional NAD  
520 biosynthesis and nicotinate/vitamin B3 salvage genes (*nadB*, *pncB*, *niaP*, *nadR*).

521 In  $\alpha$ -proteobacteria and several species of  $\beta$ - and  $\gamma$ -proteobacteria we found a novel TF,  
522 termed NadQ, which presumably controls the NAD biosynthesis genes. Proteins from the NadQ  
523 orthologous group belong to yet uncharacterized protein family (COG4111) that is characterized by a  
524 characteristic C-terminal DNA-binding domain with a helix-turn-helix (HTH) motif, which is  
525 homologous to another regulator of NAD metabolism, NrtR (Rodionov, et al. 2008). However, the N-  
526 terminal effector binding domain of NadQ is unique as it is not similar to the ADP ribose-binding  
527 domain of NrtR. Palindromic DNA binding motifs for NadQ identified in seven lineages of  
528 Proteobacteria are characterized by the common consensus sequence ttATRCTCannntGAGYATaa,  
529 where R and Y stand for purines or pyrimidines, respectively. The *nadQ* genes are often clustered on  
530 the chromosome with the *de novo* NAD biosynthesis genes (*nadABC*). Thus, the core of  
531 reconstructed NadQ regulons in proteobacteria includes these central NAD biosynthesis genes. In  
532 the *Rhodobacteriales* and *Caulobacteriales*, the NadQ regulon is expanded to include the lower NAD  
533 biosynthesis pathway genes (*nadE* and *nadD*). Effector molecule for the novel NadQ regulator is to  
534 be determined experimentally but the regulon content suggests that it can be either NAD itself or  
535 one of pathway intermediates.

### 536 Conclusions

537 We used the comparative genomics approach for reconstruction of regulatory networks for amino  
538 acid and other central metabolic pathways that are controlled by specific groups of TFs. The results  
539 of this study demonstrate considerable variability of the TF regulons for the central metabolic  
540 pathways in Gram-negative bacteria from the phylum Proteobacteria. The core members of the  
541 characterized TF regulons are involved in arginine biosynthesis (ArgR), biotin biosynthesis (BirA),  
542 fatty acid biosynthesis (FabR) and degradation (FadR, FadP, PsrA), glycolate, lactate and pyruvate  
543 utilization (GlcC, LldR, PdhR), central carbohydrate metabolism (HexR), histidine and  
544 hydroxyproline/proline utilization (HutC, HypR), branched-chain amino acid degradation (LiuR, LiuQ),  
545 methionine metabolism (MetJ, MetR, SahR), nitrogen assimilation (NtrC), deoxyribonucleotide

546 biosynthesis (NrdR), N-acetylglucosamine utilization (NagC, NagQ, NagR), pyrimidine degradation  
547 (RutR), tyrosine and phenylalanine metabolism (TyrR) and tryptophan biosynthesis (TrpR). Large-  
548 scale phylogenomic and comparative genomics analyses of these TFs reveal numerous examples of  
549 various evolutionary processes for regulators and their regulons both at the levels of a taxonomic  
550 group/class of bacteria and an individual genome. These predicted evolutionary processes can be  
551 classified into three distinct types: (i) “regulon expansion” in certain taxa compared to other lineages  
552 that can be ranged from additions of several regulons members to large-scale shifts in the regulated  
553 metabolic pathways (e.g., PdhR, TyrR and TrpR regulons in *Shewanella* spp.); (ii) “fuzzy regulons”  
554 when a regulon contains a small conserved core and a large periphery of taxon- and genome-specific  
555 genes (e.g. ArgR, HexR and NtrC regulons); (iii) “regulon loss or acquisition” when entire regulon  
556 (including a TF and all its TFBSs and target genes) is absent or present only in specific genomes  
557 within a taxonomic group of bacteria (e.g. GlcC and HypR that are present in individual species of  
558 *Enterobacteria* or NagR that was found in all but one *Shewanella* spp.). The most conserved  
559 regulatory interactions were identified within TF regulons that are involved in the control of certain  
560 essential biosynthetic pathways (e.g. BirA, NrdR, and FabR). Overall, this study provides new insights  
561 into the evolutionary mechanisms that shape transcriptional regulatory networks in Bacteria.

562

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## 563 ABBREVIATIONS

564 TF, Transcription factor; TFBS, transcription factor binding site; PWM, positional weight matrix;  
565 CRON, cluster of co-regulated orthologous operons.

566

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713

714 **FIGURES AND TABLES**

715 **Figure 1. Taxonomic distribution of 33 studied transcription factor regulons in four major**  
 716 **classes of Proteobacteria.** Circles include number of TFs that are either taxonomic class-  
 717 specific or shared between several classes.

718 **Figure 2. Examples of motifs changes in four orthologous groups of studied TFs.**  
 719 Conservative positions between motifs within groups are boxed with the same color.

720 **Figure 3. Arginine metabolism and its regulation by ArgR in Proteobacteria.**

721 **Figure 4. Aromatic amino acid metabolism and its regulation by TyrR, TrpR and other**  
 722 **transcription factors in Proteobacteria.**

723 **Figure 5. Hydroxyproline and proline utilization pathway and its regulation by HypR in**  
 724 **Proteobacteria.**

725 **Figure 6. Histidine metabolism and its regulation by HutC in Proteobacteria.**

726

727 **Table 1. Statistics for the studied TF regulons in Proteobacteria.**

TF <sup>1</sup>	Protein family	Metabolic pathways controlled by a TF	Genomes (taxa) <sup>2</sup>	TFBSs total <sup>3</sup>	Genes, total <sup>3</sup>	Genes, average <sup>4</sup>
ArgR	ArgR	Arginine metabolism	62 (6)	1079	1223	19.7
BioR*	GntR	Biotin biosynthesis	13 (2)	34	59	4.5
BirA	BirA	Biotin biosynthesis	94 (11)	185	495	5.3
FabR	TetR	Fatty acid biosynthesis	74 (10)	361	392	5.3
FadP*	TetR	Fatty acid degradation	25 (3)	194	448	17.9
FadR	GntR	Fatty acid degradation	61 (6)	374	423	6.9
GlcC	GntR	Glycolate utilization	23 (7)	83	133	5.8
HexR	RpiR	Central carbohydrate metabolism	87 (11)	897	1178	13.5
HmgQ*	LysR	Tyrosine degradation	17 (2)	35	50	2.9
HmgR*	IcIR	Tyrosine degradation	5 (1)	12	24	4.8
HmgS*	MarR	Tyrosine degradation	3 (1)	6	9	3.0
HutC	GntR	Histidine utilization	113 (18)	386	857	7.6
HypR	GntR	Proline / 4-hydroxyproline utilization	44 (12)	190	265	6.0

LiuQ*	TetR	Branched-chain amino acid utilization	14 (3)	54	73	5.2
LiuR	MerR	Branched-chain amino acid utilization	103 (15)	671	1411	13.7
LldR	GntR	Lactate utilization	55 (13)	146	241	4.4
MetJ	MetJ	Methionine metabolism	62 (6)	1026	857	13.8
MetR	LysR	Methionine metabolism	117 (14)	570	480	4.1
NadR*	NadR	NAD biosynthesis	11 (1)	27	35	3.2
NadQ*	NadQ	NAD biosynthesis	30 (7)	67	109	3.6
NagC	ROK	N-acetylglucosamine utilization	31 (5)	304	431	13.9
NagQ*	GntR	N-acetylglucosamine utilization	31 (10)	81	225	7.3
NagR*	Lacl	N-acetylglucosamine utilization	25 (4)	168	288	11.5
NrdR	NrdR	Deoxyribonucleotide biosynthesis	186 (20)	638	591	3.2
NrtR	NrtR	NAD biosynthesis	28 (11)	75	96	3.4
NtrC	Fis	Nitrogen assimilation	169 (19)	921	1804	10.7
PdhR	GntR	Pyruvate metabolism	55 (6)	200	399	7.3
PsrA	TetR	Fatty acid degradation	76 (12)	673	845	11.1
RutR	TetR	Pyrimidine catabolism	68 (13)	273	743	10.9
SahR*	ArsR	Methionine metabolism	62 (9)	156	266	4.3
SamR*	ArsR	Methionine metabolism	4 (1)	17	30	7.5
TrpR	TrpR	Aromatic amino acid metabolism	53 (8)	142	314	5.9
TyrR	TyrR	Aromatic amino acid metabolism	67 (7)	618	896	13.4

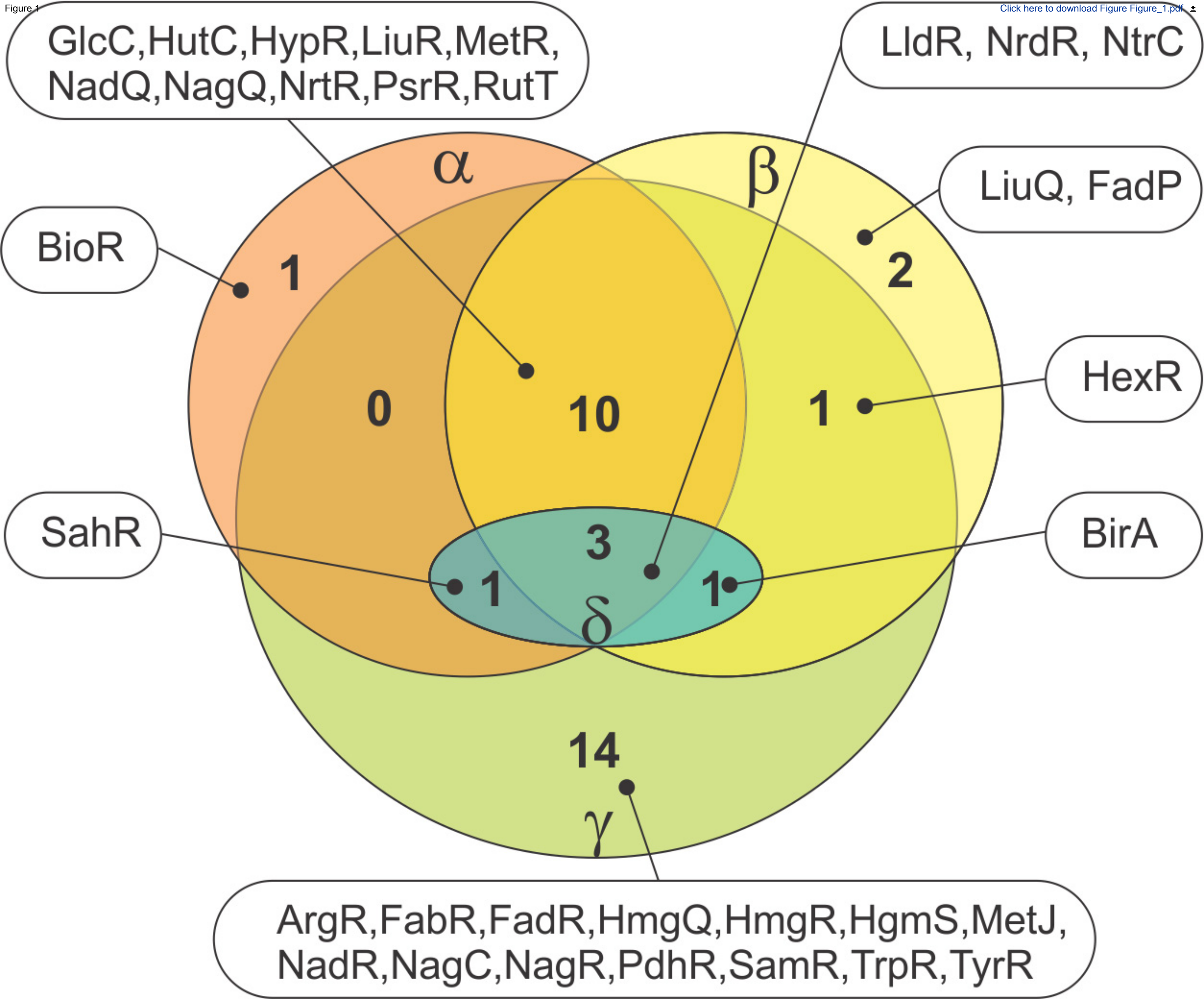
728 <sup>1</sup>Initially, we studied 21 TFs that are present in *E. coli* and/or *Shewanella* spp. and that are  
729 conserved in five or more taxonomic groups of Proteobacteria. Additionally, we studied TFs  
730 that represent non-orthologous replacements of the initial set of TFs in some taxonomic  
731 groups are marked by asterisk.

732 <sup>2</sup>Number of genomes and taxonomic groups (in parenthesis) of Proteobacteria that contain  
733 the studied TF regulon. The detailed distribution of regulons and regulogs is provided in  
734 Figure S2.

735 <sup>3</sup>Total number of candidate TF-binding sites (TFBSs) and TF-regulated genes (target genes) in  
736 all studied genomes.

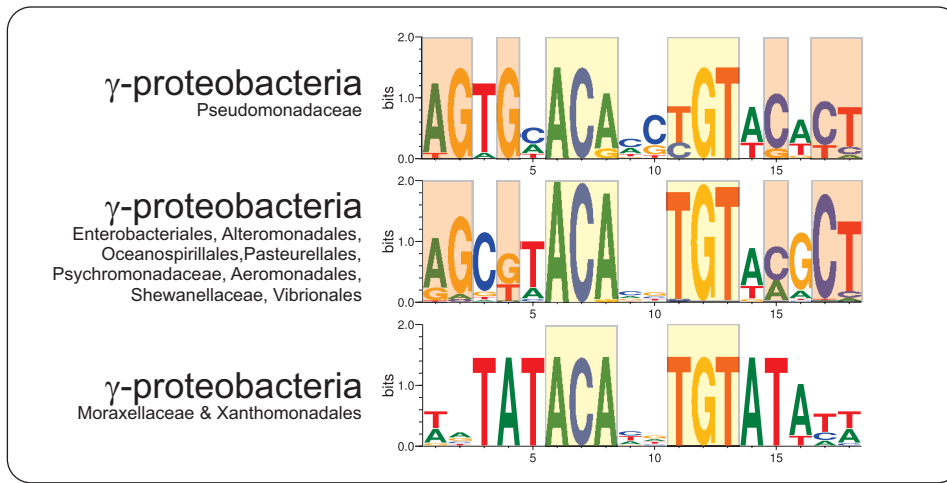
737 <sup>4</sup>Average number of candidate TFBSs per genome.

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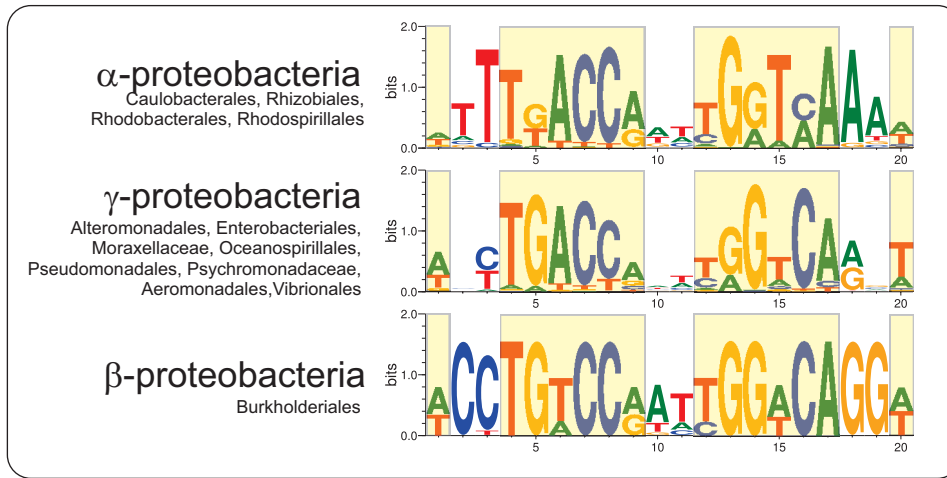




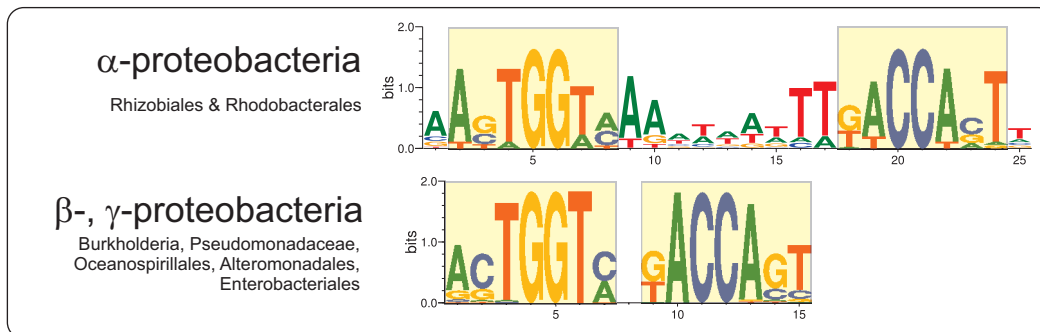
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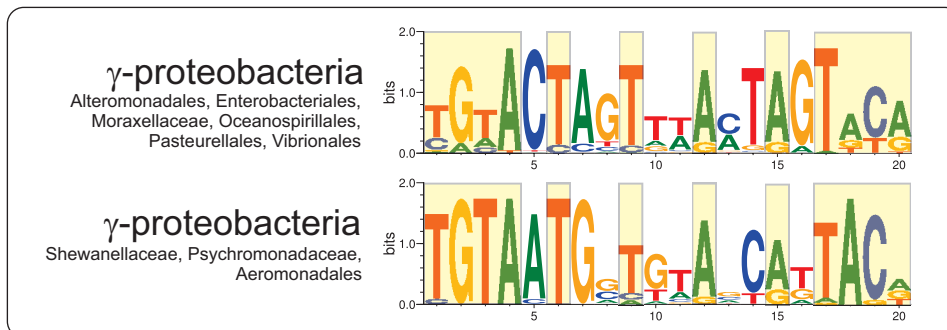
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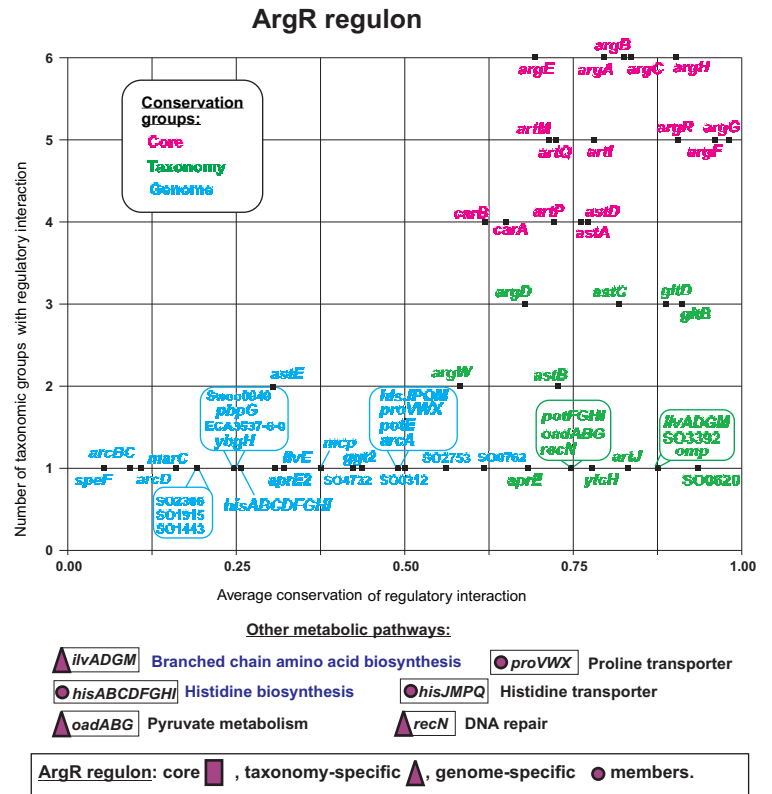
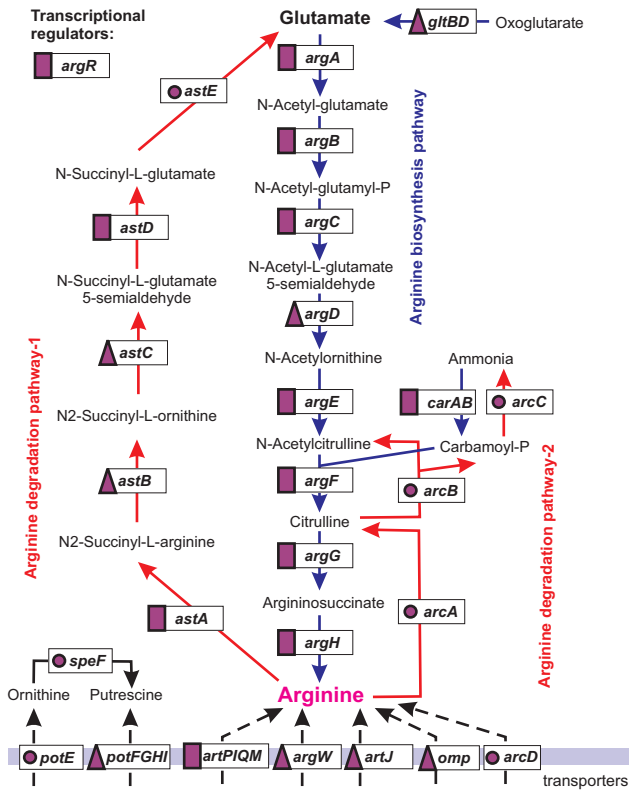


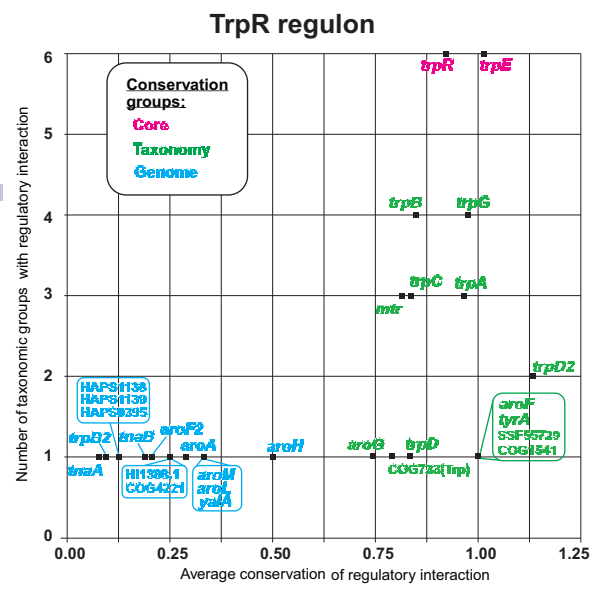
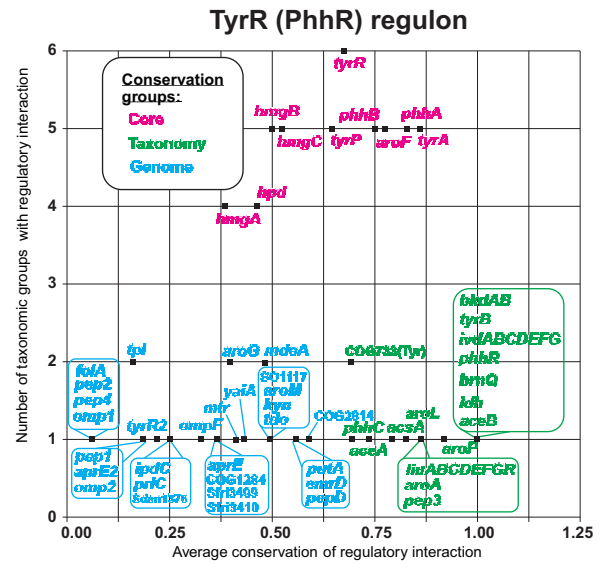
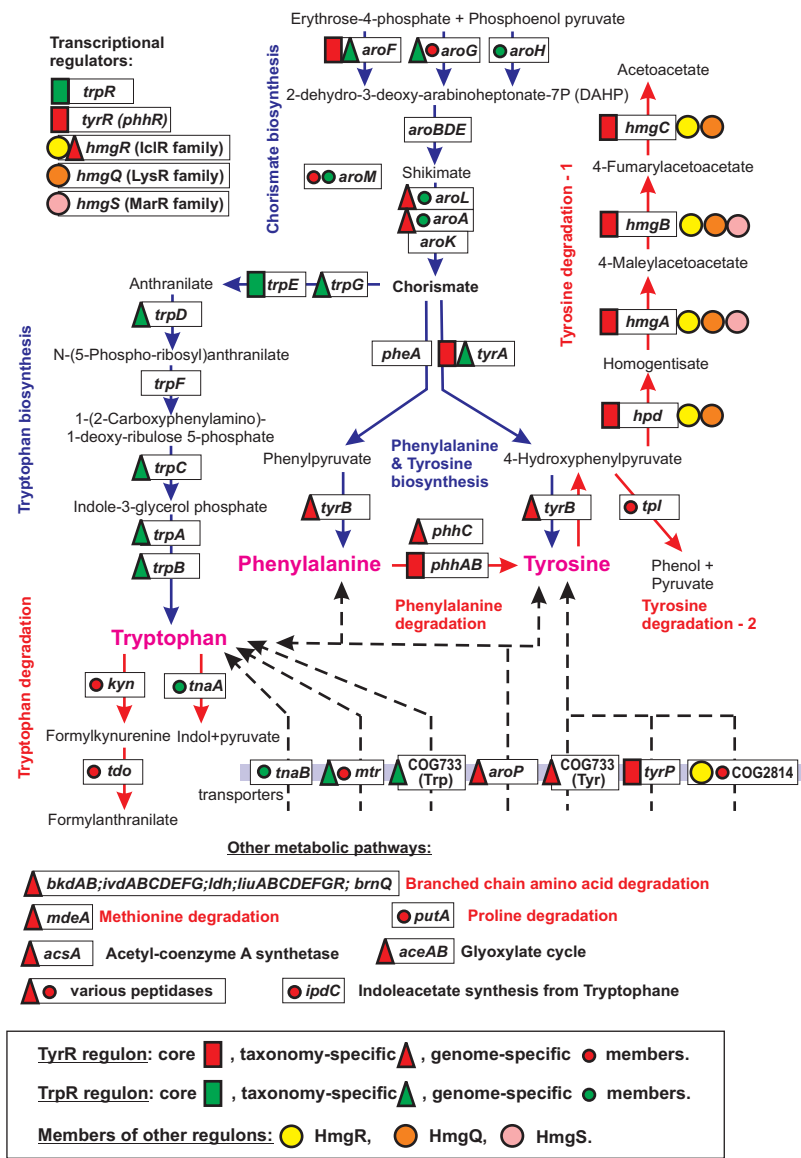
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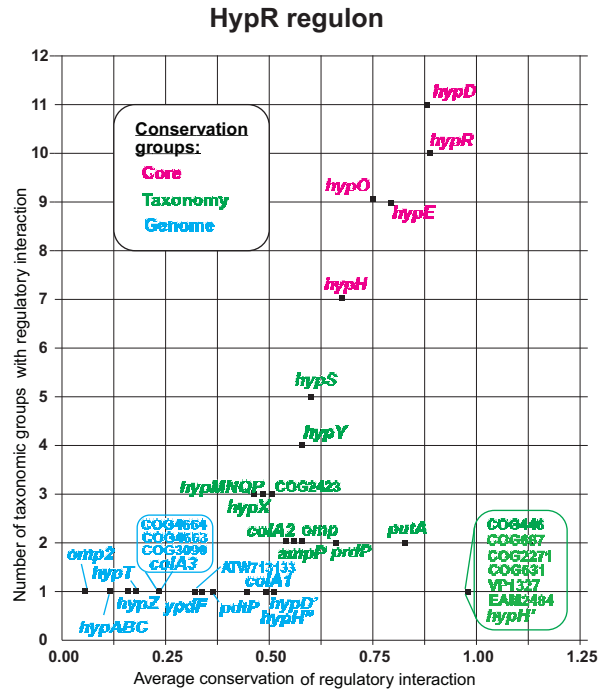
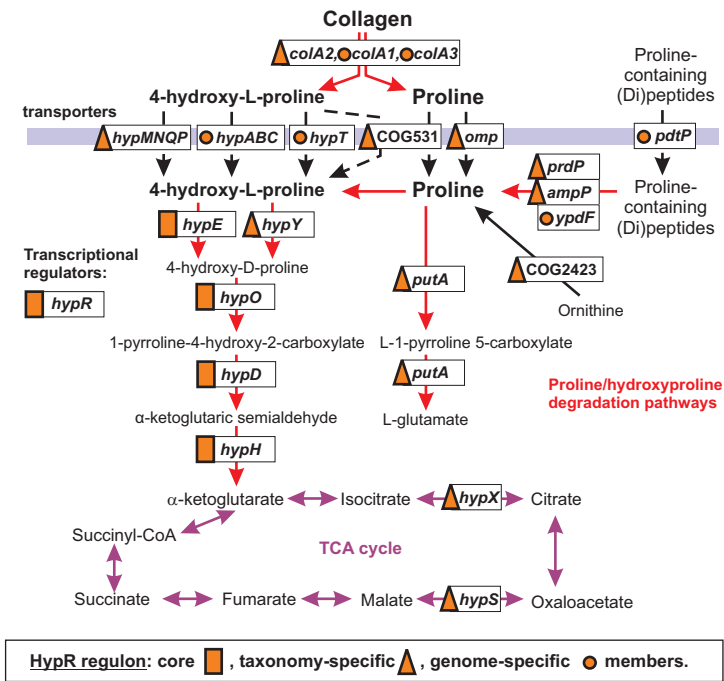


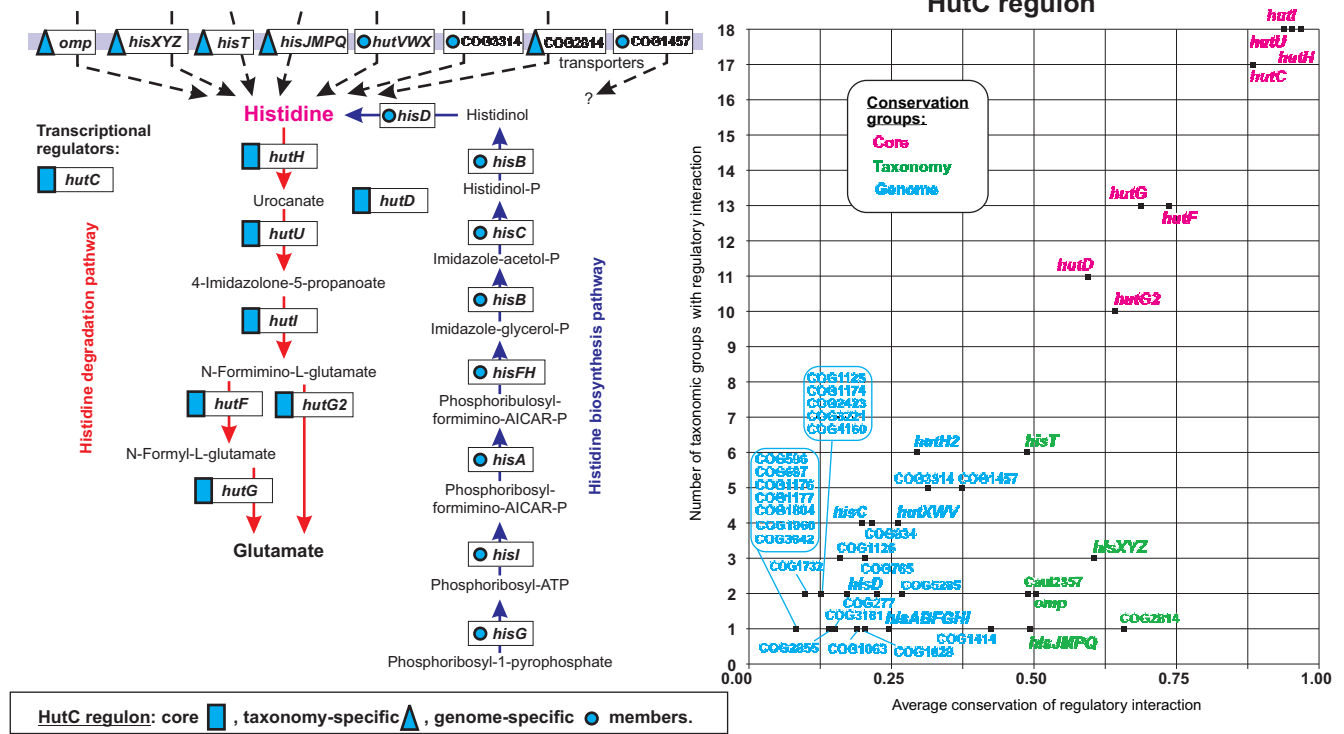
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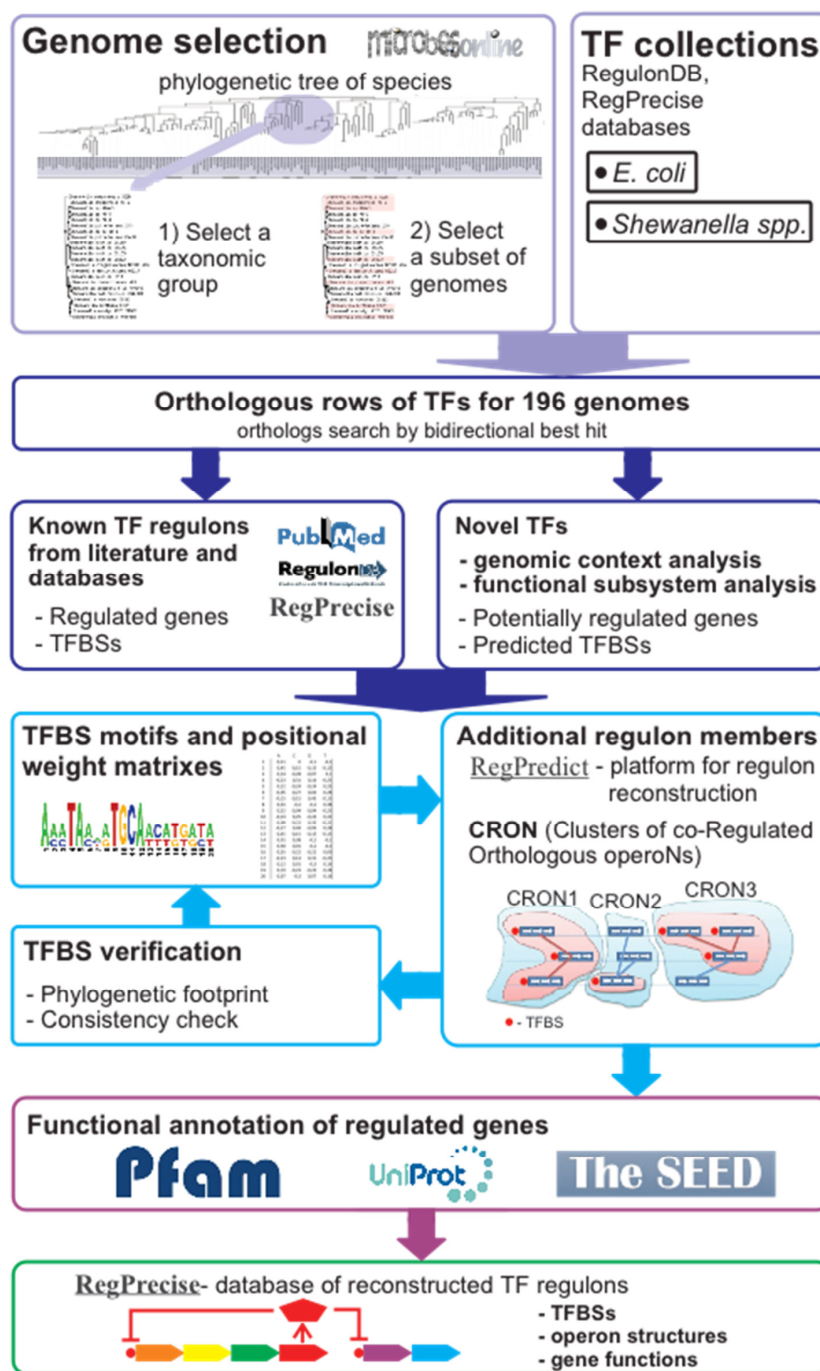












**Figure S1. Bioinformatics workflow used for reconstruction of TF regulons.**

For regulon reconstruction we started from collections of known TFs in *Escherichia coli* and *Shewanella* species and identification of their orthologs. Collections of TFs were obtained from RegulonDB (Gama-Castro, et al. 2016) for *E. coli* and the RegPrecise (Novichkov et al., 2013) for *Shewanella* spp. For subsequent reconstruction steps we used genomes from MicrobesOnline (Dehal, et al. 2010) database because the RegPredict platform for reconstruction of transcription regulation is linked with genomes in MicrobesOnline. In each taxonomic group, from 4 to 16 representative genomes were selected based on the MicrobesOnline species tree. Closely related strains were eliminated from our analysis to

avoid skews in the consistency check approach and to simplify the simultaneous analysis in the RegPredict web server. At that we preferably selected most well studied genome representative in each set of closely-related genomes. Next we searched for orthologous TFs in the selected genomes using the bidirectional best hits approach and protein BLAST server at NCBI (Altschul, et al. 1997).

For regulon reconstruction in each group of genomes possessing TF orthologs we used standard comparative genomics approach (Rodionov 2007) that consists of the next steps:

1. Obtain training set of potential TFBS;
2. Build positional weight matrix (PWM);
3. Whole-genomic search for additional TFBSs and regulon members;
4. False positive filtering;
5. PWM refinement and continue from step 2.

For collection of training sets we used two strategies. (i) For studied known regulons we collected upstream regions of known to be regulated genes with attention for more precise information about location of TFBSs (as electrophoretic mobility shift assay or DNase footprinting assay). (ii) For novel TF regulons, we used genomic context analysis where we predicted regulation of neighborhood genes by their conservative co-localization in one locus mapped to phylogenetic tree of TF. Another approach is functional analysis based on assumption that genes from one metabolic pathway or one process should be regulated simultaneously. Based on this approach we taken upstreams of genes from one process. Association of TF with regulation was made by conservative co-localization of TF gene with genes from this pathway.

Collected upstream regions were used to identify a common DNA motif using the Discover Profiles tool in the RegPredict platform (Novichkov et al., 2010). We searched for DNA motifs either palindromic or tandem repeat symmetry. Sequences of identified DNA motif sites were used to build PWM. The constructed PWMs were further used to search for additional potential TFBSs across upstreams of all genes in genomes using the RegPredict server. Typically we searched the regions beginning 400 nt upstream to and ending 50 nt downstream to the translational start of each gene. Typical threshold for site search procedure was selected as 10% less of the lowest site score from the training set.

The whole genomic searches in RegPredict result in construction of a set of CRONs (Clusters of co-Regulated Orthologous operONs). Each CRONs in RegPredict was built by the following algorithm: 1) PWM found potential TFBSs above threshold; 2) operon predicted by taking gene with potential TFBS as the first gene of operon and prolong operon to all genes with the same direction and intergenic distance less than 200 nt; 3) identification of orthologs and paralogs for each gene in this operon based on Orthologous Groups in MicrobesOnline database; 4) steps 2 and 3 repeated until convergence. Automatic construction of CRONs and manual curation of the obtained CRONs in the RegPredict server allowed us to filter out false positive site predictions by utilizing the consistency check approach. The consistency check approach is based on the assumption that true sites are conserved in evolution. It should be noted that the cases of operon gene content rearrangement are also taken into consideration in the course of CRON analysis and curation. On next step, the identified true positive TFBSs were added to refine PWM and further repeat the genomic site searches.

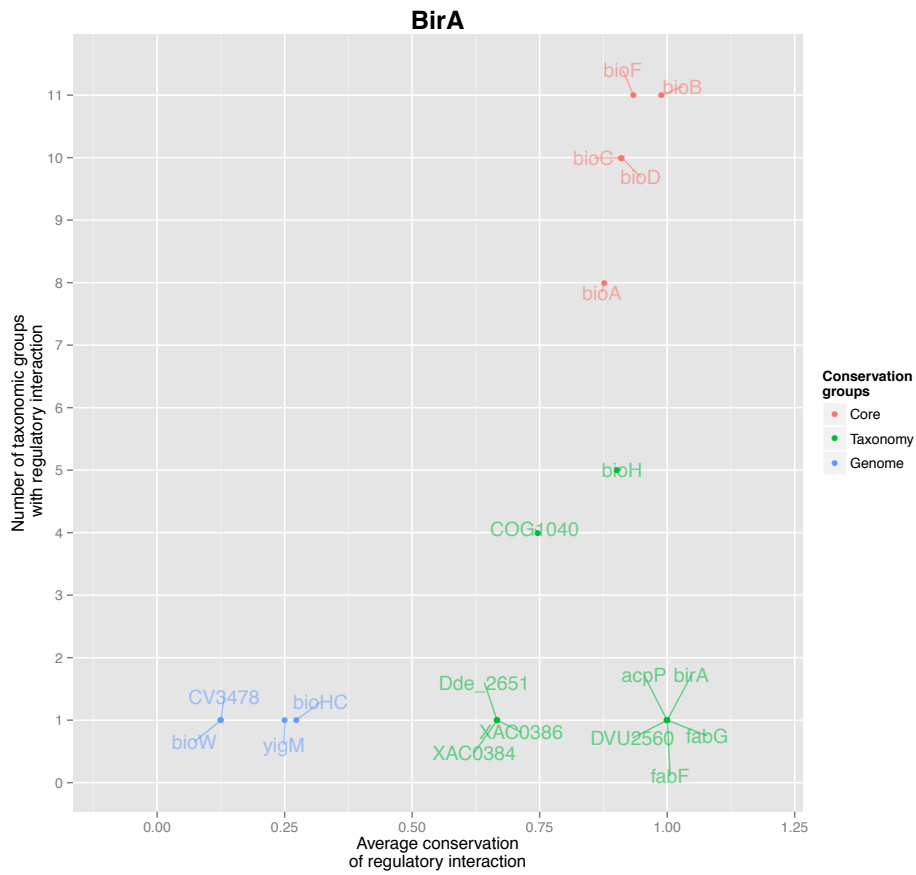
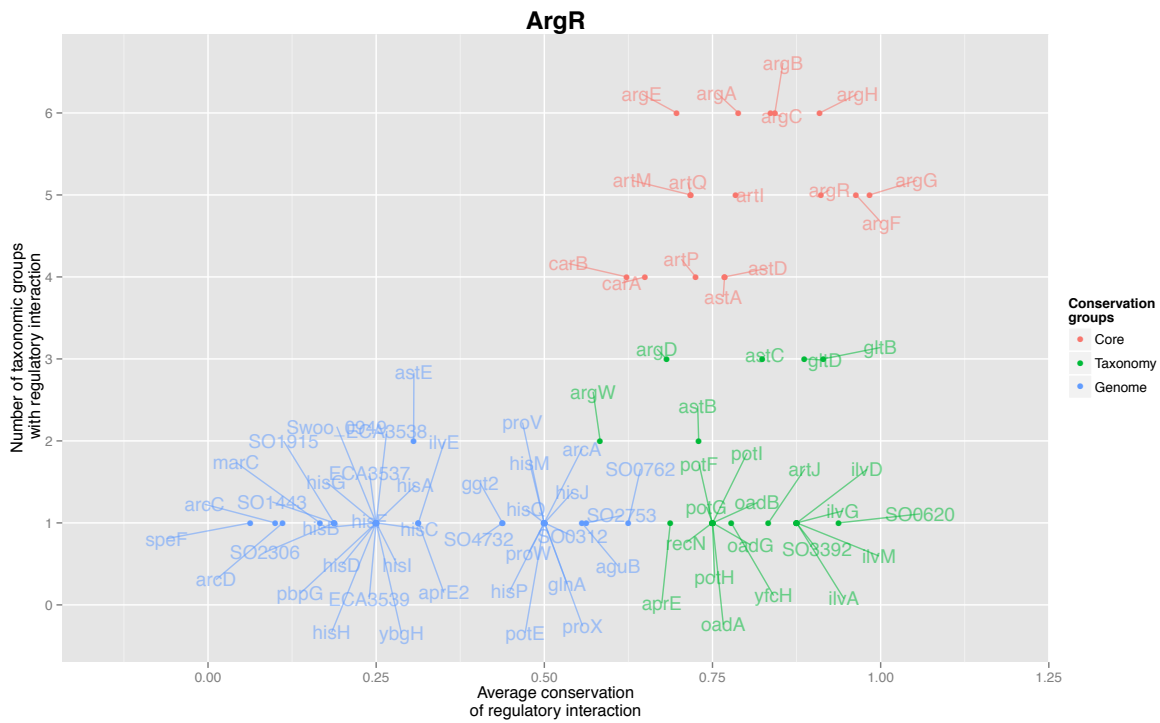
At the final step of the manual regulon annotation, gene functions are assigned using the existing gene annotations in Genbank and SEED databases (Overbeek, et al. 2005), annotations of homologous proteins in SwissProt / UniProt database (UniProt 2015) and analysis of Pfam domains (Finn, et al. 2016). All reconstructed regulons were finally deposited in the latest release of the RegPrecise database (<http://regprecise.lbl.gov>) (Novichkov, et al. 2013).

TF	<i>Escherichia coli</i>	γ-proteobacteria										β-proteobacteria				α-proteobacteria				δ-proteob.		TOTAL reguloGs	TOTAL reguloNs	
		Enterobacteriales (12)	Vibrionales (10)	Pasteurellales (9)	Shewanellaceae (16)	Other Alteromonadales (9)	Psychromonadaceae/ Aeromonadales (6)	Oceanospirillales/ Alteromonadales (12)	Pseudomonadaceae (8)	Moraxellaceae (4)	Xanthomonadales (4)	Ralstonia (6)	Burkholderia (8)	Comamonadaceae (11)	Other various β-proteobacteria (12)	Rhizobiales (15)	Rhodobacteriales (15)	Rhodospirillales (9)	Spingomonadales (7)	Caulobacteriales (4)	Desulfovibrionales (10)			Desulfuromonadales (9)
ArgR	+	12	10	9	16	9	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	62
BioR*	-	0	0	0	0	0	0	0	0	0	0	0	0	0	7	6	0	0	0	0	0	0	2	13
BirA	+	12	10	0	16	9	6	11	8	0	3	0	0	0	8	0	0	0	0	0	3	8	11	94
FabR	+	12	10	8	16	9	4	6	8	2	3	0	0	0	0	0	0	0	0	0	0	0	10	78
FadP*	-	0	0	0	0	0	0	0	0	0	0	6	8	11	0	0	0	0	0	0	0	0	3	25
FadR	+	12	10	9	16	9	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	61
GlcC	+	1	0	0	0	0	0	3	6	0	0	0	4	2	6	1	0	0	0	0	0	0	7	23
HexR	+	11	10	0	16	5	6	6	16	0	0	6	8	9	2	0	0	0	0	0	0	0	13	95
HmgQ*	-	0	0	0	16	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	2	17
HmgR*	-	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	1	5
HmgS*	-	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3
HutC	-	8	10	0	16	8	4	3	6	2	3	6	8	7	1	10	10	5	2	4	0	0	18	113
HypR	-	1	1	0	16	3	3	2	1	0	0	1	3	0	0	6	8	1	0	0	0	0	13	46
LiuQ*	-	0	0	0	0	0	0	0	0	0	0	4	8	2	0	0	0	0	0	0	0	0	3	14
LiuR	-	0	6	0	16	8	2	6	8	0	0	6	2	10	5	9	13	3	6	4	0	0	16	104
LidR	+	5	0	0	0	0	0	4	7	2	1	4	8	3	5	0	2	4	0	0	6	4	13	55
MetJ	+	12	10	9	16	9	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	62
MetR	+	12	10	8	16	4	5	12	8	0	3	6	7	5	8	0	13	0	0	0	0	0	14	117
NadQ*	-	0	0	0	0	0	0	0	0	2	0	0	0	2	1	12	2	7	0	4	0	0	7	30
NadR*	+	11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	11
NagC	+	12	10	2	0	0	6	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	31
NagQ*	-	0	0	0	0	0	0	3	2	0	2	1	7	0	1	7	4	1	0	3	0	0	10	31
NagR*	-	0	0	0	15	3	0	3	0	0	4	0	0	0	0	0	0	0	0	0	0	0	4	25
NrdR	+	12	10	9	16	9	6	12	8	4	4	6	8	11	12	15	15	9	7	4	0	9	20	186
NrtR	-	1	4	0	3	0	3	2	4	2	0	0	0	4	2	2	1	0	0	0	0	0	11	28
NtrC	+	12	9	0	16	9	6	12	8	4	4	6	8	11	9	14	14	8	6	4	0	9	19	169
PdhR	+	12	10	0	16	9	6	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	55
PsrA	-	0	8	0	16	4	3	8	8	0	3	6	8	0	5	3	0	0	4	0	0	0	12	76
RutR	+	7	2	0	0	5	1	8	20	2	0	4	7	0	0	9	13	1	0	2	0	0	17	81
SahR*	-	0	0	0	0	0	0	9	8	0	0	0	0	0	10	2	7	7	4	9	6	9	62	
SamR*	-	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	1	4
TrpR	+	12	10	8	16	0	2	2	0	2	1	0	0	0	0	0	0	0	0	0	0	0	8	53
TyrR	+	12	10	9	16	9	4	0	7	0	0	0	0	0	0	0	0	0	0	0	0	0	8	67
TOTAL regulogs	17	20	19	9	19	21	19	21	22	9	12	13	14	12	13	13	15	10	5	9	3	5	283	
TOTAL regulons	-	189	160	71	290	124	84	115	139	22	35	62	94	75	61	110	104	46	28	33	18	36		1896

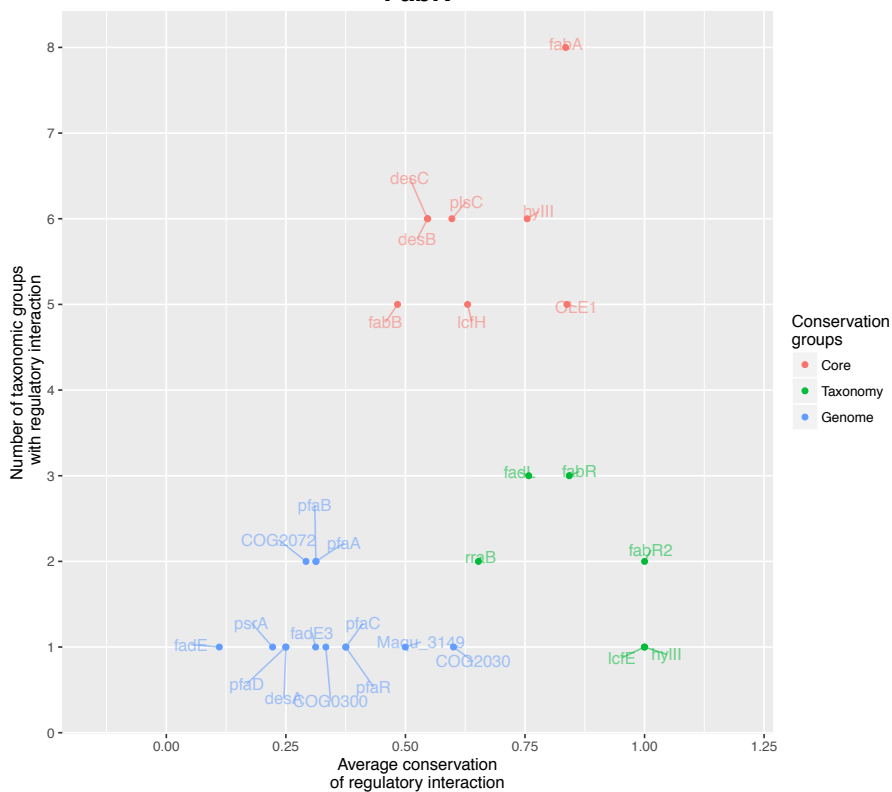
**Figure S2. Taxonomic distribution of studied TF regulons and regulogs in 21 taxonomic groups of Proteobacteria**  
 21 TFs are present in *E. coli* and/or *Shewanella* spp. and are conserved in five or more taxonomic groups of Proteobacteria.  
 12 TFs that represent non-orthologous replacements of the initial set of TFs in some taxonomic groups are marked by asterisk (\*).  
 Each cell in represents a TF regulog; each number corresponds to the number of TF regulons per regulog.  
 Numbers in red font highlight TFs/taxonomic groups that have multiple regulogs represented by paralogous TFs.



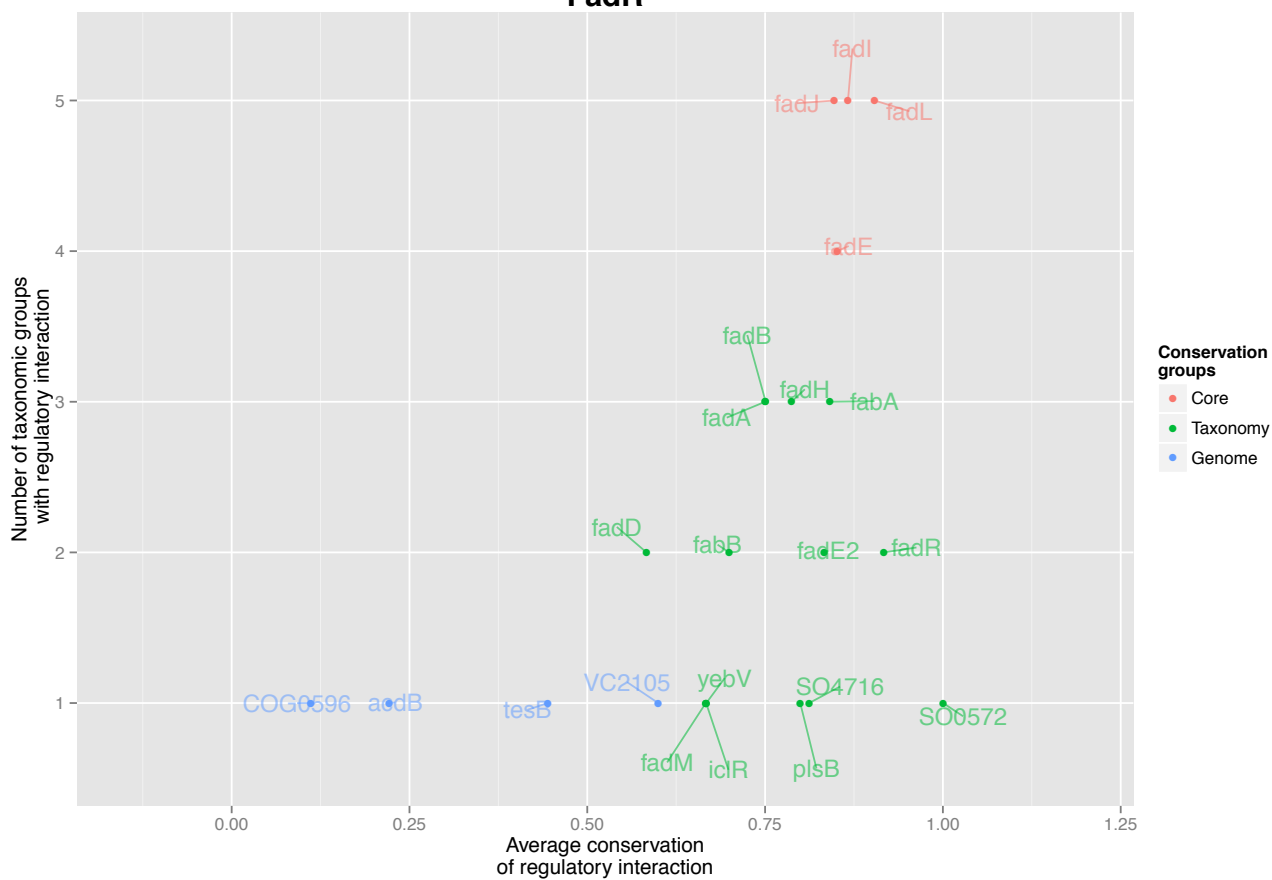
**Figure S3.** Conservation of regulatory interactions in the reconstructed regulons. Core, Taxonomy-specific and Genome-specific groups are highlighted with red, green and blue color respectively. Regulon member names are connected with respective dots by dashes. Functional belonging of regulon members is listed in table S3.



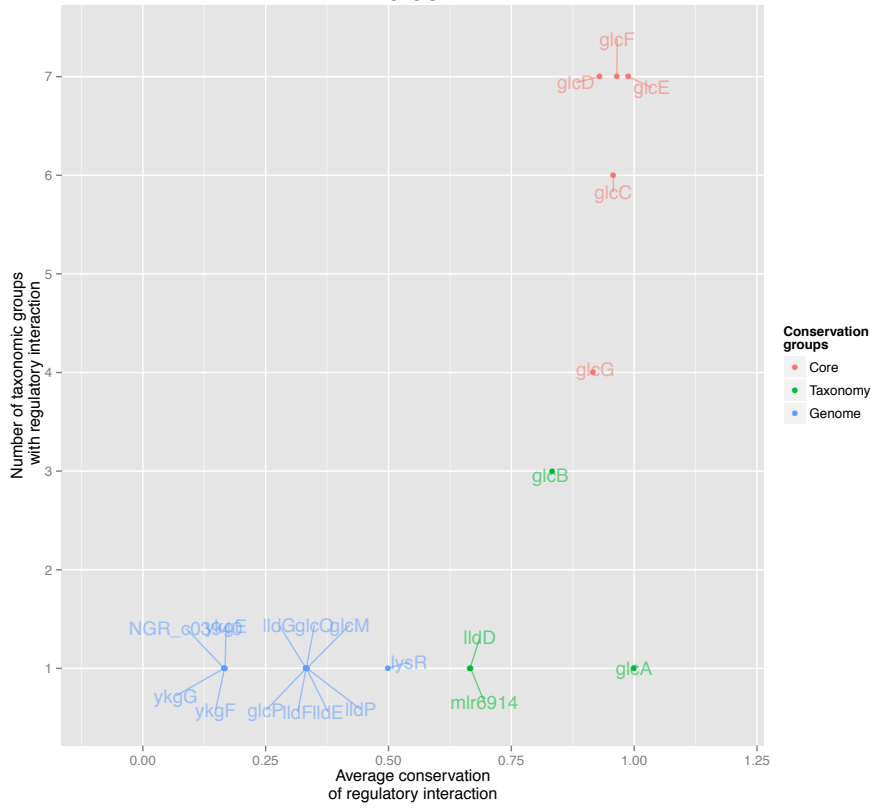
### FabR



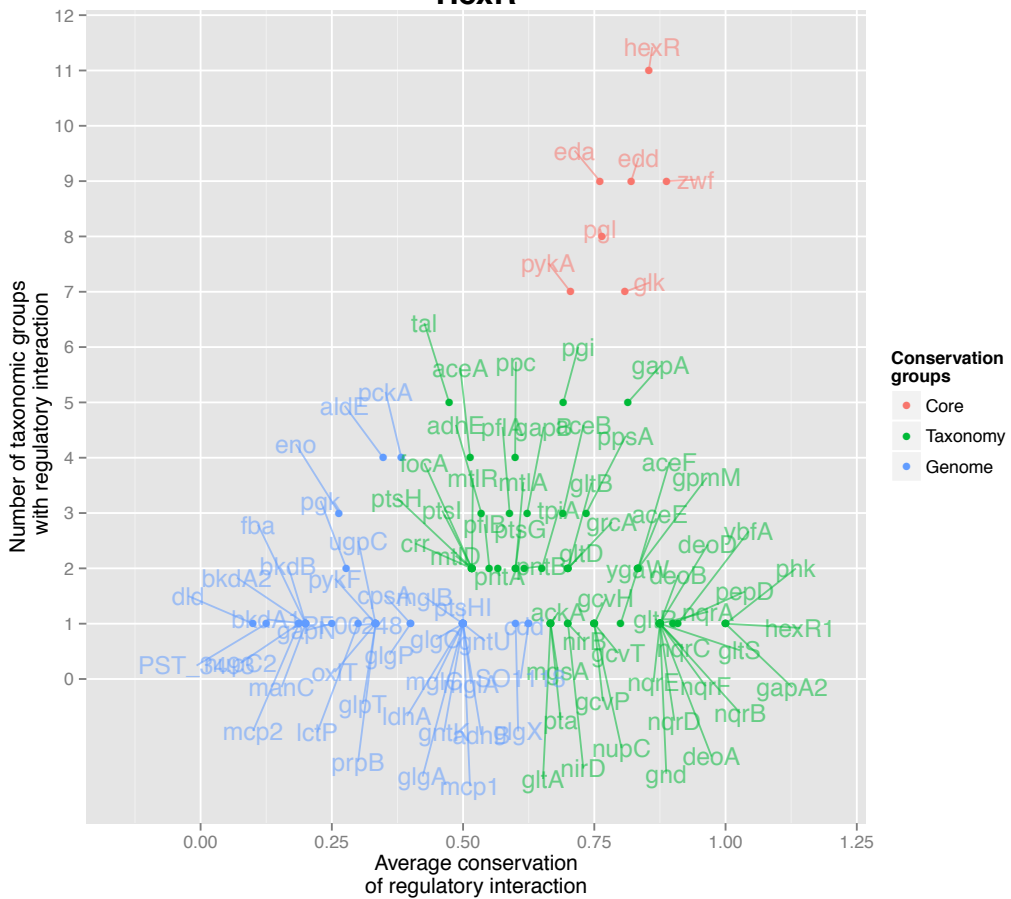
### FadR



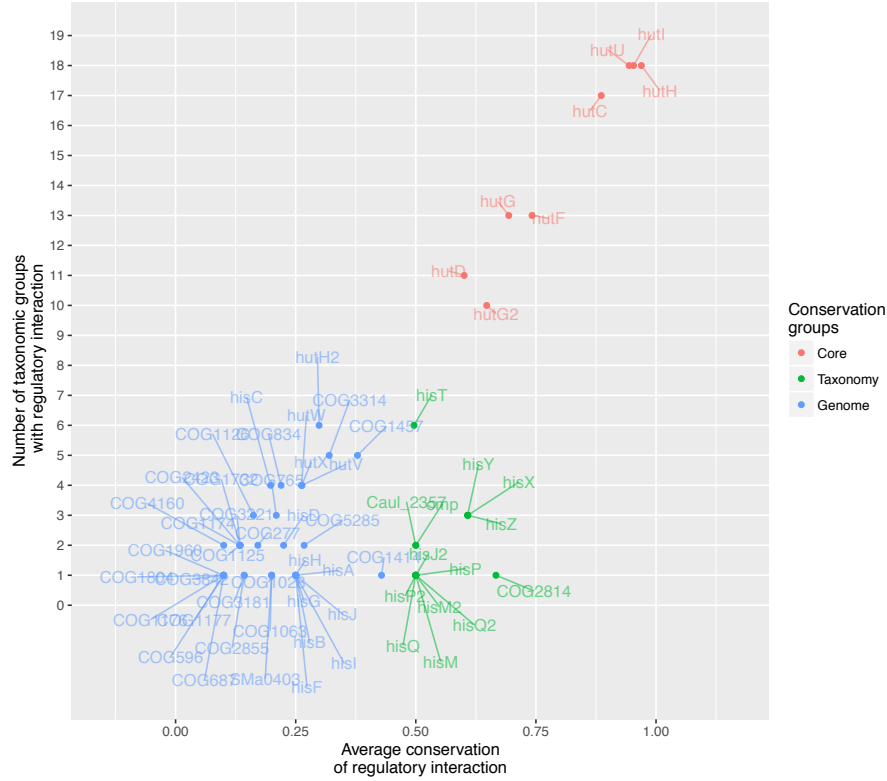
### GlcC



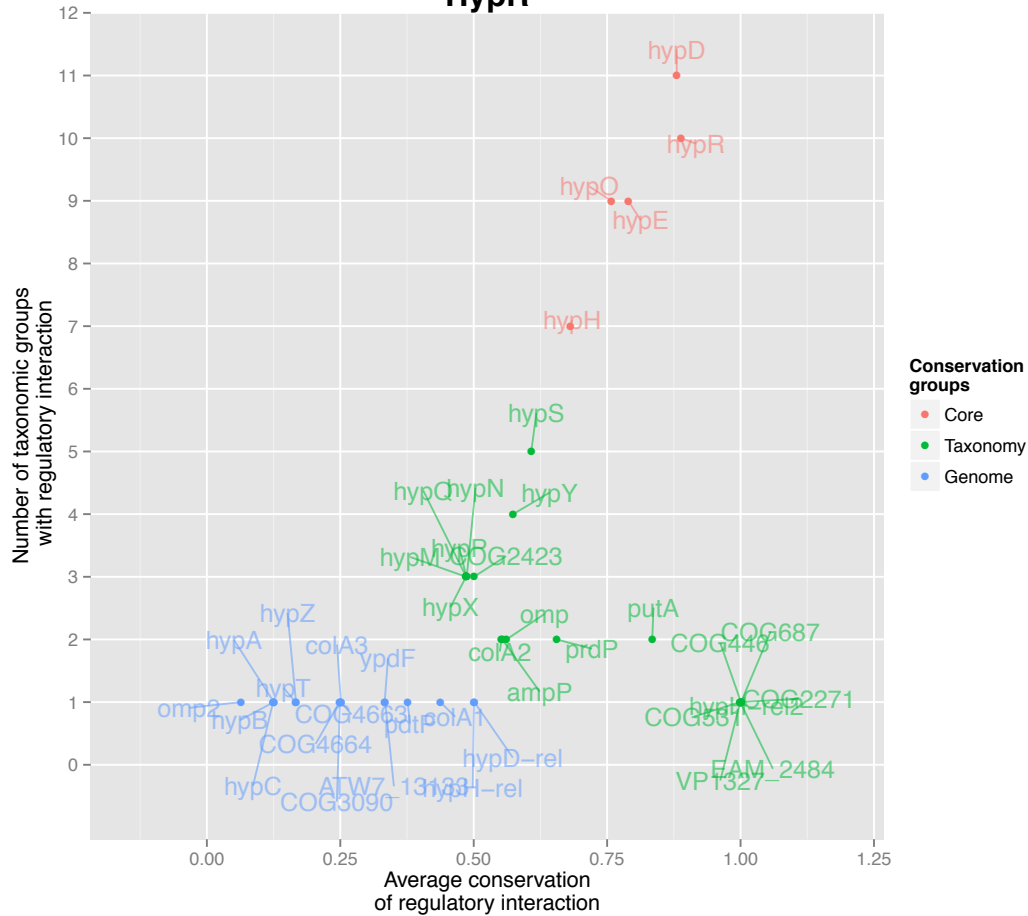
### HexR



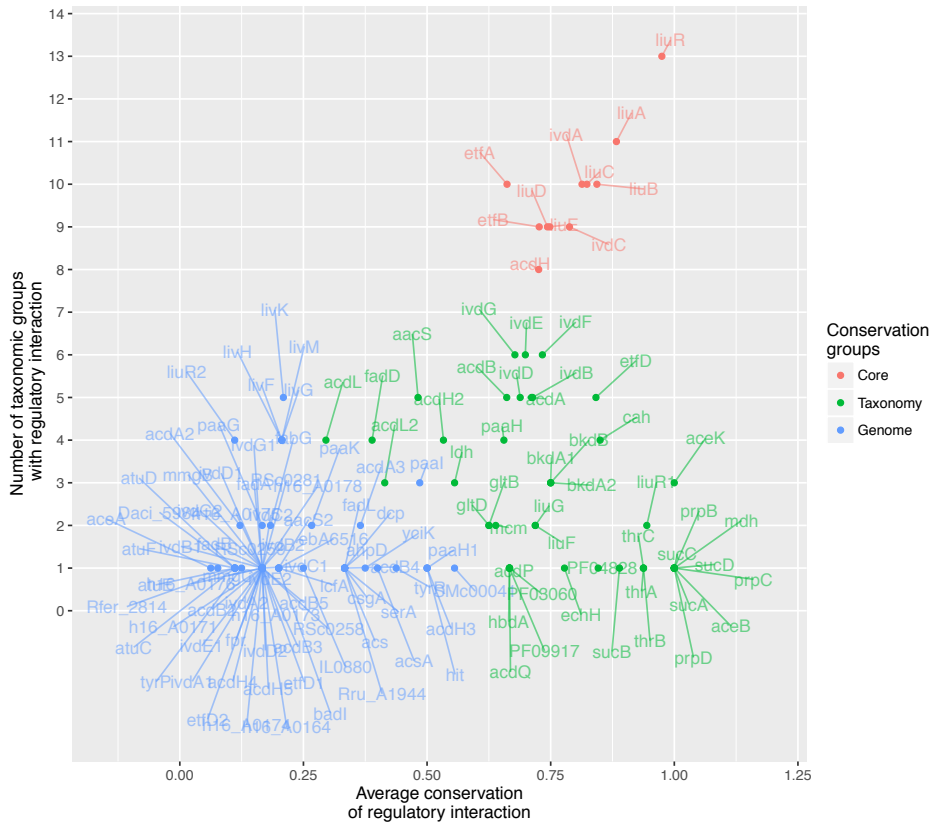
### HutC



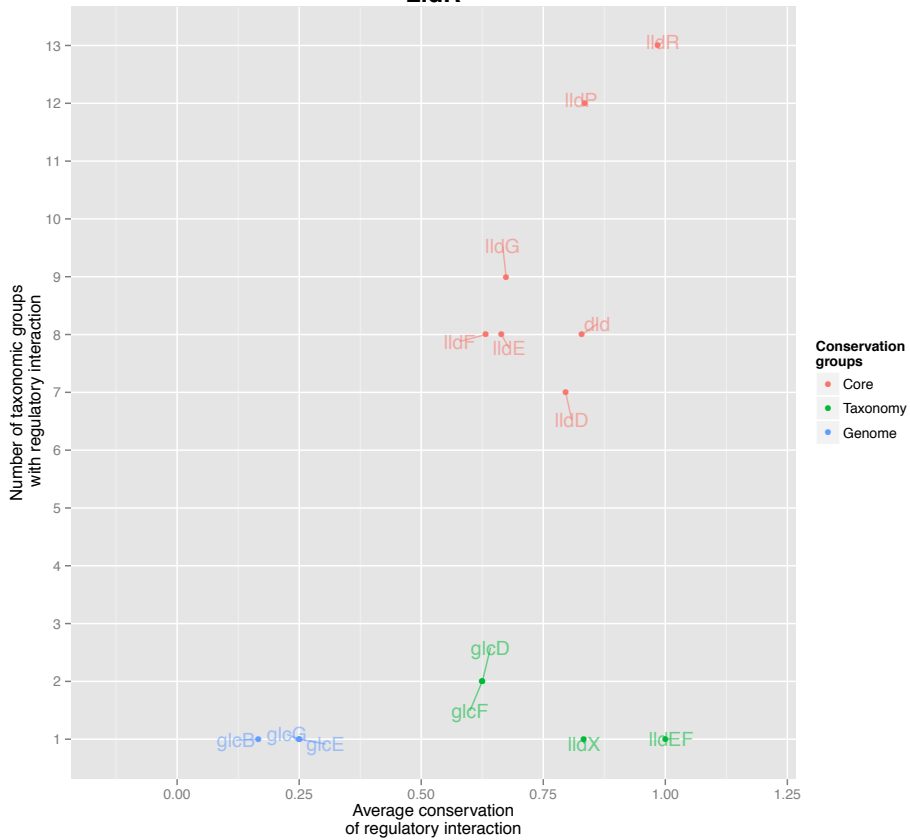
### HypR



### LiuR

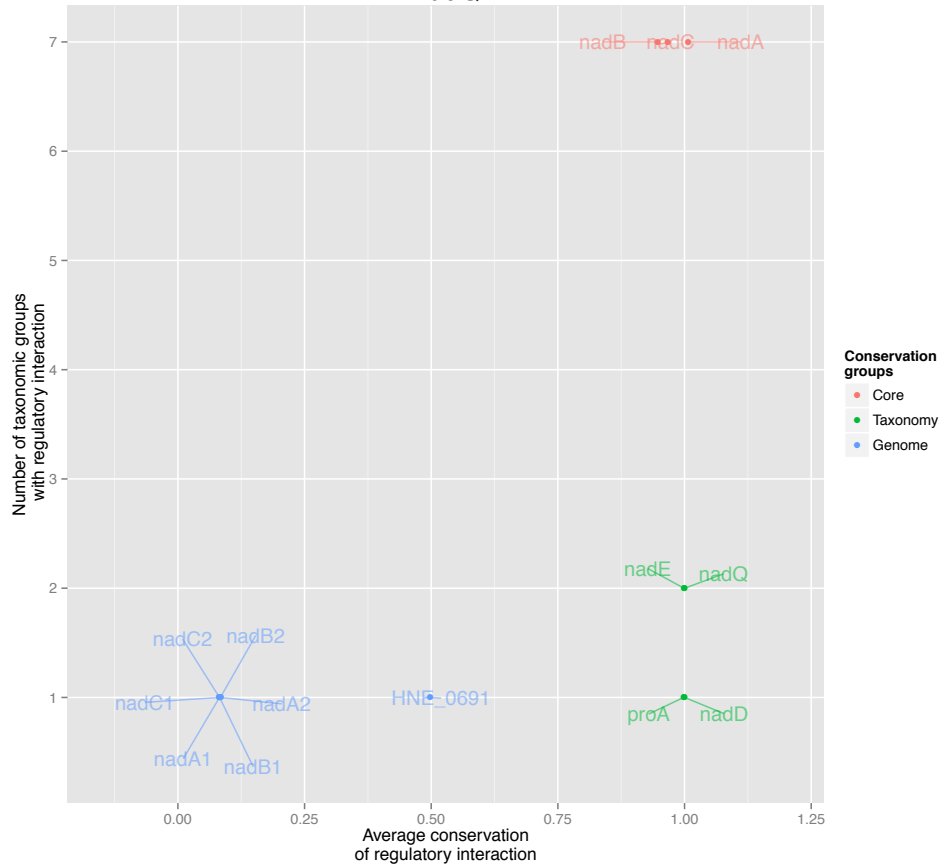


### LidR

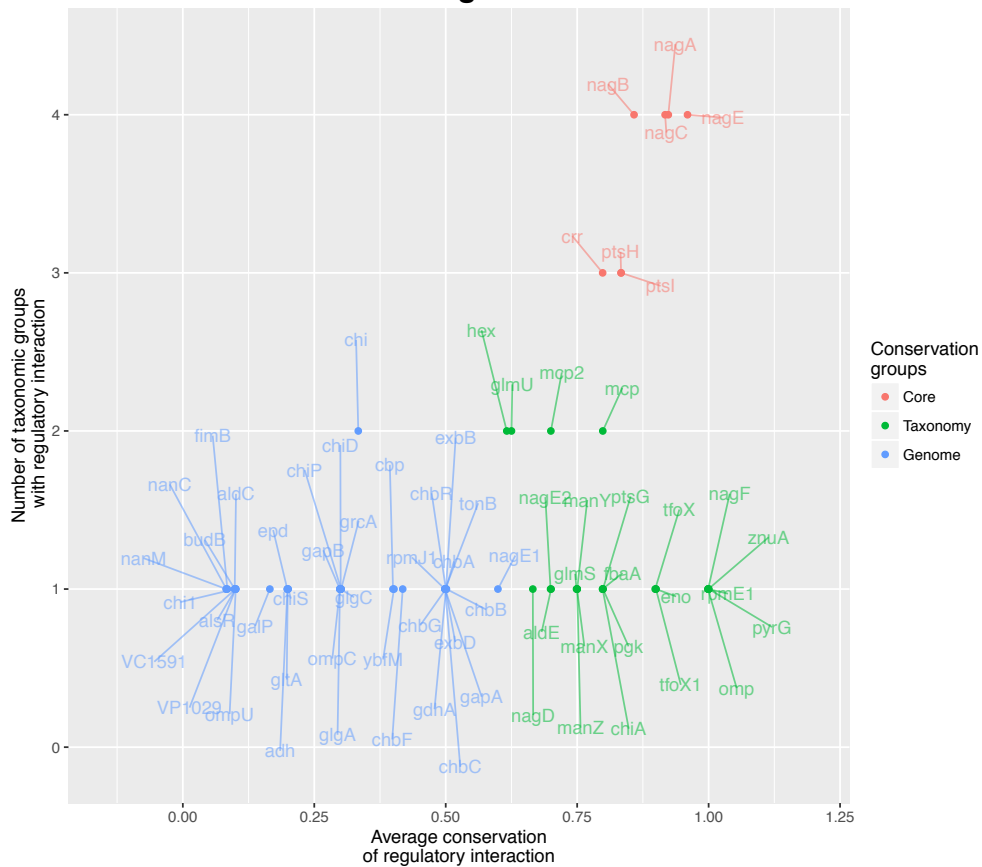




### NadQ

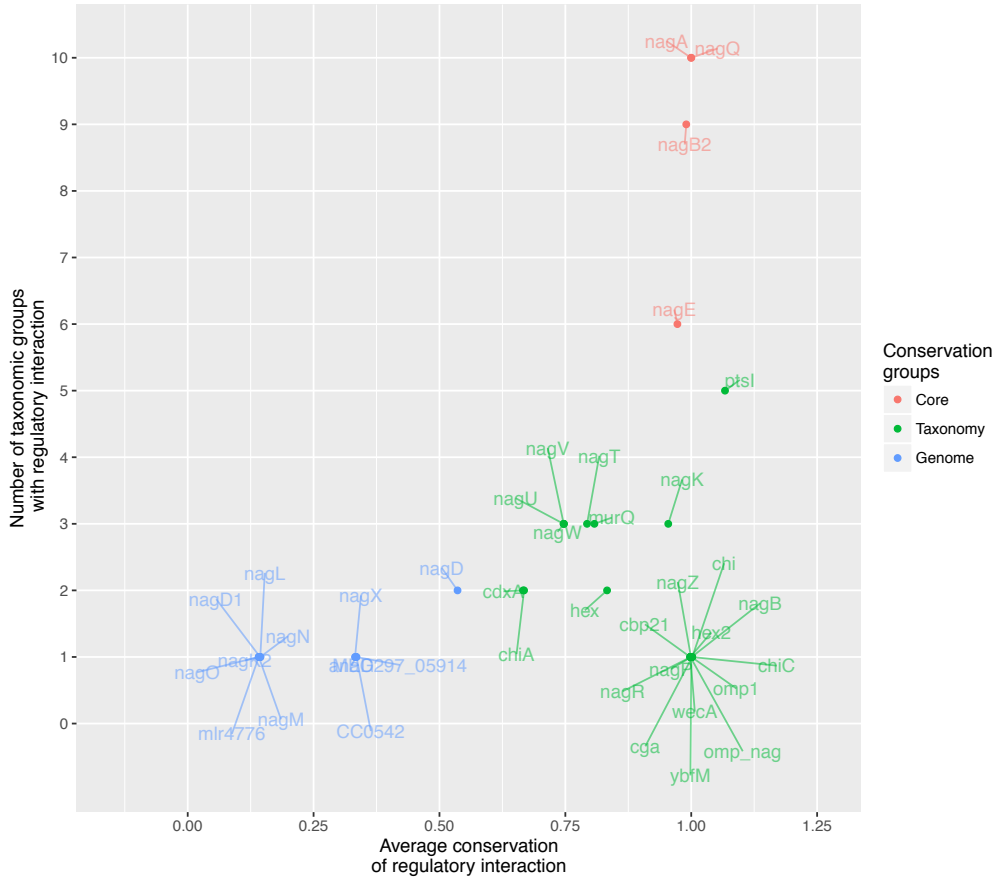


### NagC

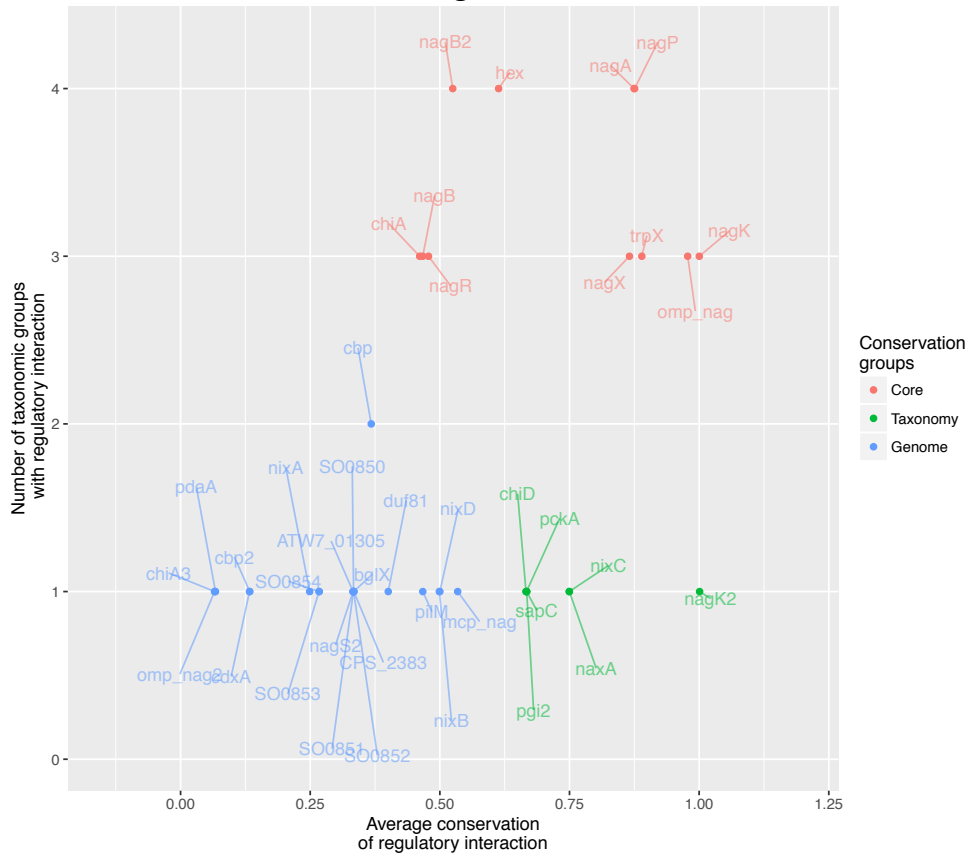




## NagQ



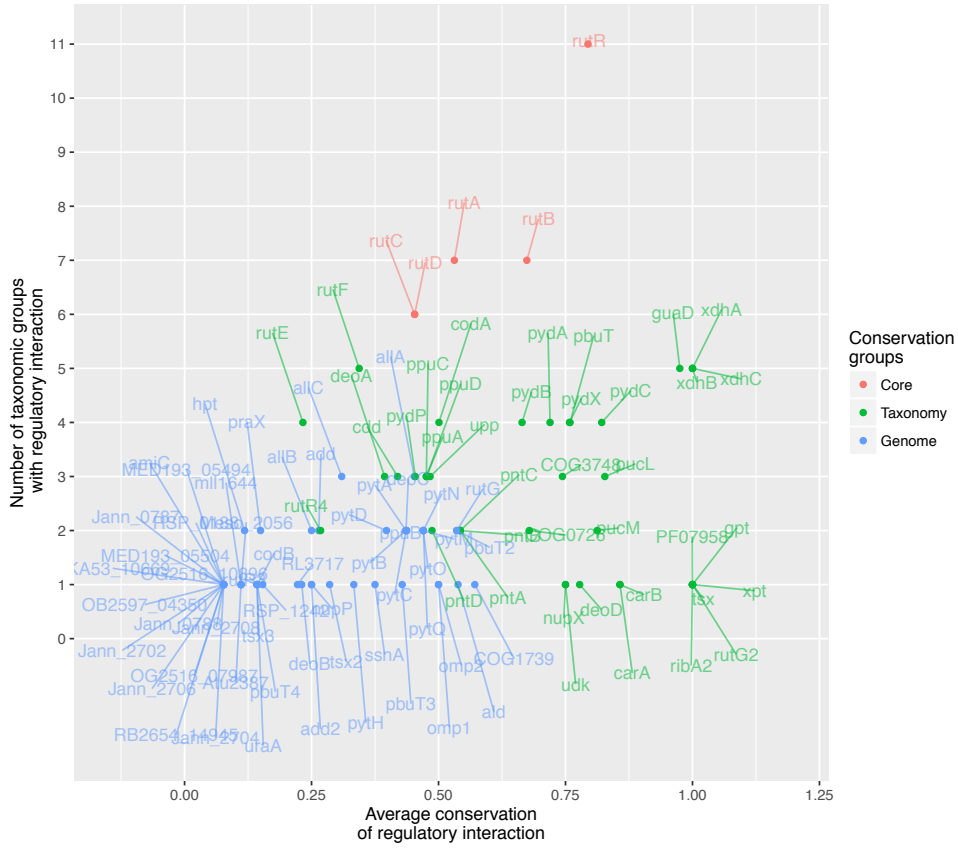
## NagR



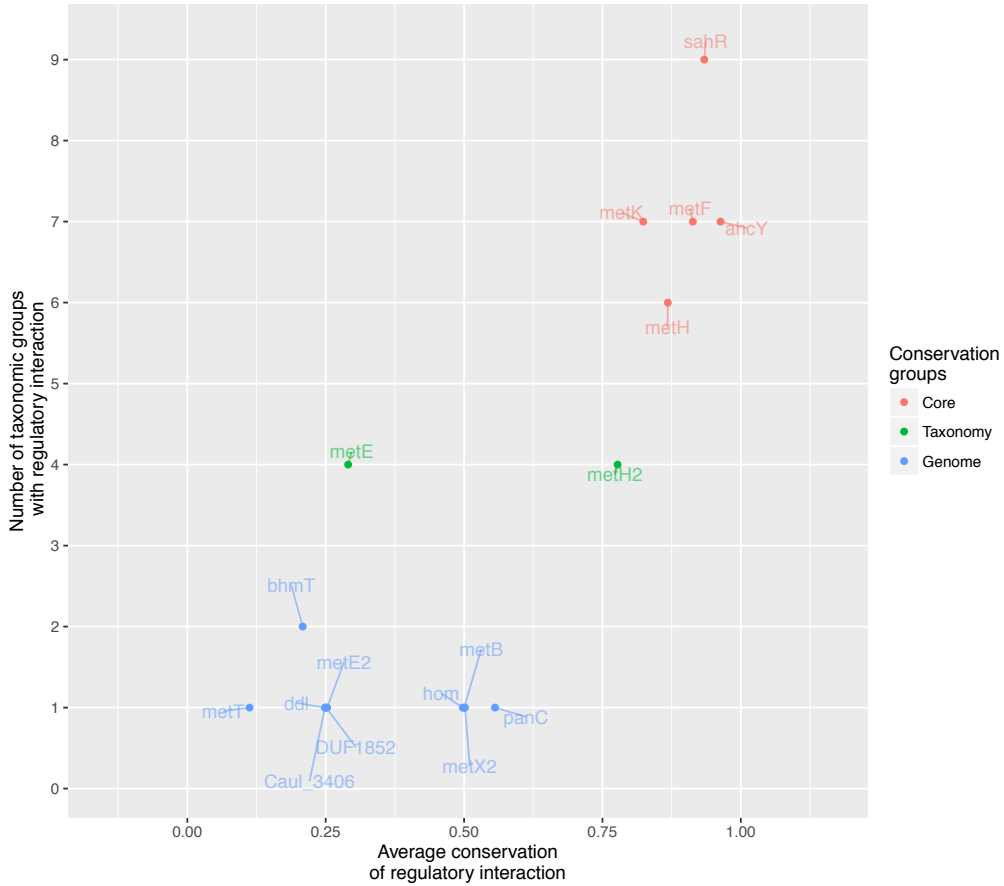




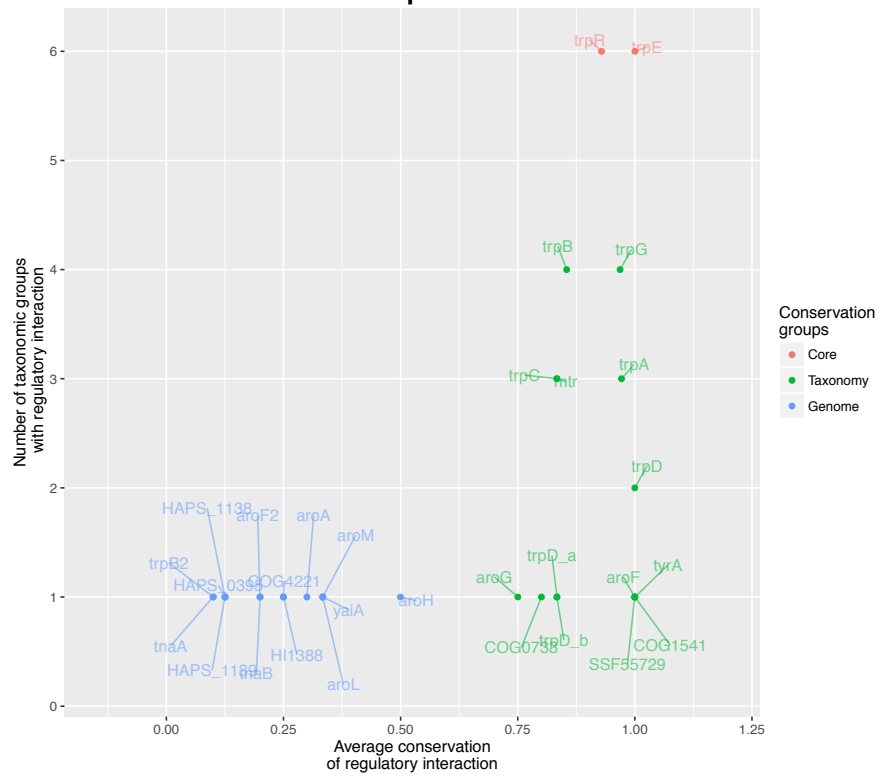
### RutR



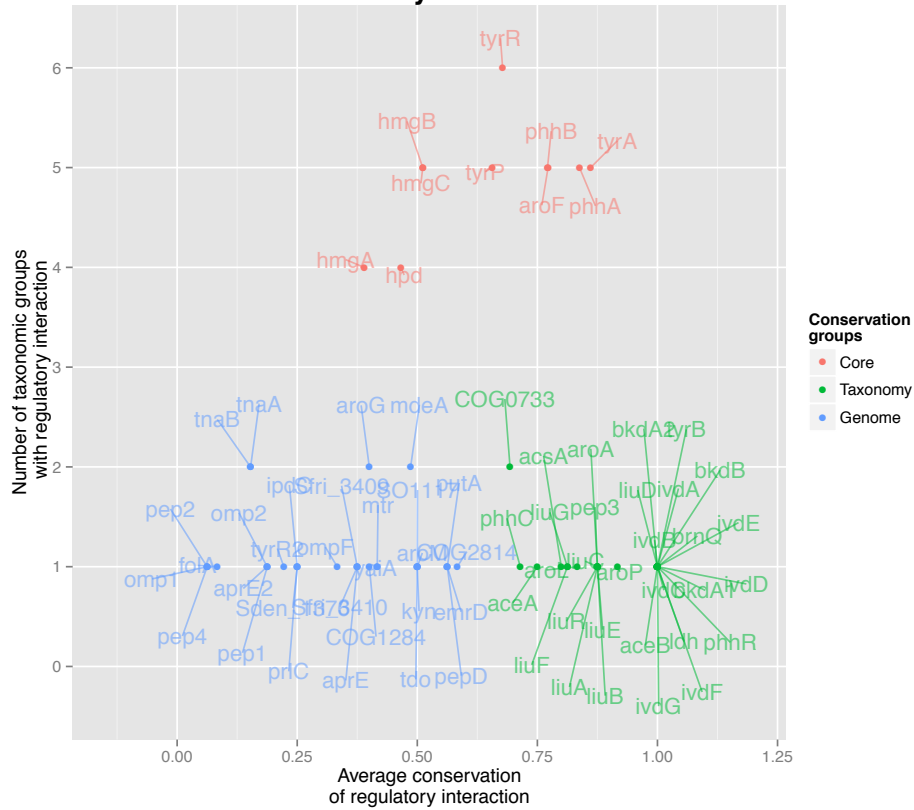
### SahR



### TrpR



### TyrR



**Table S1. Studied genomes and taxonomic groups of Proteobacteria.**

Tax ID	Phylum / Class / Taxonomic collection <sup>1</sup> / Genome	Number of genomes
<b>Phylum</b>	<b>Proteobacteria</b>	<b>196</b>
<b>Class</b>	<b>Gammaproteobacteria</b>	<b>90</b>
	<b>Enterobacteriales</b>	<b>12</b>
511145	Escherichia coli str. K-12 substr. MG1655	
99287	Salmonella typhimurium LT2	
290338	Citrobacter koseri ATCC BAA-895	
272620	Klebsiella pneumoniae subsp. pneumoniae MGH 78578	
399742	Enterobacter sp. 638	
716540	Erwinia amylovora ATCC 49946	
187410	Erwinia amylovora ATCC 49946	
399741	Serratia proteamaculans 568	
218491	Erwinia carotovora subsp. atroseptica SCRI1043	
498217	Edwardsiella tarda EIB202	
529507	Proteus mirabilis HI4320	
243265	Photorhabdus luminescens subsp. laumondii TTO1	
	<b>Pasteurellales</b>	<b>9</b>
71421	Haemophilus influenzae Rd KW20	
634176	Aggregatibacter aphrophilus NJ8700	
272843	Pasteurella multocida subsp. multocida str. Pm70	
221988	Mannheimia succiniciproducens MBEL55E	
339671	Actinobacillus succinogenes 130Z	
228400	Haemophilus somnus 2336	
537457	Actinobacillus pleuropneumoniae serovar 7 str. AP76	
233412	Haemophilus ducreyi 35000HP	
557723	Haemophilus parasuis SH0165	
	<b>Vibrionales</b>	<b>10</b>
243277	Vibrio cholerae O1 biovar eltor str. N16961	
216895	Vibrio vulnificus CMCP6	
338187	Vibrio harveyi ATCC BAA-1116	
223926	Vibrio parahaemolyticus RIMD 2210633	
391591	Vibrio shilonii AK1	
575788	Vibrio splendidus LGP32	
312309	Vibrio fischeri ES114	
316275	Vibrio salmonicida LFI1238	
314292	Vibrio angustum S14	
298386	Photobacterium profundum SS9	
	<b>Psychromonadaceae/Aeromonadales</b>	<b>6</b>
357804	Psychromonas ingrahamii 37	
314282	Psychromonas sp. CNPT3	
58051	Moritella sp. PE36	
380703	Aeromonas hydrophila subsp. hydrophila ATCC 7966	
382245	Aeromonas salmonicida subsp. salmonicida A449	
595494	Tolumonas auensis DSM 9187	
	<b>Shewanellaceae</b>	<b>16</b>
211586	Shewanella oneidensis MR-1	
319224	Shewanella putrefaciens CN-32	
351745	Shewanella sp W3-18-1	

94122	Shewanella sp ANA-3	
60480	Shewanella sp MR-4	
60481	Shewanella sp MR-7	
325240	Shewanella baltica OS155	
318161	Shewanella denitrificans OS217	
318167	Shewanella frigidimarina NCIMB 400	
326297	Shewanella amazonensis SB2B	
323850	Shewanella loihica PV-4	
398579	Shewanella pealeana ATCC 700345	
458817	Shewanella halifaxensis HAW-EB4	
225849	Shewanella piezotolerans WP3	
425104	Shewanella sediminis HAW-EB3	
392500	Shewanella woodyi ATCC 51908	
	<b>Alteromonadales</b>	<b>9</b>
342610	Pseudoalteromonas atlantica T6c	
314275	Alteromonas macleodii 'Deep ecotype'	
455436	Glaciecola sp. HTCC2999	
167879	Colwellia psychrerythraea 34H	
156578	Alteromonadales bacterium TW-7	
326442	Pseudoalteromonas haloplanktis TAC125	
87626	Pseudoalteromonas tunicata D2	
314276	Idiomarina baltica OS145	
283942	Idiomarina loihiensis L2TR	
	<b>Oceanospirillales/Alteromonadales</b>	<b>12</b>
349521	Hahella chejuensis KCTC 2396	
351348	Marinobacter aqueolei	
270374	Marinobacter sp. ELB17	
207949	Oceanobacter sp. RED65	
207954	Oceanospirillum sp. MED92	
400668	Marinomonas sp. MWYL1	
203122	Saccharophagus degradans 2-40	
377629	Teredinibacter turnerae T7901	
498211	Cellvibrio japonicus Ueda107	
290398	Chromohalobacter salexigens DSM 3043	
314283	Reinekea sp. MED297	
393595	Alcanivorax borkumensis SK2	
	<b>Pseudomonadaceae</b>	<b>8</b>
208964	Pseudomonas aeruginosa PAO1	
384676	Pseudomonas entomophila L48	
160488	Pseudomonas putida KT2440	
223283	Pseudomonas syringae pv. tomato str. DC3000	
220664	Pseudomonas fluorescens Pf-5	
399739	Pseudomonas mendocina ymp	
379731	Pseudomonas stutzeri A1501	
322710	Azotobacter vinelandii AvOP	
	<b>Moraxellaceae</b>	<b>4</b>
62977	Acinetobacter sp. ADP1	
480119	Acinetobacter baumannii AB0057	
259536	Psychrobacter arcticum 273-4	
349106	Psychrobacter sp. PRwf-1	
	<b>Xanthomonadales</b>	

160492	Xylella fastidiosa 9a5c	
190486	Xanthomonas axonopodis pv. citri str. 306	
190485	Xanthomonas campestris pv. campestris str. ATCC 33913	
522373	Stenotrophomonas maltophilia K279a	
<b>Class</b>	<b>Betaproteobacteria</b>	<b>37</b>
	<b>Ralstonia</b>	<b>6</b>
381666	Ralstonia eutropha H16	
164546	Cupriavidus taiwanensis	
266264	Ralstonia metallidurans CH34	
264198	Ralstonia eutropha JMP134	
267608	Ralstonia solanacearum GMI1000	
402626	Ralstonia pickettii 12J	
	<b>Burkholderia</b>	<b>8</b>
272560	Burkholderia pseudomallei K96243	
243160	Burkholderia mallei ATCC 23344	
269483	Burkholderia sp. 383	
339670	Burkholderia cepacia AMMD (Burkholderia ambifaria AMMD)	
269482	Burkholderia vietnamiensis G4	
626418	Burkholderia glumae BGR1	
266265	Burkholderia xenovorans LB400	
391038	Burkholderia phymatum STM815	
	<b>Comamonadaceae</b>	<b>11</b>
397945	Acidovorax avenae subsp. citrulli AAC00-1	
232721	Acidovorax sp. JS42	
399795	Comamonas testosteroni KF-1	
398578	Delftia acidovorans SPH-1	
365044	Polaromonas naphthalenivorans CJ2	
296591	Polaromonas sp. JS666	
338969	Rhodoferrax ferrireducens DSM 15236	
543728	Variovorax paradoxus S110	
391735	Verminephrobacter eiseniae EF01-2	
420662	Methylbium petroleiphilum PM1	
395495	Leptothrix cholodnii SP-6	
	<b>Various betaproteobacteria</b>	<b>12</b>
76114	Azoarcus sp. EbN1	
85643	Thauera sp. MZ1T	
159087	Dechloromonas aromatica RCB	
228410	Nitrosomonas europaea ATCC 19718	
323848	Nitrospira multiformis ATCC 25196	
292415	Thiobacillus denitrificans	
243365	Chromobacterium violaceum ATCC 12472	
122586	Neisseria meningitidis MC58	
557598	Laribacter hongkongensis HLHK9	
265072	Methylobacillus flagellatus KT	
583345	Methylotenera mobilis JLW8	
383631	Methylophilales bacterium HTCC2181	
<b>Class</b>	<b>Alphaproteobacteria</b>	<b>50</b>
	<b>Rhizobiales</b>	<b>15</b>
266834	Sinorhizobium meliloti 1021	
394	Rhizobium sp. NGR234	
216596	Rhizobium leguminosarum bv. viciae 3841 from www.microbiologyresearch.org by	



347834	Rhizobium etli CFN 42	
176299	Agrobacterium tumefaciens str. C58 (Cereon)	
266779	Mesorhizobium sp. BNC1	
266835	Mesorhizobium loti MAFF303099	
224914	Brucella melitensis 16M	
283165	Bartonella quintana str. Toulouse	
258594	Rhodopseudomonas palustris CGA009	
224911	Bradyrhizobium japonicum USDA 110	
288000	Bradyrhizobium sp. BTAi1	
323098	Nitrobacter winogradskyi Nb-255	
438753	Azorhizobium caulinodans ORS 571	
78245	Xanthobacter autotrophicus Py2	
	<b>Rhodobacterales</b>	<b>15</b>
272943	Rhodobacter sphaeroides 2.4.1	
318586	Paracoccus denitrificans PD1222	
290400	Jannaschia sp. CCS1	
314271	Rhodobacterales bacterium HTCC2654	
314256	Oceanicola granulosus HTCC2516	
314232	Loktanella vestfoldensis SKA53	
252305	Oceanicola batsensis HTCC2597	
89187	Roseovarius nubinhibens ISM	
314264	Roseovarius sp. 217	
52598	Sulfitobacter sp. EE-36	
292414	Silicibacter TM1040	
246200	Silicibacter pomeroyi DSS-3	
314262	Roseobacter sp. MED193	
228405	Hyphomonas neptunium ATCC 15444	
314254	Oceanicaulis alexandrii HTCC2633	
	<b>Rhodospirillales</b>	<b>9</b>
269796	Rhodospirillum rubrum ATCC 11170	
342108	Magnetospirillum magneticum AMB-1	
272627	Magnetospirillum magnetotacticum MS-1	
137722	Azospirillum sp. B510	
414684	Rhodospirillum centenum SW	
272568	Gluconacetobacter diazotrophicus PAI 5	
634452	Acetobacter pasteurianus IFO 3283-01	
290633	Gluconobacter oxydans 621H	
391165	Granulibacter bethesdensis CGDNIH1	
	<b>Sphingomonadales</b>	<b>7</b>
314225	Erythrobacter litoralis HTCC2594	
237727	Erythrobacter sp. NAP1	
279238	Novosphingobium aromaticivorans DSM 12444	
317655	Sphingopyxis alaskensis RB2256	
452662	Sphingobium japonicum UT26S	
392499	Sphingomonas wittichii RW1	
264203	Zymomonas mobilis subsp. mobilis ZM4	
	<b>Caulobacterales</b>	<b>4</b>
190650	Caulobacter crescentus CB15	
509190	Caulobacter segnis ATCC 21756	
366602	Caulobacter sp. K31	
450851	Phenylobacterium zucineum HLK1	

<b>Class</b>	<b>Proteobacteria/Delta</b>	<b>19</b>
	<b>Desulfovibrionales</b>	<b>10</b>
882	Desulfovibrio vulgaris Hildenborough	
883	Desulfovibrio vulgaris str. Miyazaki F	
207559	Desulfovibrio desulfuricans G20	
525146	Desulfovibrio desulfuricans subsp. desulfuricans str. ATCC 27774	
411464	Desulfovibrio piger ATCC 29098	
526222	Desulfovibrio salexigens DSM 2638	
573370	Desulfovibrio magneticus RS-1	
363253	Lawsonia intracellularis PHE/MN1-00	
525897	Desulfomicrobium baculatum DSM 4028	
485915	Desulfohalobium retbaense DSM 5692	
	<b>Desulfuromonadales</b>	<b>9</b>
269799	Geobacter metallireducens GS-15	
243231	Geobacter sulfurreducens PCA	
351605	Geobacter uraniumreducens Rf4	
316067	Geobacter sp. FRC-32	
443144	Geobacter sp. M21	
398767	Geobacter lovleyi SZ	
338966	Pelobacter propionicus DSM 2379	
338963	Pelobacter carbinolicus str. DSM 2380	
281689	Desulfuromonas acetoxidans DSM 684	

<sup>1</sup> Taxonomic collections are according to the standardized genomic collections in the RegPrecise database.

**Table S2. Examples of experimentally studied TFs analyzed in this work.**

TF	Genome	Reference
ArgR	<i>Escherichia coli</i>	(Tian et al., 1992;Caldara et al., 2007;Paul et al., 2007;Cho et al., 2015)
	<i>Salmonella typhimurium</i>	(Lu and Abdelal, 1999)
BioR	<i>Brucella melitensis</i>	(Feng et al., 2013)
	<i>Paracoccus denitrificans</i>	(Feng et al., 2015)
BirA	<i>Escherichia coli</i>	(Bower et al., 1995;Xu et al., 1995)
FabR	<i>Escherichia coli</i>	(Zhang et al., 2002;Fujita et al., 2007)
FadR	<i>Escherichia coli</i>	(DiRusso et al., 1992;Fujita et al., 2007)
GlcC	<i>Escherichia coli</i>	(Pellicer et al., 1999)
HexR	<i>Shewanella oneidensis</i>	(Leyn et al., 2011)
	<i>Pseudomonas putida</i>	(del Castillo et al., 2008;Daddaoua et al., 2009)
HmgR	<i>Pseudomonas putida</i>	(Arias-Barrau et al., 2004)
HutC	<i>Salmonella typhimurium</i>	(Hagen et al., 1975)
HypR	<i>Sinorhizobium meliloti</i>	(White et al., 2012)
LldR	<i>Pseudomonas aeruginosa</i>	(Gao et al., 2012)
	<i>Escherichia coli</i>	(Aguilera et al., 2008)
MetJ	<i>Escherichia coli</i>	(Merlin et al., 2002)
MetR	<i>Escherichia coli</i>	(Cai et al., 1989)
	<i>Vibrio cholerae</i>	(Bogard et al., 2012)
NadR	<i>Salmonella typhimurium</i>	(Foster et al., 1990)
NagC	<i>Escherichia coli</i>	(Plumbridge, 1995; 2001)
NagQ	<i>Xanthomonas campestris</i>	(Boulanger et al., 2010)
NagR	<i>Xanthomonas campestris</i>	(Boulanger et al., 2010)
	<i>Shewanella oneidensis</i>	(Rodionov et al., 2011)
NrdR	<i>Escherichia coli</i>	(Torrents et al., 2007)
	<i>Salmonella typhimurium</i>	(Panosa et al., 2010)
	<i>Pseudomonas aeruginosa</i>	(Crespo et al., 2015)
NrtR	<i>Shewanella oneidensis</i>	(Rodionov et al., 2008)
NtrC	<i>Escherichia coli</i>	(Muse and Bender, 1998;Zimmer et al., 2000)
PdhR	<i>Escherichia coli</i>	(Quail and Guest, 1995;Ogasawara et al., 2007)
PsrA	<i>Pseudomonas putida</i>	(Kojic et al., 2002;Fonseca et al., 2014)
	<i>Pseudomonas aeruginosa</i>	(Kang et al., 2009)
RutR	<i>Escherichia coli</i>	(Shimada et al., 2007;Nguyen Ple et al., 2010;Nguyen Le Minh et al., 2015)
SahR	<i>Desulfovibrio alaskensis</i>	(Novichkov et al., 2014)
TrpR	<i>Escherichia coli</i>	(Czernik et al., 1994;Jeeves et al., 1999)
TyrR	<i>Escherichia coli</i>	(Camakaris and Pittard, 1982;Yang et al., 2002), (Yang et al., 2004;Pittard et al., 2005)
TyrR	<i>Enterobacter cloacae</i>	(Coulson and Patten, 2015)
TyrR	<i>Citrobacter freundii</i>	(Smith and Somerville, 1997)
PhhR	<i>Pseudomonas aeruginosa</i>	(Palmer et al., 2010)
PhhR	<i>Pseudomonas putida</i>	(Herrera et al., 2009;Herrera et al., 2010)

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**Table S3. Reconstructed regulatory interactions and functional annotations for the analyzed TF regulons of Proteobacteria.**

Regulon	Target gene	RI <sup>1</sup>	Taxa <sup>2</sup>	Functional role	Metabolic pathway / Biological process
ArgR	argH	57	6	Argininosuccinate lyase (EC 4.3.2.1)	Arginine biosynthesis
ArgR	argB	54	6	Acetylglutamate kinase (EC 2.7.2.8)	Arginine biosynthesis
ArgR	argC	53	6	N-acetyl-gamma-glutamyl-phosphate reductase (EC 1.2.1.38)	Arginine biosynthesis
ArgR	argG	52	5	Argininosuccinate synthase (EC 6.3.4.5)	Arginine biosynthesis
ArgR	argF	52	5	Ornithine carbamoyltransferase (EC 2.1.3.3)	Arginine biosynthesis
ArgR	argA	51	6	N-acetylglutamate synthase (EC 2.3.1.1)	Arginine biosynthesis
ArgR	argR	48	5	Arginine biosynthesis transcription regulator ArgR, ArgR family	Arginine biosynthesis
ArgR	argE	42	6	Acetylornithine deacetylase (EC 3.5.1.16)	Arginine biosynthesis
ArgR	artI	41	5	Arginine ABC transporter, substrate-binding protein	Arginine transport
ArgR	artQ	39	5	Arginine ABC transporter, permease protein 1	Arginine transport
ArgR	artM	39	5	Arginine ABC transporter, permease protein 2	Arginine transport
ArgR	astD	37	4	Succinylglutamic semialdehyde dehydrogenase (EC 1.2.1.71)	Arginine degradation
ArgR	astA	37	4	Arginine N-succinyltransferase (EC 2.3.1.109)	Arginine degradation
ArgR	astC	31	3	Acetylornithine aminotransferase (EC 2.6.1.11) / N-succinyl-L,L-diaminopimelate aminotransferase (EC 2.6.1.17) / Succinylornithine transaminase (EC 2.6.1.81)	Arginine degradation
ArgR	astB	21	2	Succinylarginine dihydrolase (EC 3.5.3.23)	Arginine degradation
ArgR	artP	28	4	Arginine ABC transporter, ATP-binding protein	Arginine transport
ArgR	carA	25	4	Carbamoyl-phosphate synthase small chain (EC 6.3.5.5)	Arginine and pyrimidine biosynthesis
ArgR	carB	24	4	Carbamoyl-phosphate synthase large chain (EC 6.3.5.5)	Arginine and pyrimidine biosynthesis
ArgR	argD	22	3	Acetylornithine aminotransferase (EC 2.6.1.11)	Arginine biosynthesis
ArgR	gltB	34	3	Glutamate synthase [NADPH] large chain (EC 1.4.1.13)	Glutamate biosynthesis
ArgR	gltD	33	3	Glutamate synthase [NADPH] small chain (EC 1.4.1.13)	Glutamate biosynthesis
ArgR	argW	17	2	Predicted arginine uptake transporter, COG3314 family	Arginine transport
ArgR	SO0620	15	1	Conserved hypothetical protein	
ArgR	ilvM	14	1	Acetolactate synthase small subunit (EC 2.2.1.6)	Branched-chain amino acid biosynthesis
ArgR	SO3392	14	1	NADH-dependent flavin oxidoreductase, Oye family	
ArgR	ilvG	14	1	Acetolactate synthase large subunit (EC 2.2.1.6)	Branched-chain amino acid biosynthesis
ArgR	ilvD	14	1	Dihydroxy-acid dehydratase (EC 4.2.1.9)	Branched-chain amino acid biosynthesis
ArgR	ilvA	14	1	Threonine dehydratase biosynthetic (EC 4.3.1.19)	Branched-chain amino acid biosynthesis
ArgR	artJ	10	1	arginine ABC transporter, substrate-binding protein	Arginine transport
ArgR	yfcH	7	1	Conserved hypothetical protein	
ArgR	omp	14	1	TonB-dependent outer membrane transporter	Arginine transport ?
ArgR	oadA	12	1	Oxaloacetate decarboxylase, alpha chain (EC 4.1.1.3)	Pyruvate metabolism
ArgR	oadB	12	1	Oxaloacetate decarboxylase, beta chain (EC 4.1.1.3)	Pyruvate metabolism
ArgR	oadG	12	1	Oxaloacetate decarboxylase gamma chain (EC 4.1.1.3)	Pyruvate metabolism
ArgR	potF	12	1	Putrescine ABC transporter, substrate-binding protein (TC 3.A.1.11.2)	Putrescine transport
ArgR	potG	12	1	Putrescine ABC transporter, ATP-binding protein (TC 3.A.1.11.2)	Putrescine transport
ArgR	potH	12	1	Putrescine ABC transporter, permease protein 1 (TC 3.A.1.11.2)	Putrescine transport
ArgR	potI	12	1	Putrescine ABC transporter, permease protein 2 (TC 3.A.1.11.2)	Putrescine transport
ArgR	recN	12	1	DNA repair protein RecN	DNA repair
ArgR	aprE	11	1	Alkaline serine protease	
ArgR	SO0762	10	1	Isochorismate hydrolase (EC 3.3.2.1)	
ArgR	astE	7	2	succinylglutamate desuccinylase	Arginine degradation
ArgR	SO2753	9	1	Prolyl endopeptidase (EC 3.4.21.26)	
ArgR	arcA	5	1	Arginine deiminase (EC 3.5.3.6)	Arginine degradation
ArgR	arcB	1	1	Ornithine carbamoyltransferase (EC 2.1.3.3), catabolic	Arginine degradation
ArgR	arcC	1	1	Carbamate kinase (EC 2.7.2.2)	Arginine degradation

ArgR	arcD	1	1	Arginine/ornithine antiporter	Arginine degradation
ArgR	hisJ	6	1	histidine ABC transporter, substrate-binding protein	Histidine transport
ArgR	hisM	6	1	histidine ABC transporter, inner membrane permease	Histidine transport
ArgR	hisP	6	1	histidine ABC transporter, ATP-binding protein	Histidine transport
ArgR	hisQ	6	1	histidine ABC transporter, permease protein	Histidine transport
ArgR	potE	8	1	Putrescine/ornithine antiporter	Putrescine transport
ArgR	proV	3	1	Glycine betaine/L-proline ABC transporter, ATP-binding protein	Proline transport
ArgR	proW	3	1	Glycine betaine/L-proline ABC transporter, permease protein	Proline transport
ArgR	proX	3	1	Glycine betaine/L-proline ABC transporter, substrate-binding protein	Proline transport
ArgR	SO0312	8	1	Predicted outer membrane porin	
ArgR	ggt2	7	1	Gamma-glutamyltranspeptidase (EC 2.3.2.2)	Glutathione metabolism
ArgR	SO4732	7	1	Conserved hypothetical protein	
ArgR	mcp	6	1	Methyl-accepting chemotaxis protein	
ArgR	aprE2	5	1	Cold-active alkaline serine protease (EC 3.4.21.62)	
ArgR	ilvE	5	1	Branched-chain amino acid aminotransferase (EC 2.6.1.42)	Branched-chain amino acid biosynthesis
ArgR	ECA3537	3	1	amino acid-binding protein	
ArgR	ECA3538	3	1	polar amino acid ABC transporter, inner membrane subunit	
ArgR	ECA3539	3	1	amino acid ABC transporter, ATP-binding protein	
ArgR	hisA	4	1	Phosphoribosylformimino-5-aminoimidazole carboxamide ribotide isomerase (EC 5.3.1.16)	Histidine biosynthesis
ArgR	hisB	4	1	Histidinol-phosphatase (EC 3.1.3.15) / Imidazoleglycerol-phosphate dehydratase (EC 4.2.1.19)	Histidine biosynthesis
ArgR	hisC	4	1	Histidinol-phosphate aminotransferase (EC 2.6.1.9)	Histidine biosynthesis
ArgR	hisD	4	1	Histidinol dehydrogenase (EC 1.1.1.23)	Histidine biosynthesis
ArgR	hisF	4	1	Imidazole glycerol phosphate synthase cyclase subunit (EC 4.1.3.-)	Histidine biosynthesis
ArgR	hisG	4	1	ATP phosphoribosyltransferase (EC 2.4.2.17)	Histidine biosynthesis
ArgR	hisH	4	1	Imidazole glycerol phosphate synthase amidotransferase subunit (EC 2.4.2.-)	Histidine biosynthesis
ArgR	hisI	4	1	Phosphoribosyl-AMP cyclohydrolase (EC 3.5.4.19) / Phosphoribosyl-ATP pyrophosphatase (EC 3.6.1.31)	Histidine biosynthesis
ArgR	pbpG	4	1	D-alanyl-D-alanine endopeptidase	
ArgR	Swoo_0949	4	1	Peptidase U32	
ArgR	ybgH	3	1	amino acid/peptide transporter	
ArgR	SO1443	3	1	Conserved hypothetical protein	
ArgR	SO1915	3	1	Serine protease, subtilase family	
ArgR	SO2306	3	1	Cell division protein FtsK	
ArgR	marC	1	1	Membrane protein, MarC family	
ArgR	speF	1	1	Ornithine decarboxylase (EC 4.1.1.17)	Putrescine metabolism
BioR	bioB	12	2	Biotin synthase (EC 2.8.1.6)	Biotin biosynthesis
BioR	bioR	10	2	Biotin metabolism regulatory protein BioR, GntR family	Transcription regulation
BioR	bioY	8	2	Substrate-specific component BioY of biotin ECF transporter	Biotin transport
BioR	bioF	7	2	8-amino-7-oxononanoate synthase (EC 2.3.1.47)	Biotin biosynthesis
BioR	bioD	7	2	Dethiobiotin synthetase (EC 6.3.3.3)	Biotin biosynthesis
BioR	bioA	7	2	Adenosylmethionine-8-amino-7-oxononanoate aminotransferase (EC 2.6.1.62)	Biotin biosynthesis
BioR	bioZ	3	1	Biotin synthesis protein bioZ	Biotin biosynthesis
BioR	bioM	1	1	ATPase component BioM of energizing module of biotin ECF transporter	Biotin transport
BioR	bioG	1	1	Biotin synthesis protein bioG	Biotin biosynthesis
BioR	bioN	1	1	Transmembrane component BioN of energizing module of biotin ECF transporter	Biotin transport
BioR	bioC	1	1	Biotin synthesis protein bioC	Biotin biosynthesis
BioR	panD	1	1	aspartate alpha-decarboxylase	Pantothenate biosynthesis
BirA	bioB	93	11	Biotin synthase (EC 2.8.1.6)	Biotin biosynthesis
BirA	bioF	86	11	8-amino-7-oxononanoate synthase (EC 2.3.1.47)	Biotin biosynthesis



<b>BirA</b>	bioD	83	10	Dethiobiotin synthetase (EC 6.3.3.3)	Biotin biosynthesis
<b>BirA</b>	bioC	84	10	Biotin synthesis protein bioC	Biotin biosynthesis
<b>BirA</b>	bioA	65	8	Adenosylmethionine-8-amino-7-oxononanoate aminotransferase (EC 2.6.1.62)	Biotin biosynthesis
<b>BirA</b>	bioH	33	5	Biotin synthesis protein bioH	Biotin biosynthesis
<b>BirA</b>	COG1040	23	4	competence protein F	
<b>BirA</b>	fabF	3	1	3-oxoacyl-[acyl-carrier-protein] synthase, KASII (EC 2.3.1.41)	Fatty acid biosynthesis
<b>BirA</b>	birA	3	1	Biotin-protein ligase (EC 6.3.4.15) / Biotin operon repressor	Transcription regulation
<b>BirA</b>	fabG	3	1	3-oxoacyl-[acyl-carrier protein] reductase (EC 1.1.1.100)	Fatty acid biosynthesis
<b>BirA</b>	DVU2560	3	1	conserved domain protein	
<b>BirA</b>	acpP	3	1	acyl carrier protein, putative	
<b>BirA</b>	Dde_2651	2	1	hypothetical thioesterase domain protein	
<b>BirA</b>	XAC0384	2	1	putative short chain dehydrogenase	
<b>BirA</b>	XAC0386	2	1	hypothetical protein	
<b>BirA</b>	bioHC	3	1	Biotin synthesis protein BioH / Biotin synthesis protein BioC	Biotin biosynthesis
<b>BirA</b>	yigM	3	1	Predicted biotin transporter YigM	Biotin transport
<b>BirA</b>	CV3478	1	1	Phosphatidylethanolamine N-methyltransferase (EC 2.1.1.17)	Phosphatidylcholine biosynthesis
<b>BirA</b>	bioW	1	1	Pimeloyl-CoA synthase (EC 6.2.1.14)	Biotin biosynthesis
<b>FabR</b>	fabA	62	8	3-hydroxydecanoyl-[acyl-carrier-protein] dehydratase (EC 4.2.1.60)	Fatty acid biosynthesis
<b>FabR</b>	hylI	30	6	COG1272: Predicted membrane protein hemolysin III homolog	Fatty acid metabolism
<b>FabR</b>	OLE1	38	5	Fatty acid desaturase (EC 1.14.19.1)	Unsaturated fatty acid biosynthesis
<b>FabR</b>	plsC	30	6	1-acyl-sn-glycerol-3-phosphate acyltransferase (EC 2.3.1.51)	Glycerolipid metabolism
<b>FabR</b>	desB	13	6	Acyl-CoA delta-9-desaturase, DesB	Unsaturated fatty acid biosynthesis
<b>FabR</b>	desC	13	6	Flavodoxin reductases (ferredoxin-NADPH reductases) family 1	Unsaturated fatty acid biosynthesis
<b>FabR</b>	lcfH	25	5	putative long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid biosynthesis
<b>FabR</b>	fabR	26	3	Unsaturated fatty acid biosynthesis repressor FabR, TetR family	Transcription regulation
<b>FabR</b>	fadL	25	3	Long-chain fatty acid transport protein	Fatty acid biosynthesis
<b>FabR</b>	fabR2	5	2	Unsaturated fatty acid biosynthesis repressor FabR, TetR family	Transcription regulation
<b>FabR</b>	fabB	20	4	3-oxoacyl-[acyl-carrier-protein] synthase, KASI (EC 2.3.1.41)	Fatty acid biosynthesis
<b>FabR</b>	rraB	17	2	Ribonuclease E inhibitor RraB	
<b>FabR</b>	lcfE	16	1	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid biosynthesis
<b>FabR</b>	hylII	17	2	COG1272: Predicted membrane protein hemolysin III homolog	
<b>FabR</b>	Maqu_3149	2	1	AraC family transcriptional regulator	Transcription regulation
<b>FabR</b>	pfaA	7	2	omega-3 polyunsaturated fatty acid synthase subunit, PfaA	Unsaturated fatty acid biosynthesis
<b>FabR</b>	pfaB	7	2	omega-3 polyunsaturated fatty acid synthase subunit, PfaB	Unsaturated fatty acid biosynthesis
<b>FabR</b>	COG2030	6	1	Putative acyl dehydratase, COG2030	
<b>FabR</b>	pfaR	6	1	transcriptional regulator for synthesis of eicosapentaenoic acid, PfaR	Transcription regulation
<b>FabR</b>	pfaC	6	1	omega-3 polyunsaturated fatty acid synthase subunit, PfaC	Unsaturated fatty acid biosynthesis
<b>FabR</b>	desA	1	1	Fatty acid desaturase (EC 1.14.99.-)	Unsaturated fatty acid biosynthesis
<b>FabR</b>	fadE3	5	1	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Fatty acid degradation
<b>FabR</b>	pfaD	4	1	Enoyl-[acyl-carrier-protein] reductase [FMN] (EC 1.3.1.9), inferred for PFA pathway	Fatty acid biosynthesis
<b>FabR</b>	psrA	2	1	Predicted transcriptional regulator for fatty acid degradation PsrA, TetR family	Unsaturated fatty acid biosynthesis
<b>FabR</b>	fadE	1	1	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Fatty acid degradation
<b>FabR</b>	COG2072	3	2	probable flavin-containing monooxygenase, COG2072	
<b>FabR</b>	COG0300	2	1	probable short-chain dehydrogenase, COG0300	
<b>FadP</b>	fadP	24	3	Predicted transcriptional regulator for fatty acid degradation FadP, TetR family	Transcription regulation
<b>FadP</b>	etfA	23	3	Electron transfer flavoprotein alpha subunit	Electron transfer chain for fatty acid degradation
<b>FadP</b>	etfB	23	3	Electron transfer flavoprotein, beta subunit	Electron transfer chain for fatty acid degradation
<b>FadP</b>	acdH	23	3	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>FadP</b>	fadA	22	3	3-ketoacyl-CoA thiolase (EC 2.3.1.16)	Fatty acid degradation

<b>FadP</b>	fadB	22	3	Enoyl-CoA hydratase (EC 4.2.1.17) / Delta(3)-cis-delta(2)-trans-enoyl-CoA isomerase (EC 5.3.3.8) / 3-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.35) / 3-hydroxybutyryl-CoA epimerase (EC 5.1.2.3)	Fatty acid degradation
<b>FadP</b>	acdB	22	3	Enoyl-CoA hydratase (EC 4.2.1.17) / 3,2-trans-enoyl-CoA isomerase (EC 5.3.3.8) / 3-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.35)	Fatty acid degradation
<b>FadP</b>	acdA	22	3	3-ketoacyl-CoA thiolase (EC 2.3.1.16) @ Acetyl-CoA acetyltransferase (EC 2.3.1.9)	Fatty acid degradation
<b>FadP</b>	etfD	21	3	Electron transfer flavoprotein-ubiquinone oxidoreductase (EC 1.5.5.1)	Electron transfer chain for fatty acid degradation
<b>FadP</b>	acdH2	20	3	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>FadP</b>	echH	19	3	Enoyl-CoA hydratase (EC 4.2.1.17)	Fatty acid degradation
<b>FadP</b>	acdP	18	3	acyl-CoA dehydrogenase domain protein	Fatty acid degradation
<b>FadP</b>	acdQ	18	3	Acyl-CoA dehydrogenase (EC 1.3.99.-)	Fatty acid degradation
<b>FadP</b>	fadD1	13	2	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid degradation
<b>FadP</b>	maoC	13	2	Putative (R)-specific enoyl-CoA hydratase, MaoC- like	
<b>FadP</b>	echI	13	2	MaoC domain protein dehydratase	
<b>FadP</b>	pncA	13	2	Nicotinamidase (EC 3.5.1.19)	Nicotinate biosynthesis
<b>FadP</b>	fadD2	11	2	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid degradation
<b>FadP</b>	nppD	11	2	2-nitropropane dioxygenase NPD	
<b>FadP</b>	acdH3	12	3	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>FadP</b>	paaG4	7	2	Enoyl-CoA hydratase (EC 4.2.1.17)	Fatty acid degradation
<b>FadP</b>	paaH1	7	2	3-hydroxybutyryl-CoA dehydrogenase, phenylacetic acid degradation	Fatty acid degradation
<b>FadP</b>	RSc1638	6	1	hypothetical protein	
<b>FadP</b>	BPSL1235	6	1	Phosphotransferase enzyme family protein	
<b>FadP</b>	bktB	6	1	3-ketoacyl-CoA thiolase (EC 2.3.1.16)	Fatty acid degradation
<b>FadP</b>	alkK	6	1	Medium-chain-fatty-acid-CoA ligase	Fatty acid degradation
<b>FadP</b>	Rsc1773	6	1	putative 4-hydroxybenzoyl-CoA thioesterase	
<b>FadP</b>	RSc1772	6	1	Alpha/beta hydrolase fold-3 domain protein	
<b>FadP</b>	RSc2046	6	1	conserved hypothetical protein, DUF1178	
<b>FadP</b>	BPSL1236	5	1	Putative phosphoglycerate mutase	Glycolysis
<b>FadP</b>	liuR	4	1	Predicted transcriptional regulator LiuR of leucine degradation pathway, MerR family	Transcription regulation
<b>FadP</b>	degV	4	1	conserved hypothetical protein, DegV family	
<b>FadP</b>	acsA	4	1	Acetyl-coenzyme A synthetase (EC 6.2.1.1)	Acetyl-coenzyme A synthetase
<b>FadP</b>	h16_A1555	4	1	conserved hypothetical protein, UPF0065	
<b>FadP</b>	Rmet_0145	3	1	TesB-like acyl-CoA thioesterase 2	
<b>FadP</b>	paal	2	1	phenylacetic acid degradation protein Paal	Fatty acid degradation
<b>FadP</b>	Rsc1774	2	1	GCN5-related N-acetyltransferase	
<b>FadP</b>	acdH4	1	1	Acyl-CoA dehydrogenase domain protein	Fatty acid degradation
<b>FadR</b>	fadL	50	5	Long-chain fatty acid transport protein	Fatty acid degradation
<b>FadR</b>	fadI	47	5	FadI component of anaerobic fatty acid oxidation complex	Fatty acid degradation
<b>FadR</b>	fadJ	46	5	FadJ component of anaerobic fatty acid oxidation complex	Fatty acid degradation
<b>FadR</b>	fadE	38	4	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Fatty acid degradation
<b>FadR</b>	fabA	26	3	3-hydroxydecanoyl-[acyl-carrier-protein] dehydratase (EC 4.2.1.60)	Fatty acid biosynthesis
<b>FadR</b>	fadH	25	3	2,4-dienoyl-CoA reductase [NADPH] (EC 1.3.1.34)	Fatty acid degradation
<b>FadR</b>	fadB	24	3	fatty oxidation complex, alpha subunit FadB	Fatty acid degradation
<b>FadR</b>	fadA	24	3	fatty oxidation complex, beta subunit FadA	Fatty acid degradation
<b>FadR</b>	fadR	26	2	Transcriptional regulator for fatty acid degradation FadR, GntR family	Transcription regulation
<b>FadR</b>	fadE2	16	2	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Fatty acid degradation
<b>FadR</b>	fabB	14	2	fatty oxidation complex, alpha subunit FadB	Fatty acid biosynthesis
<b>FadR</b>	fadD	13	2	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid degradation
<b>FadR</b>	SO0572	16	1	Enoyl-CoA hydratase (EC 4.2.1.17)	Fatty acid degradation
<b>FadR</b>	SO4716	13	1	Acetyltransferase, GNAT family	

<b>FadR</b>	plsB	8	1	Glycerol-3-phosphate acyltransferase (EC 2.3.1.15)	Glycerolipid metabolism
<b>FadR</b>	iclR	8	1	Acetate operon transcriptional repressor, IclR family	Transcription regulation
<b>FadR</b>	fadM	8	1	Long-chain acyl-CoA thioesterase FadM (EC=3.1.2.-)	Fatty acid degradation
<b>FadR</b>	yebV	8	1	hypothetical protein	
<b>FadR</b>	VC2105	6	1	Thioesterase/thiol ester dehydrase-isomerase	
<b>FadR</b>	tesB	4	1	Acyl-CoA thioesterase	Fatty acid degradation
<b>FadR</b>	acdB	2	1	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>FadR</b>	COG0596	1	1	Predicted hydrolase/acetyltransferase	
<b>GlcC</b>	glcE	23	7	Glycolate dehydrogenase (EC 1.1.99.14), FAD-binding subunit GlcE	Glycolate utilization
<b>GlcC</b>	glcF	22	7	Glycolate dehydrogenase (EC 1.1.99.14), iron-sulfur subunit GlcF	Glycolate utilization
<b>GlcC</b>	glcD	21	7	Glycolate dehydrogenase (EC 1.1.99.14), subunit GlcD	Glycolate utilization
<b>GlcC</b>	glcC	22	6	Glycolate utilization operon transcriptional activator GlcC	Transcription regulation
<b>GlcC</b>	glcG	13	4	Hypothetical protein GlcG in glycolate utilization operon	Glycolate utilization
<b>GlcC</b>	glcB	8	3	Malate synthase G (EC 2.3.3.9)	Tricarboxylic acid cycle
<b>GlcC</b>	glcA	1	1	Glycolate permease	Glycolate transport
<b>GlcC</b>	lldD	4	1	L-lactate dehydrogenase (EC 1.1.2.3)	Lactate utilization
<b>GlcC</b>	mlr6914	4	1	uncharacterized conserved membrane protein	
<b>GlcC</b>	lysR	3	1	Transcriptional regulator, LysR family, in glycolate utilization operon	Transcription regulation
<b>GlcC</b>	lldG	1	1	L-lactate dehydrogenase, subunit LldG	Lactate utilization
<b>GlcC</b>	lldE	1	1	L-lactate dehydrogenase, Fe-S oxidoreductase subunit LldE	Lactate utilization
<b>GlcC</b>	glcQ	1	1	Predicted TRAP-type glycolate transport system, small permease component	Glycolate transport
<b>GlcC</b>	glcM	1	1	Predicted TRAP-type glycolate transport system, large permease component	Glycolate transport
<b>GlcC</b>	lldP	2	1	L-lactate permease	Lactate utilization
<b>GlcC</b>	lldF	1	1	L-lactate dehydrogenase, Iron-sulfur cluster-binding subunit LldF	Lactate utilization
<b>GlcC</b>	glcP	1	1	Predicted TRAP-type glycolate transport system, periplasmic component	Glycolate transport
<b>GlcC</b>	NGR_c03940	1	1	hypothetical protein	
<b>GlcC</b>	ykgE	1	1	L-lactate dehydrogenase, Fe-S oxidoreductase subunit YkgE	Lactate utilization
<b>GlcC</b>	ykgF	1	1	L-lactate dehydrogenase, Iron-sulfur cluster-binding subunit YkgF	Lactate utilization
<b>GlcC</b>	ykgG	1	1	L-lactate dehydrogenase, hypothetical protein subunit YkgG	Lactate utilization
<b>HexR</b>	hexR	74	11	Central carbohydrate metabolism transcription regulator HexR, RpiR family	Transcription regulation
<b>HexR</b>	zwf	72	9	Glucose-6-phosphate 1-dehydrogenase (EC 1.1.1.49)	Pentose phosphate pathway
<b>HexR</b>	edd	55	9	Phosphogluconate dehydratase (EC 4.2.1.12)	Entner-Doudoroff pathway
<b>HexR</b>	eda	53	9	2-keto-3-deoxy-D-arabino-heptulosonate-7-phosphate synthase I alpha (EC 2.5.1.54) # AroA I alpha	Entner-Doudoroff pathway
<b>HexR</b>	pgl	53	8	6-phosphogluconolactonase (EC 3.1.1.31), eukaryotic type	Pentose phosphate pathway
<b>HexR</b>	glk	33	7	Glucokinase (EC 2.7.1.2)	Glycolysis
<b>HexR</b>	pykA	40	7	Pyruvate kinase (EC 2.7.1.40)	Glycolysis
<b>HexR</b>	gapA	28	5	NAD-dependent glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.12)	Glycolysis
<b>HexR</b>	pgi	31	5	Glucose-6-phosphate isomerase (EC 5.3.1.9)	Glycolysis
<b>HexR</b>	ppc	20	4	Phosphoenolpyruvate carboxylase (EC 4.1.1.31)	Glycolysis
<b>HexR</b>	tal	23	5	Transaldolase (EC 2.2.1.2)	Pentose phosphate pathway
<b>HexR</b>	ppsA	20	3	Phosphoenolpyruvate synthase (EC 2.7.9.2)	Gluconeogenesis
<b>HexR</b>	aceB	25	3	Malate synthase (EC 2.3.3.9)	Tricarboxylic acid cycle
<b>HexR</b>	aceA	21	4	Isocitrate lyase (EC 4.1.3.1)	Tricarboxylic acid cycle
<b>HexR</b>	gapB	19	3	NADPH-dependent glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.13)	Glycolysis
<b>HexR</b>	pflA	12	3	Pyruvate formate-lyase activating enzyme (EC 1.97.1.4)	Fermentation
<b>HexR</b>	aceE	10	2	Pyruvate dehydrogenase E1 component (EC 1.2.4.1)	Pyruvate metabolism
<b>HexR</b>	aceF	10	2	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex (EC 2.3.1.12)	Pyruvate metabolism
<b>HexR</b>	gpmM	12	2	2,3-bisphosphoglycerate-independent phosphoglycerate mutase (EC 5.4.2.1)	Glycolysis
<b>HexR</b>	adhE	18	3	Alcohol dehydrogenase (EC 1.1.1.1)	Fermentation

HexR	pckA	10	4	Phosphoenolpyruvate carboxykinase [ATP] (EC 4.1.1.49)	Gluconeogenesis
HexR	grcA	12	2	Autonomous glycy radical cofactor	
HexR	gltD	12	2	Glutamate synthase [NADPH] small chain (EC 1.4.1.13)	Glutamate biosynthesis
HexR	gltB	12	2	Glutamate synthase [NADPH] large chain (EC 1.4.1.13)	Glutamate biosynthesis
HexR	aldE	7	4	Aldose 1-epimerase	Glycolysis
HexR	tpiA	11	2	Triosephosphate isomerase (EC 5.3.1.1)	Glycolysis
HexR	pntB	11	2	NAD(P) transhydrogenase subunit beta (EC 1.6.1.2)	NAD metabolism
HexR	ptsG	8	2	PTS system, glucose-specific IIB component (EC 2.7.1.69) / PTS system, glucose-specific IIC component (EC 2.7.1.69)	Glucose transport
HexR	mtIA	10	2	PTS system, mannitol-specific IIC component (EC 2.7.1.69) / PTS system, mannitol-specific IIB component (EC 2.7.1.69) / PTS system, mannitol-specific IIA component (EC 2.7.1.69)	Mannitol utilization
HexR	pntA	10	2	NAD(P) transhydrogenase alpha subunit (EC 1.6.1.2)	NAD metabolism
HexR	pflB	7	2	Pyruvate formate-lyase (EC 2.3.1.54)	Fermentation
HexR	mtlR	9	2	Mannitol operon repressor	Transcription regulation
HexR	ptsI	7	2	Phosphoenolpyruvate-protein phosphotransferase of PTS system (EC 2.7.3.9)	Glucose transport
HexR	focA	7	2	Formate efflux transporter (TC 2.A.44 family)	Fermentation
HexR	ptsH	7	2	Phosphocarrier protein of PTS system	Glucose transport
HexR	mtID	9	2	Mannitol-1-phosphate 5-dehydrogenase (EC 1.1.1.17)	Mannitol utilization
HexR	crr	7	2	PTS system, glucose-specific IIA component (EC 2.7.1.69)	Glucose transport
HexR	phk	16	1	Xylulose-5-phosphate phosphoketolase (EC 4.1.2.9)	Pentose phosphate pathway
HexR	hexR1	8	1	Central carbohydrate metabolism transcription regulator HexR, RpiR family	Transcription regulation
HexR	gapA2	16	1	glyceraldehyde-3-phosphate dehydrogenase, type I	Glycolysis
HexR	ybfA	10	1	Putative exported protein	
HexR	pepD	9	1	Aminoacyl-histidine dipeptidase (Peptidase D) (EC 3.4.13.3)	
HexR	deoD	14	1	Purine nucleoside phosphorylase (EC 2.4.2.1)	Nucleoside metabolism
HexR	gnd	14	1	6-phosphogluconate dehydrogenase, decarboxylating (EC 1.1.1.44)	Pentose phosphate pathway
HexR	nqrD	14	1	NADH:ubiquinone oxidoreductase, Na translocating, hydrophobic membrane protein NqrD	Electron transport chain
HexR	nqrC	14	1	NADH:ubiquinone oxidoreductase, Na translocating, gamma subunit	Electron transport chain
HexR	gltR	7	1	DNA-binding response regulator GltR, controls specific porins for the entry of glucose	Transcription regulation
HexR	nqrF	14	1	NADH:ubiquinone oxidoreductase, Na translocating, beta subunit	Electron transport chain
HexR	nqrA	14	1	NADH:ubiquinone oxidoreductase, Na translocating, alpha subunit	Electron transport chain
HexR	deoA	14	1	Thymidine phosphorylase (EC 2.4.2.4)	Nucleoside metabolism
HexR	nqrE	14	1	NADH:ubiquinone oxidoreductase, Na translocating, hydrophobic membrane protein NqrE	Electron transport chain
HexR	deoB	14	1	Phosphopentomutase (EC 5.4.2.7)	Nucleoside metabolism
HexR	nqrB	14	1	NADH:ubiquinone oxidoreductase, Na translocating, hydrophobic membrane protein NqrB	Electron transport chain
HexR	gltS	7	1	Integral membrane sensor signal transduction histidine kinase (EC 2.7.13.3), glucose catabolism cluster	Transcription regulation
HexR	ygaW	8	1	Putative inner membrane protein	
HexR	eno	4	3	Enolase (EC 4.2.1.11)	Glycolysis
HexR	gcvT	12	1	Aminomethyltransferase (glycine cleavage system T protein) (EC 2.1.2.10)	Glycine cleavage system
HexR	gcvP	12	1	Glycine dehydrogenase [decarboxylating] (glycine cleavage system P protein) (EC 1.4.4.2)	Glycine cleavage system
HexR	nupC	12	1	nucleoside transporter, NupC family	Nucleoside metabolism
HexR	gcvH	12	1	Glycine cleavage system H protein	Glycine cleavage system
HexR	nirB	7	1	Nitrite reductase [NAD(P)H] large subunit (EC 1.7.1.4)	Nitrogen metabolism
HexR	nirD	7	1	Nitrite reductase [NAD(P)H] small subunit (EC 1.7.1.4)	Nitrogen metabolism
HexR	pta	4	1	Phosphate acetyltransferase (EC 2.3.1.8)	Fermentation
HexR	mgsA	2	1	Methylglyoxal synthase (EC 4.2.3.3)	Methylglyoxal metabolism
HexR	gltA	2	1	Citrate synthase (si) (EC 2.3.3.1)	Tricarboxylic acid cycle

HexR	ackA	4	1	Acetate kinase (EC 2.7.2.1)	Fermentation
HexR	PF00248	2	1	Putative aldo/keto reductase	
HexR	SO1118	10	1	hypothetical protein	
HexR	cdd	10	1	cytidine deaminase	Nucleoside metabolism
HexR	glgX	6	1	Glycogen debranching enzyme (EC 3.2.1.-)	Glycogen utilization
HexR	pgk	3	2	Phosphoglycerate kinase (EC 2.7.2.3)	Glycolysis
HexR	glgA	5	1	Glycogen synthase, ADP-glucose transglucosylase (EC 2.4.1.21)	Glycogen utilization
HexR	adhB	8	1	alcohol dehydrogenase II	Fermentation
HexR	ldhA	3	1	D-lactate dehydrogenase (EC 1.1.1.28)	Fermentation
HexR	gntU	1	1	Low-affinity gluconate/H <sup>+</sup> symporter GntU	Gluconate utilization
HexR	glgC	5	1	Glucose-1-phosphate adenyltransferase (EC 2.7.7.27)	Glycogen utilization
HexR	mgIB	3	1	Galactose/methyl galactoside ABC transport system, D-galactose-binding periplasmic protein MglB (TC 3.A.1.2.3)	Galactose transport
HexR	mcp1	8	1	methyl-accepting chemotaxis protein	
HexR	ptsHI	1	1	PTS system, glucose-specific IIA component (EC 2.7.1.69) / Phosphocarrier protein of PTS system / Phosphoenolpyruvate-protein phosphotransferase of PTS system (EC 2.7.3.9)	Glucose transport
HexR	gntK	1	1	Gluconokinase (EC 2.7.1.12)	Gluconate utilization
HexR	mgIA	3	1	Galactose/methyl galactoside ABC transport system, ATP-binding protein MglA (EC 3.6.3.17)	Galactose transport
HexR	mgIC	3	1	Galactoside transport system permease protein mgIC (TC 3.A.1.2.3)	Galactose transport
HexR	cpsA	2	1	Capsular polysaccharide synthesis enzyme CpsA, sugar transferase	
HexR	glgP	2	1	Glycogen phosphorylase (EC 2.4.1.1)	Glycogen utilization
HexR	prpB	1	1	Carboxyphosphoenolpyruvate phosphonmutase (EC 2.7.8.23)	
HexR	oxlT	1	1	Putative oxalate:formate antiporter	Tricarboxylic acid cycle
HexR	ugpC	1	1	SN-glycerol-3-phosphate transport ATP-binding protein UgpC (TC 3.A.1.1.3)	Glycerol-3-phosphate transport
HexR	glpT	2	1	Glycerol-3-phosphate transporter	Glycerol-3-phosphate transport
HexR	pykF	1	1	Pyruvate kinase (EC 2.7.1.40)	Glycolysis
HexR	lctP	3	1	L-lactate permease	Lactate utilization
HexR	gapN	2	1	NADP-dependent glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.9)	Glycolysis
HexR	fba	1	1	Fructose-bisphosphate aldolase class II (EC 4.1.2.13)	Glycolysis
HexR	manC	1	1	Mannose-1-phosphate guanylyltransferase (GDP) (EC 2.7.7.22)	Mannose utilization
HexR	bkdA2	1	1	Branched-chain alpha-keto acid dehydrogenase, E1 component, beta subunit (EC 1.2.4.4)	Branched-chain amino acid degradation
HexR	bkdB	1	1	Dihydrolipoamide acyltransferase component of branched-chain alpha-keto acid dehydrogenase complex (EC 2.3.1.168)	Branched-chain amino acid degradation
HexR	bkdA1	1	1	Branched-chain alpha-keto acid dehydrogenase, E1 component, alpha subunit (EC 1.2.4.4)	Branched-chain amino acid degradation
HexR	nupC2	3	1	putative nucleoside transporter, NupC family	Nucleoside metabolism
HexR	mcp2	3	1	methyl-accepting chemotaxis sensory transducer	
HexR	PST_3493	1	1	Aldo/keto reductase	
HexR	dld	1	1	D-Lactate dehydrogenase (EC 1.1.2.5)	Lactate utilization
HmgQ	hpd	16	2	4-hydroxyphenylpyruvate dioxygenase (EC 1.13.11.27)	Tyrosine degradation
HmgQ	hmgA	14	1	Homogentisate 1,2-dioxygenase (EC 1.13.11.5)	Tyrosine degradation
HmgQ	hmgB	1	1	Maleylacetoacetate isomerase (EC 5.2.1.2)	Tyrosine degradation
HmgQ	hmgC	1	1	Fumarylacetoacetase (EC 3.7.1.2)	Tyrosine degradation
HmgQ	gloA	1	1	Predicted homogentisate dioxygenase, GloA family	Tyrosine degradation
HmgQ	hmgQ	16	1	Tyrosine degradation transcriptional regulator, LysR family	Transcription regulation
HmgR	hpd	1	1	4-hydroxyphenylpyruvate dioxygenase (EC 1.13.11.27)	Tyrosine degradation
HmgR	hmgA	5	1	Homogentisate 1,2-dioxygenase (EC 1.13.11.5)	Tyrosine degradation
HmgR	hmgB	5	1	Maleylacetoacetate isomerase (EC 5.2.1.2)	Tyrosine degradation
HmgR	hmgC	5	1	Fumarylacetoacetase (EC 3.7.1.2)	Tyrosine degradation
HmgR	COG2814	3	1	Predicted tyrosine transporter, COG2814 family	Tyrosine transport

HmgR	hmgR	5	1	Tyrosine degradation transcriptional regulator, lclR family	Transcription regulation
HmgS	hmgA	3	1	Homogentisate 1,2-dioxygenase (EC 1.13.11.5)	Tyrosine degradation
HmgS	hmgB	3	1	Maleylacetoacetate isomerase (EC 5.2.1.2)	Tyrosine degradation
HmgS	hmgS	3	1	Tyrosine degradation transcriptional regulator, MarR family	Transcription regulation
HutC	hutU	106	18	Urocanate hydratase (EC 4.2.1.49)	Histidine degradation
HutC	hutH	108	18	Histidine ammonia-lyase (EC 4.3.1.3)	Histidine degradation
HutC	hutI	108	18	Imidazolonepropionase (EC 3.5.2.7)	Histidine degradation
HutC	hutC	103	17	Histidine utilization repressor, GntR family	Transcription regulation
HutC	hutF	59	13	Formiminoglutamic iminohydrolase (EC 3.5.3.13)	Histidine degradation
HutC	hutG	53	13	N-formylglutamate deformylase (EC 3.5.1.68)	Histidine degradation
HutC	hutD	41	11	Conserved hypothetical protein related to histidine degradation	Histidine degradation
HutC	hutG2	32	10	Formiminoglutamase (EC 3.5.3.8)	Histidine degradation
HutC	hisT	18	6	Histidine transport protein (permease)	Histidine transport
HutC	hutH2	14	6	Histidine ammonia-lyase ( EC:4.3.1.3 )	Histidine degradation
HutC	COG3314	6	5	Predicted histidine uptake transporter	Histidine transport
HutC	COG1457 (CodB)	11	5	Permease, cytosine/purines, uracil, thiamine, allantoin family protein	Transport
HutC	hutX	8	4	Histidine ABC transporter, histidine-binding protein (TC 3.A.1)	Histidine transport
HutC	hutW	8	4	Histidine ABC transporter, permease protein (TC 3.A.1)	Histidine transport
HutC	hutV	8	4	Histidine ABC transporter, ATP-binding protein (TC 3.A.1)	Histidine transport
HutC	COG834 (HisJ)	7	4	ABC amino acid transporter, periplasmic binding protein	Histidine transport
HutC	hisC	6	4	Histidinol-phosphate aminotransferase	Histidine biosynthesis
HutC	COG1126 (GlnQ)	4	3	ABC amino acid transporter, ATPase component	Histidine transport
HutC	COG765 (HisM)	5	3	ABC amino acid transporter, permease component	Histidine transport
HutC	hisX	13	3	Putative histidine ABC transporter, substrate binding protein	Histidine transport
HutC	hisY	13	3	Putative histidine ABC transporter, permease protein	Histidine transport
HutC	hisZ	13	3	Putative histidine ABC transporter, ATPase protein	Histidine transport
HutC	Cau_2357	3	2	Optional hypothetical component of omp transporter	Transport
HutC	omp	3	2	TonB-dependent outer membrane transporter	Histidine transport?
HutC	COG5285	4	2	Phytanoyl-CoA dioxygenase	
HutC	COG4160 (ArtM)	2	2	ABC amino acid transporter, permease component	Transport
HutC	COG277(GlcD)	2	2	FAD linked oxidase domain protein	
HutC	COG1125 (OpuBA)	2	2	ABC proline/glycine/betaine transporter, ATPase component	Transport
HutC	COG1174 (OpuBB)	2	2	ABC proline/glycine/betaine transporter, permease component	Transport
HutC	COG1732 (OpuBC)	2	2	ABC proline/glycine/betaine transporter, periplasmic binding domain	Transport
HutC	COG2423	2	2	Predicted ornithine cyclodeaminase, mu-crystallin homolog (EC 4.3.1.12)	
HutC	COG3221 (PhnD)	2	2	ABC phosphate/phosphonate transporter, periplasmic binding component	Transport
HutC	hisD	4	2	Histidinol dehydrogenase (EC 1.1.1.23)	Histidine biosynthesis
HutC	hisI	2	1	Phosphoribosyl-AMP cyclohydrolase (EC 3.5.4.19) / Phosphoribosyl-ATP pyrophosphatase (EC 3.6.1.31)	Histidine biosynthesis
HutC	hisG	2	1	ATP phosphoribosyltransferase (EC 2.4.2.17)	Histidine biosynthesis
HutC	hisF	2	1	Imidazole glycerol phosphate synthase cyclase subunit (EC 4.1.3.-) Phosphoribosylformimino-5-aminoimidazole carboxamide ribotide isomerase (EC 5.3.1.16)	Histidine biosynthesis
HutC	hisA	2	1	Imidazole glycerol phosphate synthase amidotransferase subunit (EC 2.4.2.-)	Histidine biosynthesis
HutC	hisH	2	1	Histidinol-phosphatase (EC 3.1.3.15) / Imidazoleglycerol-phosphate dehydratase (EC 4.2.1.19)	Histidine biosynthesis
HutC	COG2814 (AraJ)	4	1	Putative histidine permease, major facilitator superfamily	Histidine transport
HutC	hisP	4	1	Histidine ABC transporter, ATP-binding protein HisP (TC 3.A.1.3.1)	Histidine transport
HutC	hisP2	4	1	Histidine ABC transporter, ATP-binding protein HisP (TC 3.A.1.3.1)	Histidine transport
HutC	COG1960 (CaiA)	1	1	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	
HutC	COG1804 (CaiB)	1	1	CAIB/BAIF family protein	

HutC	hisJ2	4	1	Histidine ABC transporter, histidine-binding periplasmic protein precursor HisJ (TC 3.A.1.3.1)	Histidine transport
HutC	hisM	4	1	Histidine ABC transporter, permease protein HisM (TC 3.A.1.3.1)	Histidine transport
HutC	hisM2	4	1	Histidine ABC transporter, permease protein HisM (TC 3.A.1.3.1)	Histidine transport
HutC	hisQ	4	1	Histidine ABC transporter, permease protein HisQ (TC 3.A.1.3.1)	Histidine transport
HutC	hisQ2	4	1	Histidine ABC transporter, permease protein HisQ (TC 3.A.1.3.1)	Histidine transport
HutC	COG1414	3	1	Transcriptional regulator, IclR family	
HutC	COG2855	1	1	Predicted membrane protein	
HutC	COG3181	1	1	Uncharacterized conserved putative exported protein	
HutC	hisJ	2	1	Histidine ABC transporter, histidine-binding periplasmic protein precursor HisJ (TC 3.A.1.3.1)	Histidine transport
HutC	COG3842 (PotA)	1	1	ABC transporter, ATPase component	Transport
HutC	COG1176 (PotB)	1	1	ABC transporter, permease component	Transport
HutC	COG1177 (PotC)	1	1	ABC transporter, permease component	Transport
HutC	COG687 (PotD)	1	1	ABC transporter, periplasmic binding protein	Transport
HutC	COG1028 (FabG)	2	1	Short-chain alcohol dehydrogenase	
HutC	COG1063 (Tdh)	2	1	Zn-dependent dehydrogenase	
HutC	SMa0403	2	1	hypothetical protein	
HutC	COG596 (MhpC)	1	1	Putative hydrolases or acyltransferases (alpha/beta hydrolase superfamily)	
HypR	hypD	31	11	1-pyrroline-4-hydroxy-2-carboxylate deaminase (EC 3.5.4.22) # predicted	Hydroxyproline/proline degradation
HypR	hypR	32	10	Predicted regulator for proline and hydroxyproline utilization, GntR family D-amino acid dehydrogenase (EC 1.4.99.1) family protein in hydroxy-L-proline catabolic cluster	Transcription regulation
HypR	hypO	20	9		Hydroxyproline/proline degradation
HypR	hypE	21	9	Proline racemase /4-hydroxyproline epimerase (EC 5.1.1.8)	Hydroxyproline/proline degradation
HypR	hypH	17	7	Ketoglutarate semialdehyde dehydrogenase (EC 1.2.1.26) # hydroxy-L-proline-inducible	Hydroxyproline/proline degradation
HypR	hypS	8	5	Putative L-lactate/Malate dehydrogenase	TCA cycle
HypR	hypY	9	4	Proline racemase /4-hydroxyproline epimerase (EC 5.1.1.8)	Hydroxyproline/proline degradation
HypR	COG2423	8	3	Predicted ornithine cyclodeaminase, mu-crystallin homolog	Proline degradation
HypR	hypP	4	3	Predicted hydroxyproline ABC transporter, permease protein	Hydroxyproline transport
HypR	hypM	4	3	Predicted hydroxyproline ABC transporter, substrate-binding protein	Hydroxyproline transport
HypR	hypN	4	3	Predicted hydroxyproline ABC transporter, permease protein	Hydroxyproline transport
HypR	hypQ	4	3	Predicted hydroxyproline ABC transporter, ATP-binding protein	Hydroxyproline transport
HypR	hypX	4	3	Putative citrate/isocitrate isomerase or aconitase ## predicted from clustering to proline racemase Proline dehydrogenase (EC 1.5.99.8) (Proline oxidase) / Delta-1-pyrroline-5-carboxylate dehydrogenase (EC 1.5.1.12)	TCA cycle
HypR	putA	18	2		Proline degradation
HypR	prdP	8	2	Proline dipeptidase	Proline degradation
HypR	ampP	9	2	Xaa-Pro aminopeptidase (EC 3.4.11.9)	Proline degradation
HypR	omp	5	2	TonB-dependent receptor, collagen-binding surface protein	Proline transport?
HypR	colA2	9	2	Microbial collagenase, secreted (EC 3.4.24.3)	Collagen degradation
HypR	COG4663	2	1	TRAP-type C4-dicarboxylate transport system, periplasmic component	
HypR	COG3090	2	1	TRAP-type C4-dicarboxylate transport system, small permease component	
HypR	COG4664	2	1	TRAP-type C4-dicarboxylate transport system, large permease component	
HypR	hypD'	1	1	1-pyrroline-4-hydroxy-2-carboxylate deaminase (EC 3.5.4.22) # predicted	Hydroxyproline/proline degradation
HypR	hypH'	1	1	Ketoglutarate semialdehyde dehydrogenase (EC 1.2.1.26) # hydroxy-L-proline-inducible Putative ketoglutarate semialdehyde dehydrogenase (EC 1.2.1.26) # hydroxy-L-proline-inducible	Hydroxyproline/proline degradation
HypR	hypH'-2	1	1		Hydroxyproline/proline degradation
HypR	EAM_2484	1	1	Oxidase	
HypR	COG446 (HcaD)	1	1	Putative oxidoreductase in 4-hydroxyproline catabolic gene cluster	
HypR	COG687 (PotD)	1	1	Probable binding protein component of ABC transporter	
HypR	VP1327	1	1	hypothetical protein	
HypR	COG2271 (UhpC)	1	1	Transporter, MFS superfamily	

<b>HypR</b>	hypT	1	1	Putative hydroxyproline transporter	Hydroxyproline transport
<b>HypR</b>	hypZ	1	1	OsmC/Ohr family protein	
<b>HypR</b>	COG531 (PotE)	1	1	Putative proline/hydroxyproline permease, PotE family	Hydroxyproline/proline transport
<b>HypR</b>	colA1	7	1	Microbial collagenase, secreted (EC 3.4.24.3)	Collagen degradation
<b>HypR</b>	pdtP	6	1	Predicted proline dipeptide/tripeptide permease, MFS family	Proline transport
<b>HypR</b>	ATW7_13133	1	1	hypothetical protein	
<b>HypR</b>	ypdF	1	1	Aminopeptidase YpdF (MP-, MA-, MS-, AP-, NP- specific)	Collagen degradation
<b>HypR</b>	hypA	1	1	Predicted hydroxyproline TRAP-type transport system, small permease component	Hydroxyproline transport
<b>HypR</b>	hypB	1	1	Predicted hydroxyproline TRAP-type transport system, large permease component	Hydroxyproline transport
<b>HypR</b>	hypC	1	1	Predicted hydroxyproline TRAP-type transport system, periplasmic component	Hydroxyproline transport
<b>HypR</b>	colA3	4	1	Microbial collagenase, secreted (EC 3.4.24.3)	Collagen degradation
<b>HypR</b>	omp2	1	1	TonB-dependent receptor	
<b>LiuQ</b>	liuD	14	3	Methylcrotonyl-CoA carboxylase carboxyl transferase subunit (EC 6.4.1.4)	Branched_chain amino acid degradation
<b>LiuQ</b>	liuB	14	3	Methylcrotonyl-CoA carboxylase biotin-containing subunit (EC 6.4.1.4)	Branched_chain amino acid degradation
<b>LiuQ</b>	liuQ	12	3	Predicted branched-chain amino acid degradation regulator LiuQ, TetR family	Branched_chain amino acid degradation
<b>LiuQ</b>	liuA	11	3	Isovaleryl-CoA dehydrogenase (EC 1.3.99.10)	Branched_chain amino acid degradation
<b>LiuQ</b>	liuC	11	3	Methylglutaconyl-CoA hydratase (EC 4.2.1.18)	Branched_chain amino acid degradation
<b>LiuQ</b>	aacS	4	1	AMP-dependent synthetase and ligase	Branched_chain amino acid degradation
<b>LiuQ</b>	liuE	2	2	Hydroxymethylglutaryl-CoA lyase (EC 4.1.3.4)	Branched_chain amino acid degradation
<b>LiuQ</b>	ivd2	1	1	Isovaleryl-CoA dehydrogenase (EC 1.3.99.10)	Branched_chain amino acid degradation
<b>LiuQ</b>	liuQ2	1	1	Predicted transcriptional regulator LiuQ of leucine degradation pathway, TetR family	Transcription regulation
<b>LiuQ</b>	atuB	1	1	Short-chain dehydrogenase/reductase SDR	
<b>LiuQ</b>	liuQ1	1	1	Predicted transcriptional regulator LiuQ of leucine degradation pathway, TetR family	Transcription regulation
<b>LiuQ</b>	acsA	1	1	Acetyl-coenzyme A synthetase (EC 6.2.1.1)	Acyl-coenzyme A synthetase
<b>LiuR</b>	etfA	49	10	Electron transfer flavoprotein, alpha subunit	Electron transfer chain for branched-chain amino acid degradation
<b>LiuR</b>	etfB	48	9	Electron transfer flavoprotein, beta subunit	Electron transfer chain for branched-chain amino acid degradation
<b>LiuR</b>	ivdA	54	10	Acetyl-CoA C-acyltransferase (EC 2.3.1.16) @ Acetyl-CoA acetyltransferase (EC 2.3.1.9)	Branched-chain amino acid degradation
<b>LiuR</b>	ivdC	47	9	Branched-chain acyl-CoA dehydrogenase (EC 1.3.99.12)	Branched-chain amino acid degradation
<b>LiuR</b>	liuA	65	11	Isovaleryl-CoA dehydrogenase (EC 1.3.99.10); Butyryl-CoA dehydrogenase (EC 1.3.99.2)	Branched-chain amino acid degradation
<b>LiuR</b>	liuB	55	10	Methylcrotonyl-CoA carboxylase biotin-containing subunit (EC 6.4.1.4)	Branched-chain amino acid degradation
<b>LiuR</b>	liuC	54	10	Methylglutaconyl-CoA hydratase (EC 4.2.1.18)	Branched-chain amino acid degradation
<b>LiuR</b>	liuD	46	9	Methylcrotonyl-CoA carboxylase carboxyl transferase subunit (EC 6.4.1.4)	Branched-chain amino acid degradation
<b>LiuR</b>	liuE	49	9	Hydroxymethylglutaryl-CoA lyase (EC 4.1.3.4)	Branched-chain amino acid degradation
<b>LiuR</b>	liuR	90	13	Predicted transcriptional regulator LiuR of leucine degradation pathway, MerR family	Transcriptional regulator
<b>LiuR</b>	aacS2	1	1	Acetoacetyl-CoA synthetase (EC 6.2.1.16) / Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Branched-chain amino acid degradation
<b>LiuR</b>	acdA2	2	2	3-ketoacyl-CoA thiolase (EC 2.3.1.16) @ Acetyl-CoA acetyltransferase (EC 2.3.1.9)	Branched-chain amino acid degradation
<b>LiuR</b>	acdA3	6	2	3-ketoacyl-CoA thiolase (EC 2.3.1.16) @ Acetyl-CoA acetyltransferase (EC 2.3.1.9)	Branched-chain amino acid degradation
<b>LiuR</b>	acdB2	1	1	Enoyl-CoA hydratase (EC 4.2.1.17)	Branched-chain amino acid degradation
<b>LiuR</b>	acdB3	1	1	Enoyl-CoA hydratase (EC 4.2.1.17)	Branched-chain amino acid degradation
<b>LiuR</b>	acdB4	2	1	Enoyl-CoA hydratase [valine degradation] (EC 4.2.1.17)	Branched-chain amino acid degradation
<b>LiuR</b>	acdB5	1	1	Enoyl-CoA hydratase (EC 4.2.1.17)	Branched-chain amino acid degradation
<b>LiuR</b>	acdH3	3	1	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Branched-chain amino acid degradation
<b>LiuR</b>	acdH4	1	1	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Branched-chain amino acid degradation
<b>LiuR</b>	acdH5	1	1	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Branched-chain amino acid degradation



LiuR	aceA	1	1	isocitrate lyase	Tricarboxylic acid cycle
LiuR	acs	2	1	acyl-CoA synthase	Acyl-coenzyme A synthetase
LiuR	acsA	2	1	Acyl-coenzyme A synthetases/AMP-(fatty) acid ligases	Acyl-coenzyme A synthetase
LiuR	ahpD	2	1	alkylhydroperoxidase AhpD family core domain protein	
LiuR	badI	1	1	2-ketocyclohexanecarboxyl-CoA hydrolase (EC 4.1.3.36)	
LiuR	csgA	1	1	Short-chain dehydrogenase/reductase SDR( EC:1.1.1.184 )	
LiuR	Daci_5984	1	1	Alpha/beta hydrolase fold (EC 3.8.1.5)	
LiuR	dcp	2	1	Peptidyl-dipeptidase dcp (EC 3.4.15.5)	
LiuR	ebA6516	1	1	Enoyl-CoA hydratase (EC 4.2.1.17)	Enoyl-CoA hydratase
LiuR	eftB	1	1	Electron transfer flavoprotein, beta subunit	Electron transfer chain for branched-chain amino acid degradation
LiuR	etfD1	1	1	Electron transfer flavoprotein-ubiquinone oxidoreductase (EC 1.5.5.1)	Electron transfer chain for branched-chain amino acid degradation
LiuR	etfD2	1	1	Electron transfer flavoprotein-ubiquinone oxidoreductase (EC 1.5.5.1)	Electron transfer chain for branched-chain amino acid degradation
LiuR	fabG	2	2	3-oxoacyl-[acyl-carrier protein] reductase (EC 1.1.1.100)	Fatty acid biosynthesis
LiuR	fadA	1	1	acetyl-CoA acyltransferase	Fatty acid degradation
LiuR	fadB	1	1	3-hydroxyacyl-CoA dehydrogenase	Fatty acid degradation
LiuR	fadL	1	1	Long-chain fatty acid transport protein	Fatty acid degradation
LiuR	fpr	1	1	Flavodoxin reductases (ferredoxin-NADPH reductases) family 1	
LiuR	h16_A0164	1	1	Metallo-beta-lactamase family protein	
LiuR	h16_A0171	1	1	Dehydrogenases with different specificities (related to short-chain alcohol dehydrogenases)	
LiuR	h16_A0173	1	1	2-Hydroxychromene-2-carboxylate isomerase	
LiuR	h16_A0174	1	1	Putative phosphatase YieH	
LiuR	h16_A0175	1	1	hypothetical protein	
LiuR	h16_A0176	1	1	Maleylacetoacetate isomerase (EC 5.2.1.2) / Glutathione S-transferase	
LiuR	h16_A0178	1	1	Dienelactone hydrolase or related enzyme	
LiuR	hit	3	1	Bis(5'-nucleosyl)-tetrphosphatase (asymmetrical) (EC 3.6.1.17)	
LiuR	IL0880	2	1	Sensory box/GGDEF family protein	
LiuR	ivdA1	1	1	3-ketoacyl-CoA thiolase [isoleucine degradation] (EC 2.3.1.16)	Branched-chain amino acid degradation
LiuR	ivdA2	1	1	3-ketoacyl-CoA thiolase [isoleucine degradation] (EC 2.3.1.16)	Branched-chain amino acid degradation
LiuR	ivdB1	1	1	Methylmalonate-semialdehyde dehydrogenase (EC 1.2.1.27)	Branched-chain amino acid degradation
LiuR	ivdB2	1	1	Methylmalonate-semialdehyde dehydrogenase (EC 1.2.1.27)	Branched-chain amino acid degradation
LiuR	ivdC1	1	1	Branched-chain acyl-CoA dehydrogenase (EC 1.3.99.12)	Branched-chain amino acid degradation
LiuR	ivdC2	1	1	Branched-chain acyl-CoA dehydrogenase (EC 1.3.99.12)	Branched-chain amino acid degradation
LiuR	ivdD1	1	1	3-hydroxyisobutyryl-CoA hydrolase (EC 3.1.2.4)	Branched-chain amino acid degradation
LiuR	ivdD2	1	1	3-hydroxyisobutyryl-CoA hydrolase (EC 3.1.2.4)	Branched-chain amino acid degradation
LiuR	ivdE1	1	1	Enoyl-CoA hydratase [valine degradation] (EC 4.2.1.17) / Enoyl-CoA hydratase [isoleucine degradation] (EC 4.2.1.17)	Branched-chain amino acid degradation
LiuR	ivdE2	1	1	Enoyl-CoA hydratase [valine degradation] (EC 4.2.1.17) / Enoyl-CoA hydratase [isoleucine degradation] (EC 4.2.1.17)	Branched-chain amino acid degradation
LiuR	ivdG1	1	1	3-hydroxyacyl-CoA dehydrogenase [isoleucine degradation] (EC 1.1.1.135)	Branched-chain amino acid degradation
LiuR	ivdG2	1	1	3-hydroxyacyl-CoA dehydrogenase [isoleucine degradation] (EC 1.1.1.135)	Branched-chain amino acid degradation
LiuR	lcfA	1	1	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid degradation
LiuR	livF	4	4	Branched-chain amino acid transport ATP-binding protein LivF (TC 3.A.1.4.1)	Branched-chain amino acid transport
LiuR	livG	4	4	Branched-chain amino acid transport ATP-binding protein LivG (TC 3.A.1.4.1)	Branched-chain amino acid transport
LiuR	livH	4	4	Branched-chain amino acid transport permease protein LivH (TC 3.A.1.4.1)	Branched-chain amino acid transport
LiuR	livK	6	5	Branched-chain amino acid transport substrate-binding protein LivK (TC 3.A.1.4.1)	Branched-chain amino acid transport
LiuR	livM	4	4	Branched-chain amino acid transport system permease protein LivM (TC 3.A.1.4.1)	Branched-chain amino acid transport
LiuR	mmgB	1	1	3-hydroxybutyryl-CoA dehydrogenase (EC 1.1.1.157)	Branched-chain amino acid degradation
LiuR	mmgC	1	1	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	

LiuR	paaG	2	2	Enoyl-CoA hydratase/isomerase	
LiuR	paaH1	3	1	3-hydroxybutyryl-CoA dehydrogenase (EC 1.1.1.157)	Branched-chain amino acid degradation
LiuR	paal	10	3	Phenylacetic acid degradation-related protein	
LiuR	paaK	2	2	Phenylacetate-coenzyme A ligase (EC 6.2.1.30)	
LiuR	Rru_A1944	1	1	2-hydroxychromene-2-carboxylate isomerase (EC 5.3.99.-)	
LiuR	RSc0258	1	1	Beta-lactamase domain protein	
LiuR	RSc0259	1	1	Protein of unknown function DUF1289	
LiuR	RSc0281	1	1	Metallo-beta-lactamase family protein	
LiuR	serA	2	1	D-3-phosphoglycerate dehydrogenase (EC 1.1.1.95)	Serine biosynthesis
LiuR	SMc00041	5	1	hypothetical protein	
LiuR	tyrP	1	1	Tyrosine-specific transport protein (HAAAP family)	
LiuR	tyrR	7	1	aromatic amino acid biosynthesis/transport transcriptional regulator	Transcriptional regulator
LiuR	yciK	3	1	Oxidoreductase, short-chain dehydrogenase/reductase family	
LiuR	aacS	12	5	Acetoacetyl-CoA synthetase [leucine] (EC 6.2.1.16)	Branched-chain amino acid degradation
LiuR	acdA	28	5	Enoyl-CoA hydratase (EC 4.2.1.17)	Branched-chain amino acid degradation
LiuR	acdB	27	5	3-ketoacyl-CoA thiolase (EC 2.3.1.16) @ Acetyl-CoA acetyltransferase (EC 2.3.1.9)	Branched-chain amino acid degradation
LiuR	acdH	43	8	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Branched-chain amino acid degradation
LiuR	acdH2	14	4	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Branched-chain amino acid degradation
LiuR	acdL	7	4	Acyl-CoA dehydrogenase, long-chain specific, mitochondrial precursor (EC 1.3.99.13)	Branched-chain amino acid degradation
LiuR	acdL2	6	3	Acyl-CoA dehydrogenase, long-chain specific, mitochondrial precursor (EC 1.3.99.13)	Branched-chain amino acid degradation
LiuR	acdP	4	1	Acyl-CoA dehydrogenase family protein	Branched-chain amino acid degradation
LiuR	acdQ	4	1	Acyl-CoA dehydrogenases	Branched-chain amino acid degradation
LiuR	aceB	16	1	malate synthase A	Tricarboxylic acid cycle
LiuR	aceK	17	3	Isocitrate dehydrogenase phosphatase (EC 2.7.11.5)/kinase (EC 3.1.3.-)	Tricarboxylic acid cycle
LiuR	atuC	1	1	Geranyl-CoA carboxylase carboxyl transferase subunit	Branched-chain amino acid degradation
LiuR	atuD	1	1	Isovaleryl-CoA dehydrogenase (EC 1.3.99.10)	Branched-chain amino acid degradation
LiuR	atuE	1	1	Isohexenylglutaconyl-CoA hydratase	Branched-chain amino acid degradation
LiuR	atuF	1	1	Methylcrotonyl-CoA carboxylase biotin-containing subunit (EC 6.4.1.4)	Branched-chain amino acid degradation
LiuR	bkdA1	25	3	Branched-chain alpha-keto acid dehydrogenase, E1 component, alpha subunit (EC 1.2.4.4)	Branched-chain amino acid degradation
LiuR	bkdA2	25	3	Branched-chain alpha-keto acid dehydrogenase, E1 component, beta subunit (EC 1.2.4.4)	Branched-chain amino acid degradation
LiuR	bkdB	25	3	Dihydrolipoamide acyltransferase component of branched-chain alpha-keto acid dehydrogenase complex (EC 2.3.1.168)	Branched-chain amino acid degradation
LiuR	cah	19	4	Carbonic anhydrase (EC 4.2.1.1)	Carbonic anhydrase
LiuR	echH	7	1	Enoyl-CoA hydratase (EC 4.2.1.17)	Branched-chain amino acid degradation
LiuR	etfD	23	5	Electron transfer flavoprotein-ubiquinone oxidoreductase (EC 1.5.5.1)	Electron transfer chain for branched-chain amino acid degradation
LiuR	fadD	9	4	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid degradation
LiuR	gltB	18	2	Glutamate synthase [NADPH] large chain (EC 1.4.1.13)	Glutamate biosynthesis
LiuR	gltD	18	2	Glutamate synthase [NADPH] small chain (EC 1.4.1.13)	Glutamate biosynthesis
LiuR	hbdA	6	1	3-hydroxybutyryl-CoA dehydrogenase (EC 1.1.1.157)	Branched-chain amino acid degradation
LiuR	ivdB	28	5	Methylmalonate-semialdehyde dehydrogenase (EC 1.2.1.27)	Branched-chain amino acid degradation
LiuR	ivdD	27	5	3-hydroxyisobutyryl-CoA hydrolase (EC 3.1.2.4)	Branched-chain amino acid degradation
LiuR	ivdE	31	6	Enoyl-CoA hydratase [valine degradation] (EC 4.2.1.17)	Branched-chain amino acid degradation
LiuR	ivdF	32	6	3-hydroxyisobutyrate dehydrogenase (EC 1.1.1.31)	Branched-chain amino acid degradation
LiuR	ivdG	31	6	3-hydroxybutyryl-CoA dehydrogenase (EC 1.1.1.157)	Branched-chain amino acid degradation
LiuR	ldh	21	3	Leucine dehydrogenase (EC 1.4.1.9)	Branched-chain amino acid degradation
LiuR	liuF	19	2	Succinyl-CoA:3-ketoacid-coenzyme A transferase subunit A (EC 2.8.3.5)	Branched-chain amino acid degradation
LiuR	liuG	19	2	Succinyl-CoA:3-ketoacid-coenzyme A transferase subunit B (EC 2.8.3.5)	Branched-chain amino acid degradation

<b>LiuR</b>	liuR1	10	2	Predicted transcriptional regulator LiuR of leucine degradation pathway, MerR family	
<b>LiuR</b>	liuR2	5	4	Predicted transcriptional regulator LiuR of leucine degradation pathway, MerR family	
<b>LiuR</b>	mcm	9	2	Methylmalonyl-CoA mutase (EC 5.4.99.2)	Branched-chain amino acid degradation
<b>LiuR</b>	mdh	9	1	Malate dehydrogenase (EC 1.1.1.37)	Tricarboxylic acid cycle
<b>LiuR</b>	paaH	17	4	3-hydroxybutyryl-CoA dehydrogenase (EC 1.1.1.157)	Branched-chain amino acid degradation
<b>LiuR</b>	PF03060	6	1	Dioxygenases related to 2-nitropropane dioxygenase	
<b>LiuR</b>	PF04828	11	1	Glutathione S-transferase, unnamed subgroup (EC 2.5.1.18)	
<b>LiuR</b>	PF09917	6	1	Protein of unknown function, PF09917	
<b>LiuR</b>	prpB	2	1	Methylisocitrate lyase (EC 4.1.3.30)	Propionate metabolism
<b>LiuR</b>	prpC	2	1	2-methylcitrate synthase (EC 2.3.3.5)	Propionate metabolism
<b>LiuR</b>	prpD	2	1	2-methylcitrate dehydratase (EC 4.2.1.79)	Propionate metabolism
<b>LiuR</b>	Rfer_2814	1	1	protein of unknown function DUF849	
<b>LiuR</b>	sucA	9	1	2-oxoglutarate dehydrogenase E1 component (EC 1.2.4.2)	Tricarboxylic acid cycle
<b>LiuR</b>	sucB	8	1	Dihydrolipoamide succinyltransferase component (E2) of 2-oxoglutarate dehydrogenase complex (EC 2.3.1.61)	Tricarboxylic acid cycle
<b>LiuR</b>	sucC	9	1	Succinyl-CoA ligase [ADP-forming] beta chain (EC 6.2.1.5)	Tricarboxylic acid cycle
<b>LiuR</b>	sucD	9	1	Succinyl-CoA ligase [ADP-forming] alpha chain (EC 6.2.1.5)	Tricarboxylic acid cycle
<b>LiuR</b>	thrA	15	1	aspartate kinase	Threonine biosynthesis
<b>LiuR</b>	thrB	15	1	homoserine kinase	Threonine biosynthesis
<b>LiuR</b>	thrC	15	1	threonine synthase	Threonine biosynthesis
<b>LidR</b>	lldR	54	13	Lactate-responsive regulator LldR, GntR family	Transcription regulation
<b>LidR</b>	lldP	41	12	L-lactate permease	Lactate transport
<b>LidR</b>	dld	23	8	D-Lactate dehydrogenase (EC 1.1.2.5)	Lactate utilization
<b>LidR</b>	lldG	29	9	L-lactate dehydrogenase, hypothetical protein subunit LldG	Lactate utilization
<b>LidR</b>	lldD	21	7	L-lactate dehydrogenase (EC 1.1.2.3)	Lactate utilization
<b>LidR</b>	lldE	26	8	L-lactate dehydrogenase, Fe-S oxidoreductase subunit	Lactate utilization
<b>LidR</b>	lldF	25	8	L-lactate dehydrogenase, iron-sulfur cluster-binding subunit	Lactate utilization
<b>LidR</b>	glcF	5	2	Glycolate dehydrogenase (EC 1.1.99.14), iron-sulfur subunit GlcF	Glycolate utilization
<b>LidR</b>	glcD	5	2	Glycolate dehydrogenase (EC 1.1.99.14), subunit GlcD	Glycolate utilization
<b>LidR</b>	lldEF	4	1	L-lactate dehydrogenase, Fe-S oxidoreductase subunit LldE / L-lactate dehydrogenase, Iron-sulfur cluster-binding subunit LldF	Lactate utilization
<b>LidR</b>	lldX	5	1	predicted lactate permease, DUF81 family	Lactate transport
<b>LidR</b>	glcE	1	1	Glycolate dehydrogenase (EC 1.1.99.14), FAD-binding subunit GlcE	Glycolate utilization
<b>LidR</b>	glcG	1	1	Hypothetical protein GlcG in glycolate utilization operon	Glycolate utilization
<b>LidR</b>	glcB	1	1	Malate synthase G (EC 2.3.3.9)	Tricarboxylic acid cycle
<b>MetJ</b>	metA	50	5	Homoserine O-succinyltransferase (EC 2.3.1.46)	Methionine biosynthesis
<b>MetJ</b>	metB	46	6	Cystathionine gamma-synthase (EC 2.5.1.48)	Methionine biosynthesis
<b>MetJ</b>	metE	44	6	5-methyltetrahydropteroyltriglutamate--homocysteine methyltransferase (EC 2.1.1.14)	Methionine biosynthesis
<b>MetJ</b>	metF	43	6	5,10-methylenetetrahydrofolate reductase (EC 1.5.1.20)	Methionine biosynthesis
<b>MetJ</b>	metH	36	4	5-methyltetrahydrofolate--homocysteine methyltransferase (EC 2.1.1.13)	Methionine biosynthesis
<b>MetJ</b>	metI	36	4	Methionine ABC transporter permease protein	Methionine transport
<b>MetJ</b>	metJ	59	6	S-adenosylmethionine-responsive transcriptional repressor MetJ	Transcription regulation
<b>MetJ</b>	metK	55	6	S-adenosylmethionine synthetase (EC 2.5.1.6)	Methionine biosynthesis
<b>MetJ</b>	metL	48	5	Aspartokinase (EC 2.7.2.4) / Homoserine dehydrogenase (EC 1.1.1.3)	Methionine biosynthesis
<b>MetJ</b>	metN	37	4	Methionine ABC transporter ATP-binding protein	Methionine transport
<b>MetJ</b>	metQ	38	4	Methionine ABC transporter substrate-binding protein	Methionine transport
<b>MetJ</b>	metR	44	5	Homocysteine-responsive transcriptional regulator of methionine metabolism, LysR family	Transcription regulation
<b>MetJ</b>	metT	32	4	Methionine transporter MetT, NhaC antiporter family	Methionine transport
<b>MetJ</b>	ahpC	5	1	Alkyl hydroperoxide reductase protein C (EC 1.6.4.-)	

MetJ	ahpF	3	1	Alkyl hydroperoxide reductase protein F (EC 1.6.4.-)	
MetJ	ASA_2534	1	1	Erythronate-4-phosphate dehydrogenase (EC 1.1.1.290)	
MetJ	asd	1	1	Aspartate-semialdehyde dehydrogenase (EC 1.2.1.11)	Methionine biosynthesis
MetJ	btuB2	1	1	TonB-dependent outer membrane transporter for vitamin B12	Vitamin B12 transport
MetJ	btuC	1	1	Vitamin B12 ABC transporter, permease component BtuC	Vitamin B12 transport
MetJ	btuD	1	1	Vitamin B12 ABC transporter, ATPase component BtuD	Vitamin B12 transport
MetJ	btuF	1	1	Vitamin B12 ABC transporter, B12-binding component BtuF	Vitamin B12 transport
MetJ	CKO_03982	1	1	hypothetical protein	
MetJ	COG0235	3	1	Ribulose-5-phosphate 4-epimerase and related epimerases and aldolases	
MetJ	COG4948	3	1	L-alanine-DL-glutamate epimerase and related enzymes of enolase superfamily	
MetJ	COG5276	4	1	Hypothetical protein, COG5276 family	
MetJ	folE	3	1	GTP cyclohydrolase I (EC 3.5.4.16) type 1	
MetJ	mccA	3	1	Cystathionine beta-synthase (EC 4.2.1.22)	Methionine biosynthesis
MetJ	mccB	3	1	Cystathionine gamma-lyase (EC 4.4.1.1)	Methionine biosynthesis
MetJ	mdeA2	3	1	Methionine gamma-lyase (EC 4.4.1.11)	Methionine biosynthesis
MetJ	metC	12	2	Cystathionine beta-lyase (EC 4.4.1.8)	Methionine biosynthesis
MetJ	metE2	8	2	Methionine synthase II, vitamin-B12 independent (EC 2.1.1.14)	Methionine biosynthesis
MetJ	metF-II	4	1	5,10-methylenetetrahydrofolate reductase, non-orthologous isozyme (EC 1.5.1.20)	Methionine biosynthesis
MetJ	metQ2	5	3	Methionine ABC transporter substrate-binding protein	Methionine transport
MetJ	mmuM	11	4	Homocysteine S-methyltransferase (EC 2.1.1.10)	Methionine biosynthesis
MetJ	mmuP	10	3	S-methylmethionine transporter	Methionine transport
MetJ	mtnA	6	1	Methylthioribose-1-phosphate isomerase (EC 5.3.1.23)	Methylthioribose recycling
MetJ	mtnB	8	2	Methylthioribulose-1-phosphate dehydratase (EC 4.2.1.109)	Methylthioribose recycling
MetJ	mtnC	7	2	2,3-diketo-5-methylthiopentyl-1-phosphate enolase-phosphatase (EC 3.1.3.77)	Methylthioribose recycling
MetJ	mtnD	7	2	1,2-dihydroxy-3-keto-5-methylthiopentene dioxygenase (EC 1.13.11.54)	Methylthioribose recycling
MetJ	mtnE	7	1	Methionine aminotransferase	Methylthioribose recycling
MetJ	mtnK	7	2	5-methylthioribose kinase (EC 2.7.1.100)	Methylthioribose recycling
MetJ	mtnX	5	1	Predicted methylthioribose ABC transporter, ATP-binding protein	Methylthioribose recycling
MetJ	mtnY	5	1	Predicted methylthioribose ABC transporter, permease protein	Methylthioribose recycling
MetJ	mtnZ	5	1	Predicted methylthioribose ABC transporter, substrate-binding protein	Methylthioribose recycling
MetJ	pcbC	3	1	putative 2OG-Fe(II) oxygenase	
MetJ	PCNPT3_05874	1	1	Homoserine/homoserine lactone efflux protein	
MetJ	pduO	1	1	Cob(I)alamin adenosyltransferase (EC 2.5.1.17)	Vitamin B12 biosynthesis
MetJ	PF08908	2	1	Protein of unknown function DUF1852	
MetJ	serA	4	1	D-3-phosphoglycerate dehydrogenase (EC 1.1.1.95)	Serine biosynthesis
MetJ	thrA	3	1	Aspartokinase (EC 2.7.2.4) / Homoserine dehydrogenase (EC 1.1.1.3)	Threonine biosynthesis
MetJ	thrB	3	1	Homoserine kinase (EC 2.7.1.39)	Threonine biosynthesis
MetJ	thrC	3	1	Threonine synthase (EC 4.2.3.1)	Threonine biosynthesis
MetJ	ybdH	3	1	Uncharacterized oxidoreductase YbdH	
MetJ	btuB	30	5	TonB-dependent outer membrane transporter for vitamin B12	Vitamin B12 transport
MetJ	COG3126	14	1	Lipoprotein-related protein	
MetJ	csd	7	1	Cysteine desulfurase (EC 2.8.1.7)	Methionine metabolism
MetJ	metX	10	2	Homoserine O-acetyltransferase (EC 2.3.1.31)	Methionine biosynthesis
MetJ	metY	18	3	O-acetylhomoserine sulfhydrylase (EC 2.5.1.49) / O-succinylhomoserine sulfhydrylase (EC 2.5.1.48)	Methionine biosynthesis
MetJ	msrA	19	2	Peptide methionine sulfoxide reductase MsrA (EC 1.8.4.11)	Methionine metabolism
MetJ	mtsA	8	1	Substrate-specific component MtsA of methionine-regulated ECF transporter	Methionine transport
MetJ	mtsB	8	1	Duplicated ATPase component MtsB of energizing module of methionine-regulated ECF transporter	Methionine transport
MetJ	mtsC	8	1	Transmembrane component MtsC of energizing module of methionine-regulated ECF transporter	Methionine transport

MetR	metR	111	14	Homocysteine-responsive transcriptional regulator of methionine metabolism, LysR family	Transcription regulation
MetR	metE	88	12	5-methyltetrahydropteroyltrimethylglutamate--homocysteine methyltransferase (EC 2.1.1.14)	Methionine biosynthesis
MetR	metE2	23	6	Methionine synthase II, vitamin-B12 independent (EC 2.1.1.14)	Methionine biosynthesis
MetR	metF	43	6	5,10-methylenetetrahydrofolate reductase (EC 1.5.1.20)	Methionine biosynthesis
MetR	glyA	43	6	Serine hydroxymethyltransferase (EC 2.1.2.1)	Methionine biosynthesis
MetR	PF08908	20	6	Protein of unknown function DUF1852	
MetR	metH	26	5	5-methyltetrahydrofolate--homocysteine methyltransferase (EC 2.1.1.13)	Methionine biosynthesis
MetR	luxS	21	2	S-ribosylhomocysteine lyase (EC 4.4.1.21) / Autoinducer-2 production protein LuxS	SAM recycling
MetR	metA	14	2	Homoserine O-succinyltransferase (EC 2.3.1.46)	Methionine biosynthesis
MetR	metE2-2	7	2	Methionine synthase II, vitamin-B12 independent (EC 2.1.1.14)	Methionine biosynthesis
MetR	PF03358	3	1	NADPH-dependent FMN reductase	
MetR	ilvI	15	1	Acetolactate synthase large subunit (EC 2.2.1.6)	Branched-chain amino acid biosynthesis
MetR	ilvH	15	1	Acetolactate synthase small subunit (EC 2.2.1.6)	Branched-chain amino acid biosynthesis
MetR	hmp	9	1	Flavo-hemoprotein (Hemoglobin-like protein) (Flavo-hemoglobin) (Nitric oxide dioxygenase) (EC 1.14.12.17)	Nitric oxide cell defense
MetR	metF-II	3	1	5,10-methylenetetrahydrofolate reductase, non-orthologous isozyme (EC 1.5.1.20)	Methionine biosynthesis
MetR	metC	7	1	Cystathionine beta-lyase (EC 4.4.1.8)	Methionine biosynthesis
MetR	HI0736	3	1	hypothetical sodium-dependent transporter	
MetR	PF01613	3	1	Flavin reductase-like, FMN-binding	
MetR	PF02677	1	1	Protein of unknown function DUF208	
MetR	pfl	3	1	Pyruvate formate-lyase (EC 2.3.1.54)	
MetR	dsbC	2	1	Thiol:disulfide interchange protein DsbC	
MetR	metQ2	3	1	Methionine ABC transporter substrate-binding protein	Methionine transport
MetR	thrC	2	1	Threonine synthase (EC 4.2.3.1)	Threonine biosynthesis
MetR	hom	2	1	Homoserine dehydrogenase (EC 1.1.1.3)	Methionine biosynthesis
MetR	metF2	2	1	5,10-methylenetetrahydrofolate reductase (EC 1.5.1.20)	Methionine biosynthesis
MetR	metH2	5	2	5-methyltetrahydrofolate--homocysteine methyltransferase (EC 2.1.1.13)	Methionine biosynthesis
MetR	metR2	1	1	Homocysteine-responsive transcriptional regulator of methionine metabolism, LysR family	Transcription regulation
MetR	gcvP	1	1	Glycine dehydrogenase [decarboxylating] (glycine cleavage system P protein) (EC 1.4.4.2)	Glycine cleavage system
MetR	gcvH	1	1	Glycine cleavage system H protein	Glycine cleavage system
MetR	mdeA	1	1	Methionine gamma-lyase (EC 4.4.1.11)	Methionine biosynthesis
MetR	bhmT	2	1	Betaine--homocysteine S-methyltransferase (EC 2.1.1.5)	Methionine biosynthesis
NadR	nadA	10	1	Quinolinate synthetase (EC 4.1.99.-)	NAD biosynthesis
NadR	pnuC	11	1	Ribosyl nicotinamide transporter	Niacin or Ribosyl nicotinamide transport
NadR	pncB	6	1	Nicotinate phosphoribosyltransferase (EC 2.4.2.11)	NAD metabolism
NadR	nadB	5	1	L-aspartate oxidase (EC 1.4.3.16)	NAD biosynthesis
NadR	nadR	2	1	Transcriptional regulator of NAD metabolism / Nicotinamide-nucleotide adenyltransferase, NadR family (EC 2.7.7.1) / Ribosylnicotinamide kinase (EC 2.7.1.22)	NAD metabolism
NadR	niaP	1	1	Niacin transporter, MFS family	Niacin or Ribosyl nicotinamide transport
NadQ	nadA	30	7	Quinolinate synthetase (EC 4.1.99.-)	NAD biosynthesis
NadQ	nadC	28	7	Quinolinate phosphoribosyltransferase [decarboxylating] (EC 2.4.2.19)	NAD biosynthesis
NadQ	nadB	27	7	L-aspartate oxidase (EC 1.4.3.16)	NAD biosynthesis
NadQ	nadE	6	2	NAD synthetase (EC 6.3.1.5) / Glutamine amidotransferase chain of NAD synthetase	NAD biosynthesis
NadQ	nadQ	3	2	Transcriptional regulator of NAD metabolism, COG4111 family	Transcription regulation
NadQ	nadD	4	1	Nicotinate-nucleotide adenyltransferase (EC 2.7.7.18) ## bacterial NadD family	NAD biosynthesis
NadQ	proA	4	1	Gamma-glutamyl phosphate reductase (EC 1.2.1.41)	Proline biosynthesis

<b>NadQ</b>	HNE_0691	1	1	hypothetical protein	
<b>NadQ</b>	nadC2	1	1	Quinolate phosphoribosyltransferase [decarboxylating] (EC 2.4.2.19)	NAD biosynthesis
<b>NadQ</b>	nadA1	1	1	Quinolate synthetase (EC 4.1.99.-)	NAD biosynthesis
<b>NadQ</b>	nadA2	1	1	Quinolate synthetase (EC 4.1.99.-)	NAD biosynthesis
<b>NadQ</b>	nadB2	1	1	L-aspartate oxidase (EC 1.4.3.16)	NAD biosynthesis
<b>NadQ</b>	nadB1	1	1	L-aspartate oxidase (EC 1.4.3.16)	NAD biosynthesis
<b>NadQ</b>	nadC1	1	1	Quinolate phosphoribosyltransferase [decarboxylating] (EC 2.4.2.19)	NAD biosynthesis
<b>NagC</b>	nagE	21	4	PTS system, N-acetylglucosamine-specific IIB component (EC 2.7.1.69) / PTS system, glucose-specific IIC component (EC 2.7.1.69)	N-acetylglucosamine utilization
<b>NagC</b>	nagA	31	4	N-acetylglucosamine-6-phosphate deacetylase (EC 3.5.1.25)	N-acetylglucosamine utilization
<b>NagC</b>	nagC	27	4	N-acetylglucosamine-6P-responsive transcriptional repressor NagC, ROK family	Transcription regulation
<b>NagC</b>	nagB	29	4	Glucosamine-6-phosphate deaminase (EC 3.5.99.6)	N-acetylglucosamine utilization
<b>NagC</b>	ptsI	15	3	Phosphoenolpyruvate-protein phosphotransferase of PTS system (EC 2.7.3.9)	Sugar transport
<b>NagC</b>	ptsH	15	3	Phosphocarrier protein of PTS system	Sugar transport
<b>NagC</b>	crr	14	3	PTS system, glucose-specific IIA component (EC 2.7.1.69)	Sugar transport
<b>NagC</b>	nagF	2	1	PTS system, glucose-specific IIA component (EC 2.7.1.69) / Phosphocarrier protein of PTS system / Phosphoenolpyruvate-protein phosphotransferase of PTS system (EC 2.7.3.9)	N-acetylglucosamine utilization
<b>NagC</b>	mcp	7	2	N-acetylglucosamine regulated methyl-accepting chemotaxis protein	Chemotaxis
<b>NagC</b>	omp	3	1	Outer membrane receptor protein	N-acetylglucosamine utilization
<b>NagC</b>	mcp2	5	2	N-acetylglucosamine regulated methyl-accepting chemotaxis protein	Chemotaxis
<b>NagC</b>	glmU	14	2	N-acetylglucosamine-1-phosphate uridylyltransferase (EC 2.7.7.23) / Glucosamine-1-phosphate N-acetyltransferase (EC 2.3.1.157)	N-acetylglucosamine utilization
<b>NagC</b>	hex	11	2	Beta-hexosaminidase (EC 3.2.1.52)	Chitin degradation
<b>NagC</b>	rpmE1	2	1	50S ribosomal protein L31	
<b>NagC</b>	znuA	2	1	Zinc ABC transporter, periplasmic-binding protein ZnuA	
<b>NagC</b>	pyrG	10	1	CTP synthase (EC 6.3.4.2)	
<b>NagC</b>	eno	9	1	Enolase (EC 4.2.1.11)	Glycolysis
<b>NagC</b>	tfoX	9	1	DNA transformation protein TfoX	
<b>NagC</b>	tfoX1	9	1	DNA transformation protein TfoX1 (Sxy)	
<b>NagC</b>	ptsG	8	1	PTS system, glucose-specific IIB component (EC 2.7.1.69) / PTS system, glucose-specific IIC component (EC 2.7.1.69)	Mannose and glucose transport
<b>NagC</b>	fbaA	8	1	Fructose-bisphosphate aldolase class II (EC 4.1.2.13)	Glycolysis
<b>NagC</b>	pgk	8	1	Phosphoglycerate kinase (EC 2.7.2.3)	Glycolysis
<b>NagC</b>	chiA	8	1	Chitinase (EC 3.2.1.14)	Chitin degradation
<b>NagC</b>	manX	9	1	PTS system, mannose-specific IAB component	Mannose and glucose transport
<b>NagC</b>	glmS	9	1	Glucosamine--fructose-6-phosphate aminotransferase [isomerizing] (EC 2.6.1.16)	N-acetylglucosamine utilization
<b>NagC</b>	manZ	9	1	PTS system, mannose-specific IID component	Mannose and glucose transport
<b>NagC</b>	manY	9	1	PTS system, mannose-specific IIc component	Mannose and glucose transport
<b>NagC</b>	nagE2	7	1	PTS system, N-acetylglucosamine-specific IIA component (EC 2.7.1.69) / PTS system, N-acetylglucosamine-specific IIB component (EC 2.7.1.69) / PTS system, N-acetylglucosamine-specific IIC component (EC 2.7.1.69)	N-acetylglucosamine utilization
<b>NagC</b>	aldE	7	1	Aldose 1-epimerase	
<b>NagC</b>	chi	6	2	Chitinase (EC 3.2.1.14)	Chitin degradation
<b>NagC</b>	nagD	8	1	Phosphatase NagD predicted to act in N-acetylglucosamine utilization subsystem	N-acetylglucosamine utilization
<b>NagC</b>	nagE1	6	1	PTS system, N-acetylglucosamine-specific IIB component (EC 2.7.1.69) / PTS system, N-acetylglucosamine-specific IIC component (EC 2.7.1.69)	N-acetylglucosamine utilization
<b>NagC</b>	gapA	5	1	NAD-dependent glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.12)	Glycolysis
<b>NagC</b>	chbR	6	1	Chitobiose-specific regulator ChbR, AraC family	Transcription regulation
<b>NagC</b>	chbB	6	1	PTS system, chitobiose-specific IIB component (EC 2.7.1.69)	Chitobiose utilization
<b>NagC</b>	gdhA	1	1	NADP-specific glutamate dehydrogenase (EC 1.4.1.4)	Glutamate degradation
<b>NagC</b>	rpmJ1	1	1	ribosomal protein L36	

NagC	chbA	6	1	N,N'-diacetylchitobiose-specific PTS system, EIIA component	Chitobiose utilization
NagC	exbD	1	1	Biopolymer transport protein ExbD/ToIR	
NagC	tonB	1	1	Periplasmic binding protein TonB	
NagC	chbC	6	1	PTS system, chitobiose-specific IIC component (EC 2.7.1.69)	Chitobiose utilization
NagC	exbB	1	1	Biopolymer transport protein ExbB	
NagC	chbG	6	1	Cellobiose phosphotransferase system YdjC-like protein	
NagC	chbF	5	1	Chitobiose-specific 6-phospho-beta-glucosidase ChbF (EC 3.2.1.86)	Chitobiose utilization
NagC	ybfM	4	1	N-acetylglucosamine-regulated outer membrane porin	Chitobiose utilization
NagC	cbp	4	1	Chitin binding protein	Chitin degradation
NagC	glgA	3	1	Glycogen synthase, ADP-glucose transglucosylase (EC 2.4.1.21)	Glycogen metabolism
NagC	grcA	3	1	autonomous glycyl radical cofactor GrcA	
NagC	chiP	3	1	Outer membrane chitoporin	Chitobiose transport
NagC	chiD	3	1	Chitodextrinase precursor (EC 3.2.1.14)	Chitin degradation
NagC	glgC	3	1	Glucose-1-phosphate adenyltransferase (EC 2.7.7.27)	Glycogen metabolism
NagC	gapB	3	1	NADPH-dependent glyceraldehyde-3-phosphate dehydrogenase (EC 1.2.1.13)	Glycolysis
NagC	ompC	3	1	Predicted OmpC-like chitoporin	Chitobiose utilization
NagC	adh	2	1	Alcohol dehydrogenase (EC 1.1.1.1); Acetaldehyde dehydrogenase (EC 1.2.1.10)	
NagC	gltA	2	1	Citrate synthase (si) (EC 2.3.3.1)	Tricarboxylic acid cycle
NagC	chiS	2	1	Chitin catabolic cascade sensor histidine kinase ChiS	Transcription regulation
NagC	epd	2	1	D-erythrose-4-phosphate dehydrogenase (EC 1.2.1.72)	
NagC	galP	2	1	D-galactose transporter	Galactose transport
NagC	chi1	1	1	Chitinase (EC 3.2.1.14)	Chitin degradation
NagC	VP1029	1	1	Hypothetical protein	
NagC	ompU	1	1	Outer membrane protein OmpU	
NagC	VC1591	1	1	Oxidoreductase, short-chain dehydrogenase/reductase family	
NagC	aldC	1	1	Alpha-acetolactate decarboxylase (EC 4.1.1.5)	
NagC	budB	1	1	Acetolactate synthase, catabolic (EC 2.2.1.6)	
NagC	alsR	1	1	Transcriptional regulator of alpha-acetolactate operon alsR	Transcription regulation
NagC	nanM	1	1	N-acetylneuraminic acid-induced hypothetical transmembrane protein	N-acetylneuraminic acid transport
NagC	fimB	1	1	type 1 fimbriae regulatory protein FimB	
NagC	nanC	1	1	N-acetylneuraminic acid outer membrane channel protein NanC	N-acetylneuraminic acid transport
NagQ	nagQ	33	10	Predicted transcriptional regulator of N-Acetylglucosamine utilization, GntR family	Transcription regulation
NagQ	nagA	30	10	N-acetylglucosamine-6-phosphate deacetylase (EC 3.5.1.25)	N-acetylglucosamine utilization
NagQ	nagB2	26	9	Glucosamine-6-phosphate deaminase [isomerizing], alternative (EC 3.5.99.6)	N-acetylglucosamine utilization
NagQ	nagE	15	6	PTS system, N-acetylglucosamine-specific IIB component (EC 2.7.1.69) / PTS system, N-acetylglucosamine-specific IIC component (EC 2.7.1.69)	N-acetylglucosamine utilization
NagQ	ptsl	15	5	PTS system, glucose-specific IIA component (EC 2.7.1.69) / Phosphocarrier protein of PTS system / Phosphoenolpyruvate-protein phosphotransferase of PTS system (EC 2.7.3.9)	Sugar transport
NagQ	nagK	13	3	N-acetylglucosamine kinase of eukaryotic type (EC 2.7.1.59)	N-acetylglucosamine utilization
NagQ	murQ	8	3	N-acetylmuramic acid 6-phosphate etherase (EC 4.2.-.-)	N-acetylmuramic acid utilization
NagQ	nagT	11	3	N-Acetyl-D-glucosamine ABC transport system, sugar-binding protein	N-acetylglucosamine utilization
NagQ	nagV	10	3	N-Acetyl-D-glucosamine ABC transport system, permease protein 2	N-acetylglucosamine utilization
NagQ	nagU	10	3	N-Acetyl-D-glucosamine ABC transport system, permease protein 1	N-acetylglucosamine utilization
NagQ	nagW	10	3	N-Acetyl-D-glucosamine ABC transport system, ATP-binding component	N-acetylglucosamine utilization
NagQ	hex	3	2	Beta-hexosaminidase (EC 3.2.1.52)	N-acetylglucosamine utilization
NagQ	chiA	2	2	Chitinase (EC 3.2.1.14)	Chitin degradation
NagQ	cdxA	2	2	Chitodextrinase precursor (EC 3.2.1.14)	Chitin degradation
NagQ	omp_nag	4	1	N-acetylglucosamine-regulated TonB-dependent outer membrane receptor	Chitobiose utilization
NagQ	nagD	6	2	Hypothetical oxidoreductase related to N-acetylglucosamine utilization	
NagQ	nagZ	1	1	Beta N-acetyl-glucosaminidase (EC 3.2.1.52)	Chitin degradation

<b>NagQ</b>	nagB	3	1	Glucosamine-6-phosphate deaminase (EC 3.5.99.6)	N-acetylglucosamine utilization
<b>NagQ</b>	nagR	2	1	Transcriptional regulator of N-acetylglucosamine utilization, LacI family	Transcription regulation
<b>NagQ</b>	wecA	1	1	Undecaprenyl-phosphate N-acetylglucosaminyl 1-phosphate transferase (EC 2.7.8.-)	
<b>NagQ</b>	hex2	1	1	N-Acetyl-D-glucosamine ABC transport system ATP-binding protein	Chitin degradation
<b>NagQ</b>	cga	1	1	Glucosylase (EC 3.2.1.3)	
<b>NagQ</b>	ybfM	1	1	N-acetylglucosamine-regulated outer membrane porin	Chitobiose utilization
<b>NagQ</b>	cbp21	1	1	Chitin binding protein	Chitin degradation
<b>NagQ</b>	chiC	1	1	Chitinase (EC 3.2.1.14)	Chitin degradation
<b>NagQ</b>	chi	1	1	Chitinase (EC 3.2.1.14)	Chitin degradation
<b>NagQ</b>	nagP	2	1	N-acetylglucosamine transporter, NagP	N-acetylmuramic acid utilization
<b>NagQ</b>	omp1	1	1	Outer membrane protein (porin)	Chitobiose utilization
<b>NagQ</b>	CC0542	1	1	Predicted periplasmic phosphohydrolase	
<b>NagQ</b>	MED297_05914	1	1	Hypothetical protein	
<b>NagQ</b>	nagX	1	1	N-acetylglucosamine related transporter, NagX	N-acetylmuramic acid utilization
<b>NagQ</b>	anaG	1	1	Alpha-N-acetylglucosaminidase (EC 3.2.1.50)	Alpha-N-acetylglucosaminidase
<b>NagQ</b>	mlr4776	1	1	Hypothetical protein	
<b>NagQ</b>	nagM	1	1	Predicted N-Acetylglucosamine ABC transporter, inner membrane subunit	N-acetylmuramic acid utilization
<b>NagQ</b>	nagO	1	1	Predicted N-Acetylglucosamine ABC transporter, periplasmic sugar-binding protein	N-acetylmuramic acid utilization
<b>NagQ</b>	nagN	1	1	Predicted N-Acetylglucosamine ABC transporter, permease protein	N-acetylmuramic acid utilization
<b>NagQ</b>	nagK2	1	1	N-acetylglucosamine kinase (EC 2.7.1.59), ROK family	N-acetylglucosamine utilization
<b>NagQ</b>	nagD1	1	1	Probable oxidoreductase	
<b>NagQ</b>	nagL	1	1	Predicted N-Acetylglucosamine ABC transporter, ATP-binding protein	N-acetylmuramic acid utilization
<b>NagR</b>	omp_nag	24	3	N-acetylglucosamine-regulated TonB-dependent outer membrane receptor	Chitobiose utilization
<b>NagR</b>	trpX	24	3	Tryptophan halogenase	
<b>NagR</b>	nagA	23	4	N-acetylglucosamine-6-phosphate deacetylase (EC 3.5.1.25)	N-acetylglucosamine utilization
<b>NagR</b>	nagP	23	4	PTS system, N-acetylglucosamine-specific IIB component (EC 2.7.1.69) / PTS system, N-acetylglucosamine-specific IIC component (EC 2.7.1.69)	N-acetylglucosamine utilization
<b>NagR</b>	nagK	21	3	N-acetylglucosamine kinase of eukaryotic type (EC 2.7.1.59)	N-acetylglucosamine utilization
<b>NagR</b>	nagX	19	3	N-acetylglucosamine related transporter, NagX	N-acetylglucosamine utilization
<b>NagR</b>	hex	18	4	Beta-hexosaminidase (EC 3.2.1.52)	Chitobiose utilization
<b>NagR</b>	nagB2	14	4	Glucosamine-6-phosphate deaminase [isomerizing], alternative (EC 3.5.99.6)	N-acetylglucosamine utilization
<b>NagR</b>	nagK2	6	1	Predicted N-acetylglucosamine kinase, glucokinase-like (EC 2.7.1.59)	N-acetylglucosamine utilization
<b>NagR</b>	nagR	8	3	Transcriptional regulator of N-acetylglucosamine utilization, LacI family	Transcription regulation
<b>NagR</b>	nagB	9	3	Glucosamine-6-phosphate deaminase (EC 3.5.99.6)	N-acetylglucosamine utilization
<b>NagR</b>	chiA	10	3	Chitinase (EC 3.2.1.14)	Chitin degradation
<b>NagR</b>	nixC	3	1	N-acetylglucosamine-regulated TonB-dependent outer membrane receptor	Chitobiose utilization
<b>NagR</b>	naxA	3	1	N-acetylglucosamine-regulated TonB-dependent outer membrane receptor	Chitobiose utilization
<b>NagR</b>	cbp	7	2	Chitin and N-acetylglucosamine-binding protein A	Chitin degradation
<b>NagR</b>	pckA	2	1	Phosphoenolpyruvate carboxykinase [ATP] (EC 4.1.1.49)	Gluconeogenesis
<b>NagR</b>	chiD	2	1	Chitodextrinase (EC 3.2.1.14)	Chitin degradation
<b>NagR</b>	pgi2	2	1	Glucose-6-phosphate isomerase (EC 5.3.1.9)	Glycolysis
<b>NagR</b>	sapC	10	1	Peptide transport system permease protein sapC (TC 3.A.1.5.5)	
<b>NagR</b>	mcp_nag	8	1	N-acetylglucosamine regulated methyl-accepting chemotaxis protein	Chemotaxis
<b>NagR</b>	nixD	2	1	N-acetylglucosamine-regulated TonB-dependent outer membrane receptor	Chitobiose utilization
<b>NagR</b>	nixB	2	1	N-acetylglucosamine-regulated TonB-dependent outer membrane receptor	Chitobiose utilization
<b>NagR</b>	pilM	7	1	homolog of type IV pilus assembly protein PilM	
<b>NagR</b>	duf81	6	1	protein of unknown function DUF81	
<b>NagR</b>	nagS2	1	1	Putative sulfatase (EC 3.1.6.-)	
<b>NagR</b>	SO0851	5	1	prepilin-type cleavage/methylation-like protein	



<b>NagR</b>	CPS_2383	1	1	Putative surface protein	
<b>NagR</b>	SO0852	5	1	Type IV fimbrial biogenesis protein PilV	Fimbriae biogenesis
<b>NagR</b>	ATW7_01305	1	1	Pass1-related protein	
<b>NagR</b>	bgIX	1	1	Beta-glucosidase (EC 3.2.1.21)	Glucosides utilization
<b>NagR</b>	SO0850	5	1	Type IV fimbrial biogenesis protein PilX	Fimbriae biogenesis
<b>NagR</b>	SO0854	4	1	Type IV pilus biogenesis protein PILE	Fimbriae biogenesis
<b>NagR</b>	SO0853	4	1	Type IV fimbrial biogenesis protein FimT	Fimbriae biogenesis
<b>NagR</b>	nixA	1	1	N-acetylglucosamine-regulated TonB-dependent outer membrane receptor	Chitobiose utilization
<b>NagR</b>	cbp2	2	1	putative chitin-binding protein, exported	Chitin degradation
<b>NagR</b>	cdxA	2	1	Chitodextrinase precursor (EC 3.2.1.14)	Chitin degradation
<b>NagR</b>	pdaA	1	1	Peptidoglycan N-acetylglucosamine deacetylase	N-acetylglucosamine utilization
<b>NagR</b>	omp_nag2	1	1	N-acetylglucosamine-regulated TonB-dependent outer membrane receptor	Chitobiose utilization
<b>NagR</b>	chiA3	1	1	chitodextrinase	Chitin degradation
<b>NrdR</b>	nrdA	126	19	Ribonucleotide reductase of class Ia (aerobic), alpha subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdB	117	19	Ribonucleotide reductase of class Ia (aerobic), beta subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdD	70	12	Ribonucleotide reductase of class III (anaerobic), large subunit (EC 1.17.4.2)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdG	63	12	Ribonucleotide reductase of class III (anaerobic), activating protein (EC 1.97.1.4)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdJ	46	5	Ribonucleotide reductase of class II (coenzyme B12-dependent) (EC 1.17.4.1) @ intein-containing	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	yfaE	40	7	Ferredoxin	Oxidoreductase
<b>NrdR</b>	nrdJa	21	4	Ribonucleotide reductase of class II (coenzyme B12-dependent) (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdH	16	2	Glutaredoxin-like protein NrdH, required for reduction of Ribonucleotide reductase class Ib	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdF	15	2	Ribonucleotide reductase of class Ib (aerobic), beta subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdI	15	2	Ribonucleotide reductase stimulatory protein NrdI	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdE	15	2	Ribonucleotide reductase of class Ib (aerobic), alpha subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	SO2417	16	1	Ferredoxin	Oxidoreductase
<b>NrdR</b>	trxA	4	1	Thioredoxin	Oxidoreductase
<b>NrdR</b>	topA	8	1	DNA topoisomerase I (EC 5.99.1.2)	Replication
<b>NrdR</b>	nrdJb	5	3	Ribonucleotide reductase of class II (coenzyme B12-dependent), alpha subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdA2	2	2	Ribonucleotide reductase of class Ia (aerobic), alpha subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdB2	2	2	Ribonucleotide reductase of class Ia (aerobic), beta subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	Sala_1774	2	1	protein of unknown function DUF559	
<b>NrdR</b>	Ajs_0086	3	1	hypothetical protein	
<b>NrdR</b>	nrdA1	1	1	Ribonucleotide reductase of class Ia (aerobic), alpha subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdB1	1	1	Ribonucleotide reductase of class Ia (aerobic), beta subunit (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	RSp0964	1	1	hypothetical protein	
<b>NrdR</b>	nrdJ1	1	1	Ribonucleotide reductase of class II (coenzyme B12-dependent) (EC 1.17.4.1)	Deoxyribonucleotide biosynthesis
<b>NrdR</b>	nrdD fragment	1	1	Ribonucleotide reductase of class III (anaerobic), large subunit (EC 1.17.4.2)	Deoxyribonucleotide biosynthesis
<b>NrtR</b>	nrtR	24	10	Nudix-related transcriptional regulator NrtR	Transcription regulation
<b>NrtR</b>	nrtX	7	6	NrtR-regulated hypothetical OrfX, Band 7 protein domain	Putative NAD metabolism genes
<b>NrtR</b>	pncB	15	5	Nicotinate phosphoribosyltransferase (EC 2.4.2.11)	NAD metabolism
<b>NrtR</b>	nrtY	6	5	NrtR-regulated hypothetical OrfY, PpnK-type ATP-NAD kinase domain	Putative NAD metabolism genes
<b>NrtR</b>	pncA	13	5	Nicotinamidase (EC 3.5.1.19)	NAD metabolism
<b>NrtR</b>	nadV	7	4	Nicotinamide phosphoribosyltransferase (EC 2.4.2.12)	NAD metabolism
<b>NrtR</b>	prs	6	3	Ribose-phosphate pyrophosphokinase (EC 2.7.6.1)	NAD metabolism
<b>NrtR</b>	nadE	8	4	NAD synthetase (EC 6.3.1.5)	NAD metabolism
<b>NrtR</b>	nadD	4	3	Nicotinate-nucleotide adenyltransferase (EC 2.7.7.18)	NAD metabolism
<b>NrtR</b>	nadM	4	2	Nicotinamide-nucleotide adenyltransferase, NadM family (EC 2.7.7.1) / ADP-ribose pyrophosphatase (EC 3.6.1.13)	NAD metabolism

<b>NrtR</b>	pnuC	1	1	Ribosyl nicotinamide transporter, PnuC-like	NAD metabolism
<b>NrtR</b>	nadR	1	1	Nicotinamide-nucleotide adenyltransferase, NadR family (EC 2.7.7.1) / Ribosylnicotinamide kinase (EC 2.7.1.22)	NAD metabolism
<b>NtrC</b>	glnA	163	19	Glutamine synthetase type I (EC 6.3.1.2)	Glutamine biosynthesis
<b>NtrC</b>	ntrC	157	19	nitrogen regulation protein NR(I)	Transcription regulation
<b>NtrC</b>	ntrB	157	19	Nitrogen regulation protein NR(II) (EC 2.7.3.-)	Nitrogen metabolism regulation proteins
<b>NtrC</b>	amtB	134	17	ammonium transporter	Nitrogen source transport
<b>NtrC</b>	glnK	107	13	nitrogen regulatory protein P-II	Nitrogen metabolism regulation proteins
<b>NtrC</b>	glnB	66	7	Nitrogen regulatory protein P-II	Nitrogen metabolism regulation proteins
<b>NtrC</b>	nifR3	41	5	Nitrogen assimilation transcriptional regulator NtrX, Fis family	
<b>NtrC</b>	nasD	34	8	Nitrite reductase, large subunit (EC 1.7.1.4)	Nitrogen metabolism
<b>NtrC</b>	nasE	33	8	Nitrite reductase, small subunit (EC 1.7.1.4)	Nitrogen metabolism
<b>NtrC</b>	ntrY	30	4	Nitrogen regulation protein NtrY, sensor kinase (EC 2.7.3.-)	Nitrogen metabolism
<b>NtrC</b>	amtB2	30	8	ammonium transporter	Nitrogen source transport
<b>NtrC</b>	narK	23	6	Nitrate/nitrite antiporter	Nitrogen source transport
<b>NtrC</b>	ntrX	24	3	Nitrogen assimilation transcriptional regulator NtrX, Fis family	Nitrogen metabolism
<b>NtrC</b>	ntrZ	23	3	Conserved hypothetical signal peptide protein	
<b>NtrC</b>	nasA	23	7	Assimilatory nitrate reductase, large subunit (EC:1.7.99.4)	Nitrogen metabolism
<b>NtrC</b>	nrtC	22	4	Nitrate ABC transporter, ATP-binding component	Nitrogen source transport
<b>NtrC</b>	nrtB	21	4	Nitrate ABC transporter, permease component	Nitrogen source transport
<b>NtrC</b>	nrtA	21	4	Nitrate ABC transporter, substrate-binding component	Nitrogen source transport
<b>NtrC</b>	urtB	22	3	Urea ABC transporter, permease component 2	Nitrogen source transport
<b>NtrC</b>	gdhA	13	3	NADP-specific glutamate dehydrogenase (EC 1.4.1.4)	Nitrogen metabolism
<b>NtrC</b>	ureD	20	3	Urease accessory protein, UreD	Nitrogen metabolism
<b>NtrC</b>	ureA	20	3	Urease, gamma subunit (EC 3.5.1.5)	Nitrogen metabolism
<b>NtrC</b>	ureB	19	3	Urease, beta subunit (EC 3.5.1.5)	Nitrogen metabolism
<b>NtrC</b>	ureC	19	3	Urease, alpha subunit (EC 3.5.1.5)	Nitrogen metabolism
<b>NtrC</b>	urtA	18	3	Urea ABC transporter, substrate-binding component	Nitrogen source transport
<b>NtrC</b>	urtD	16	3	Urea ABC transporter, ATP-binding component 1	Nitrogen source transport
<b>NtrC</b>	CHP02001	12	2	Conserved hypothetical protein CHP02001	
<b>NtrC</b>	dppC	10	2	Dipeptide ABC transporter, permease component 2	Nitrogen source transport
<b>NtrC</b>	dppA	10	2	Dipeptide ABC transporter, substrate-binding component	Nitrogen source transport
<b>NtrC</b>	dppB	10	2	Dipeptide ABC transporter, permease component 1	Nitrogen source transport
<b>NtrC</b>	ureE	15	2	Urease accessory protein, UreE	Nitrogen metabolism
<b>NtrC</b>	ureG	15	2	Urease accessory protein, UreG	Nitrogen metabolism
<b>NtrC</b>	ureF	15	2	Urease accessory protein, UreF	Nitrogen metabolism
<b>NtrC</b>	cysG	10	4	Uroporphyrinogen-III methyltransferase (EC 2.1.1.107)	Porphyrin biosynthesis
<b>NtrC</b>	urtE	15	3	Urea ABC transporter, ATP-binding component 1	Nitrogen source transport
<b>NtrC</b>	glnK2	12	3	nitrogen regulatory protein P-II	Nitrogen metabolism
<b>NtrC</b>	nasBA	8	1	Assimilatory nitrate reductase, large and small subunits protein fusion (EC:1.7.99.4)	Nitrogen metabolism
<b>NtrC</b>	dat	4	1	D-alanine aminotransferase (EC 2.6.1.21)	Proline degradation
<b>NtrC</b>	nasB	8	2	Assimilatory nitrate reductase, small subunit (EC:1.7.99.4)	Nitrogen metabolism
<b>NtrC</b>	gltJ	11	1	Glutamate-aspartate ABC transporter, transmembrane component 1	Nitrogen source transport
<b>NtrC</b>	gltK	11	1	Glutamate-aspartate ABC transporter, transmembrane component 2	Nitrogen source transport
<b>NtrC</b>	gltL	11	1	Glutamate-aspartate ABC transporter, ATP-binding component	Nitrogen source transport
<b>NtrC</b>	gltI	11	1	Glutamate-aspartate ABC transporter, substrate-binding component	Nitrogen source transport
<b>NtrC</b>	dppD	5	1	Dipeptide ABC transporter, ATP-binding component 1	Nitrogen source transport
<b>NtrC</b>	dppF	5	1	Dipeptide ABC transporter, ATP-binding component 2	Nitrogen source transport
<b>NtrC</b>	ntrXY	5	1	Nitrogen assimilation transcriptional regulator NtrX, Fis family	Transcription regulation
<b>NtrC</b>	nifR	7	1	Predicted oxidoreductase, FAD binding	

NtrC	urtC	10	2	Urea ABC transporter, permease component 2	Nitrogen source transport
NtrC	ybdK	6	1	Carboxylate-amine ligase	
NtrC	PF04168	6	1	Conserved hypothetical protein	
NtrC	gltB	4	2	Glutamate synthase, large chain (EC 1.4.1.13)	Glutamate biosynthesis
NtrC	gltD	4	2	Glutamate synthase, small chain (EC 1.4.1.13)	Glutamate biosynthesis
NtrC	nrtA2	8	2	Nitrate ABC transporter, substrate-binding component	Nitrogen source transport
NtrC	nifEN	6	1	Nitrogenase FeMo-cofactor scaffold and assembly protein	Nitrogen metabolism
NtrC	Gmet_0693	6	1	Conserved hypothetical protein	
NtrC	PF01841	5	1	Transglutaminase-like protein	
NtrC	rutG	5	2	Uracil permease	Nitrogen source transport
NtrC	hisM	7	1	Histidine ABC transporter, transmembrane component 2	Nitrogen source transport
NtrC	rutC	5	2	Aminoacrylate peracid reductase	Pyrimidine Degradation
NtrC	rutA	5	2	Pyrimidine oxygenase	Pyrimidine Degradation
NtrC	glnP	7	1	Glutamine ABC transporter, transmembrane component	Nitrogen source transport
NtrC	hisP	7	1	Histidine ABC transporter, ATP-binding component	Nitrogen source transport
NtrC	glnH	7	1	Glutamine ABC transporter, substrate-binding component	Nitrogen source transport
NtrC	hisQ	7	1	Histidine ABC transporter, transmembrane component 1	Nitrogen source transport
NtrC	rutB	5	2	Peroxyureidoacrylate / ureidoacrylate amido hydrolase	
NtrC	rutF	5	2	Flavin reductase	Pyrimidine Degradation
NtrC	hisJ	7	1	Histidine ABC transporter, substrate-binding component	Nitrogen source transport
NtrC	astD	6	1	Succinylglutamic semialdehyde dehydrogenase (EC 1.2.1.71)	Arginine degradation
NtrC	glnQ	6	1	Glutamine ABC transporter, ATP-binding component	Nitrogen source transport
NtrC	astB	6	1	Succinylarginine dihydrolase (EC 3.5.3.23)	Arginine degradation
NtrC	astA	6	1	Arginine N-succinyltransferase (EC 2.3.1.109)	Arginine degradation
NtrC	nac	6	1	Nitrogen assimilation transcriptional regulator, LysR family	Transcription regulation
NtrC	astC	6	1	Succinylornithine transaminase (EC 2.6.1.81)	Arginine degradation
NtrC	astE	6	1	Succinylglutamate desuccinylase (EC 3.5.1.96)	Arginine degradation
NtrC	uctA	7	1	Urea carboxylase-related ABC transporter, substrate-binding component	Nitrogen source transport
NtrC	COG0733	2	1	Predicted sodium dependent transporter	
NtrC	glnK1	4	1	Nitrogen regulatory protein P-II	Nitrogen metabolism
NtrC	uctB	6	1	Urea carboxylase-related ABC transporter, permease component	Nitrogen source transport
NtrC	nasT	6	1	Nitrogen assimilation attenuator protein NasT	Transcription regulation
NtrC	uctC	6	1	Urea carboxylase-related ABC transporter, ATP-binding component	Nitrogen source transport
NtrC	ureJ	5	1	Urease accessory protein, UreJ	Nitrogen metabolism
NtrC	alsT	3	1	Predicted alanin/sodium symporter	Nitrogen source transport
NtrC	ansA	3	1	L-asparaginase I (EC 3.5.1.1)	Asparagine degradation
NtrC	dppDE	5	1	Dipeptide ABC transporter, ATP-binding component	Nitrogen source transport
NtrC	hmp	5	2	Nitric oxide dioxygenase	Nitrogen stress response
NtrC	uahA	5	1	Urea carboxylase (EC 6.3.4.6)	Nitrogen metabolism
NtrC	uahB	5	1	Urea carboxylase-related aminomethyltransferase (EC 2.1.2.10)	Nitrogen metabolism
NtrC	uahC	5	1	Urea carboxylase-related aminomethyltransferase (EC 2.1.2.10)	Nitrogen metabolism
NtrC	EAM_0873	4	1	Predicted ABC transporter, permease component 1	
NtrC	EAM_0875	4	1	Predicted ABC transporter, ATP-binding component	
NtrC	potG	4	1	Putrescine ABC transporter, ATP-binding component	Nitrogen source transport
NtrC	potI	4	1	Putrescine ABC transporter, transmembrane component 1	Nitrogen source transport
NtrC	rutD	4	1	Aminoacrylate hydrolase	Pyrimidine Degradation
NtrC	PF09694	4	1	Conserved hypothetical protein, nitrogen assimilation associated	
NtrC	ygjG	4	1	Putrescine aminotransferase (EC 2.6.1.82)	Putrescine metabolism
NtrC	EAM_0872	4	1	Predicted ABC transporter, substrate-binding component	
NtrC	EAM_0874	4	1	Predicted ABC transporter, permease component 2	

<b>NtrC</b>	potH	4	1	Putrescine ABC transporter, transmembrane component 2	Nitrogen source transport
<b>NtrC</b>	nasB2	4	1	Assimilatory nitrate reductase, large subunit (EC:1.7.99.4)	Nitrogen metabolism
<b>NtrC</b>	nirA	4	1	Ferredoxin--nitrite reductase (EC 1.7.7.1)	Nitrogen metabolism
<b>NtrC</b>	ddpC	3	1	Dipeptide ABC transporter, transmembrane component 2 (TC 3.A.1.5.2)	Nitrogen source transport
<b>NtrC</b>	amaB	3	1	N-carbamoyl-L-amino acid hydrolase	
<b>NtrC</b>	potC	2	1	Putrescine ABC transporter, transmembrane component 2 (TC_3.A.1.11.1)	Nitrogen source transport
<b>NtrC</b>	pucG	3	1	Serine--pyruvate aminotransferase (EC 2.6.1.51) / L-alanine:glyoxylate aminotransferase (EC 2.6.1.44)	Amino acid degradation
<b>NtrC</b>	rutE	3	1	3-hydroxy propionic acid dehydrogenase	Pyrimidine Degradation
<b>NtrC</b>	ddpA	3	1	Dipeptide ABC transporter, substrate-binding component (TC 3.A.1.5.2)	Nitrogen source transport
<b>NtrC</b>	potA	2	1	Putrescine ABC transporter, ATP-binding component (TC_3.A.1.11.1)	Nitrogen source transport
<b>NtrC</b>	ddpX	3	1	D-alanyl-D-alanine dipeptidase (EC 3.4.13.-)	
<b>NtrC</b>	ddpB	3	1	Dipeptide ABC transporter, transmembrane component 1 (TC 3.A.1.5.2)	Nitrogen source transport
<b>NtrC</b>	rutE2	1	1	3-hydroxy propionic acid dehydrogenase	Pyrimidine Degradation
<b>NtrC</b>	potB	2	1	Putrescine ABC transporter, transmembrane component 1 (TC_3.A.1.11.1)	Nitrogen source transport
<b>NtrC</b>	rutR	1	1	Pyrimidine catabolism transcriptional regulator RutR, TetR family	Transcription regulation
<b>NtrC</b>	potD	2	1	Putrescine ABC transporter, substrate-binding component (TC_3.A.1.11.1)	Nitrogen source transport
<b>NtrC</b>	ddpD	3	1	Dipeptide ABC transporter, transmembrane component 3 (TC 3.A.1.5.2)	Nitrogen source transport
<b>NtrC</b>	ddpF	3	1	Dipeptide ABC transporter, ABC-binding component (TC 3.A.1.5.2)	Nitrogen source transport
<b>NtrC</b>	ybiB	2	1	Conserved hypothetical protein	
<b>NtrC</b>	CKO_01526	2	1	Predicted transcriptional regulator, RpiR family	Transcription regulation
<b>NtrC</b>	TM1040_0383	2	1	Conserved hypothetical protein	
<b>NtrC</b>	COG0547	2	1	Glycosyl transferase, family 3	
<b>NtrC</b>	atzF	2	1	Allophanate hydrolase (EC 3.5.1.54)	Nitrogen metabolism
<b>NtrC</b>	atzF2	2	1	Allophanate hydrolase (EC 3.5.1.54)	Nitrogen metabolism
<b>NtrC</b>	Jann_1753	2	1	Conserved hypothetical protein	
<b>NtrC</b>	ISBma2	1	1	Transposase, IS4	
<b>NtrC</b>	nrtB3	1	1	Nitrate ABC transporter, permease component	Nitrogen source transport
<b>NtrC</b>	nrtC3	1	1	Nitrate ABC transporter, ATP-binding component	Nitrogen source transport
<b>NtrC</b>	nrtA3	1	1	Nitrate ABC transporter, substrate-binding component	Nitrogen source transport
<b>NtrC</b>	Daro_0818	1	1	Hypothetical protein	
<b>NtrC</b>	pkn	1	1	Probable serine/threonine-protein kinase SCO3848	
<b>NtrC</b>	PF02627	1	1	Putative alkylhydroperoxidase	
<b>NtrC</b>	OB2597_07045	1	1	Conserved hypothetical protein	
<b>NtrC</b>	OB2597_07055	1	1	Hypothetical protein	
<b>NtrC</b>	Xaut_1081	1	1	Hypothetical protein	
<b>NtrC</b>	NGR_b03860	1	1	Hypothetical protein	
<b>NtrC</b>	speB	1	1	Agmatinase (EC 3.5.3.11)	Putrescine metabolism
<b>NtrC</b>	Jann_1751	1	1	Hypothetical protein	
<b>PdhR</b>	aceE	55	6	Pyruvate dehydrogenase E1 component (EC 1.2.4.1)	Pyruvate metabolism
<b>PdhR</b>	pdhR	55	6	Transcriptional repressor for pyruvate dehydrogenase complex Dihydroliipoamide acetyltransferase component of pyruvate dehydrogenase complex (EC 2.3.1.12)	Transcription regulation Pyruvate metabolism
<b>PdhR</b>	aceF	54	6		Pyruvate metabolism
<b>PdhR</b>	lpdA	49	5	Dihydroliipoamide dehydrogenase of pyruvate dehydrogenase complex (EC 1.8.1.4)	Pyruvate metabolism
<b>PdhR</b>	oadB	19	2	Oxaloacetate decarboxylase beta chain (EC 4.1.1.3)	Pyruvate metabolism
<b>PdhR</b>	oadA	19	2	Oxaloacetate decarboxylase alpha chain (EC 4.1.1.3)	Pyruvate metabolism
<b>PdhR</b>	oadG	18	2	Oxaloacetate decarboxylase gamma chain (EC 4.1.1.3)	Pyruvate metabolism
<b>PdhR</b>	pflA	16	1	Pyruvate formate-lyase activating enzyme (EC 1.97.1.4)	Formate metabolism
<b>PdhR</b>	pflB	16	1	Pyruvate formate-lyase (EC 2.3.1.54)	Formate metabolism
<b>PdhR</b>	aceB	14	1	Malate synthase (EC 2.3.3.9)	Tricarboxylic acid cycle

<b>PdhR</b>	aceA	12	1	Isocitrate lyase (EC 4.1.3.1)	Tricarboxylic acid cycle
<b>PdhR</b>	pfIX	11	1	pyruvate formate lyase-related hypothetical transporter	
<b>PdhR</b>	ndh	8	1	NADH dehydrogenase	NAD metabolism
<b>PdhR</b>	hemL	6	1	Glutamate-1-semialdehyde aminotransferase (EC 5.4.3.8)	Porphyrin biosynthesis
<b>PdhR</b>	focA	6	1	formate transporter	
<b>PdhR</b>	yfiD	4	1	stress-induced alternate pyruvate formate-lyase subunit	
<b>PdhR</b>	deaD	5	1	Cold-shock DEAD-box protein A	
<b>PdhR</b>	cyoC	3	2	Cytochrome O ubiquinol oxidase subunit III (EC 1.10.3.-)	Electron transfer chain
<b>PdhR</b>	cyoE	3	2	Heme O synthase, protoheme IX farnesyltransferase (EC 2.5.1.-) COX10-CtaB	Porphyrin biosynthesis
<b>PdhR</b>	cyoD	3	2	Cytochrome O ubiquinol oxidase subunit IV (EC 1.10.3.-)	Electron transfer chain
<b>PdhR</b>	cyoB	3	2	Cytochrome O ubiquinol oxidase subunit I (EC 1.10.3.-)	Electron transfer chain
<b>PdhR</b>	cyoA	3	2	Cytochrome O ubiquinol oxidase subunit II (EC 1.10.3.-)	Electron transfer chain
<b>PdhR</b>	dld	2	1	Predicted D-lactate dehydrogenase, Fe-S protein, FAD/FMN-containing	Lactate metabolism
<b>PdhR</b>	lldP	2	1	L-lactate permease	Lactate metabolism
<b>PdhR</b>	grcA	1	1	stress-induced alternate pyruvate formate-lyase subunit	Pyruvate metabolism
<b>PdhR</b>	glcB	1	1	Malate synthase G (EC 2.3.3.9)	Glycolate utilization
<b>PdhR</b>	glcD	1	1	Glycolate dehydrogenase (EC 1.1.99.14), subunit GlcD	Glycolate utilization
<b>PdhR</b>	glcG	1	1	Hypothetical protein GlcG in glycolate utilization operon	Glycolate utilization
<b>PdhR</b>	glcE	1	1	Glycolate dehydrogenase (EC 1.1.99.14), FAD-binding subunit GlcE	Glycolate utilization
<b>PdhR</b>	glcF	1	1	Glycolate dehydrogenase (EC 1.1.99.14), iron-sulfur subunit GlcF	Glycolate utilization
<b>PdhR</b>	SO0273	1	1	protein of unknown function DUF1439	
<b>PdhR</b>	sdhC	1	1	succinate dehydrogenase, cytochrome b556 subunit	Tricarboxylic acid cycle
<b>PdhR</b>	gltA	1	1	citrate synthase	Tricarboxylic acid cycle
<b>PdhR</b>	ppc	1	1	Phosphoenolpyruvate carboxylase (EC 4.1.1.31)	Pyruvate metabolism
<b>PdhR</b>	sdhA	1	1	succinate dehydrogenase, flavoprotein subunit	Tricarboxylic acid cycle
<b>PdhR</b>	sdhD	1	1	succinate dehydrogenase, hydrophobic membrane anchor protein	Tricarboxylic acid cycle
<b>PdhR</b>	sdhB	1	1	succinate dehydrogenase, iron-sulfur protein	Tricarboxylic acid cycle
<b>PsrA</b>	psrA	69	12	Predicted transcriptional regulator for fatty acid degradation PsrA, TetR family	Transcription regulation
<b>PsrA</b>	fadA	56	10	3-ketoacyl-CoA thiolase (EC 2.3.1.16)	Fatty acid degradation
<b>PsrA</b>	fadB	55	9	Enoyl-CoA hydratase (EC 4.2.1.17)	Fatty acid degradation
<b>PsrA</b>	fadD	25	5	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid degradation
<b>PsrA</b>	acdH	26	4	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>PsrA</b>	fadH	31	6	2,4-dienoyl-CoA reductase [NADPH] (EC 1.3.1.34)	Fatty acid degradation
<b>PsrA</b>	etfD	31	6	Electron transfer flavoprotein-ubiquinone oxidoreductase (EC 1.5.5.1) Enoyl-CoA hydratase (EC 4.2.1.17) / Delta(3)-cis-delta(2)-trans-enoyl-CoA isomerase (EC 5.3.3.8) / 3-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.35) / 3-hydroxybutyryl-CoA epimerase (EC 5.1.2.3)	Electron transfer chain for fatty acid degradation
<b>PsrA</b>	fadJ	27	3		Fatty acid degradation
<b>PsrA</b>	fadI	27	3	3-ketoacyl-CoA thiolase (EC 2.3.1.16) @ Acetyl-CoA acetyltransferase (EC 2.3.1.9)	Fatty acid degradation
<b>PsrA</b>	etfA	27	5	electron transfer flavoprotein, alpha subunit	Electron transfer chain for fatty acid degradation
<b>PsrA</b>	etfB	27	5	electron transfer flavoprotein, beta subunit	Electron transfer chain for fatty acid degradation
<b>PsrA</b>	fadE	17	5	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Fatty acid degradation
<b>PsrA</b>	fadE1	21	3	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Fatty acid degradation
<b>PsrA</b>	fabG	16	2	3-oxoacyl-[acyl-carrier protein] reductase (EC 1.1.1.100)	Fatty acid biosynthesis
<b>PsrA</b>	fabF	14	3	3-oxoacyl-[acyl-carrier-protein] synthase, KASII (EC 2.3.1.41)	Fatty acid biosynthesis
<b>PsrA</b>	fadD2	18	4	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid degradation
<b>PsrA</b>	echH	20	3	Enoyl-CoA hydratase [valine degradation] (EC 4.2.1.17)	Fatty acid degradation
<b>PsrA</b>	fadL	9	3	Long-chain fatty acid transport protein	Fatty acid degradation
<b>PsrA</b>	scp	13	3	Sterol-binding domain protein	
<b>PsrA</b>	fabH	12	2	3-oxoacyl-[acyl-carrier-protein] synthase, KASIII (EC 2.3.1.41)	Fatty acid biosynthesis
<b>PsrA</b>	fabD	12	2	Malonyl CoA-acyl carrier protein transacylase (EC 2.3.1.39)	Fatty acid biosynthesis

<b>PsrA</b>	acpP	12	2	Acyl carrier protein	
<b>PsrA</b>	acdH1	12	2	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>PsrA</b>	fadE2	18	2	Acyl-CoA dehydrogenase, short-chain specific (EC 1.3.99.2)	Fatty acid degradation
<b>PsrA</b>	fadD1	17	2	Long-chain-fatty-acid--CoA ligase (EC 6.2.1.3)	Fatty acid degradation
<b>PsrA</b>	sdhC	16	1	succinate dehydrogenase, cytochrome b556 subunit	Tricarboxylic acid cycle
<b>PsrA</b>	glfA	16	1	citrate synthase	Tricarboxylic acid cycle
<b>PsrA</b>	aroQ	3	1	3-dehydroquinate dehydratase II (EC 4.2.1.10)	Aromatic amino acid biosynthesis
<b>PsrA</b>	SO2935	16	1	oxidoreductase, short-chain dehydrogenase/reductase family	
<b>PsrA</b>	sdhA	16	1	succinate dehydrogenase, flavoprotein subunit	Tricarboxylic acid cycle
<b>PsrA</b>	rpoS	8	1	RNA polymerase sigma factor RpoS	Transcription
<b>PsrA</b>	aceB	16	1	malate synthase A	Tricarboxylic acid cycle
<b>PsrA</b>	sdhD	16	1	succinate dehydrogenase subunit D	Tricarboxylic acid cycle
<b>PsrA</b>	acdB	5	1	Enoyl-CoA hydratase (EC 4.2.1.17) / 3,2-trans-enoyl-CoA isomerase (EC 5.3.3.8) / 3-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.35)	Fatty acid degradation
<b>PsrA</b>	sdhB	16	1	succinate dehydrogenase, iron-sulfur protein	Tricarboxylic acid cycle
<b>PsrA</b>	bccP	3	1	Biotin carboxyl carrier protein of acetyl-CoA carboxylase	
<b>PsrA</b>	accC	3	1	Biotin carboxylase of acetyl-CoA carboxylase (EC 6.3.4.14)	
<b>PsrA</b>	acdA	5	1	3-ketoacyl-CoA thiolase (EC 2.3.1.16) @ Acetyl-CoA acetyltransferase (EC 2.3.1.9)	Fatty acid degradation
<b>PsrA</b>	acdH2	5	4	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>PsrA</b>	SO0881	14	1	conserved hypothetical protein	
<b>PsrA</b>	SO0882	14	1	oxidoreductase, GMC family	
<b>PsrA</b>	paal	3	1	Phenylacetic acid degradation protein paal	
<b>PsrA</b>	algQ	6	1	Regulator of RNA polymerase sigma(70) subunit, Rsd/AlgQ	Transcription
<b>PsrA</b>	phhB	3	1	Pterin-4-alpha-carbinolamine dehydratase (EC 4.2.1.96)	
<b>PsrA</b>	fabL	3	1	ENOYL-[ACYL-CARRIER-PROTEIN] REDUCTASE (fabL) (NADPH) (EC 1.3.1.9)	Fatty acid biosynthesis
<b>PsrA</b>	aceA	12	1	isocitrate lyase	Tricarboxylic acid cycle
<b>PsrA</b>	SO0080	9	1	thioesterase superfamily protein	
<b>PsrA</b>	mdh	4	1	Malate synthase (EC 2.3.3.9)	Tricarboxylic acid cycle
<b>PsrA</b>	ldh	2	1	Leucine dehydrogenase (EC 1.4.1.9)	Branched_chain amino acid biosynthesis
<b>PsrA</b>	fadH1	2	1	2,4-dienoyl-CoA reductase [NADPH] (EC 1.3.1.34)	Fatty acid degradation
<b>PsrA</b>	fadE3	5	1	acyl-CoA dehydrogenase	Fatty acid degradation
<b>PsrA</b>	acdH3	2	2	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>PsrA</b>	paal2	1	1	Phenylacetic acid degradation protein paal	
<b>PsrA</b>	Sbal_0657	4	1	hypothetical protein	
<b>PsrA</b>	fabK	1	1	Enoyl-[acyl-carrier-protein] reductase [FMN] (EC 1.3.1.9)	Fatty acid biosynthesis
<b>PsrA</b>	SO3908	1	1	Enoyl-CoA hydratase (EC 4.2.1.17)	Fatty acid degradation
<b>PsrA</b>	acdH4	1	1	Acyl-CoA dehydrogenase (EC 1.3.99.3)	Fatty acid degradation
<b>PsrA</b>	fadL2	1	1	Long-chain fatty acid transport protein	Fatty acid degradation
<b>PsrA</b>	fadD3	1	1	long-chain-fatty-acid--CoA ligase	Fatty acid degradation
<b>RutR</b>	rutR	52	11	Transcriptional regulator RutR of pyrimidine catabolism, TetR family	Transcription regulation
<b>RutR</b>	rutB	13	7	Peroxyureidoacrylate / ureidoacrylate amido hydrolase	Pyrimidine degradation
<b>RutR</b>	rutA	12	7	Pyrimidine oxygenase	Pyrimidine degradation
<b>RutR</b>	xdhC	22	5	XdhC protein (assists in molybdopterin insertion into xanthine dehydrogenase)	Purine degradation
<b>RutR</b>	xdhA	22	5	Xanthine dehydrogenase, iron-sulfur cluster and FAD-binding subunit A (1.17.1.4)	Purine degradation
<b>RutR</b>	xdhB	22	5	Xanthine dehydrogenase, molybdenum binding subunit (EC 1.17.1.4)	Purine degradation
<b>RutR</b>	guaD	21	5	Guanine deaminase (EC 3.5.4.3)	Purine degradation
<b>RutR</b>	rutC	11	6	Aminoacrylate peracid reductase	Pyrimidine degradation
<b>RutR</b>	rutD	11	6	Aminoacrylate hydrolase	Pyrimidine degradation
<b>RutR</b>	pydC	31	4	Beta-ureidopropionase (EC 3.5.1.6)	Pyrimidine degradation

RutR	pydX	29	4	Pyridine nucleotide-disulphide oxidoreductase associated with reductive pyrimidine catabolism	Pyrimidine degradation
RutR	pydA	27	4	Dihydropyrimidine dehydrogenase [NADP+] (EC 1.3.1.2)	Pyrimidine degradation
RutR	rutF	9	5	Flavin reductase	Pyrimidine degradation
RutR	pydB	26	4	Dihydropyrimidinase (EC 3.5.2.2)	Pyrimidine degradation
RutR	pbuT	14	4	Xanthine/uracil permease	Nucleoside transport
RutR	pucL	15	3	Uricase (EC 1.7.3.3)	Pyrimidine degradation
RutR	COG3748	14	3	hypothetical protein, COG3748	
RutR	rutE	6	4	3-hydroxy propionic acid dehydrogenase	Pyrimidine degradation
RutR	rutR2	3	2	Transcriptional regulator RutR of pyrimidine catabolism, TetR family	Transcription regulation
RutR	codA	13	4	Cytosine deaminase (EC 3.5.4.1)	Pyrimidine degradation
RutR	pydP	10	3	Pyrimidine permease in reductive pathway	Pyrimidine transport
RutR	pucM	9	2	Hydroxyisourate hydrolase (EC 3.5.2.17)	Pyrimidine degradation
RutR	upp	9	3	Uracil phosphoribosyltransferase (EC 2.4.2.9)	Pyrimidine degradation
RutR	ppuD	10	3	Predicted ABC transporter, inner membrane protein precursor	Nucleoside transport
RutR	ppuC	10	3	Predicted ABC transporter, permease protein	Nucleoside transport
RutR	ppuA	10	3	Predicted ABC transporter, ATP-binding protein	
RutR	allA	9	3	Ureidoglycolate hydrolase (EC 3.5.3.19)	Purine degradation
RutR	COG0726	8	2	putative polysaccharide deacetylase family protein Nucleoside-binding outer membrane protein	
RutR	tsx	9	1		Nucleoside transport
RutR	cdd	11	3	Cytidine deaminase (EC 3.5.4.5)	Pyrimidine degradation
RutR	pbuT2	7	2	Xanthine/uracil permease	Nucleoside transport
RutR	deoA	10	3	Thymidine phosphorylase (EC 2.4.2.4)	Pyrimidine degradation
RutR	pntB	11	2	Predicted nucleoside ABC transporter, permease protein 1	Nucleoside transport
RutR	pntC	11	2	Predicted nucleoside ABC transporter, permease protein 2	Nucleoside transport
RutR	pntA	11	2	Predicted nucleoside ABC transporter, ATP-binding protein	Nucleoside transport
RutR	rutG	5	2	Uracil permease	Pyrimidine transport
RutR	rutG2	2	1	Uracil permease	Pyrimidine transport
RutR	gpt	1	1	Xanthine-guanine phosphoribosyltransferase (EC 2.4.2.22)	Purine degradation
RutR	xpt	1	1	Xanthine phosphoribosyltransferase (EC 2.4.2.22)	Purine degradation
RutR	PF07958	4	1	Conserved hypothetical protein	
RutR	ribA2	4	1	GTP cyclohydrolase II (EC 3.5.4.25 ) homolog	
RutR	pntD	10	2	Predicted nucleoside ABC transporter, substrate-binding protein	Nucleoside transport
RutR	pytO	10	2	Predicted pyrimidine ABC transporter, permease protein 1	Pyrimidine transport
RutR	pytM	10	2	Predicted pyrimidine ABC transporter, substrate-binding protein	Pyrimidine transport
RutR	pytN	10	2	Predicted pyrimidine ABC transporter, ATP-binding protein	Pyrimidine transport
RutR	pytQ	10	2	Predicted pyrimidine ABC transporter, permease protein 2	Pyrimidine transport
RutR	allC	6	3	Allantoicase (EC 3.5.3.4)	Purine degradation
RutR	ppuB	6	2	Predicted ABC transporter, substrate-binding protein precursor	
RutR	pytC	10	2	Pyrimidine ABC transporter, permease protein 2	Pyrimidine transport
RutR	pytB	10	2	Pyrimidine ABC transporter, permease protein 1	Pyrimidine transport
RutR	deoC	10	2	Deoxyribose-phosphate aldolase (EC 4.1.2.4)	Pyrimidine degradation
RutR	pytA	10	2	Pyrimidine ABC transporter, ATP-binding protein	Pyrimidine transport
RutR	carA	6	1	Carbamoyl-phosphate synthase small chain (EC 6.3.5.5)	Arginine and pyrimidine biosynthesis
RutR	carB	6	1	Carbamoyl-phosphate synthase large chain (EC 6.3.5.5)	Arginine and pyrimidine biosynthesis
RutR	pytD	9	2	Pyrimidine ABC transporter, substrate-binding protein	Pyrimidine transport
RutR	deoD	7	1	Purine nucleoside phosphorylase (EC 2.4.2.1)	Purine degradation
RutR	nupX	3	1	Nucleoside permease	Nucleoside transport
RutR	udk	3	1	Uridine kinase (EC 2.7.1.48)	Pyrimidine metabolism
RutR	COG1739	4	1	hypothetical protein, COG1739	

RutR	ald	7	1	Aldehyde dehydrogenase (EC 1.2.1.3)	
RutR	add	5	2	Adenosine deaminase (EC 3.5.4.4)	Purine degradation
RutR	allB	3	2	Allantoinase (EC 3.5.2.5)	Purine degradation
RutR	omp1	2	1	putative TonB-dependent outer membrane transporter	Nucleoside transport
RutR	omp2	2	1	putative TonB-dependent outer membrane transporter	Nucleoside transport
RutR	pbuT3	3	1	Xanthine/uracil permease	Nucleoside transport
RutR	ssnA	3	1	Predicted chlorohydrolase/aminohydrolase	
RutR	pytH	3	1	Predicted hydrolase	
RutR	praX	3	2	Omega-amino acid--pyruvate aminotransferase (EC 2.6.1.18) Nucleoside-binding outer membrane protein	
RutR	tsx2	2	1		Nucleoside transport
RutR	codB	1	1	Cytosine permease	Nucleoside transport
RutR	nupP	2	1	Predicted purine nucleoside permease	
RutR	add2	1	1	Adenosine deaminase (EC 3.5.4.4)	Purine degradation
RutR	hpt	2	2	Hypoxanthine-guanine phosphoribosyltransferase (EC 2.4.2.8)	Purine degradation
RutR	deoB	3	1	Phosphopentomutase (EC 5.4.2.7)	Purine degradation
RutR	RL3717	2	1	Hypothetical protein	
RutR	RSP_1242	2	1	Predicted lyase Nucleoside-binding outer membrane protein	
RutR	tsx3	1	1		Nucleoside transport
RutR	pbuT4	1	1	Xanthine/uracil permease	Nucleoside transport
RutR	uraA	1	1	Uracil permease	Nucleoside transport
RutR	rutR3	1	1	Transcriptional regulator RutR of pyrimidine catabolism, TetR family	Transcription regulation
RutR	Meso_2056	1	1	Hypothetical protein	
RutR	Atu2387	1	1	NTP pyrophosphohydrolase, MutT family	
RutR	mll1644	1	1	Predicted methyltransferase	
RutR	OG2516_07987	1	1	Conserved hypothetical protein	
RutR	Jann_2708	1	1	Hypothetical protein	
RutR	Jann_2706	1	1	hypothetical protein	
RutR	MED193_05504	1	1	Hypothetical protein	
RutR	MED193_05494	1	1	Hypothetical protein	
RutR	Jann_0788	1	1	Hypothetical protein	
RutR	Jann_0787	1	1	Hypothetical protein	
RutR	Jann_2704	1	1	Hypothetical protein	
RutR	RSP_0188	1	1	DedA family integral membrane protein	
RutR	OB2597_04350	1	1	Hypothetical protein	
RutR	Jann_2702	1	1	Predicted N-acetyltransferase	
RutR	SKA53_10669	1	1	Hypothetical protein	
RutR	RB2654_14945	1	1	Hypothetical protein	
RutR	OG2516_10896	1	1	Hypothetical protein	
RutR	amiC	1	1	Predicted amidase	
SahR	sahR	61	9	Predicted regulator of methionine metabolism, ArsR family	Transcription regulation
SahR	ahcY	50	7	Adenosylhomocysteinase (EC 3.3.1.1)	Methionine metabolism
SahR	metF	43	7	5,10-methylenetetrahydrofolate reductase (EC 1.5.1.20)	Methionine biosynthesis
SahR	metK	41	7	S-adenosylmethionine synthetase (EC 2.5.1.6)	Methionine metabolism
SahR	metH	32	6	5-methyltetrahydrofolate--homocysteine methyltransferase (EC 2.1.1.13)	Methionine biosynthesis
SahR	metH2	14	4	5-methyltetrahydrofolate--homocysteine methyltransferase (EC 2.1.1.13)	Methionine biosynthesis
SahR	metE	8	4	5-methyltetrahydropteroyltryglutamate--homocysteine methyltransferase (EC 2.1.1.14)	Methionine biosynthesis
SahR	bhmT	4	2	Betaine--homocysteine S-methyltransferase (EC 2.1.1.5)	Methionine biosynthesis
SahR	panC	5	1	Pantoate--beta-alanine ligase (EC 6.3.2.1)	Alanine metabolism



<b>SahR</b>	metB	1	1	Cystathionine gamma-synthase (EC 2.5.1.48)	Methionine biosynthesis
<b>SahR</b>	metX2	1	1	Homoserine O-acetyltransferase (EC 2.3.1.31)	Methionine biosynthesis
<b>SahR</b>	hom	1	1	Homoserine dehydrogenase (EC 1.1.1.3)	Methionine biosynthesis
<b>SahR</b>	metE2	1	1	methionine synthase	Methionine biosynthesis
<b>SahR</b>	DUF1852	1	1	Protein of unknown function DUF1852	
<b>SahR</b>	ddl	1	1	D-alanine--D-alanine ligase B (EC 6.3.2.4)	Alanine metabolism
<b>SahR</b>	Caul_3406	1	1	PIN domain protein	
<b>SahR</b>	metT	1	1	Methionine transporter MetT	Methionine transport
<b>SamR</b>	metE	1	1	5-methyltetrahydropteroyltriglutamate--homocysteine methyltransferase (EC 2.1.1.14)	Methionine biosynthesis
<b>SamR</b>	metF2	4	1	5,10-methylenetetrahydrofolate reductase (EC 1.5.1.20)	Methionine biosynthesis
<b>SamR</b>	metX2	4	1	Homoserine O-acetyltransferase (EC 2.3.1.31)	Methionine biosynthesis
<b>SamR</b>	metB	4	1	Cystathionine gamma-synthase (EC 2.5.1.48)	Methionine biosynthesis
<b>SamR</b>	hom	3	1	Homoserine dehydrogenase (EC 1.1.1.3)	Methionine biosynthesis
<b>SamR</b>	metK	4	1	S-adenosylmethionine synthetase (EC 2.5.1.6)	SAM biosynthesis
<b>SamR</b>	samR	4	1	Transcriptional regulator of methionine metabolism, ArsR family	Transcription regulation
<b>SamR</b>	metH1	3	1	5-methyltetrahydrofolate--homocysteine methyltransferase (EC 2.1.1.13)	Methionine biosynthesis
<b>SamR</b>	metH2	3	1	5-methyltetrahydrofolate--homocysteine methyltransferase (EC 2.1.1.13)	Methionine biosynthesis
<b>TrpR</b>	trpE	36	6	Anthranilate synthase, aminase component (EC 4.1.3.27)	Tryptophan biosynthesis
<b>TrpR</b>	trpR	37	6	Trp operon repressor	Transcription regulation
<b>TrpR</b>	trpG	12	4	Anthranilate synthase, amidotransferase component (EC 4.1.3.27)	Tryptophan biosynthesis
<b>TrpR</b>	trpB	30	4	Tryptophan synthase beta chain (EC 4.2.1.20)	Tryptophan biosynthesis
<b>TrpR</b>	trpC	27	3	Indole-3-glycerol phosphate synthase (EC 4.1.1.48)	Tryptophan biosynthesis
<b>TrpR</b>	trpA	29	3	Tryptophan synthase alpha chain (EC 4.2.1.20)	Tryptophan biosynthesis
<b>TrpR</b>	mtr	17	3	Tryptophan-specific transport protein	Tryptophan transport
<b>TrpR</b>	trpD	24	2	Anthranilate phosphoribosyltransferase (EC 2.4.2.18)	Tryptophan biosynthesis
<b>TrpR</b>	trpD_a	10	1	Anthranilate synthase, amidotransferase component (EC 4.1.3.27)	Tryptophan biosynthesis
<b>TrpR</b>	trpD_b	10	1	Anthranilate phosphoribosyltransferase (EC 2.4.2.18)	Tryptophan biosynthesis
<b>TrpR</b>	tyrA	16	1	Chorismate mutase I (EC 5.4.99.5) / Prephenate dehydrogenase [EC:5.4.99.5 1.3.1.12]	Tyrosine & Phenylalanine biosynthesis
<b>TrpR</b>	COG1541	1	1	Coenzyme F390 synthetase	
<b>TrpR</b>	aroF	16	1	2-keto-3-deoxy-D-arabino-heptulosonate-7-phosphate synthase (EC 2.5.1.54)	Aromatic amino acid biosynthesis
<b>TrpR</b>	SSF55729	1	1	Acyl-CoA N-acyltransferase	
<b>TrpR</b>	COG0733(Trp)	8	1	Predicted tryptophan transporter, SNF family	Tryptophan transport
<b>TrpR</b>	aroG	6	1	2-keto-3-deoxy-D-arabino-heptulosonate-7-phosphate synthase (EC 2.5.1.54)	Aromatic amino acid biosynthesis
<b>TrpR</b>	aroH	6	1	2-keto-3-deoxy-D-arabino-heptulosonate-7-phosphate synthase (EC 2.5.1.54)	Aromatic amino acid biosynthesis
<b>TrpR</b>	aroM	4	1	AroM family protein	Aromatic amino acid biosynthesis
<b>TrpR</b>	aroL	4	1	Shikimate kinase III (EC 2.7.1.71)	Aromatic amino acid biosynthesis
<b>TrpR</b>	yaiA	4	1	putative cytoplasmic protein	
<b>TrpR</b>	aroA	3	1	5-Enolpyruvylshikimate-3-phosphate synthase (EC 2.5.1.19)	Aromatic amino acid biosynthesis
<b>TrpR</b>	COG4221	2	1	Short-chain alcohol dehydrogenase of unknown specificity	
<b>TrpR</b>	HI1388	2	1	Anthranilate synthase, amidotransferase component (EC 4.1.3.27)	Tryptophan biosynthesis
<b>TrpR</b>	tnaB	2	1	Tryptophan-specific transport protein	Tryptophan transport
<b>TrpR</b>	aroF2	2	1	2-keto-3-deoxy-D-arabino-heptulosonate-7-phosphate synthase (EC 2.5.1.54)	Aromatic amino acid biosynthesis
<b>TrpR</b>	HAPS_1139	1	1	ABC transporter, inner-membrane component	
<b>TrpR</b>	HAPS_0395	1	1	ABC transporter, substrate binding component	
<b>TrpR</b>	HAPS_1138	1	1	ABC transporter, ATP-binding protein	
<b>TrpR</b>	tnaA	1	1	Tryptophanase (EC 4.1.99.1)	Tryptophan utilization
<b>TrpR</b>	trpB2	1	1	Tryptophan synthase beta chain like (EC 4.2.1.20)	Tryptophan utilization
<b>TyrR</b>	phhA	41	5	Phenylalanine-4-hydroxylase (EC 1.14.16.1)	Phenylalanine degradation
<b>TyrR</b>	phhB	38	5	Pterin-4-alpha-carbinolamine dehydratase (EC 4.2.1.96)	Phenylalanine degradation

<b>TyrR</b>	tyrA	39	5	Chorismate mutase I (EC 5.4.99.5) / Prephenate dehydrogenase [EC:5.4.99.5 1.3.1.12]	Tyrosine & Phenylalanine biosynthesis
<b>TyrR</b>	tyrR	45	6	Transcriptional regulator of aromatic amino acid biosynthesis	Transcription regulation
<b>TyrR</b>	aroF	35	5	2-keto-3-deoxy-D-arabino-heptulosonate-7-phosphate synthase (EC 2.5.1.54)	Aromatic amino acid biosynthesis
<b>TyrR</b>	COG2814	7	1	Predicted tyrosine transporter, COG2814 family	Tyrosine transport
<b>TyrR</b>	emrD	9	1	multidrug resistance protein D	
<b>TyrR</b>	pepD	9	1	Aminoacyl-histidine dipeptidase (Peptidase D) (EC 3.4.13.3)	
				Proline dehydrogenase (EC 1.5.99.8) (Proline oxidase) / Delta-1-pyrroline-5-carboxylate dehydrogenase (EC 1.5.1.12)	Proline degradation
<b>TyrR</b>	putA	9	1		
<b>TyrR</b>	kyn	8	1	kynureninase (tryptophan degradation)	Tryptophan degradation
<b>TyrR</b>	aroM	6	1	AroM family protein	Aromatic amino acid biosynthesis
<b>TyrR</b>	SO1117	8	1	peptidase M17, leucyl aminopeptidase	
<b>TyrR</b>	tdo	8	1	tryptophan 2,3-dioxygenase	Tryptophan degradation
<b>TyrR</b>	mtr	5	1	Tryptophan-specific transport protein	Tryptophan transport
<b>TyrR</b>	yaiA	5	1	hypothetical protein	
<b>TyrR</b>	aroG	5	2	2-keto-3-deoxy-D-arabino-heptulosonate-7-phosphate synthase I alpha (EC 2.5.1.54)	Aromatic amino acid biosynthesis
<b>TyrR</b>	COG1284	4	1	Hypothetical protein	
<b>TyrR</b>	Sfri_3409	6	1	Hypothetical protein	
<b>TyrR</b>	aprE	6	1	Alkaline serine protease	
<b>TyrR</b>	Sfri_3410	6	1	transcriptional regulator, XRE family protein	
<b>TyrR</b>	ompF	4	1	outer membrane porin F	
<b>TyrR</b>	ipdC	7	2	Indole-3-pyruvate decarboxylase (EC 4.1.1.74)	Tryptophan degradation
<b>TyrR</b>	prlC	4	1	Oligopeptidase A (EC 3.4.24.70)	
<b>TyrR</b>	pep1	3	1	Alkaline serine exoprotease A precursor (EC 3.4.21.-)	
<b>TyrR</b>	aprE2	3	1	Cold-active alkaline serine protease (EC 3.4.21.62)	
<b>TyrR</b>	omp2	3	1	putative TonB-dependent outer membrane receptor	
<b>TyrR</b>	tpl	3	2	Tyrosine phenol-lyase (EC 4.1.99.2)	Tyrosine degradation
<b>TyrR</b>	folA	1	1	Dihydrofolate reductase (EC 1.5.1.3)	Tetrahydrofolate biosynthesis
<b>TyrR</b>	pep2	1	1	peptidase M4 thermolysin	
<b>TyrR</b>	omp1	1	1	TonB-dependent receptor	
<b>TyrR</b>	pep4	1	1	prolyl oligopeptidase family protein	
<b>TyrR</b>	tyrP	32	5	Tyrosine-specific transport protein	Tyrosine transporter
<b>TyrR</b>	hmgB	29	5	Maleylacetoacetate isomerase (EC 5.2.1.2)	Tyrosine degradation
<b>TyrR</b>	hmgC	29	5	Fumarylacetoacetase (EC 3.7.1.2)	Tyrosine degradation
<b>TyrR</b>	hpd	14	4	4-hydroxyphenylpyruvate dioxygenase (EC 1.13.11.27)	Tyrosine degradation
<b>TyrR</b>	hmgA	13	4	Homogentisate 1,2-dioxygenase (EC 1.13.11.5)	Tyrosine degradation
<b>TyrR</b>	aceA	12	1	Isocitrate lyase (EC 4.1.3.1)	Tricarboxylic acid cycle
<b>TyrR</b>	aceB	16	1	Malate synthase (EC 2.3.3.9)	Tricarboxylic acid cycle
<b>TyrR</b>	acsA	8	1	Acetoacetyl-CoA synthetase (EC 6.2.1.16)	Acetyl-coenzyme A synthetase
<b>TyrR</b>	aroA	14	1	5-Enolpyruvylshikimate-3-phosphate synthase (EC 2.5.1.19)	Aromatic amino acid biosynthesis
<b>TyrR</b>	aroL	10	1	Shikimate kinase III (EC 2.7.1.71)	Aromatic amino acid biosynthesis
<b>TyrR</b>	aroP	11	1	Aromatic amino acid transport protein AroP	Aromatic amino acid transport
<b>TyrR</b>	bkdA1	16	1	Branched-chain alpha-keto acid dehydrogenase, E1 component, alpha subunit (EC 1.2.4.4)	Branched_chain amino acid degradation
<b>TyrR</b>	bkdA2	16	1	Branched-chain alpha-keto acid dehydrogenase, E1 component, beta subunit (EC 1.2.4.4)	Branched_chain amino acid degradation
<b>TyrR</b>	bkdB	16	1	Dihydrolipoamide acyltransferase component of branched-chain alpha-keto acid dehydrogenase complex (EC 2.3.1.168)	Branched_chain amino acid degradation
<b>TyrR</b>	brnQ	16	1	Branched-chain amino acid transport system carrier protein	Branched_chain amino acid transport
<b>TyrR</b>	COG0733(Tyr)	13	2	Predicted tyrosine transporter, SNF family	
<b>TyrR</b>	tyrR2	2	1	Tyrosine and phenylalanine degradation transcriptional activator, TyrR family	Transcription regulation
<b>TyrR</b>	ivdA	16	1	3-ketoacyl-CoA thiolase [isoleucine degradation] (EC 2.3.1.16)	Branched_chain amino acid degradation

<b>TyrR</b>	ivdB	16	1	Methylmalonate-semialdehyde dehydrogenase (EC 1.2.1.27)	Branched_chain amino acid degradation
<b>TyrR</b>	ivdC	16	1	Branched-chain acyl-CoA dehydrogenase (EC 1.3.99.12)	Branched_chain amino acid degradation
<b>TyrR</b>	ivdD	16	1	Enoyl-CoA hydratase [valine degradation] (EC 4.2.1.17) / Enoyl-CoA hydratase [isoleucine degradation] (EC 4.2.1.17)	Branched_chain amino acid degradation
<b>TyrR</b>	ivdE	16	1	3-hydroxyisobutyryl-CoA hydrolase (EC 3.1.2.4)	Branched_chain amino acid degradation
<b>TyrR</b>	ivdF	16	1	3-hydroxyisobutyrate dehydrogenase (EC 1.1.1.31)	Branched_chain amino acid degradation
<b>TyrR</b>	ivdG	16	1	3-hydroxyacyl-CoA dehydrogenase [isoleucine degradation] (EC 1.1.1.35)	Branched_chain amino acid degradation
<b>TyrR</b>	ldh	16	1	Leucine dehydrogenase (EC 1.4.1.9)	Branched_chain amino acid degradation
<b>TyrR</b>	liuA	14	1	Isovaleryl-CoA dehydrogenase (EC 1.3.99.10)	Branched_chain amino acid degradation
<b>TyrR</b>	liuB	14	1	Methylcrotonyl-CoA carboxylase carboxyl transferase subunit (EC 6.4.1.4)	Branched_chain amino acid degradation
<b>TyrR</b>	liuC	14	1	Methylglutaconyl-CoA hydratase (EC 4.2.1.18)	Branched_chain amino acid degradation
<b>TyrR</b>	liuD	16	1	Methylcrotonyl-CoA carboxylase biotin-containing subunit (EC 6.4.1.4)	Branched_chain amino acid degradation
<b>TyrR</b>	liuE	14	1	Hydroxymethylglutaryl-CoA lyase (EC 4.1.3.4)	Branched_chain amino acid degradation
<b>TyrR</b>	liuF	13	1	Succinyl-CoA:3-ketoacid-coenzyme A transferase subunit A (EC 2.8.3.5)	Branched_chain amino acid degradation
<b>TyrR</b>	liuG	13	1	Succinyl-CoA:3-ketoacid-coenzyme A transferase subunit B (EC 2.8.3.5)	Branched_chain amino acid degradation
<b>TyrR</b>	liuR	14	1	Predicted transcriptional regulator LiuR of leucine degradation pathway, MerR family	Transcription regulation
<b>TyrR</b>	mdeA	14	2	Methionine gamma-lyase (EC 4.4.1.11)	Methionine degradation
<b>TyrR</b>	pep3	14	1	peptidase, M13 family	
<b>TyrR</b>	phhC	5	1	Aromatic-amino-acid aminotransferase (EC 2.6.1.57)	Phenylalanine degradation
<b>TyrR</b>	phhR	7	1	Phenylalanine degradation transcriptional activator, TyrR family	Transcription regulation
<b>TyrR</b>	tyrB	16	1	Tyrosine aminotransferase (EC 2.6.1.42)	Tyrosine biosynthesis / Tyrosine degradation

<sup>1</sup> Number of regulatory interactions

<sup>2</sup> Number of taxa with regulation

**Table S4. Metabolic and gene content of reconstructed TF regulons in Proteobacteria classified by conservation of regulatory interactions.**

TF name	TF regulon members	Assigned metabolic pathway or process <sup>1</sup>	Major function	TF effector
<b>ArgR</b>	<b>Core</b>		<b>Arginine metabolism</b>	<b>Arginine</b>
	argH, argB, argC, argG, argF, argA, argE	Arginine biosynthesis		
	argR	Transcription regulation		
	artI, artQ, artM, artP	Arginine transport		
	astD, astA	Arginine degradation		
	carA, carB	Arginine and pyrimidine biosynthesis		
	<b>Taxonomy-specific</b>			
	argD	Arginine biosynthesis		
	argW, artJ, omp	Arginine transport		
	gltB, gltD	Glutamate biosynthesis		
	ilvM, ilvG, ilvD, ilvA	Branched-chain amino acid biosynthesis		
	potF, potG, potH, potI	Putrescine transport		
	recN	DNA repair		
	oadA, oadB, oadG	Pyruvate metabolism		
	astC, astB	Arginine degradation		
	<b>Genome-specific</b>			
	ilvE	Branched-chain amino acid biosynthesis		
	hisJ, hisM, hisP, hisQ	Histidine transport		
	arcA, arcB, arcC, arcD, astE	Arginine degradation		
	hisA, hisB, hisC, hisD, hisF, hisG, hisH, hisI	Histidine biosynthesis		
	proV, proW, proX	Proline transport		
speF, potE	Putrescine metabolism			
<b>BioR</b>	<b>All target genes</b>		<b>Biotin biosynthesis</b>	<b>Unknown</b>
	bioY, bioM, bioN	Biotin transport		
	bioB, bioF, bioD, bioA, bioZ, bioG, bioC	Biotin biosynthesis		
	bioR	Transcription regulation		
<b>BirA</b>	<b>Core</b>		<b>Biotin biosynthesis</b>	<b>Biotin</b>
	bioB, bioF, bioD, bioC, bioA	Biotin biosynthesis		
	<b>Taxonomy-specific</b>			
	bioH	Biotin biosynthesis		
	birA	Transcription regulation		
	fabF, fabG	Fatty acid biosynthesis		
	<b>Genome-specific</b>			
	yigM	Biotin transport		
bioW	Biotin biosynthesis			
<b>FabR</b>	<b>Core</b>		<b>Fatty acid biosynthesis</b>	<b>Unsaturated acyl-ACP</b>
	OLE1 (desA)	Unsaturated fatty acid biosynthesis		
	fabA, fabB, lcfH	Fatty acid biosynthesis		
	plsC	Glycerolipid metabolism		
	hylI	Fatty acid metabolism		
	<b>Taxonomy-specific</b>			
	desB, desC	Unsaturated fatty acid biosynthesis		
	fadL, lcfE	Fatty acid biosynthesis		
	fabR, fabR2	Transcription regulation		
	<b>Genome-specific</b>			
	pfaA, pfaB, pfaC, pfaD	Unsaturated fatty acid biosynthesis		
	pfaR, psrA	Transcription regulation		
	fadE	Fatty acid degradation		

<b>FadP</b>	<b>Core</b>		<b>Fatty acid degradation</b>	<b>Unknown</b>
		fadA, fadB, acdA, acdB, acdH, echH, acdP, acdQ, fadD	Fatty acid degradation	
		etfA, etfB, etfD	Electron transfer chain for fatty acid degradation	
		pncA	Nicotinate biosynthesis	
		fadP	Transcription regulation	
		<b>Taxonomy-specific and Genome-specific</b>		
		acsA	Acetyl-coenzyme A synthetase	
		BPSL1236	Glycolysis	
		liuR	Transcription regulation	
		paal, paaG4, paaH1, bktB, alkK	Fatty acid degradation	
<b>FadR</b>	<b>Core</b>		<b>Fatty acid degradation</b>	<b>Palmitoyl-CoA; Oleoyl-CoA</b>
		fadL, fadI, fadJ, fadE	Fatty acid degradation	
		<b>Taxonomy-specific</b>		
		fabA, fabB	Fatty acid biosynthesis	
		plsB	Glycerolipid metabolism	
		fadA, fadD, fadH, fadB, fadM, SO0572	Fatty acid degradation	
		fadR, iclR	Transcription regulation	
		<b>Genome-specific</b>		
	acdB, tesB	Fatty acid degradation		
<b>GlcC</b>	<b>Core</b>		<b>Glycolate utilization</b>	<b>Glycolate</b>
		glcE, glcF, glcD, glcG	Glycolate utilization	
		glcC	Transcription regulation	
		<b>Taxonomy-specific</b>		
		glcB	Tricarboxylic acid cycle	
		glcA	Glycolate transport	
		lldD	Lactate utilization	
		<b>Genome-specific</b>		
		glcQ, glcM, glcP	Glycolate transport	
		lldG, lldE, lldF, ykgE, ykgF, ykgG, lldP	Lactate utilization	
	lysR	Transcription regulation		
<b>HexR</b>	<b>Core</b>		<b>Central carbohydrate metabolism</b>	<b>2-keto-3-deoxy-6-phosphogluconate</b>
		glk, pykA	Glycolysis	
		edd, eda	Entner-Doudoroff pathway	
		zwf, pgl	Pentose phosphate pathway	
		hexR	Transcription regulation	
		<b>Taxonomy-specific</b>		
		tal, phk, gnd	Pentose phosphate pathway	
		nqrD, nqrC, nqrF, nqrA, nqrE, nqrB	Electron transport chain	
		adhE, pflA, pflB, ackA, pta, focA	Fermentation	
		ppsA	Gluconeogenesis	
	ptsI, ptsH, ptsG, crr	Glucose transport		
	gltD, gltB	Glutamate biosynthesis		
	gcvT, gcvP, gcvH	Glycine cleavage system		
	gapA, pgi, ppc, tpiA, gapB, gpmM	Glycolysis		
	mtlA, mtlD	Mannitol utilization		
	pntB, pntA	NAD metabolism		
	nirB, nirD	Nitrogen metabolism		
	deoD, deoA, deoB, nupC	Nucleoside metabolism		
	mtlR, gltR, gltS	Transcription regulation		

aceB, aceA	Tricarboxylic acid cycle
<b>Genome-specific</b>	
bkdA2, bkdB, bkdA1	Branched-chain amino acid degradation
adhB, ldhA	Fermentation
mgIA, mgIB, mgIC	Galactose transport
gntU, gntK	Gluconate utilization
pckA	Gluconeogenesis
ptsHI	Glucose transport
glpT	Glycerol-3-phosphate transport
glgX, glgA, glgC, glgP	Glycogen utilization
gapN, eno, pgk, fba, aldE	Glycolysis
lctP, dld	L-lactate utilization
manC	Mannose utilization
cdd	Nucleoside metabolism

<b>HmgQ</b>	<b>All target genes</b>	<b>Tyrosine degradation</b>	<b>Unknown</b>
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hmgA, hmgB, hmgC, hpd, gloA	Tyrosine degradation
hmgQ	Transcription regulation

<b>HmgR</b>	<b>All target genes</b>	<b>Tyrosine degradation</b>	<b>Homogentisate</b>
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hmgA, hmgB, hmgC, hpd	Tyrosine degradation
COG2814	Tyrosine transport
hmgR	Transcription regulation

<b>HmgS</b>	<b>All target genes</b>	<b>Tyrosine degradation</b>	<b>Unknown</b>
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hmgA, hmgB	Tyrosine degradation
hmgS	Transcription regulation

<b>HutC</b>	<b>Core</b>	<b>Histidine utilization</b>	<b>Urocanate</b>
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hutU, hutH, hutI, hutD, hutF, hutG, hutG2	Histidine degradation
hutC	Transcription regulation

<b>Taxonomy-specific</b>	
hisT, hisX, hisY, hisZ, hisP, hisQ, hisM, hisJ, COG2814, omp	Histidine transport

<b>Genome-specific</b>	
hutV, hutW, hutX, COG3314	Histidine transport
hutH2	Histidine degradation
hisA, hisB, hisC, hisD, hisF, hisG, hisH, hisI	Histidine biosynthesis

<b>HypR</b>	<b>Core</b>	<b>Proline and 4-hydroxyproline utilization</b>	<b>Proline; 4-hydroxyproline</b>
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hypD, hypE, hypH, hypO	Hydroxyproline/proline degradation
hypR	Transcription regulation

<b>Taxonomy-specific</b>	
hypY, hypH'-2	Hydroxyproline/proline degradation
putA, prdP, ampP	Proline degradation
hypP, hypM, hypN, hypQ	Hydroxyproline transport
COG531, omp	Hydroxyproline/proline transport
hypX, hypS	TCA cycle
colA2	Collagen degradation

<b>Genome-specific</b>	
pdtP	Proline transport
hypA, hypB, hypC, hypT	Hydroxyproline transport

hypD', hypH'  
colA1, ypdF, colA3

Hydroxyproline/proline degradation  
Collagen degradation

<b>LiuQ</b>	<b>Core</b>		<b>Branched-chain amino acid degradation</b>	<b>Unknown</b>
	liuA, liuB, liuC, liuD liuQ	Branched-chain amino acid degradation Transcription regulation		
	<b>Taxonomy-specific and Genome-specific</b>			
	liuE, aacS, ivd2 acsA	Branched-chain amino acid degradation Acyl-coenzyme A synthetase		

<b>LiuR</b>	<b>Core</b>		<b>Branched-chain amino acid degradation</b>	<b>Unknown</b>
	liuA, liuB, liuC, liuD, liuE, ivdA, ivdC, acdH liuR	Branched-chain amino acid degradation Transcription regulation		
	etfA, etfB	Electron transfer chain for branched-chain amino acid degradation		
	<b>Taxonomy-specific</b>			
	aacS, acdA, acdB, acdL, acdP, acdQ, bkdA, bkdB, hbdA, ivdB, ivdD, ivdE, ivdF, ivdG, ldh, liuF, liuG, mcm, paaH, echH	Branched-chain amino acid degradation		
		Electron transfer chain for branched-chain amino acid degradation		
	etfD			
	atuC, atuD, atuE, atuF	Acyclic terpenes degradation		
	gltB, gltD	Glutamate biosynthesis		
	prpB, prpC, prpD	Propionate metabolism		
	fadD	Fatty acid degradation		
	aceB, mdh, sucA, sucB, sucC, sucD, aceK	Tricarboxylic acid cycle		
	thrA, thrB, thrC	Threonine biosynthesis		
	cah	Carbonic anhydrase		
	<b>Genome-specific</b>			
	livF, livG, livH, livK, livM	Branched-chain amino acid transport		
	mngB	Branched-chain amino acid degradation		
	fadA, fadB, fadL, lcfA	Fatty acid degradation		
	fabG	Fatty acid biosynthesis		
	serA	Serine biosynthesis		
	acs, acsA	Acyl-coenzyme A synthetase		
	aceA	Tricarboxylic acid cycle		
	tyrR	Transcription regulation		

<b>LldR</b>	<b>Core</b>		<b>Lactate utilization</b>	<b>Lactate</b>
	lld, lldD, lldE, lldF, lldG	Lactate utilization		
	lldP	Lactate transport		
	lldR	Transcription regulation		
	<b>Taxonomy-specific</b>			
	lldX	Lactate transport		
	glcF, glcD	Glycolate utilization		
	<b>Genome-specific</b>			
	glcE, glcG	Glycolate utilization		
	glcB	Tricarboxylic acid cycle		

<b>MetJ</b>	<b>Core</b>		<b>Methionine metabolism</b>	<b>S-adenosyl-methionine</b>
	metI, metN, metQ, metT	Methionine transport		
	metJ, metR	Transcription regulation		
	metA, metB, metE, metF, methH, metK, metL	Methionine biosynthesis		

btuB	Vitamin B12 transport
<b>Taxonomy-specific</b>	
mtsA, mtsB, mtsC	Methionine transport
metX, metY	Methionine biosynthesis
msrA, csd	Methionine metabolism
<b>Genome-specific</b>	
btuC, btuD, btuF	Vitamin B12 transport
asd, mccA, mccB, mdeA2, metC, metF-II, mmuM	Methionine biosynthesis
mmuP	Methionine transport
mtnA, mtnB, mtnC, mtnD, mtnE, mtnK, mtnX, mtnY, mtnZ	Methylthioribose recycling
pduO	Vitamin B12 biosynthesis
serA	Serine biosynthesis
thrA, thrB, thrC	Threonine biosynthesis

<b>MetR</b>	<b>Core</b>	<b>Methionine metabolism</b>	<b>Homocysteine</b>
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metE	Methionine biosynthesis
metR	Transcription regulation
<b>Taxonomy-specific</b>	
metF, glyA, methH, metA, metF-II	Methionine biosynthesis
luxS	SAM recycling
hmp	Nitric oxide cell defense
ilvI, ilvH	Branched-chain amino acid biosynthesis
<b>Genome-specific</b>	
gcvP, gcvH	Glycine cleavage system
metQ2	Methionine transport
thrC	Threonine biosynthesis
metC, hom, mdeA, bhmT	Methionine biosynthesis

<b>NadR</b>	<b>All target genes</b>	<b>NAD metabolism</b>	<b>NAD</b>
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pnuC, niaP	Niacin or Ribosyl nicotinamide transport (NAD salvage)
nadA, nadB	NAD biosynthesis
nadR, pncB	NAD salvage

<b>NadQ</b>	<b>Core</b>	<b>NAD metabolism</b>	<b>Unknown</b>
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nadA, nadC, nadB	NAD biosynthesis
<b>Taxonomy-specific</b>	
nadE, nadD	NAD biosynthesis
proA	Proline biosynthesis
nadQ	Transcription regulation

<b>NagC</b>	<b>Core</b>	<b>N-acetylglucosamine utilization</b>	<b>N-acetylglucosamine</b>
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nagA, nagB, nagE	N-acetylglucosamine utilization
ptsI, ptsH, crr	Sugar transport
nagC	Transcription regulation
<b>Taxonomy-specific</b>	
eno, pgk, fbaA	Glycolysis
omp, glmU, glmS, nagD, nagF	N-acetylglucosamine utilization
manX, manZ, manY, ptsG	Mannose and glucose transport
chiA, hex	Chitin degradation
mcp	Chemotaxis protein (toward chitin?)
<b>Genome-specific</b>	
chbB, chbA, chbC, chbF, chiP, ompC, ybfM	Chitobiose utilization
chi, cbp, chiD, chi1	Chitin degradation



galP	Galactose transport
gapA, gapB	Glycolysis
chbR, chiS, alsR	Transcription regulation
glgA, glgC	Glycogen metabolism
gdhA	Glutamate degradation
gltA	Tricarboxylic acid cycle
nanM, nanC	N-acetylneuraminic acid transport

<b>NagQ</b>	<b>Core</b>	<b>N-acetylglucosamine utilization</b>	<b>Unknown</b>
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nagA, nagB2, nagE	N-acetylglucosamine utilization
nagQ	Transcription regulation

<b>Taxonomy-specific</b>
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chiA, cdxA, cbp21, chiC, chi, hex	Chitin degradation
nagB, nagK, nagZ, nagT, nagV, nagU, nagW, nagP	N-acetylglucosamine utilization
ybfM, omp_nag, omp1	Chitobiose utilization
murQ	N-acetylmuramic acid utilization
ptsI	Sugar transport
nagR	Transcription regulation

<b>Genome-specific</b>
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nagX, nagM, nagO, nagN, nagL, nagK2	N-acetylglucosamine utilization
anaG	Alpha-N-acetylglucosaminidase

<b>NagR</b>	<b>Core</b>	<b>N-acetylglucosamine utilization</b>	<b>N-acetylglucosamine-6-phosphate</b>
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nagA, nagK, nagB, nagB2, nagP, nagX	N-acetylglucosamine utilization
hex, omp_nag	Chitobiose utilization
chiA	Chitin degradation
nagR	Transcription regulation

<b>Taxonomy-specific</b>
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nagK2	N-acetylglucosamine utilization
chiD	Chitin degradation
nixC, naxA	Chitobiose utilization
pgi2	Glycolysis
pckA	Gluconeogenesis

<b>Genome-specific</b>
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cbp, cbp2, cdxA, chiA3	Chitin degradation
nixD, nixB, nixA, omp_nag2	Chitobiose utilization
bgIX	Glucosides utilization
SO0852, SO0850, SO0854, SO0853	Fimbriae biogenesis
pdaA	N-acetylglucosamine utilization
mcp	Chemotaxis protein (toward chitin?)

<b>NrdR</b>	<b>Core</b>	<b>Deoxyribonucleotide biosynthesis</b>	<b>Deoxyribonucleotides</b>
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nrdA, nrdB, nrdD, nrdG	Deoxyribonucleotide biosynthesis
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<b>Taxonomy-specific</b>
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nrdJ, nrdH, nrdF, nrdI, nrdE	Deoxyribonucleotide biosynthesis
topA	Replication
yfaE, SO2417, trxA	Oxidoreductase

<b>NrtR</b>	<b>Core</b>	<b>NAD metabolism</b>	<b>Adenosine diphosphate ribose</b>
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nrtR	Transcription regulation
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<b>Taxonomy- and Genome-specific</b>
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pncB, pncA, nadV, nadE, nadD, nadM, nadR, pncC, prs	NAD biosynthesis; NAD salvage
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<b>NtrC</b>	<b>Core</b>	<b>Nitrogen assimilation</b>	<b>Phosphorylated NtrB</b>
	glnA	Glutamine biosynthesis	
	amtB	Nitrogen source transport	
	ntrB, glnB, glnK	Nitrogen metabolism regulation proteins	
	ntrC	Transcription regulation	
	<b>Taxonomy-specific</b>		
	dat	Proline degradation	
	narK, nrtC, nrtB, nrtA, gltJ, gltK, gltL, gltI, dppC, dppA, dppB, dppD, dppF	Nitrogen source transport	
	ntrXY	Transcription regulation	
	nasD, nasE, ntrY, ntrX, nasA, gdhA, nasBA, nasB, nifEN	Nitrogen metabolism	
	<b>Genome-specific</b>		
	ureD, ureA, ureB, ureC, ureE, ureG, ureF, ureJ, hmp, uahA, uahB, uahC, nirA, atzE	Nitrogen metabolism	
	hisQ, hisJ, hisM, glnH, glnQ, uctA, uctB, uctC, alsT, potG, potI, potH, potA, potB, potC, potD, gltB, gltD	Nitrogen source transport	
	speB, ygjG	Glutamate biosynthesis	
	astD, astB, astA, astC, astE	Putrescine metabolism	
	rutC, rutA, rutF, rutD, rutE, rutE2	Arginine degradation	
	ansA	Pyrimidine degradation	
	hmp	Asparagine degradation	
	nac, nasT, rutR	Nitrogen stress response	
		Transcription regulation	
<b>PdhR</b>	<b>Core</b>	<b>Pyruvate metabolism</b>	<b>Pyruvate</b>
	aceE, aceF, lpdA	Pyruvate utilization	
	pdhR	Transcription regulation	
	<b>Taxonomy-specific</b>		
	ndh	NAD metabolism	
	aceB, aceA	Tricarboxylic acid cycle	
	oadB, oadA, oadG	Pyruvate metabolism	
	pflA, pflB	Formate metabolism	
	<b>Genome-specific</b>		
	sdhC, gltA, sdhA, sdhD, sdhB	Tricarboxylic acid cycle	
	cyoC, cyoD, cyoB, cyoA	Electron transfer chain	
	lldP, dld	Lactate metabolism	
	ppc, grcA	Pyruvate metabolism	
	hemL, cyoE	Prophyrin biosynthesis	
	glcB, glcD, glcG, glcE, glcF	Glycolate utilization	
<b>PsrA</b>	<b>Core</b>	<b>Fatty acid degradation</b>	<b>Oleate</b>
	fadA, fadB	Fatty acid degradation	
	psrA	Transcription regulation	
	<b>Taxonomy-specific</b>		
	fadD, fadE, fadH, fadJ, fadI, fadL, acdH, echH, acdB, acdA	Fatty acid degradation	
	fabG, fabF, fabH, fabD, fabL	Fatty acid biosynthesis	
	aceA, aceB, gltA, sdhA, sdhB, sdhC, sdhD	Tricarboxylic acid cycle	
	etfD, etfA, etfB	Electron transfer chain for fatty acid degradation	
	rpoS, algQ	Transcription	
	aroQ	Aromatic amino acid biosynthesis	
	<b>Genome-specific</b>		
	ldh	Branched-chain amino acid biosynthesis	

mdh Tricarboxylic acid cycle  
 SO3908 Fatty acid degradation  
 fabK Fatty acid biosynthesis

<b>RutR</b>	<b>Core</b>	<b>Pyrimidine utilization</b>	<b>Uracil</b>
	rutB, rutA, rutC, rutD	Pyrimidine degradation	
	rutR	Transcription regulation	
	<b>Taxonomy-specific</b>		
	carA, carB	Arginine and pyrimidine biosynthesis	
	rutG, pydP	Pyrimidine transport	
	xdhC, xdhA, xdhB, guaD, gpt, xpt, deoD	Purine degradation	
	rutF, pydC, pydX, pydA, pydB, rutE, codA, upp, cdd, deoA, pucM, pucL	Pyrimidine degradation	
	pbuT, pntB, pntC, pntA, ppuD, ppuC, pntD	Nucleoside transport	
	<b>Genome-specific</b>		
	pytO, pytM, pytN, pytQ, pytC, pytB, pytA, pytD	Pyrimidine transport	
	add, allB, allA, allC, hpt, deoB	Purine degradation	
	deoC	Pyrimidine degradation	
<b>SahR</b>	<b>Core</b>	<b>Methionine metabolism</b>	<b>S-adenosyl-homocysteine</b>
	ahcY	Methionine metabolism	
	metF, metH	Methionine biosynthesis	
	sahR	Transcription regulation	
	metK	Methionine metabolism	
	<b>Taxonomy-specific</b>		
	metE, meth2	Methionine biosynthesis	
	<b>Genome-specific</b>		
	metT	Methionine transport	
	bhmT, metB, metX, hom	Methionine biosynthesis	
<b>SamR</b>	<b>All target genes</b>	<b>Methionine metabolism</b>	<b>Unknown</b>
	metE, metF2, metX2, metB, metH, hom	Methionine biosynthesis	
	samR	Transcription regulation	
	metK	SAM biosynthesis	
<b>TyrR</b>	<b>Core</b>	<b>Tyrosine metabolism</b>	<b>Tyrosine</b>
	aroF	Chorismate biosynthesis	
	tyrA	Tyrosine & Phenylalanine biosynthesis	
	phhA, phhB	Phenylalanine degradation	
	hmgB, hmgC, hpd, hmgA	Tyrosine degradation	
	tyrP	Tyrosine transporter	
	tyrR (phhR)	Transcription regulation	
	<b>Taxonomy-specific</b>		
	brnQ	Branched-chain amino acid transport	
	mdeA	Methionine degradation	
	putA	Proline degradation	
	bkdA, bkdB, ivdA, ivdB, ivdC, ivdD, ivdE, ivdF, ivdG, Idh, liuA, liuB, liuC, liuD, liuE, liuF, liuG	Branched-chain amino acid degradation	
	hmgR, liuR	Transcription regulation	
	tyrB	Tyrosine biosynthesis / Tyrosine degradation	
	aceA, aceB	Tricarboxylic acid cycle	
	aroA, aroL	Chorismate biosynthesis	

aroP	Aromatic amino acid transport
acsA	Acetyl-coenzyme A synthetase
phhC	Phenylalanine degradation
COG0733	Tyrosine transport

**Genome-specific**

aroM, aroG	Chorismate biosynthesis
kyn, tdo, ipdC	Tryptophan degradation
mtr	Tryptophan transport
tpl	Tyrosine degradation
COG2814	Tyrosine transport
folA	Tetrahydrofolate biosynthesis

<b>TrpR</b>	<b>Core</b>	<b>Tryptophan biosynthesis</b>	<b>Tryptophan</b>
	trpE	Tryptophan biosynthesis	
	trpR	Transcription regulation	
	<b>Taxonomy-specific</b>		
	aroF, aroG	Chorismate biosynthesis	
	trpG, trpB, trpC, trpA, trpD	Tryptophan biosynthesis	
	tyrA	Tyrosine biosynthesis	
	mtr, COG0733	Tryptophan transport	
	<b>Genome-specific</b>		
	aroH, aroM, aroL, aroA	Chorismate biosynthesis	
	tnaA, tnaB	Tryptophan transport and degradation	

<sup>1</sup> annotated gene functions and metabolic pathways are listed in Table S3. This table excludes functionally unassigned genes.

**Table S5. (A) Content of reconstructed TyrR (PhhR), HmgR, HmgQ, HmgS regulons for aromatic amino acid metabolism in gamma-proteobacteria.**

	TyrR	AroL	AroH	AroG	AroF	TyrA	TyrB	AroP	TyrP	Mtr	COG2814	Tpl	IpdC	TyrR regulon		
<b>Enterobacteriales</b>																
<i>Escherichia coli</i> K-12	+	+	+	+	+	+	+	+	+	+	-	-	-	-	aroF-tyrA; tyrP; tyrR; aroP; aroL-yaiA-aroM; mtr	
<i>Salmonella typhimurium</i> LT2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; tyrR; aroP; aroL-yaiA-aroM; mtr; ipdC	
<i>Citrobacter koseri</i> ATCC BAA-895	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; tyrR; aroP; aroL-yaiA-aroM; mtr; COG2814; tpl; ipdC	
<i>Klebsiella pneumoniae</i> MGH 78578	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; tyrR; aroP; aroL-yaiA-aroM; mtr; COG2814; ipdC	
<i>Enterobacter</i> sp. 638	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; tyrR; aroP; aroL-yaiA-aroM; mtr; COG2814	
<i>Erwinia amylovora</i> ATCC 49946	+	+	-	+	+	+	+	+	+	-	+	-	-	-	aroF-tyrA; tyrP; tyrR; aroP; aroL-yaiA-aroM	
<i>Yersinia pestis</i> KIM	+	+	+	+	+	+	+	+	+	+	+	+	-	-	aroF-tyrA; tyrP; aroP; aroL; COG2814	
<i>Serratia proteamaculans</i> 568	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; tyrR; aroP; aroL; COG2814	
<i>Erwinia carotovora</i> SCRI1043	+	+	+	+	+	+	+	+	+	+	+	+	-	-	aroF-tyrA; tyrP; aroP; COG2814	
<i>Edwardsiella tarda</i> EIB202	+	-	+	+	+	+	+	+	+	+	+	+	-	-	aroF-tyrA; tyrP; aroP; COG2814	
<i>Proteus mirabilis</i> H4320	+	+	+	+	+	+	+	+	+	+	+	+	-	-	aroF-tyrA; tyrP; tyrR; aroP; aroL	
<i>Photobacterium luminescens</i> TTO1	+	+	+	+	+	+	+	+	+	+	+	-	-	-	aroF-tyrA; tyrP; tyrR; aroL	
<b>Vibrionales</b>																
	TyrR	AroA	AroH	AroG	AroF	TyrA	TyrB	TyrP	COG0733	Hpd	HmgA	HmgB	HmgC	PhhAB	TyrR regulon	
<i>Vibrio cholerae</i> N16961	+	+	+	-	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; COG733; phhAB; hpd-hmgACB	
<i>Vibrio vulnificus</i> CMCP6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; COG733; phhAB; hpd-hmgACB; aroG	
<i>Vibrio harveyi</i> ATCC BAA-1116	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; COG733; phhAB; hpd-hmgACB	
<i>Vibrio parahaemolyticus</i> RIMD 2210633	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; COG733; phhAB; hpd-hmgACB; aroG	
<i>Vibrio shilonii</i> AK1	+	+	+	+	+	+	+	+	++	+	+	+	+	+	aroF-tyrA; tyrP; COG733-1, COG733-2; phhAB; hpd-hmgACB	
<i>Vibrio splendidus</i> LGP32	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; COG733; phhAB; hpd-hmgACB; tyrR; aroG	
<i>Vibrio fischeri</i> ES114	+	+	+	+	+	+	+	+	+	-	-	-	-	-	aroF-tyrA; tyrP; COG733; tyrR	
<i>Vibrio salmonicida</i> LF11238	+	+	+	+	+	+	+	+	+	-	-	-	-	-	aroF-tyrA; tyrP; COG733; tyrR	
<i>Vibrio angustum</i> S14	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; COG733; phhAB; tyrR; hmgACB	
<i>Photobacterium profundum</i> SS9	+	+	+	+	+	+	+	+	+	+	+	+	+	+	aroF-tyrA; tyrP; COG733; phhAB; hmgACB	
<b>Pasteurellales</b>																
	TyrR	AroA	AroH	AroG	AroF	TyrA	TyrB	TyrP	Mtr	Tpl	Hpd	HmgA	HmgB	HmgC	PhhAB	TyrR regulon
<i>Haemophilus influenzae</i> Rd KW20	+	-	-	+	+	+	+	+	+	-	-	-	-	-	-	tyrA; tyrR
<i>Aggregatibacter aphrophilus</i> NJ8700	+	-	-	-	+	+	+	+	+	+	+	-	-	-	-	tyrR; tpl
<i>Pasteurella multocida</i> Pm70	+	-	+	+	+	+	+	+	+	+	+	-	-	-	-	aroF-tyrA; tyrP2; tyrR; tpl
<i>Mannheimia succiniciproducens</i> MBEL55E	+	-	+	+	+	+	+	+	+	+	+	-	-	-	-	aroF-tyrA; tyrP2; tyrR
<i>Actinobacillus succinogenes</i> 1302	+	-	+	+	+	+	+	+	+	+	+	-	-	-	-	aroF-tyrA; tyrR
<i>Haemophilus somnus</i> 2336	+	-	+	-	+	+	+	+	+	-	-	-	-	-	-	tyrA; tyrP1
<i>Actinobacillus pleuropneumoniae</i> AP76	+	-	+	+	+	+	+	++	+	-	-	-	-	-	-	aroF-tyrA; tyrP1-tyrP2; tyrR
<i>Haemophilus ducreyi</i> 35000HP	+	-	-	+	+	+	-	+	-	-	-	-	-	-	-	aroF; tyrR
<i>Haemophilus parasuis</i> SH0165	+	-	-	+	+	+	++	-	-	-	-	-	-	-	-	aroF-tyrA; tyrP1; tyrP2; tyrR
<b>Shewanellaceae</b>																
	TyrR	AroA	AroH	AroG	AroF	TyrA	TyrB	TyrP	IpdC	Hpd	HmgA	HmgB	HmgC	PhhAB	Tdo-kyn	TyrR; HmgQ regulon
<i>Shewanella oneidensis</i> MR-1	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; tdo-kyn; hmgA-hpd; hmgQ
<i>Shewanella putrefaciens</i> CN-32	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; tdo-kyn; hmgA-hpd; hmgQ
<i>Shewanella</i> sp W3-18-1	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; tdo-kyn; hmgA-hpd; hmgQ
<i>Shewanella</i> sp ANA-3	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; tdo-kyn; hmgA-hpd; hmgQ
<i>Shewanella</i> sp MR-4	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; tdo-kyn; hmgA-hpd; hmgQ
<i>Shewanella</i> sp MR-7	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; tdo-kyn; hmgA-hpd; hmgQ
<i>Shewanella baltica</i> OS155	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; tdo-kyn; hmgA-hpd; hmgQ
<i>Shewanella denitrificans</i> OS217	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; tdo-kyn; ipdC; hmgA-hpd; hmgQ
<i>Shewanella frigidimarina</i> NCIMB 400	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	tyrR; phhAB; hmgCB; aroA; tyrB; hmgA-hpd; hmgQ
<i>Shewanella amazonensis</i> SB28	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; ipdC; hmgA-hpd; hmgQ
<i>Shewanella loihica</i> PV-4	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; ipdC; hmgA-hpd; hmgQ
<i>Shewanella pealeana</i> ATCC 700345	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; aroA; tyrB; hmgA-hpd; hmgQ
<i>Shewanella halifaxensis</i> HAW-EB4	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	tyrR; phhAB; hmgCB; tyrB; hmgA-hpd; hmgQ
<i>Shewanella piezotolerans</i> WP3	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	tyrR; phhAB; hmgCB; tyrB; hmgA-hpd; hmgQ
<i>Shewanella sediminis</i> HAW-EB3	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	tyrR; phhAB; hmgCB; aroA; tyrB; ipdC; hpd; hmgQ
<i>Shewanella woodyi</i> ATCC 51908	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	tyrR; phhAB; hmgCB; aroA; tyrB; hpd; hmgQ
<b>Alteromonadales</b>																
	TyrR	AroL	AroH	AroG	AroF	TyrA	TyrB	TyrP	Hpd	HmgA	HmgB	HmgC	PhhAB	TyrR1 regulon; HmgS regulon		
<i>Pseudoalteromonas atlantica</i> T6c	+	-	-	-	+	+	-	-	+	+	+	+	+	tyrR; phhA; aroF-tyrA; hpd		
<i>Alteromonas macleodii</i> 'Deep ecotype'	+	-	-	-	+	+	-	-	-	+	+	+	+	tyrR; phhA; aroF-tyrA		
<i>Glaciecola</i> sp. HTC2999	+	-	-	-	+	+	-	-	-	-	-	-	-	tyrR; aroF-tyrA		
<i>Colwellia psychrerythraea</i> 34H	+	-	-	-	+	+	-	-	-	-	+	+	+	tyrR; phhA; aroF-tyrA		
<i>Alteromonadales bacterium</i> TW-7	+	-	-	-	+	+	-	-	-	+	+	+	+	tyrR; phhAB; tyrA; tyrP; hmgAB		
<i>Pseudoalteromonas haloplanktis</i> TAC125	+	-	-	-	+	+	-	-	-	+	+	+	+	tyrR; phhAB; tyrA; tyrP; hmgAB		
<i>Pseudoalteromonas tunicata</i> D2	+	-	-	-	+	+	-	-	-	+	+	+	+	tyrR; phhAB; tyrA; tyrP; hmgAB		
<i>Idiomarina baltica</i> OS145	+	-	-	-	+	+	-	-	-	+	+	+	+	tyrR2; mdeA-phhAB; hpd-hmgACB		
<i>Idiomarina loihiensis</i> L2TR	+	-	-	-	+	+	-	-	-	+	+	+	+	mdeA-phhAB-tyrR2; hpd-hmgACB		
<b>Psychromonadaceae/Aeromonadales</b>																
	TyrR	AroL	AroH	AroG	AroF	TyrA	TyrB	TyrP	Hpd	HmgA	HmgB	HmgC	PhhAB	TyrR regulon		

Psychromonas spp. (2 genomes)	-															
Moritella sp. PE36	+				+	+	+	+								tyrR; tyrP
Aeromonas hydrophila ATCC 7966	+			+	+	+	+	+	+	+	+	+	+			aroF-tyrA; phhAB; aroG; hpd-hmgACB
Aeromonas salmonicida A449	+			+	+	+	+	+	+	+	+	+	+			aroF-tyrA; phhAB; aroG; hpd-hmgACB
Tolomonas auensis DSM 9187	+			+	+	+	+									aroF-tyrA
<b>Oceanospirillales/Alteromonadales</b>	<b>TyrR</b>	AroL	AroH	AroG	AroF	TyrA	TyrB		Hpd	HmgA	HmgB	HmgC	PhhAB			No TyrR regulon
Hahella chejuensis KCTC 2396	-															
Marinobacter aqueolei	-															
Marinobacter sp. ELB17	-															
Oceanobacter sp. RED65	-															
Oceanospirillum sp. MED92	-															
Marinomonas sp. MWYL1	-															
Saccharophagus degradans 2-40	-															
Teredinibacter turnerae T7901	-															
Cellvibrio japonicus Ueda107	-															
Chromohalobacter salexigens DSM 3043	-															
Reinekea sp. MED297	-															
Alcanivorax borkumensis SK2	-															
<b>Pseudomonadaceae</b>	<b>PhhR</b>	AroL	AroH	AroG	AroF	TyrA	TyrB	COG2814 COG0733	Hpd	HmgA	HmgB	HmgC	PhhAB			<b>PhhR (TyrR) regulon; HmgR regulon; HmgQ regulon</b>
Pseudomonas aeruginosa PAO1	+							+	+	+	+	+	+			phhR; phhABC; hpd; hmgACB-COG2814; hmgR
Pseudomonas entomophila L48	+							+	+	+	+	+	+			phhR; phhABC; hmgACB-COG2814; hmgR
Pseudomonas putida KT2440	+							+	+	+	+	+	+			phhR; phhABC; hmgACB; hmgR
Pseudomonas syringae DC3000	+							+	+	+	+	+	+			phhR; phhABC; hmgAC; hmgB-hpd; hmgR
Pseudomonas fluorescens Pf-5	+							+	+	+	+	+	+			phhR; phhABC; hmgACB-COG2814; hmgR
Pseudomonas mendocina ymp	+							+	+	+	+	+	+			phhR; phhABC; hpd-hmgACB-COG733
Pseudomonas stutzeri A1501	+							+	+	+	+	+	+			phhR; phhABC; hpd-hmgACB-COG733
Azotobacter vinelandii AvOP	-							+	+*	+	+	+	+			hmgQ; hpd-gloA-hmgCB
<b>Moraxellaceae</b>	<b>TyrR</b>	AroL	AroH	AroG	AroF	TyrA	TyrB		Hpd	HmgA	HmgB	HmgC	PhhAB			No TyrR regulon
Acinetobacter sp. ADP1	-															
Acinetobacter baumannii AB0057	-															
Psychrobacter arcticum 273-4	-															
Psychrobacter sp. PRwf-1	-															
<b>Xanthomonadales</b>	<b>TyrR</b>	AroL	AroH	AroG	AroF	TyrA	TyrB		Hpd	HmgA	HmgB	HmgC	PhhAB			No TyrR regulon
Xylella fastidiosa 9a5c	-															
Xanthomonas axonopodis 306	-															
Xanthomonas campestris ATCC 33913	-															
Stenotrophomonas maltophilia K279a	-															

The presence or absence of gene orthologs is shown by +/- signs. Colored '+' signs (red, purple, green, blue) indicate that the gene belongs to TyrR(PhhR), HmgR, HmgQ, HmgS regulons, respectively.

Last column shows the list of all corresponding operons from reconstructed regulons. Additional members of TyrR regulons that are not involved in aromatic amino acid metabolism are not included.

Color code for genes in the table:

- TyrR (PhhR) regulator gene
- Chorismate biosynthesis genes
- Tyr biosynthesis pathway genes
- Tyr transporter genes
- Tyr degradation genes