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Polynucleotide Phosphorylase Activity May Be Modulated by Metabolites in *Escherichia coli**[S]◆

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RNA turnover is an essential element of cellular homeostasis and response to environmental change. Whether the ribonucleases that mediate RNA turnover can respond to cellular metabolic status is an unresolved question. Here we present evidence that the Krebs cycle metabolite citrate affects the activity of *Escherichia coli* polynucleotide phosphorylase (PNPase) and, conversely, that cellular metabolism is affected widely by PNPase activity. An *E. coli* strain that requires PNPase for viability has suppressed growth in the presence of increased citrate concentration. Transcriptome analysis reveals a PNPase-mediated response to citrate, and PNPase deletion broadly impacts on the metabolome. *In vitro*, citrate directly binds and modulates PNPase activity, as predicted by crystallographic data. Binding of metal-chelated citrate in the active site at physiological concentrations appears to inhibit enzyme activity. However, metal-free citrate is bound at a vestigial active site, where it stimulates PNPase activity. Mutagenesis data confirmed a potential role of this vestigial site as an allosteric binding pocket that recognizes metal-free citrate. Collectively, these findings suggest that RNA degradative pathways communicate with central metabolism. This communication appears to be part of a feedback network that may contribute to global regulation of metabolism and cellular energy efficiency.

Ribonucleases play key roles in post-transcriptional regulation of gene expression in organisms from all domains of life. One well studied ribonuclease is polynucleotide phosphorylase (PNPase; E.C. 2.7.7.8),[3] a phosphorolytic exoribonuclease found in most bacteria as well as the eukaryotic organelles, the mitochondrion, and chloroplast (1, 2). In bacterial species PNPase affects complex processes, such as tissue invasive virulence of *Salmonella enterica* (3, 4) and the regulation of virulence secretion systems in *Yersinia* sp. (5). In *Escherichia coli*, PNPase contributes to the decay of bulk RNA, the quality control of ribosomal RNA, the turnover of small regulatory RNA, and cold shock response (1, 6–13).

A proportion of cellular PNPase is recruited into an RNA degrading machine, known as the degradosome, in *E. coli* and other γ-proteobacteria (14, 15). The degradosome is assembled upon an extensive scaffolding domain of the endoribonuclease RNase E (EC 3.1.26.12) (14, 16, 17); its other canonical components are the ATP-dependent DEAD-box RNA helicase RhlB (EC 3.6.4.13) and the glycolytic enzyme enolase (EC 4.2.1.11) (14, 15, 18). Small regions in the RNase E C-terminal domain mediate interactions with RNA (16) and with the cytoplasmic membrane to localize the degradosome assembly (19). This multienzyme complex provides a major contribution to RNA decay and, consequently, post-transcriptional gene regulation (20, 21).

Previous observations have hinted at a connection between RNA degradosome activity and central metabolism. The physical association of enolase, a glycolytic enzyme, with RNase E in the degradosome is required for response to phosphosugar stress (22). The importance of this interaction is highlighted by the observation that the recognition site for enolase is highly conserved in RNase E of γ-proteobacteria (23, 24). We have recently identified the Krebs cycle aconitase as a component of the RNase E-mediated RNA degradosome from *Caulobacter crescentus* (25). Although the Gram-positive bacterium *Bacillus subtilis* lacks an RNase E homologue, it has a functionally analogous ribonuclease (RNase J) that also interacts with glycolytic enzymes (26). The recurrence of stable interactions between ribonucleases and metabolic enzymes illustrates a remarkable evolutionary convergence that implies an important contribution of the interaction for organism fitness. Furthermore, the *E. coli* degradosome affects the abundance of transcripts encoding enzymes of central metabolism (20). Also suggestive of a link between RNA degradation and metabolism is the finding that PNPase activity can be regulated by nucleotides. *In vitro*, *E. coli* PNPase is allosterically inhibited by ATP (27), and its homologues from *Nonomuraea sp.* and *Streptomyces* are inhibited by the signaling molecule (p)ppGpp (28, 29). Although these observations implicate a communication between RNA degradative machines and central metabolism, evidence of such a linkage is missing.

Our earlier crystallographic studies of *E. coli* PNPase revealed the presence of citrate, originating from the crystallization buffer, at both the active site and at a "vestigial" active site,

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◆ This article was selected as a Paper of the Week.

[S] The on-line version of this article (available at http://www.jbc.org) contains supplemental Tables S1–S4 and Figs. S1–S4.

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[3] The abbreviations used are: PNPase, polynucleotide phosphorylase; PLS-DA, partial least squares-discriminant analysis.

which is related to the former through approximate molecular symmetry (30). These observations led us to explore whether citrate can affect the activity of *E. coli* PNPase *in vivo* and *in vitro*. Our data show that citrate influences PNPase activity in physiologically relevant concentration ranges. Our data also identify the vestigial active site of PNPase as a potential allosteric pocket that responds to metal-free citrate. Based on these findings, we propose a communication mechanism with feedback between RNA metabolism and central metabolism.

EXPERIMENTAL PROCEDURES

Ribonuclease Mutant Strain Growth Rate and Microarray Analyses

Ribonuclease null strains were provided by M. P. Deutscher (University of Miami). MG1655* I^- (Δ*rna*) in which the frameshift in the *rph* gene has been corrected was used as a parental control for the ribonuclease null strains; we will refer to this as wild-type throughout. MG1655* I^- (Δ*rna*), MG1655* I^- PNP^- (Δ*rna* Δ*pnp::kan* Kan^R), a PNPase null strain, and MG1655* I^- II^- R^- (Δ*rna* Δ*rnb::Tn10* Δ*rnr::kan* Tet^RKan^R), a RNase II/RNase R double null strain, were grown at 37 °C in M9-glucose in the presence or absence of 50 mM magnesium chloride, 50 mM sodium citrate. Doubling times were calculated from A_{600} measurements taken at 10-min intervals.

For global transcript analysis by microarray, wild-type MG1655* I^- (Δ*rna*) and PNPase null MG1655* I^- PNP^- (Δ*rna* Δ*pnp::kan* Kan^R) strains were grown at 37 °C in M9-glucose to mid-exponential phase (A_{600} = 0.5–0.6). Cells were then grown at 37 °C for a further 30 min in the presence or absence of 50 mM magnesium chloride, 50 mM sodium citrate. Total RNA was extracted using the RNeasy RNA extraction kit (Qiagen) and analyzed using microarrays by Oxford Gene Technology, Oxford, UK.

Relative mRNA abundances were determined for the following experimental groups: (i) genes in the wild-type strain, MG1655* I^-, in the presence of citrate compared with the absence of citrate, (ii) genes in the PNPase null strain, MG1655* I^- PNP^-, in the presence of citrate compared with the absence of citrate, and (iii) genes in the wild-type strain in the absence of citrate compared with the PNPase null strain in the absence of citrate. Only gene probes for which the raw intensity was greater than 100 were considered. Genes displaying a PNPase-mediated response to citrate were identified as those for which the effect of citrate was different by 2-fold or more in the PNPase null strain compared with the wild-type strain. Genes generally affected by PNPase were identified as those for which the relative mRNA abundance in the PNPase null was different by 2-fold or more relative to the wild-type strain. Gene Ontology terms as defined by the Gene Ontology website were assigned to each gene. The distribution among the Gene Ontology terms was compared for the genes displaying a PNPase-mediate response to citrate and those affected generally by PNPase.

Metabolome Analyses

Cells, Growth Conditions, and Sample Extraction—E. coli MC1061-derivative strains including PNPase parent, SVK29 (*pnp* null strain), AC21 (RNase E-parent), and AC27 (RNase E lacking the last 477 residues from the C-terminal degradosome-scaffolding domain, *i.e.* a degradosome null strain) (31, 32) were provided by A. J. Carpousis (CNRS, Toulouse, France) and have a Tn10 marker linked to the *rne* allele. Strains were cultured at 37 °C in LB + antibiotic to an $A_{600} \sim 1$ and then harvested by centrifugation at 4200 × *g* at 4 °C for 20 min. Samples were recovered and stored at −80 °C. Metabolite samples were extracted using a methanol-chloroform method (33) to generate dried cell extract of the aqueous metabolites.

Metabolite Measurements by ^1H Nuclear Magnetic Resonance (NMR) Spectroscopy and Gas Phase Chromatography Mass Spectrometry (GC-MS)—Spectra were collected using a Bruker 500 MHz NMR spectrometer interfaced with a 5 mm TXI probe and processed using the ACD Labs one-dimensional NMR processor (ACD, Toronto, Canada) as previously described (34, 35). Dried aqueous extracts were derivatized before GC-MS as previously described (33). SIMCA-*p* + v.11.0 (Umetrics) was used for multivariate analysis. Data were processed using principal components analysis and partial least squares-discriminant analysis (PLS-DA). Details of these procedures are provided in the supplementary information.

Expression and Purification of PNPase Core

E. coli PNPase ΔKΔH1 (PNPase core) (36) was expressed using the auto-induction method (37) and purified as described previously (30).

Cloning, Overexpression, and Purification of PNPase and PNPase (R153A,R372A,R405A,R409A) Mutant

The *pnp* gene was generated by restriction digestion with NcoI and NotI from the pETDuet-1-*pnp-enol* (38). The pETDuet-1-*pnp* vector was constructed by subcloning the fragment of *pnp* bounded by NcoI and NotI into the multiple cloning site of expression vector pETDuet-1. The Arg-153 → Ala, Arg-372 → Ala, Arg-405 → Ala, and Arg-409 → Ala mutations were introduced into *pnp* using the QuikChange® site-directed mutagenesis method (Stratagene) with PCR primers PNPR153A_fw (5′-CCC GAT TGG TGC TGC CGC CGT AGG TTA CAT CAA T-3′) and PNPR153A_rev (5′-ATT GAT GTA ACC TAC GGC GGC AGC ACC AAT CGG G-3′), PNPR372A_fw (5′-CTT GAT GAA CTG ATG GGC GAA GCT ACC GAT ACC TTC CT-3′) and PNPR372A_rev (5′-AGG AAG GTA TCG GTA GCT TCG CCC ATC AGT TCA TCA AG-3′), and PNPR405A_R409A_fw (5′-GAA ATT GGT CAC GGT GCT CTG GCG AAG GCC GGC GTG C-3′) and PNPR405A_R409A_rev (5′-GCA CGC CGG CCT TCG CCA GAG CAC CGT GAC CAA TTT C-3′. The construct pETDuet-1-*pnp* was used as template for the site-directed mutagenesis experiments. The resulting construct pETDuet-*pnp(R153A,R372A,R405A,R409A)* was transformed into *E. coli* strain Rosetta (DE3). Cells were grown in an orbital shaker at 37 °C until the culture reached an absorbance at 600 nm of 0.5–0.6 and were then induced by the addition of 0.5 mM isopropyl 1-thio-β-D-galactopyranoside at 20 °C overnight. The cells were harvested by centrifugation, resuspended in lysis buffer (20 mM Tris, pH 8.0, 150 mM NaCl, 5 mM $MgCl_2$, 5 units/ml DNase I, 1 tablet/50 ml protease inhibitor mixture tablet), and lysed using a high pressure homogenizer (Emulsiflex). Cellular debris was removed by centrifugation at 31,500 rpm (SW32 Ti) for 30 min at 4 °C. PNPase(*R153A*, *R372A*, *R405A*, *R409A*) was precipitated from the supernatant by adding $(NH_4)_2SO_4$ to 51.3% saturation. The mixture was rotated at 4 °C for 1 h, and the pellet was collected by centrifugation at 22,000 rpm (SW32 Ti) for 20 min at 4 °C. The pellet was resuspended in buffer A (20 mM Tris pH 8.5, 30 mM NaCl, 5 mM $MgCl_2$, 5 mM DTT) and dialyzed against buffer A overnight. Sample was then loaded onto a HiTrap Q HP column and eluted with a linear gradient from 0 to 100% of the buffer A supplemented with 1 M NaCl. The fractions containing PNPase(*R153A*,*R372A*,*R405A*,*R409A*) were pooled, concentrated, and loaded onto a Sephacryl^{TM} S500 HR XK 16/70 prep grade column equilibrated with GF buffer (20 mM Tris, pH 8.0,150 mM NaCl, 5 mM $MgCl_2$). Fractions containing purified PNPase(*R153A*,*R372A*,*R405A*,*R409A*) mutant protein were pooled and concentrated using a VIVA Spin column (molecular weight cutoff = 30 kDa). The PNPase parent was overexpressed and purified using the same procedure.

PNPase Activity Assays

Degradation Assay—The assay mix contained 0.05 mM poly(rA) 15-mer RNA, 10 mM $MnSO_4$ or $MgCl_2$, 10 mM phosphate, 20 mM Tris, pH 7.5, and 2 μM PNPase core with 0–20 mM sodium citrate. Assay samples were quenched with an equal volume of 200 mM EDTA at time 0 and 2 min after the addition of PNPase core. Assay samples (5 μl) were analyzed for RNA degradation by ion exchange HPLC (Dionex DNAPac 200 column, 25 °C, 0–1 M NaCl gradient in 20 mM Tris buffer pH 8.0 run over 8 min at 1 ml/min). Chromatograms were processed and analyzed in Dionex Chromeleon software.

Polymerization Assays—The assay mix contained 6.25 μM poly(rA) 15-mer RNA, 1 mM ADP, 20 mM Tris, pH 7.5, 1 mM $MgCl_2$ or 1 mM $MnSO_4$, 0–20 mM sodium citrate, and 2 μM PNPase. Five μl were quenched with an equal volume of 200 mM EDTA at time 0 and 1 min after the addition of PNPase core. Assay samples (5 μl) were analyzed for RNA polymerization by HPLC using the same conditions as for the degradation assay.

RESULTS

Citrate Affects PNPase Activity in Vivo—Whether PNPase activity is repressed by a metabolite *in vivo* can be evaluated by examining the impact of that metabolite on a strain that requires PNPase for viability. PNPase is essential in *E. coli* in the absence of either of the two other processive exoribonucleases, RNase II (39, 40) or RNase R (8, 41). A strain lacking RNase II and RNase R together is anticipated to be sensitive to the inhibition of PNPase activity because the double null mutants PNPase/RNase II (39, 40) and PNPase/RNase R (8, 41) are both inviable.

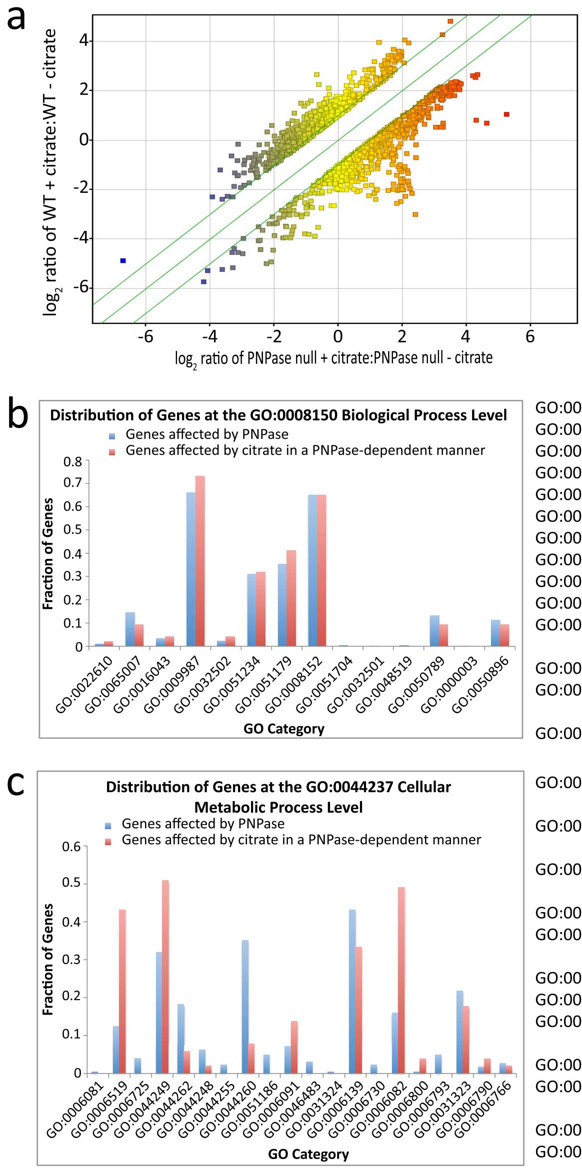
Within 30 min of adding magnesium-citrate to the culture medium, intracellular citrate levels increase significantly (supplemental Table S1). We observed that in the presence of 50 mM magnesium-citrate, an RNase II/RNase R double null mutant grew with a doubling time of 59.4 ± 3.2 min, compared with a doubling time of 49.0 ± 2.3 min in the absence of magnesium-citrate. In contrast, a PNPase null strain grew with similar doubling times in the presence and absence of 50 mM magnesium-citrate (53.5 ± 2.2 min in the presence of magnesium-citrate and 54.3 ± 2.6 min in the absence of magnesium-citrate). These observations suggest that magnesium-citrate has a negative effect on an RNase II/RNase R double mutant, probably through inhibition of PNPase, which is required for viability in this strain. The parental strain was also insensitive to exogenously added magnesium-citrate, growing with a doubling time of 49.2 ± 1.9 min in the presence of 50 mM magnesium-citrate and a doubling time of 48.7 ± 2.6 min in its absence. This was not unexpected as this strain contains both RNases II and R, which could compensate for any loss in PNPase activity (8, 39–41).

Identification of Transcripts Impacted by PNPase-mediated Citrate Response—To identify transcripts that may be affected in a PNPase-mediated response to magnesium-citrate, we utilized gene expression microarray analyses. Comparison of the relative abundance of mRNAs revealed that 126 genes respond differently upon the addition of magnesium-citrate to the growth media in the parental strain compared with the PNPase null strain (Fig. 1*a*). Of those genes, roughly half were also sensitive to a loss of PNPase alone (the mRNA level of 655 genes was altered in the PNPase null strain relative to the parental strain grown on normal media), whereas the remaining portion was uniquely affected, suggesting an additional level of gene regulation by PNPase in response to magnesium-citrate.

The affected genes were clustered based on gene ontology (supplemental Table S2, a and b). The broad groups of functionally clustered genes that are affected by PNPase loss are similarly affected by the PNPase-mediated magnesium-citrate response (Fig. 1*b*). Closer inspection of the sub-groupings indicate that the PNPase-mediated magnesium-citrate response specifically affects transcripts of enzymes involved in processes of amino acid and derivative metabolism, cellular biosynthesis, and organic acid metabolism (Fig. 1*c*).

The relative abundance of *cirA*, *fkpA*, *gdhA*, and *rpoB* mRNAs in the PNPase null and wild-type strains in the presence of magnesium-citrate were explored by quantitative RT-PCR after rifampicin treatment to inhibit transcription. *cirA* and *fkpA* have previously been reported to be regulated by PNPase (10, 20). These transcripts were affected in a PNPase-mediated magnesium-citrate response in both our quantitative RT-PCR (supplemental Table S3) and microarray analyses. In contrast, the *gdhA* and *rpoB* transcripts were not significantly affected by a PNPase-mediated magnesium-citrate response by either quantitative RT-PCR (supplemental Table S3) or microarray. There are conflicting reports in the literature as to whether *gdhA* and *rpoB* transcripts are affected (20) or unaffected (10) by the absence of PNPase. Nonetheless, our results support the hypothesis that PNPase is involved either directly or indirectly in the response to changes in magnesium-citrate concentration *in vivo*.

PNPase Impacts the Metabolome—Having shown that the metabolite citrate may affect PNPase activity *in vivo*, we next investigated whether PNPase activity levels influence the cellular metabolome. Such an influence would enable a feedback loop that may regulate metabolite levels through their reciprocal impact on PNPase activity. Metabolite concentrations for a



GO:0022610	Biological adhesion
GO:0065007	Biological regulation
GO:0016043	Cellular component organization
GO:0009987	Cellular process
GO:0032502	Developmental process
GO:0051234	Establishment of localization
GO:0051179	Localization
GO:0008152	Metabolic process
GO:0051704	Multi-organism process
GO:0032501	Multicellular organismal process
GO:0048519	Negative regulation of biological process
GO:0050789	Regulation of biological process
GO:0000003	RNA splicing via endonucleolytic cleavage and ligation
GO:0050896	Response to stimulus

GO:0006081	Cellular aldehyde metabolic process
GO:0006519	Cellular amino acid and derivative metabolic process
GO:0006725	Cellular aromatic compound metabolic process
GO:0044249	Cellular biosynthetic process
GO:0044262	Cellular carbohydrate metabolic process
GO:0044248	Cellular catabolic process
GO:0044255	Cellular lipid metabolic process
GO:0044260	Cellular macromolecule metabolic process
GO:0051186	Cofactor metabolic process
GO:0006091	Generation of precursor metabolites and energy
GO:0046483	Heterocycle metabolic process
GO:0031324	Negative regulation of cellular metabolic process
GO:0006139	Nucleobase, nucleoside, nucleotide and nucleic acid metabolic process
GO:0006730	One-carbon metabolic process
GO:0006082	Organic acid metabolic process
GO:0006800	Oxygen and reactive oxygen species metabolic process
GO:0006793	Phosphorus metabolic process
GO:0031323	Regulation of cellular metablic process
GO:0006790	Sulfur metabolic process
GO:0006766	Vitamin metabolic process

FIGURE 1. **The impact of citrate on global gene expression.** *a*, genes affected by citrate in a PNPase-dependent manner are shown. A plot of the log$_2$ ratios for signal intensity for microarray probes in the presence of citrate relative to the absence of citrate for the wild-type strain *versus* the PNPase null strain is shown. This reflects the impact of citrate treatment on the relative mRNA abundance for the wild-type strain compared with the PNPase null mutant. Only shown are probes for which the relative abundance differs by 2-fold or more between the wild-type and PNPase null strain upon treatment with citrate. A single mRNA can be represented by multiple microarray probes. The data points are colored according to the *x* axis value (*blue* is negative, and *red* is positive) to aid visualization of individual points. *b*, the PNPase-mediated citrate response and PNPase ablation have a similar impact on gene expression. Genes affected by PNPase were determined by comparing the relative mRNA abundances that differ 2-fold or greater for the wild-type strain and a PNPase null strain in the absence of citrate. Genes affected by PNPase-mediated citrate response were determined as described in *a*. Groupings were made by Gene Ontology at the level of GO:0008150 Biological Process. *c*, PNPase-mediated citrate response broadly affects genes involved in cellular metabolic processes. Genes were grouped by Gene Ontology at the level of GO:0044237 Cellular Metabolic Process. In comparison to the genes that are affected by PNPase activity, those genes affected by citrate in a PNPase-dependent manner are involved more specifically with cellular amino acid and derivative metabolic processes, cellular biosynthetic processes, and organic acid metabolic processes than carbohydrate metabolic processes and cellular macromolecule metabolic processes.

PNPase null strain and the parental strain were determined by ^{1}H NMR spectroscopy and gas chromatography mass spectrometry. Many metabolites throughout central metabolism are affected by the loss of PNPase (supplemental Fig. S1). Notably, the Krebs cycle metabolite succinate decreases, whereas citrate concentrations increase, the latter possibly reflecting the disruption of a feedback loop.

Metabolite concentrations were also examined in a strain for which PNPase activity is uncoupled from the degradosome through the deletion of the C-terminal degradosome-scaffold-

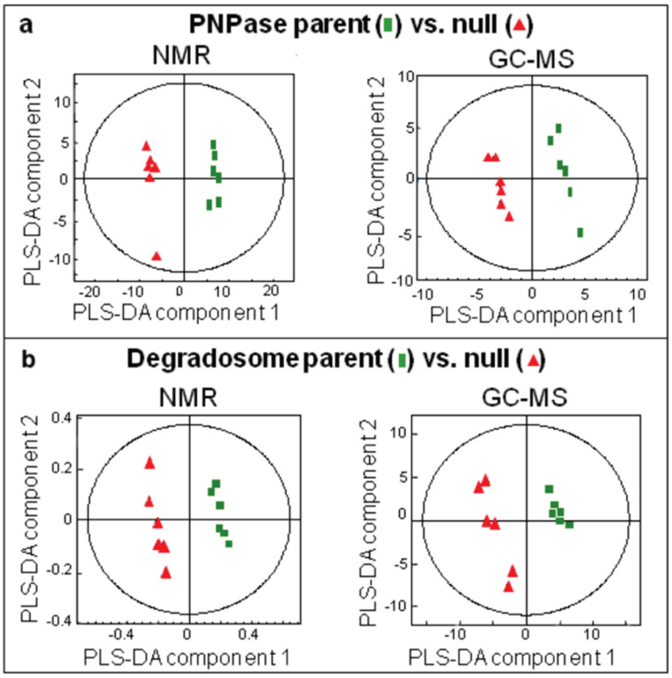


FIGURE 2. **Impact of PNPase and the degradosome on metabolism.** *a*, projection maps of the effects of PNPase deficiency on metabolic profiles with PLS-DA scores generated from PNPase parent (■) and null (▲) strains. A combination of high resolution ^{1}H NMR spectroscopy and GC-MS were used to provide coverage of the *E. coli* aqueous endometabolome. The distribution of extracted metabolites was analyzed by principal component analysis to examine the variation of metabolite concentration and composition within the dataset and PLS-DA to identify significant metabolite differences between the PNPase null and parental strains. The graph represents a two-dimensional projection map of PLS-DA scores generated from the multivariate analysis of the aqueous metabolites extracted from the respective parent (■) and null (▲) strains. This multivariate statistical technique correlates variables (metabolites or integral regions) with PLS-DA component 1, representing the dominant trend in the dataset, and PLS-DA component 2, representing the second largest amount of variation in the data. Each data point represents the pool of metabolites in each sample; the experiments were repeated six times. Plots are shown for extracts from cells grown in LB medium and analyzed by NMR (*left panel*) or GC-MS (*right panel*). R^2 and Q^2 values are 58 and 95% (NMR) and 46 and 84% (GC-MS), respectively. Typically a $Q^2 > 40\%$, calculated by cross-validation of every sixth sample iteratively, is indicative of a robust and predictive model. *b*, the degradosome affects on metabolism are shown. A projection map of the effects of degradosome deficiency on metabolic profiles is shown. PLS-DA scores plots were generated from the multivariate analysis of the aqueous metabolites extracted from the parent strain (■) and the degradosome deficient derivative (▲). Plots are shown for extracts from cells grown in LB medium and analyzed by NMR (*left panel*) or GC-MS (*right panel*). R^2 and Q^2 values are 47% and 95% (NMR) and 41%, 82% (GC-MS), respectively.

ing domain of RNase E (degradosome null). Compared with the parental strain, significant differences are distributed across many metabolic pathways, including the Krebs cycle, amino acid synthesis, and glycolysis (supplemental Table S4). Salient differences are seen for amino acids and increases in the concentrations of succinate, fumarate, and malate, suggesting uncoupling of the two halves of the Krebs cycle (supplemental Fig. S2).

The distribution of extracted metabolites may be represented graphically using principal components analysis to examine the variation of metabolite concentration and composition within the dataset and PLS-DA to identify significant metabolite differences between the null and parental strains. The projection maps in Fig. 2 are two-dimensional graphs of the dominant variations in the first two components of the PLS-DA scores. These representations show that it is possible to distinguish on the basis of metabolite distributions the PNPase null from the parental strain (Fig. 2*a*) as well as the degradosome null and its parent (Fig. 2*b*).

Collectively, these findings suggest that PNPase and the degradosome have a wide-ranging impact on metabolism. In contrast, mutants lacking single enzymes of central metabolism are reported to have small metabolome changes due to re-routing of metabolic fluxes (42). The more global effects of RNA degradative machines on metabolism suggest that they potentially contribute to robust metabolic regulation.

Citrate Affects PNPase Activity in Vitro—The mechanism of communication between the metabolite citrate and PNPase could be indirect, direct, or a combination of both effects. We next sought to investigate if citrate can interact physically with PNPase and modulate its activity *in vitro*. We tested the impact of both free citrate and magnesium-citrate as *in vivo* citrate can exist in free- and magnesium-chelated forms.

We first tested whether citrate can bind directly at physiologically relevant concentrations to PNPase. Interaction of magnesium-citrate with PNPase could be detected using surface plasmon resonance, and the K_D was determined to be in the low mM range (supplemental Fig. S3a). This is in the same concentration range as our observed intracellular citrate concentrations for *E. coli* grown in minimal media (supplemental Table S1) and values previously reported (43) (1.2–4.4 mM in minimal media with glucose or glycerol as carbon source, increasing to 22 mM in acetate minimal media). The affinity of PNPase for free citrate is roughly 10-fold lower than the affinity for magnesium-citrate (supplemental Fig. S3b). It is possible that free citrate and magnesium-citrate bind PNPase at the same site with magnesium, significantly enhancing the interaction. Alternatively, the free citrate and magnesium-citrate may bind at distinct sites; from recent structural data, this appears to be the case (see below and PDB code 3GCM; Ref. 30).

Having demonstrated that citrate can bind directly to PNPase at physiological concentrations, we next investigated its effect on PNPase activity. Degradation of RNA by PNPase *in vitro* requires inorganic phosphate and the presence of divalent metal cation as a co-factor with 10 mM Mg^{2+} being optimal. In the presence of mM concentrations of citrate, conditions in which the citrate would be predominantly complexed as magnesium-citrate given the Mg^{2+} concentration, the degradative activity of PNPase is inhibited (Fig. 3, *a* and *b*). The observed inhibition was not solely due to loss of available metal co-factor, as citrate remains inhibitory in the presence of Mg^{2+} in a 2-fold excess over citrate (Fig. supplemental Fig. S4*b*; degradation is inhibited in the presence of 5 mM citrate, 10 mM Mg^{2+}). Furthermore, manganese can substitute for magnesium as the catalytic metal in PNPase, and RNA degradation was unaffected in the presence of mM concentrations of manganese and citrate. This suggests that the inhibition seen with magnesium-citrate requires a specific ligand geometry and is not due simply to sequestering the required metal cofactor (Fig. 3*b*).

In addition to its degradative role, PNPase can also function as a polymerase, adding 3′ tails to transcripts (1, 12). This reaction is the reverse of degradation and is favored when nucleoside diphosphate rather than inorganic phosphate is present in

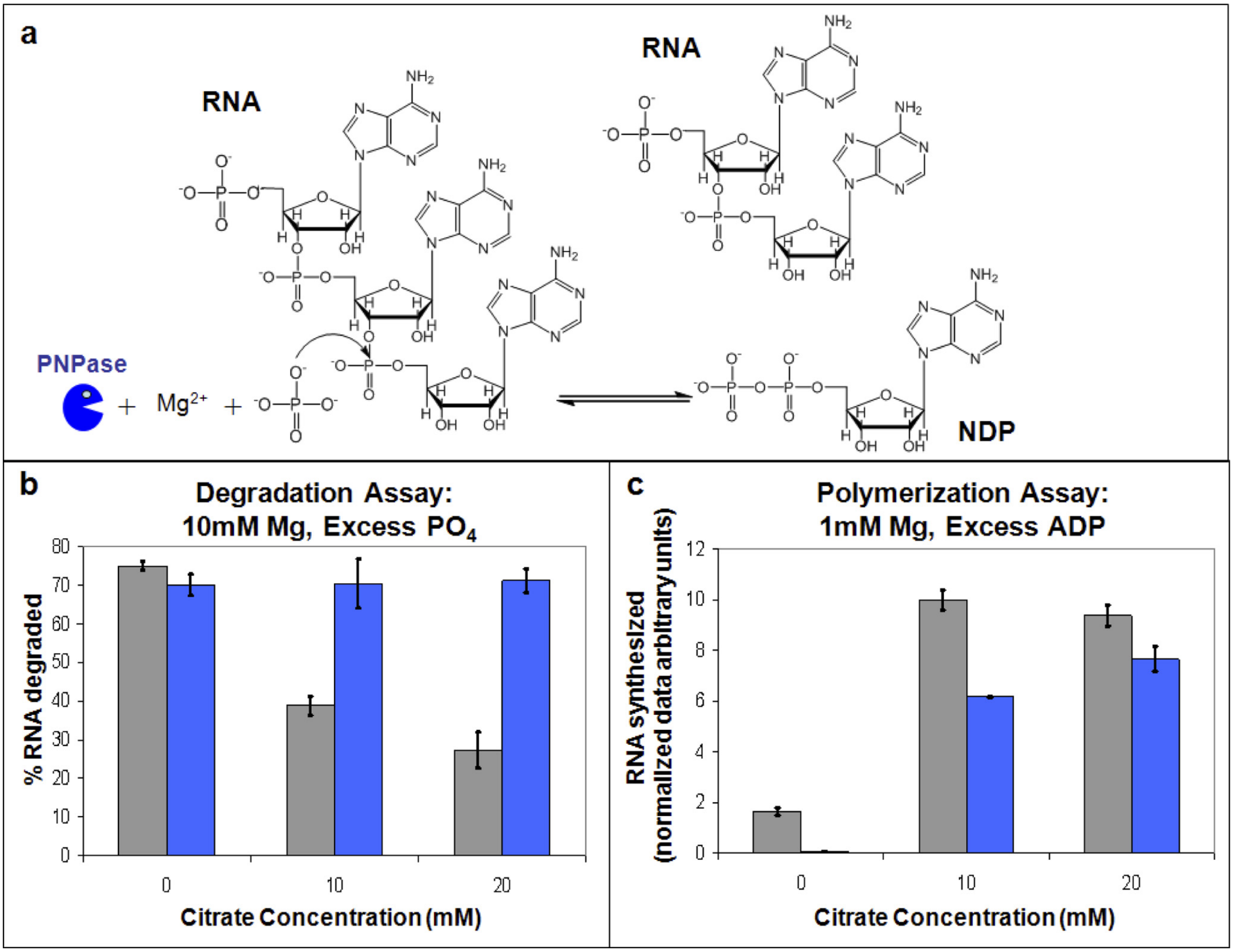


FIGURE 3. **Effect of citrate on the *in vitro* activity of PNPase.** *a*, shown is a schematic representation of the RNA degradation (forward) and polymerization (reverse) mechanisms of PNPase. Note that different experimental assay conditions are used to "switch" PNPase between RNA degradation and polymerization modes. *b* and *c*, analysis of PNPase core activity catalyzed by Mg^{2+} (*gray*) and Mn^{2+} (*blue*) in the presence of varying citrate concentrations is shown. Data represent experimental repeat averages with S.D. indicated by *bars*. *b*, a RNA degradation assay shows the amount of 15-mer RNA degraded as a percentage at the end of the assay period. *c*, RNA substrate-based polymerization assay is shown under metal-limited conditions (described in the main text). Total oligonucleotide produced from the 15-mer RNA substrate at the end of the assay period is shown. Data are normalized to the highest concentration of RNA synthesized.

excess. Optimal polymerization rates are achieved at low mM concentrations of divalent metal ions. Given that magnesium-citrate inhibits degradation, it would be expected that the chelate would also inhibit the polymerization activity. To test the effect of citrate on PNPase polymerization activity, we assayed the polymerization of ADP on an RNA substrate. At low concentrations of citrate, polymerization is inhibited, as expected (supplemental Fig. S4*a*).

Overall, our *in vitro* work suggests that PNPase is affected by the metabolite citrate. From our binding data, one high affinity site, potentially at the catalytic site, binds magnesium-chelated citrate to mediate an inhibitory effect on degradative activity. Support for metabolite binding sites within PNPase comes from structural studies discussed below.

Citrate in the PNPase Crystal Structure—The co-crystal of *E. coli* PNPase and RNA (30) was prepared in the presence of 200 mM citrate. In the 2.6 Å resolution structure (PDB code 3GCM) four molecules of citrate are seen bound to a PNPase protomer. Two are found at the catalytic site (Fig. 4, *b* and *d*) and two are located at a distant vestigial site (Fig. 4, *b* and *e*).

At the catalytic site the citrate molecules occupy the proposed location of the catalytic intermediate (Fig. 4*c*). One of the molecules has the conformation observed in the small molecule crystal structure of magnesium-citrate, and occupies the binding site for the orthophosphate substrate in PNPase. The adjacent second citrate mimics the position of the scissile phosphate in the backbone of the RNA (Fig. 4*d*). At these positions the citrate molecules would be expected to prevent the formation of the Michaelis complex and provide a potential means of enzyme inhibition, in accord with the observed inhibitory effects seen *in vitro* (Fig. 3*b*). Under conditions in which citrate is magnesium-chelated, the metabolite inhibits both the forward and backwards reactions, *i.e.* degradation as well as polymerization.

Evidence for an Allosteric Regulation Pocket in PNPase—In addition to the magnesium-citrate and unchelated-citrate mol-

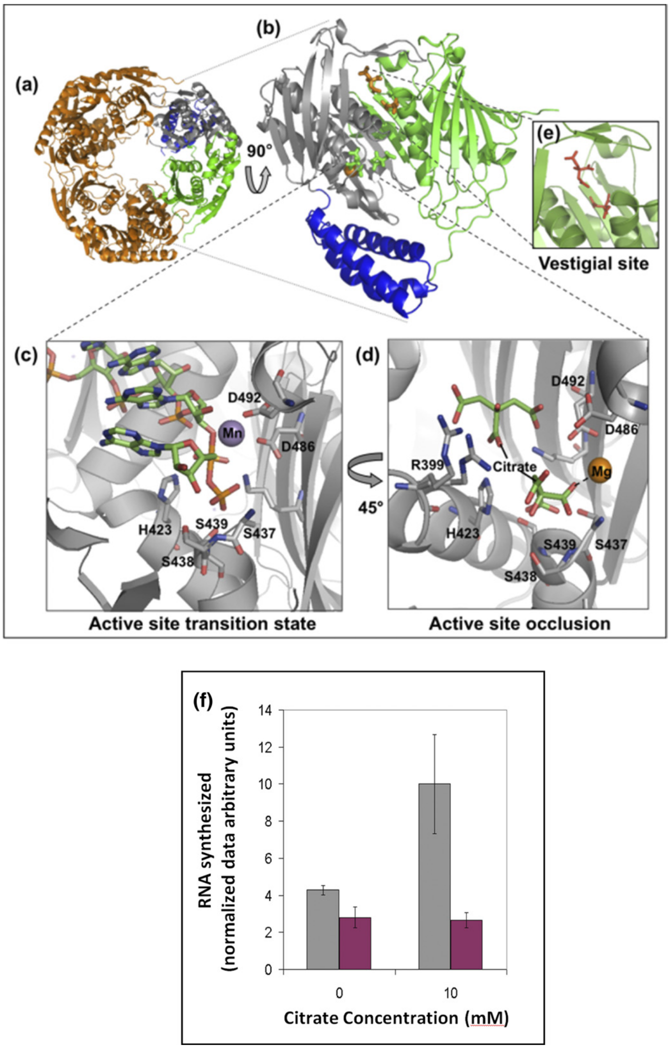


FIGURE 4. **Metabolite-bound PNPase structure and evidence for an allosteric pocket.** *a*, shown is the PNPase trimer enclosing the central channel, as viewed from above. One monomer is colored according to sub-domain structure as in *b*, and the other two monomers of the trimer are shown in *orange*. *b*, shown is the PNPase core monomer unit, as viewed from the side and colored according to subdomain structure with the N-terminal PH domain in *green*, the C-terminal PH domain in *gray*, and the helical domain in *blue*. Citrate is found at the vestigial active site (*orange*) and at the active site in Mg-chelated and free forms (*green*). Mg^{2+} is shown as an *orange sphere*. *c*, shown is an active site transition state model based on the PNPase core-manganese co-crystal structure (30). Shown is the active site within the RNase PH-domain (*gray*), catalytic Mn^{2+} (*purple sphere*), and modeled bound RNA (*orange* and *green*). *d*, shown is active site occlusion by citrate (*green*) and Mg-citrate (*green* and *orange sphere*) within the C-terminal RNase PH-domain (*gray*). *e*, citrate (*orange*) bound to the vestigial site within the N-terminal RNase PH-domain (*green*). *f*, analysis of the RNA substrate-based polymerization activity of PNPase parent (*gray*) and PNPase vestigial site mutant (*purple*) catalyzed by Mg^{2+} in the presence of varying citrate concentrations. Total oligonucleotide produced from the 15-mer RNA substrate at the end of the assay period are shown, normalized to the highest concentration of RNA synthesized. Data represent experimental repeat averages with S.D. indicated by *bars*.

ecules found in the active site, two free citrate molecules are located at a vestigial site in one of the three protomers of the crystallographic asymmetric unit (Fig. 4, *b* and *e*). This vestigial site is related to the true active site by internal structural duplication, and in the course of evolution it has lost capacity to catalyze phosphorolysis (44, 45). In this respect it is analogous to the evolutionarily conserved, phosphorolytically inactive archaeal and eukaryotic exosome subunits (46, 47). The function of these inactive sites remains unknown, and similarly, the role of the vestigial site in PNPase has not been established. The observation that the PNPase vestigial site binds citrate in a similar manner to the true active site indicates a capacity for regulatory metabolite binding.

Under our *in vitro* assay conditions, when citrate is predominantly in the metal-free form, polymerization of the substrate is enhanced (Fig. 3*c*). Correspondingly, at high concentrations of citrate (30 – 60 mM), the reverse process, *i.e.* degradation, is also enhanced (supplemental Fig. S4*b*). These activating effects are entirely the opposite of the inhibition seen under conditions in which magnesium-citrate may be the predominate species. It must be emphasized that the above results do not violate the principle of microscopic reversibility; instead, they suggest that citrate has two different binding sites; one where it is an inhibitor as the metal-bound form and one where it is an activator in its metal-free state. Evidence that the activating effect is due to binding at a distinct site comes from the observation that free citrate enhances the polymerization reactions catalyzed by manganese (Fig. 3*c*), whereas inhibition by metal-bound citrate depends upon the nature of the metal. Inhibition is observed in the presence of equimolar amounts of magnesium and citrate but not in the presence of equimolar amounts of manganese and citrate (Fig. 3*b*).

We suggest that the activating effects are due to free citrate bound at the vestigial site. The interactions of the vestigial site with citrate molecules are mediated by guanidinium groups of several arginines that are conserved in PNPase homologues. Mutations of the conserved vestigial site arginines Arg-153, Arg-372, Arg-405, and Arg-409 to alanine completely abolished the enhancement effect of free citrate (Fig. 4*f*). Nevertheless, this mutant is also inhibited by magnesium citrate (supplemental Fig. S5), just as seen for the wild-type enzyme (Fig. 3*b*), supporting the hypothesis that the metal-chelated citrate acts at a different location from the vestigial site; *e.g.* the active site.

These data indicate that the vestigial active site is a ligand binding allosteric pocket that responds to metal-free citrate. The binding of a ligand at the vestigial site may influence the location of a β-ribbon formed by residues 362–375 that is part of a central ring controlling the entry of RNA to the active site (30) and in this manner could influence substrate channeling to and from the catalytic site through an allosteric mechanism.

DISCUSSION

Decades of efforts to engineer metabolic pathways have revealed the complex behavior of metabolite concentrations and pathway fluxes in response to changing levels of enzymes. These observations illustrate how cellular metabolism requires regulation not only at the level of individual enzymes but also at a broader level that orchestrates the activities of many different enzymes distributed among branching pathways (48, 49). One possible contribution to such control might be post-transcriptional regulation, mediated through the regulatory effects of metabolites on ribonucleases.

We initially found that citrate could bind to PNPase after crystallization of PNPase core (30). Such binding could have been an artifact due to the high concentration of citrate present in the crystallization buffer. Here we present substantial evidence that the Krebs cycle metabolite citrate does modulate the activity of the processive exoribonuclease PNPase *in vitro* and *in vivo* at physiological concentrations and that PNPase activities impact on the metabolome. Our findings suggest a key role for PNPase in the normal cellular response to citrate.

At the protein level, we show that the enzymatic activity of PNPase is inhibited in the presence of magnesium-chelated citrate, and we propose that this is due to its binding at, and occluding the catalytic site. The inhibition is observed at concentrations that correspond to physiological ranges (Ref. 43 and this study). In a cellular context, both magnesium homeostasis and citrate flux may in principle affect PNPase activity.

We also observe that PNPase activity is enhanced in the presence of free citrate and propose that this is due to binding at a vestigial site and acting as an allosteric regulator. Our mutagenesis data confirm that the vestigial active site mediates the response to free-citrate and could be an allosteric site. Metal-free citrate could be the natural ligand or it may mimic the effect of a natural regulatory ligand yet to be identified.

The ability to modulate PNPase activity through metabolite binding provides a mechanism for wide-ranging regulation of RNA transcript levels in response to changes in the cellular environment. Our microarray gene expression analyses demonstrate that many transcripts are affected in a PNPase-mediated response to citrate. Inhibition of the degradative activity by magnesium-chelated citrate is anticipated to stabilize certain transcripts and decay intermediates or re-route the degradation through hydrolytic pathways, which are perhaps most costly in terms of product recycling. The impact of PNPase activity upon gene expression is likely to result in changes in the proteome, which in turn will result in changes in the metabolome. We show that cells lacking PNPase or degradosome-coupled PNPase activities differ in their metabolite concentrations when compared with parental strains. The other canonical components of the degradosome also seem to be involved in regulation of the metabolome in response to environmental change (see the data for the null mutant of the DEAD-box helicase RhlB and parent in supplemental Table S4 and Fig. S6). This indicates that the activities of RNA degradative machines impact upon metabolic control.

Taken together our results support a link between the cellular metabolic status and RNA degradative activity. Metabolites impact on ribonuclease function, and this has a wide ranging impact on many transcripts, which in turn regulates the cellular proteome and metabolome. Finally, changes in the metabolome can feed back to modulate ribonuclease activity.

The metabolite-mediated PNPase effect shown here for *E. coli* is potentially conserved in PNPase homologues found in archaea and eukaryotes. Human PNPase regulates RNA import in the mitochondria (50), the location of the Krebs cycle, where citrate is present at low mM concentrations, comparable with the concentrations used in our studies. In addition, the PNPase vestigial site of unknown function, now proposed to be involved in responding to citrate or other metabolites, is evolutionarily conserved in the phosphorolytically inactive archaeal and eukaryotic exosome subunits (46, 47). A combination of wide ranging control by PNPase and the degradosome and the direct or indirect effects of metabolites on their constituent activities represents a hitherto unrecognized integrative control mechanism that regulates homeostasis and response to environmental change.

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Note Added in Proof—A recent report identifies PNPase as a direct target of the messenger cyclic diguanylic acid in *E. coli* (51).

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Supporting Information

Table S1. Estimates of intracellular citrate concentrations in *Escherichia coli* MG1655* I- and its PNPase null and RNase II/RNase R double null derivatives.

Table S2a. Genes affected by the absence of PNPase and/or in a PNPase-mediated response to citrate. Genes are listed according to their Gene Ontology groupings at the level of GO:8150, Biological Process. Genes in bold are affected both by the absence of PNPase and in a PNPase-mediated response to citrate. The magnitude of the changes are expressed as Log_2 ratios and are the average of duplicate experiments.

Table S2b. Genes affected by the absence of PNPase and/or in a PNPase-mediated response to citrate. Genes are listed according to their Gene Ontology groupings at the level of GO:44237, Cellular Metabolic Process. Genes in bold are affected both by the absence of PNPase and in a PNPase-mediated response to citrate. The magnitude of the changes are expressed as Log_2 ratios and are the average of duplicate experiments.

Table S3. Effect of Mg-citrate on PNPase-mediated transcript decay *in vivo*. The relative abundance of selected transcripts was measured by quantitative RT-PCR for the PNPase null and wild-type strains in the presence of citrate and compared to the relative abundances determined from microarray analysis.

Table S4. Summary of the main metabolite differences for PNPase null, degradosome null and RhlB null compared to the corresponding parental strains and response to environmental stress.
Data are for *E. coli* PNPase parent and null strains, degradosome parent and null strains and RhlB parent and null strains. Metabolite changes were detected using multivariate analysis following both NMR and GC-MS. Conditions and metabolic profiles: Comparing the degradosome null and parent without alpha-methyl glucoside (control), NMR data ($R^2 = 47\%$, $Q^2 = 95\%$) and GC-MS data ($R^2 = 41\%$, $Q^2 = 82\%$) and in the presence of alpha-methyl glucoside

(phosphosugar stress), NMR data (R^2 = 63%, Q^2 = 52%) and GC-MS data (R^2 = 37%, Q^2 = 82%). Comparing RhlB parent and RhlB null at 16 °C (cold shock): NMR data (R^2 = 42%, Q^2 = 49%) and GC-MS data (R^2 = 29%, Q^2 = 16%) amd at 37 °C (control): NMR data (R^2 = 31%, Q^2 = 52%) and GC-MS data (R^2 = 24%, Q^2 = 28%). PNPase null vs PNPase parent: NMR data (R^2=74%; Q^2=98%) and GC-MS data (R^2=70%, Q^2=98%). Samples showing no change are labelled Nc; increases are labelled as + and decreases as -.

Figure S1. NMR spectra of metabolite extracts for degradosome parent vs. null strains.
High resolution 500 MHz ^{1}H NMR spectra are overlaid for parent and degradosome null strains of *E. coli* under normal growth conditions (black) or phosphosugar stress (blue). The salient differences are highlighted on the spectra with the increased metabolites indicated by green circles and decreased metabolites with red circles. The osmolytes betaine and proline are marked with yellow diamonds. These have opposing behavior under the two conditions. The numbered peaks are identified as the following compounds: 1) Isoleucine/ Valine/ Leucine, 2) Lactate, 3) Alanine 4) Lysine/ Leucine, 5) Lysine 6) Acetate, 7) N-acetyl groups. 8) Glutamate/ Glutamine, 9) Methionine, 10) Valine, 11) Proline, 12) Glutamate, 13) Pyruvate, 14) Succinate, 15) Methionine, 16) Lysine/ 2-oxoglutarate, 17) Histidine, 18) Betaine, 19) scyllo-inositol, 20) alpha-methyl glucoside, 21) Glycine, 22) Threonine, 23) Isoleucine, 24) α -glucose, 25) Tyrosine, 26) Tryptophan, 27) Phenylalanine

Figure S2. Summary of degradosome-mediated effects on metabolites of the glycolytic pathway and Krebs cycle.
Metabolites with red lettering are decreased in the degradosome null strain compared to the parent, while metabolites in green are increased. The transcripts encoding enzymes involved in the pathways are in blue.

Figure S3. Analysis of citrate and magnesium-citrate binding by PNPase.
Surface plasmon resonance was used to monitor magnesium citrate (A) and citrate (B) binding to immobilized PNPase core. The concentrations of magnesium citrate and citrate used were 0-4 mM and 0-16 mM respectively. The running buffer contained 20 mM Tris pH 7.5, 150 mM NaCl. The binding data for each magnesium citrate or citrate concentration at equilibrium is shown (red data points) and represents the average of triplicate experimental repeats. The steady state fit to the data (black line) gives a K_D of ~3 mM for magnesium citrate and ~25 mM for citrate. The binding response suggests that in both cases at least 2 molecules of citrate and magnesium citrate bind to the PNPase core monomer.

Figure S4. Mg-citrate inhibits polymerization (a), and free citrate enhances degradation (b)

(a) Mg-citrate inhibits PNPase polymerization activity: Assay conditions of excess dADP, 10 mM Mg^{2+} (i) or Mg-citrate (ii). Chromatograms resolving RNA 15-mer (substrate) and RNA 16-mer produced by polymerization of dADP to 15-mer by PNPase core in the presence of Mg (i) and Mg-citrate (ii) at time 0 and 2.5 min post assay start. At 2.5 min, a significant amount of the 15-mer substrate has been polymerized to 16mer by the addition of dADP when only Mg^{2+} is present whereas when Mg-citrate is present, the formation of 16-mer is reduced and 15-mer remains demonstrating Mg-citrate inhibition of polymerization.

(b) Free citrate enhances PNPase degradation activity: Assay conditions of excess PO_4, 10mM Mg^{2+}, increasing citrate concentrations (0-60 mM). Experimental details are described in the Materials and Methods. Percentage RNA degradation of 15-mer substrate by PNPase core is shown for varying citrate concentrations. At low citrate concentrations, when citrate will be present as Mg-citrate, we observe the expected inhibition. At high citrate concentrations, when free citrate is present over the Mg-citrate level, we begin to see enhancement of degradation activity.

Figure S5: Magnesium-citrate still inhibits PNPase degradation activity in the vestigial site mutant.

RNA degradation assay; shown is the amount of 15-mer RNA degraded, as a percentage, at the end of the assay period. Experimental details are in the Materials and Methods.

Figure S6. Effects of degradosome deficiency (a) and RhlB deficiency (b) on metabolic profiles and response to environmental stress.

a) Degradosome null. A projection map of the effects of degradosome deficiency on metabolic profiles. PLS-DA scores plots generated from the multivariate analysis of the aqueous metabolites extracted from the parent strain (■) and the degradosome null (Δ). Plots are shown for extracts from cells grown in LB medium and analyzed by NMR (upper left panel) or GC-MS (upper right panel). R^2 and Q^2 values are (NMR) 47%, 95% (GC-MS) 41%, 82%, respectively. Typically a Q^2>40%, calculated by cross-validation of every sixth sample iteratively, is indicative of a robust and predictive model. The lower panels show the effects of degradosome deficiency on metabolic response to phosphosugar stress. Extracts from cells grown in the

presence of alpha-methyl glucoside, analyzed by NMR (lower left panel) and GC-MS (lower right panel). R^2 and Q^2 values are (NMR) 63%, 52%, (GC-MS) 37%, 82%, respectively.
b) RhlB null. PLS-DA scores plots generated from the multivariate analysis of the aqueous metabolites extracted from parent (●) and RhlB null (◊). NMR data (upper left panel) and GC-MS data (upper right panel) at 37 °C; the lower panels show the effects of RhlB deficiency on metabolic response to cold shock. NMR data (lower left panel) and GC-MS data (lower right panel) at 16 ºC. R^2 and Q^2 values are respectively: 42%, 49% for NMR at 37 °C; 29%, 16% for GC-MS at 37 °C; 31%, 52% for NMR at 16 °C, and 24%, 28% for GC-MS at 16 °C.

Materials and Methods

Intracellular Citrate Concentration Measurements

Strains were provided by M.P. Deutscher (University of Miami, Florida). MG1655* I^- (Δ*rna*) in which the frameshift in the *rph* gene has been corrected was considered wild-type. MG1655* I^- (Δ*rna*), MG1655* I^- PNP^- ((Δ*rna* Δ*pnp::kan* Kan^R), a PNPase null strain, and MG1655* I^- II^- R^- ((Δ*rna* Δ*rnb::Tn10* Δ*rnr::kan* $Tet^R Kan^R$), a RNase II/RNase R double null strain, were grown at 37 ºC in M9-glucose and intracellular citrate concentrations were determined before and 30 min after the addition of 50 mM magnesium chloride-50 mM sodium citrate.

Cells were harvested at 0.3 to 1.0 A_{600} by centrifugation for 5 min at 6000 ***g***, or filtration with 47 mm diameter 0.2 micron membranes (PALL Life Science), rapidly frozen in liquid nitrogen, and then metabolites extracted using methanol-chloroform and sonication, as described below in the sub-section on metabolome analysis. Citrate concentrations were estimated from proton-NMR spectra from ratios of the integrate peaks for citrate and a 0.5 mM sodium-3-(tri-methylsilyl)-2,2,3,3-tetradeuteriopropionate (TSP) reference and matching these with a calibration curve prepared using a range of citrate standards (0.1 to 3 mM). Intracellular volume was estimated using assumptions that *E. coli* cell volume at mid-log growth is 0.65 x 10^{-12} ml and that 1 A_{600} corresponds to 10^9 cells/ml (1-2).

Quantitative RT-PCR

The PNPase null mutant and its parent K-12 *E. coli* wild-type strain (BW25113) were obtained from the NARA Institute of Genetics, Japan. The cells were grown in LB-enriched media to an optical density A_{600} of ~0.6 and then supplemented with 50 mM sodium citrate and 50 mM $MgCl_2$. 500 μg/ml of rifampicin was added to stop transcription. Samples were collected 5 min after the addition of the Mg-citrate and rifampicin. Total RNA was extracted (Qiagen RNeasy) and reverse-transcriptase polymerase chain reaction (RT-PCR) was performed using a one-step RT-PCR kit (Qiagen) with 50 ng of total RNA per reaction in a Techne Genius Thermal Cycler for 30 cycles. Primers for the transcripts tested were purchased from Eurofins MWG Operon.

The RT-PCR products were analyzed by agarose gel electrophoresis; this was followed by densitometry using the Syngene Gene Genius Bioimaging System (Syngene) and ImageJ software (NIH) for analysis of band intensity. Each transcript was tested in triplicate. For each experiment, the RT-PCR product was analyzed by gel electrophoresis in duplicate to account for error within each experiment. To assess the effect of citrate on transcript decay we calculated the relative abundance between the parent and PNPase null strains in the presence of citrate.

Metabolome analyses:

Cells and growth conditions *E. coli* MC1061-derivative strains including AC21 (RNase E-parent) and AC27 (RNase E lacking the last 477 residues from the C-terminal degradosome-scaffolding domain, i.e. a degradosome null strain) (3-4) and RhlB parent and SVK1 RhlB null strains were provided by A.J. Carpousis, (CNRS, Toulouse) and have a Tn10 marker linked to the *rne* allele. Strains were cultured at 37 ºC in LB + antibiotic. Strains for phosphosugar stress experiments were grown in LB supplemented with 1% w/v alpha-methyl glucoside and strains for cold shock experiments were grown to an A_{600} ~0.6 and then grown overnight at 16 °C to induce cold shock. The MC1061 background used for these studies also contains the ara-leu 7696 deletion rendering the strain incapable of metabolizing arabinose and sensitive to the glucose analogue alpha-methyl glucoside; this is likely due to the deletion of SgsR-SgsS. Once at an A_{600} ~1, stains were harvested by centrifugation at 4200 g at 4 ºC for 20 min. Samples were recovered and stored at -80 ºC.

Sample extraction

Metabolite samples were extracted using a methanol-chloroform method (5) to generate dried cell extract.

Metabolite measurements by ^{1}H NMR spectroscopy

Dried cell extract was rehydrated in 15 mM sodium phosphate buffered D_2O, pH 7.0, containing 1 mM (sodium-3-(tri-methylsilyl)-2,2,3,3-tetradeuteriopropionate (TSP), and analyzed using an AVANCE II+ spectrometer operating at 500.13 MHz for the ^{1}H frequency (Bruker, Germany) with a 5 mm TXI Inverse ATMA probe. Spectra were collected using: relaxation delay = 2 s, t_1= 4 μs, mixing time=150 ms, and processed using the ACD Labs 1D NMR processor (ACD, Toronto, Canada) as previously described (5-6). Spectral regions were normalized to a total value of 10000 and data were analyzed using PCA and PLS-DA techniques (SIMCA-P package (Umetrics, Sweden)).

Metabolite evaluation by gas phase chromatography mass spectrometry (GC-MS)

Dried aqueous extract was derivatized by methoxylation and silylation; samples were diluted (1:10) with hexane prior to GC-MS analysis in a Thermo Electron Corporation Trace GC-Ultra (Split/Splitless injector temperature 230 ^{o}C, helium used as a carrier gas at flow rate 1.2 ml min^{-1}) as previously described (7). GC-MS chromatogram peaks were integrated individually (Xcalibur, version 2.0 (Thermo Electron)) and overlapping peaks were deconvoluted using a selection of single/multiple representative ions and structures were assigned (NIST database (2002)). The integrated peaks in a sample were normalised so that the total sum of peaks was 10000.

Data evaluation for NMR and GC-MS

SIMCA-P+ v.11.0 (Umetrics) used for multivariate analysis. Data processed using principal components analysis (PCA) and partial least squares-discriminant analysis (PLS-DA). Data were mean centered before univariate scaling for GC-MS analysis and Pareto scaling for NMR data. Statistical robustness was assessed using $R^2$and Q^2 values. Coefficients of a PLS-DA dataset describe the contribution of a variable to the overall model; these were used to determine variables that were significant to a given classification. Those coefficients with the highest modulus value and deemed to contribute significantly to a component, as assessed by a jack-knifing procedure within SIMCA, were selected.

Surface plasmon resonance analysis

PNPase core was immobilized covalently using amine coupling to the surface of a Biacore CM5 sensor chip (GE Healthcare). Immobilization levels obtained ranged from 1500 to 3000 RUs. Assessment of citrate and magnesium citrate binding were conducted by injecting 0-16 mM buffered citrate in 20 mM Tris pH 7.5, 150 mM NaCl or 0-4 mM buffered magnesium citrate in 20 mM Tris pH 7.5, 150 mM NaCl at flow rates of 30-90 μl/min for 30-60 s over the reference and test flow cells. A Biacore T100 instrument was used and the data collected was reference and buffer subtracted prior to steady state analysis using data fitting functions provided in the Biacore T100 Evaluation Software.

PNPase activity assays:

Degradation assay

The assay mix contained 0.05 mM 15-mer RNA, 10 mM $MgCl_2$, 10 mM phosphate and 2 μM PNPase core, with 0-60 mM sodium citrate. Assay samples were quenched with an equal volume of 200 mM EDTA at time 0 and 2 min following addition of PNPase core. Assay samples (5μl) were analyzed for RNA degradation by ion exchange HPLC (Dionex DNAPac 200 column, 25 ºC, 0-1 M NaCl gradient in 20 mM Tris buffer pH 8.0 run over 8 min at 1 ml/min). Chromatograms were processed and analyzed in Dionex Chromeleon software.

Degradation assay (vestigial site mutant)

The assay mix contained 0.05 mM 15-mer RNA, 10 mM $MgCl_2$, 10 mM phosphate and 2 μM PNPase vestigial site mutant, with 0-10 mM sodium citrate. Assay samples were quenched with an equal volume of 200 mM EDTA at time 0 and 2 min following addition of PNPase core. Assay samples (5 μl) were analyzed for RNA degradation by ion exchange HPLC (Dionex DNAPac 200 column, 25 ºC, 0-1 M NaCl gradient in 20 mM Tris buffer pH 8.0 run over 8 min at 1 ml/min). Chromatograms were processed and analyzed in Dionex Chromeleon software.

Polymerization assays

The assay mix contained 6.25 μM poly(rA) 15-mer RNA, 100 μM dADP, 20 mM Tris pH 7.5, 10 mM $MgCl_2$, 0-10 mM sodium citrate and 2 μM PNPase. Five μl were quenched with an equal volume of 200 mM EDTA at time 0 and 2.5 min following addition of PNPase core.

Assay samples (5μl) were analyzed for RNA polymerization by HPLC using the same conditions as for the degradation assay.

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Table S1. Estimates of intracellular citrate concentrations in *Escherichia coli* MG1655* I- and its PNPase null and RNase II/RNase R double null derivatives

Strain	**Intracellular citrate concentration (mM)**	
	M9 glucose media	**M9 glucose media** **30 min post addition of 50 mM Mg-citrate**
Parent	6.7	not measured
PNPase null	2.9	58.9
RNase II/RNase R double null	4.3	61.4

Table S2a. Genes affected by the absence of PNPase and/or in a PNPase-mediated response to citrate. Genes are listed according to their Gene Ontology groupings at the level of GO:8150, Biological Process. Genes in bold are affected both by the absence of PNPase and in a PNPase-mediated response to citrate. The magnitude of the changes are expressed as Log2 ratios and are the average of duplicate experiments.

Biological Process

GO Term	**Gene**	**Function**	**Log$_2$ of the ratio of PNPase null (no citrate):Wild-type (no citrate)**	**Log$_2$ of the ratio of Wild-type plus citrate:Wild-type (no citrate)**	**Log$_2$ of the ratio of PNPase null plus citrate:PNPase null (no citrate)**	**Log2 of the ratio of fold-change from wild-type plus/minus citrate and PNPase null plus/minus citrate**
22610 biological adhesion	fimI	Required for pilus biosynthesis, FimA homolog	1.3809748			
	fliD	Hook-associated protein 2, axial family	-1.0269284			
	sfmA	Function unknown, FimA homolog		-1.382384642	-2.958069183	1.575684542
	ycgV	Overexpression increases adhesion and biofilm formation; probable adhesin, function unknown	1.2697777			
	ygiL	Function unknown, FimA homolog		0.097937983	-0.852435761	0.950373744
	ypjA	Overexpression increases adhesion, function unknown; OM autotransporter homolog	1.2955649			
	znuA	High-affinity ABC transport system for zinc, periplasmic	-1.5015092			
65007 biological regulation	**acrR**	**AcrR transcriptional repressor for acrAB (AcrAB-TolC mulltidrugefflux pump)**	**-1.0204067**	**0.968588206**	**1.712429133**	**-0.743840928**
	arcB	Tripartite sensor/histidine protein kinase; repression of aerobic genes and activationof some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has respones regulator and second transmitter domains	1.0271903			
	barA	Sensor histidine protein kinase, pleiotropic; controls the expresion of csrB/C sRNAs; works in concert with UvrY response regulator	1.6353183			
	cheA	Histidine protein kinase sensor of chemotactic response; CheY is cognate response regulator; autophosphorylating; CheAS is a short form produced by an internal start at codon 98	-1.1959176			
	cheW	Chemotaxis signal transducer; bridges CheA to chemoreceptors to regulate phophotransfer to CheY and CheB	-1.2323792			
	cheY	Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein	-1.2030091			
	csgD	Transcriptional activator for csgBA and other genes		-1.859434883	-0.292246188	-1.567188696

	csiE	Stationary phase inducible protein; sigma S-dependent promoter	1.3574634			
	cusS	Copper ion sensor regulating cusCFBA expression; may also sense silver	1.4919264			
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		1.44637671	0.350969162	1.095407548
	dcuR	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system response regulator	1.0233135			
	dcuS	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system sensory histidine kinase	1.2036445			
	deaD	ATP-dependent RNA helicase, 50S ribosomal subunit biogenesis; translation factor W2; facilitates translation of mRNAs with 5' secondary structures; multicopy suppressor of rpsB(Ts) mutations	1.1617334			
	deoR	Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer	1.2066016			
	dhaR	Transcription activator of the dhaKLM operon	1.127254			
	envY	Thermoregulatory activator of porin expression, AraC family	1.679985			
	fimB	**Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE**	**-1.1248107**	**0.473670149**	**1.76544683**	**-1.291776681**
	fliC	Flagellin, structural gene, H-antigen	-1.5392385			
	ftsI	Transpetidase, PBP3; penicillin-binding protein 3 involved in septal peptidoglycan synthesis	2.2227626			
	gadE	Transcriptional regulator of the gadABC operon		-1.613297865	1.91643444	-3.529732305
	galS	Repressor of the mgl operon and isorepressor of the gal operon; autoregulatory; homodimeric	1.2070732			
	glcC	Transcriptional positive regulator for glc operon	1.077054			
	gmr	Cyclic-di-GMP phosphodiesterase, csgD regulator; modulates protein stability of RNase II	1.123914			
	grxB	Glutaredoxin 2; regulated by RpoS and ppGpp	1.6855459			
	hyfR	Formate-sensing regulator for hyf operon	1.2317433			
	iscR	Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro	-1.1579247			
	kdgR	Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK	-1.064749			
	ldcA	L,D-carboxypeptidase A; cytoplasmic protease that cleaves the terminal D-alanine from cytoplasmic muropeptides	1.003866			
	lldR	Dual role activator/repressor for lldPRD operon		-1.022032736	-0.102462884	-0.919569852
	mlrA	Transcriptional regulator of csgD	1.208386			
	mreB	MreB filaments participate in directional chromosome movement and segregation; mecillinam resistance; forms membrane-associated coiled arrays; actin homolog; morphology	-1.0813851			
	murA	UDP-N-acetylglucosamine enoylpyruvyl transferase; fosfomycin resistance	-1.2009416			
	nanR	Repressor of the nan operon, induced by sialic acid; homodimeric	1.6356357			
	narQ	Nitrate/nitrite sensor-transmitter protein; anaerobic respiratory path; cognate regulator is NarP; function redundant with narX	1.0795679			
	narX	Two-component nitrate/nittrite sensor-transmitter protein; NarL is cognate regulator; functional redundance with narQ	1.0639569			
	nhaA	Na+/H+ antiporter 1, strongly pH-dependent; helps regulate intracellular pH and extrude lithium; nhaA_P1 activated by NhaR, repressed by H-NS and stimulated by Na(+)	1.3487701			
	paaX	**Phenylacetic acid degradation**	**1.0424947**	**0.378975841**	**-0.246470978**	**0.625446818**

	phoQ	Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP	1.4622464			
	prpR	Transcriptional regulator of prp operon; propionate catabolism via 2-methlycitrate cycle, characterized primarily in Salmonella	1.6797161			
	purR	Purine regulon repressor	-1.0262108			
	rcsA	Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene		0.300528606	-1.142561372	1.443089978
	rcsC	Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase	-1.6430304			
	rhaR	Transcriptional activator for rhaSR, AraC family	2.2165618			
	rob	Right oriC-binding protein, AraC family	1.3771441			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	sgcR	Putative sgc cluster transcriptional regulator	1.3975518			
	slyA	Activates crytpic hemolysin gene hlyE; global transcriptional regulator	1.015482			
	stpA	RNA chaperone and DNA-binding protein; suppresses T4 td mutant; modulates micF stability; forms heteromers with, and stabilzed against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS	-1.2432377			
	tar	Aspartate, maltose chemoreceptor, methyl-accepting; MCP II; also senses repellents cobalt and nickel; flagellar regulon	-1.1869416			
	torS	Sensor kinase for torCAD operon	2.9209745			
	treR	Repressor of trehalose operon	1.5542111			
	trg	Ribose, galactose chemoreceptor, methyl-accepting; MCP III; flagellar regulon	-1.3795029			
	tsr	Serine chemoreceptor, methyl-accepting; MCP I; also senses repellents; flagellar regulon	-1.9566808			
	uxuR	Repressor for UxuR regulon; true inducer is fructuronate	1.0230589			
	yahA	c-di-GMP-specific phosphodiesterase, PDE-A; reaction product is 5'pGpG; dependent on Mg+2 or Mn+2, Ca+2 inhibitory; optimum pH 9.35; monomeric	-2.0166183			
	yahB	LysR family of transcriptional regulators, function unknown	1.046875			
	ybaO	Function unknown, Lrp family; putative transcriptional regulator	1.0301518			
	ybeF	Putative LysR-family transcriptional regulator, function unknown LysR-family transcriptional regulator, function unknown	1.0823689			
	ybhD	Putative LysR-family transcriptional regulator, function unknown	1.1145554			
	yccA	Membrane-associated protein that binds to FtsH(HflB) and HflKC proteins; mutant YccA stabilizes SecY(Ts); suppression requires HflKC; YccA is a native substrate for the FtsH(HflB) protease	-1.0077734			
	ydfT	Function unknown	1.6117142			
	yecI	Function unknown	1.016995			
	yegE	Putative c-di-GMP dual activity enzyme, function unknown	1.6381769			
	yfaX	Putative transcriptional regulator, function unknown	1.2188423			
	yfeG	Function unknown	1.1252446			
	yfeR	Required for swarming phenotype, function unknown; predicted transcriptional regulator	1.2977767			
	ygfI	Putative LysR-family transcriptional regulator, function unknown	1.4685719			
	yhiF	**Probable repressor of dctA dicarboxylate transporter gene**	**1.2616509**	**-1.6261956**	**0.509971635**	**-2.136167235**

	yhjB	Function unknown	1.5886974			
	yjiR	Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family	1.0690143			
	ypdA	Putative sensor kinase, function unknown	-1.0332007			
	yqeI	Part of T3SS PAI ETT2 remnant, ToxR homolog	-1.067694			
16043 cellular component organisation	dbpA	ATP-dependent 3'-5' RNA helicase, specific for 23S rRNA	1.1279364			
	flgF	**Flagellar basal body rod subunit**	**-2.318077**	**1.818358267**	**2.829423308**	**-1.011065042**
	flgG	**Flagellar basal body rod major subunit**	**-2.7651777**	**1.72109801**	**2.74639891**	**-1.0253009**
	flgJ	Flagellum-specific muramidase	-1.6338248			
	flgK	Flagellar synthesis, hook-associated protein	-1.3041476			
	fliD	Hook-associated protein 2, axial family	-1.0269284			
	fliI	**Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits**	**-2.8425198**	**2.053080188**	**3.095328983**	**-1.042248796**
	fliK	**Hook filament junction; controls hook length**	**-2.6773417**	**1.939810007**	**2.765864679**	**-0.826054671**
	fliO	Flagellin export apparatus, integral membrane protein	-1.882103			
	ftsI	Transpetidase, PBP3; penicillin-binding protein 3 involved in septal peptidoglycan synthesis	2.2227626			
	hofQ	Required for the utilization of DNA as a carbon source; H. influenzae competence protein ComE homolog; putative fimbrial transport protein; expression not detected	2.0593238			
	mreB	MreB filaments participate in directional chromosome movement and segregation; mecillinam resistance; forms membrane-associated coiled arrays; actin homolog; morphology	-1.0813851			
	murA	UDP-N-acetylglucosamine enoylpyruvyl transferase; fosfomycin resistance	-1.2009416			
	yhbC	Function unknown				
	ypdA	Putative sensor kinase, function unknown	-1.0332007			
9987 cellular process	aaeA	AaeAB p-hydroxybenzoic acid efflux pump MFP component; membrane fusion protein	1.1153295			
	abgB	Required for p-aminobenzoyl-glutamate usage	1.1240034			
	accD	Acetyl-CoA carboxylase, carboxyltransferase beta subunit	-1.0916588			
	acnA	Aconitase A, stationary phase induced; iron-sulfur cluster; apo-enzyme binds mRNA for negative translational autoregulation; negatively regulated by ryhB RNA as part of indirect positive regulation by Fur	1.6737623			
	acnB	Aconitase B; 2-methylaconitate hydratase; apo-enzyme binds mRNA for negative translational autoregulation; iron-sulfur cluster; monomeric	1.0271903			
	acpS	Acyl carrier protein, ACP-CoA phosphopantetheinyltransferase; Holo-ACP synthase		0.020738638	-1.374399075	1.395137713
	acrF	AcrEF-TolC efflux pump, multidrug/solvent resistance; osmotically remedial envelope defect	1.513372			
	acrR	**AcrR transcriptional repressor for acrAB (AcrAB-TolC mulltidrug efflux pump)**	**-1.0204067**	**0.968588206**	**1.712429133**	**-0.743840928**
	adhE	Alcohol dehydrogenase, largely anaerobic; aerobic antioxidant; acetaldehyde-CoA dehydrogenase, CoA-linked; allyl alcohol resistance	1.0416784			
	adiA	Arginine decarboxylase, acid-inducible; arginine-dependent acid resistance	1.1271622			

	amtB	Ammonia gas channel; sequesters GlnK, a negative regulator of AmtB activity, to the inner membrane; bi-directional facilitated diffusion	1.316608			
	ansA	L-Asparaginase I	-1.1030908			
	ansB	L-Asparaginase II	1.5445883			
	arcB	Tripartite sensor/histidine protein kinase; repression of aerobic genes and activationof some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has respones regulator and second transmitter domains	2.5143914			
	argA	**N-acetylglutamate synthase; first step in arginine biosynthesis; amino-acid acetyltransferase; growth on acetylornithine**	**1.3041081**	**2.991781138**	**1.434967896**	**1.556813242**
	argB	**N-acetylglutamate kinase**	**1.044384**	**2.818308386**	**1.527225825**	**1.291082561**
	argC	**N-acetyl-gamma-glutamyl-phosphate reductase**	**1.7869039**	**3.319065683**	**1.757350161**	**1.561715522**
	argD	Acetylornithine aminotransferase; succinyldiaminopimelate aminotransferase, PLP-dependent		2.58062465	1.749457164	0.831167486
	argF	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase; CP4-6 putative prophage remnant		2.345750989	0.780893261	1.564857729
	argG	Argininosuccinate synthase		2.6295392	1.468532017	1.161007183
	argH	**Argininosuccinate lyase**	**1.2643517**	**2.489928442**	**1.442275936**	**1.047652506**
	argI	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase		2.843476333	1.517740469	1.325735865
	arnT	4-amino-4-deoxy-L-arabinose(Ara4N):Lipid A transferase; modifies lipid A phosphates with aminoarabinose and confers resistance to polymyxin B and cationic antimicrobial peptides; glycolipid donor is undecaprenyl phosphate-alpha-L-Ara4N	1.0203366			
	aroF	3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP) synthase; tyrosine repressible; TyrR regulon	1.0875133			
	aroK	Shikimate kinase I; alkali-inducible	-1.2647691			
	asd	Aspartate semialdehyde dehydrogenase		-0.796322194	-1.579930631	0.783608438
	aspA	L-Aspartate ammonia-lyase; L-aspartase	3.0522566			
	aspC	Aspartate aminotransferase, AspAT; kynurenine aminotransferase; glutamine transaminase K	-1.0659509			
	atpA	ATP synthase subunit alpha, membrane-bound, F1 sector	1.33844			
	atpB	ATP synthase subunit a, membrane-bound, F0 sector	-1.0947847			
	atpE	ATP synthase subunit c, membrane-bound, F0 sector; DCCD-binding	-1.2534213			
	atpF	ATP synthase subunit b, membrane-bound, F0 sector	-1.1470773			
	atpH	ATP synthase subunit delta, membrane-bound, F1 sector	-1.1472812			
	barA	Sensor histidine protein kinase, pleiotropic; controls the expresion of csrB/C sRNAs; works in concert with UvrY response regulator	1.6353183			
	bcr	Efflux pump for bicyclomycin, cysteine and sulfonamides	1.2833695			
	bioB	**Biotin synthase; dethiobiotin to biotin pathway; iron-sulfur enzyme**	**-1.5355635**	**-0.360614381**	**0.797467665**	**-1.158082046**
	bioC	Biotin synthesis blocked prior to pimeloyl CoA formation; putative SAM-dependent methyltransferase	-1.0316381			
	bioF	**7-keto-8-amino pelargonic acid synthase**	**-1.3357835**	**0.006936511**	**1.062414033**	**-1.055477522**
	cheA	Histidine protein kinase sensor of chemotactic response; CheY is cognate response regulator; autophosphorylating; CheAS is a short form produced by an internal start at codon 98	-1.1959176			
	cheW	Chemotaxis signal transducer; bridges CheA to chemoreceptors to regulate phophotransfer to CheY and CheB	-1.2323792			

	cheY	Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein	-1.2030091			
	cheZ	CheY-P phosphatase	-1.0379796			
	citE	Putative citrate lyase beta chain	1.1568863			
	citG	Putative cit operon gene, function unknown	2.3438559			
	cld	Regulator of lipopolysaccharide O-chain length; gene studied in Salmonella and non-K-12 strains	-1.0316088			
	coaA	Pantothenate kinase	-1.1887982			
	cobC	Probable alpha-ribazole-5'-phosphate phosphatase; potential partial cobalamin biosynthesis pathway	1.7467084			
	csgD	Transcriptional activator for csgBA and other genes		-1.859434883	-0.292246188	-1.567188696
	csiE	Stationary phase inducible protein; sigma S-dependent promoter	1.3574634			
	cusS	Copper ion sensor regulating cusCFBA expression; may also sense silver	1.4919264			
	cynX	Putative transporter, function unknown, cyn operon	1.084173			
	cyoB	Cytochrome o oxidase subunit I; cytochrome bo(3) ubiquinol oxidase subunit I	1.0475307			
	cyoE	**Cytochrome o oxidase subunit, protoheme IX farnesyltransferase**	**-1.0276141**	**0.195029502**	**1.040158488**	**-0.845128986**
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		0.442750627	1.32534585	-0.882595223
	cysD	Sulfate adenylyltransferase	-1.4373238			
	dadA	D-amino acid dehydrogenase		-0.368920809	-1.625476173	1.256555364
	dadX	Alanine racemase; homodimeric		-0.155438273	-1.291326758	1.135888485
	dapB	**Dihydrodipicolinate reductase**	**1.2919754**	**-0.563659431**	**-2.013465644**	**1.449806213**
	dapD	2,3,4,5-tetrahydropyridine-2-carboxylate N-succinyltransferase; mutations suppress growth defects of strains lacking superoxide dismutase	-1.0075407			
	dbpA	ATP-dependent 3'-5' RNA helicase, specific for 23S rRNA	1.1279364			
	dcuR	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system response regulator	1.0233135			
	dcuS	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system sensory histidine kinase	1.2036445			
	deaD	ATP-dependent RNA helicase, 50S ribosomal subunit biogenesis; translation factor W2; facilitates translation of mRNAs with 5' secondary structures; multicopy suppressor of rpsB(Ts) mutations	1.1617334			
	degP	Periplasmic, membrane-associated serine endoprotease; protease Do, required for high-temperature growth and the degradation of damaged proteins		-0.366102641	0.625276117	-0.991378758
	deoR	Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer	1.2066016			
	dhaR	Transcription activator of the dhaKLM operon	1.127254			
	dxs	DXP synthase; DXP is precursor to isoprenoids, thiamin, pyridoxol	1.8676739			
	eno	Enolase; phosphoprotein; component of RNA degradosome	-1.0622171			
	envC	Periplasmic murein hydrolase septal ring factor; sensitivity to crystal violet; filamentous	1.3034105			
	envY	Thermoregulatory activator of porin expression, AraC family	1.679985			
	eutB	Ethanolamine ammonia lyase, large subunit, adenosylcobalamine-dependent; concerted induction requires both B12 and ethanolamine; heterodimeric	1.7656298			
	exuT	Hexuronate permease, for glucuronate and galacturonate	1.0179187			
	fabB	beta-Ketoacyl-ACP synthase I; KAS I; homodimeric		1.148054475	2.149240165	-1.00118569
	fabI	Enoyl-ACP reductase, NADH dependent	-1.0237877			

	fbaB	Fructose 1,6-bisphosphate aldolase, class I	1.0204077			
	fcl	NADPH-dependent GDP-L-fucose synthase, colanic acid synthesis; two step reaction at a single active site: GDP-4-keto-6-deoxy-D-mannose epimerase, then reductase	1.6897135			
	fepE	Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains	-1.1662207			
	fimB	**Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE**	**-1.1248107**	**0.473670149**	**1.76544683**	**-1.291776681**
	fimI	Required for pilus biosynthesis, FimA homolog	1.3809748			
	fkpA	Periplasmic peptidylprolyl cis,trans isomerase; heat shock inducible; PPIase-independent chaperone activity, binds FK506	1.2272221			
	flgB	**Flagellar basal body rod subunit**	**-2.9897075**	**2.114201933**	**3.5668911**	**-1.452689167**
	flgC	**Flagellar basal body rod subunit**	**-3.2366333**	**1.918144667**	**3.290344417**	**-1.37219975**
	flgE	**Flagellar hook subunit protein**	**-3.2993827**	**1.879339905**	**3.128954345**	**-1.24961444**
	flgF	**Flagellar basal body rod subunit**	**-2.318077**	**1.818358267**	**2.829423308**	**-1.011065042**
	flgG	**Flagellar basal body rod major subunit**	**-2.7651777**	**1.72109801**	**2.74639891**	**-1.0253009**
	flgH	**Flagellar synthesis, basal body L-ring lipoprotein**	**-1.9212251**	**1.901291464**	**2.870884957**	**-0.969593493**
	flgI	Basal body P-ring flagellar protein	-2.6527514			
	flgJ	Flagellum-specific muramidase	-1.6338248			
	flgK	Flagellar synthesis, hook-associated protein	-1.3041476			
	flgL	Flagellar synthesis, hook-associated protein	-1.0269798			
	fliC	Flagellin, structural gene, H-antigen	-1.5392385			
	fliD	Hook-associated protein 2, axial family	-1.0269284			
	fliF	**Flagellar basal body M-ring protein**	**-2.1452103**	**2.21798513**	**3.623918913**	**-1.405933783**
	fliG	**Rotor protein for flagellar motor switching and energizing; role in flagellar assembly**	**-2.774952**	**2.130965744**	**3.2673922**	**-1.136426456**
	fliH	**Negative regulator of FliI ATPase activity; involved in flagellar assembly and export**	**-2.0643058**	**1.950296025**	**2.756911638**	**-0.806615613**
	fliI	**Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits**	**-2.8425198**	**2.053080188**	**3.095328983**	**-1.042248796**
	fliJ	**Flagellin export apparatus soluble chaperone**	**-1.861196**	**2.017483883**	**2.880704117**	**-0.863220233**
	fliK	**Hook filament junction; controls hook length**	**-2.6773417**	**1.939810007**	**2.765864679**	**-0.826054671**
	fliL	Affects rotational direction of flagella during chemotaxis	-1.5788474			
	fliM	**Flagellar synthesis, motor switching and energizing**	**-2.746443**	**2.032106006**	**2.845598856**	**-0.81349285**
	fliN	Flagellar switch protein	-1.9425316			
	fliO	Flagellin export apparatus, integral membrane protein	-1.882103			
	fliP	Flagellin export apparatus, integral membrane protein	-1.3490691			
	fliQ	Flagellin export apparatus, integral membrane protein	-1.7036285			
	folE	GTP cyclohydrolase I	-1.0409135			
	ftsI	Transpetidase, PBP3; penicillin-binding protein 3 involved in septal peptidoglycan synthesis	2.2227626			
	ftsN	Cell division and growth; multicopy suppresses ftsA12	1.7090788			
	fusA	Elongation Factor EF-G; GTPase required for translocation from the A-site to the P-site in the ribosome; fusidic acid resistance	-1.1621015			
	gabP	GABA permease, membrane protein	1.2657433			
	gadA	Glutamate decarboxylase A	1.1232334			
	gadB	Glutamate decarboxylase B, vitamin B6-dependent; hexameric	1.0481529			
	gadE	Transcriptional regulator of the gadABC operon		-1.613297865	1.91643444	-3.529732305
	galK	Galactokinase	1.7365794			

	galS	Repressor of the mgl operon and isorepressor of the gal operon; autoregulatory; homodimeric	1.2070732			
	gatA	Galactitol-specific enzyme IIA of phosphotransferase system (PTS)	-1.6841471			
	gatC	Galactitol-specific enzyme IIC of PTS	-1.4637866			
	gatY	D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability	-1.1761272			
	gatZ	Tagatose bisphosphate aldolase GatYZ subunit; required for full activity and stabilty of GatY	-1.2347231			
	gcl	Glyoxylate carboligase, glyoxylate-inducible	1.2727609			
	gdhA	Glutamate dehydrogenase		-0.965960622	-2.004323596	1.038362974
	glf	UDP-galactopyranose mutase	-1.4456341			
	glgA	Glycogen synthase		-0.611356637	-1.254026216	0.642669579
	glgB	**1,4-alpha-glucan branching enzyme; glycogen branching enzyme**	**1.0104895**	**-0.518011066**	**-1.447500807**	**0.929489741**
	glgC	**Glucose-1-phosphate adenylyltransferase; ADP-glucosepyrophosphorylase**	**1.077054**	**-0.717255721**	**-1.435926535**	**0.718670815**
	glnA	Glutamine synthase	1.0619159			
	glpK	Glycerol kinase	1.7542315			
	glyA	Serine hydroxymethyltransferase; binds Zn(II)	-1.2570169			
	glyS	Glycine--tRNA ligase, beta-subunit	-1.1524415			
	gmr	Cyclic-di-GMP phosphodiesterase, csgD regulator; modulates protein stability of RNase II	1.123914			
	gnd	6-phosphogluconate dehydrogenase, decarboxylating	-1.1842852			
	gntU	Low-affinity gluconate transport protein, membrane protein	1.0674934			
	gpmA	Phosphoglycerate mutase 1, 2,3-bisphosphoglycerate-dependent; Fur regulon; dimeric	-1.1640095			
	grpE	Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase	-1.0346646			
	grxB	Glutaredoxin 2; regulated by RpoS and ppGpp	1.6855459			
	gspC	**Part of H-NS-silenced gsp divergon, type II protein secretion;cloned gsp divergon secretes ChiA**	**1.2146425**	**-0.862021266**	**-2.680390988**	**1.818369721**
	gspD	**Part of H-NS-silenced gsp divergon, type II protein secretion; OM secretin; cloned gsp divergon secretes ChiA**	**1.3587675**	-0.682023174	-2.018471739	**1.336448565**
	gspE	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		-0.574179631	-1.777101815	1.202922185
	gspF	**Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA**	**1.0381198**	**-0.571653549**	**-1.758766291**	**1.187112742**
	gspG	**Pseudopilin in H-NS-silenced gsp divergon, type II secreton; cloned gsp divergon secretes ChiA**	**1.3308105**	**-0.964730177**	**-2.1795117**	**1.214781523**
	gspH	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA	1.1772904			
	gspI	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		0.112665963	-0.927333212	1.039999175
	gspJ	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		0.136944905	-1.110237463	1.247182368
	gspK	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		-0.002275476	-0.831979946	0.829704469
	hcaE	3-phenylpropionate/cinnamic acid dioxygenase, alpha subunit; hca genes catabolize 3-phenylpropionate and cinnamic acid, feeding the products into the the mhp pathway	1.170918			
	hemB	5-aminolevulinate dehydratase; also known as porphobilinogen synthase; binds Zn(II)	-1.1517999			
	hemD	Uroporphyrinogen III cosynthase; neomycin sensitivity	1.0766261			
	hisS	Histidine--tRNA ligase	-1.0382023			

	hofC	Homologous to PilC of P. aeruginosa; function not established, insertion mutation gives no phenotype	1.3816845			
	hofQ	Required for the utilization of DNA as a carbon source; H. influenzae competence protein ComE homolog; putative fimbrial transport protein; expression not detected	2.0593238			
	hsdM	DNA methyltransferase M, host modification of foreign DNA	1.1989958			
	hsrA	Putative transporter, blocks RspA-mediated RpoS down-regulation; membrane protein; overexpression causes homocysteine accumulation due to MetE inhibition and methionine auxotrophy in absense of cobalamin; no overexpression resistances found	1.1956267			
	htrL		-1.0534656			
	hyfR	Formate-sensing regulator for hyf operon	1.2317433			
	ilvC	**Ketol-acid reductoisomerase**	**-1.0233388**	**0.607905905**	**2.038941914**	**-1.43103601**
	ilvN	Acetohydroxy acid synthase I (AHAS-I); acetolactate synthase I (ALS-I); valine sensitive; small subunit		1.33800575	-0.51491624	1.85292199
	insA-6		1.4929194			
	insA-7		1.4931407			
	insC-6		1.4933076			
	insD-6		1.874304			
	insF-5		1.4364634			
	insG	IS4 gene, transposition function	1.3130264			
	insI-3		2.618895			
	iscR	Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro	-1.1579247			
	iscS	Cysteine desulfurase used in synthesis of Fe-S clusters and 4-thiouridine; ThiI transpersulfidase; SirA(TusA) transpersulfidase; pyridoxal phosphate cofactor linked to Lys206	-1.2212651			
	iscU	Iron-sulfur cluster assembly scaffold protein	-1.092907			
	ispE	4-diphosphocytidyl-2-C-methylerythritol kinase; isopentenyl phosphate kinase; alternative nonmevalonate (DXP) pathway for terpenoid biosynthesis; essential gene	2.0409093			
	katE	Catalase hydroperoxidase II, heme d-containing; response to oxidative stress; chromate resistance	1.2447912			
	katG	Catalase-hydrogen peroxidase I		0.208642701	-0.610920661	0.819563361
	kdgR	Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK	-1.064749			
	kdtA		1.5366621			
	kduI	4-deoxy-L-threo-5-hexosulose-uronate ketol-isomerase; 5-keto-4-deoxyuronate isomerase	1.4980454			
	kefB	NEM-activatable K+/H+ antiporter	1.0485537			
	kgtP	alpha-Ketoglutarate permease		-0.953824419	0.208527791	-1.16235221
	ldcA	L,D-carboxypeptidase A; cytoplasmic protease that cleaves the terminal D-alanine from cytoplasmic muropeptides	1.003866			
	leuA	alpha-Isopropylmalate synthase		-0.414798339	-1.432033122	1.017234783
	leuB	beta-Isopropylmalate dehydrogenase		-0.199455562	-1.235586059	1.036130497
	leuC	alpha-Isopropylmalate isomerase large subunit		-0.415228459	-1.46720426	1.051975801
	leuD	alpha-Isopropylmalate isomerase small subunit		-0.170246462	-1.315692056	1.145445594
	lldR	Dual role activator/repressor for lldPRD operon		-1.022032736	-0.102462884	-0.919569852
	lpxL	Lipid A synthesis, KDO2-lipid IVA lauroyl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high-temperature survival	1.2080741			
	lpxM	Lipid A synthesis, KDO2-lauroyl-lipid IVA myristoyl-ACP acyltransferase	1.418642			

	map	Methionine aminopeptidase	-1.051142			
	mdlB	ABC exporter permease-ATPase, function unknown	1.090272			
	mdtD	Putative transporter, function unknown; no MDR phenotype when mutated or cloned; fourth gene in mdtABCDbaeRS operon	1.009489			
	mdtE	**MdtEF-TolC multidrug resistance efflux transporter; membrane fusion protein (MFP) component, lipoprotein; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype**	**1.103848**	**-0.943962914**	**1.637187912**	**-2.581150826**
	mlrA	Transcriptional regulator of csgD	1.208386			
	motA	H+-driven stator protein of flagellar rotation	-1.1367812			
	mreB	MreB filaments participate in directional chromosome movement and segregation; mecillinam resistance; forms membrane-associated coiled arrays; actin homolog; morphology	-1.0813851			
	murA	UDP-N-acetylglucosamine enoylpyruvyl transferase; fosfomycin resistance	-1.2009416			
	nadD	Nicotinate mononucleotide adenylyltransferase, NAD(P) biosynthesis	1.1660845			
	nanR	Repressor of the nan operon, induced by sialic acid; homodimeric	1.6356357			
	napA	Nitrate reductase, periplasmic	1.479877			
	narQ	Nitrate/nitrite sensor-transmitter protein; anaerobic respiratory path; cognate regulator is NarP; function redundant with narX	1.0795679			
	narX	Two-component nitrate/nittrite sensor-transmitter protein; NarL is cognate regulator; functional redundance with narQ	1.0639569			
	nlpD	Lipoprotein, function unknown; may be involved in cell wall formation; may have murein hydrolytic activity	1.0051479			
	nlpI	Lipoprotein, osmotic sensitivity and filamentation	1.8954201			
	nudD		1.783473			
	ompT	Outer membrane protease VII, DLP12 prophage; OM protein 2b; omptin	-1.2738028			
	oxc	Probable oxalyl-CoA decarboxylase, oxalate catabolism		-0.336075069	1.512178216	-1.848253285
	paaJ	Phenylacetic acid degradation; mutants are unable to use phenylacetate as a carbon source	2.1441832			
	paaX	**Phenylacetic acid degradation**	**1.0424947**	**0.378975841**	**-0.246470978**	**0.625446818**
	panB	Ketopantoate hydroxymethyltransferase	-1.0029793			
	pcnB	Poly(A) polymerase; controls plasmid copy number; rare AUU start codon, growth-rate regulated; monomeric	2.1234794			
	pdxB	2-hydroxyacid dehydrogenase involved in pyridoxine biosynthesis upstream of 4-phospho-hydroxy-threonine; isoniazid resistance	1.6453347			
	pheA	Phenylalanine synthesis, bifunctional: chorismate mutase (N) and prephenate dehydratase (central); also contains Phe-binding regulatory domain (C); FPA resistance	-1.0391736			
	phoQ	Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP	1.4622464			
	ppiB	Periplasmic peptidylprolyl-cis-trans-isomerase B, rotamase	-1.5020874			
	pqqL	Putative secreted zinc protease, function unknown; induced by AI-2 pheromone	-1.293534			
	prc	Periplasmic carboxy-terminal protease with specificity for non-polar C-termini	-1.0079885			
	prfA	Peptide chain release factor 1, RF-1; translation termination factor recognizes UAG and UAA.	-1.1390026			
	proP	Proline/betaine permease, minor; osmosensor/osmoregulator	1.1124482			

	prpR	Transcriptional regulator of prp operon; propionate catabolism via 2-methlycitrate cycle, characterized primarily in Salmonella	1.6797161			
	purF	Amidophosphoribosyltransferase, purine synthesis; also known as glutamine 5'-phosphoribosylpyrophosphate amidotransferase, GPATase	1.5669665			
	purR	Purine regulon repressor	-1.0262108			
	puuD	gamma-Glutamyl-GABA hydrolase, putrescine utilization pathway	1.0298939			
	puuP	Putrescine importer	1.1621327			
	pyrB	Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamoylase		2.405384692	1.399913513	1.005471179
	rbsD	D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU	-1.7281728			
	rcsA	Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene		0.300528606	-1.142561372	1.443089978
	rcsC	Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase	1.8229611			
	rfaJ	UDP-D-glucose: (galactosyl)LPS-glucosyltransferase	-1.0780096			
	rfaQ	Glycosyltransferase needed for heptose region of LPS core	-1.1963794			
	rfaS	LPS core, not affecting attachment of O antigen	-1.0442805			
	rfaZ	2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis,	-1.3851705			
	rfbA	TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidylyltransferase; needed for dTDP-L-rhamnose synthesis	-1.325498			
	rfbB	TDP-glucose oxidoreductase-4,6 dehydratase	-1.0411434			
	rfbC	dTDP-4-deoxyrhamnose-3,5-epimerase	-1.3006554			
	rfbX	Putative polisoprenol-linked O-antigen translocase	-1.0625052			
	rhaR	Transcriptional activator for rhaSR, AraC family	1.0716362			
	ribA	GTP cyclohydrolase II, riboflavin biosynthesis	1.9398031			
	ribB	**3,4-dihydroxy-2-butanone 4-phosphate synthase; riboflavin biosynthesis; acid-inducible; homodimeric**	**-3.7772803**	**0.081360818**	**1.346423538**	**-1.265062721**
	rob	Right oriC-binding protein, AraC family	1.3771441			
	rplB	50S ribosomal subunit protein L2; binds Zn(II)	1.1556873			
	rplC	50S ribosomal subunit protein L3	-1.0714864			
	rplF	50S ribosomal subunit protein L6; gentamicin sensitivity	-1.1512773			
	rplO	50S ribosomal subunit protein L15	-1.0819453			
	rplP	50S ribosomal subunit protein L16	-1.1343815			
	rplQ	50S ribosomal subunit protein L17	1.612936			
	rplU	50S ribosomal subunit protein L21	-1.2566199			
	rplX	50S ribosomal subunit protein L24	-1.030241			
	rpmG	50S ribosomal subunit protein L33	-1.1044912			
	rpsC	30S ribosomal subunit protein S3	-1.4378805			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	rpsG	30S ribosomal subunit protein S7	-1.2602897			
	rpsH	30S ribosomal subunit protein S8	-1.019196			
	rpsK	30S ribosomal subunit protein S11	-1.0231135			
	rpsM	30S ribosomal subunit protein S13	-1.0838764			
	rpsQ	30S ribosomal subunit protein S17	-1.0870361			
	rrmJ		1.1538243			

	rspA	Bifunctional D-altronate/D-mannonate dehydratase; overproduction prevents homoserine lactone-induced synthesis of RpoS	1.478749			
	sdhC	Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0607324			
	sdhD	Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0157504			
	secB	Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone	-1.3555017			
	secG	SecG inner membrane secretion protein; complexes with and assists the SecYE core translocon to interact with SecA to export proteins	-1.0875401			
	serA	D-3-Phosphoglycerate dehydrogenase	-1.0648217			
	sfmA	Function unknown, FimA homolog		-1.382384642	-2.958069183	1.575684542
	sgcR	Putative sgc cluster transcriptional regulator	1.3975518			
	slyA	Activates crytpic hemolysin gene hlyE; global transcriptional regulator	1.015482			
	sodA	**Superoxide dismutase, Mn**	**1.120604**	**-0.384140377**	**-1.40051441**	**1.016374033**
	sodB	Superoxide dismutase, Fe; response to oxidative stress; chromate resistance; negatively regulated by ryhB RNA as part of indirect positive regulation by Fur; acid-inducible		4.006849988	3.110075363	0.896774625
	stpA	RNA chaperone and DNA-binding protein; suppresses T4 td mutant; modulates micF stability; forms heteromers with, and stabilzed against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS	-1.2432377			
	sulA	Inhibits cell division and ftsZ ring formation; lexA regulon	1.9572544			
	surA	Periplasmic OM porin chaperone, has PPIase activity; required for stationary-phase survival	1.1290984			
	tar	Aspartate, maltose chemoreceptor, methyl-accepting; MCP II; also senses repellents cobalt and nickel; flagellar regulon	-1.1869416			
	thrA	**Aspartokinase I and homoserine dehydrogenase I, bifunctional**	**-1.004643**	**1.18802236**	**1.733920514**	**-0.545898154**
	tig	Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains	-1.0661763			
	torS	Sensor kinase for torCAD operon	2.9209745			
	treF	Cytoplasmic trehalase	1.0018826			
	treR	Repressor of trehalose operon	1.5542111			
	trg	Ribose, galactose chemoreceptor, methyl-accepting; MCP III; flagellar regulon	-1.3795029			
	trkG	Major constitutive K+ uptake permease TrkAG; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane; Rac prophage	1.2485242			
	trkH	Major constitutive K+ uptake permease TrkAH; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane	1.0318046			
	tsr	Serine chemoreceptor, methyl-accepting; MCP I; also senses repellents; flagellar regulon	-1.9566808			
	tufA	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3282719			
	tufB	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3645415			
	uvrC	Excision nuclease subunit C; repair of UV damage to DNA; multicopy causes mucoidy	1.2626269			
	uxuR	Repressor for UxuR regulon; true inducer is fructuronate	1.0230589			
	wbbH		-1.004085			

	wbbI	d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis	-1.0572133			
	wbbJ	Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase	-1.3040595			
	wbbK	Involved in lipopolysaccharide biosynthesis	-1.4321501			
	wcaI	Putative colanic acid biosynthesis glycosyl transferase	1.883362			
	yaaU	Putative transporter, function unknown	1.4289691			
	yadB	Glutamyl-queuosine tRNA(Asp) synthase	1.391839			
	yahA	c-di-GMP-specific phosphodiesterase, PDE-A; reaction product is 5'pGpG; dependent on Mg+2 or Mn+2, Ca+2 inhibitory; optimum pH 9.35; monomeric	-2.0166183			
	yahB	LysR family of transcriptional regulators, function unknown	1.046875			
	ybaO	Function unknown, Lrp family; putative transcriptional regulator	1.0301518			
	ybaS	Glutaminase	1.2362571			
	ybaT	Mutant inhibits reduction of selenate, function unknown; predicted transporter	1.8074303			
	ybaX		-1.101002			
	ybbY	Putative xanthine/uracil permease, function unknown; glyoxylate-inducible	1.3393364			
	ybdG	Putative mechanosensitive channel protein, function unknown	1.1174531			
	ybeF	Putative LysR-family transcriptional regulator, function unknown LysR-family transcriptional regulator, function unknown	1.0823689			
	ybhD	Putative LysR-family transcriptional regulator, function unknown	1.1145554			
	ycaI	Competence protein ComEC homolog, function unknown	1.2410421			
	ycaM	Putative transporter, function unknown	1.6574664			
	ycgV	Overexpression increases adhesion and biofilm formation; probable adhesin, function unknown	1.2697777			
	ydfT		1.6117142			
	ydgD	Putative periplasmic serine protease; function unknown	1.9687521			
	ydiD		1.5217233			
	yeaN	Putative transporter, function unknown; membrane protein	1.3042753			
	yebQ	Putative transporter, function unknown; no overexpression resistances found	1.1920364			
	yegE	Putative c-di-GMP dual activity enzyme, function unknown	1.6381769			
	yegQ	Function unknown, U32 peptidase family	-1.0663853			
	yfaX	Putative transcriptional regulator, function unknown	1.2188423			
	yfbG		1.0953493			
	yfbJ		1.2325368			
	yfbW		1.0032601			
	yfcJ	Putative transporter, function unknown; membrane protein	1.0550871			
	yfeG		1.1252446			
	yfeR	Required for swarming phenotype, function unknown; predicted transcriptional regulator	1.2977767			
	ygeY	Peptidase homolog, function unknown; M20D family	1.1330509			
	ygfI	Putative LysR-family transcriptional regulator, function unknown	1.4685719			
	ygiL	Function unknown, FimA homolog		0.097937983	-0.852435761	0.950373744
	ygjE		1.8157401			
	ygjG		1.0237489			
	yhbC		-1.146364			
	yhdJ	DNA adenine methyltransferase, SAM-dependent	1.0355549			

	yhiF		**1.2616509**	**-1.6261956**	**0.509971635**	**-2.136167235**
	yhjB	Function unknown	1.5886974			
	yicE		**-1.8931122**	**1.018744964**	**2.526242192**	**-1.507497228**
	yieG		-1.2165263			
	yieK	Function unknown, bgl operon; glucosamine-6-phosphate isomerase homolog	1.1036859			
	yihS	D-mannose isomerase; aldose-ketose isomerase inter-converting mannose, fructose and glucose; D-lyxose isomerase	2.4466274			
	yjcD	**Putative purine permease, function unknown**	**-1.2766161**	**0.58935423**	**1.464890192**	**-0.875535962**
	yjcR		2.1817305			
	yjhB	Putative transporter, function unknown; N-acetylneuraminic acid inducible	-1.0054262			
	yjhH	Function unknown	1.0324111			
	yjiR	Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family	1.0690143			
	yjiZ		-1.4398055			
	ynfM	Putative transporter, function unknown; no overexpression resistances found	-1.059771			
	ynhG	Murein L,D-transpeptidase, periplasmic	1.1129286			
	yojI	Microcin J25 efflux pump, TolC-dependent; non-essential gene	1.117802			
	ypdA	Putative sensor kinase, function unknown	-1.0332007			
	ypjA	Overexpression increases adhesion, function unknown; OM autotransporter homolog	1.2955649			
	yqeI	Part of T3SS PAI ETT2 remnant, ToxR homolog	-1.067694			
	yrbG	Function unknown, 10 helix membrane protein similiar to Na+/Ca++ exchangers	1.0887241			
	znuA	High-affinity ABC transport system for zinc, periplasmic	-1.5015092			
	zupT	Zinc and other divalent cation uptake transporter	1.4372325			
30502 developmental process	**flgF**	**Flagellar basal body rod subunit**	**-2.318077**	**1.818358267**	**2.829423308**	**-1.011065042**
	flgG	**Flagellar basal body rod major subunit**	**-2.7651777**	**1.72109801**	**2.74639891**	**-1.0253009**
	flgJ	Flagellum-specific muramidase	-1.6338248			
	flgK	Flagellar synthesis, hook-associated protein	-1.3041476			
	fliD	Hook-associated protein 2, axial family	-1.0269284			
	fliI	**Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits**	**-2.8425198**	**2.053080188**	**3.095328983**	**-1.042248796**
	fliK	**Hook filament junction; controls hook length**	**-2.6773417**	**1.939810007**	**2.765864679**	**-0.826054671**
	fliO	Flagellin export apparatus, integral membrane protein	-1.882103			
	hofQ	Required for the utilization of DNA as a carbon source; H. influenzae competence protein ComE homolog; putative fimbrial transport protein; expression not detected	2.0593238			
	mreB	MreB filaments participate in directional chromosome movement and segregation; mecillinam resistance; forms membrane-associated coiled arrays; actin homolog; morphology	-1.0813851			
	yccA	Membrane-associated protein that binds to FtsH(HflB) and HflKC proteins; mutant YccA stabilizes SecY(Ts); suppression requires HflKC; YccA is a native substrate for the FtsH(HflB) protease	-1.0077734			

51234 establishment of localisation	aaeA	AaeAB p-hydroxybenzoic acid efflux pump MFP component; membrane fusion protein	1.1153295			
	aaeB	AaeAB p-hydroxybenzoic acid efflux pump PET component; efflux protein family	1.2832041			
	acrD	Aminoglycoside efflux pump; RND-type transporter	1.2997208			
	acrF	AcrEF-TolC efflux pump, multidrug/solvent resistance; osmotically remedial envelope defect	1.513372			
	alsA	Allose transport ABC protein	2.124423			
	alsC	Allose transport, membrane component	1.0019131			
	amtB	Ammonia gas channel; sequesters GlnK, a negative regulator of AmtB activity, to the inner membrane; bi-directional facilitated diffusion	1.316608			
	appB	Cytochrome bd-II oxidase subunit II		-1.142286168	0.73330429	-1.875590458
	appC	Cytochrome bd-II oxidase subunit I		-1.223081848	0.589787849	-1.812869697
	araG	High-affinity L-arabinose transport	2.1461978			
	argT	Periplasmic Lys-, Arg-, and Orn-binding protein		-1.31832983	-0.406379535	-0.911950296
	artJ	Periplasmic binding protein of Arg transport system		2.102985883	1.297458654	0.805527229
	ascF	PTS system EIIBC enzyme, beta-glucoside phosphotransferase; paralogous to bglF; cryptic unless AscG is mutated	1.0536551			
	atpA	ATP synthase subunit alpha, membrane-bound, F1 sector	1.33844			
	atpB	ATP synthase subunit a, membrane-bound, F0 sector	-1.0947847			
	atpE	ATP synthase subunit c, membrane-bound, F0 sector; DCCD-binding	-1.2534213			
	atpF	ATP synthase subunit b, membrane-bound, F0 sector	-1.1470773			
	atpH	ATP synthase subunit delta, membrane-bound, F1 sector	-1.1472812			
	bcr	Efflux pump for bicyclomycin, cysteine and sulfonamides	1.2833695			
	betT	High-affinity choline transporter; bet genes confer protection against osmotic stress by making the osmoprotectant glycine betaine from choline	1.1661614			
	bglF	PTS system EIIABC enzyme, beta-glucoside phosphotransferase; BglG kinase/dephosphorylase; membrane-bound protein; binds BglG	1.1257329			
	cirA	**Colicin I receptor and translocator**	**-1.0816369**	**-3.036369365**	**-1.232802369**	**-1.803566996**
	cusA	Silver and copper efflux, membrane transporter; overexpression confers low level fosfomycin resistance; confers copper and silver resistance	1.4714775			
	cydA	**Cytochrome d (bd-I) terminal oxidase subunit I; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by Fnr**	**-1.0059352**	**1.320696764**	**0.540896798**	**0.779799966**
	cydB	**Cytochrome d (bd-I) terminal oxidase subunit II; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by Fnr**	**-1.065628**	**1.44637671**	**0.350969162**	**1.095407548**
	cynX	Putative transporter, function unknown, cyn operon	1.084173			
	cyoA	**Cytochrome o oxidase subunit II, lipoprotein; also called cytochrome bo(3) ubiquinol oxidase subunit II**	**-1.3402126**	**0.208660176**	**1.206163419**	**-0.997503243**
	cyoB	Cytochrome o oxidase subunit I; cytochrome bo(3) ubiquinol oxidase subunit I	1.0475307			
	cyoD	**Cytochrome o oxidase subunit IV; cytochrome bo(3) ubiquinol oxidase subunit IV**	**-1.4617386**	**0.406981018**	**1.492060622**	**-1.085079603**
	dcuD	DcuC paralog, function unknown; mutant has no phenotype and dcuD does not complement dcuC mutations	1.0231616			

	ddpF	D,D-dipeptide permease system, ATP-binding (hydrolysis?) component	1.2672591			
	dppA	Dipeptide/heme transport, periplasmic binding protein; recognition for transport and chemotaxis	1.8925548			
	dsdX	D-serine permease; D-serine tolerance	2.2577286			
	exuT	Hexuronate permease, for glucuronate and galacturonate	1.0179187			
	fecE	Ferric citrate ATP-binding, membrane-associated transport protein	1.2498283			
	feoA	Ferrous iron uptake, required for full FeoB activity	-1.4880528			
	feoB	Ferrous iron uptake GTP-binding membrane protein; N-terminus is a cytoplasmic G protein	-1.9224972			
	fepA	**Ferrienterobactin outer membrane receptor**	**-1.5621696**	**-2.615889662**	**-1.351310187**	**-1.264579475**
	fepE	Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains	-1.1662207			
	fhuE	Outer membrane receptor for ferric-rhodotorulic acid; also receptor for ferric siderophores coprogen and ferrioxamine B		-0.995984903	0.033259204	-1.029244106
	fiu	TonB-dependent ferric iron outer membrane transporter; siderophore receptor for ferri-dihydroxybenzoylserine, ferri-dihydroxybenzoate and other catecholate siderophores; surface receptor for colicins G, H, and E492	-1.0117576			
	fliH	**Negative regulator of FliI ATPase activity; involved in flagellar assembly and export**	**-2.0643058**	**1.950296025**	**2.756911638**	**-0.806615613**
	fliI	**Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits**	**-2.8425198**	**2.053080188**	**3.095328983**	**-1.042248796**
	fliJ	**Flagellin export apparatus soluble chaperone**	**-1.861196**	**2.017483883**	**2.880704117**	**-0.863220233**
	fliP	Flagellin export apparatus, integral membrane protein	-1.3490691			
	fliQ	Flagellin export apparatus, integral membrane protein	-1.7036285			
	focB	Probable bidirectional formate transporter 2	1.0541813			
	gabP	GABA permease, membrane protein	1.2657433			
	gatA	Galactitol-specific enzyme IIA of phosphotransferase system (PTS)	-1.6841471			
	gatC	Galactitol-specific enzyme IIC of PTS	-1.4637866			
	gltP	Proton-glutamate-aspartate transport protein	-1.0238819			
	gntU	Low-affinity gluconate transport protein, membrane protein	1.0674934			
	grpE	Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase	-1.0346646			
	grxB	Glutaredoxin 2; regulated by RpoS and ppGpp	1.6855459			
	gspA	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA, requires gspAB operon	1.1330825			
	gspC	**Part of H-NS-silenced gsp divergon, type II protein secretion;cloned gsp divergon secretes ChiA**	**1.2146425**	**-0.862021266**	**-2.680390988**	**1.818369721**
	gspD	**Part of H-NS-silenced gsp divergon, type II protein secretion; OM secretin; cloned gsp divergon secretes ChiA**	**1.3587675**	**-0.682023174**	**-2.018471739**	**1.336448565**
	gspE	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		-0.574179631	-1.777101815	1.202922185
	gspF	**Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA**	**1.0381198**	**-0.571653549**	**-1.758766291**	**1.187112742**
	gspG	**Pseudopilin in H-NS-silenced gsp divergon, type II secreton; cloned gsp divergon secretes ChiA**	**1.3308105**	**-0.964730177**	**-2.1795117**	**1.214781523**
	gspH	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA	1.1772904			
	gspI	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		0.112665963	-0.927333212	1.039999175

	gspJ	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		0.136944905	-1.110237463	1.247182368
	gspK	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		-0.002275476	-0.831979946	0.829704469
	hofB	Homologous to PilB of Pseudomonas aeruginosa; function not established, insertion mutation gives no phenotype	1.6588261			
	hofC	Homologous to PilC of P. aeruginosa; function not established, insertion mutation gives no phenotype	1.3816845			
	hofQ	Required for the utilization of DNA as a carbon source; H. influenzae competence protein ComE homolog; putative fimbrial transport protein; expression not detected	2.0593238			
	hsrA	Putative transporter, blocks RspA-mediated RpoS down-regulation; membrane protein; overexpression causes homocysteine accumulation due to MetE inhibition and methionine auxotrophy in absense of cobalamin; no overexpression resistances found	1.1956267			
	kefB	NEM-activatable K+/H+ antiporter	1.0485537			
	kgtP	alpha-Ketoglutarate permease		-0.953824419	0.208527791	-1.16235221
	livF	High-affinity branched-chain amino acid transport, ATP-binding membrane protein	-1.2960677			
	livJ	Leu/Ile/Val-binding protein, periplasmic, high-affinity transport; LIV-I system; also involved in phenylalanine accumulation	-1.0355506			
	livK	Leucine-specific binding protein, periplasmic, high-affinity transport for leucine; LS system; also involved in isoleucine, valine, and phenylalanine accumulation	-1.3484504			
	lldP	L-lactate permease; also involved in glycolate uptake		-0.984811318	-0.085681014	-0.899130305
	lsrC	Autoinducer-2 (AI-2) uptake	1.0987494			
	lsrD	Autoinducer-2 (AI-2) uptake	1.0535583			
	malX	PTS enzyme II homolog; malI regulated	1.1802423			
	mdlB	ABC exporter permease-ATPase, function unknown	1.090272			
	mdtD	Putative transporter, function unknown; no MDR phenotype when mutated or cloned; fourth gene in mdtABCDbaeRS operon	1.009489			
	mdtE	**MdtEF-TolC multidrug resistance efflux transporter; membrane fusion protein (MFP) component, lipoprotein; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype**	**1.103848**	**-0.943962914**	**1.637187912**	**-2.581150826**
	mdtF	MdtEF-TolC multidrug resistance efflux RND-type transporter; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenoype		-0.396000539	1.441295899	-1.837296438
	melB	Melibiose permease; thiomethylgalactoside permease II	1.1329398			
	metQ	Periplasmic methionine binding lipoprotein; methionine sulfoximine sensitivity	-1.0314264			
	mgtA	**Magnesium transporter, ATP-dependent; mutant has cobalt resistance; mediates Mg(2+) influx**	**-2.2685869**	**0.414117157**	**2.015561195**	**-1.601444038**
	modA	Molybdate uptake; chlorate resistance; periplasmic molybdate binding protein	-1.0889276			
	motA	H+-driven stator protein of flagellar rotation	-1.1367812			
	napA	Nitrate reductase, periplasmic	1.479877			
	nhaA	Na+/H+ antiporter 1, strongly pH-dependent; helps regulate intracellular pH and extrude lithium; nhaA_P1 activated by NhaR, repressed by H-NS and stimulated by Na(+)	1.3487701			
	nirC	Nitrite uptake transporter; membrane protein	-1.0733091			
	npr	NPr, N-regulated HPr-like protein	1.8415642			
	ompF	Outer membrane porin F	-1.0644927			
	oppD	Oligopeptide transport, ATP-binding protein	-1.0622754			

	phnL	Carbon-phosphorus lyase complex subunit	1.0372381			
	pntA	Proton-translocating NAD(P) transhydrogenase, alpha subunit; membrane protein	-1.123445			
	pnuC	Nicotinamide mononucleotide transporter, putative, by homology with Salmonella		-0.383646904	-1.343392607	0.959745703
	potA	Spermidine/putrescine ABC transporter ATP-binding protein	-1.0903093			
	proP	Proline/betaine permease, minor; osmosensor/osmoregulator	1.1124482			
	ptsG	Glucose phophotransferase enzyme IIBC(Glc); glucose permease	-1.1116796			
	puuP	Putrescine importer	1.1621327			
	rbsA	D-ribose high-affinity transport system	-1.086268			
	rbsC	D-ribose high-affinity transport system, membrane component	-1.6430304			
	rbsD	D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU	-1.7281728			
	rfbX	Putative polisoprenol-linked O-antigen translocase	-1.0625052			
	rsxC	Required for the reduction of SoxR; putative membrane-associated NADH oxidoreductase	-1.300488			
	rsxE	Required for the reduction of SoxR; membrane protein	-1.038332			
	sdaC	Serine:H+ symport permease, threonine-insensitive	-1.1312735			
	sdhC	Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0607324			
	sdhD	Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0157504			
	secB	Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone	-1.3555017			
	secG	SecG inner membrane secretion protein; complexes with and assists the SecYE core translocon to interact with SecA to export proteins	-1.0875401			
	sugE	Multidrug efflux pump; overexpression resistance to cetylpyridinium; suppresses groL mutation	1.8585258			
	tig	Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains	-1.0661763			
	trkG	Major constitutive K+ uptake permease TrkAG; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane; Rac prophage	1.2485242			
	trkH	Major constitutive K+ uptake permease TrkAH; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane	1.0318046			
	uup	DNA-binding ATPase involved in replication; cytosolic; mutant displays an increased frequency of precise excision of transposons and defective growth of bacteriophage Mu	1.0175562			
	yaaJ	Function unknown	1.0547018			
	yaaU	Putative transporter, function unknown	1.4289691			
	yadI	Putative PTS Enzyme IIA, sugar specificity unknown	1.0017041			
	ybaE	Function unknown	1.0258374			
	ybaT	Mutant inhibits reduction of selenate, function unknown; predicted transporter	1.8074303			
	ybbY	Putative xanthine/uracil permease, function unknown; glyoxylate-inducible	1.3393364			
	ybfM		1.4339647			
	ycaM	Putative transporter, function unknown	1.6574664			
	yccZ		1.6202683			
	ydcU	Putative ABC transporter permease protein; function unknown	1.1136831			

	yddB	Putative TonB-dependent outer membrane receptor; function unknown	2.1117015			
	ydhK	Putative efflux protein family (PET) component of YdhJK efflux pump, function unknown	1.3457184			
	ydjN	Function unknown	-1.0541339			
	yeaN	Putative transporter, function unknown; membrane protein	1.3042753			
	yebQ	Putative transporter, function unknown; no overexpression resistances found	1.1920364			
	yecI		1.016995			
	yeiU		1.4640794			
	yejA	ABC transporter periplasmic binding protein for microcin C; regulated by rydC sRNA	1.0284705			
	yfbJ		1.2325368			
	yfbW		1.0032601			
	ygbN	Putative GntP family transporter, function unknown	1.262356			
	ygiS	Putative periplasmic binding protein, function unknown	1.4980664			
	ygjE		1.8157401			
	yhaO	Putative amino acid:H+ symport permease, function unknown	1.8030388			
	yhcD	Putative outer membrane fimbrial subunit usher; function unknown	1.1889033			
	yhdX	Putative ABC transporter permease protein; function unknown	1.2737434			
	yhdY	Putative ABC transporter permease protein; function unknown	1.0240188			
	yhiP		1.1875293			
	yhjV	Putative amino acid:H+ symport permease, function unknown	-1.3462486			
	yicE		**-1.8931122**	**1.018744964**	**2.526242192**	**-1.507497228**
	yieG		-1.2165263			
	yjcD	**Putative purine permease, function unknown**	**-1.2766161**	**0.58935423**	**1.464890192**	**-0.875535962**
	yjcR		2.1817305			
	yjdA	Function unknown	-1.1101673			
	yjfF	Putative ABC transporter permease protein; part of a predicted ABC transporter YtfQRT-YjfF probably specific for galactofuranse transport	1.0845251			
	yjhB	Putative transporter, function unknown; N-acetylneuraminic acid inducible	-1.0054262			
	ynfM	Putative transporter, function unknown; no overexpression resistances found	-1.059771			
	ynjC	Function unknown	1.0072496			
	ynjD	Function unknown	1.1847191			
	yodB	Function unknown		0.694684412	1.62745419	-0.932769778
	yojI	Microcin J25 efflux pump, TolC-dependent; non-essential gene	1.117802			
	yphE	Putative ABC transporter ATP-binding protein; function unknown	1.5556669			
	znuA	High-affinity ABC transport system for zinc, periplasmic	-1.5015092			
51179 localisation	aaeA	AaeAB p-hydroxybenzoic acid efflux pump MFP component; membrane fusion protein	1.1153295			
	aaeB	AaeAB p-hydroxybenzoic acid efflux pump PET component; efflux protein family	1.2832041			
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	alsA	Allose transport ABC protein	2.124423			
	alsC	Allose transport, membrane component	1.0019131			
	amtB	Ammonia gas channel; sequesters GlnK, a negative regulator of AmtB activity, to the inner membrane; bi-directional facilitated diffusion	1.316608			
	appB	Cytochrome bd-II oxidase subunit II		-1.142286168	0.73330429	-1.875590458
	appC	Cytochrome bd-II oxidase subunit I		-1.223081848	0.589787849	-1.812869697
	araG	High-affinity L-arabinose transport	2.1461978			
	argT	Periplasmic Lys-, Arg-, and Orn-binding protein		-1.31832983	-0.406379535	-0.911950296
	artJ	Periplasmic binding protein of Arg transport system		2.102985883	1.297458654	0.805527229
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	atpE	ATP synthase subunit c, membrane-bound, F0 sector; DCCD-binding	-1.2534213			
	atpF	ATP synthase subunit b, membrane-bound, F0 sector	-1.1470773			
	atpH	ATP synthase subunit delta, membrane-bound, F1 sector	-1.1472812			
	bcr	Efflux pump for bicyclomycin, cysteine and sulfonamides	1.2833695			
	betT	High-affinity choline transporter; bet genes confer protection against osmotic stress by making the osmoprotectant glycine betaine from choline	1.1661614			
	bglF	PTS system EIIABC enzyme, beta-glucoside phosphotransferase; BglG kinase/dephosphorylase; membrane-bound protein; binds BglG	1.1257329			
	cheY	Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein	-1.2030091			
	cheZ	CheY-P phosphatase	-1.0379796			
	cirA	**Colicin I receptor and translocator**	**-1.0816369**	**-3.036369365**	**-1.232802369**	**-1.803566996**
	cusA	Silver and copper efflux, membrane transporter; overexpression confers low level fosfomycin resistance; confers copper and silver resistance	1.4714775			
	cydA	**Cytochrome d (bd-I) terminal oxidase subunit I; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by Fnr**	**-1.0059352**	**1.320696764**	**0.540896798**	**0.779799966**
	cydB	**Cytochrome d (bd-I) terminal oxidase subunit II; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by Fnr**	**-1.065628**	**1.44637671**	**0.350969162**	**1.095407548**
	cynX	Putative transporter, function unknown, cyn operon	1.084173			
	cyoA	**Cytochrome o oxidase subunit II, lipoprotein; also called cytochrome bo(3) ubiquinol oxidase subunit II**	**-1.3402126**	**0.208660176**	**1.206163419**	**-0.997503243**
	cyoB	Cytochrome o oxidase subunit I; cytochrome bo(3) ubiquinol oxidase subunit I	1.0475307			
	cyoD	**Cytochrome o oxidase subunit IV; cytochrome bo(3) ubiquinol oxidase subunit IV**	**-1.4617386**	**0.406981018**	**1.492060622**	**-1.085079603**
	dcuD	DcuC paralog, function unknown; mutant has no phenotype and dcuD does not complement dcuC mutations	1.0231616			
	ddpF	D,D-dipeptide permease system, ATP-binding (hydrolysis?) component	1.2672591			
	dppA	Dipeptide/heme transport, periplasmic binding protein; recognition for transport and chemotaxis	1.8925548			
	dsdX	D-serine permease; D-serine tolerance	2.2577286			
	exuT	Hexuronate permease, for glucuronate and galacturonate	1.0179187			

	fecE	Ferric citrate ATP-binding, membrane-associated transport protein	1.2498283			
	feoA	Ferrous iron uptake, required for full FeoB activity	-1.4880528			
	feoB	Ferrous iron uptake GTP-binding membrane protein; N-terminus is a cytoplasmic G protein	-1.9224972			
	fepA	**Ferrienterobactin outer membrane receptor**	**-1.5621696**	**-2.615889662**	**-1.351310187**	**-1.264579475**
	fepE	Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains	-1.1662207			
	fhuE	Outer membrane receptor for ferric-rhodotorulic acid; also receptor for ferric siderophores coprogen and ferrioxamine B		-0.995984903	0.033259204	-1.029244106
	fiu	TonB-dependent ferric iron outer membrane transporter; siderophore receptor for ferri-dihydroxybenzoylserine, ferri-dihydroxybenzoate and other catecholate siderophores; surface receptor for colicins G, H, and E492	-1.0117576			
	flgB	**Flagellar basal body rod subunit**	**-2.9897075**	**2.114201933**	**3.5668911**	**-1.452689167**
	flgC	**Flagellar basal body rod subunit**	**-3.2366333**	**1.918144667**	**3.290344417**	**-1.37219975**
	flgE	**Flagellar hook subunit protein**	**-3.2993827**	**1.879339905**	**3.128954345**	**-1.24961444**
	flgF	**Flagellar basal body rod subunit**	**-2.318077**	**1.818358267**	**2.829423308**	**-1.011065042**
	flgG	**Flagellar basal body rod major subunit**	**-2.7651777**	**1.72109801**	**2.74639891**	**-1.0253009**
	flgH	**Flagellar synthesis, basal body L-ring lipoprotein**	**-1.9212251**	**1.901291464**	**2.870884957**	**-0.969593493**
	flgI	Basal body P-ring flagellar protein	-2.6527514			
	flgJ	Flagellum-specific muramidase	-1.6338248			
	flgK	Flagellar synthesis, hook-associated protein	-1.3041476			
	flgL	Flagellar synthesis, hook-associated protein	-1.0269798			
	fliC	Flagellin, structural gene, H-antigen	-1.5392385			
	fliD	Hook-associated protein 2, axial family	-1.0269284			
	fliF	**Flagellar basal body M-ring protein**	**-2.1452103**	**2.21798513**	**3.623918913**	**-1.405933783**
	fliH	**Negative regulator of FliI ATPase activity; involved in flagellar assembly and export**	**-2.0643058**	**1.950296025**	**2.756911638**	**-0.806615613**
	fliI	**Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits**	**-2.8425198**	**2.053080188**	**3.095328983**	**-1.042248796**
	fliJ	**Flagellin export apparatus soluble chaperone**	**-1.861196**	**2.017483883**	**2.880704117**	**-0.863220233**
	fliG	**Rotor protein for flagellar motor switching and energizing; role in flagellar assembly**	**-2.774952**	**2.130965744**	**3.2673922**	**-1.136426456**
	fliL	Affects rotational direction of flagella during chemotaxis	-1.5788474			
	fliM	**Flagellar synthesis, motor switching and energizing**	**-2.746443**	**2.032106006**	**2.845598856**	**-0.81349285**
	fliN	Flagellar switch protein	-1.9425316			
	fliO	Flagellin export apparatus, integral membrane protein	-1.882103			
	fliP	Flagellin export apparatus, integral membrane protein	-1.3490691			
	fliQ	Flagellin export apparatus, integral membrane protein	-1.7036285			
	focB	Probable bidirectional formate transporter 2	1.0541813			
	gabP	GABA permease, membrane protein	1.2657433			
	gatA	Galactitol-specific enzyme IIA of phosphotransferase system (PTS)	-1.6841471			
	gatC	Galactitol-specific enzyme IIC of PTS	-1.4637866			
	gltP	Proton-glutamate-aspartate transport protein	-1.0238819			
	gntU	Low-affinity gluconate transport protein, membrane protein	1.0674934			
	grpE	Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase	-1.0346646			
	grxB	Glutaredoxin 2; regulated by RpoS and ppGpp	1.6855459			

	gspA	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA, requires gspAB operon	1.1330825			
	gspC	**Part of H-NS-silenced gsp divergon, type II protein secretion;cloned gsp divergon secretes ChiA**	**1.2146425**	**-0.862021266**	**-2.680390988**	**1.818369721**
	gspD	**Part of H-NS-silenced gsp divergon, type II protein secretion; OM secretin; cloned gsp divergon secretes ChiA**	**1.3587675**	**-0.682023174**	**-2.018471739**	**1.336448565**
	gspE	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		-0.574179631	-1.777101815	1.202922185
	gspF	**Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA**	**1.0381198**	**-0.571653549**	**-1.758766291**	**1.187112742**
	gspG	**Pseudopilin in H-NS-silenced gsp divergon, type II secreton; cloned gsp divergon secretes ChiA**	**1.3308105**	**-0.964730177**	**-2.1795117**	**1.214781523**
	gspH	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA	1.1772904			
	gspI	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		0.112665963	-0.927333212	1.039999175
	gspJ	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		0.136944905	-1.110237463	1.247182368
	gspK	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA		-0.002275476	-0.831979946	0.829704469
	hofB	Homologous to PilB of Pseudomonas aeruginosa; function not established, insertion mutation gives no phenotype	1.6588261			
	hofC	Homologous to PilC of P. aeruginosa; function not established, insertion mutation gives no phenotype	1.3816845			
	hofQ	Required for the utilization of DNA as a carbon source; H. influenzae competence protein ComE homolog; putative fimbrial transport protein; expression not detected	2.0593238			
	hsrA	Putative transporter, blocks RspA-mediated RpoS down-regulation; membrane protein; overexpression causes homocysteine accumulation due to MetE inhibition and methionine auxotrophy in absense of cobalamin; no overexpression resistances found	1.1956267			
	kefB	NEM-activatable K+/H+ antiporter	1.0485537			
	kgtP	alpha-Ketoglutarate permease		-0.953824419	0.208527791	-1.16235221
	livF	High-affinity branched-chain amino acid transport, ATP-binding membrane protein	-1.2960677			
	livJ	Leu/Ile/Val-binding protein, periplasmic, high-affinity transport; LIV-I system; also involved in phenylalanine accumulation	-1.0355506			
	livK	Leucine-specific binding protein, periplasmic, high-affinity transport for leucine; LS system; also involved in isoleucine, valine, and phenylalanine accumulation	-1.3484504			
	lldP	L-lactate permease; also involved in glycolate uptake		-0.984811318	-0.085681014	-0.899130305
	lsrC	Autoinducer-2 (AI-2) uptake	1.0987494			
	lsrD	Autoinducer-2 (AI-2) uptake	1.0535583			
	malX	PTS enzyme II homolog; malI regulated	1.1802423			
	mdlB	ABC exporter permease-ATPase, function unknown	1.090272			
	mdtD	Putative transporter, function unknown; no MDR phenotype when mutated or cloned; fourth gene in mdtABCDbaeRS operon	1.009489			
	mdtE	**MdtEF-TolC multidrug resistance efflux transporter; membrane fusion protein (MFP) component, lipoprotein; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype**	**1.103848**	**-0.943962914**	**1.637187912**	**-2.581150826**
	mdtF	MdtEF-TolC multidrug resistance efflux RND-type transporter; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenoype		-0.396000539	1.441295899	-1.837296438

	melB	Melibiose permease; thiomethylgalactoside permease II	1.1329398			
	metQ	Periplasmic methionine binding lipoprotein; methionine sulfoximine sensitivity	-1.0314264			
	mgtA	**Magnesium transporter, ATP-dependent; mutant has cobalt resistance; mediates Mg(2+) influx**	**-2.2685869**	**0.414117157**	**2.015561195**	**-1.601444038**
	modA	Molybdate uptake; chlorate resistance; periplasmic molybdate binding protein	-1.0889276			
	motA	H+-driven stator protein of flagellar rotation	-1.1367812			
	napA	Nitrate reductase, periplasmic	1.479877			
	nhaA	Na+/H+ antiporter 1, strongly pH-dependent; helps regulate intracellular pH and extrude lithium; nhaA_P1 activated by NhaR, repressed by H-NS and stimulated by Na(+)	1.3487701			
	nirC	Nitrite uptake transporter; membrane protein	-1.0733091			
	npr	NPr, N-regulated HPr-like protein	1.8415642			
	ompF	Outer membrane porin F	-1.0644927			
	oppD	Oligopeptide transport, ATP-binding protein	-1.0622754			
	phnL	Carbon-phosphorus lyase complex subunit	1.0372381			
	pntA	Proton-translocating NAD(P) transhydrogenase, alpha subunit; membrane protein	-1.123445			
	pnuC	Nicotinamide mononucleotide transporter, putative, by homology with Salmonella		-0.383646904	-1.343392607	0.959745703
	potA	Spermidine/putrescine ABC transporter ATP-binding protein	-1.0903093			
	proP	Proline/betaine permease, minor; osmosensor/osmoregulator	1.1124482			
	ptsG	Glucose phophotransferase enzyme IIBC(Glc); glucose permease	-1.1116796			
	puuP	Putrescine importer	1.1621327			
	rbsA	D-ribose high-affinity transport system	-1.086268			
	rbsC	D-ribose high-affinity transport system, membrane component	-1.6430304			
	rbsD	D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU	-1.7281728			
	rfbX	Putative polisoprenol-linked O-antigen translocase	-1.0625052			
	rsxC	Required for the reduction of SoxR; putative membrane-associated NADH oxidoreductase	-1.300488			
	rsxE	Required for the reduction of SoxR; membrane protein	-1.038332			
	sdaC	Serine:H+ symport permease, threonine-insensitive	-1.1312735			
	sdhC	Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0607324			
	sdhD	Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0157504			
	secB	Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone	-1.3555017			
	secG	SecG inner membrane secretion protein; complexes with and assists the SecYE core translocon to interact with SecA to export proteins	-1.0875401			
	sugE	Multidrug efflux pump; overexpression resistance to cetylpyridinium; suppresses groL mutation	1.8585258			
	tig	Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains	-1.0661763			
	trkG	Major constitutive K+ uptake permease TrkAG; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane; Rac prophage	1.2485242			

	trkH	Major constitutive K+ uptake permease TrkAH; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane	1.0318046			
	uup	DNA-binding ATPase involved in replication; cytosolic; mutant displays an increased frequency of precise excision of transposons and defective growth of bacteriophage Mu	1.0175562			
	yaaJ	Function unknown	1.0547018			
	yaaU	Putative transporter, function unknown	1.4289691			
	yadI	Putative PTS Enzyme IIA, sugar specificity unknown	1.0017041			
	ybaE	Function unknown	1.0258374			
	ybaT	Mutant inhibits reduction of selenate, function unknown; predicted transporter	1.8074303			
	ybbY	Putative xanthine/uracil permease, function unknown; glyoxylate-inducible	1.3393364			
	ybfM		1.4339647			
	ycaM	Putative transporter, function unknown	1.6574664			
	yccZ		1.6202683			
	ydcU	Putative ABC transporter permease protein; function unknown	1.1136831			
	yddB	Putative TonB-dependent outer membrane receptor; function unknown	2.1117015			
	ydhK	Putative efflux protein family (PET) component of YdhJK efflux pump, function unknown	1.3457184			
	ydjN	Function unknown	-1.0541339			
	yeaN	Putative transporter, function unknown; membrane protein	1.3042753			
	yebQ	Putative transporter, function unknown; no overexpression resistances found	1.1920364			
	yecI		1.016995			
	yeiU		1.4640794			
	yejA	ABC transporter periplasmic binding protein for microcin C; regulated by rydC sRNA	1.0284705			
	yfbJ		1.2325368			
	yfbW		1.0032601			
	ygbN	Putative GntP family transporter, function unknown	1.262356			
	ygiS	Putative periplasmic binding protein, function unknown	1.4980664			
	ygjE		1.8157401			
	yhaO	Putative amino acid:H+ symport permease, function unknown	1.8030388			
	yhcD	Putative outer membrane fimbrial subunit usher; function unknown	1.1889033			
	yhdX	Putative ABC transporter permease protein; function unknown	1.2737434			
	yhdY	Putative ABC transporter permease protein; function unknown	1.0240188			
	yhiP		1.1875293			
	yhjV	Putative amino acid:H+ symport permease, function unknown	-1.3462486			
	yicE		**-1.8931122**	**1.018744964**	**2.526242192**	**-1.507497228**
	yieG		-1.2165263			
	yjcD	**Putative purine permease, function unknown**	**-1.2766161**	**0.58935423**	**1.464890192**	**-0.875535962**
	yjcR		2.1817305			
	yjdA	Function unknown	-1.1101673			
	yjfF	Putative ABC transporter permease protein; part of a predicted ABC transporter YtfQRT-YjfF probably specific for galactofuranse transport	1.0845251			
	yjhB	Putative transporter, function unknown; N-acetylneuraminic acid inducible	-1.0054262			

	ynfM	Putative transporter, function unknown; no overexpression resistances found	-1.059771			
	ynjC	Function unknown	1.0072496			
	ynjD	Function unknown	1.1847191			
	yodB	Function unknown		0.694684412	1.62745419	-0.932769778
	yojI	Microcin J25 efflux pump, TolC-dependent; non-essential gene	1.117802			
	yphE	Putative ABC transporter ATP-binding protein; function unknown	1.5556669			
	znuA	High-affinity ABC transport system for zinc, periplasmic	-1.5015092			
8152 metabolic process	abgB	Required for p-aminobenzoyl-glutamate usage	1.1240034			
	accD	Acetyl-CoA carboxylase, carboxyltransferase beta subunit	-1.0916588			
	acnA	Aconitase A, stationary phase induced; iron-sulfur cluster; apo-enzyme binds mRNA for negative translational autoregulation; negatively regulated by ryhB RNA as part of indirect positive regulation by Fur	1.6737623			
	acnB	Aconitase B; 2-methylaconitate hydratase; apo-enzyme binds mRNA for negative translational autoregulation; iron-sulfur cluster; monomeric	1.0271903			
	acpS	Acyl carrier protein, ACP-CoA phosphopantetheinyltransferase; Holo-ACP synthase		0.020738638	-1.374399075	1.395137713
	acrR	**AcrR transcriptional repressor for acrAB (AcrAB-TolC mulltidrug efflux pump)**	**-1.0204067**	**0.968588206**	**1.712429133**	**-0.743840928**
	adhE	Alcohol dehydrogenase, largely anaerobic; aerobic antioxidant; acetaldehyde-CoA dehydrogenase, CoA-linked; allyl alcohol resistance	1.0416784			
	adiA	Arginine decarboxylase, acid-inducible; arginine-dependent acid resistance	1.1271622			
	aidB	Flavin-containing, DNA binding protein; low level isovaleryl CoA dehydrogenase activity; Ada-regulated adaptive response to DNA methylation damage	1.1255507			
	aldA	**Aldehyde dehydrogenase, NAD-dependent; active on lactaldehyde, glycolaldehyde, and other aldehydes**	**-1.016096**	**0.322882306**	**1.393713239**	**-1.070830933**
	alsK	Allose kinase	1.203258			
	ansA	L-Asparaginase I	-1.1030908			
	ansB	L-Asparaginase II	1.5445883			
	appB	Cytochrome bd-II oxidase subunit II		-1.07989973	0.092777038	-1.172676768
	appC	Cytochrome bd-II oxidase subunit I		-1.142286168	0.73330429	-1.875590458
	arcB	Tripartite sensor/histidine protein kinase; repression of aerobic genes and activationof some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has respones regulator and second transmitter domains	2.5143914			
	argA	**N-acetylglutamate synthase; first step in arginine biosynthesis; amino-acid acetyltransferase; growth on acetylornithine**	**1.3041081**	**2.991781138**	**1.434967896**	**1.556813242**
	argB	**N-acetylglutamate kinase**	**1.044384**	**2.818308386**	**1.527225825**	**1.291082561**
	argC	**N-acetyl-gamma-glutamyl-phosphate reductase**	**1.7869039**	**3.319065683**	**1.757350161**	**1.561715522**
	argD	Acetylornithine aminotransferase; succinyldiaminopimelate aminotransferase, PLP-dependent		2.58062465	1.749457164	0.831167486
	argF	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase; CP4-6 putative prophage remnant		2.345750989	0.780893261	1.564857729
	argG	Argininosuccinate synthase		2.6295392	1.468532017	1.161007183
	argH	**Argininosuccinate lyase**	**1.2643517**	**2.489928442**	**1.442275936**	**1.047652506**

	argI	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase		2.843476333	1.517740469	1.325735865
	arnT	4-amino-4-deoxy-L-arabinose(Ara4N):Lipid A transferase; modifies lipid A phosphates with aminoarabinose and confers resistance to polymyxin B and cationic antimicrobial peptides; glycolipid donor is undecaprenyl phosphate-alpha-L-Ara4N	1.0203366			
	aroF	3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP) synthase; tyrosine repressible; TyrR regulon	1.0875133			
	aroK	Shikimate kinase I; alkali-inducible	-1.2647691			
	asd	Aspartate semialdehyde dehydrogenase		-0.796322194	-1.579930631	0.783608438
	aspA	L-Aspartate ammonia-lyase; L-aspartase	3.0522566			
	aspC	Aspartate aminotransferase, AspAT; kynurenine aminotransferase; glutamine transaminase K	-1.0659509			
	atpA	ATP synthase subunit alpha, membrane-bound, F1 sector	1.33844			
	atpB	ATP synthase subunit a, membrane-bound, F0 sector	-1.0947847			
	atpE	ATP synthase subunit c, membrane-bound, F0 sector; DCCD-binding	-1.2534213			
	atpF	ATP synthase subunit b, membrane-bound, F0 sector	-1.1470773			
	atpH	ATP synthase subunit delta, membrane-bound, F1 sector	-1.1472812			
	barA	Sensor histidine protein kinase, pleiotropic; controls the expresion of csrB/C sRNAs; works in concert with UvrY response regulator	1.6353183			
	bglX	Periplasmic beta-glucosidase	1.188965			
	bioB	**Biotin synthase; dethiobiotin to biotin pathway; iron-sulfur enzyme**	**-1.5355635**	**-0.360614381**	**0.797467665**	**-1.158082046**
	bioC	Biotin synthesis blocked prior to pimeloyl CoA formation; putative SAM-dependent methyltransferase	-1.0316381			
	bioF	**7-keto-8-amino pelargonic acid synthase**	**-1.3357835**	**0.006936511**	**1.062414033**	**-1.055477522**
	cheA	Histidine protein kinase sensor of chemotactic response; CheY is cognate response regulator; autophosphorylating; CheAS is a short form produced by an internal start at codon 98	-1.1959176			
	citC	Putative acetate:SH-citrate lyase ligase	1.741257			
	citE	Putative citrate lyase beta chain	1.1568863			
	citG	Putative cit operon gene, function unknown	2.3438559			
	cld	Regulator of lipopolysaccharide O-chain length; gene studied in Salmonella and non-K-12 strains	-1.0316088			
	coaA	Pantothenate kinase	-1.1887982			
	cobC	Probable alpha-ribazole-5'-phosphate phosphatase; potential partial cobalamin biosynthesis pathway	1.7467084			
	csgD	Transcriptional activator for csgBA and other genes		-1.859434883	-0.292246188	-1.567188696
	cusS	Copper ion sensor regulating cusCFBA expression; may also sense silver	1.4919264			
	cydA	**Cytochrome d (bd-I) terminal oxidase subunit I; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by Fnr**	**-1.0059352**	**1.320696764**	**0.540896798**	**0.779799966**
	cydB	**Cytochrome d (bd-I) terminal oxidase subunit II; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by Fnr**	**-1.065628**	**1.44637671**	**0.350969162**	**1.095407548**
	cyoA	**Cytochrome o oxidase subunit II, lipoprotein; also called cytochrome bo(3) ubiquinol oxidase subunit II**	**-1.3402126**	**0.208660176**	**1.206163419**	**-0.997503243**
	cyoB	Cytochrome o oxidase subunit I; cytochrome bo(3) ubiquinol oxidase subunit I	1.0475307			
	cyoD	**Cytochrome o oxidase subunit IV; cytochrome bo(3) ubiquinol oxidase subunit IV**	**-1.4617386**	**0.406981018**	**1.492060622**	**-1.085079603**

	cyoE	**Cytochrome o oxidase subunit, protoheme IX farnesyltransferase**	**-1.0276141**	**0.195029502**	**1.040158488**	**-0.845128986**
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		0.442750627	1.32534585	-0.882595223
	cysD	Sulfate adenylyltransferase	-1.4373238			
	dadA	D-amino acid dehydrogenase		-0.368920809	-1.625476173	1.256555364
	dadX	Alanine racemase; homodimeric		-0.155438273	-1.291326758	1.135888485
	dapB	**Dihydrodipicolinate reductase**	**1.2919754**	**-0.563659431**	**-2.013465644**	**1.449806213**
	dapD	2,3,4,5-tetrahydropyridine-2-carboxylate N-succinyltransferase; mutations suppress growth defects of strains lacking superoxide dismutase	-1.0075407			
	dcuR	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system response regulator	1.0233135			
	dcuS	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system sensory histidine kinase	1.2036445			
	ddg		1.3459754			
	deaD	ATP-dependent RNA helicase, 50S ribosomal subunit biogenesis; translation factor W2; facilitates translation of mRNAs with 5' secondary structures; multicopy suppressor of rpsB(Ts) mutations	1.1617334			
	degP	Periplasmic, membrane-associated serine endoprotease; protease Do, required for high-temperature growth and the degradation of damaged proteins		-0.366102641	0.625276117	-0.991378758
	deoR	Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer	1.2066016			
	dhaR	Transcription activator of the dhaKLM operon	1.127254			
	dinB	DNA polymerase IV, capable of translesion synthesis; overexpression enhances mutagenesis; mediates targeted mutagenesis by 4-NQO; intrinsic AP lyase activity	1.0903935			
	dnaN	DNA polymerase III sliding clamp beta subunit; required for high processivity; required for regulatory inactivation of DnaA	1.1078105			
	dusB	tRNA-dihydrouridine synthase B	-1.1940618			
	dxs	DXP synthase; DXP is precursor to isoprenoids, thiamin, pyridoxol	1.8676739			
	eno	Enolase; phosphoprotein; component of RNA degradosome	-1.0622171			
	envC	Periplasmic murein hydrolase septal ring factor; sensitivity to crystal violet; filamentous	1.3034105			
	envY	Thermoregulatory activator of porin expression, AraC family	1.679985			
	eutB	Ethanolamine ammonia lyase, large subunit, adenosylcobalamine-dependent; concerted induction requires both B12 and ethanolamine; heterodimeric	1.7656298			
	fabB	beta-Ketoacyl-ACP synthase I; KAS I; homodimeric		1.148054475	2.149240165	-1.00118569
	fabI	Enoyl-ACP reductase, NADH dependent	-1.0237877			
	fbaB	Fructose 1,6-bisphosphate aldolase, class I	1.0204077			
	fcl	NADPH-dependent GDP-L-fucose synthase, colanic acid synthesis; two step reaction at a single active site: GDP-4-keto-6-deoxy-D-mannose epimerase, then reductase	1.6897135			
	fepE	Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains	-1.1662207			
	fimB	**Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE**	**-1.1248107**	**0.473670149**	**1.76544683**	**-1.291776681**
	fkpA	Periplasmic peptidylprolyl cis,trans isomerase; heat shock inducible; PPIase-independent chaperone activity, binds FK506	1.2272221			
	flgJ	Flagellum-specific muramidase	-1.6338248			

	fliI	**Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits**	**-2.8425198**	**2.053080188**	**3.095328983**	**-1.042248796**
	fliJ	Flagellin export apparatus soluble chaperone	-1.861196	**2.017483883**	**2.880704117**	-0.863220233
	fliZ	RpoS antagonist, transiently in post-exponential phase; timing factor allowing motility to continue for a while during starvation; not required for normal motility	1.1728091			
	folE	GTP cyclohydrolase I	-1.0409135			
	ftsI	Transpetidase, PBP3; penicillin-binding protein 3 involved in septal peptidoglycan synthesis	2.2227626			
	ftsN	Cell division and growth; multicopy suppresses ftsA12	1.7090788			
	fusA	Elongation Factor EF-G; GTPase required for translocation from the A-site to the P-site in the ribosome; fusidic acid resistance	-1.1621015			
	gadA	Glutamate decarboxylase A	1.1232334			
	gadB	Glutamate decarboxylase B, vitamin B6-dependent; hexameric	1.0481529			
	gadE	Transcriptional regulator of the gadABC operon		-1.613297865	1.91643444	-3.529732305
	galK	Galactokinase	1.7365794			
	galS	Repressor of the mgl operon and isorepressor of the gal operon; autoregulatory; homodimeric	1.2070732			
	gatA	Galactitol-specific enzyme IIA of phosphotransferase system (PTS)	-1.6841471			
	gatC	Galactitol-specific enzyme IIC of PTS	-1.4637866			
	gatY	D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability	-1.1761272			
	gatZ	Tagatose bisphosphate aldolase GatYZ subunit; required for full activity and stabilty of GatY	-1.2347231			
	gcl	Glyoxylate carboligase, glyoxylate-inducible	1.2727609			
	gdhA	Glutamate dehydrogenase		-0.965960622	-2.004323596	1.038362974
	glcC	Transcriptional positive regulator for glc operon	1.077054			
	glf	UDP-galactopyranose mutase	-1.4456341			
	glgA	Glycogen synthase		-0.611356637	-1.254026216	0.642669579
	glgB	**1,4-alpha-glucan branching enzyme; glycogen branching enzyme**	**1.0104895**	**-0.518011066**	**-1.447500807**	**0.929489741**
	glgC	Glucose-1-phosphate adenylyltransferase; ADP-glucosepyrophosphorylase		-0.717255721	-1.435926535	0.718670815
	glmM	Phosphoglucosamine mutase; UDP-GlcNAc pathway, peptidoglycan, lipopolysaccharide synthesis; mRNA stability effects	-1.2160809			
	glnA	Glutamine synthase	1.0619159			
	glnD	Bifunctional uridylyltransferase/uridylyl-removing enzyme; (UTase/UR); controls uridylylation state and activity of PII(GlnB)	1.5173011			
	glpK	Glycerol kinase	1.7542315			
	glyA	Serine hydroxymethyltransferase; binds Zn(II)	-1.2570169			
	glyS	Glycine--tRNA ligase, beta-subunit	-1.1524415			
	gnd	6-phosphogluconate dehydrogenase, decarboxylating	-1.1842852			
	gntU	Low-affinity gluconate transport protein, membrane protein	1.0674934			
	gpmA	Phosphoglycerate mutase 1, 2,3-bisphosphoglycerate-dependent; Fur regulon; dimeric	-1.1640095			
	grpE	Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase	-1.0346646			
	grxB	Glutaredoxin 2; regulated by RpoS and ppGpp	1.6855459			
	gspA	Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA, requires gspAB operon	1.1330825			

	gyrB	DNA gyrase, subunit B; novobiocin, coumermycin resistance	1.1973567			
	hcaE	3-phenylpropionate/cinnamic acid dioxygenase, alpha subunit; hca genes catabolize 3-phenylpropionate and cinnamic acid, feeding the products into the the mhp pathway	1.170918			
	hemB	5-aminolevulinate dehydratase; also known as porphobilinogen synthase; binds Zn(II)	-1.1517999			
	hemD	Uroporphyrinogen III cosynthase; neomycin sensitivity	1.0766261			
	hisS	Histidine--tRNA ligase	-1.0382023			
	hsdM	DNA methyltransferase M, host modification of foreign DNA	1.1989958			
	hsdR	Endonuclease R, host restriction of foreign DNA; ClpXP-dependent degradation	1.2009877			
	htrL		-1.0534656			
	hyfR	Formate-sensing regulator for hyf operon	1.2317433			
	hyaB	Hydrogenase 1 large subunit [NiFe], periplasmic		-0.191647795	0.952972455	-1.14462025
	ilvC	**Ketol-acid reductoisomerase**	**-1.0233388**	**0.607905905**	**2.038941914**	**-1.43103601**
	ilvN	Acetohydroxy acid synthase I (AHAS-I); acetolactate synthase I (ALS-I); valine sensitive; small subunit		1.33800575	-0.51491624	1.85292199
	insA-6		1.4929194			
	insA-7		1.4931407			
	insC-6		1.4933076			
	insD-6		1.874304			
	insF-5		1.4364634			
	insG	IS4 gene, transposition function	1.3130264			
	insI-3		2.618895			
	intD	Integrase gene within defective prophage DLP12	1.4847395			
	intF	Putative integrase gene, CP4-6 putative prophage remnant	1.1676054			
	intS	Integrase, CPS-53/KpLE1 prophage	-1.029356			
	iscR	Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro	-1.1579247			
	iscS	Cysteine desulfurase used in synthesis of Fe-S clusters and 4-thiouridine; ThiI transpersulfidase; SirA(TusA) transpersulfidase; pyridoxal phosphate cofactor linked to Lys206	-1.2212651			
	iscU	Iron-sulfur cluster assembly scaffold protein	-1.092907			
	ispA	Farnesyl diphosphate synthase, isoprenoid biosynthesis	1.3927091			
	ispE	4-diphosphocytidyl-2-C-methylerythritol kinase; isopentenyl phosphate kinase; alternative nonmevalonate (DXP) pathway for terpenoid biosynthesis; essential gene	2.0409093			
	katE	Catalase hydroperoxidase II, heme d-containing; response to oxidative stress; chromate resistance	1.2447912			
	katG	Catalase-hydrogen peroxidase I		0.208642701	-0.610920661	0.819563361
	kdgR	Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK	-1.064749			
	kdtA		1.5366621			
	kduD	2-deoxy-D-gluconate 3-dehydrogenase	1.0039684			
	kduI	4-deoxy-L-threo-5-hexosulose-uronate ketol-isomerase; 5-keto-4-deoxyuronate isomerase	1.4980454			
	kefB	NEM-activatable K+/H+ antiporter	1.0485537			
	kptA	2'-phosphotransferase, ligated tRNA substrate in vitro, physiological role and in vivo substrate unknown	-1.0849328			
	lacZ	beta-D-Galactosidase	2.3031547			
	ldcA	L,D-carboxypeptidase A; cytoplasmic protease that cleaves the terminal D-alanine from cytoplasmic muropeptides	1.003866			

	leuA	alpha-Isopropylmalate synthase		-0.414798339	-1.432033122	1.017234783
	leuB	beta-Isopropylmalate dehydrogenase		-0.199455562	-1.235586059	1.036130497
	leuC	alpha-Isopropylmalate isomerase large subunit		-0.415228459	-1.46720426	1.051975801
	leuD	alpha-Isopropylmalate isomerase small subunit		-0.170246462	-1.315692056	1.145445594
	lldD	L-lactate dehydrogenase, FMN dependent		-1.218356827	-0.349690385	-0.868666442
	lldR	Dual role activator/repressor for lldPRD operon		-1.022032736	-0.102462884	-0.919569852
	lpxL	Lipid A synthesis, KDO2-lipid IVA lauroyl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high-temperature survival	1.2080741			
	lpxM	Lipid A synthesis, KDO2-lauroyl-lipid IVA myristoyl-ACP acyltransferase	1.418642			
	malP	Maltodextrin phosphorylase	1.0782759			
	map	Methionine aminopeptidase	-1.051142			
	melA	alpha-Galactosidase	1.1843722			
	mgtA	**Magnesium transporter, ATP-dependent; mutant has cobalt resistance; mediates Mg(2+) influx**	**-2.2685869**	**0.414117157**	**2.015561195**	**-1.601444038**
	miaA	Dimethylallyl diphosphate:tRNA dimethylallyltransferase; 2-methylthio-N6-(dimethylallyl)adenosine tRNA hypermodification	2.5113444			
	mlrA	Transcriptional regulator of csgD	1.208386			
	murA	UDP-N-acetylglucosamine enoylpyruvyl transferase; fosfomycin resistance	-1.2009416			
	mutS	Methyl-directed mismatch repair protein; dimeric/tetrameric	-1.0045633			
	nadD	Nicotinate mononucleotide adenylyltransferase, NAD(P) biosynthesis	1.1660845			
	nanR	Repressor of the nan operon, induced by sialic acid; homodimeric	1.6356357			
	napA	Nitrate reductase, periplasmic	1.479877			
	narQ	Nitrate/nitrite sensor-transmitter protein; anaerobic respiratory path; cognate regulator is NarP; function redundant with narX	1.0795679			
	narX	Two-component nitrate/nittrite sensor-transmitter protein; NarL is cognate regulator; functional redundance with narQ	1.0639569			
	nhoA	N-hydroxyarylamine O-acetyltransferase	1.1406503			
	nirC	Nitrite uptake transporter; membrane protein	-1.0733091			
	nlpD	Lipoprotein, function unknown; may be involved in cell wall formation; may have murein hydrolytic activity	1.0051479			
	nrdA	Ribonucleoside diphosphate reductase, subunit alpha; class I, aerobic; ribonucleotide reductase; B1 protein, R1 subunit	-1.0100503			
	nudD		1.783473			
	nuoE	NADH:ubiquinone oxidoreductase subunit E, complex I; NADH dehydrogenase I	1.1405885			
	ompT	Outer membrane protease VII, DLP12 prophage; OM protein 2b; omptin	-1.2738028			
	osmC	Osmotically inducible, stress-inducible membrane protein; involved in defense against oxidative compounds; required for long-term survival in stationary phase	1.022247			
	otsB	Trehalose phosphate phosphatase; cold- and heat- induced; required for viability at 4C; rpoS regulon; HAD17	1.0189233			
	oxc	Probable oxalyl-CoA decarboxylase, oxalate catabolism		-0.336075069	1.512178216	-1.848253285
	paaJ	Phenylacetic acid degradation; mutants are unable to use phenylacetate as a carbon source	2.1441832			
	paaX	**Phenylacetic acid degradation**	**1.0424947**	**0.378975841**	**-0.246470978**	**0.625446818**
	panB	Ketopantoate hydroxymethyltransferase	-1.0029793			
	parC		2.1262205			

	pcnB	Poly(A) polymerase; controls plasmid copy number; rare AUU start codon, growth-rate regulated; monomeric	2.1234794			
	pdxB	2-hydroxyacid dehydrogenase involved in pyridoxine biosynthesis upstream of 4-phospho-hydroxy-threonine; isoniazid resistance	1.6453347			
	pheA	Phenylalanine synthesis, bifunctional: chorismate mutase (N) and prephenate dehydratase (central); also contains Phe-binding regulatory domain (C); FPA resistance	-1.0391736			
	phoA	Alkaline phosphatase, periplasmic; binds Zn(II); dimeric	1.3444939			
	phoQ	Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP	1.4622464			
	php	Putative phosphotriesterase; substrate unknown	1.7269516			
	pinQ	DNA invertase, site-specific recombination, Qin prophage	1.1538181			
	pinR	DNA invertase, site-specific recombination, Rac prophage	1.1496861			
	plsC	1-Acyl-n-glycerol-3-phosphate acyltransferase; affects partitioning	1.6378386			
	pntA	Proton-translocating NAD(P) transhydrogenase, alpha subunit; membrane protein	-1.123445			
	ppiB	Periplasmic peptidylprolyl-cis-trans-isomerase B, rotamase	-1.5020874			
	pqqL	Putative secreted zinc protease, function unknown; induced by AI-2 pheromone	-1.293534			
	prc	Periplasmic carboxy-terminal protease with specificity for non-polar C-termini	-1.0079885			
	prfA	Peptide chain release factor 1, RF-1; translation termination factor recognizes UAG and UAA.	-1.1390026			
	prpR	Transcriptional regulator of prp operon; propionate catabolism via 2-methlycitrate cycle, characterized primarily in Salmonella	1.6797161			
	purC	**Phosphoribosyl-aminoimidazole-succinocarboxamide synthase; purine synthesis**	**-1.6214104**	**0.671627539**	**1.519014342**	**-0.847386803**
	purF	Amidophosphoribosyltransferase, purine synthesis; also known as glutamine 5'-phosphoribosylpyrophosphate amidotransferase, GPATase	1.5669665			
	purM	**Phosphoribosyl-aminoimidazole (AIR) synthase; homodimeric**	**-1.3292446**	**0.734599861**	**2.273001511**	**-1.538401651**
	purN	**Glycinamide ribonucleotide transformylase (GART) 1, purine synthesis; glycinamide ribonucleotide formyltransferase**	**-1.2978582**	**1.019235695**	**1.86684724**	**-0.847611545**
	purR	Purine regulon repressor	-1.0262108			
	purT	**Glycinamide ribonucleotide transformylase (GART) 2, non-folate-requiring, purine synthesis**	**-2.2606297**	**1.08852949**	**2.6678463**	**-1.57931681**
	puuD	gamma-Glutamyl-GABA hydrolase, putrescine utilization pathway	1.0298939			
	pyrB	Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamoylase		2.405384692	1.399913513	1.005471179
	pyrD	Dihydroorotate dehydrogenase, UMP biosynthesis	-1.0465689			
	pyrI	Aspartate carbamoyltransferase, regulatory subunit; aspartate transcarbamylase; ATCase; aspartate transcarbamoylase		2.193177888	1.177744341	1.015433546
	queA	S-adenosylmethionine:tRNA ribosyltransferase-isomerase; queuosine biosynthesis,	-1.0753493			
	rbsD	D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU	-1.7281728			
	rcsA	Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene		0.300528606	-1.142561372	1.443089978
	rcsC	Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase	1.8229611			

	recT	RecET recombinase, annealing protein, Rac prophage; recombination and repair	1.6986904			
	relA	ATP:GTP 3'-pyrophosphotransferase, ppGpp synthetase I; required for ppGpp synthesis during stringent response to amino acid starvation; self regulated	1.068548			
	rfaJ	UDP-D-glucose: (galactosyl)LPS-glucosyltransferase	-1.0780096			
	rfaQ	Glycosyltransferase needed for heptose region of LPS core	-1.1963794			
	rfaS	LPS core, not affecting attachment of O antigen	-1.0442805			
	rfaZ	2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis,	-1.3851705			
	rfbA	TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidylyltransferase; needed for dTDP-L-rhamnose synthesis	-1.325498			
	rfbB	TDP-glucose oxidoreductase-4,6 dehydratase	-1.0411434			
	rfbC	dTDP-4-deoxyrhamnose-3,5-epimerase	-1.3006554			
	rfbX	Putative polisoprenol-linked O-antigen translocase	-1.0625052			
	rhaR	Transcriptional activator for rhaSR, AraC family	1.0716362			
	ribA	GTP cyclohydrolase II, riboflavin biosynthesis	1.9398031			
	ribB	**3,4-dihydroxy-2-butanone 4-phosphate synthase; riboflavin biosynthesis; acid-inducible; homodimeric**	**-3.7772803**	**0.081360818**	**1.346423538**	**-1.265062721**
	rihC	Ribonucleoside hydrolase	-1.0441272			
	rpe	D-ribulose-5-phosphate 3-epimerase	1.0808909			
	rplB	50S ribosomal subunit protein L2; binds Zn(II)	1.1556873			
	rplC	50S ribosomal subunit protein L3	-1.0714864			
	rplF	50S ribosomal subunit protein L6; gentamicin sensitivity	-1.1512773			
	rplO	50S ribosomal subunit protein L15	-1.0819453			
	rplP	50S ribosomal subunit protein L16	-1.1343815			
	rplQ	50S ribosomal subunit protein L17	1.612936			
	rplU	50S ribosomal subunit protein L21	-1.2566199			
	rplX	50S ribosomal subunit protein L24	-1.030241			
	rpmG	50S ribosomal subunit protein L33	-1.1044912			
	rpsC	30S ribosomal subunit protein S3	-1.4378805			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	rpsG	30S ribosomal subunit protein S7	-1.2602897			
	rpsH	30S ribosomal subunit protein S8	-1.019196			
	rpsK	30S ribosomal subunit protein S11	-1.0231135			
	rpsM	30S ribosomal subunit protein S13	-1.0838764			
	rpsQ	30S ribosomal subunit protein S17	-1.0870361			
	rrmJ		1.1538243			
	rspA	Bifunctional D-altronate/D-mannonate dehydratase; overproduction prevents homoserine lactone-induced synthesis of RpoS	1.478749			
	rsxC	Required for the reduction of SoxR; putative membrane-associated NADH oxidoreductase	-1.300488			
	rsxE	Required for the reduction of SoxR; membrane protein	-1.038332			
	rumA	23S rRNA m(5)U1939 methyltransferase, SAM-dependent	1.9303648			
	sbcD	DNA hairpin dsDNA 3'-exonuclease SbcCD, Mn(2+), ATP-dependent; ATP-independent 5' ssDNA endonuclease; cosuppressor with sbcB of recB recC mutations; heterodimeric	1.08962			
	sdhC	Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0607324			

	sdhD	Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0157504			
	secB	Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone	-1.3555017			
	secG	SecG inner membrane secretion protein; complexes with and assists the SecYE core translocon to interact with SecA to export proteins	-1.0875401			
	sgcQ	Putative gene in sgc gene cluster, function unknown	2.1578507			
	sgcR	Putative sgc cluster transcriptional regulator	1.3975518			
	slyA	Activates crytpic hemolysin gene hlyE; global transcriptional regulator	1.015482			
	sodA	**Superoxide dismutase, Mn**	**1.120604**	**-0.384140377**	**-1.40051441**	**1.016374033**
	sodB	Superoxide dismutase, Fe; response to oxidative stress; chromate resistance; negatively regulated by ryhB RNA as part of indirect positive regulation by Fur; acid-inducible		4.006849988	3.110075363	0.896774625
	srlD	Sorbitol-6-phosphate dehydrogenase	-1.2612939			
	surA	Periplasmic OM porin chaperone, has PPIase activity; required for stationary-phase survival	1.1290984			
	tesA	Acyl-CoA thioesterase I; also protease I; also lysophospholipase L1; monomeric	1.0010815			
	thrA	**Aspartokinase I and homoserine dehydrogenase I, bifunctional**	**-1.004643**	**1.18802236**	**1.733920514**	**-0.545898154**
	tig	Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains	-1.0661763			
	tktB	Transketolase B; binds Zn(II)	1.0192213			
	torS	Sensor kinase for torCAD operon	2.9209745			
	treF	Cytoplasmic trehalase	1.0018826			
	treR	Repressor of trehalose operon	1.5542111			
	tufA	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3282719			
	tufB	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3645415			
	uxuR	Repressor for UxuR regulon; true inducer is fructuronate	1.0230589			
	wbbH		-1.004085			
	wbbI	d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis	-1.0572133			
	wbbJ	Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase	-1.3040595			
	wbbK	Involved in lipopolysaccharide biosynthesis	-1.4321501			
	wcaI	Putative colanic acid biosynthesis glycosyl transferase	1.883362			
	xdhA	Probable xanthine dehydrogenase molybdenum-binding subunit; involved in limited purine catabolism; mutation confers adenine sensitivity	1.3941514			
	xdhD	Probable hypoxanthine oxidase; mutation confers adenine sensitivity	1.2296381			
	yadB	Glutamyl-queuosine tRNA(Asp) synthase	1.391839			
	yadE	Polysaccharide deacetylase-like protein, function unknown	1.055563			
	yahB	LysR family of transcriptional regulators, function unknown	1.046875			
	ybaO	Function unknown, Lrp family; putative transcriptional regulator	1.0301518			
	ybaS	Glutaminase	1.2362571			
	ybaX		-1.101002			

	ybeF	Putative LysR-family transcriptional regulator, function unknown LysR-family transcriptional regulator, function unknown	1.0823689			
	ybhD	Putative LysR-family transcriptional regulator, function unknown	1.1145554			
	ybhJ	AcnA homolog, function unknown; not responsible for the residual aconitase activity in acnAB double mutants	1.4566447			
	ycaK	Putative NAD(P)H oxidoreductase, function unknown	-1.1524379			
	ycbB	Murein L,D-transpeptidase, periplasmic	1.1077027			
	yddE	Function unknown	1.1745566			
	ydeP	Required for acid resistance conferred by EvgA overexpression; oxidoreductase homolog		0.165101808	1.134409366	-0.969307558
	ydfT		1.6117142			
	ydgD	Putative periplasmic serine protease; function unknown	1.9687521			
	ydgJ	Putative oxidoreductase; yhhX paralog	1.0867878			
	ydiD		1.5217233			
	yecI		1.016995			
	yedF	Function unknown	-1.1209044			
	yegQ	Function unknown, U32 peptidase family	-1.0663853			
	yfaX	Putative transcriptional regulator, function unknown	1.2188423			
	yfbG		1.0953493			
	yfbJ		1.2325368			
	yfbQ	**Function unknown**	**-1.0475144**	**-0.044862622**	**0.847759504**	**-0.892622126**
	yfbW		1.0032601			
	yfeG		1.1252446			
	yfeR	Required for swarming phenotype, function unknown; predicted transcriptional regulator	1.2977767			
	yfiF	Putative methyltransferase, function unknown; spoU paralog; non-essential gene	-1.4608327			
	ygeY	Peptidase homolog, function unknown; M20D family	1.1330509			
	ygfI	Putative LysR-family transcriptional regulator, function unknown	1.4685719			
	ygjG		1.0237489			
	yhdJ	DNA adenine methyltransferase, SAM-dependent	1.0355549			
	yhiF		**1.2616509**	**-1.6261956**	**0.509971635**	**-2.136167235**
	yhjB	Function unknown	1.5886974			
	yicI	alpha-Xylosidase; hexameric	1.2212114			
	yieK	Function unknown, bgl operon; glucosamine-6-phosphate isomerase homolog	1.1036859			
	yihS	D-mannose isomerase; aldose-ketose isomerase inter-converting mannose, fructose and glucose; D-lyxose isomerase	2.4466274			
	yjdJ	Putative acetyltransferase	1.3598251			
	yjeS	Putative electron transport protein, iron-sulfur center	1.1133585			
	yjhC	Putative oxidoreductase; N-acetylneuraminic acid inducible	-1.0411266			
	yjhG	Function unknown	1.064939			
	yjhH	Function unknown	1.0324111			
	yjiR	Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family	1.0690143			
	yliI	Soluble aldose sugar dehydrogenase; Asd; binds PQQ; outer membrane protein	1.2631116			
	ymdC	Function unknown	1.1792688			
	ynhG	Murein L,D-transpeptidase, periplasmic	1.1129286			
	yodB	Function unknown		0.694684412	1.62745419	-0.932769778

	ypfI		1.067775			
	yqeI	Part of T3SS PAI ETT2 remnant, ToxR homolog	-1.067694			
	zupT	Zinc and other divalent cation uptake transporter	1.4372325			
51704 multi-organism process	ompF	Outer membrane porin F	-1.0644927			
	slyA	Activates crytpic hemolysin gene hlyE; global transcriptional regulator	1.015482			
48519 negative regulation	treR	Repressor of trehalose operon	1.5542111			
	yccA	Membrane-associated protein that binds to FtsH(HflB) and HflKC proteins; mutant YccA stabilizes SecY(Ts); suppression requires HflKC; YccA is a native substrate for the FtsH(HflB) protease	-1.0077734			
50789 regulation of biological process	**acrR**	**AcrR transcriptional repressor for acrAB (AcrAB-TolC mulltidrugefflux pump)**	**-1.0204067**	**0.968588206**	**1.712429133**	**-0.743840928**
	arcB	Tripartite sensor/histidine protein kinase; repression of aerobic genes and activationof some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has respones regulator and second transmitter domains	1.0271903			
	barA	Sensor histidine protein kinase, pleiotropic; controls the expresion of csrB/C sRNAs; works in concert with UvrY response regulator	1.6353183			
	cheA	Histidine protein kinase sensor of chemotactic response; CheY is cognate response regulator; autophosphorylating; CheAS is a short form produced by an internal start at codon 98	-1.1959176			
	cheW	Chemotaxis signal transducer; bridges CheA to chemoreceptors to regulate phophotransfer to CheY and CheB	-1.2323792			
	cheY	Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein	-1.2030091			
	cheZ	CheY-P phosphatase	-1.0379796			
	csgD	Transcriptional activator for csgBA and other genes		-1.859434883	-0.292246188	-1.567188696
	csiE	Stationary phase inducible protein; sigma S-dependent promoter	1.3574634			
	cusS	Copper ion sensor regulating cusCFBA expression; may also sense silver	1.4919264			
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		1.44637671	0.350969162	1.095407548
	dcuR	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system response regulator	1.0233135			
	dcuS	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system sensory histidine kinase	1.2036445			
	deaD	ATP-dependent RNA helicase, 50S ribosomal subunit biogenesis; translation factor W2; facilitates translation of mRNAs with 5' secondary structures; multicopy suppressor of rpsB(Ts) mutations	1.1617334			
	deoR	Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer	1.2066016			
	dhaR	Transcription activator of the dhaKLM operon	1.127254			

	envY	Thermoregulatory activator of porin expression, AraC family	1.679985			
	fimB	**Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE**	**-1.1248107**	**0.473670149**	**1.76544683**	**-1.291776681**
	fliC	Flagellin, structural gene, H-antigen	-1.5392385			
	gadE	Transcriptional regulator of the gadABC operon		-1.613297865	1.91643444	-3.529732305
	galS	Repressor of the mgl operon and isorepressor of the gal operon; autoregulatory; homodimeric	1.2070732			
	glcC	Transcriptional positive regulator for glc operon	1.077054			
	gmr	Cyclic-di-GMP phosphodiesterase, csgD regulator; modulates protein stability of RNase II	1.123914			
	hyfR	Formate-sensing regulator for hyf operon	1.2317433			
	iscR	Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro	-1.1579247			
	kdgR	Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK	-1.064749			
	lldR	Dual role activator/repressor for lldPRD operon		-1.022032736	-0.102462884	-0.919569852
	mlrA	Transcriptional regulator of csgD	1.208386			
	nanR	Repressor of the nan operon, induced by sialic acid; homodimeric	1.6356357			
	narQ	Nitrate/nitrite sensor-transmitter protein; anaerobic respiratory path; cognate regulator is NarP; function redundant with narX	1.0795679			
	narX	Two-component nitrate/nittrite sensor-transmitter protein; NarL is cognate regulator; functional redundance with narQ	1.0639569			
	paaX	**Phenylacetic acid degradation**	**1.0424947**	**0.378975841**	**-0.246470978**	**0.625446818**
	phoQ	Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP	1.4622464			
	prpR	Transcriptional regulator of prp operon; propionate catabolism via 2-methlycitrate cycle, characterized primarily in Salmonella	1.6797161			
	purR	Purine regulon repressor	-1.0262108			
	rcsA	Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene		0.300528606	-1.142561372	1.443089978
	rcsC	Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase	-1.6430304			
	rhaR	Transcriptional activator for rhaSR, AraC family	2.2165618			
	rob	Right oriC-binding protein, AraC family	1.3771441			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	sgcR	Putative sgc cluster transcriptional regulator	1.3975518			
	slyA	Activates crytpic hemolysin gene hlyE; global transcriptional regulator	1.015482			
	stpA	RNA chaperone and DNA-binding protein; suppresses T4 td mutant; modulates micF stability; forms heteromers with, and stabilzed against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS	-1.2432377			
	tar	Aspartate, maltose chemoreceptor, methyl-accepting; MCP II; also senses repellents cobalt and nickel; flagellar regulon	-1.1869416			
	torS	Sensor kinase for torCAD operon	2.9209745			
	treR	Repressor of trehalose operon	1.5542111			
	trg	Ribose, galactose chemoreceptor, methyl-accepting; MCP III; flagellar regulon	-1.3795029			
	tsr	Serine chemoreceptor, methyl-accepting; MCP I; also senses repellents; flagellar regulon	-1.9566808			
	uxuR	Repressor for UxuR regulon; true inducer is fructuronate	1.0230589			

	yahA	c-di-GMP-specific phosphodiesterase, PDE-A; reaction product is 5'pGpG; dependent on Mg+2 or Mn+2, Ca+2 inhibitory; optimum pH 9.35; monomeric	-2.0166183			
	yahB	LysR family of transcriptional regulators, function unknown	1.046875			
	ybaO	Function unknown, Lrp family; putative transcriptional regulator	1.0301518			
	ybeF	Putative LysR-family transcriptional regulator, function unknown LysR-family transcriptional regulator, function unknown	1.0823689			
	ybhD	Putative LysR-family transcriptional regulator, function unknown	1.1145554			
	yccA	Membrane-associated protein that binds to FtsH(HflB) and HflKC proteins; mutant YccA stabilizes SecY(Ts); suppression requires HflKC; YccA is a native substrate for the FtsH(HflB) protease	-1.0077734			
	ydfT	Function unknown	1.6117142			
	yegE	Putative c-di-GMP dual activity enzyme, function unknown	1.6381769			
	yfaX	Putative transcriptional regulator, function unknown	1.2188423			
	yfeG	Function unknown	1.1252446			
	yfeR	Required for swarming phenotype, function unknown; predicted transcriptional regulator	1.2977767			
	ygfI	Putative LysR-family transcriptional regulator, function unknown	1.4685719			
	yhiF	**Probable repressor of dctA dicarboxylate transporter gene**	**1.2616509**	**-1.6261956**	**0.509971635**	**-2.136167235**
	yhjB	Function unknown	1.5886974			
	yjiR	Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family	1.0690143			
	ypdA	Putative sensor kinase, function unknown	-1.0332007			
	yqeI	Part of T3SS PAI ETT2 remnant, ToxR homolog	-1.067694			
50896 response to stimulus	bcr	Efflux pump for bicyclomycin, cysteine and sulfonamides	1.2833695			
	betT	High-affinity choline transporter; bet genes confer protection against osmotic stress by making the osmoprotectant glycine betaine from choline	1.1661614			
	cheA	Histidine protein kinase sensor of chemotactic response; CheY is cognate response regulator; autophosphorylating; CheAS is a short form produced by an internal start at codon 98	-1.1959176			
	cheR	Chemotaxis MCP protein methyltransferase, SAM-dependent; binds C-terminus of chemoreceptors; makes glutamate methyl esters	-1.229362			
	cheW	Chemotaxis signal transducer; bridges CheA to chemoreceptors to regulate phophotransfer to CheY and CheB	-1.2323792			
	cheY	Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein	-1.2030091			
	cheZ	CheY-P phosphatase	-1.0379796			
	deaD	ATP-dependent RNA helicase, 50S ribosomal subunit biogenesis; translation factor W2; facilitates translation of mRNAs with 5' secondary structures; multicopy suppressor of rpsB(Ts) mutations	1.1617334			
	degP	Periplasmic, membrane-associated serine endoprotease; protease Do, required for high-temperature growth and the degradation of damaged proteins		-0.366102641	0.625276117	-0.991378758
	dinB	DNA polymerase IV, capable of translesion synthesis; overexpression enhances mutagenesis; mediates targeted mutagenesis by 4-NQO; intrinsic AP lyase activity	1.0903935			

	dppA	Dipeptide/heme transport, periplasmic binding protein; recognition for transport and chemotaxis	1.8925548			
	ecnB	Bacteriolytic lipoprotein entericidin B toxin	1.641038			
	fabI	Enoyl-ACP reductase, NADH dependent	-1.0237877			
	fliG	**Rotor protein for flagellar motor switching and energizing; role in flagellar assembly**	**-2.774952**	**2.130965744**	**3.2673922**	**-1.136426456**
	fliJ	**Flagellin export apparatus soluble chaperone**	**-1.861196**	**2.017483883**	**2.880704117**	**-0.863220233**
	fliL	Affects rotational direction of flagella during chemotaxis	-1.5788474			
	fliM	**Flagellar synthesis, motor switching and energizing**	**-2.746443**	**2.032106006**	**2.845598856**	**-0.81349285**
	fliN	Flagellar switch protein	-1.9425316			
	fliO	Flagellin export apparatus, integral membrane protein	-1.882103			
	ftsI	Transpetidase, PBP3; penicillin-binding protein 3 involved in septal peptidoglycan synthesis	2.2227626			
	grpE	Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase	-1.0346646			
	gyrB	DNA gyrase, subunit B; novobiocin, coumermycin resistance	1.1973567			
	hscC	Hsc62, DnaK-like chaperone; binds to RpoD and inhibits transcription; inhibits growth when overexpressed; Hsc56(DjlC) is DnaJ-like co-chaperone; ATPase activity is stimulated by GrpE, DjlC; mutant grows slow and is hypersensitive to Cd(II) and UV	1.0540187			
	hsrA	Putative transporter, blocks RspA-mediated RpoS down-regulation; membrane protein; overexpression causes homocysteine accumulation due to MetE inhibition and methionine auxotrophy in absense of cobalamin; no overexpression resistances found	1.1956267			
	iscR	Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro	-1.1579247			
	katE	Catalase hydroperoxidase II, heme d-containing; response to oxidative stress; chromate resistance	1.2447912			
	katG	Catalase-hydrogen peroxidase I		0.208642701	-0.610920661	0.819563361
	lpxL	Lipid A synthesis, KDO2-lipid IVA lauroyl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high-temperature survival	1.2080741			
	mdtD	Putative transporter, function unknown; no MDR phenotype when mutated or cloned; fourth gene in mdtABCDbaeRS operon	1.009489			
	mdtE	**MdtEF-TolC multidrug resistance efflux transporter; membrane fusion protein (MFP) component, lipoprotein; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype**	**1.103848**	**-0.943962914**	**1.637187912**	**-2.581150826**
	mdtF	MdtEF-TolC multidrug resistance efflux RND-type transporter; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenoype		-0.396000539	1.441295899	-1.837296438
	motA	H+-driven stator protein of flagellar rotation	-1.1367812			
	mutS	Methyl-directed mismatch repair protein; dimeric/tetrameric	-1.0045633			
	ompF	Outer membrane porin F	-1.0644927			
	osmC	Osmotically inducible, stress-inducible membrane protein; involved in defense against oxidative compounds; required for long-term survival in stationary phase	1.022247			
	phoH	ATP-binding protein, function unknown	2.0218205			
	rcsA	Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene		0.300528606	-1.142561372	1.443089978

	recD	RecBCD Exonuclease V subunit, recombination and repair; recD mutants are constitutively activated for recombination; RecBCD 5'-3' fast helicase subunit; RecD alone has 5'-3' helicase activity; contains ATP-binding site; binds RecC; inhibits RecA loading	1.1258063			
	ribB	**3,4-dihydroxy-2-butanone 4-phosphate synthase; riboflavin biosynthesis; acid-inducible; homodimeric**	**-3.7772803**	**0.081360818**	**1.346423538**	**-1.265062721**
	rplF	50S ribosomal subunit protein L6; gentamicin sensitivity	-1.1512773			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	rpsQ	30S ribosomal subunit protein S17	-1.0870361			
	rrmJ		1.1538243			
	sulA	Inhibits cell division and ftsZ ring formation; lexA regulon	1.9572544			
	tar	Aspartate, maltose chemoreceptor, methyl-accepting; MCP II; also senses repellents cobalt and nickel; flagellar regulon	-1.1869416			
	trg	Ribose, galactose chemoreceptor, methyl-accepting; MCP III; flagellar regulon	-1.3795029			
	tsr	Serine chemoreceptor, methyl-accepting; MCP I; also senses repellents; flagellar regulon	-1.9566808			
	tufA	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3282719			
	tufB	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3645415			
	uvrC	Excision nuclease subunit C; repair of UV damage to DNA; multicopy causes mucoidy	1.2626269			
	ycaI	Competence protein ComEC homolog, function unknown	1.2410421			
	yebQ	Putative transporter, function unknown; no overexpression resistances found	1.1920364			
	yfbG		1.0953493			
	yhfA	Function unknown	1.1060753			
	yjcR		2.1817305			
	yojI	Microcin J25 efflux pump, TolC-dependent; non-essential gene	1.117802			

Table S2b. Genes affected by the absence of PNPase and/or in a PNPase-mediated response to citrate. Genes are listed according to their Gene Ontology groupings at the level of GO:44237, Cellular Metabolic Process. Genes in bold are affected both by the absence of PNPase and in a PNPase-mediated response to citrate. The magnitude of the changes are expressed as Log2 ratios and are the average of duplicate experiments.

Cellular Metabolic Process

GO Term	**Gene**	**Function**	**Log$_2$ of the ratio of PNPase null (no citrate):Wild-type (no citrate)**	**Log$_2$ of the ratio of Wild-type plus citrate:Wild-type (no citrate)**	**Log$_2$ of the ratio of PNPase null plus citrate:PNPase null (no citrate)**	**Log2 of the ratio of fold-change from wild-type plus/minus citrate and PNPase null plus/minus citrate**
6081 cellular aldehyde metabolic process	gcl	Glyoxylate carboligase, glyoxylate-inducible	1.2727609			
6519 cellular amino acid and derivative metabolic process	adiA	Arginine decarboxylase, acid-inducible; arginine-dependent acid resistance	1.1271622			
	ansA	L-Asparaginase I	-1.1030908			
	ansB	L-Asparaginase II	1.5445883			
	argA	**N-acetylglutamate synthase; first step in arginine biosynthesis; amino-acid acetyltransferase; growth on acetylornithine**	**1.3041081**	**2.991781138**	**1.434967896**	**1.556813242**
	argB	**N-acetylglutamate kinase**	**1.044384**	**2.818308386**	**1.527225825**	**1.291082561**
	argC	**N-acetyl-gamma-glutamyl-phosphate reductase**	**1.7869039**	**3.319065683**	**1.757350161**	**1.561715522**
	argD	Acetylornithine aminotransferase; succinyldiaminopimelate aminotransferase, PLP-dependent		2.58062465	1.749457164	0.831167486
	argF	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase; CP4-6 putative prophage remnant		2.345750989	0.780893261	1.564857729
	argG	Argininosuccinate synthase		2.6295392	1.468532017	1.161007183
	argH	**Argininosuccinate lyase**	**1.2643517**	**2.489928442**	**1.442275936**	**1.047652506**
	argI	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase		2.843476333	1.517740469	1.325735865
	asd	Aspartate semialdehyde dehydrogenase		-0.796322194	-1.579930631	0.783608438
	aspA	L-Aspartate ammonia-lyase; L-aspartase	3.0522566			
	aspC	Aspartate aminotransferase, AspAT; kynurenine aminotransferase; glutamine transaminase K	-1.0659509			
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		0.442750627	1.32534585	-0.882595223

	dadA	D-amino acid dehydrogenase		-0.368920809	-1.625476173	1.256555364
	dadX	Alanine racemase; homodimeric		-0.155438273	-1.291326758	1.135888485
	dapB	**Dihydrodipicolinate reductase**	**1.2919754**	**-0.563659431**	**-2.013465644**	**1.449806213**
	dapD	2,3,4,5-tetrahydropyridine-2-carboxylate N-succinyltransferase; mutations suppress growth defects of strains lacking superoxide dismutase	-1.0075407			
	eutB	Ethanolamine ammonia lyase, large subunit, adenosylcobalamine-dependent; concerted induction requires both B12 and ethanolamine; heterodimeric	1.7656298			
	gadA	Glutamate decarboxylase A	1.1232334			
	gadB	Glutamate decarboxylase B, vitamin B6-dependent; hexameric	1.0481529			
	gdhA	Glutamate dehydrogenase		-0.965960622	-2.004323596	1.038362974
	glnA	Glutamine synthase	1.0619159			
	glyA	Serine hydroxymethyltransferase; binds Zn(II)	-1.2570169			
	glyS	Glycine--tRNA ligase, beta-subunit	-1.1524415			
	hisS	Histidine--tRNA ligase	-1.0382023			
	ilvC	**Ketol-acid reductoisomerase**	**-1.0233388**	**0.607905905**	**2.038941914**	**-1.43103601**
	ilvN	Acetohydroxy acid synthase I (AHAS-I); acetolactate synthase I (ALS-I); valine sensitive; small subunit		1.33800575	-0.51491624	1.85292199
	iscS	Cysteine desulfurase used in synthesis of Fe-S clusters and 4-thiouridine; ThiI transpersulfidase; SirA(TusA) transpersulfidase; pyridoxal phosphate cofactor linked to Lys206	-1.2212651			
	leuA	alpha-Isopropylmalate synthase		-0.414798339	-1.432033122	1.017234783
	leuB	beta-Isopropylmalate dehydrogenase		-0.199455562	-1.235586059	1.036130497
	leuC	alpha-Isopropylmalate isomerase large subunit		-0.415228459	-1.46720426	1.051975801
	leuD	alpha-Isopropylmalate isomerase small subunit		-0.170246462	-1.315692056	1.145445594
	purF	Amidophosphoribosyltransferase, purine synthesis; also known as glutamine 5'-phosphoribosylpyrophosphate amidotransferase, GPATase	1.5669665			
	puuD	gamma-Glutamyl-GABA hydrolase, putrescine utilization pathway	1.0298939			
	pyrB	Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamoylase		2.405384692	1.399913513	1.005471179
	serA	D-3-Phosphoglycerate dehydrogenase	-1.0648217			
	thrA	**Aspartokinase I and homoserine dehydrogenase I, bifunctional**	**-1.004643**	**1.18802236**	**1.733920514**	**-0.545898154**
	yadB	Glutamyl-queuosine tRNA(Asp) synthase	1.391839			
	ybaS	Glutaminase	1.2362571			
	ybaX		-1.101002			
	yjhH	Function unknown	-1.4842229			
6725 cellular aromatic compound metabolic process	citE	Putative citrate lyase beta chain	1.1568863			
	folE	GTP cyclohydrolase I	-1.0409135			
	hcaE	3-phenylpropionate/cinnamic acid dioxygenase, alpha subunit; hca genes catabolize 3-phenylpropionate and cinnamic acid, feeding the products into the the mhp pathway	1.170918			
	napA	Nitrate reductase, periplasmic	1.479877			
	rihC	Ribonucleoside hydrolase	-1.0441272			

	xdhA	Probable xanthine dehydrogenase molybdenum-binding subunit; involved in limited purine catabolism; mutation confers adenine sensitivity	1.3941514			
	xdhD	Probable hypoxanthine oxidase; mutation confers adenine sensitivity	1.2296381			
	zupT	Zinc and other divalent cation uptake transporter	1.4372325			
44249 cellular biosynthetic process	**argA**	**N-acetylglutamate synthase; first step in arginine biosynthesis; amino-acid acetyltransferase; growth on acetylornithine**	**1.3041081**	**2.991781138**	**1.434967896**	**1.556813242**
	argB	**N-acetylglutamate kinase**	**1.044384**	**2.818308386**	**1.527225825**	**1.291082561**
	argC	**N-acetyl-gamma-glutamyl-phosphate reductase**	**1.7869039**	**3.319065683**	**1.757350161**	**1.561715522**
	argD	Acetylornithine aminotransferase; succinyldiaminopimelate aminotransferase, PLP-dependent		2.58062465	1.749457164	0.831167486
	argF	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase; CP4-6 putative prophage remnant		2.345750989	0.780893261	1.564857729
	argG	Argininosuccinate synthase		2.6295392	1.468532017	1.161007183
	argH	**Argininosuccinate lyase**	**1.2643517**	**2.489928442**	**1.442275936**	**1.047652506**
	argI	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase		2.843476333	1.517740469	1.325735865
	arnT	4-amino-4-deoxy-L-arabinose(Ara4N):Lipid A transferase; modifies lipid A phosphates with aminoarabinose and confers resistance to polymyxin B and cationic antimicrobial peptides; glycolipid donor is undecaprenyl phosphate-alpha-L-Ara4N	1.0203366			
	aroF	3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP) synthase; tyrosine repressible; TyrR regulon	1.0875133			
	aroK	Shikimate kinase I; alkali-inducible	-1.2647691			
	asd	Aspartate semialdehyde dehydrogenase		-0.796322194	-1.579930631	0.783608438
	bioB	**Biotin synthase; dethiobiotin to biotin pathway; iron-sulfur enzyme**	**-1.5355635**	**-0.360614381**	**0.797467665**	**-1.158082046**
	bioC	Biotin synthesis blocked prior to pimeloyl CoA formation; putative SAM-dependent methyltransferase	-1.0316381			
	bioF	**7-keto-8-amino pelargonic acid synthase**	**-1.3357835**	**0.006936511**	**1.062414033**	**-1.055477522**
	cld	Regulator of lipopolysaccharide O-chain length; gene studied in Salmonella and non-K-12 strains	-1.0316088			
	cobC	Probable alpha-ribazole-5'-phosphate phosphatase; potential partial cobalamin biosynthesis pathway	1.7467084			
	cyoE	**Cytochrome o oxidase subunit, protoheme IX farnesyltransferase**	**-1.0276141**	**0.195029502**	**1.040158488**	**-0.845128986**
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		0.442750627	1.32534585	-0.882595223
	dapB	**Dihydrodipicolinate reductase**	**1.2919754**	**-0.563659431**	**-2.013465644**	**1.449806213**
	dapD	2,3,4,5-tetrahydropyridine-2-carboxylate N-succinyltransferase; mutations suppress growth defects of strains lacking superoxide dismutase	-1.0075407			
	fcl	NADPH-dependent GDP-L-fucose synthase, colanic acid synthesis; two step reaction at a single active site: GDP-4-keto-6-deoxy-D-mannose epimerase, then reductase	1.6897135			
	fepE	Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains	-1.1662207			
	fusA	Elongation Factor EF-G; GTPase required for translocation from the A-site to the P-site in the ribosome; fusidic acid resistance	-1.1621015			
	glf	UDP-galactopyranose mutase	-1.4456341			

	glgA	Glycogen synthase		-0.611356637	-1.254026216	0.642669579
	glgB	**1,4-alpha-glucan branching enzyme; glycogen branching enzyme**	**1.0104895**	**-0.518011066**	**-1.447500807**	**0.929489741**
	glgC	Glucose-1-phosphate adenylyltransferase; ADP-glucose pyrophosphorylase		-0.717255721	-1.435926535	0.718670815
	glyS	Glycine--tRNA ligase, beta-subunit	-1.1524415			
	hemB	5-aminolevulinate dehydratase; also known as porphobilinogen synthase; binds Zn(II)	-1.1517999			
	hemD	Uroporphyrinogen III cosynthase; neomycin sensitivity	1.0766261			
	hisS	Histidine--tRNA ligase	-1.0382023			
	htrL		-1.0534656			
	ilvC	**Ketol-acid reductoisomerase**	**-1.0233388**	**0.607905905**	**2.038941914**	**-1.43103601**
	ilvN	Acetohydroxy acid synthase I (AHAS-I); acetolactate synthase I (ALS-I); valine sensitive; small subunit		1.33800575	-0.51491624	1.85292199
	kdtA		1.5366621			
	leuA	alpha-Isopropylmalate synthase		-0.414798339	-1.432033122	1.017234783
	leuB	beta-Isopropylmalate dehydrogenase		-0.199455562	-1.235586059	1.036130497
	leuC	alpha-Isopropylmalate isomerase large subunit		-0.415228459	-1.46720426	1.051975801
	leuD	alpha-Isopropylmalate isomerase small subunit		-0.170246462	-1.315692056	1.145445594
	lpxL	Lipid A synthesis, KDO2-lipid IVA lauroyl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high-temperature survival	1.2080741			
	lpxM	Lipid A synthesis, KDO2-lauroyl-lipid IVA myristoyl-ACP acyltransferase	1.418642			
	nadD	Nicotinate mononucleotide adenylyltransferase, NAD(P) biosynthesis	1.1660845			
	nudD		1.783473			
	pheA	Phenylalanine synthesis, bifunctional: chorismate mutase (N) and prephenate dehydratase (central); also contains Phe-binding regulatory domain (C); FPA resistance	-1.0391736			
	prfA	Peptide chain release factor 1, RF-1; translation termination factor recognizes UAG and UAA.	-1.1390026			
	purF	Amidophosphoribosyltransferase, purine synthesis; also known as glutamine 5'-phosphoribosylpyrophosphate amidotransferase, GPATase	1.5669665			
	pyrB	Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamoylase		2.405384692	1.399913513	1.005471179
	pyrD	Dihydroorotate dehydrogenase, UMP biosynthesis	-1.0465689			
	pyrI	Aspartate carbamoyltransferase, regulatory subunit; aspartate transcarbamylase; ATCase; aspartate transcarbamoylase		2.193177888	1.177744341	1.015433546
	rfaJ	UDP-D-glucose: (galactosyl)LPS-glucosyltransferase	-1.0780096			
	rfaQ	Glycosyltransferase needed for heptose region of LPS core	-1.1963794			
	rfaS	LPS core, not affecting attachment of O antigen	-1.0442805			
	rfaZ	2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis,	-1.3851705			
	rfbA	TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidylyltransferase; needed for dTDP-L-rhamnose synthesis	-1.325498			
	rfbB	TDP-glucose oxidoreductase-4,6 dehydratase	-1.0411434			
	rfbC	dTDP-4-deoxyrhamnose-3,5-epimerase	-1.3006554			
	rfbX	Putative polisoprenol-linked O-antigen translocase	-1.0625052			
	rplB	50S ribosomal subunit protein L2; binds Zn(II)	1.1556873			

	rplC	50S ribosomal subunit protein L3	-1.0714864			
	rplF	50S ribosomal subunit protein L6; gentamicin sensitivity	-1.1512773			
	rplO	50S ribosomal subunit protein L15	-1.0819453			
	rplP	50S ribosomal subunit protein L16	-1.1343815			
	rplQ	50S ribosomal subunit protein L17	1.612936			
	rplU	50S ribosomal subunit protein L21	-1.2566199			
	rplX	50S ribosomal subunit protein L24	-1.030241			
	rpmG	50S ribosomal subunit protein L33	-1.1044912			
	rpsC	30S ribosomal subunit protein S3	-1.4378805			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	rpsG	30S ribosomal subunit protein S7	-1.2602897			
	rpsH	30S ribosomal subunit protein S8	-1.019196			
	rpsK	30S ribosomal subunit protein S11	-1.0231135			
	rpsM	30S ribosomal subunit protein S13	-1.0838764			
	rpsQ	30S ribosomal subunit protein S17	-1.0870361			
	serA	D-3-Phosphoglycerate dehydrogenase	-1.0648217			
	thrA	**Aspartokinase I and homoserine dehydrogenase I, bifunctional**	**-1.004643**	**1.18802236**	**1.733920514**	**-0.545898154**
	tufA	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3282719			
	tufB	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3645415			
	wbbH		-1.004085			
	wbbI	d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis	-1.0572133			
	wbbJ	Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase	-1.3040595			
	wbbK	Involved in lipopolysaccharide biosynthesis	-1.4321501			
	wcaI	Putative colanic acid biosynthesis glycosyl transferase	1.883362			
	yadB	Glutamyl-queuosine tRNA(Asp) synthase	1.391839			
	yfbG		1.0953493			
	yfbJ		1.2325368			
	yfbW		1.0032601			
44262 cellular carbohydrate metabolic process	arnT	4-amino-4-deoxy-L-arabinose(Ara4N):Lipid A transferase; modifies lipid A phosphates with aminoarabinose and confers resistance to polymyxin B and cationic antimicrobial peptides; glycolipid donor is undecaprenyl phosphate-alpha-L-Ara4N	1.0203366			
	cld	Regulator of lipopolysaccharide O-chain length; gene studied in Salmonella and non-K-12 strains	-1.0316088			
	fcl	NADPH-dependent GDP-L-fucose synthase, colanic acid synthesis; two step reaction at a single active site: GDP-4-keto-6-deoxy-D-mannose epimerase, then reductase	1.6897135			
	fepE	Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains	-1.1662207			
	galK	Galactokinase	1.7365794			

	gatA	Galactitol-specific enzyme IIA of phosphotransferase system (PTS)	-1.6841471			
	gatC	Galactitol-specific enzyme IIC of PTS	-1.4637866			
	gatY	D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability	-1.6480765			
	gatZ	Tagatose bisphosphate aldolase GatYZ subunit; required for full activity and stabilty of GatY	-1.2347231			
	glf	UDP-galactopyranose mutase	-1.4456341			
	glgA	Glycogen synthase		-0.611356637	-1.254026216	0.642669579
	glgB	**1,4-alpha-glucan branching enzyme; glycogen branching enzyme**	**1.0104895**	**-0.518011066**	**-1.447500807**	**0.929489741**
	glgC	Glucose-1-phosphate adenylyltransferase; ADP-glucose pyrophosphorylase		-0.717255721	-1.435926535	0.718670815
	gnd	6-phosphogluconate dehydrogenase, decarboxylating	-1.1842852			
	gntU	Low-affinity gluconate transport protein, membrane protein	1.0674934			
	htrL		-1.0534656			
	kdtA		1.5366621			
	kduI	4-deoxy-L-threo-5-hexosulose-uronate ketol-isomerase; 5-keto-4-deoxyuronate isomerase	1.4980454			
	lpxL	Lipid A synthesis, KDO2-lipid IVA lauroyl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high-temperature survival	1.2080741			
	lpxM	Lipid A synthesis, KDO2-lauroyl-lipid IVA myristoyl-ACP acyltransferase	1.418642			
	nudD		1.783473			
	rfaJ	UDP-D-glucose: (galactosyl)LPS-glucosyltransferase	-1.0780096			
	rfaQ	Glycosyltransferase needed for heptose region of LPS core	-1.1963794			
	rfaS	LPS core, not affecting attachment of O antigen	-1.0442805			
	rfaZ	2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis,	-1.3851705			
	rfbA	TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidylyltransferase; needed for dTDP-L-rhamnose synthesis	-1.325498			
	rfbB	TDP-glucose oxidoreductase-4,6 dehydratase	-1.0411434			
	rfbC	dTDP-4-deoxyrhamnose-3,5-epimerase	-1.3006554			
	rfbX	Putative polisoprenol-linked O-antigen translocase	-1.0625052			
	rhaR	Transcriptional activator for rhaSR, AraC family	1.0716362			
	treF	Cytoplasmic trehalase	1.0018826			
	treR	Repressor of trehalose operon	1.5542111			
	wbbH		-1.004085			
	wbbI	d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis	-1.0572133			
	wbbJ	Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase	-1.3040595			
	wbbK	Involved in lipopolysaccharide biosynthesis	-1.4321501			
	wcaI	Putative colanic acid biosynthesis glycosyl transferase	1.883362			
	yfbG		1.0953493			
	yfbJ		1.2325368			
	yfbW		1.0032601			
	yieK	Function unknown, bgl operon; glucosamine-6-phosphate isomerase homolog	1.1036859			

	yihS	D-mannose isomerase; aldose-ketose isomerase inter-converting mannose, fructose and glucose; D-lyxose isomerase	2.4466274			
44248 cellular catabolic process	acnA	Aconitase A, stationary phase induced; iron-sulfur cluster; apo-enzyme binds mRNA for negative translational autoregulation; negatively regulated by ryhB RNA as part of indirect positive regulation by Fur	1.6737623	0.208642701	-0.610920661	0.819563361
	acnB	Aconitase B; 2-methylaconitate hydratase; apo-enzyme binds mRNA for negative translational autoregulation; iron-sulfur cluster; monomeric	1.0271903			
	aspA	L-Aspartate ammonia-lyase; L-aspartase	3.0522566			
	gatY	D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability	-1.6480765			
	gatZ	Tagatose bisphosphate aldolase GatYZ subunit; required for full activity and stabilty of GatY	-1.2347231			
	hcaE	3-phenylpropionate/cinnamic acid dioxygenase, alpha subunit; hca genes catabolize 3-phenylpropionate and cinnamic acid, feeding the products into the the mhp pathway	1.170918			
	katE	Catalase hydroperoxidase II, heme d-containing; response to oxidative stress; chromate resistance	1.2447912			
	katG	Catalase-hydrogen peroxidase I				
	nlpD	Lipoprotein, function unknown; may be involved in cell wall formation; may have murein hydrolytic activity	1.0051479			
	rbsD	D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU	-1.7281728			
	rspA	Bifunctional D-altronate/D-mannonate dehydratase; overproduction prevents homoserine lactone-induced synthesis of RpoS	1.478749			
	sdhC	Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0607324			
	sdhD	Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0157504			
	ynhG	Murein L,D-transpeptidase, periplasmic	1.1129286			
44255 cellular lipid metabolic process	arnT	4-amino-4-deoxy-L-arabinose(Ara4N):Lipid A transferase; modifies lipid A phosphates with aminoarabinose and confers resistance to polymyxin B and cationic antimicrobial peptides; glycolipid donor is undecaprenyl phosphate-alpha-L-Ara4N	1.0203366			
	ydiD		1.5217233			
	yfbG		1.0953493			
	yfbJ		1.2325368			
	yfbW		1.0032601			
44260 cellular macromolecule metabolic process	abgB	Required for p-aminobenzoyl-glutamate usage	1.1240034			

	arcB	Tripartite sensor/histidine protein kinase; repression of aerobic genes and activationof some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has respones regulator and second transmitter domains	2.5143914			
	arnT	4-amino-4-deoxy-L-arabinose(Ara4N):Lipid A transferase; modifies lipid A phosphates with aminoarabinose and confers resistance to polymyxin B and cationic antimicrobial peptides; glycolipid donor is undecaprenyl phosphate-alpha-L-Ara4N	1.0203366			
	barA	Sensor histidine protein kinase, pleiotropic; controls the expresion of csrB/C sRNAs; works in concert with UvrY response regulator	1.6353183			
	cheA	Histidine protein kinase sensor of chemotactic response; CheY is cognate response regulator; autophosphorylating; CheAS is a short form produced by an internal start at codon 98	-1.1959176			
	cld	Regulator of lipopolysaccharide O-chain length; gene studied in Salmonella and non-K-12 strains	-1.0316088			
	cusS	Copper ion sensor regulating cusCFBA expression; may also sense silver	1.4919264			
	dcuS	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system sensory histidine kinase	1.2036445			
	degP	Periplasmic, membrane-associated serine endoprotease; protease Do, required for high-temperature growth and the degradation of damaged proteins		-0.366102641	0.625276117	-0.991378758
	envC	Periplasmic murein hydrolase septal ring factor; sensitivity to crystal violet; filamentous	1.3034105			
	fcl	NADPH-dependent GDP-L-fucose synthase, colanic acid synthesis; two step reaction at a single active site: GDP-4-keto-6-deoxy-D-mannose epimerase, then reductase	1.6897135			
	fepE	Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains	-1.1662207			
	fkpA	Periplasmic peptidylprolyl cis,trans isomerase; heat shock inducible; PPIase-independent chaperone activity, binds FK506	1.2272221			
	ftsN	Cell division and growth; multicopy suppresses ftsA12	1.7090788			
	fusA	Elongation Factor EF-G; GTPase required for translocation from the A-site to the P-site in the ribosome; fusidic acid resistance	-1.1621015			
	glf	UDP-galactopyranose mutase	-1.4456341			
	glgA	Glycogen synthase		-0.611356637	-1.254026216	0.642669579
	glgB	**1,4-alpha-glucan branching enzyme; glycogen branching enzyme**	**1.0104895**	**-0.518011066**	**-1.447500807**	**0.929489741**
	glgC	Glucose-1-phosphate adenylyltransferase; ADP-glucose pyrophosphorylase		-0.717255721	-1.435926535	0.718670815
	glyS	Glycine--tRNA ligase, beta-subunit	-1.1524415			
	grpE	Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase	-1.0346646			
	hisS	Histidine--tRNA ligase	-1.0382023			
	htrL		-1.0534656			
	kdtA		1.5366621			
	kduI	4-deoxy-L-threo-5-hexosulose-uronate ketol-isomerase; 5-keto-4-deoxyuronate isomerase	1.4980454			
	lpxL	Lipid A synthesis, KDO2-lipid IVA lauroyl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high-temperature survival	1.2080741			

	lpxM	Lipid A synthesis, KDO2-lauroyl-lipid IVA myristoyl-ACP acyltransferase	1.418642			
	map	Methionine aminopeptidase	-1.051142			
	narQ	Nitrate/nitrite sensor-transmitter protein; anaerobic respiratory path; cognate regulator is NarP; function redundant with narX	1.0795679			
	narX	Two-component nitrate/nittrite sensor-transmitter protein; NarL is cognate regulator; functional redundance with narQ	1.0639569			
	nlpD	Lipoprotein, function unknown; may be involved in cell wall formation; may have murein hydrolytic activity	1.0051479			
	nudD		1.783473			
	ompT	Outer membrane protease VII, DLP12 prophage; OM protein 2b; omptin	-1.2738028			
	phoQ	Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP	1.4622464			
	ppiB	Periplasmic peptidylprolyl-cis-trans-isomerase B, rotamase	-1.5020874			
	pqqL	Putative secreted zinc protease, function unknown; induced by AI-2 pheromone	-1.293534			
	prc	Periplasmic carboxy-terminal protease with specificity for non-polar C-termini	-1.0079885			
	prfA	Peptide chain release factor 1, RF-1; translation termination factor recognizes UAG and UAA.	-1.1390026			
	rcsC	Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase	1.8229611			
	rfaJ	UDP-D-glucose: (galactosyl)LPS-glucosyltransferase	-1.0780096			
	rfaQ	Glycosyltransferase needed for heptose region of LPS core	-1.1963794			
	rfaS	LPS core, not affecting attachment of O antigen	-1.0442805			
	rfaZ	2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis,	-1.3851705			
	rfbA	TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidylyltransferase; needed for dTDP-L-rhamnose synthesis	-1.325498			
	rfbB	TDP-glucose oxidoreductase-4,6 dehydratase	-1.0411434			
	rfbC	dTDP-4-deoxyrhamnose-3,5-epimerase	-1.3006554			
	rfbX	Putative polisoprenol-linked O-antigen translocase	-1.0625052			
	rplB	50S ribosomal subunit protein L2; binds Zn(II)	1.1556873			
	rplC	50S ribosomal subunit protein L3	-1.0714864			
	rplF	50S ribosomal subunit protein L6; gentamicin sensitivity	-1.1512773			
	rplO	50S ribosomal subunit protein L15	-1.0819453			
	rplP	50S ribosomal subunit protein L16	-1.1343815			
	rplQ	50S ribosomal subunit protein L17	1.612936			
	rplU	50S ribosomal subunit protein L21	-1.2566199			
	rplX	50S ribosomal subunit protein L24	-1.030241			
	rpmG	50S ribosomal subunit protein L33	-1.1044912			
	rpsC	30S ribosomal subunit protein S3	-1.4378805			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	rpsG	30S ribosomal subunit protein S7	-1.2602897			
	rpsH	30S ribosomal subunit protein S8	-1.019196			
	rpsK	30S ribosomal subunit protein S11	-1.0231135			
	rpsM	30S ribosomal subunit protein S13	-1.0838764			
	rpsQ	30S ribosomal subunit protein S17	-1.0870361			

	secB	Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone	-1.3555017			
	surA	Periplasmic OM porin chaperone, has PPIase activity; required for stationary-phase survival	1.1290984			
	tig	Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains	-1.0661763			
	torS	Sensor kinase for torCAD operon	2.9209745			
	tufA	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3282719			
	tufB	EF-Tu, Elongation Factor-Translation, unstable; GTP-dependent binding of aa-tRNA to the A-site of ribosomes; has intrinsic GTPase activity when bound to kirromycin	-1.3645415			
	wbbH		-1.004085			
	wbbI	d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis	-1.0572133			
	wbbJ	Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase	-1.3040595			
	wbbK	Involved in lipopolysaccharide biosynthesis	-1.4321501			
	wcaI	Putative colanic acid biosynthesis glycosyl transferase	1.883362			
	yadB	Glutamyl-queuosine tRNA(Asp) synthase	1.391839			
	ydfT		1.6117142			
	ydgD	Putative periplasmic serine protease; function unknown	1.9687521			
	yegQ	Function unknown, U32 peptidase family	-1.0663853			
	yfbG		1.0953493			
	yfbJ		1.2325368			
	yfbW		1.0032601			
	ygeY	Peptidase homolog, function unknown; M20D family	1.1330509			
51186 cofactor metabolic process	acnA	Aconitase A, stationary phase induced; iron-sulfur cluster; apo-enzyme binds mRNA for negative translational autoregulation; negatively regulated by ryhB RNA as part of indirect positive regulation by Fur	1.6737623			
	acnB	Aconitase B; 2-methylaconitate hydratase; apo-enzyme binds mRNA for negative translational autoregulation; iron-sulfur cluster; monomeric	1.0271903			
	aspA	L-Aspartate ammonia-lyase; L-aspartase	3.0522566			
	citE	Putative citrate lyase beta chain	1.1568863			
	coaA	Pantothenate kinase	-1.1887982			
	hemB	5-aminolevulinate dehydratase; also known as porphobilinogen synthase; binds Zn(II)	-1.1517999			
	hemD	Uroporphyrinogen III cosynthase; neomycin sensitivity	1.0766261			
	iscU	Iron-sulfur cluster assembly scaffold protein	-1.092907			
	panB	Ketopantoate hydroxymethyltransferase	-1.0029793			
	sdhC	Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0607324			
	sdhD	Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0157504			

6091 generation of precursor metabolites and energy	appB	Cytochrome bd-II oxidase subunit II		-1.142286168	0.73330429	-1.875590458
	appC	Cytochrome bd-II oxidase subunit I		-1.223081848	0.589787849	-1.812869697
	cydA	**Cytochrome d (bd-I) terminal oxidase subunit I; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by Fnr**	**-1.0059352**	**1.320696764**	**0.540896798**	**0.779799966**
	cydB	**Cytochrome d (bd-I) terminal oxidase subunit II; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by Fnr**	**-1.065628**	**1.44637671**	**0.350969162**	**1.095407548**
	cyoA	**Cytochrome o oxidase subunit II, lipoprotein; also called cytochrome bo(3) ubiquinol oxidase subunit II**	**-1.3402126**	**0.208660176**	**1.206163419**	**-0.997503243**
	cyoB	Cytochrome o oxidase subunit I; cytochrome bo(3) ubiquinol oxidase subunit I	1.0475307			
	cyoD	**Cytochrome o oxidase subunit IV; cytochrome bo(3) ubiquinol oxidase subunit IV**	**-1.4617386**	**0.406981018**	**1.492060622**	**-1.085079603**
	eno	Enolase; phosphoprotein; component of RNA degradosome	-1.0622171			
	fbaB	Fructose 1,6-bisphosphate aldolase, class I	1.0204077			
	gatY	D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability	-1.6480765			
	gpmA	Phosphoglycerate mutase 1, 2,3-bisphosphoglycerate-dependent; Fur regulon; dimeric	-1.1640095			
	grxB	Glutaredoxin 2; regulated by RpoS and ppGpp	1.6855459			
	napA	Nitrate reductase, periplasmic	1.479877			
	rsxC	Required for the reduction of SoxR; putative membrane-associated NADH oxidoreductase	-1.300488			
	rsxE	Required for the reduction of SoxR; membrane protein	-1.038332			
	sdhC	Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0607324			
	sdhD	Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration	1.0157504			
	yodB	Function unknown		0.694684412	1.62745419	-0.932769778
46483 heterocycle metabolic process	folE	GTP cyclohydrolase I	-1.0409135			
	hemB	5-aminolevulinate dehydratase; also known as porphobilinogen synthase; binds Zn(II)	-1.1517999			
	hemD	Uroporphyrinogen III cosynthase; neomycin sensitivity	1.0766261			
	rihC	Ribonucleoside hydrolase	-1.0441272			
	xdhA	Probable xanthine dehydrogenase molybdenum-binding subunit; involved in limited purine catabolism; mutation confers adenine sensitivity	1.3941514			
	xdhD	Probable hypoxanthine oxidase; mutation confers adenine sensitivity	1.2296381			

31324 negative regulation of cellular metabolic process	treR	Repressor of trehalose operon	1.5542111			
6139 nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	**acrR**	**Transcriptional repressor for acrAB**	**-1.0204067**	0.968588206	1.712429133	**-0.743840928**
	arcB	Tripartite sensor/histidine protein kinase; repression of aerobic genes and activationof some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has respones regulator and second transmitter domains	2.5143914			
	atpA	ATP synthase subunit alpha, membrane-bound, F1 sector	1.33844			
	atpB	ATP synthase subunit a, membrane-bound, F0 sector	-1.0947847			
	atpE	ATP synthase subunit c, membrane-bound, F0 sector; DCCD-binding	-1.2534213			
	atpF	ATP synthase subunit b, membrane-bound, F0 sector	-1.1470773			
	atpH	ATP synthase subunit delta, membrane-bound, F1 sector	-1.1472812			
	barA	Sensor histidine protein kinase, pleiotropic; controls the expresion of csrB/C sRNAs; works in concert with UvrY response regulator	1.6353183			
	cheY	Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein	-1.2030091			
	csgD	Transcriptional activator for csgBA and other genes		-1.859434883	-0.292246188	-1.567188696
	csiE	Stationary phase inducible protein; sigma S-dependent promoter	1.3574634			
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		0.442750627	1.32534585	-0.882595223
	dcuR	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system response regulator	1.0233135			
	dcuS	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system sensory histidine kinase	1.2036445			
	deaD	ATP-dependent RNA helicase, 50S ribosomal subunit biogenesis; translation factor W2; facilitates translation of mRNAs with 5' secondary structures; multicopy suppressor of rpsB(Ts) mutations	1.1617334			
	deoR	Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer	1.2066016			
	dhaR	Transcription activator of the dhaKLM operon	1.127254			
	dusB	tRNA-dihydrouridine synthase B	-1.1940618			
	envY	Thermoregulatory activator of porin expression, AraC family	1.679985			
	fimB	**Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE**	**-1.1248107**	**0.473670149**	**1.76544683**	**-1.291776681**
	fliI	**Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits**	**-2.8425198**	**2.053080188**	**3.095328983**	**-1.042248796**
	fliZ	RpoS antagonist, transiently in post-exponential phase; timing factor allowing motility to continue for a while during starvation; not required for normal motility	1.1728091			

	gadE	Transcriptional regulator of the gadABC operon		-1.613297865	1.91643444	-3.529732305
	galS	Repressor of the mgl operon and isorepressor of the gal operon; autoregulatory; homodimeric	1.2070732			
	glcC	Transcriptional positive regulator for glc operon	1.077054			
	gmr	Cyclic-di-GMP phosphodiesterase, csgD regulator; modulates protein stability of RNase II	1.123914			
	gnd	6-phosphogluconate dehydrogenase, decarboxylating	-1.1842852			
	gyrB	DNA gyrase, subunit B; novobiocin, coumermycin resistance	1.1973567			
	hyfR	Formate-sensing regulator for hyf operon	1.2317433			
	insA-6		1.4929194			
	insA-7		1.4931407			
	insC-6		1.4933076			
	insD-6		1.874304			
	insF-5		1.4364634			
	insG		1.3130264			
	insI-3		2.618895			
	intD	Integrase gene within defective prophage DLP12	1.4847395			
	intF	Putative integrase gene, CP4-6 putative prophage remnant	1.1676054			
	intS	Integrase, CPS-53/KpLE1 prophage	-1.029356			
	iscR	Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro	-1.1579247			
	iscS	Cysteine desulfurase used in synthesis of Fe-S clusters and 4-thiouridine; ThiI transpersulfidase; SirA(TusA) transpersulfidase; pyridoxal phosphate cofactor linked to Lys206	-1.2212651			
	kdgR	Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK	-1.064749			
	kptA	2'-phosphotransferase, ligated tRNA substrate in vitro, physiological role and in vivo substrate unknown	-1.0849328			
	lldR	Dual role activator/repressor for lldPRD operon		-1.022032736	-0.102462884	-0.919569852
	mgtA	**Magnesium transporter, ATP-dependent; mutant has cobalt resistance; mediates Mg(2+) influx**	**-2.2685869**	**0.414117157**	**2.015561195**	**-1.601444038**
	miaA	Dimethylallyl diphosphate:tRNA dimethylallyltransferase; 2-methylthio-N6-(dimethylallyl)adenosine tRNA hypermodification	2.5113444			
	mlrA	Transcriptional regulator of csgD	1.208386			
	nadD	Nicotinate mononucleotide adenylyltransferase, NAD(P) biosynthesis	1.1660845			
	nanR	Repressor of the nan operon, induced by sialic acid; homodimeric	1.6356357			
	paaX	**Phenylacetic acid degradation**	**1.0424947**	**0.378975841**	**-0.246470978**	**0.625446818**
	parC	Topoisomerase IV, subunit A, ATP-dependent, type II; chromosome decatenase; relaxes both positive and negative supercoils; DNA unknotting activity; heterotetrameric	2.1262205			
	pcnB	Poly(A) polymerase; controls plasmid copy number; rare AUU start codon, growth-rate regulated; monomeric	2.1234794			
	pinQ	DNA invertase, site-specific recombination, Qin prophage	1.1538181			
	pinR	DNA invertase, site-specific recombination, Rac prophage	1.1496861			
	prpR	Transcriptional regulator of prp operon; propionate catabolism via 2-methlycitrate cycle, characterized primarily in Salmonella	1.6797161			
	purC	**Phosphoribosyl-aminoimidazole-succinocarboxamide synthase; purine synthesis**	**-1.6214104**	**0.671627539**	**1.519014342**	**-0.847386803**

	purF	Amidophosphoribosyltransferase, purine synthesis; also known as glutamine 5'-phosphoribosylpyrophosphate amidotransferase, GPATase	1.5669665			
	purM	**Phosphoribosyl-aminoimidazole (AIR) synthase; homodimeric**	**-1.3292446**	**0.734599861**	**2.273001511**	**-1.538401651**
	purN	**Glycinamide ribonucleotide transformylase (GART) 1, purine synthesis; glycinamide ribonucleotide formyltransferase**	**-1.2978582**	**1.019235695**	**1.86684724**	**-0.847611545**
	purR	Purine regulon repressor	-1.0262108			
	purT	**Glycinamide ribonucleotide transformylase (GART) 2, non-folate-requiring, purine synthesis**	**-2.2606297**	**1.08852949**	**2.6678463**	**-1.57931681**
	pyrB	Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamoylase		2.405384692	1.399913513	1.005471179
	pyrD	Dihydroorotate dehydrogenase, UMP biosynthesis	-1.0465689			
	pyrI	Aspartate carbamoyltransferase, regulatory subunit; aspartate transcarbamylase; ATCase; aspartate transcarbamoylase		2.193177888	1.177744341	1.015433546
	queA	S-adenosylmethionine:tRNA ribosyltransferase-isomerase; queuosine biosynthesis,	-1.0753493			
	rcsA	Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene		0.300528606	-1.142561372	1.443089978
	rcsC	Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase	1.8229611			
	recT	RecET recombinase, annealing protein, Rac prophage; recombination and repair	1.6986904			
	relA	ATP:GTP 3'-pyrophosphotransferase, ppGpp synthetase I; required for ppGpp synthesis during stringent response to amino acid starvation; self regulated	1.068548			
	rfbB	TDP-glucose oxidoreductase-4,6 dehydratase	-1.0411434			
	rhaR	Transcriptional activator for rhaSR, AraC family	1.0716362			
	rihC	Ribonucleoside hydrolase	-1.0441272			
	rob	Right oriC-binding protein, AraC family	1.3771441			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	rrmJ		1.1538243			
	rumA	23S rRNA m(5)U1939 methyltransferase, SAM-dependent	1.9303648			
	sbcD	DNA hairpin dsDNA 3'-exonuclease SbcCD, Mn(2+), ATP-dependent; ATP-independent 5' ssDNA endonuclease; cosuppressor with sbcB of recB recC mutations; heterodimeric	1.08962			
	sgcR	Putative sgc cluster transcriptional regulator	1.3975518			
	slyA	Activates crytpic hemolysin gene hlyE; global transcriptional regulator	1.015482			
	stpA	RNA chaperone and DNA-binding protein; suppresses T4 td mutant; modulates micF stability; forms heteromers with, and stabilzed against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS	-1.2432377			
	torS	Sensor kinase for torCAD operon	2.9209745			
	treR	Repressor of trehalose operon	1.5542111			
	uxuR	Repressor for UxuR regulon; true inducer is fructuronate	1.0230589			
	xdhA	Probable xanthine dehydrogenase molybdenum-binding subunit; involved in limited purine catabolism; mutation confers adenine sensitivity	1.3941514			
	xdhD	Probable hypoxanthine oxidase; mutation confers adenine sensitivity	1.2296381			

	yahA	c-di-GMP-specific phosphodiesterase, PDE-A; reaction product is 5'pGpG; dependent on Mg+2 or Mn+2, Ca+2 inhibitory; optimum pH 9.35; monomeric	-2.0166183			
	yahB	LysR family of transcriptional regulators, function unknown	1.046875			
	ybaO	Function unknown, Lrp family; putative transcriptional regulator	1.0301518			
	ybaX		-1.101002			
	ybeF	Putative LysR-family transcriptional regulator, function unknown LysR-family transcriptional regulator, function unknown	1.0823689			
	ybhD	Putative LysR-family transcriptional regulator, function unknown	1.1145554			
	ydfT		1.6117142			
	yedF	Function unknown	-1.1209044			
	yegE	Putative c-di-GMP dual activity enzyme, function unknown	1.6381769			
	yfaX	Putative transcriptional regulator, function unknown	1.2188423			
	yfeG		1.1252446			
	yfeR	Required for swarming phenotype, function unknown; predicted transcriptional regulator	1.2977767			
	yfiF	Putative methyltransferase, function unknown; spoU paralog; non-essential gene	-1.4608327			
	ygfI	Putative LysR-family transcriptional regulator, function unknown	1.4685719			
	yhiF		**1.2616509**	**-1.6261956**	**0.509971635**	**-2.136167235**
	yhjB	Function unknown	1.5886974			
	yjiR	Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family	1.0690143			
	yqeI	Part of T3SS PAI ETT2 remnant, ToxR homolog	-1.067694			
6730 one-carbon metabolic process	folE	GTP cyclohydrolase I	-1.0409135			
	glyA	Serine hydroxymethyltransferase; binds Zn(II)	-1.2570169			
	hsdM	DNA methyltransferase M, host modification of foreign DNA	1.1989958			
	rrmJ		1.1538243			
	yhdJ	DNA adenine methyltransferase, SAM-dependent	1.0355549			
6082 organic acid metabolic process	accD	Acetyl-CoA carboxylase, carboxyltransferase beta subunit	-1.0916588			
	acpS	Acyl carrier protein; ACP-CoA phosphopantetheinyltransferase; Holo-ACP synthase		0.020738638	-1.374399075	1.395137713
	adiA	Arginine decarboxylase, acid-inducible; arginine-dependent acid resistance	1.1271622			
	ansA	L-Asparaginase I	-1.1030908			
	ansB	L-Asparaginase II	1.5445883			
	argA	**N-acetylglutamate synthase; first step in arginine biosynthesis; amino-acid acetyltransferase; growth on acetylornithine**	**1.3041081**	**2.991781138**	**1.434967896**	**1.556813242**
	argB	**N-acetylglutamate kinase**	**1.044384**	**2.818308386**	**1.527225825**	**1.291082561**
	argC	**N-acetyl-gamma-glutamyl-phosphate reductase**	**1.7869039**	**3.319065683**	**1.757350161**	**1.561715522**

	argD	Acetylornithine aminotransferase; succinyldiaminopimelate aminotransferase, PLP-dependent		2.58062465	1.749457164	0.831167486
	argF	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase; CP4-6 putative prophage remnant		2.345750989	0.780893261	1.564857729
	argG	Argininosuccinate synthase		2.6295392	1.468532017	1.161007183
	argH	**Argininosuccinate lyase**	**1.2643517**	**2.489928442**	**1.442275936**	**1.047652506**
	argI	Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase		2.843476333	1.517740469	1.325735865
	aroF	3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP) synthase; tyrosine repressible; TyrR regulon	1.0875133			
	aroK	Shikimate kinase I; alkali-inducible	-1.2647691			
	asd	Aspartate semialdehyde dehydrogenase		-0.796322194	-1.579930631	0.783608438
	aspA	L-Aspartate ammonia-lyase; L-aspartase	3.0522566			
	aspC	Aspartate aminotransferase, AspAT; kynurenine aminotransferase; glutamine transaminase K	-1.0659509			
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		0.442750627	1.32534585	-0.882595223
	dadA	D-amino acid dehydrogenase		-0.368920809	-1.625476173	1.256555364
	dadX	Alanine racemase; homodimeric		-0.155438273	-1.291326758	1.135888485
	dapB	**Dihydrodipicolinate reductase**	**1.2919754**	**-0.563659431**	**-2.013465644**	**1.449806213**
	dapD	2,3,4,5-tetrahydropyridine-2-carboxylate N-succinyltransferase; mutations suppress growth defects of strains lacking superoxide dismutase	-1.0075407			
	eutB	Ethanolamine ammonia lyase, large subunit, adenosylcobalamine-dependent; concerted induction requires both B12 and ethanolamine; heterodimeric	1.7656298			
	fabB	beta-Ketoacyl-ACP synthase I; KAS I; homodimeric		1.148054475	2.149240165	-1.00118569
	fabI	Enoyl-ACP reductase, NADH dependent	-1.0237877			
	gadA	Glutamate decarboxylase A	1.1232334			
	gadB	Glutamate decarboxylase B, vitamin B6-dependent; hexameric	1.0481529			
	gcl	Glyoxylate carboligase, glyoxylate-inducible	1.2727609			
	gdhA	Glutamate dehydrogenase		-0.965960622	-2.004323596	1.038362974
	glnA	Glutamine synthase	1.0619159			
	glyA	Serine hydroxymethyltransferase; binds Zn(II)	-1.2570169			
	glyS	Glycine--tRNA ligase, beta-subunit	-1.1524415			
	hisS	Histidine--tRNA ligase	-1.0382023			
	ilvC	**Ketol-acid reductoisomerase**	**-1.0233388**	**0.607905905**	**2.038941914**	**-1.43103601**
	ilvN	Acetohydroxy acid synthase I (AHAS-I); acetolactate synthase I (ALS-I); valine sensitive; small subunit		1.33800575	-0.51491624	1.85292199
	iscS	Cysteine desulfurase used in synthesis of Fe-S clusters and 4-thiouridine; ThiI transpersulfidase; SirA(TusA) transpersulfidase; pyridoxal phosphate cofactor linked to Lys206	-1.2212651			
	leuA	alpha-Isopropylmalate synthase		-0.414798339	-1.432033122	1.017234783
	leuB	beta-Isopropylmalate dehydrogenase		-0.199455562	-1.235586059	1.036130497
	leuC	alpha-Isopropylmalate isomerase large subunit		-0.415228459	-1.46720426	1.051975801
	leuD	alpha-Isopropylmalate isomerase small subunit		-0.170246462	-1.315692056	1.145445594
	oxc	Probable oxalyl-CoA decarboxylase, oxalate catabolism		-0.336075069	1.512178216	-1.848253285
	paaJ	Phenylacetic acid degradation; mutants are unable to use phenylacetate as a carbon source	2.1441832			

	pheA	Phenylalanine synthesis, bifunctional: chorismate mutase (N) and prephenate dehydratase (central); also contains Phe-binding regulatory domain (C); FPA resistance	-1.0391736			
	prpR	Transcriptional regulator of prp operon; propionate catabolism via 2-methlycitrate cycle, characterized primarily in Salmonella	1.6797161			
	purF	Amidophosphoribosyltransferase, purine synthesis; also known as glutamine 5'-phosphoribosylpyrophosphate amidotransferase, GPATase	1.5669665			
	puuD	gamma-Glutamyl-GABA hydrolase, putrescine utilization pathway	1.0298939			
	pyrB	Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamoylase		2.405384692	1.399913513	1.005471179
	serA	D-3-Phosphoglycerate dehydrogenase	-1.0648217			
	thrA	**Aspartokinase I and homoserine dehydrogenase I, bifunctional**	**-1.004643**	**1.18802236**	**1.733920514**	**-0.545898154**
	yadB	Glutamyl-queuosine tRNA(Asp) synthase	1.391839			
	ybaS	Glutaminase	1.2362571			
	ybaX		-1.101002			
	yjhH	Function unknown	-1.4842229			
6800 oxygen and reactive oxygen species metabolic process	**sodA**	**Superoxide dismutase, Mn**	**1.120604**	**-0.384140377**	**-1.40051441**	**1.016374033**
	sodB	Superoxide dismutase, Fe; response to oxidative stress; chromate resistance; negatively regulated by ryhB RNA as part of indirect positive regulation by Fur; acid-inducible		4.006849988	3.110075363	0.896774625
6793 phosphorus metabolic process	barA	Sensor histidine protein kinase, pleiotropic; controls the expresion of csrB/C sRNAs; works in concert with UvrY response regulator	1.6353183			
	cheA	Histidine protein kinase sensor of chemotactic response; CheY is cognate response regulator; autophosphorylating; CheAS is a short form produced by an internal start at codon 98	-1.1959176			
	citG	Putative cit operon gene, function unknown	2.3438559			
	cusS	Copper ion sensor regulating cusCFBA expression; may also sense silver	1.4919264			
	dcuS	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system sensory histidine kinase	1.2036445			
	galK	Galactokinase	1.7365794			
	ispE	4-diphosphocytidyl-2-C-methylerythritol kinase; isopentenyl phosphate kinase; alternative nonmevalonate (DXP) pathway for terpenoid biosynthesis; essential gene	2.0409093			
	phoQ	Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP	1.4622464			
	rcsC	Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase	1.8229611			
	torS	Sensor kinase for torCAD operon	2.9209745			

31323 regulation of cellular metabolic process	**acrR**	**Transcriptional repressor for acrAB**	**-1.0204067**	**0.968588206**	**1.712429133**	**-0.743840928**
	arcB	Tripartite sensor/histidine protein kinase; repression of aerobic genes and activationof some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has respones regulator and second transmitter domains	2.5143914			
	barA	Sensor histidine protein kinase, pleiotropic; controls the expresion of csrB/C sRNAs; works in concert with UvrY response regulator	1.6353183			
	cheY	Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein	-1.2030091			
	csgD	Transcriptional activator for csgBA and other genes		-1.859434883	-0.292246188	-1.567188696
	csiE	Stationary phase inducible protein; sigma S-dependent promoter	1.3574634			
	cysB	Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase		0.442750627	1.32534585	-0.882595223
	dcuR	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system response regulator	1.0233135			
	dcuS	C4-dicarboxylate regulation of anaerobic fumurate respiratory system; two-component system sensory histidine kinase	1.2036445			
	deaD	ATP-dependent RNA helicase, 50S ribosomal subunit biogenesis; translation factor W2; facilitates translation of mRNAs with 5' secondary structures; multicopy suppressor of rpsB(Ts) mutations	1.1617334			
	deoR	Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer	1.2066016			
	dhaR	Transcription activator of the dhaKLM operon	1.127254			
	envY	Thermoregulatory activator of porin expression, AraC family	1.679985			
	fimB	**Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE**	**-1.1248107**	**0.473670149**	**1.76544683**	**-1.291776681**
	gadE	Transcriptional regulator of the gadABC operon		-1.613297865	1.91643444	-3.529732305
	galS	Repressor of the mgl operon and isorepressor of the gal operon; autoregulatory; homodimeric	1.2070732			
	glcC	Transcriptional positive regulator for glc operon	1.077054			
	gmr	Cyclic-di-GMP phosphodiesterase, csgD regulator; modulates protein stability of RNase II	1.123914			
	hyfR	Formate-sensing regulator for hyf operon	1.2317433			
	iscR	Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro	-1.1579247			
	kdgR	Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK	-1.064749			
	lldR	Dual role activator/repressor for lldPRD operon		-1.022032736	-0.102462884	-0.919569852
	mlrA	Transcriptional regulator of csgD	1.208386			
	nanR	Repressor of the nan operon, induced by sialic acid; homodimeric	1.6356357			
	paaX	**Phenylacetic acid degradation**	**1.0424947**	**0.378975841**	**-0.246470978**	**0.625446818**
	prpR	Transcriptional regulator of prp operon; propionate catabolism via 2-methlycitrate cycle, characterized primarily in Salmonella	1.6797161			
	purR	Purine regulon repressor	-1.0262108			

	rcsA	Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene		0.300528606	-1.142561372	1.443089978
	rcsC	Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase	1.8229611			
	rhaR	Transcriptional activator for rhaSR, AraC family	1.0716362			
	rob	Right oriC-binding protein, AraC family	1.3771441			
	rpsD	30S ribosomal subunit protein S4; NusA-like antitermination factor	-1.0738251			
	rpsH	30S ribosomal subunit protein S8	-1.019196			
	sgcR	Putative sgc cluster transcriptional regulator	1.3975518			
	slyA	Activates crytpic hemolysin gene hlyE; global transcriptional regulator	1.015482			
	stpA	RNA chaperone and DNA-binding protein; suppresses T4 td mutant; modulates micF stability; forms heteromers with, and stabilzed against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS	-1.2432377			
	torS	Sensor kinase for torCAD operon	2.9209745			
	treR	Repressor of trehalose operon	1.5542111			
	uxuR	Repressor for UxuR regulon; true inducer is fructuronate	1.0230589			
	yahA	c-di-GMP-specific phosphodiesterase, PDE-A; reaction product is 5'pGpG; dependent on Mg+2 or Mn+2, Ca+2 inhibitory; optimum pH 9.35; monomeric	-2.0166183			
	yahB	LysR family of transcriptional regulators, function unknown	1.046875			
	ybaO	Function unknown, Lrp family; putative transcriptional regulator	1.0301518			
	ybeF	Putative LysR-family transcriptional regulator, function unknown LysR-family transcriptional regulator, function unknown	1.0823689			
	ybhD	Putative LysR-family transcriptional regulator, function unknown	1.1145554			
	ydfT		1.6117142			
	yegE	Putative c-di-GMP dual activity enzyme, function unknown	1.6381769			
	yfaX	Putative transcriptional regulator, function unknown	1.2188423			
	yfeG		1.1252446			
	yfeR	Required for swarming phenotype, function unknown; predicted transcriptional regulator	1.2977767			
	ygfI	Putative LysR-family transcriptional regulator, function unknown	1.4685719			
	yhiF		**1.2616509**	**-1.6261956**	**0.509971635**	**-2.136167235**
	yhjB	Function unknown	1.5886974			
	yjiR	Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family	1.0690143			
	yqeI	Part of T3SS PAI ETT2 remnant, ToxR homolog	-1.067694			
6790 sulfur metabolic process	**bioB**	**Biotin synthase; dethiobiotin to biotin pathway; iron-sulfur enzyme**	**-1.5355635**	**-0.360614381**	**0.797467665**	**-1.158082046**
	bioC	Biotin synthesis blocked prior to pimeloyl CoA formation; putative SAM-dependent methyltransferase	-1.0316381			
	bioF	**7-keto-8-amino pelargonic acid synthase**	**-1.3357835**	**0.006936511**	**1.062414033**	**-1.055477522**
	cysD	Sulfate adenylyltransferase	-1.4373238			

6766 vitamin metabolic process	cobC	Probable alpha-ribazole-5'-phosphate phosphatase; potential partial cobalamin biosynthesis pathway	1.7467084			
	dxs	DXP synthase; DXP is precursor to isoprenoids, thiamin, pyridoxol	1.8676739			
	nadD	Nicotinate mononucleotide adenylyltransferase, NAD(P) biosynthesis	1.1660845			
	pdxB	2-hydroxyacid dehydrogenase involved in pyridoxine biosynthesis upstream of 4-phospho-hydroxy-threonine; isoniazid resistance	1.6453347			
	ribA	GTP cyclohydrolase II, riboflavin biosynthesis	1.9398031			
	ribB	**3,4-dihydroxy-2-butanone 4-phosphate synthase; riboflavin biosynthesis; acid-inducible; homodimeric**	**-3.7772803**	**0.081360818**	**1.346423538**	**-1.265062721**

Table S3. Effect of Mg-citrate on PNPase-mediated transcript levels in vivo. The relative abundance of selected transcripts was measured by quantitative RT-PCR for the PNPase null and wild-type strains in the presence of citrate and compared to the relative abundances determined from microarray analysis.

Transcript	**Relative abundance of mRNA in the PNPase null strain relative to the wild-type strain in the presence of Mg-citrate**	
	qRT-PCR	**Microarray**
cirA	1.71	2.87
fkpA	1.97	1.76
gdhA	0.92	0.56
rpoB	1	1.29

Table S4. Summary of the main metabolite differences for PNPase null, degradosome null and RhlB null compared to the corresponding parental strains and response to environmental stress.

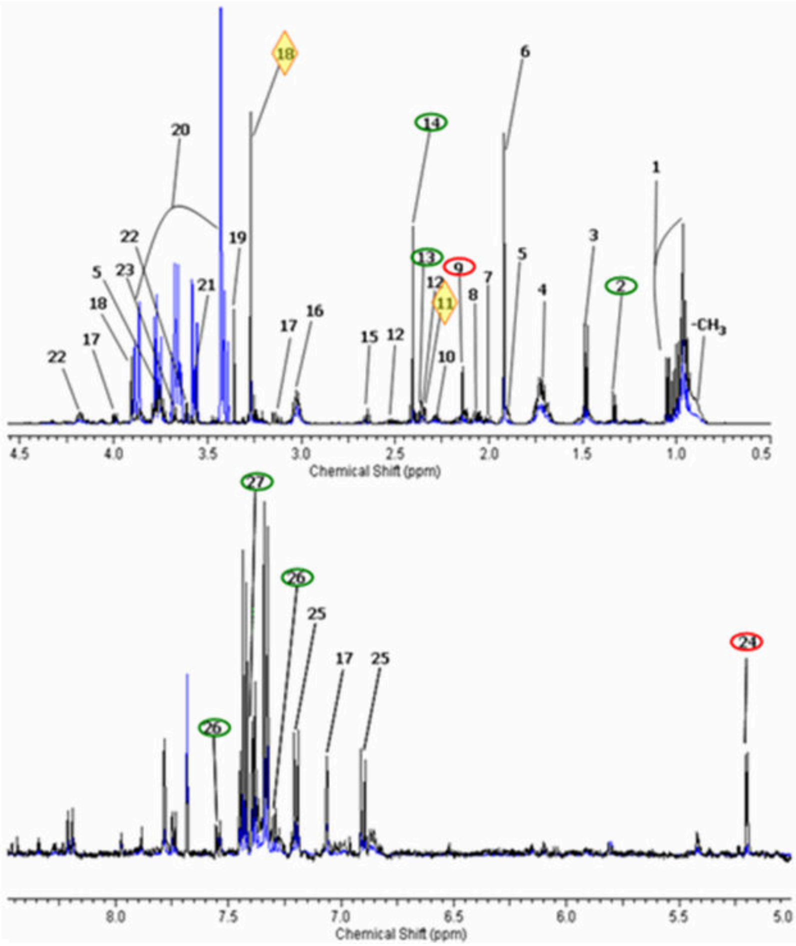
Data are for *E. coli* PNPase parent and null strains, degradosome parent and null strains and RhlB parent and null strains. Metabolite changes were detected using multivariate analysis following both NMR and GC-MS. Conditions and metabolic profiles: Comparing the degradosome null and parent without alpha-methyl glucoside (control), NMR data (R^2 = 47%, Q^2 = 95%) and GC-MS data (R^2 = 41%, Q^2 = 82%) and in the presence of alpha-methyl glucoside (phosphosugar stress), NMR data (R^2 = 63%, Q^2 = 52%) and GC-MS data (R^2 = 37%, Q^2 = 82%). Comparing RhlB parent and RhlB null at 16 °C (cold shock): NMR data (R^2 = 42%, Q^2 = 49%) and GC-MS data (R^2 = 29%, Q^2 = 16%) amd at 37 °C (control): NMR data (R^2 = 31%, Q^2 = 52%) and GC-MS data (R^2 = 24%, Q^2 = 28%). PNPase null vs PNPase parent: NMR data (R^2=74%; Q^2=98%) and GC-MS data (R^2=70%, Q^2=98%). Samples showing no change are labelled Nc; increases are labelled as + and decreases as -.

Metabolite Classification	**Degradosome null (vs. degradosome parent)**	**Degradosome null (vs. degradosome parent)**	**RhlB null (vs. RhlB parent)**	**RhlB null (vs. RhlB parent)**	**PNPase null (vs PnPase parent)**
	No α-methyl glucoside (Control)	**With 1% α-methyl glucoside (Phosphosugar stress)**	**37ºC (Control)**	**16ºC (Cold shock)**	
Amino Acids					
Alanine	Nc	+	+	+	+
Amino-butyric acid	-	-	Nc	Nc	-
Betaine	+	-	-	-	-
Glutamate	-	-	-	+	+
Glutamine	-	Nc	Nc	Nc	Nc
Glycine	+	+	+	Nc	+
Isoleucine	-	-	Nc	-	_
Leucine	-	-	Nc	Nc	Nc
Lysine	-	-	+	+	_
Methionine	-	Nc	-	Nc	Nc
Ornithine	-	Nc	Nc	+	Nc
Phenylalanine	Nc	Nc	-	Nc	
Proline	-	+	+	+	_
Serine	Nc	+	Nc	Nc	Nc

Threonine	+	+	Nc	Nc	_
Tryptophan	+	+	Nc	+	Nc
Tyrosine	-	Nc	Nc	Nc	Nc
Valine	-	-	Nc	-	Nc
Glycolysis					
Glucose	-	Nc	-	+	+
Glyceric acid	Nc	+	Nc	Nc	Nc
Lactate	+	+	+	+	+
Pyruvate	+	Nc	Nc	Nc	Nc
Krebs Cycle					
Fumarate	+	+	Nc	Nc	+
Malate	+	+	Nc	Nc	Nc
Succinate	+	+	+	+	+
Acetate*	-	+/(-)	Nc	Nc	-
Lipid Metabolites					
Pentanoic acid	-	-	Nc	Nc	Nc
Pentandioic acid	+	+	Nc	+	Nc
Secondary					
A-hydroxyisobutyric	-	-	Nc	Nc	-
Putrescine	-	-	+	Nc	+
Cadaverine	Nc	+	Nc	Nc	+
Inositol	-	-	Nc	-	Nc
Phosphate	Nc	-	Nc	Nc	Nc
Urea Cycle					
Urea	-	Nc	Nc	Nc	Nc

*The results for the acetate metabolite are in conflict, metabolomic analysis by NMR shows this metabolite to have the second most significant difference, whereas GC-MS shows a very slight decrease this may be due to the high sensitivity of GC-MS for small molecules or alternatively that another pool of acetate contributed to the GC-MS results possibly as a result of derivatisation (e.g. the degradation of acetyl-CoA).

Degradosome parent vs. null



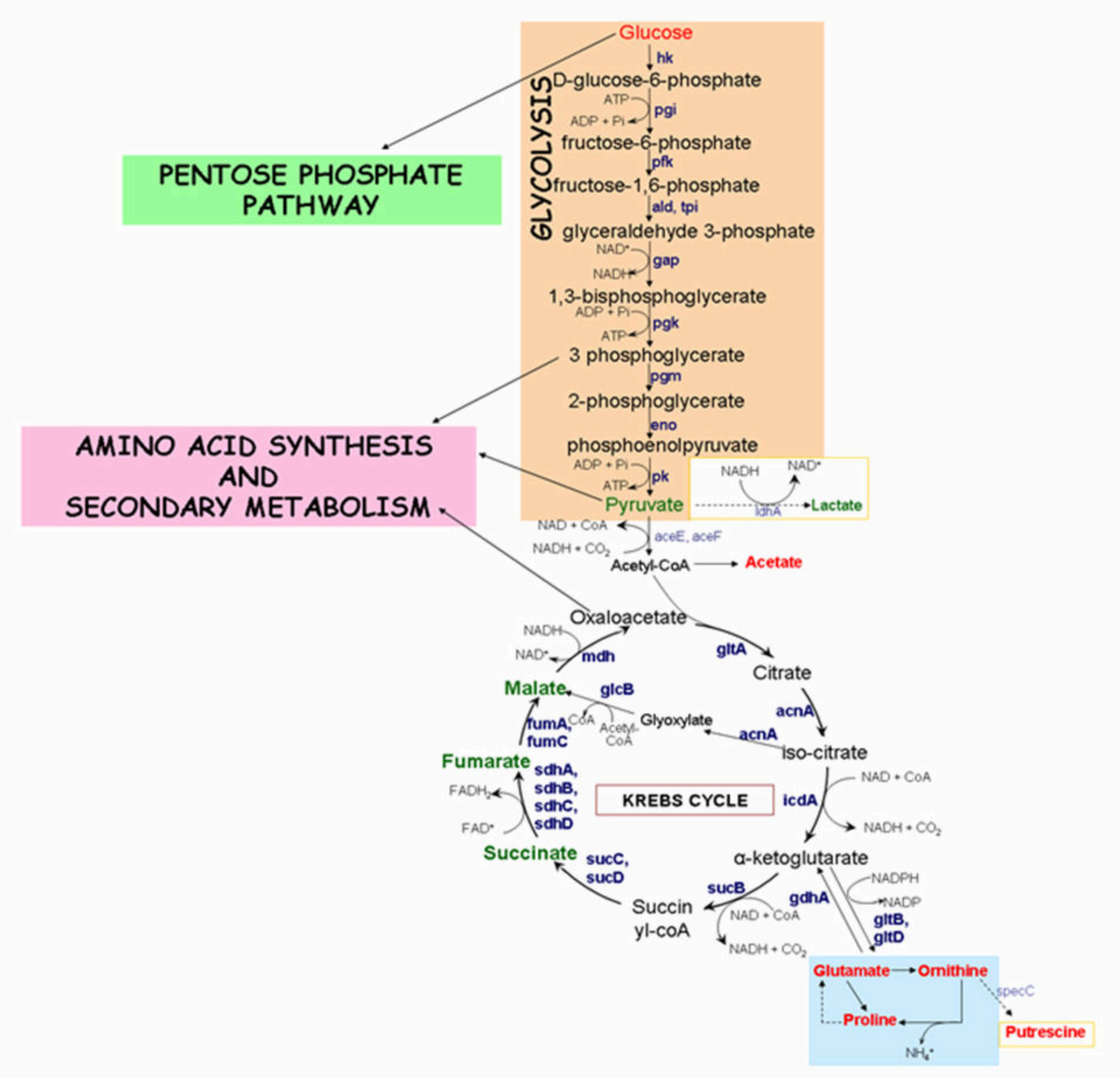
Unstressed condition

Increase:	**Decrease:**
18) Betaine	24) α –glucose
27) Phenylalanine	9) Methionine
14) Succinate	11) Proline
26) Tryptophan	
13) Pyruvate	
2) Lactate	

Phosphosugar Stress

Increase:	**Decrease:**
11) Proline	18) Betaine

Figure S1



Glucose
hk
D-glucose-6-phosphate
ATP
ADP + Pi
pgi
fructose-6-phosphate
pfk
fructose-1,6-phosphate
ald, tpi
glyceraldehyde 3-phosphate
NAD+
NADH
gap
1,3-bisphosphoglycerate
ADP + Pi
ATP
pgk
3 phosphoglycerate
pgm
2-phosphoglycerate
eno
phosphoenolpyruvate
ADP + Pi
ATP
pk
Pyruvate
GLYCOLYSIS
PENTOSE PHOSPHATE PATHWAY
AMINO ACID SYNTHESIS AND SECONDARY METABOLISM
NADH
NAD+
ldhA
Lactate
NAD + CoA
NADH + CO2
aceE, aceF
Acetyl-CoA
Acetate
Oxaloacetate
NADH
NAD+
mdh
gltA
Citrate
acnA
Malate
glcB
CoA
Acetyl-CoA
Glyoxylate
acnA
iso-citrate
fumA, fumC
Fumarate
sdhA, sdhB, sdhC, sdhD
FADH2
FAD+
KREBS CYCLE
icdA
NAD + CoA
NADH + CO2
α-ketoglutarate
Succinate
sucC, sucD
sucB
Succinyl-coA
NAD + CoA
NADH + CO2
gdhA
NADPH
NADP
gltB, gltD
Glutamate
Ornithine
specC
Proline
NH4+
Putrescine

Figure S2

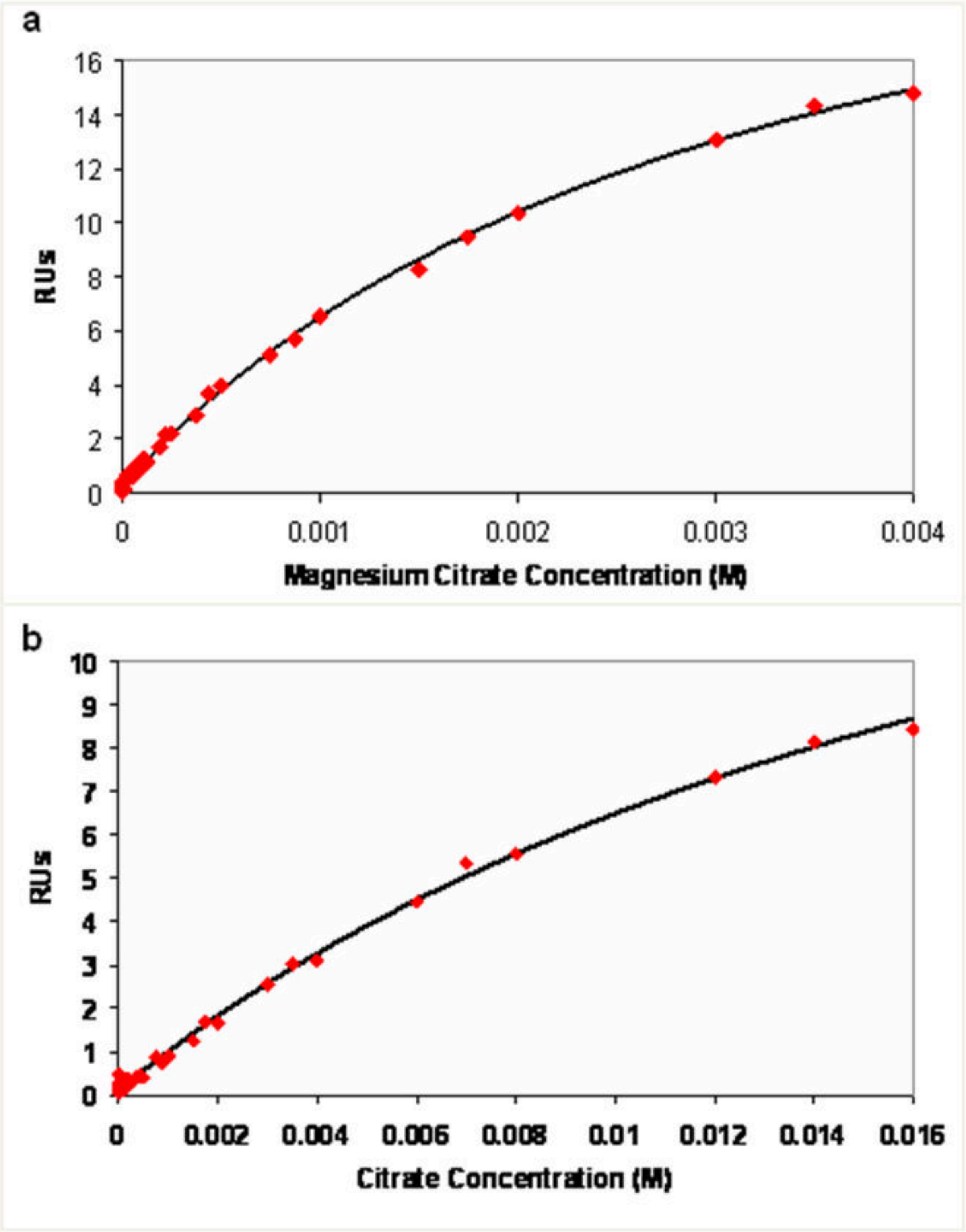

a
16
14
12
10
8
6
4
2
0
RUs
0
0.001
0.002
0.003
0.004
Magnesium Citrate Concentration (M)
b
10
9
8
7
6
5
4
3
2
1
0
RUs
0
0.002
0.004
0.006
0.008
0.01
0.012
0.014
0.016
Citrate Concentration (M)

Figure S3

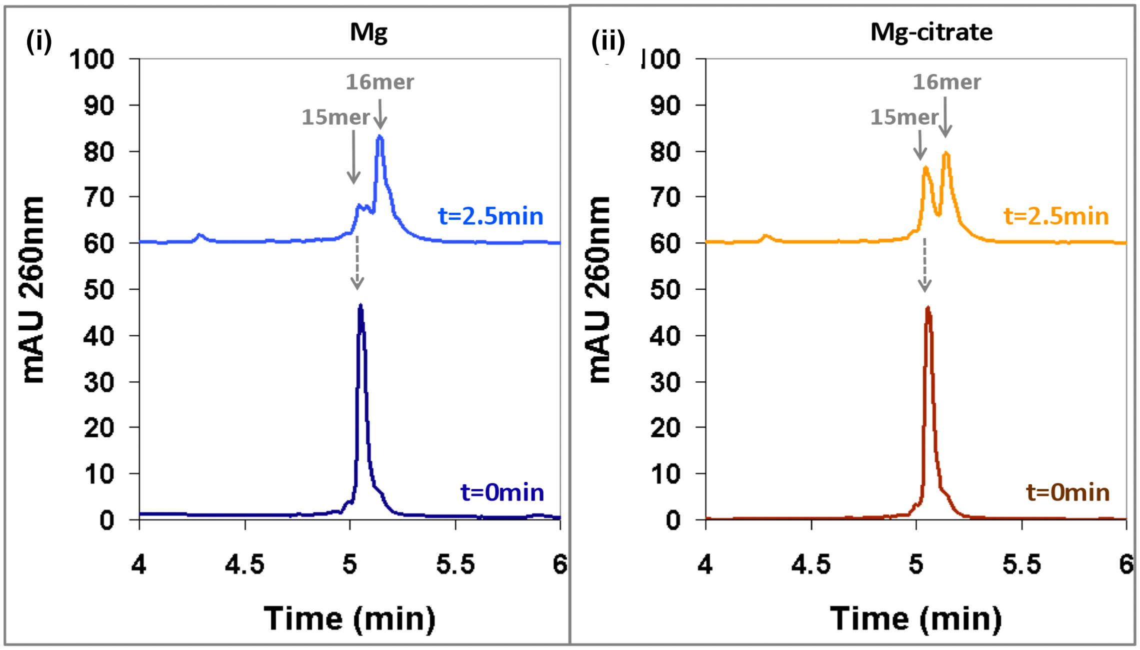


Figure S4 (a)

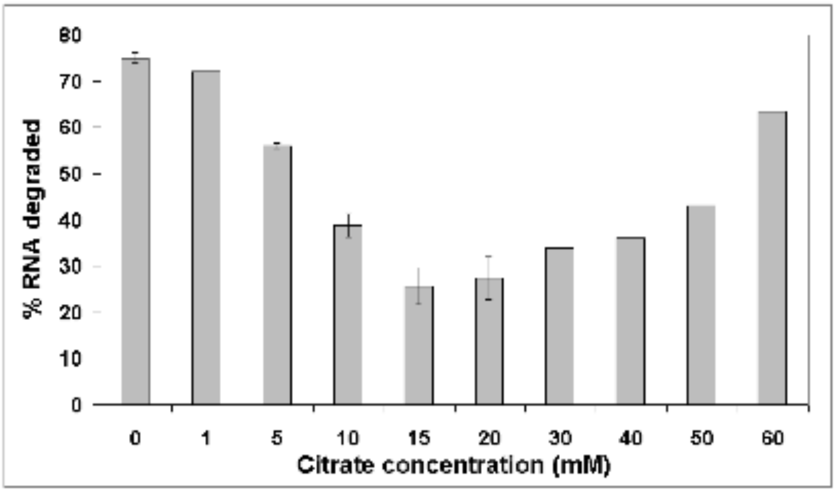
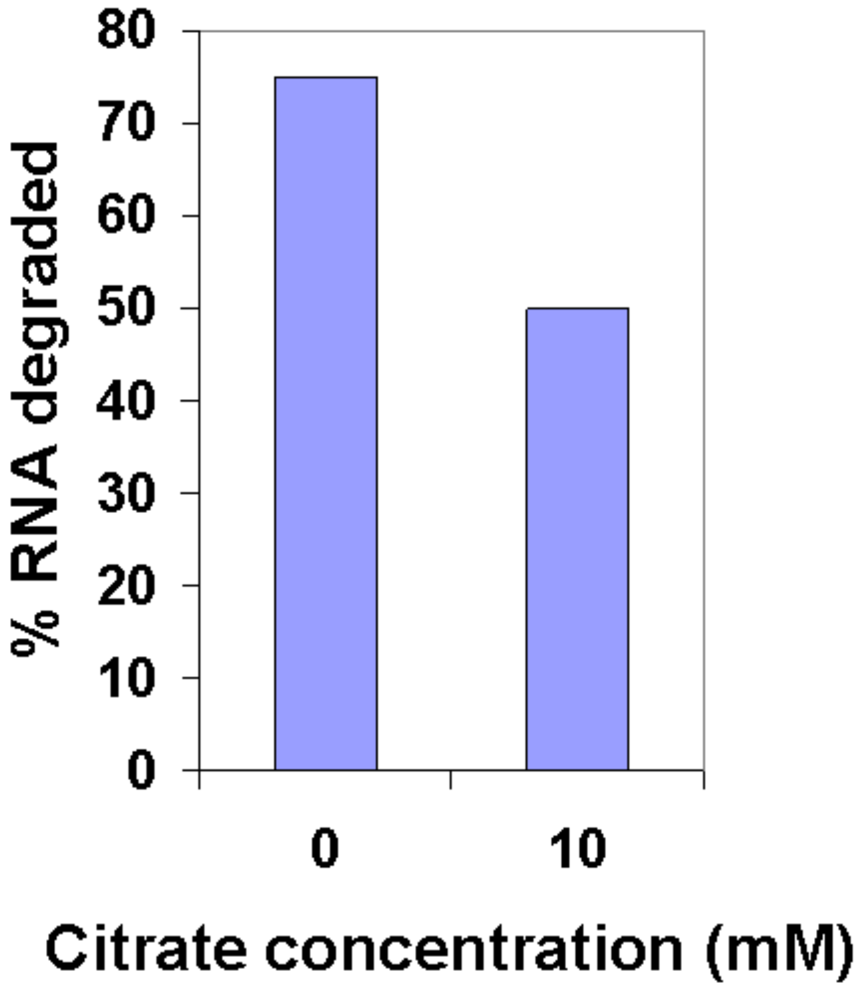


Figure S4(b)



80
70
60
50
40
30
20
10
0
% RNA degraded
0
10
Citrate concentration (mM)

Figure S5

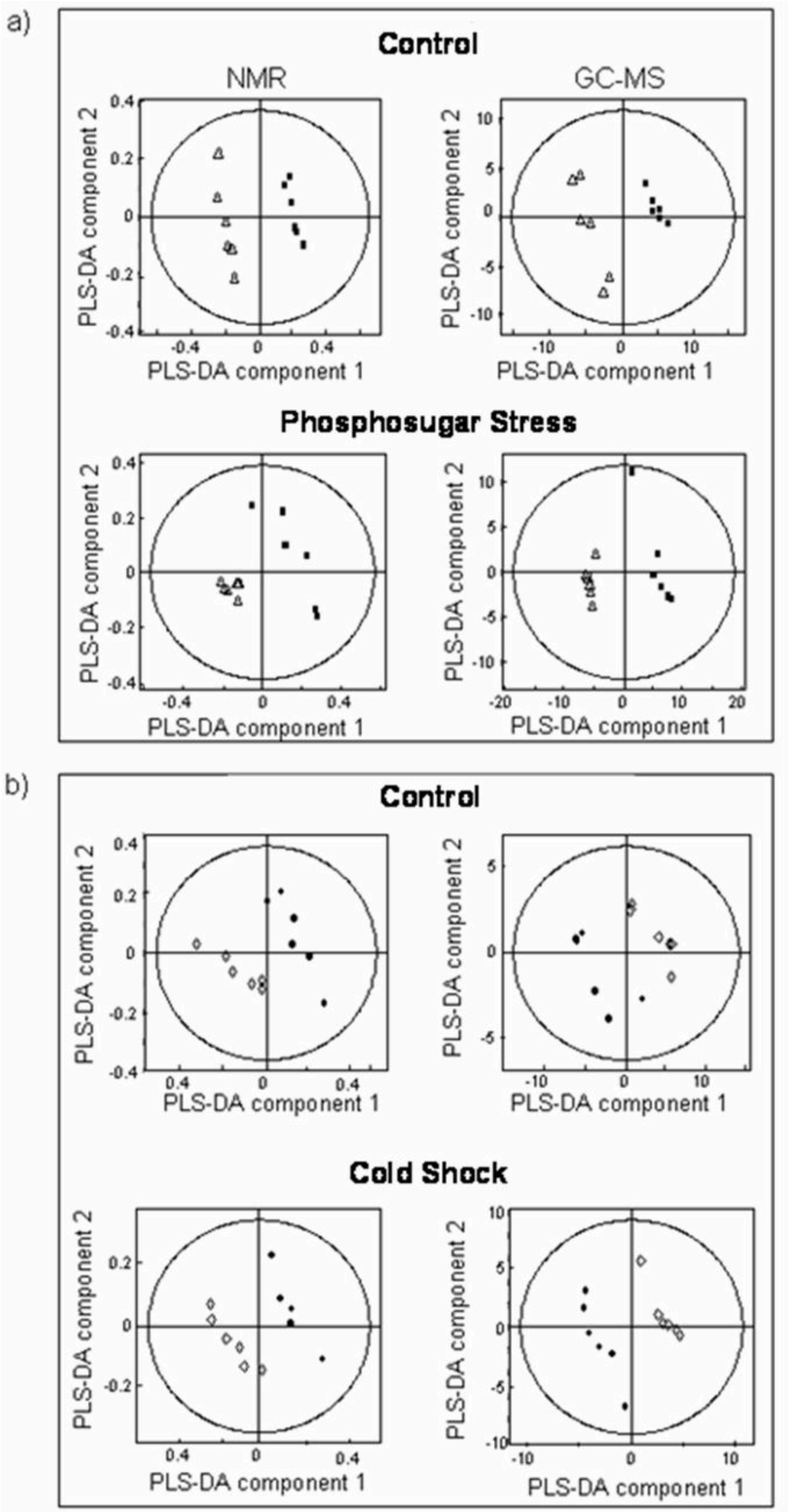

a)
Control
NMR
GC-MS
PLS-DA component 2
PLS-DA component 1
Phosphosugar Stress
PLS-DA component 2
PLS-DA component 1
b)
Control
PLS-DA component 2
PLS-DA component 1
Cold Shock
PLS-DA component 2
PLS-DA component 1

Figure S6

Polynucleotide Phosphorylase Activity May Be Modulated by Metabolites in *Escherichia coli*

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