Polynucleotide Phosphorylase Activity May Be Modulated by Metabolites in Escherichia coli*5*6

Received for publication, November 12, 2010, and in revised form, January 14, 2011 Published, JBC Papers in Press, February 14, 2011DOI 10.1074/jbc.M110.00741

Salima Nurmohamed11, Helen A. Vincent51, Christopher M. Titman1, Vidya Chandran4, Michael R. Pears6, Dijun Du4, Julian L. Griffin5, Anastasia J. Callaghan52, and Ben F. Luisi2

From the 1Department of Biochemistry, University of Cambridge, 80 Tennis Court Road, Cambridge CB2 1GA and 2Biophysics Laboratories, School of Biological Sciences, Institute of Biomedical and Biomolecular Sciences, University of Portsmouth, Portsmouth PO1 2DY, United Kingdom

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 physiologically significant 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), 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,
PNPase Activity May Be Modulated by Metabolites in E. coli

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 Δ(rna) in which the frame-shift 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 Δ(rna), MG1655 Δ(rna Δpnp::kan KanR), a PNPase null strain, and MG1655 Δ(rna Δpnp::kan KanR) Δ(rna Δrnb::Tn10 KanR), 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. Total RNA was 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 ΔK2AH (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 Core (R153A, R372A, R405A, R409A) Mutant

The pnp gene was generated by restriction digestion with Ncol and NotI from the pETDuet-1-pnp-enol (38). The pETDuet-1-pnp vector was constructed by subcloning the fragment of pnp bounded by Ncol 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 TCG CGT AGG TTA CAT CAA T-3′) and PNPR153A_rev (5′-ATT GAT GTA ACC TAC GGC GGC ACC AAC ATG GGC 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 AG-3′), and PNPR405A_R409A_fw (5′-GAA ATT GGT CAC GGT CTC GGT CGG 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 isopropl 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 MgCl2, 5 units/ml DNase I, 1 table/50 ml protease inhibitor mixture tablet), and lysed using a high pressure homogenizer (Emulsi-
PNPase Activity May Be Modulated by Metabolites in E. coli

Degradation Assays—The assay mix contained 0.05 mM poly(rA)-15-mer RNA, 10 mM MnSO₄ or MgCl₂, 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 mM 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 Chromelon 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 MgCl₂, or 1 mM MnSO₄, 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 sensitive 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. 1a). 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. 1b). Closer inspection of the sub-groupings indicates 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. 1c).

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...
PNPase null strain and the parental strain were determined by 1H 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.

PNPase Activity May Be Modulated by Metabolites in E. coli

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 log2 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 Activity May Be Modulated by Metabolites in E. coli

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 PNPase 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. 2a) as well as the degradosome null and its parent (Fig. 2b).

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 $\text{Mg}^{2+}$ being optimal. In the presence of mM concentrations of citrate, conditions in which the citrate would be predominantly complexed as magnesium–citrate given the $\text{Mg}^{2+}$ 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 $\text{Mg}^{2+}$ in a 2-fold excess over citrate (Fig. supplemental Fig. S4b; degradation is inhibited in the presence of 5 mM citrate, 10 mM $\text{Mg}^{2+}$). 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. 3b).

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...
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. S4a).

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. 4c). 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. 4d). 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. 3b). 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-
PNPase Activity May Be Modulated by Metabolites in E. coli

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. 3c). Correspondingly, at high concentrations of citrate (30–60 mM), the reverse process, i.e. degradation, is also enhanced (supplemental Fig. S4b). These activating effects are entirely the opposite of the inhibition seen under conditions in which magnesium–citrate may be the predominant 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. 3c), 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. 3b).

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. 4f). Nevertheless, this mutant is also inhibited by magnesium citrate (supplemental Fig. S5), just as seen for the wild-type enzyme (Fig. 3b), 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 evi-
PNPase Activity May Be Modulated by Metabolites in E. coli

dence 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 vestibial site and acting as an allosteric regulator. Our mutagenesis data confirm that the vestibial active site mediates the response to free-citrate and could be an allosteric site. Metalfree 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 the 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 vestibial site of unknown function, now proposed to be involved in responding to citrate or other metabolites, is evolutionarily conserved in the phosphorolytically inactive archael 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.

Acknowledgments—We thank Martyn Symmons, Steve Oliver, René Frank, James Milner-White, Kenny McDowall, A. J. Carpousis, Toby Gibson, Madan Babu, Kevin Brindle, and Sarath Janga for discussions. We thank A. J. Carpousis for providing E. coli strains with RNase E truncations, Murray Deutscher for the ribonuclease null strains used in the growth and microarray analyses, and George Mackie for providing the expression vector for core PNPase. We thank T. J. Ragan for assistance with microarray data collation and critical comments on the manuscript. We thank Hal Dixon for comments on earlier aspects of this work.

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

REFERENCES
1. Mohanty, B. K., and Kushner, S. R. (2000) Proc. Natl. Acad. Sci. U.S.A. 97, 11966–11971
2. Schuster, G., and Stern, D. (2009) Prog. Mol. Biol. Transl. Sci. 85, 393–422
3. Clements, M. O., Eriksson, S., Thompson, A., Luchcini, S., Hinton, J. C., Normark, S., and Rhen, M. (2002) Proc. Natl. Acad. Sci. U.S.A. 99, 8784–8789
4. Ygberg, S. E., Clements, M. O., Rytkönen, A., Thompson, A., Holden, D. W., Hinton, J. C., and Rhen, M. (2006) Infect. Immun. 74, 1243–1254
5. Yang, J., Iain, C., and Schesser, K. (2008) J. Bacteriol. 190, 3774–3778
6. Andrade, J. M., and Arraiain, C. M. (2008) RNA 14, 543–551
7. Awano, N., Inouye, M., and Phadatre, S. (2008) J. Bacteriol. 190, 5924–5933
8. Cheng, Z. F., and Deutscher, M. P. (2003) Proc. Natl. Acad. Sci. U.S.A. 100, 6388–6393
9. Deutscher, M. P. (2006) Nucleic Acids Res. 34, 659–666
10. Mohanty, B. K., and Kushner, S. R. (2003) Mol. Microbiol. 50, 645–658
11. Mohanty, B. K., and Kushner, S. R. (2006) Nucleic Acids Res. 34, 5695–5704
12. Slomovic, S., Portnoy, V., Yehudai-Reishe, S., Bronshtein, E., and Schuster, G. (2008) Biochim. Biophys. Acta 1779, 247–255
13. Viegas, S. C., Pfeiffer, V., Sittka, A., Silva, I. J., Vogel, J., and Arraiain, C. M. (2007) Nucleic Acids Res. 35, 7651–7664
14. Carpousis, A. J. (2007) Annu. Rev. Microbiol. 61, 71–87
15. Marcaida, M. J., DePristo, M. A., Chandran, V., Carposiss, A. J., and Luisi, B. F. (2006) Trends Biochem. Sci. 31, 359–365
16. Callaghan, A. J., Aurikko, J. P., Ilag, L. L., Günter Grossmann, J., Chandran, V., Kühnel, K., Poljak, L., Carposiss, A. J., Robinson, C. V., Symmons, M. F., and Luisi, B. F. (2004) J. Mol. Biol. 340, 965–979
17. Callaghan, A. J., Marcaida, M. J., Stead, J. A., McDowall, K. J., Scott, W. G., and Luisi, B. F. (2005) Nature 437, 1187–1191
18. Py, B., Higgins, C. F., Krish, H. M., and Carposiss, A. J. (1996) Nature 381, 169–172
19. Khermici, V., Poljak, L., Luisi, B. F., and Carposiss, A. J. (2008) Mol. Microbiol. 70, 799–813
20. Bernstein, J. A., Lin, P. H., Cohen, S. N., and Lin-Chao, S. (2004) Proc. Natl. Acad. Sci. U.S.A. 101, 2758–2763
21. Lopez, P. J., Marchand, I., Joyce, S. A., and Dreyfus, M. (1999) Mol. Microbiol. 33, 188–199
22. Morita, T., Kawamoto, H., Mizuta, T., Inada, T., and Aiba, H. (2004) Mol. Microbiol. 54, 1063–1075
23. Chandran, V., and Luisi, B. F. (2006) J. Mol. Biol. 358, 8–15
24. Erce, M. A., Low, J. K., March, P. E., Wilkins, M. R., and Takayama, K. M. (2009) Biochim. Biophys. Acta 1794, 1107–1114
25. Hardwick, S. W., Chan, V. S., Broadhurst, R. W., and Luisi, B. F. (2011) Nucleic Acids Res. 39, 1449–1459
26. Commichau, F. M., Rothe, F. M., Herzberg, C., Wagner, E., Hellwig, D.,
Lehnik-Habrink, M., Hammer, E., Völker, U., and Stülke, J. (2009) *Mol. Cell. Proteomics* **8**, 1350–1360

27. Del Favero, M., Mazzantini, E., Briani, F., Zangrossi, S., Tortora, P., and Dehò, G. (2008) *J. Biol. Chem.* **283**, 27355–27359

28. Gatewood, M. L., and Jones, G. H. (2010) *J. Bacteriol.* **192**, 4275–4280

29. Siculella, L., Damiano, F., di Summa, R., Tredici, S. M., Alduina, R., Gnoni, G. V., and Alifano, P. (2010) *Mol. Microbiol.* **77**, 716–729

30. Nurmohamed, S., Vaidialingam, B., Callaghan, A. J., and Luisi, B. F. (2009) *J. Mol. Biol.* **389**, 17–33

31. Khemici, V., Toesca, I., Poljak, L., Vanzo, N. F., and Carpousis, A. J. (2004) *Mol. Microbiol.* **54**, 1422–1430

32. Leroy, A., Vanzo, N. F., Sousa, S., Dreyfus, M., and Carpousis, A. J. (2002) *Mol. Microbiol.* **45**, 1231–1243

33. Le Belle, J. E., Harris, N. G., Williams, S. R., and Bhakoo, K. K. (2002) *NMR Biomed.* **15**, 37–44

34. Atherton, H. J., Gulston, M. K., Bailey, N. J., Cheng, K. K., Zhang, W., Clarke, K., and Griffin, J. L. (2009) *Mol. Syst. Biol.* **5**, 207–234

35. Pears, M. R., Cooper, J. D., Mitchison, H. M., Mortishire-Smith, R. J., Pearce, D. A., and Griffin, J. L. (2005) *J. Biol. Chem.* **280**, 42508–42514

36. Stickney, L. M., Hankins, J. S., Miao, X., and Mackie, G. A. (2005) *J. Bacteriol.* **187**, 7214–7221

37. Studier, F. W. (2005) *Protein Expr. Purif.* **41**, 207–234

38. Worrall, J. A., Görna, M., Crump, N. T., Phillips, L. G., Tuck, A. C., Price, A. I., Bavro, V. N., and Luisi, B. F. (2008) *J. Mol. Biol.* **382**, 870–883

39. Donovan, W. P., and Kushner, S. R. (1983) *Nucleic Acids Res.* **11**, 265–275

40. Donovan, W. P., and Kushner, S. R. (1986) *Proc. Natl. Acad. Sci. U.S.A.* **83**, 120–124

41. Cheng, Z. F., Zuo, Y., Li, Z., Rudd, K. E., and Deutscher, M. P. (1998) *J. Biol. Chem.* **273**, 14077–14080

42. Ishii, N., Nakahigashi, K., Baba, T., Robert, M., Soga, T., Kanai, A., Hirasawa, T., Naba, M., Hirai, K., Hoque, A., Ho, P. Y., Kakazu, Y., Sugawara, K., Igarashi, S., Harada, S., Masuda, T., Sugiyama, N., Togashi, T., Hasegawa, M., Takai, Y., Yugi, K., Arakawa, K., Iwata, N., Toya, Y., Nakayama, Y., Nishioka, T., Shimizu, K., Mori, H., and Tomita, M. (2007) *Science* **316**, 593–597

43. Bennett, B. D., Kimball, E. H., Gao, M., Osterhout, R., Van Dien, S. J., and Rabinowitz, J. D. (2009) *Nat. Chem. Biol.* **5**, 593–599

44. Symmons, M. F., Jones, G. H., and Luisi, B. F. (2000) *Structure* **8**, 1215–1226

45. Symmons, M. F., Williams, M. G., Luisi, B. F., Jones, G. H., and Carpousis, A. J. (2002) *Trends Biochem. Sci.* **27**, 11–18

46. Liu, Q., Greimann, J. C., and Lima, C. D. (2006) *Cell* **127**, 1223–1237

47. Schmid, M., and Jensen, T. H. (2008) *Trends Biochem. Sci.* **33**, 501–510

48. Daran-Lapujade, P., Rossell, S., van Gulik, W. M., Luttik, M. A., de Groot, M. J., Sliper, M., Heck, A. J., Daran, J. M., de Winde, J. H., Westerhoff, H. V., Pronk, J. T., and Bakker, B. M. (2007) *Proc. Natl. Acad. Sci. U.S.A.* **104**, 15753–15758

49. Hardiman, T., Lemuth, K., Keller, M. A., Reuss, M., and Siemann-Herzberg, M. (2007) *J. Biotechnol.* **132**, 359–374

50. Wang, G., Chen, H. W., Oktay, Y., Zhang, J., Allen, E. L., Smith, G. M., Fan, K. C., Hong, J. S., French, S. W., McCaffery, J. M., Lightowlers, R. N., Morse, H. C., 3rd, Koehler, C. M., and Teitell, M. A. (2010) *Cell* **142**, 456–467

51. Tuckerman, J. R., Gonzalez, G., and Gilles-Gonzalez, M. A. (2011) *J. Mol. Biol.*, in press
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 Log₂ 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 Log₂ 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 ($R^2 = 29\%, Q^2 = 16\%$) and 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 ¹H 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 °C. $R^2$ 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* Δ (Δrna) in which the frameshift in the rph gene has been corrected was considered wild-type. MG1655* Δ (Δrna), MG1655* Δ PNP’ ((Δrna Δpnp::kan KanR), a PNPase null strain, and MG1655* Δ II’ R’ ((Δrna Δrnb::Tn10 Δrnr::kan TetR KanR), a RNase II/RNase R double null strain, were grown at 37 °C 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-(trimethylsilyl)-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 $\mu$g/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 °C 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 °C for 20 min. Samples were recovered and stored at -80 °C.
**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$_2$O, pH 7.0, containing 1 mM (sodium-3-(tri-methylsilyl)-2,2,3,3-tetradeteriopropionate (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 $\mu$s, 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 ºC, 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 MgCl₂, 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 (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.

**Degradation assay (vestigial site mutant)**

The assay mix contained 0.05 mM 15-mer RNA, 10 mM MgCl₂, 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 °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, 100 µM dADP, 20 mM Tris pH 7.5, 10 mM MgCl₂, 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.

References

1. Kubitschek, H. E. (1990) *J Gen Microbiol* **136**, 599-606

2. Sezonov, G., Joseleau-Petit, D., and D’Ari, R. (2007) *J Bacteriol* **189**, 8746-8749

3. Leroy, A., Vanzo, N. F., Sousa, S., Dreyfus, M., and Carpousis, A. J. (2002) *Mol Microbiol* **45**, 1231-1243

4. Vanzo, N. F., Li, Y. S., Py, B., Blum, E., Higgins, C. F., Raynal, L. C., Krisch, H. M., and Carpousis, A. J. (1998) *Genes Dev* **12**, 2770-2781

5. Le Belle, J. E., Harris, N. G., Williams, S. R., and Bhakoo, K. K. (2002) *NMR Biomed* **15**, 37-44

6. Pears, M. R., Cooper, J. D., Mitchison, H. M., Mortishire-Smith, R. J., Pearce, D. A., and Griffin, J. L. (2005) *J Biol Chem* **280**, 42508-42514
7. Atherton, H. J., Gulston, M. K., Bailey, N. J., Cheng, K. K., Zhang, W., Clarke, K., and Griffin, J. L. (2009) *Mol Syst Biol* 5, 259

8. Worrall, J. A., Gorna, M., Crump, N. T., Phillips, L. G., Tuck, A. C., Price, A. J., Bavro, V. N., and Luisi, B. F. (2008) *J Mol Biol* 382, 870-883
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 |
|-------------------------------|------------------------------------------|------------------|
|                               |                                          | 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 | Log₂ of the ratio of PNPase null (no citrate):Wild-type (no citrate) | Log₂ of the ratio of Wild-type plus citrate:Wild-type (no citrate) | Log₂ 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 | -1.0269284 | -1.38238462 | -2.958069183 | 1.575684542 |
| | fliD | Hook-associated protein 2, axial family | 0.097937983 | 0.097937983 | 0.097937983 | 0.097937983 | 0.097937983 |
| | sfmA | Function unknown, FimA homolog | 1.0271903 | 1.0271903 | 1.0271903 | 1.0271903 | 1.0271903 |
| | ycgV | Overexpression increases adhesion and biofilm formation; probable adhesin, function unknown | 1.2697777 | 1.2697777 | 1.2697777 | 1.2697777 | 1.2697777 |
| | ygiL | Function unknown, FimA homolog | 1.6353183 | 1.6353183 | 1.6353183 | 1.6353183 | 1.6353183 |
| | ypjA | Overexpression increases adhesion, function unknown; OM autotransporter homolog | 1.2955649 | 1.2955649 | 1.2955649 | 1.2955649 | 1.2955649 |
| | znuA | High-affinity ABC transport system for zinc, periplasmic | -1.5015092 | -1.5015092 | -1.5015092 | -1.5015092 | -1.5015092 |
| 65007 biological regulation | acrR | AcrR transcriptional repressor for acrAB (AcrAB–ToIC multidrug efflux pump) | -1.0204067 | 0.96858206 | 1.712429133 | -0.743840928 |
| | arcB | Tripartite sensor/histidine protein kinase; repression of aerobic genes and activation of some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has respones regulator and second transmitter domains | 1.0271903 | 1.0271903 | 1.0271903 | 1.0271903 | 1.0271903 |
| | barA | Sensor histidine protein kinase, pleiotropic; controls the expression of csrB/C sRNAs; works in concert with UvrY response regulator | 1.6353183 | 1.6353183 | 1.6353183 | 1.6353183 | 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 | -1.1959176 | -1.1959176 | -1.1959176 | -1.1959176 |
| | cheW | Chemotaxis signal transducer; bridges CheA to chemoreceptors to regulate phosphotransfer to CheY and CheB | -1.2323792 | -1.2323792 | -1.2323792 | -1.2323792 | -1.2323792 |
| | cheY | Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein Transcriptional activator for csgBA and other genes | -1.2030091 | -1.2030091 | -1.2030091 | -1.2030091 | -1.2030091 |
| | csgD | -1.859434883 | -1.859434883 | -2.92246188 | -1.567188696 | -1.567188696 | -1.567188696 |
| Gene | Description                                                                                   | Expression 1 | Expression 2 | Expression 3 |
|------|-------------------------------------------------------------------------------------------------|--------------|--------------|--------------|
| 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 ssuEADCBC; cysteine desulfhydrase | 1.4463767    | 0.350969162  | 1.095407548  |
| dcaR | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system response regulator | 1.0233135    |              |              |
| dcaS | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system sensory histidine kinase | 1.2036445    |              |              |
| deaD | Repressor for deo operon, nupG and tsx; binds deoxyribose-S-phosphate inducer                 | 1.1617334    |              |              |
| deoR | Transcriptional activator of the dhaKLM operon                                                | 1.127254     |              |              |
| envY | Thermoregulatory activator of porin expression, ArsC family                                  | 1.679985     |              |              |
| fimB | Site-specific recombinase, fimbria 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 | Transpeptidase, PBPs; 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  | 1.2070372    |              |              |
| glcC | Transcriptional positive regulator for glc operon                                             | 1.077054     |              |              |
| gmr  | Cyclic-di-GMP phosphodiesterase, csgD regulator; modulates protein stability of RtuP 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   |              |              |
| narQ | Nitrate/nitrite sensor-transmitter protein; anaerobic respiratory path; cognate regulator is NarP; function redundant with narX | 1.0795679    |              |              |
| narX | Two-component nitrate/nitrite sensor-transmitter protein; NarL is cognate regulator; functional redundancy with narQ | 1.0639569    |              |              |
| nhaA | Repressor of the nan operon, induced by sialic acid; homodimeric                              | 1.6356357    |              |              |
| paaX | Phenylacetic acid degradation                                                                | 1.0424947    | 0.378975841  | -0.246470978 | 0.625446818  |
| Gene   | Description                                                                 | Log2 Value 1 | Log2 Value 2 | Log2 Value 3 |
|--------|------------------------------------------------------------------------------|--------------|--------------|--------------|
| 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-methylcitrate 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   | 3OS ribosomal subunit protein S4; NusA-like antitermination factor           | -1.0738251   |              |              |
| sgrR   | Putative sgc cluster transcriptional regulator                               | 1.3975518    |              |              |
| slyA   | Activates cryptic hemolysin gene hlyE; global transcriptional regulator      | 1.015482     |              |              |
| rtpA   | RNA chaperone and DNA-binding protein; suppresses T4 td mutant; modulates mic; stability; forms heteromers with, and stabilized 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   | LysR family of transcriptional regulators, function unknown                 | -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             | 1.0823689    |              |              |
| ybhD   | Putative LysR-family transcriptional regulator, function unknown             | 1.1145554    |              |              |
| yccA   | Membrane-associated protein that binds to FtsH(HflB) and FtsK proteins; mutant YccA stabilizes SecY(Ts); suppression requires FIKC; 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    |              |              |
| ygfF   | 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 |
| Gene  | Description                                                                 | Log2 Fold Change |
|-------|-----------------------------------------------------------------------------|-----------------|
| yhjB  | Function unknown                                                            | 1.5886974       |
| yjrK  | Putative HTH transcriptional regulator with aminotransferase domain, 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       |
| flgG  | Flagellar basal body rod major subunit                                      | -2.7651777      |
| 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; involving export of flagellar axial protein subunits | -2.8425198      |
| flIK  | Hook filament junction; controls hook length                                | -2.6773417      |
| flIO  | Flagellin export apparatus, integral membrane protein                       | -1.882103       |
| ftsI  | Transpeptidase, PBP3; penicillin-binding protein 3 involved in septal peptidoglycan synthesis | 2.2227626       |
| hofQ  | MreB filaments participate in directional chromosome movement and segregation; murein resistance; forms membrane-associated coiled arrays; actin homolog; morphology | 2.0593238       |
| mreB  | UDP-N-acetylgulosamine enolpyruvyl 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 rhb RNA as part of indirect positive regulation by Fur | 1.6737623       |
| acnB  | Aconitase B; 2-methylacooxilate hydratase; apo-enzyme binds mRNA for negative translational autoregulation; iron-sulfur cluster; monomeric ACP carrier protein, ACoA phosphopantetheinyltransferase; Holo-ACP synthase | 1.0271903       |
| acPS  | AcrEF-ToIC efflux pump, multidrug/solvent resistance; osmotically remedial envelope defect | 0.020738638     |
| acRF  | AcrR transcriptional repressor for acrAB (AcrAB-ToIC multidrug efflux pump) | -1.0204067      |
| aclE  | Alcohol dehydrogenase, anaerobic/ aerobic antioxidant; acetahydro-CoA dehydrogenase, CoA-linked; allyl alcohol resistance | 1.0416784       |
| aclA  | Arginase decarboxylase, acid-inducible; arginine-dependent acid base resistance | 1.1271622       |
| Gene | Description | Value 1 | Value 2 | Value 3 | Value 4 |
|------|-------------|---------|---------|---------|---------|
| **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 activation of some anaerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has response 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 | |
| **argB** | N-acetyl-gamma-glutamyl-phosphate reductase | 1.044384 | 2.818308386 | 1.527225825 | 1.291082561 |
| **argC** | Acetylornithine aminotransferase; succinylaminomimidate aminotransferase, PLP-dependent | 1.7869039 | 3.319065683 | 1.757350161 | 1.561715522 |
| **argD** | Acetylornithine aminotransferase; ornithine transcarbamylase; OTCase; CP4-6 putative prohage remnant | 1.044384 | 2.818308386 | 1.527225825 | 1.291082561 |
| **argF** | Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase | 2.345750989 | | 0.780893261 | 1.564857729 |
| **argG** | Argininosuccinate synthase | 2.6295392 | | 1.468532017 | |
| **argH** | Argininosuccinate lyase | 1.2643517 | 2.489928442 | 1.442275936 | 1.047652506 |
| **argJ** | 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 | -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 expression of csrB/C sRNAs; works in concert with UvrY response regulator | 1.6353183 | | | |
| **bcr** | Biotin synthase; dethiobiotin to biotin pathway; iron-sulfur enzyme | -1.5355635 | -0.360614381 | 0.797467665 | -1.158082046 |
| **bioB** | Biotin synthesis blocked prior to pimeloyl CoA formation; putative SAM-dependent methyltransferase | -1.0316381 | | | |
| **bioC** | 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 | | | |
| Gene | Description | Fold Change |
|------|-------------|-------------|
| 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 |
| csgE | Stationary phase inducible protein; sigma S-dependent promoter | 1.3574634 |
| cusS | Copper ion sensor regulating cusCFBA expression; may also sense silver | 1.4919264 |
| cyoB | Cytochrome o oxidase subunit I; cytochrome bo(3) ubiquinol oxidase subunit | 1.0475307 |
| cysB | Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase | 0.442750627 |
| cysD | Sulfate adenylyltransferase | -1.4373238 |
| dhpA | Dihydrosqualene reductase | 1.449806213 |
| dcuR | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system response regulator | 1.0233135 |
| dcm | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system sensory histidine kinase | 1.2036445 |
| deaD | Periplasmic, membrane-associated serine endoprotease; protease Do, required for high-temperature growth and the degradation of damaged proteins | 1.1617334 |
| degP | Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer | -0.366102641 |
| deoR | Transcription activator of the dhaKLM operon | 1.2066016 |
| dhrA | DXP synthase; DXP is precursor to isoprenoids, thiamin, pyridoxol | 1.127254 |
| dks | Enolase; phosphoprotein; component of RNA degradosome | 1.8676739 |
| eno | Periplasmic murein hydrolase septal ring factor; sensitivity to crystal violet; filamentous | 1.0622171 |
| envC | Thermoregulatory activator of porin expression, AnaC family | 1.3034105 |
| envY | Ethanolamine ammonia lyase, large subunit, adenosylcobalamine-dependent; concerted induction requires both B12 and ethanolamine; heterodimeric | 1.7656298 |
| eutB | Hexuronate permease, for glucuronate and galacturonate | 1.0179187 |
| fabB | Enoyl-ACP reductase, NADH dependent | 1.148054475 |
| fabI | Enoyl-ACP reductase | 1.49240165 |
| Gene | Description | Protein 1 | Protein 2 | Protein 3 |
|------|-------------|-----------|-----------|-----------|
| **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** | Fermenterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains | -1.1662078 |          |          |
| **fimB** | Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE | -1.1248107 | 0.473670149 | 1.76544638 |
| **fimD** | 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 |
| **flgC** | Flagellar basal body rod subunit | -3.2366333 | 1.918144667 | 3.290344417 |
| **flgE** | Flagellar hook subunit protein | -3.2993827 | 1.879339905 | 3.128954345 |
| **flgF** | Flagellar basal body rod subunit | -2.3180777 | 1.813582677 | 2.829423308 |
| **flgG** | Flagellar basal body rod major subunit | -2.7651777 | 1.721089011 | 2.746398912 |
| **flgH** | Flagellar synthesis, basal body L-ring lipoprotein | -1.9212251 | 1.901291464 | 2.870884957 |
| **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 |          |          |
| **flgC** | Flagellin, structural gene, H-antigen | -1.5392385 |          |          |
| **flgD** | Hook-associated protein 2, axial family | -1.0269284 |          |          |
| **flfF** | Flagellar basal body M-ring protein | -2.1452103 | 2.21798513 | 3.623918913 |
| **flfG** | Rotor protein for flagellar motor switching and energizing; role in flagellar assembly | -2.774952 | 2.13065744 | 3.2673922 |
| **flfH** | Negative regulator of FlII ATPase activity; involved in flagellar assembly and export | -2.0643058 | 1.950296025 | 2.756911638 |
| **flfI** | Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits | -2.8425198 | 2.053080188 | 3.095328983 |
| **flfJ** | Flagellin export apparatus soluble | -1.861196 | 2.017483883 | 2.880704117 |
| **flfK** | Hook filament junction; controls hook length | -2.6773417 | 1.939810007 | 2.765864679 |
| **flfL** | Affects rotational direction of flagella during chemotaxis | -1.5788474 |          |          |
| **flfM** | Flagellar synthesis, motor switching and energizing | -2.7464433 | 2.032106006 | 2.845598856 |
| **flfN** | Flagellar switch protein | -1.9425316 |          |          |
| **flfO** | Flagellin export apparatus, integral membrane protein | -1.882103 |          |          |
| **flfP** | Flagellin export apparatus, integral membrane protein | -1.3490691 |          |          |
| **flfQ** | Flagellin export apparatus, integral membrane protein | -1.7036285 |          |          |
| **folE** | GTP cyclohydrolase I | -1.0409135 |          |          |
| **ftsI** | Transpetidase, HBP3; penicillin-binding protein 3 involved in septal peptidoglycan synthesis | 2.2227626 |          |          |
| **ftsN** | Cell division and growth; multicyclic suppresses ftsA12 | 1.7090788 |          |          |
| **fusA** | Elongation Factor EF-G; GTase 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 |
| **gaoK** | Galactokinase | 1.7365794 |          |          |
| Gene | Description | Log2 Fold Change | P-Value |
|------|-------------|-----------------|---------|
| galS | Repressor of the mgl operon and isorepressor of the gal operon; autoregulatory; homodimeric | 1.2070732 | |
| galA | Galactitol-specific enzyme IIA of phosphotransferase system (PTS) | -1.6841471 | |
| galC | Galactitol-specific enzyme IIC of PTS | -1.4637866 | |
| galY | D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability | -1.1761272 | |
| galZ | Tagatose bisphosphate aldolase GatYZ subunit; required for full activity and stability of GatY | -1.2347231 | |
| gcl | Glyoxylate carboligase, glyoxylate-inducible | 1.2727609 | |
| gdhA | Glutamate dehydrogenase | -0.965960622 | 2.004323596 | 1.038362974 |
| gif | UDP-galactopyranose mutase | -1.4456341 | |
| glgA | Uroporphyrinogen III cosynthase; neomycin sensitivity | -0.611356637 | -1.254026216 | 0.642669579 |
| glgB | 1,4-alpha-glucom 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 | |
| glk | Glycerol kinase | 1.7542315 | |
| gpyA | Serine hydroxymethyltransferase; binds Zn(II) | -1.2570169 | |
| gpyS | Glycine-β-tRNA ligase, beta-subunit | -1.1524415 | |
| gmr | Glycogen synthase | |
| gntU | Decarboxylating | |
| gntU | Low-affinity glucione transport protein, membrane protein | 1.0674934 | |
| gpmA | Phosphoglycerate mutase 1, 2,3-bisphosphoglycerate-dependent; Fur regulon; homodimeric | -1.1640095 | |
| grpE | Cyclic-di-GMP phosphodiesterase, csgD regulator; modulates protein stability of RNase II 6-phosphogluconate dehydrogenase, decarboxylating | |
| grxB | Cyclic-di-GMP phosphodiesterase, csgD | -1.1842852 | |
| glpK | Nucleotide exchange factor for the DnaKJ chaperone; heat shock | 1.123914 | |
| gnd | Nucleotide exchange factor for the DnaKJ chaperone; heat shock | -1.1524415 | |
| gntU | Decarboxylating | |
| gntU | Low-affinity glucione transport protein, membrane protein | 1.0674934 | |
| gntU | Phosphoglycerate mutase 1, 2,3-bisphosphoglycerate-dependent; Fur regulon; homodimeric | -1.1640095 | |
| gpmA | Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC | -1.1524415 | |
| grxB | ATPase | |
| 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 | -0.682033174 | -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 | Pseudopilin in H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA | 1.0381198 | -0.571663549 | -1.758766291 | 1.871127424 |
| gspG | Pseudopilin in H-NS-silenced gsp divergon, type II protein secretion; 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 catalyze 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 | Hematoporphyrinogen III cosynthase; neomycin sensitivity | 1.0766261 | |
| hisS | His-HOMA-2,2-tRNA ligase | -1.0382023 | |
| Gene | Description | Log2 FC | Log10 P | E-Value |
|------|-------------|---------|---------|---------|
| 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 absence of cobalamin; no overexpression resistances found | 1.1956267 |       |         |
| hyfR | Formate-sensing regulator for hyf operon | 1.2317433 |       |         |
| ilvC | Ketol-acid reductoisomerase | -1.023338 | 0.6079059 | 1.4310360 |
| ilvN | Ketoisovalerate reductoisomerase | 1.3380057 | -0.5149162 | 1.8529219 |
| 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; Thil transpersulfidase; SnR(TuA) 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 | 0.2086427 | -0.6109206 | 0.8195636 |
| kdgR | Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK | -1.064749 |       |         |
| kdtA | 4-deoxy-L-threo-5-hexulosate-uronate ketol-isomerase; 5-keto-4-deoxyuronate isomerase | 1.5366621 |       |         |
| kduI | NEM-activatable K+/H+ antiporter | 1.4980454 |       |         |
| kexB | alpha-Ketoglutarate permease | 0.1064749 |       |         |
| ldpA | 4-deoxy-L-threo-5-hexulosate-uronate ketol-isomerase; 5-keto-4-deoxyuronate isomerase | 1.0485537 |       |         |
| ldcA | alpha-Isopropylmalate synthase | -0.4147983 | -1.4320331 | 1.0172347 |
| leuA | alpha-Isopropylmalate synthase | -0.1994555 | -1.2355860 | 1.0361304 |
| leuB | beta-Isopropylmalate dehydrogenase | -0.4152284 | -1.4672042 | 1.0519758 |
| leuC | alpha-Isopropylmalate isomerase large subunit | -0.1702464 | -1.1956920 | 1.0172347 |
| leuD | alpha-Isopropylmalate isomerase small subunit | -0.9538244 | 0.2085277 | -1.6235221 |
| 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 |       |         |
| Gene | Description | Log2 Fold Change | p Value | FDR Corrected p Value |
|------|-------------|-----------------|---------|-----------------------|
| map | Methionine aminopeptidase | -1.051142 | 1.0087 | 2.581150826 |
| mdtB | mdlB ABC exporter permease-ATPase, function unknown | 1.090272 | | |
| mdtD | MdtEF-ToLC multidrug resistance efflux transporter; membrane fusion protein (MFP) component, lipoprotein; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype | 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 |
| mdlA | 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 | -0.813851 | | |
| murA | Nicotinate mononucleotide adenylyltransferase, NAD(P) biosynthesis | 1.1660845 | | |
| napA | Nitrite reductase, periplasmic | 1.479877 | | |
| narQ | Two-component nitrate/nitrite sensor–transmitter protein; NarL is cognate regulator; functional redundance with narQ | 1.0639569 | | |
| narX | Two-component nitrate/nitrite sensor–transmitter protein; NarL is cognate regulator; functional redundance with narQ | 1.0795679 | | |
| nlpI | Lipoprotein, osmotic sensitivity and filamentation | 1.0079885 | | |
| nudD | Outer membrane protease VII, DLP12 prophage; OM protein 2b; omptin | 1.1124482 | | |
| oxc | Probable oxalyl-CoA decarboxylase, oxalate catabolism | -1.2738028 | | |
| paaA | Phenylacetic acid degradation; mutants are unable to use phenylacetate as a carbon source | 1.2441832 | | |
| paaX | Phenylacetic acid degradation | 1.0424947 | 0.378975841 | -0.246470978 |
| panB | Ketopantoate hydroxymethyltransferase | -1.0029793 | | |
| pcdB | Poly(A) polymerase; controls plasmid copy number; rare AUU start codons, growth-rate regulated; monomeric | 2.1234794 | | |
| pheA | 2-hydroxyacid dehydrogenase involved in pyridoxine biosynthesis upstream of 4-phospho-hydroxy-threonine; isoniazid resistance | 1.6453347 | | |
| pheB | Phenylalanine synthesis, bifunctional: chorismate mutase (N) and prephenate dehydratase (central); also contains Phe-binding regulatory domain (C); PPA resistance | -1.0391736 | | |
| phoQ | Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP | 1.4622464 | | |
| prfA | Peptide chain release factor 1, RF-1; translation termination factor recognizes UAG and UAA. | 1.1244482 | | |
| Gene   | Description                                                                 | Log2 Ratio | E-Value  | P-value  |
|--------|------------------------------------------------------------------------------|------------|----------|----------|
| prpR   | Transcriptional regulator of prp operon; propionate catabolism via 2-methylcitrate cycle, characterized primarily in Salmonella | 1.6797161  |          |          |
| purF   | Amidophosphoribosyltransferase, puromidine 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   | D-ribose pyranose; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU | 2.40538492  | 1.399913513 | 1.005471179 |
| rbsD   | Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene | -1.7281728  |          |          |
| rcsA   | Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase | 0.300528606 | -1.142561372 | 1.443089978 |
| rcsC   | UDP-4-glucose: (galactosyl)LPS-glucosyltransferase                           | 1.8229611  |          |          |
| rfaJ   | Glycosyltransferase needed for heptose region of LPS core                   | -1.0780096  |          |          |
| rfaS   | LPS core, not affecting attachment of O antigen                            | -1.0442805  |          |          |
| rfaZ   | TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidyltransferase; needed for dTDP-L-rhamnose synthesis | -1.3851705  |          |          |
| rfaA   | TDP-glucose oxidoreductase-4,6 dehydratase                                  | -1.325498  |          |          |
| rfaB   | dTDP-4-deoxyrhamnose-3,5-epimerase                                          | -1.3006554  |          |          |
| rfaC   | Putative polyisoprenol-linked O-antigen translocase                         | -1.0625052  |          |          |
| rfaD   | GTP cyclohydrolase II, riboflavin biosynthesis, 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   | SOS ribosomal subunit protein L2; binds Zn(II)                              | 1.1556873  |          |          |
| rplC   | SOS ribosomal subunit protein L3                                            | -1.0714864  |          |          |
| rplF   | SOS ribosomal subunit protein L6; gentamicin sensitivity                    | -1.1512773  |          |          |
| rplD   | SOS ribosomal subunit protein L15                                           | -1.0819453  |          |          |
| rplP   | SOS ribosomal subunit protein L16                                           | -1.1343815  |          |          |
| rplQ   | SOS ribosomal subunit protein L17                                           | 1.612936   |          |          |
| rplU   | SOS ribosomal subunit protein L21                                           | -1.2566199  |          |          |
| rplX   | SOS ribosomal subunit protein L24                                           | -1.030241   |          |          |
| rpmG   | SOS ribosomal subunit protein L33                                           | -1.1044912  |          |          |
| rpsC   | SOS 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                                                                |            |          |          |
| Gene | Function |
|------|----------|
| **rspA** | Bifunctional D-altronate/D-mannonate dehydratase; overproduction prevents homoserine lactone-induced synthesis of RpoS |
| **sdcH** | Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration |
| **sdcD** | Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration |
| **secB** | General protein chaperone; SecG inner membrane secretion protein; complexes with and assists the SecYE core translocon to interact with SecA to export proteins |
| **secA** | D-3-Phosphoglycerate dehydrogenase |
| **sfnA** | Function unknown, FimA homolog |
| **sgcR** | Putative sgc cluster transcriptional regulator |
| **slyA** | Activates cryptic hemolysin gene hlyE; global transcriptional regulator |
| **sodA** | Superoxide dismutase, Mn |
| **sodB** | RNA chaperone and DNA-binding protein; suppresses T4 ld mutant; modulates micF stability; forms heteromers with, and stabilized against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS |
| **tsgA** | Aspartokinase I and homoserine dehydrogenase I, bifunctional |
| **tig** | Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains |
| **torS** | Sensor kinase for torCAD operon |
| **tref** | Cytoplasmic trehalase |
| **treK** | Repressor of trehalose operon |
| **trg** | Ribose, galactose chemoreceptor, methyl-accepting; MCP III; flagellar regulator |
| **trkG** | Major constitutive K+ uptake permease TrkAG; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane; Rac prophase |
| **trkH** | Major constitutive K+ uptake permease TrkAH; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane |
| **tsr** | Serine chemoreceptor, methyl-accepting; MCP I; also senses repellents; flagellar regulator |
| **tuB** | 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 |
| **tuA** | 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 |
| **uvrC** | Excision nuclease subunit C; repair of UV damage to DNA; multicopy causes mucoidy |
| **uxuR** | Repressor for UxuR regulon; true inducer is fructuronate |
| **wbbH** | |
| Gene | Description | Log2 Value |
|------|-------------|------------|
| wbbI | d-Galp: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 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 | 1.391839 |
| yahA | LysR family of transcriptional regulators, function unknown | -2.0166183 |
| yahB | Function unknown, Lrp family; putative transcriptional regulator | 1.046875 |
| ybaO | Mutant inhibits reduction of selenate, function unknown; predicted transporter | 1.0301518 |
| ybaS | Glutaminase | 1.2362571 |
| 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 |
| ybfD | 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 | Putative periplasmic serine protease; function unknown | 1.6117142 |
| ydgD | Putative transporter, function unknown; membrane protein | 1.9687521 |
| ydiD | Putative transporter, function unknown; membrane protein | 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 |
| yfB | Putative transporter, function unknown; membrane protein | 1.0953493 |
| yfB | Putative transporter, function unknown; membrane protein | 1.0032601 |
| yfCJ | Required for swarming phenotype, function unknown; membrane protein | 1.0550871 |
| yfeG | Putative LysR-family transcriptional regulator, function unknown | 1.1252446 |
| yfeR | Putative LysR-family transcriptional regulator, function unknown | 1.2977767 |
| ygeY | Peptidase homolog, function unknown; M20D family | 1.1330509 |
| ygfT | Putative LysR-family transcriptional regulator, function unknown | 1.4685719 |
| yglL | Function unknown, FimA homolog | 0.097937983 |
| yglE | Peptidase homolog, function unknown; predicted transcriptional regulator | -0.852435761 |
| yglG | DNA adenine methyltransferase, SAM-dependent | 0.950373744 |
| yhbC | DNA adenine methyltransferase, SAM-dependent | -1.146364 |
| yhdJ | DNA adenine methyltransferase, SAM-dependent | 0.0355549 |
| Gene  | Description                                                                                     | log2| 0 log2 | 1 log2 | 2 log2 |
|-------|-----------------------------------------------------------------------------------------------|-----|--------|--------|--------|
| yhiF  | Function unknown                                                                               | 1.2616509 | -1.6261956 | 0.509971635 | -2.136167235 |
| yhiB  |                                                                                               | 1.5886974 |        |        |        |
| yicE  | Function unknown                                                                               | -1.8931122 | 1.018744964 | 2.526242192 | -1.507497228 |
| yicG  |                                                                                                |        |        |        |        |
| yieG  | Function unknown                                                                               | -1.2165263 |        |        |        |
| yieK  | D-mannose isomerase; aldose-ketose isomerase inter-converting mannose, fructose and glucose; D-lyxose isomerase | 1.1036859 |        |        |        |
| yihS  | Putative purine permease, function unknown                                                     | 2.4466274 |        |        |        |
| yjCD  |                                                                                                | -1.2766161 | 0.58935423 | 1.464890192 | -0.875535962 |
| yjC   | Putative transporter, function unknown                                                         | 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 |        |        |        |
| yjFM  | 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  |                                                                                                | 1.2955649 |        |        |        |
| yqEL  | Part of T3SS PAI ETT2 remnant, ToxR homolog                                                   | -1.067694 |        |        |        |
| yrbG  | Function unknown                                                                               | 1.0887241 |        |        |        |
| znuA  |                                                                                                | -1.5015092 |        |        |        |
| ZupT  | Zinc and other divalent cation uptake transporter                                              | 1.4372325 |        |        |        |

**30502 developmental process**

| Gene  | Description                                                                                     | log2| 0 log2 | 1 log2 | 2 log2 |
|-------|-----------------------------------------------------------------------------------------------|-----|--------|--------|--------|
| 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  | Membrane-associated protein that binds to FtsH(HfIB) and HfIKC proteins; mutant YccA stabilizes SecY(Ts); suppression requires HfKIC; YccA is a native substrate for the FtsH(HfIB) protease | -1.0813851 |        |        |        |
| yccA  |                                                                                                | -1.0077734 |        |        |        |
| **S1234** | **establishment of localisation** |
|---|---|
| aeeA | AaeAB p-hydroxybenzoic acid efflux pump MFP component; membrane fusion protein | 1.1153295 |
| aeeB | AaeAB p-hydroxybenzoic acid efflux pump PET component; efflux protein family | 1.2832041 |
| acrD | AcrEF-ToIC efflux pump, multidrug/solvent resistance; osmotically remedial envelope defect | 1.513372 |
| acrF | Aminoglycoside efflux pump; RND-type transporter | 2.124423 |
| alsA | Allose transport ABC protein | 2.124423 |
| alsC | Allose transport, membrane component | 1.0019131 |
| amtB | Ammonia gas channel; sequencers GinK, 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 |
| appC | Cytochrome bd-II oxidase subunit I | 1.223081848 |
| argT | Periplasmic Lys-, Arg-, and Orn-binding protein | 2.102985883 |
| artJ | Periplasmic binding protein of Arg transport system | 1.084173 |
| 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 | PTS system EIIABC enzyme, beta-glucoside phosphotransferase; BglG kinase/dephosphorylase; membrane-bound protein; binds BglG | 1.1661614 |
| cirA | Colicin I receptor and translocator | -1.0816369 |
| cnuA | 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 |
| 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 |
| 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 |
| 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 |
| dacA | DcuC paralog, function unknown; mutant has no phenotype and dcuD does not complement dcuC mutations | 1.0231616 |
| Gene  | Description                                                                 | Value 1     | Value 2     | Value 3     | Value 4     |
|-------|------------------------------------------------------------------------------|-------------|-------------|-------------|-------------|
| 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  | Ferric citrate ATP-binding, membrane-associated transport protein             | 1.0179187   |             |             |             |
| fecE  | Ferrous iron uptake, required for full FeoB activity                         | 1.2498283   |             |             |             |
| feoA  | Ferrous iron uptake GTP-binding membrane protein; N-terminus is a cytoplasmic G protein | -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  | Outer membrane receptor for ferric-rhodotorulic acid; also receptor for ferric siderophores | -1.1662207  |             |             |             |
| fhuE  | TonB-dependent ferric iron outer membrane transporter; siderophore receptor for ferri-dihydroxybenzoic acid, ferri-dihydroxybenzoate and other catecholate siderophores; surface receptor for colicins G, H, and E492 | -0.995984903| 0.033259204 | -1.029244106|             |
| fiu   | Negative regulator of FliI ATPase activity; involved in flagellar assembly and export | -2.0643058  | 1.950296025 | 2.756911638 | -0.806615613|
| fliH  | Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits | -2.8425198  | 2.053080188 | 3.09328893 | -1.042248796|
| fliI  | Flagellin export apparatus soluble chaperone                                  | -1.861196   | 2.017483883 | 2.880704117 | -0.863220233|
| fliJ  | Flagellin export apparatus, integral membrane protein                         | -1.3490691  |             |             |             |
| fliK  | Flagellin export apparatus, integral membrane protein                         | -1.7036285  |             |             |             |
| fliP  | Flagellin export apparatus, integrant membrane protein                        | 1.0541813   |             |             |             |
| fliQ  | Flagellin export apparatus, integrant membrane protein                        | 1.2657433   |             |             |             |
| gatA  | Galactitol-specific enzyme IIA of phosphotransferase system (PTS)             | -1.6841471  |             |             |             |
| gatC  | Galactitol-specific enzyme IIC of PTS                                          | -1.4637866  |             |             |             |
| gtP   | Proton-glutamate-aspartate transport protein                                  | -1.0238819  |             |             |             |
| gntU  | Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC | 1.0674934   |             |             |             |
| grpE  | 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| 1.8138369721|
| gspD  | Part of H-NS-silenced gsp divergon, type II protein secretion; 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  | Pseudopilin in H-NS-silenced gsp divergon, type II secretion; cloned gsp divergon secretes ChiA | 1.0381198   | -0.571653549| -1.758766291| 1.187112742 |
| gspG  | Pseudopilin in H-NS-silenced gsp divergon, type II secretion; 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  | ChiA                                                                          | 0.112665963 | -0.927333212| 1.039999175 |             |
| Gene  | Description                                                                 | ChIA   | ChIB   | ChIC   |
|-------|------------------------------------------------------------------------------|--------|--------|--------|
| gspJ  | Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA | 0.136944905 | -1.110237463 | 1.247182368 |
| gspK  | Homologous to PilB of Pseudomonas aeruginosa; function not established, insertion mutation gives no phenotype | -0.002275476 | -0.831979946 | 0.829704469 |
| hofB  | Homologous to PIC of P. aeruginosa; function not established, insertion mutation gives no phenotype | 1.6588261 |
| hofC  | Required for the utilization of DNA as a carbon source; H. influenzae competence protein ComE homolog; putative fimbrial transport protein; expression not detected | 1.3816845 |
| hofQ  | Putative transporter, blocks RspA-mediated RpoS down-regulation; membrane protein; overexpression causes homocysteine accumulation due to MoeE inhibition and methionine auxotrophy in absence of cobalamin; no overexpression resistances found | 2.0593238 |
| hsrA  | Putative transporter, blocks RspA-mediated RpoS down-regulation; membrane protein; overexpression causes homocysteine accumulation due to MoeE inhibition and methionine auxotrophy in absence of cobalamin; no overexpression resistances found | 1.1956267 |
| kefB  | NEM-activatable K+/H+ antiporter | 1.0485537 |
| kgtP  | alpha-Ketoglutarate permease | -1.2960677 |
| livF  | High-affinity branched-chain amino acid transport, ATP-binding membrane protein | 1.0987494 |
| 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 |
| ildP  | L-lactate permease; also involved in glycolate uptake | -0.984811318 | -0.085681014 | -0.899130305 |
| lsrC  | Autoinducer-2 (AI-2) uptake | 1.1802423 |
| lsrD  | Autoinducer-2 (AI-2) uptake | 1.0535583 |
| malX  | PTS enzyme II homolog; malt regulated ABC exporter permease-ATPase, function unknown | 1.090272 |
| mdlB  | Putative transporter, function unknown; no MDR phenotype when mutated or cloned; fourth gene in mdtABCDbaeRS operon | 1.009489 |
| mdtE  | MdtEF-ToIC 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-ToIC multidrug resistance efflux RND-type transporter; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype | -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  | Molylodate uptake; chloride resistance; periplasmic molydate binding protein | -1.0889276 |
| motA  | H+-driven stator protein of flagellar rotation | -1.1367812 |
| napA  | Nitrate reductase, periplasmic | 1.479877 |
| nhaA  | NhaA, P1 activated by NhaR, repressed by H-NS and stimulated by Na(+) | 1.3487701 |
| nirC  | Nitrile 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 |
| Gene | Description |
|------|-------------|
| phnL | Carbon-phosphorus lyase complex subunit |
| pntA | Proton-translocating NAD(P) transhydrogenase, alpha subunit; membrane protein |
| pnuC | Nicotinamide mononucleotide transporter, putative, by homology with Salmonella |  
| potA | Proline/betaine permease, minor; osmosensor/osmoregulator |
| proP | Glucose phophotransferase enzyme IIIC(Glc); glucose permease |
| pnuC | Nicotinamide mononucleotide transporter, putative, by homology with Salmonella |  
| potA | Proline/betaine permease, minor; osmosensor/osmoregulator |
| proP | Glucose phophotransferase enzyme IIIC(Glc); glucose permease |
| ptsG | D-ribose high-affinity transport system |
| rbsA | D-ribose high-affinity transport system, membrane component |
| rbsC | D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU |
| rbsD | Putative polisoprenol-linked O-antigen translocase |
| rfx | Required for the reduction of SoxR; putative membrane-associated NADH oxidoreductase |
| rfx | Required for the reduction of SoxR; putative membrane protein |
| sdaC | Succinate dehydrogenase (SQ) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQ); complex II of aerobic respiration |
| sdaC | Succinate dehydrogenase (SQ) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQ); complex II of aerobic respiration |
| secB | Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone |
| secG | SecG inner membrane secretion protein; complexes with and assists the SecYE core translocon to interact with SecA to export proteins |
| sugE | Multidrug efflux pump; overexpression resistance to cetylpyridinium; suppresses groL mutation |
| tig | Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains |
| trkG | Major constitutive K+ uptake permease TrkAG; high-rate, low-affinity transport; K+ translocating subunit; binds TrkA to inner membrane; Rac prophage |
| trkH | DNA-binding ATPase involved in replication; cytotoxic; mutant displays an increased frequency of precise excision of transposons and defective growth of bacteriophage Mu |  
| ybaE | Function unknown |
| ybbY | Mutant inhibits reduction of selenate, function unknown; predicted transporter |
| ybbY | Putative xanthine/uracil permease, function unknown; glyoxylate-inducible |
| ybaE | Function unknown |
| ybaE | Function unknown |
| ybbY | Putative xanthine/uracil permease, function unknown; glyoxylate-inducible |
| ybbY | Putative xanthine/uracil permease, function unknown; glyoxylate-inducible |
| ybdM | Function unknown |
| ycaM | Putative transporter, function unknown |
| yccZ | Putative ABC transporter permease protein; function unknown |  
| yccZ | Putative ABC transporter permease protein; function unknown |
| Gene   | Description                                                                 |
|--------|------------------------------------------------------------------------------|
| yddB   | Putative TonB-dependent outer membrane receptor; function unknown            |
| ydhK   | Putative efflux protein family (PET) component of YdhJK efflux pump, function unknown |
| ydjN   | Function unknown                                                              |
| yeaN   | Putative transporter, function unknown; membrane protein                     |
| yebQ   | Putative transporter, function unknown; no overexpression resistances found   |
| yecI   | Function unknown                                                              |
| yeiU   | ABC transporter periplasm binding protein for microcin C; regulated by rydC sRNA |
| yejA   | Function unknown                                                              |
| yfbJ   | Function unknown                                                              |
| yfbW   | Putative GntP family transporter, function unknown                           |
| ygbN   | Putative periplasmic binding protein, function unknown                        |
| ygiS   | Function unknown                                                              |
| ygiE   | Function unknown                                                              |
| yhaO   | Putative amino acid:H+ symport permease, function unknown                    |
| yhdO   | Putative outer membrane fimbrial subunit usher; function unknown              |
| yhdX   | Putative ABC transporter permease protein; function unknown                  |
| yhdY   | Putative ABC transporter permease protein; function unknown                  |
| yhiP   | Putative ABC transporter permease protein; function unknown                  |
| yhiV   | Putative amino acid:H+ symport permease, function unknown                    |
| yicE   | Putative purine permease, function unknown                                    |
| yieG   | Function unknown                                                              |
| yicD   | Putative purine permease, function unknown                                    |
| yjcR   | Function unknown                                                              |
| yjD    | Putative ABC transporter permease protein; part of a predicted ABC transporter YffQRT-YjFF probably specific for galactofuranse transport |
| yjF    | Function unknown                                                              |
| yjH    | Putative transporter, function unknown; N-acytelyneuraminic acid inducible    |
| ynfJ   | Putative transporter, function unknown; no overexpression resistances found   |
| ynjC   | Function unknown                                                              |
| ynjD   | Function unknown                                                              |
| yodB   | Function unknown                                                              |
| yoiJ   | Microcin J25 efflux pump, TolC-dependent; non-essential gene                  |
| yphE   | Putative ABC transporter ATP-binding protein; function unknown               |
| znuA   | Function unknown                                                              |

**S1179 localisation**

| Gene   | Description                                                                 |
|--------|------------------------------------------------------------------------------|
| aaeA   | AaeAB p-hydroxybenzoic acid efflux pump MFP component; membrane fusion protein |
| aaeB   | AaeAB p-hydroxybenzoic acid efflux pump PET component; efflux protein family  |
| acrD   | AcrEF-TolC efflux pump, multidrug/solvent resistance; osmotically remedial envelope defect |
| acrF   | Function unknown                                                              |

| Gene   | Description                                                                 |
|--------|------------------------------------------------------------------------------|
| aaeA   | AaeAB p-hydroxybenzoic acid efflux pump MFP component; membrane fusion protein |
| aaeB   | AaeAB p-hydroxybenzoic acid efflux pump PET component; efflux protein family  |
| acrD   | AcrEF-TolC efflux pump, multidrug/solvent resistance; osmotically remedial envelope defect |
| acrF   | Function unknown                                                              |
| Gene | Description                                                                 | log2 Fold Change A/B | log2 Fold Change C/D | log2 Fold Change E/F | log2 Fold Change G/H |
|------|------------------------------------------------------------------------------|---------------------|---------------------|---------------------|---------------------|
| alsA | Allose transport ABC protein                                                  | 2.124423            |                     |                     |                     |
| alsC | Allose transport, membrane component                                         | 1.0019131           |                     |                     |                     |
| amtB | Ammonia gas channel; sequesters GinK, a negative regulator of AmtB activity, to the inner membrane; bi-directional facilitated diffusion | 1.316608            |                     |                     |                     |
| appB | Cytochrome bd-II oxidase subunit II                                          | -1.32081848         | 0.589787849         | -1.812869697        |                     |
| appC | Cytochrome bd-II oxidase subunit I                                           |                     |                     |                     |                     |
| araG | High-affinity L-arabinose transport                                          | 2.1461978           |                     |                     |                     |
| argT | Periplasmic Lys-, Arg-, and Orn-binding protein                              |                     |                     |                     |                     |
| argE | Periplasmic binding protein of Arg transport system                          |                     |                     |                     |                     |
| ascF | PTS system EIIBC enzyme, beta-glucoside phosphotransferase; paralogous to bgIF; cryptic unless AscG is mutated | 1.0536551           |                     |                     |                     |
| atpA | ATP synthase subunit alpha, membrane-bound, F1 sector                       | 1.5548844           |                     |                     |                     |
| atpB | ATP synthase subunit a, membrane-bound, F0 sector                           | -1.0947847          |                     |                     |                     |
| atpE | ATP synthase subunit c, membrane-bound, F0 sector                           | -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           |                     |                     |                     |
| bgF  | Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein | 1.1257329           |                     |                     |                     |
| cheY | CheY-P phosphatase                                                          |                     |                     |                     |                     |
| cheZ | CheY-P phosphatase                                                          | -1.0379796          |                     |                     |                     |
| cirA | Colicin I receptor and translocator                                          | -1.0816369          | -3.03639365         | -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 | -1.54617386         | 0.040691018         | 1.492060622         | -1.085079603       |
| dcvD | D,D-dipeptide permease system, ATP-binding (hydrolysis?) component           | 1.023161            |                     |                     |                     |
| dppF | Dipeptide/heme transport, periplasmic binding protein; recognition for transport and chemotaxis | 1.0231613           |                     |                     |                     |
| dppA | D-serine permease; D-serine tolerance                                        | 2.2577286           |                     |                     |                     |
| dscX | Hexuronate permease, for glucuronate and galacturonate                       | 1.0179187           |                     |                     |                     |
| Genes | Description                                                                                                                                          | Log2 Fold Change |
|-------|------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| 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      |
| fepE  | Lipopolysaccharide chains                                                                                                                                                                       | -1.1662207      |
| fnuE  | Outer membrane receptor for ferric-rhodotorulic acid; also receptor for ferric siderophores coprogen and ferrioxamine B                                                                           | -0.995984903    |
| fhuE  | TonB-dependent ferric iron outer membrane transporter; siderophore receptor for ferric-dihydroxybenzoylserine, ferri-dihydroxybenzoate and other catecholate siderophores; surface receptor for colicins G, H, and E492 | -1.0117576      |
| fliB  | Flagellar basal body rod subunit                                                                                                               | -2.9897075      |
| fliC  | Flagellar basal body rod subunit                                                                                                               | -3.2366333      |
| fliD  | Flagellar hook subunit protein                                                                                                                  | -3.2993827      |
| fliF  | Flagellar basal body rod subunit                                                                                                               | -2.318077       |
| fliG  | Flagellar basal body major subunit                                                                                                             | -2.7651777      |
| fliH  | Flagellar synthesis, basal body L-ring lipoprotein                                                                                           | -1.9212251      |
| fliI  | Basal body F-ring flagellar protein                                                                                                            | -2.6527514      |
| fliJ  | Flagellum-specific muramidase                                                                                                                  | -1.6338248      |
| fliK  | Flagellar synthesis, hook-associated protein                                                                                                 | -1.3041476      |
| fliL  | Flagellar synthesis, hook-associated protein                                                                                                 | -1.0269798      |
| fliM  | Hook-associated protein 2, axial family                                                                                                        | -1.0269284      |
| fliN  | Flagellar basal body M-ring protein                                                                                                            | -2.1452103      |
| fliH  | Negative regulator of FlII ATPase activity; involved in flagellar assembly and export                                                          | -2.0643058      |
| fliI  | Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits                              | -2.8425198      |
| fliJ  | Flagellar export apparatus soluble chaperone                                                                                                  | -1.861196       |
| fliG  | Rotor protein for flagellar motor switching and energizing; role in flagellar assembly                                                                                   | -2.774952       |
| fliL  | Flagellar synthesis, motor switching and energizing                                                                                           | -1.5788474      |
| fliM  | 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  | Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase                   | 1.0674934       |
| grpE  | Glutaredoxin 2; regulated by RpoS and ppGpp                                                                                                    | 1.0346646       |
| grxB  |                                                                                                                                                    | 1.6855459       |
| Gene  | Description                                                                 | Fold Change |
|-------|------------------------------------------------------------------------------|-------------|
| 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   |
| gspD  | Part of H-NS-silenced gsp divergon, type II protein secretion; OM secretin; cloned gsp divergon secretes ChiA | 1.3587675   |
| gspE  | Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA | 1.0.574179631   |
| gspF  | Pseudopilin in H-NS-silenced gsp divergon, type II secretion; cloned gsp divergon secretes ChiA | 1.0.3811998   |
| gspG  | Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA | 1.3308105   |
| gspH  | Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA | 1.1772904   |
| gspI  | ChiA, putative fimbrial transport protein; homolog; putative fimbrial transport protein; expression not detected no phenotype | 1.6588261   |
| gspJ  | ChiA, putative fimbrial transport protein; homolog; putative fimbrial transport protein; expression not detected no phenotype | 1.3816845   |
| gspK  | ChiA, putative fimbrial transport protein; homolog; putative fimbrial transport protein; expression not detected no phenotype | 2.0593238   |
| hsrA  | Homologous to PilB of Pseudomonas aeruginosa; function not established, insertion mutation gives no phenotype | 1.1956267   |
| kefB  | NEM-activatable K+/H+ antiporter | 1.0485537   |
| kgtP  | alpha-Ketoglutarate permease | -0.953824419   |
| livF  | High-affinity branched-chain amino acid transport, ATP-binding membrane protein | -1.2960677   |
| liv3  | 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   |
| lidP  | L-lactate permease; also involved in glycolate uptake | -0.984811318   |
| lsrC  | Autoinducer-2 (AI-2) uptake | 1.0987494   |
| lsrD  | Autoinducer-2 (AI-2) uptake | 1.0535583   |
| malX  | PTS enzyme II homolog; malt regulated ABC exporter permease-ATPase, function unknown | 1.1802423   |
| mdrB  | Putative transporter, function unknown; no MDR phenotype when mutated or cloned; fourth gene in mdrABCDbaeRS operon | 1.090272   |
| mdtD  | MdtEF-ToIC multidrug resistance efflux transporter; membrane fusion protein (MFP) component, lipoprotein; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype | 1.009489   |
| mdtE  | MdtEF-ToIC multidrug resistance efflux RND-type transporter; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype | 1.103484   |
| mdtF  | MdtEF-ToIC multidrug resistance efflux RND-type transporter; overexpression resistance to erythromycin, deoxycholate, octane and rhodamine; no mutant phenotype | -0.396000539   |
| Gene  | Function                                                                 | Description                                                                 | Ratio 1  | Ratio 2  | Ratio 3  | Ratio 4  |
|-------|---------------------------------------------------------------------------|----------------------------------------------------------------------------|----------|----------|----------|----------|
| melB  | Melibiose permease; thiomethylgalactoside permease II                     |                                                                              | 1.132939 |          |          |          |
| metQ  | Periplasmic methionine binding lipoprotein; methionine sulfoximine sensitivity |                                                                              |          | -1.03142 |          |          |
| mgtA  | Magnesium transporter, ATP-dependent; mutant has cobalt resistance; mediates Mg(2+) influx |                                                                              | -2.265869 | 0.414117 | 2.015561 | -1.60144 |
| modA  | Molybdate uptake; chloride resistance; periplasmic molybdate binding protein |                                                                              |          |          |          |          |
| motA  | H+-driven stator protein of flagellar rotation                            |                                                                              |          |          |          |          |
| napA  | Nitrile reductase, periplasmic                                              |                                                                              |          |          |          |          |
| 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(+)     |          |          |          |          |
| nirC  | Nitrite uptake transporter; membrane protein                              |                                                                              |          | -0.383649 | -1.343393 | 0.959745 |
| npr   | NPR, N-regulated HPr-like protein                                          |                                                                              |          |          |          |          |
| ompF  | Outer membrane porin F                                                    |                                                                              |          | -0.064492 |          |          |
| oppD  | Oligopeptide transport, ATP-binding protein                               |                                                                              |          |          |          |          |
| phnL  | Carbon-phosphorus lyase complex subunit                                    |                                                                              |          |          |          |          |
| pntA  | Proton-translocating NAD(P) transhydrogenase, alpha subunit; membrane protein |                                                                              |          |          |          |          |
| pnuC  | Nicotinamide mononucleotide transporter, putative, by homology with Salmonella |                                                                              |          |          |          |          |
| potA  | Multidrug efflux pump; overexpression resistance to cetylpyridinium; suppresses groL mutation |                                                                              |          |          |          |          |
| proP  | Proline/betaine permease, minor; osmosensor/osmoregulator                 |                                                                              |          |          |          |          |
| ptsG  | Glucose phosphotransferase enzyme II(Glc); glucose permease               |                                                                              |          | -1.111679 |          |          |
| puuP  | Putrescine importer                                                       |                                                                              |          |          |          |          |
| rbsA  | D-ribose high-affinity transport system                                    |                                                                              |          | -1.086268 |          |          |
| rbsC  | D-ribose high-affinity transport system, membrane component               |                                                                              |          | -1.643030 |          |          |
| rbsD  | D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU | Putative polioisopren-linked O-antigen translocase                      |          | -1.7281728 |          |          |
| rfxX  | Required for the reduction of SoxR; membrane protein                       |                                                                              |          | -1.0625052 |          |          |
| rsxC  | Required for the reduction of SoxR; putative membrane-associated NADH oxidoreductase |                                                                              |          | -1.300488 |          |          |
| rsxE  | Serine:H+ symport permease, threonine-insensitive                          |                                                                              |          | -1.038332 |          |          |
| sdaC  | Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration |                                                                              | -1.1312735 |          |          |          |
| sdc   | Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration |                                                                              |          |          |          |          |
| sddD  | Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone |                                                                              |          |          |          |          |
| secB  | SecG inner membrane secretion protein; complexes with and assists the SecYE core translocon to interact with SecA to export proteins |                                                                              |          |          |          |          |
| secG  | Multidrug efflux pump; overexpression resistance to cetylpyridinium; suppresses groL mutation |                                                                              |          |          |          |          |
| sugE  | Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains |                                                                              |          |          |          |          |
| tig   | Major constitutive K+ uptake permease TrkAG; high-rate, low-affinity transport; K+ translocating subunit; binds TrkA to inner membrane; Rac prophage |                                                                              | -1.0661763 |          |          |          |
| trkG  |                                                                              |                                                                              |          |          |          |          |
| Gene | Function |
|------|----------|
| **trkH** | Major constitutive K+ uptake permease TrkAH; high-rate, low-affinity transport; K+-translocating subunit; binds TrkA to inner membrane |
| **sup** | DNA-binding ATPase involved in replication; cytosolic; mutant displays an increased frequency of precise excision of transposons and defective growth of bacteriophage Mu |
| **yaaJ** | Function unknown |
| **yaaU** | Putative transporter, function unknown |
| **yadI** | Unknown |
| **ybaE** | Function unknown |
| **ybaT** | Mutant inhibits reduction of selenate, function unknown; predicted transporter |
| **ybbY** | Putative xanthine/uracil permease, function unknown; glyoxylate-inducible |
| **ybfM** | Function unknown |
| **ycAM** | Putative transporter, function unknown |
| **yccZ** | Function unknown |
| **ydcU** | Putative ABC transporter permease protein; function unknown |
| **ydhK** | Putative efflux protein family (PET) component of YdhJK efflux pump, function unknown |
| **ydJN** | Function unknown |
| **yeaN** | Putative transporter, function unknown; membrane protein |
| **yebQ** | Putative transporter, function unknown; no overexpression resistances found |
| **yeC** | Function unknown |
| **yeiU** | ABC transporter periplasmic binding protein for microcin C; regulated by rydC sRNA |
| **yejA** | Putative amino acid:H+ symport permease, function unknown |
| **yhcD** | Putative outer membrane fimbrial subunit usher; function unknown |
| **yhdX** | Putative ABC transporter permease protein; function unknown |
| **yhdY** | Putative ABC transporter permease protein; function unknown |
| **yhp** | Putative amino acid:H+ symport permease, function unknown |
| **yijV** | Putative purine permease, function unknown |
| **yicE** | Putative purine permease, function unknown |
| **yieG** | Putative transporter, function unknown |
| **yjcD** | Putative transporter, function unknown |
| **yjcR** | Putative transporter, function unknown |
| **yjdA** | Function unknown |
| **yjFF** | Putative ABC transporter permease protein; part of a predicted ABC transporter YffQRT-YjFF probably specific for galactofuranose transport |
| **yjHB** | Putative transporter, function unknown; N-acetylneuraminic acid inducible |
| Gene | Function | Log2 Fold Change | ΔLog2 Fold Change | Absolute Log2 Fold Change |
|------|----------|-----------------|------------------|--------------------------|
| ynmF | Putative transporter, function unknown; no overexpression resistances found | -1.059771 | -0.932769778 | 1.062541358 |
| ynjC | Function unknown | 1.0072496 | -0.932769778 | 1.940019358 |
| ynjD | Function unknown | 1.1847191 | 1.712429133 | -0.743840928 |
| yodB | Function unknown | 1.117802 | -0.743840928 | 1.861641856 |
| yojI | Microcin J25 efflux pump, TolC-dependent; non-essential gene | 1.117802 | -0.743840928 | 1.861641856 |
| yphE | Putative ABC transporter ATP-binding protein; function unknown | 1.5556669 | 1.875590458 | -0.6269235 |
| znuA | High-affinity ABC transport system for zinc, periplasmic | -1.5015092 | -1.070830933 | 2.572340163 |
| 8152 metabolic process | | | | |
| abgB | Required for p-aminobenzoyl-glutamate usage | 1.1240034 | -0.743840928 | 1.867844342 |
| acdD | 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 | -0.916588 | -0.743840928 | 1.660429856 |
| acmA | Aconitase B; 2-methylaconitate hydratase; apo-enzyme binds mRNA for negative translational autoregulation; iron-sulfur cluster; monomeric Acyl carrier protein, ACP-CoA synthase | 1.6737623 | -0.743840928 | 2.417603254 |
| acnB | Aconitase B; 2-methylaconitate hydratase; apo-enzyme binds mRNA for negative translational autoregulation; iron-sulfur cluster; monomeric Acyl carrier protein, ACP-CoA synthase | 1.0271903 | -0.743840928 | 1.770931242 |
| acPS | Aldehyde dehydrogenase, NAD-dependent; active on lactaldehyde, glycolaldehyde, and other aldehydes | -0.1016096 | 1.395137713 | -1.070830933 |
| aidA | Aldehyde dehydrogenase, NAD-dependent; active on lactaldehyde, glycolaldehyde, and other aldehydes | 1.322882306 | 1.395137713 | -1.070830933 |
| alsK | Allose kinase | 1.203258 | -0.743840928 | 1.947136816 |
| ansA | L-Asparaginase I | -1.1030908 | -0.743840928 | 1.846931736 |
| ansB | L-Asparaginase II | 1.5445883 | -0.743840928 | 2.288430254 |
| appB | Cytochrome bd-II oxidase subunit II | -1.07989973 | 1.374399075 | -1.454249003 |
| appC | Cytochrome bd-II oxidase subunit I | -1.142286168 | 0.73330429 | -1.875590458 |
| arcB | Tripartite sensor/histidine protein kinase; repression of aerobic genes and activation of some anaerobic genes under aerobic growth conditions; phosphorylates response regulator protein (ArcA); has responses regulator and second transmitter domains | 2.5143914 | -0.743840928 | 3.258230846 |
| argA | N-acetylglutamate synthase; growth on acetylornithine | 1.3041081 | 1.434967896 | 2.739076782 |
| argB | N-acetylglutamate kinase | 1.044384 | 1.527225825 | 2.574550653 |
| argC | N-acetyl-gamma-glutamyl-phosphate reductase | 1.7869039 | 1.757350161 | 3.543650322 |
| argD | Ornithine carbamoyltransferase; ornithine transcarbamylase, OTCase; CP4-6 putative prophage remnant | 2.58062465 | 1.749457164 | 4.329081818 |
| argF | Argininosuccinate synthase | 2.345750989 | 0.780893261 | 3.12663425 |
| argG | Argininosuccinate lyase | 2.489928442 | 1.442275936 | 3.932204878 |
| Gene  | Description                                                                 | Percent Fold Change |
|-------|-----------------------------------------------------------------------------|---------------------|
| argI  | Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase           | 2.843476333         |
| 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-α-L-Ara4N 3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP) synthase; tyrosine repressible; TvrR regulon | 1.0203366           |
| aroF  | Shikimate kinase I; alkali-inducible                                        | -1.2647691          |
| aroK  | Aspartate semialdehyde dehydrogenase                                        |                     |
| aroF  | L-Aspartate ammonia-lyase; L-aspartase                                      | 3.0522566           |
| aroA  | Aspartate aminotransferase, AspAT; kynurenine aminotransferase; glutamine transaminase K ATP synthase subunit alpha, membrane-bound, F1 sector                              | 1.3357835           |
| atpB  | ATP synthase subunit A, membrane-bound, F0 sector                            | -1.0947847          |
| atpE  | ATP synthase subunit c, membrane-bound, F0 sector                            | -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 expression of csrB/C sRNAs; works in concert with UvrY response regulator | 1.6353183           |
| bggL  | Periplasmic beta-glucosidase                                                 | 1.188965            |
| bioB  | Biotin synthase; dethiobiotin to biotin pathway; iron-sulfur enzyme          | -1.5355635          |
| bioC  | Biotin synthase blocked prior to pemeloyl CoA formation; putative SAM-dependent methyltransferase | -0.360614381 |
| bioF  | 7-keto-8-α-methylabscisic acid synthase                                       | 0.006936511         |
| cheA  | Histidine protein kinase sensor of chemotactc 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  | Amplification of cobA and other genes                                        | 1.7467084           |
| csgD  | Copper ion sensor regulating csgCB                                             | -1.859434883        |
| cysS  | Copper ion sensor regulating cysCFBA expression; may also sense silver      | 1.4919264           |
| cydA  | Cytochrome d (bd-1) terminal oxidase subunit I; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by FnR | -1.0059352           |
| cydB  | Cytochrome d (bd-1) terminal oxidase subunit II; upregulated in biofilms and microaerobic conditions; aerobically repressed by H-NS; anaerobically repressed by FnR | -1.065628           |
| cyoA  | Cytochrome o oxidase subunit II, lipoprotein; also called cytochrome bo(3) ubiquinol oxidase subunit II | -1.3402126           |
| cyoB  | Cytochrome o oxidase subunit I; cytochrome bo(3) ubiquinol oxidase subunit I | 1.0475307           |
| cyoC  | Cytochrome o oxidase subunit IV; cytochrome bo(3) ubiquinol oxidase subunit IV | -1.4617386           |
| Gene | Function | Description |
|------|----------|-------------|
| cyoE | Cytochrome o oxidase subunit, protoheme IX farnesyltransferase | Positive regulator for Cys regulon, acetylserine desulfhydrylase; downregulates ssuEADCB; cysteine desulfhydrylase |
| cysB | Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrylase |
| cysD | Sulfate adenylyltransferase | |
| dadA | D-amino acid dehydrogenase | |
| dadX | Alanine racemase; homodimeric | |
| dapB | Dihydropicolinate reductase | 2,3,4,5-tetrahydropyridine-2-carboxylate N-succinyltransferase; mutations suppress growth defects of strains lacking superoxide dismutase |
| dapD | C4-carboxylate regulation of anaerobic fumarate respiratory system; two-component system response regulator |
| dccR | C4-carboxylate regulation of anaerobic fumarate respiratory system; two-component system sensory histidine kinase |
| dccS | C4-carboxylate regulation of anaerobic fumarate respiratory system; two-component system sensory histidine kinase |
| ddg | 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 |
| deaD | Periplasmic, membrane-associated serine endoprotease; protease Do, required for high-temperature growth and the degradation of damaged proteins |
| degP | Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer |
| deoR | DNA polymerase III sliding clamp beta subunit; required for high processivity; required for regulatory inactivation of DnaA |
| dhaR | Transcription activator of the dhaKLM operon DNA polymerase IV, capable of translesion synthesis; overexpression enhances mutagenesis; mediates targeted mutagenesis by DNA polymerase III sliding clamp beta subunit; | |
| dinB | DNA polymerase III sliding clamp beta subunit; required for high processivity; required for regulatory inactivation of DnaA |
| dnaN | DNA polymerase III sliding clamp beta subunit; required for high processivity; required for regulatory inactivation of DnaA |
| dusB | tRNA-dihydrouridine synthase B |
| dxa | DXP synthase; DXP is precursor to isoprenoids, thiamin, pyridoxol |
| eno | Enolase; phosphoprotein; component of RNA degradosome |
| envC | Periplasmic murein hydrolase septal ring factor; sensitivity to crystal violet; filamentous |
| envY | Thermoregulatory activator of porin expression, AraC family |
| eutB | Ethanolamine ammonia lyase, large subunit, adenosylcobalamine-dependent; concerted induction requires both B12 and ethanolamine; heterodimeric |
| fabB | beta-Ketoacyl-ACP synthase I; KAS I; homodimeric |
| fabI | Enoyl-ACP reductase, NADH dependent |
| fabE | Fructose 1,6-bisphosphate aldolase, class I |
| fcl | NADPH-dependent GDP-L-acucose synthase, colanic acid synthesis; two-step reaction at a single active site: GDP-4-keto-6-deoxy-D-mannose epimerase, then reductase |
| fePE | Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains |
| fimB | Site-specific recombinase, fim promoter inversion; mediates flagellar phase switching, along with FimE |
| fkpA | Periplasmic peptidylprolyl cis,trans isomerase; heat shock inducible; PPIase-independent chaperone activity, binds FK506 |
| fig | Flagellum-specific muramidase |
| GenBank Accession | Description | Fold Change (log2) | Fold Change (log2) | Fold Change (log2) | Fold Change (log2) |
|-------------------|-------------|-------------------|-------------------|-------------------|-------------------|
| 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; RpoS antagonist, transiently in post-exponential phase; timing factor allowing motility to continue for a while during starvation; not required for normal motility | -1.861196        | 2.017483883       | 2.880704117       | -0.863220233      |
| fliZ              | GTP cyclohydrolase I Transpetidase, PB3; penicillin-binding protein 3 involved in septal peptidoglycan synthesis | 1.1728091        |                  |                  |                  |
| ftsI              | Elongation Factor EF-G; GTPase required for translocation from the A-site to the P-site in the ribosome; fusidic acid resistance | -1.1621015       |                  |                  |                  |
| ftsN              | Flagellin export apparatus soluble chaperone | 1.1232334        |                  |                  |                  |
| gadA              | Glutamate decarboxylase A | 1.0481529        |                  |                  |                  |
| 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 stability 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-galactopyranosyl mutase | -1.4456341       |                  |                  |                  |
| glgA              | Glycogen synthase | -0.611356637     | -1.25402616      | 0.642669579      |                  |
| glgB              | 1,4-alpha-glucan branching enzyme; glycogen branching enzyme | 0.10104895       | -0.518011066     | -1.447500807     | 0.929489741      |
| glgC              | Glucose-1-phosphate adenyltransferase; ADP-glucosepyrophosphorylase | -0.717255721     | -1.435926535     | 0.718670815      |                  |
| glgM              | Phosphoglucomutase mutase; UDP-GlcNAc pathway, peptidoglycan, lipopolysaccharide synthesis; mRNA stability effects | -1.2160809       |                  |                  |                  |
| glmA              | Glutamine synthase | 1.0619159        |                  |                  |                  |
| glmB              | Bifunctional uridylyltransferase/uridylyl-removing enzyme; (UTase/UR); controls uridylylation state and activity of PII(GlnB) | 1.5173011        |                  |                  |                  |
| glmD              | Glycerol kinase | 1.7542315        |                  |                  |                  |
| glpK              | Serine hydroxymethyltransferase; binds Zn(II) | -1.2570169       |                  |                  |                  |
| glyA              | Glycine--tRNA ligase, beta-subunit | -1.1524415       |                  |                  |                  |
| glyS              | 6-phosphogluconate dehydrogenase, decarboxylating | -1.1842852       |                  |                  |                  |
| gnd               | Low-affinity glucose transport protein, membrane protein | 1.0674934        |                  |                  |                  |
| gntU              | Phosphoglycerate mutase 1, 2,3-bisphosphoglycerate-dependent; Fur regulon; dimeric | -1.1640095       |                  |                  |                  |
| gpmA              | Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase | -1.0346646       |                  |                  |                  |
| grpE              | Glutaredoxin 2; regulated by RpoS and ppGpp | 1.6855459        |                  |                  |                  |
| grxB              | Part of H-NS-silenced gsp divergon, type II protein secretion; cloned gsp divergon secretes ChiA, requires gspAB operon | 1.1330825        |                  |                  |                  |
| gspA              |                        |                  |                  |                  |                  |
| Gene | Description |
|------|-------------|
| gyrB | DNA gyrase, subunit B; novobiocin, coumermycin resistance |
| hcaE | 3-phenylpropionate/cinnamic acid dioxygenase, alpha subunit; hca genes catalyze 3-phenylpropionate and cinnamic acid, feeding the products into the the mhp pathway |
| hemB | 5-aminolevulinate dehydratase; also known as porphobilinogen synthase; binds Zn(II) |
| hemD | Uroporphyrinogen III cosynthase; neomycin sensitivity |
| hisS | Histidine--tRNA ligase |
| hsdM | DNA methyltransferase M, host modification of foreign DNA |
| hsdR | Endonuclease R, host restriction of foreign DNA; ClpXP-dependent degradation |
| htrL | Formate-sensing regulator for hyf operon |
| hyaB | Hydrogenase 1 large subunit [NiFe], periplasmic |
| ilvC | Ketol-acid reductoisomerase |
| ilvN | Acetohydroxy acid synthase I (AHAS-I); acetolactate synthase I (ALS-I); valine sensitive; small subunit |
| insA | IS4 gene, transposition function |
| intD | Integrase gene within defective prophage DLP12 |
| intF | Putative integrase gene, CPS-6 putative prophage remnant |
| intS | Integrate, CPS-53/KpLE1 prophage |
| iscR | Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro |
| iscS | Cysteine desulfurase used in synthesis of Fe-S clusters and 4-thiouridine; ThrL transpersulfidase; SirA(TusA) transpersulfidase; pyridoxal phosphate cofactor linked to Lys206 |
| iscU | Iron-sulfur cluster assembly scaffold protein |
| ispA | Farnesyl diphosphate synthase, isoprenoid biosynthesis |
| ispE | 4-diphosphocytidyl-2-C-methylerythritol kinase; isopentenyl phosphate kinase; alternative nonmevalonate (DXP) pathway for terpenoid biosynthesis; essential gene |
| katE | Catalase hydroperoxidase II, heme d-containing; response to oxidative stress; chromosome resistance |
| katG | Catalase-hydrogen peroxidase I |
| kdgR | Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK |
| kdtA | 2'-deoxy-D-glucanate 3-dehydrogenase |
| kduB | 4-deoxy-L-threo-5-hexosulose-urionate ketol-isomerase; 5-keto-4-deoxyurionate isomerase |
| ktpA | NEM-activatable K+/H+ antiporter |
| lacZ | beta-D-Galactosidase |
| ldcA | L,D-carboxypeptidase A; cytoplasmic protease that cleaves the terminal D-alanine from cytoplasmic muropeptides |
| Gene  | Function                                                                 | log2(fold change) |
|-------|---------------------------------------------------------------------------|-------------------|
| leuA  | alpha-Isopropylmalate synthase                                            | -0.414798339      |
| leuB  | beta-Isopropylmalate dehydrogenase                                        | -0.199455562      |
| leuC  | alpha-Isopropylmalate isomerase large subunit                             | -0.415228459      |
| leuD  | alpha-Isopropylmalate isomerase small subunit                             | -0.170246462      |
| lllD  | L-lactate dehydrogenase, FMN dependent                                    | -1.218356827      |
| lllR  | Dual role activator/repressor for lllPRD operon                          | -1.022032736      |
| 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                                                 | -0.051142         |
| melA  | alpha-Galactosidase                                                       | 1.1843722         |
| mgtA  | Magnesium transporter, ATP-dependent; mutant has cobalt resistance; mediates Mg(2+) influx | -2.2685869         |
| miaA  | Dimethylallyl diphosphate:RNA dimethylallyltransferase; 2-methylthio-N6-(dimethylallyl)adenosine RNA hypermodification | 2.5113444         |
| mlaA  | Transcriptional regulator of csgD                                          | 1.208386          |
| mlaA  | UTP-N-acetylglucosamine enolpyruvyl transferase; fusobomycin resistance  | -1.2009416        |
| mutS  | Methyl-directed mismatch repair protein; dimeric/tetrameric              | -1.0045633        |
| nadD  | 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; Two-component nitrate/nitrite sensor-transmitter protein; NarL is cognate regulator; functional redundancy with narX | 1.0795679         |
| narX  |                                             | 1.0639569         |
| nhaA  | N-hydroxyarylamine O-acetyltransferase                                     | 1.1406503         |
| nirC  | Nitrite uptake transporter; membrane protein Lipoprotein, function unknown; may be involved in cell wall formation; may have murein activity | -1.0733091        |
| napD  | Ribonucleoside diphosphate reductase, subunit alpha; class I; aerobic; ribonucleotide reductase; B1 protein, R1 subunit | 1.0051479         |
| nrdA  |                                             | -0.0100503        |
| nudD  |                                             | 1.783473          |
| nroE  | NADH:ubiquinone oxidoreductase subunit E, complex I; NADH dehydrogenase I | 1.1405885         |
| nusE  | Outer membrane protease VII, DLP12 prophage; OMP protein 2b; ompin | -1.2738028        |
| osmA  | Trehalose phosphate phosphatase; cold- and heat-induced; required for viability at 4C; rpoS regulon; HAD17 Probable oxalo-CoA decarboxylase, oxalate catabolism | 1.0189233         |
| oxaC  | Phenylacetic acid degradation; mutants unable to use phenylacetate as a carbon source | 1.0424947         |
| paaJ  | Phenyacetic acid degradation                                                | 2.1441832         |
| paaX  | Phenyacetic acid degradation                                               | 1.0424947         |
| panB  | Ketopantoate hydroxymethyltransferase                                      | -1.0029793        |
| parC  |                                             | 2.1262205         |
| **Gene** | **Function and Characteristics** |
|----------|---------------------------------|
| **pcnB** | Poly(A) polymerase; controls plasmid copy number; rare AUU start codon, growth-rate regulated; monomeric |
| **pdxB** | 2-hydroxyacid dehydrogenase involved in pyridoxine biosynthesis upstream of 4-phospho-hydroxy-threonine; isoniazid resistance |
| **pheA** | Phenylalanine synthesis, bifunctional: chorismate mutase (N) and prephenate dehydratase (central); also contains Phe-binding regulatory domain (C); FPA resistance |
| **phoA** | Alkaline phosphatase, periplasmic; binds Zn(II); dimeric |
| **phoQ** | Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP |
| **php** | Putative phosphotriesterase; substrate unknown |
| **pinQ** | DNA invertase, site-specific recombination, Qin prophage |
| **pinR** | DNA invertase, site-specific recombination, Rac prophage |
| **plsC** | 1-Acyl-n-glycerol-3-phosphate acyltransferase; affects partitioning |
| **pntA** | Proton-translocating NAD(P) transhydrogenase, alpha subunit; membrane protein |
| **ppiB** | Periplasmic peptidylprolyl-cis-trans-isomerase B, rotamase |
| **pqqL** | Putative secreted zinc protease, function unknown; induced by AI-2 pheromone |
| **prc** | Peptide chain release factor 1, RF-1; translation termination factor recognizes UAG and UAA. |
| **prfA** | Transcriptional regulator of prp operon; propionate catabolism via 2-methylcitrate cycle, characterized primarily in Salmonella |
| **purC** | Amidophosphoribosyltransferase, purine synthesis; also known as glutamine 5'-phosphoribosylpyrophosphate amidotransferase, GPATase |
| **purM** | Phosphoribosyl-aminomimidazole-succinocarboxamide synthase; purine synthesis; homodimeric |
| **purN** | Glycinamide ribonucleotide transformylase (GART) 1, purine synthesis; glycinamide ribonucleotide formyltransferase |
| **purP** | Glycinamide ribonucleotide transformylase (GART) 2, non-folate-requiring, purine synthesis |
| **puuD** | Gamma-Glutamyl-GABA hydrolase, putrescine utilization pathway |
| **pyrB** | Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamoylase |
| **pyrD** | Dihydrorotate dehydrogenase, UMP biosynthesis |
| **pyrT** | Aspartate carbamoyltransferase, regulatory subunit; aspartate transcarbamoylase; ATCase; aspartate transcarbamoylase |
| **queA** | S-adenosylmethionine:3RNA ribosyltransferase-isomerase; queuosine biosynthesis, D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU |
| **rbsD** | Negative regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene |
| **rcsA** | Positive regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase |
| Gene | Description |
|------|-------------|
| recT | RecET recombinase, annealing protein, Rac prophage; recombination and repair |
| relA | ATP:GTP 3'→5' pyrophosphotransferase, ppGpp synthetase I; required for ppGpp synthesis during stringent response to amino acid starvation; self regulated |
| relA | UTP:GTP 3'→5' pyrophosphotransferase, ppGpp synthetase I; required for ppGpp synthesis during stringent response to amino acid starvation; self regulated |
| rfaS | LPS core, not affecting attachment of O antigen |
| rfaZ | 2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis |
| rfbA | TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidylyltransferase; needed for dTDP-4-rhamnose synthesis |
| rfbB | TDP-glucose oxidoreductase-4,6 dehydratase |
| rfbC | dTDP-4-deoxyxylulose-3,5-epimerase; putative polisoprenol-linked O-antigen translocase |
| rhaR | Transcriptional activator for rhaSR, AraC family |
| ribA | GTP cyclohydrolase II, riboflavin biosynthesis |
| ribB | 3,4-dihydroxy-2-butanone 4-phosphate synthase; riboflavin biosynthesis; acid inducible; homodimeric |
| ribC | Ribonucleoside hydrolase |
| rplB | 50S ribosomal subunit protein L2; binds Zn(II) |
| rplC | 50S ribosomal subunit protein L3 |
| rplF | 50S ribosomal subunit protein L6; gentamicin sensitivity |
| rplD | 50S ribosomal subunit protein L15 |
| rplP | 50S ribosomal subunit protein L16 |
| rplQ | 50S ribosomal subunit protein L17 |
| rplU | 50S ribosomal subunit protein L21 |
| rpxX | 50S ribosomal subunit protein L24 |
| rpmG | 50S ribosomal subunit protein L33 |
| rpsC | 30S ribosomal subunit protein S3 |
| rpsD | 30S ribosomal subunit protein S4; NusA-like antitermination factor |
| rpsG | 30S ribosomal subunit protein S7 |
| rpsH | 30S ribosomal subunit protein S8 |
| rpsK | 30S ribosomal subunit protein S11 |
| rpsM | 30S ribosomal subunit protein S13 |
| rpsQ | 30S ribosomal subunit protein S17 |
| rrmJ | 1.538243 |
| rnoB | Bifunctional D-altronate/D-mannonate dehydratase; overproduction prevents homoserine lactone-induced synthesis of RpoS |
| rpsA | Required for the reduction of SoxR; putative membrane-associated NADH oxidoreductase |
| rsaC | Required for the reduction of SoxR; membrane protein |
| rsaE | 23S rRNA m(5)U1939 methyltransferase, SAM-dependent |
| rumA | DNA hairpin dsDNA 3'-exonuclease SbcCD, Mn(2+), ATP-dependent; ATP-independent 5' ssDNA endonuclease; cosuppressor with sbcB of recB recC mutations; heterodimeric |
| sbcD | Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration |
| sdhC | 1.0607324 |
| Gene | Description | Log2FoldChange | p-value | q-value |
|------|-------------|----------------|---------|---------|
| sdhD | Succinate dehydrogenase (SQO) 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 | -1.3555017 | - | - |
| secG | General protein chaperone; 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 | Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone | 1.015482 | - | - |
| 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 |
| treF | Cytoplasmic trehalase | 1.0018826 | - | - |
| 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 | - | - |
| 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 | - | - |
| treR | Repressor of trehalose operon; 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 | 1.5542111 | - | - |
| wbbB | d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis | -1.004085 | - | - |
| wbbI | Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase | -1.0572133 | - | - |
| wbbJ | Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase | -1.304595 | - | - |
| wbbK | Involved in lipopolysaccharide biosynthesis | -1.4321501 | - | - |
| wcaI | Putative colanic acid biosynthesis glycosyltransferase | 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 | 1.391839 | - | - |
| yadB | Glutamyl-queuosine tRNA(Asp) synthase | 1.055563 | - | - |
| yadE | LysR family of transcriptional regulators, function unknown | 1.046875 | - | - |
| yahB | Function unknown, Lrp family; putative transcriptional regulator | 1.0301518 | - | - |
| ybaO | Putative transcriptional regulator | 1.2362571 | - | - |
| ybaX | -1.101002 | - | - |
| Gene   | Function                                                                                      | p-value (GEO) | p-value (EIG) | Adjusted p-value (Bonferroni) |
|--------|----------------------------------------------------------------------------------------------|---------------|---------------|------------------------------|
| ybeF   | Putative LysR-family transcriptional regulator, function unknown                            | 1.0823689     |               |                              |
| ybdD   | 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     |               |                              |
| ycbB   | Murein L,D-transpeptidase, periplasm                                                        | 1.1077027     |               |                              |
| yddE   | Function unknown                                                                             | 1.1745566     |               |                              |
| ydeP   | Required for acid resistance conferred by EvgA overexpression; oxidoreductase homolog       | 0.165101808    | 1.134409366   | -0.969307558                 |
| ydT    | Putative periplasmic serine protease; function unknown                                       | 1.6117142     |               |                              |
| ydgD   | Putative oxidoreductase; yhhX paralog                                                       | 1.9687521     |               |                              |
| ydgJ   | Putative oxidoreductase; function unknown                                                    | 1.0867878     |               |                              |
| ydiD   | Function unknown                                                                             | 1.5217233     |               |                              |
| yecI   | Function unknown                                                                             | 1.016995      |               |                              |
| yedF   | Function unknown                                                                             | -1.1209044    |               |                              |
| yegQ   | Function unknown, U32 peptidase family                                                      | -1.0663853    |               |                              |
| yfaX   | Putative LysR-family transcriptional regulator, function unknown                            | 1.2188423     |               |                              |
| yfBG   | Function unknown                                                                             | 1.0953493     |               |                              |
| yfbJ   | Function unknown                                                                             | 1.2325368     |               |                              |
| yfBQ   | Function unknown                                                                             | -1.0475144    | -0.044862622  | 0.847759504 -0.892622126    |
| yfBW   | Function unknown                                                                             | 1.0032601     |               |                              |
| yfeG   | Function unknown                                                                             | 1.1252446     |               |                              |
| yfeR   | Required for swarming phenotype, function unknown; predicted transcriptional regulator       | 1.2977767     |               |                              |
| yfF    | Putative methyltransferase, function unknown; spoU paralog; non-essential gene               | -1.4608327    |               |                              |
| ygeY   | Peptidase homolog, function unknown; M20D family                                             | 1.1330509     |               |                              |
| ygD    | Putative LysR-family transcriptional regulator, function unknown                            | 1.4685719     |               |                              |
| ygJ    | Function unknown                                                                             | 1.0237489     |               |                              |
| yhjD   | DNA adenine methyltransferase, SAM-dependent                                                | 1.0355549     |               |                              |
| yHF    | Function unknown                                                                             | 1.2616509     | -1.6261956    | 0.509971635 -2.136167235    |
| yhjB   | Function unknown                                                                             | 1.5886974     |               |                              |
| yIC    | alpha-Xylosidase; hexameric                                                                 | 1.2212114     |               |                              |
| yieK   | Function unknown, bg1 operon; glucosamine-6-phosphate isomerase homolog                      | 1.1036859     |               |                              |
| yihS   | D-mannose isomerase; aldose-ketose isomerase inter-converting mannose, fructose and glucose;| 2.4466274     |               |                              |
| ysjE   | Putative acetyltransferase                                                                   | 1.3598251     |               |                              |
| yjeS   | Putative electron transport protein, iron-sulfur center                                     | 1.1133585     |               |                              |
| yjHC   | Putative oxidoreductase; N-acetylneuraminic acid inducible                                  | -1.0411266    |               |                              |
| yjG    | Function unknown                                                                             | 1.064939      |               |                              |
| yjHH   | Function unknown                                                                             | 1.0324111     |               |                              |
| yjJR   | Putative HTH transcriptional regulator with aminotransferase domain, function unknown;      | 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, periplasm                                                        | 1.1129286     |               |                              |
| yodB   | Function unknown                                                                             | 0.694684412   | 1.62745419    | -0.932769778                 |
| Gene | Description | Fold Change |
|------|-------------|-------------|
| ypfI | Part of T3SS PAI2 remnant, TaxR homolog | 1.067775 |
| yqeI | Zinc and other divalent cation uptake transporter | -1.067694 |
| zupT | | 1.437235 |

### 51704 multi-organism process

| Gene | Description | Fold Change |
|------|-------------|-------------|
| ompF | Outer membrane porin F | -1.0644927 |
| slyA | Activates cryptic hemolysin gene hlyE; global transcriptional regulator | 1.015482 |

### 48519 negative regulation

| Gene | Description | Fold Change |
|------|-------------|-------------|
| 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

| Gene | Description | Fold Change |
|------|-------------|-------------|
| acrR | AcrR transcriptional repressor for acrAB (AcrAB-ToIc multidrugefflux pump) | -1.0204067 |
| arcB | Tripartite sensor/histidine protein kinase; repression of aerobic genes and activation of some anaerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has responses regulator and second transmitter domains | 1.0271903 |
| barA | Sensor histidine protein kinase, pleiotropic; controls the expression of csrB/C sRNAs; works in concert with UvrY response regulator | 1.6353183 |
| cheA | Histidine kinase protein sensor of chemotactic response; CheY is cognate response regulator; autophosphorylates; 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 phototransfer 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 | Transcription activator for csgBA and other genes | -1.859434883 |
| 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 | Cysteine desulfhydrase | 1.44637671 |
| dcuR | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system response regulator | 1.0233135 |
| dcuS | C4-dicarboxylate regulation of anaerobic fumarate 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 |
| Gene | Function | Value | Standard Error | t-value | P-value |
|------|----------|-------|----------------|---------|---------|
| envY | Thermoregulatory activator of porin expression, AraC family | 1.679985 | 0.473670149 | 1.76544683 | 1.291776681 |
| fimB | Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE | -1.1248107 | 0.473670149 | 1.76544683 | 1.291776681 |
| fimC | Flagellin, structural gene, H-antigen | -1.5392385 | 0.473670149 | 1.76544683 | 1.291776681 |
| gadE | Transcriptional regulator of the gadABC operon | -1.613297865 | 0.473670149 | 1.76544683 | 1.291776681 |
| galS | Transcriptional positive regulator for glc operon | 1.2070732 | 0.473670149 | 1.76544683 | 1.291776681 |
| glmC | Transcriptional positive regulator for glm operon | 1.2070732 | 0.473670149 | 1.76544683 | 1.291776681 |
| gnr | Cyclic-di-GMP phosphodiesterase, csgD regulator; modulates protein stability of RNase II | 1.123914 | 0.473670149 | 1.76544683 | 1.291776681 |
| hyfR | Formate-sensing regulator for hyf operon | 1.2317433 | 0.473670149 | 1.76544683 | 1.291776681 |
| iscR | Transcriptional repressor for isc operon; contains Fe-S cluster; binds RNA in vitro | -1.1579247 | 0.473670149 | 1.76544683 | 1.291776681 |
| kdgR | Regulator of kdgK, kdgT, eda; possibly regulates several other genes, e.g. yjgK | -1.064749 | 0.473670149 | 1.76544683 | 1.291776681 |
| lldR | Dual role activator/repressor for lldPRD operon | -1.022032736 | 0.473670149 | 1.76544683 | 1.291776681 |
| mtaA | Transcriptional regulator of csgD | 1.208386 | 0.473670149 | 1.76544683 | 1.291776681 |
| nanR | Nitrate/nitrite sensor-transmitter protein; anaerobic respiratory path; cognate regulator is NarP; function redundant with narX | 1.6356357 | 0.473670149 | 1.76544683 | 1.291776681 |
| narQ | Two-component nitrate/nitrite sensor-transmitter protein; NarL is cognate regulator; functional redundance with narX | 1.0795679 | 0.473670149 | 1.76544683 | 1.291776681 |
| narX | Two-component nitrate/nitrite sensor-transmitter protein; NarL is cognate regulator; functional redundance with narX | 1.0639569 | 0.473670149 | 1.76544683 | 1.291776681 |
| paaX | Phenylacetic acid degradation | 1.0424947 | 0.378975841 | 0.62544681 | 0.378975841 |
| phoQ | Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP | 1.4622464 | 0.473670149 | 1.76544683 | 1.291776681 |
| prpR | Transcriptional regulator of prp operon; propionate catabolism via 2-methylcitrate cycle, characterized primarily in Salmonella | 1.6797161 | 0.473670149 | 1.76544683 | 1.291776681 |
| purR | Purine regulon repressor | -1.0262108 | 0.473670149 | 1.76544683 | 1.291776681 |
| rcsA | Negative regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene | 0.300528606 | 0.473670149 | 1.76544683 | 1.291776681 |
| rcsC | TerF; probable histidine kinase | -1.6430304 | 0.473670149 | 1.76544683 | 1.291776681 |
| rhaR | Transcriptional activator for rhaSR, AraC family | 2.2165618 | 0.473670149 | 1.76544683 | 1.291776681 |
| rob | Right oriC-binding protein, AraC family | 1.3771441 | 0.473670149 | 1.76544683 | 1.291776681 |
| rpsD | 3OS ribosomal subunit protein S4; NusA-like antitermination factor | -1.0738251 | 0.473670149 | 1.76544683 | 1.291776681 |
| sgcR | Putative sgc cluster transcriptional regulator | 1.3975518 | 0.473670149 | 1.76544683 | 1.291776681 |
| slyA | Activates cryptic hemolysin gene hlyE; global transcriptional regulator | 1.015482 | 0.473670149 | 1.76544683 | 1.291776681 |
| stpA | RNA chaperone and DNA-binding protein; suppresses T4 td mutant; forms heteromers with, and stabilized against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS | -1.2432377 | 0.473670149 | 1.76544683 | 1.291776681 |
| tar | Serine chemoreceptor, methyl-accepting; also senses repellents cobalt and nickel; flagellar regulon | -1.1869416 | 0.473670149 | 1.76544683 | 1.291776681 |
| torS | Sensor kinase for torCAD operon | 2.9209745 | 0.473670149 | 1.76544683 | 1.291776681 |
| treR | Repressor of trehalose operon | 1.5542111 | 0.473670149 | 1.76544683 | 1.291776681 |
| trp | Riboce, galactose chemoreceptor, methyl-accepting; flagellar regulon | -1.3795029 | 0.473670149 | 1.76544683 | 1.291776681 |
| tsr | Serine chemoreceptor, methyl-accepting; flagellar regulon | -1.9566808 | 0.473670149 | 1.76544683 | 1.291776681 |
| uxuR | Repressor for UxuR regulon; true inducer is fructuronate | 1.0230589 | 0.473670149 | 1.76544683 | 1.291776681 |
| **Gene** | **Function/Description**                                                                                                                                                                                                                   | **log2 Ratio**  |
|----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| **yahA** | c-di-GMP-specific phosphodiesterase, PDE-A; reaction product is S'pGpG; dependent on Mg+2 or Mn+2, Ca+2 inhibitory; optimum pH 9.35; monomeric LysR family of transcriptional regulators, function unknown                                                                                   | -2.0166183     |
| **yahB** | Function unknown, Lrp family; putative transcriptional regulator                                                                                                                                                                            | 1.046875        |
| **ybaO** | Putative LysR-family transcriptional regulator, function unknown                                                                                                                                                                          | 1.0301518       |
| **ybeF** | Putative LysR-family transcriptional regulator, function unknown                                                                                                                                                                          | 1.0823689       |
| **ybdD** | 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       |
| **yflF** | Putative LysR-family transcriptional regulator, function unknown                                                                                                                                                                          | 1.4685719       |
| **yhiF** | **Probable repressor of dctA dicarboxylate transporter gene**                                                                                                                                                                              | 1.2616509       |
| **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 phosphotransfer 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 S’ 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    |
| **dinB** | DNA polymerase IV, capable of translesion synthesis; overexpression enhances mutagenesis; mediates targeted mutagenesis by 4-NQO; intrinsic AP lyase activity                                                                                       | 1.0903935       |
| Gene | Description | Score1 | Score2 | Score3 | Score4 |
|------|-------------|--------|--------|--------|--------|
| 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 | ATPase | -1.0346646 |  |  |  |
| gyrA | 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(DJC) is DnaJ-like co-chaperone; ATPase activity is stimulated by GrpE, DJC; 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 absence of cobalamin; no overexpression resistance 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 | -0.61092661 | 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-ToIC 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 |
| motA | MotA 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 |  |
| Gene  | Description                                                                 | Log2 Fold Change |
|-------|-----------------------------------------------------------------------------|-----------------|
| 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-butane-4-phosphate synthase; riboflavin biosynthesis; acid-inducible; homodimeric | -3.7772803      |
| rplF  | 30S 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      |
| rmJ   | Inhibits cell division and ftsZ ring formation; lexA regulon | 1.1538243       |
| sulA  | Aspartate, maltose chemoreceptor, methyl-accepting; MCP II; also senses repellents cobalt and nickel; flagellar regulon | 1.9572544       |
| tar   | Ribose, galactose chemoreceptor, methyl-accepting; MCP III; flagellar regulon | -1.1869416      |
| trg   | Serine chemoreceptor, methyl-accepting; MCP I; also senses repellents; flagellar regulon | -1.3795029      |
| tsr   | 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 | -1.9566808      |
| 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       |
| ybgG  | Function unknown | 1.0953493       |
| yhaA  | 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.

| GO Term                                      | Gene | Function                                                                 | Log2 of the ratio of PNPase null (no citrate):Wild-type (no citrate) | Log2 of the ratio of Wild-type plus citrate:Wild-type (no citrate) | Log2 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 |
|----------------------------------------------|------|--------------------------------------------------------------------------|--------------------------------------------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Cellular Metabolic Process                   |      |                                                                          |                                                                    |                                                                |                                                                        |                                                                                                   |
| 6081 cellular aldehyde metabolic process     |      |                                                                          |                                                                    |                                                                |                                                                        |                                                                                                   |
|                                              | gcl  | Glyoxylate carboligase, glyoxylate-inducible                            | 1.2727609                                                          |                                                                |                                                                        |                                                                                                   |
| 6519 cellular amino acid and derivative      |      |                                                                          |                                                                    |                                                                |                                                                        |                                                                                                   |
| metabolic process                           |      |                                                                          |                                                                    |                                                                |                                                                        |                                                                                                   |
|                                              | adA  | 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 1.61007183 |                                                                |                                                                        |                                                                                                   |
|                                              | 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, acetylserylme induced; downregulates ssuEADCB; cysteine desulfhydrase | 0.442750627 1.32534585 -0.882595223 |                                                                |                                                                        |                                                                                                   |
| Gene | Description | Entry | Z-score | P-value | Fold-change |
|------|-------------|-------|---------|---------|-------------|
| dadA | D-amino acid dehydrogenase | 1.2919754 | -0.36892089 | -1.625476173 | 1.256555364 |
| dadB | Dihydrolipide dehydratase | -1.0075407 | -0.965960622 | -2.004323596 | 1.449806213 |
| glnA | Glutamine synthase | 0.155438273 | -0.563659431 | -2.038941914 | 1.03862974 |
| glyA | Serine hydroxymethyltransferase | -1.2570169 | -1.315692056 | -1.10524415 | 1.1232334 |
| hisS | Histidine-tRNA ligase | -1.0075407 | -0.965960622 | -2.004323596 | 1.449806213 |
| ilvC | Ketol-acid reductoisomerase | -1.0233388 | 0.607905905 | 2.038941914 | -1.43103601 |
| purF | Amidophosphoribosyltransferase, purine synthesis | 1.5669665 | 1.33800575 | -0.51491624 | 1.85292199 |
| purD | Aspartate carboxamidase | 0.415228459 | -0.170246462 | -1.315692056 | 1.145445594 |
| thrA | Aspartokinase I and homoserine dehydrogenase | -1.004643 | 1.18802236 | 2.038941914 | -1.43103601 |
| yapA | Nitrate reductase, periplasmic | 1.19802236 | 1.33800575 | -0.51491624 | 1.85292199 |

6725 cellular aromatic compound metabolic process

- citE | Putative citrate lyase beta chain | 1.1568863 |
- folE | GTP cyclohydrolase I | -1.0049135 |
- hcaE | 3-phenylpropionate/cinnamic acid dioxygenase, alpha subunit; hca genes catalyze 3-phenylpropionate and cinnamic acid oxidation, feedback the products into the mhp pathway | 1.170918 |
- napA | Ribonucleoside hydrolase | 1.479877 |
- rihC | Ribonucleoside hydrolase | -1.0441272 |
**44249 cellular biosynthetic process**

| Gene | Description | Promoter | Pathway | Metabolite | Function |
|------|-------------|----------|---------|------------|----------|
| xdhA | Probable xanthine dehydrogenase molybdenum-binding subunit; involved in limited purine catabolism; mutation confers adenine sensitivity | 1.394154 | | | |
| xhdD | Probable hypoxanthine oxidase; mutation confers adenine sensitivity | 1.2296381 | | | |
| zipT | Zinc and other divalent cation uptake transporter | 1.4372325 | | | |
| argA | N-acetylglutamate synthase; first step in arginine biosynthesis; amino-acid acetyltransferase; growth on acetylornithine | 1.3041081 | | | |
| argB | N-acetylglutamate kinase | 1.044384 | | | |
| argC | N-acetyl-gamma-glutamyl-phosphate reductase | 1.7869039 | | | |
| argD | Acetylornithine aminotransferase; succinylpyridoxal phosphate 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 | 1.466532017 | 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 |
| ornA | 4-amino-4-deoxy-L-arabinose(Ara4N):Lipid A transferase; modifies lipid A phosphates with aminosugars and confers resistance to polymyxin B and cationic antimicrobial peptides; glycolipid donor is undecaprenyl phosphate-alpha-L-Ara4N | 1.0203366 | | |
| ornT | 3-deoxy-D-arabinofuranosyl-7-phosphate (DAHP) synthase; tyrosine repressible; TyrR regulon | 1.0875133 | | |
| aroF | Shikimate kinase I; auxotrophic | -1.2647691 | | |
| aroK | 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 | 0.006935611 | 1.062414033 | -1.055477522 |
| cld | Regulator of lipopolysaccharide O-chain length; gene studied in Salmonella and non-K-12 strains | -1.0316088 | | | |
| cobC | Cytochrome c oxidase subunit | 1.7467084 | | | |
| cyoE | Positive regulator for Cys regulon, cysteine inducer; downregulates cysteine desulphhydrase | -1.0276141 | 0.195029502 | 1.040158488 | -0.845128986 |
| cysB | cysteine desulphhydrase | 0.442750627 | 1.32534585 | -0.882595223 |
| dapA | Dihydrodipicolinate reductase | 1.2919754 | -0.563659431 | -2.013465644 | 1.449806213 |
| dapD | Dihydrodipicolinate reductase; growth defects of strains lacking superoxide dismutase | -1.0075407 | | | |
| fcl | Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains | 1.6897135 | | | |
| fepE | Elongation Factor EF-G; GTPase required for translocation from the A-site to the P-site in the ribosome; fusidic acid resistance | -1.1662207 | | | |
| fusA | UDP-galactopyranose mutase | -1.1621015 | | | |
| glf | UDP-galactopyranose mutase | -1.4456341 | | | |
| Gene   | Description                                                                 | log2FoldChange (up) | log2FoldChange (down) | p-value  |
|--------|------------------------------------------------------------------------------|---------------------|-----------------------|----------|
| glgA   | Glycogen synthase                                                           | -0.611356637        | -1.254026216          | 0.642669579 |
| glgB   | 1,4-alpha-glucan branching enzyme; glycogen branching enzyme                 | 1.0104895           | -0.518011066          | 0.929489741 |
| glgC   | Glucose-1-phosphate adenylyltransferase; ADP-glucose pyrophosphorylase        | -0.717255721        | -1.435926535          | 0.718670815 |
| gtyS   | Glycine-3'-RNA ligase, beta-subunit                                        | -1.1524415          | -1.46720426           | 1.051975801 |
| hemB   | Uroporphyrinogen III cosynthase; neomycin sensitivity                       | 1.0766261           | -1.46720426           | 1.051975801 |
| leuB   | beta-Isopropylmalate dehydrogenase                                          | -0.199455562        | -1.235586059          | 1.036130497 |
| leuD   | Isopropylmalate isomerase small subunit                                     | -0.170246462        | -1.315692056          | 1.145445594 |
| purF   | Aspartate carbamoyltransferase, regulatory subunit; aspartate transcarbamoylase; catalytic subunit; ATCase; aspartate transcarbamoylase | 2.193177888          | 1.177744341           | 1.015433546 |
| pyrB   | transcarbamoylase                                                           | 2.405384692         | 1.399913513           | 1.005471179 |
| pyrD   | Dihydroorotate dehydrogenase, UMP biosynthesis                              | -1.0465689          | -1.399913513          | 1.005471179 |
| pyrI   | Aspartate carbamoyltransferase, regulatory subunit; aspartate transcarbamoylase; ATCase; aspartate transcarbamoylase | 2.193177888          | 1.177744341           | 1.015433546 |
| rfaJ   | Glycolysis transferase needed for heptose region of LPS core                | -1.0780096          | -1.9637394            | -1.0442805 |
| rfaQ   | LPS core, not affecting attachment of O antigen                             | -1.3851705          | 2.4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis, | -1.0442805 |
| rfaS   | 2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis, | -1.3851705          | 2.4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis, | -1.0442805 |
| rfaZ   | TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidyltransferase; needed for dTDP-L-rhamnose synthesis | -1.3851705          | 2.4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis, | -1.0442805 |
| rfbX   | Putative polisoprenol-linked O-antigen translocase                          | -1.252498           | -1.252498             | -1.252498 |
| rfbC   | dTDP-4-deoxyxynamnose-3,5-epimerase                                          | -1.3006554          | -1.252498             | -1.252498 |
| rfbB   | TDP-glucose oxidoreductase-4,6 dehydrogenase                                 | -1.0411434          | -1.252498             | -1.252498 |
| rfbA   | TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidyltransferase; needed for dTDP-L-rhamnose synthesis | -1.3851705          | 2.4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis, | -1.0442805 |
| rplB   | SOS ribosomal subunit protein L2; binds Zn(II)                              | 1.22875676          | -1.3851705            | 2.4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis, | 1.556873 |
| Gene | Description | Fold Change |
|------|-------------|-------------|
| rplC | 50S ribosomal subunit protein L3 | -0.0714864 |
| rplF | 50S ribosomal subunit protein L6; gentamicin sensitivity | -1.1512773 |
| rplO | 50S ribosomal subunit protein L15 | -0.0819453 |
| 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** | d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis | -1.004085 |

**wbbI** | Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase | -1.0572133 |

**wbbJ** | Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase | -1.3040595 |

**wbbK** | Involved in lipopolysaccharide biosynthesis Putative colanic acid biosynthesis glycosyl transferase | -1.4321501 |

**wcaI** | Glutamyl-queuosine tRNA(Asp) synthase | 1.883362 |

**yadB** | 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 |

**arnT** | Regulator of lipopolysaccharide O-chain length; gene studied in Salmonella and non-K-12 strains | 1.0203366 |

**cld** | 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 |

**fcl** | Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains | -1.1662207 |

**galK** | Galactokinase | 1.7365794 |

---

### 44262 cellular carbohydrate metabolic process

| Gene | Description | Fold Change |
|------|-------------|-------------|
| 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 | 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 |
| fcl | Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains | -1.1662207 |
| galK | Galactokinase | 1.7365794 |
| Gene | Description                                                                 | Log2 Ratio |
|------|------------------------------------------------------------------------------|------------|
| gatA | Galactitol-specific enzyme IIA of phosphotransferase system (PTS)             | -1.6841471 |
| gatC | Galactitol-specific enzyme IIC of PTS D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability | -1.4637866 |
| gatY | Tagatose bisphosphate aldolase GatYZ subunit; required for full activity and stability of GatY | -1.6480765 |
| gatZ | UDP-galactopyranosyl mutase                                                   | -1.4456341 |
| glgA | Glycogen synthase                                                             | -0.61135637 -1.25402616 0.64266979 |
| 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 | 4-deoxy-L-threo-5-hexosulose-uronate ketol-isomerase; 5-keto-4-deoxyuronate isomerase | 1.5366621 |
| kduI | Lipid A synthesis, KDO2-lipid IVA lauroyl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high temperature survival | 1.4980454 |
| lpxL | Lipid A synthesis, KDO2-lauroyl-lipid IVA myristoyl-ACP acyltransferase       | 1.2080741 |
| lpxM | Lipid A synthesis, KDO2-lauroyl-lipid IVA myristoyl-ACP acyltransferase       | 1.418642 |
| nudD | UDP-D-glucose: (galactosyl)LPS-glucosyltransferase                             | 1.783473 |
| rfaJ | Glucosyltransferase needed for heptose region of LPS core                     | -1.1963794 |
| rfaQ | LPS core, not affecting attachment of O antigen                               | -1.0442805 |
| rfaS | 2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis, | -1.3851705 |
| rfaZ | TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidylyltransferase; needed for dTDP-L-rhamnose synthesis | -1.325498 |
| rfbA | TDP-glucose oxidoreductase-4,6 dehydratase                                     | -1.0411434 |
| rfbB | dTDP-4-deoxyxyrhamnose-3,5-epimerase Putative polysacrenol-linked O-antigen translocase | -1.3006554 |
| rfbC | Transcriptional activator for rhaSR, AraC family                              | -1.0625052 |
| rfaI | Cytoplasmic trehalase                                                         | 1.0018826 |
| treR | Repressor of trehalose operon                                                 | 1.5542111 |
| wbbH | d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis | -1.004085 |
| wbbI | Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase      | -1.0572133 |
| wbbJ | Involved in lipopolysaccharide biosynthesis, possible O-acetyltransferase      | -1.3040595 |
| wbbK | Putative colanic acid biosynthesis glycosyl transferase                        | -1.4321501 |
| wcaI | d-Galf:alpha-d-Glc beta-1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis | 1.883362 |
| ybgB | Function unknown, bgl operon; glucosamine-6-phosphate isomerase homolog       | 1.0953493 |
| ybeJ | 1.2325368 |
| ybfW | 1.0032601 |
| Gene | Description | Log2 Fold Change |
|------|-------------|-----------------|
| yiHS | D-mannose isomerase; aldose-ketose isomerase inter-converting mannose, fructose and glucose; D-lyxose isomerase | 2.4466274 |
| acnA | Aconitase A, stationary phase induced; iron-sulfur cluster; apo-enzyme binds mRNA for negative translational autoregulation; negatively regulated by rynB 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 D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability | 3.0522566 |
| gatY | Tagatose bisphosphate aldolase GatYZ subunit; required for full activity and stability of GatY | -1.6480765 |
| gatZ | 3-phenylpropionate/cinnamic acid dioxxygenase, alpha subunit; hca genes catalyze 3-phenylpropionate and cinnamic acid, feeding the products into the mhp pathway | -1.2347231 |
| hcaE | Catalase hydroperoxidase II, heme d-containing; response to oxidative stress; chromate resistance | 1.170918 |
| katE | Catalase-hydrogen peroxidase I Lipoprotein, function unknown; may be involved in cell wall formation; may have murein hydrolytic activity | 1.2447912 |
| katG | Catalase-hydrogen peroxidase I Lipoprotein, function unknown; may be involved in cell wall formation; may have murein hydrolytic activity | 0.208642701 |
| nlpD | D-ribose pyranase; interconverts beta-pyran and beta-furan forms of D-ribose; related to fucose mutarotase FucU | -0.610920661 |
| rbsD | Bifunctional D-altronate/D-mannonate dehydratase; overproduction prevents homoserine lactone-induced synthesis of homoserine lactone | 0.819563361 |
| rspA | RpoS Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration | 1.051479 |
| sdhC | Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration | -1.7281728 |
| sdhD | Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration | 1.0607324 |
| ynhG | Murein L,D-transpeptidase, periplasmic | 1.0157504 |
| abgB | Required for p-aminobenzoyl-glutamate usage | 1.1240034 |
| Gene | Description |
|------|-------------|
| arcB | Tripartite sensor/histidine protein kinase; repression of aerobic genes and activation of some anaerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has responses regulator and second transmitter domains |
| 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 |
| barA | 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 |
| 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 |
| cld | Regulator of lipopolysaccharide O-chain length; gene studied in Salmonella and non-K-12 strains |
| cusS | Copper ion sensor regulating cusCFBA expression; may also sense silver |
| dcuS | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system sensory histidine kinase |
| degP | Periplasmic, membrane-associated serine endopeptidase; protease Do, required for high-temperature growth and the degradation of damaged proteins Periplasmic murein hydrolase septal ring factor; sensitivity to crystal violet; |
| envC | filamentous 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 |
| fcl | Ferrienterobactin transport, membrane protein; regulator of length of O-antigen component of lipopolysaccharide chains |
| fepE | Periplasmic peptidylprolyl cis,trans isomerase; heat shock inducible; PPIase-independent chaperone activity, binds FK506 |
| ftsN | Cell division and growth; multicopy suppresses ftsA12 |
| fusA | Elongation Factor EF-G; GTPase required for translocation from the A-site to the P-site in the ribosome; fusidic acid resistance |
| glf | UDP-galactopyranose mutase |
| glgA | Glycogen synthase |
| glgB | 1,4-alpha-glucan branching enzyme; glycogen branching enzyme |
| glgC | Glucose-1-phosphate adenylytransferase; ADP-glucose pyrophosphorylase |
| glyS | Glycine--tRNA ligase, beta-subunit |
| grpE | Nucleotide exchange factor for the DnaKJ chaperone; heat shock protein; mutant survives lambda induction; stimulates DnaK and HscC ATPase |
| hisS | Histidine--tRNA ligase |
| htrL | 4-deoxy-L-threo-5-hexosulose-uronate ketol-isomerase; 5-keto-4-deoxyuronate isomerase |
| kdtA | Lipid A synthesis, KDO2-lipid IVa laureryl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high-temperature survival |
| lpxL | Lipid A synthesis, KDO2-lipid IVa laureryl-ACP acyltransferase; not under heat shock regulation; membrane protein affecting cell division, growth, and high-temperature survival |
| Gene | Description |
|------|-------------|
| lpxM | Lipid A synthesis, KDO2-lauroyl-lipid IVA myristoyl-ACP acyltransferase |
| map  | Methionine aminopeptidase |
| narQ | Nitrate/nitrite sensor-transmitter protein; anaerobic respiratory pathway; cognate regulator is NarP; function redundant with narX |
| narX | Two-component nitrate/nitrite sensor-transmitter protein; NarL is cognate regulator; functional redundancy with narQ |
| nlpD | Lipoprotein, function unknown; may be involved in cell wall formation; may have murein hydrolytic activity |
| nudD | Methionine aminopeptidase |
| ompT | Outer membrane protease VII, DLP12 prophage; OM protein 2b; omptin |
| phoQ | Response to extracellular divalent cations, pH, and acetate; two-component response regulator, cognate to phoP |
| ppiB | Putative peptidylprolyl-cis-trans-isomerase B, rotamase |
| pqqL | Periplasmic carboxy-terminal protease with specificity for non-polar C-termini |
| prc | Peptide chain release factor 1, RF-1; translation termination factor recognizes UAG and UAA |
| rcsC | Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF, probable histidine kinase |
| rfaA | UDP-D-glucose: (galactosyl)LPS-glucosyltransferase |
| rfaB | Glycosyltransferase needed for heptose region of LPS core |
| rfaC | LPS core, not affecting attachment of O antigen |
| rfaD | 2,4 Kdo transferase, required for the addition of KdoIII; LPS core biosynthesis |
| rfaH | TDP-glucose pyrophosphorylase; glucose-1-phosphate thymidyltransferase; needed for dTDP-L-rhamnose synthesis |
| rfbB | TDP-glucose oxidoreductase 4,6 dehydratase |
| rfbC | dTDP-4-deoxyrhamnose-3,5-epimerase; Putative polisoprenol-linked O-antigen translocase |
| rfbX | 50S ribosomal subunit protein L2; binds Zn(II) |
| rplA | 50S ribosomal subunit protein L3 |
| rplB | 50S ribosomal subunit protein L4; gentamicin sensitivity |
| rplC | 50S ribosomal subunit protein L15 |
| rplD | 50S ribosomal subunit protein L16 |
| rplE | 50S ribosomal subunit protein L6 |
| rplF | 50S ribosomal subunit protein L17 |
| rplG | 50S ribosomal subunit protein L21 |
| rplH | 50S ribosomal subunit protein L24 |
| rplI | 50S ribosomal subunit protein L32 |
| rpsA | 30S ribosomal subunit protein S4; NusA-like antitermination factor |
| rpsB | 30S ribosomal subunit protein S5 |
| rpsC | 30S ribosomal subunit protein S6 |
| rpsD | 30S ribosomal subunit protein S7; NusA-like antitermination factor |
| rpsE | 30S ribosomal subunit protein S8 |
| rpsF | 30S ribosomal subunit protein S9 |
| rpsH | 30S ribosomal subunit protein S10 |
| rpsI | 30S ribosomal subunit protein S11 |
| rpsK | 30S ribosomal subunit protein S12 |
| rpsL | 30S ribosomal subunit protein S13 |
| rpsM | 30S ribosomal subunit protein S14 |
| rpsO | 30S ribosomal subunit protein S15 |
| rpsP | 30S ribosomal subunit protein S16 |
| rpsQ | 30S ribosomal subunit protein S17 |
| Gene | Description |
|------|-------------|
| secB | Protein export chaperone; SecB helps SecA deliver proteins to the SecYE core translocon; general protein chaperone |
| surA | Periplasmic OM porin chaperone, has PPIase activity; required for stationary-phase survival |
| tig | Trigger factor, protein folding chaperone; also peptidyl-prolyl cis-trans isomerase; interacts with nascent polypeptide chains |
| torS | Sensor kinase for torCAD operon |
| 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 |
| wbbH | d-Galf:alpha-d-Glc beta,1,6-galactofuranosyltransferase; involved in lipopolysaccharide biosynthesis |
| ydfT | Putative periplasmic serine protease; function unknown |
| yegQ | Function unknown, U32 peptidase family |
| yfbG | Peptidase homolog, function unknown; M20D family |

**51186 cofactor metabolic process**

| Gene | Description |
|------|-------------|
| 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 |
| acnB | Aconitase B; 2-methylaconitate hydratase; apo-enzyme binds mRNA for negative translational autoregulation; iron-sulfur cluster; monomeric |
| aspA | L-Aspartate ammonia-lyase; L-aspartase |
| citE | Putative citrate lyase beta chain |
| coaA | Pantothenate kinase |
| hemB | S-aminolevulinate dehydratase; also known as porphobilinogen synthase; binds Zn(II); Uroporphyrinogen III cosynthase; neomycin sensitivity |
| hemD | 51186 cofactor metabolic process |
| iscU | Iron-sulfur cluster assembly scaffold protein |
| panB | Ketopantoate hydroxymethyltransferase Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate-ubiquinone oxidoreductase (SQR); complex II of aerobic respiration |
| sdhC | Succinate dehydrogenase (SQR) hydrophobic subunit; succinate-ubiquinone oxidoreductase (SQR); complex II of aerobic respiration |
| Generation of precursor metabolites and energy | | |
|---|---|---|
| appB | Cytochrome bd-II oxidase subunit II | -1.142286168 |
| appC | Cytochrome bd-II oxidase subunit I | -1.223081848 |
| 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 |
| cydA | 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 |
| cydB | Cytochrome o oxidase subunit II, lipoprotein; also called cytochrome bo(3) ubiquinol oxidase subunit II | -1.3402126 |
| cyoA | Cytochrome o oxidase subunit I; cytochrome bo(3) ubiquinol oxidase subunit I | -1.300488 |
| cyoB | Cytochrome o oxidase subunit IV; cytochrome bo(3) ubiquinol oxidase subunit IV | -1.4617386 |
| eno | Enolase; phosphoprotein; component of RNA degradosome | -1.0622171 |
| fbaB | Fructose 1,6-bisphosphate aldolase, class I D-Tagatose-1,6-bisphosphate aldolase, class II; requires GatZ subunit for full activity and stability | -1.6480765 |
| gatY | Phosphoglycerate mutase 1, 2,3-bisphosphoglycerate-dependent; Fur regulon; dimeric | -1.1640095 |
| gpmA | Glutaredoxin 2; regulated by RpoS and ppGpp | 1.6855459 |
| grxB | Nitrate reductase, periplasmic | 1.479877 |
| napA | Required for the reduction of SoxR; putative membrane-associated NADH oxidoreductase | -1.300488 |
| rsxC | Required for the reduction of SoxR; membrane protein | -1.300488 |
| rsxE | Succinate dehydrogenase (SQR) cytochrome b556; membrane anchor; succinate-ubiquinone oxidoreductase (SQR); complex II of aerobic respiration | 1.0607324 |
| sdhC | Succinate dehydrogenase (SQR) hydrophobic subunit; succinate:ubiquinone oxidoreductase (SQR); complex II of aerobic respiration | 1.0157504 |
| yodB | Function unknown | 0.694684412 |

| Heterocycle metabolic process | | |
|---|---|---|
| folE | GTP cyclohydrolase I | -1.0409135 |
| hemB | S-aminolevulinic 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 |
| arcB | Tripartite sensor/histidine protein kinase; repression of aerobic genes and activation of some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has responses 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, F0 sector | -1.1472812 |
| barA | Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein | 1.6353183 |
| cheY | Transcriptional activator for csgBA and other genes | -1.2030091 |
| csgD | Stationary phase inducible protein; sigma S-dependent promoter | -1.859434883 |
| csiE | Positive regulator for Cys regulon, acetylserine inducer; downregulates sssEADCB; cysteine desulfhydrase | 0.442750627 |
| cysB | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system response regulator | 1.0233135 |
| dcuR | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system sensory histidine kinase | 1.2036445 |
| dcuS | ATP-dependent RNA helicase, SOS ribosomal subunit biogenesis; translation factor W2; facilitates translation of mRNAs with 5' secondary structures; multicopy suppressor of rpsB(Ts) mutations | 1.1617334 |
| deaD | Repressor for deo operon, nupG and tsx; binds deoxyribose-5-phosphate inducer | 1.2066016 |
| deoR | Transcription activator of the dhaKLM operon | 1.127254 |
| dhaR | tRNA-dihydouridine synthase B | -1.1940618 |
| dusB | Thermoregulatory activator of porin expression, AraC family | 1.679985 |
| envY | Site-specific recombinase, fimA promoter inversion; mediates flagellar phase switching, along with FimE | -1.1248107 |
| fimB | Cytoplasmic membrane ATPase involved in flagellar assembly; involved in export of flagellar axial protein subunits | -2.8425198 |
| fliI | 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 |
| Gene   | Description                                                                                                                                                                                                 | Expression Level 1 | Expression Level 2 | Expression Level 3 |
|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|--------------------|--------------------|
| 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; 1.2070732 < 1.91643444 < 3.529732305                                                                                                             |                    |                    |                    |
| glcC   | Transcriptional positive regulator for glc operon; Cyclic-di-GMP phosphodiesterase, cgD regulator; modulates protein stability of 6-phosphogluconate dehydrogenase, decarboxylating |                    |                    |                    |
| gmr    | DNA gyrase, subunit B; novobiocin, coumermycin resistance; 1.1973567                                                                                                                                             |                    |                    |                    |
| gnd    | Formate-sensing regulator for hyf operon; 1.2317433 < 1.91643444 < 3.529732305                                                                                                                               |                    |                    |                    |
| gyrB   | Putative integrase gene, CP4-6 putative prophage remnant; 1.123914 < 1.91643444 < 3.529732305                                                                                                                       |                    |                    |                    |
| hyfR   | Dual role activator/repressor for lldPRD operon; 1.022032736 < 0.102462884 < 0.919569852                                                                                                                                  |                    |                    |                    |
| mgtA   | Magnesium transporter, ATP-dependent; 2.2685869 < 0.414117157 < 2.015561195 < -1.601444038                                                                                                                               |                    |                    |                    |
| miaA   | Dimethylallyl diphosphate:tRNA dimethylallyltransferase; 2-methylthio-N6-(dimethylallyl)adenosine tRNA hypermodification; 2.5113444                                                                                             |                    |                    |                    |
| mirA   | Transcriptional regulator of csgD; 1.208386 < 1.91643444 < 3.529732305                                                                                                                                             |                    |                    |                    |
| nadD   | Nicotinate mononucleotide dehydrogenase; 1.1650845 < 1.91643444 < 3.529732305                                                                                                                                         |                    |                    |                    |
| nanR   | Repressor of the nan operon, induced by sialic acid; 1.6356357 < 1.91643444 < 3.529732305                                                                                                                                  |                    |                    |                    |
| paaX   | Phenylacetic acid degradation; 1.0424947 < 0.378975841 < -0.246470978 < 0.625446818                                                                                                                                   |                    |                    |                    |
| parC   | Topoisomerase IV, subunit A, ATP-dependent, type II; chromosome decatenase; 2.1262205 < 0.414117157 < 2.015561195 < -1.601444038                                                                                         |                    |                    |                    |
| pcnB   | Poly(A) polymerase; controls plasmid copy number; rare AUA start codon, growth-rate regulated; 2.1234794                                                                                                           |                    |                    |                    |
| pinQ   | DNA invertase, site-specific recombination, Qin prophage; 1.1538181 < 1.91643444 < 3.529732305                                                                                                                                  |                    |                    |                    |
| pinR   | DNA invertase, site-specific recombination, Rac prophage; 1.1496861 < 1.91643444 < 3.529732305                                                                                                                                  |                    |                    |                    |
| prpR   | Transcriptional regulator of prp operon; 1.6797161 < 1.91643444 < 3.529732305                                                                                                                                       |                    |                    |                    |
| purC   | Phosphoribosyl-aminomimidazole-succinocarboxamide synthase; 1.6214104 < 0.671627539 < 1.519014342 < -0.847386803                                                                                     |                    |                    |                    |
| Gene   | Description                                                                 | Description                                                                 | Description                                                                 | Description                                                                 | Description                                                                 |
|--------|------------------------------------------------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| purF   | Amidophosphoribosyltransferase, purine synthesis; also known as glutamine 5'-phosphoribosylpyrophosphate amidotransferase, GPATase | 1.5669665                                                                   |                                                                              |                                                                              |                                                                              |
| purM   | Phosphoribosyl-aminimidazole (AIR) synthase; homodimeric Glycinamide ribonucleotide transformylase (GART) 1, purine synthesis; glycinamide ribonucleotide formyltransferase | -1.3292446                                                                   | 0.734599861                                                                | 2.273001511                                                               | -1.538401651                                                                |
| purN   | formyltransferase                                                            |                                                                              |                                                                              |                                                                              |                                                                              |
| purR   | Purine regulon repressor                                                     |                                                                              |                                                                              |                                                                              |                                                                              |
| purT   | Phosphoribosyl-aminimidazole (AIR) synthase; homodimeric Glycinamide ribonucleotide transformylase (GART) 2, non-folate-requiring, purine synthesis | -2.2606297                                                                   | 1.08852949                                                                 | 2.6678463                                                                | -1.57931681                                                                |
| purT   | Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamoylase | 2.40538462                                                                   | 1.399913513                                                                | 1.005471179                                                               |                                                                              |
| pyrB   | Dihydroorotate dehydrogenase, UMP biosynthesis                               | -1.0465689                                                                   |                                                                              |                                                                              |                                                                              |
| pyrD   | Aspartate carbamoyltransferase, regulatory subunit; ATCase; aspartate transcarbamylase; S-adenosylmethionine:RNA ribosyltransferase-isomerase; queuosine biosynthesis, | 2.193177888                                                                  | 1.177744341                                                               | 1.015433546                                                               |                                                                              |
| queA   | Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene | -1.0753493                                                                   |                                                                              |                                                                              |                                                                              |
| rcsA   | Negative regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains TerF; probable histidine kinase | 0.300528606                                                                  | -1.142561372                                                               | 1.443089978                                                               |                                                                              |
| rcsC   | RecET recombinase, annealing protein, Rac prophage; recombination and repair ATP:GTP 3'-pyrophosphotransferase, ppGpp synthetase I; required for ppGpp synthesis during stringent response to amino acid starvation; self regulated | 1.8229611                                                                   |                                                                              |                                                                              |                                                                              |
| relA   | Ribonucleoside hydrolase                                                     | -1.0411434                                                                   |                                                                              |                                                                              |                                                                              |
| rfbB   | TDP-glucose oxidoreductase-4,6 dehydratase Transcriptional activator for rhASR, AraC family | 1.0716362                                                                   |                                                                              |                                                                              |                                                                              |
| rhaR   | Ribonucleoside hydrolase                                                     | -1.0411434                                                                   |                                                                              |                                                                              |                                                                              |
| 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                                    |                                                                              |                                                                              |                                                                              |                                                                              |
| slyA   | RNA chaperone and DNA-binding protein; suppresses T4 td mutant; modulates micF stability; forms heteromers with, and stabilized against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS | 1.015482                                                                    |                                                                              |                                                                              |                                                                              |
| stpA   | Sensor kinase for torCAD operon                                              | -1.2432377                                                                   |                                                                              |                                                                              |                                                                              |
| treR   | Repressor of trehalose operon                                                |                                                                              |                                                                              |                                                                              |                                                                              |
| uxuR   | Repressor for UxuR regulon; true inducer is fructuronate                     |                                                                              |                                                                              |                                                                              |                                                                              |
| 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                                                                   |                                                                              |                                                                              |                                                                              |
| Gene  | Description                                                                 | Log2 Fold Change |
|-------|------------------------------------------------------------------------------|------------------|
| 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  | Putative LysR-family transcriptional regulator, function unknown             | -1.101002        |
| ybeF  | Putative LysR-family transcriptional regulator, function unknown             | 1.0823689        |
| ybhD  | Putative LysR-family transcriptional regulator, function unknown             | 1.1145554        |
| ydT   | Function unknown                                                              | 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  | Required for swarming phenotype, function unknown; predicted transcriptional regulator | 1.1252446 |
| yfeR  | Putative methyltransferase, function unknown; spoU paralog; non-essential gene | -1.4608327       |
| ygfI  | Putative LysR-family transcriptional regulator, function unknown             | 1.4685719        |
| yhiF  | Function unknown                                                              | 1.2616509        |
| yhjB  | Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family | 1.5886974        |
| yjiR  | Part of T3SS PAI ETT2 remnant, ToxR homolog                                  | 1.0690143        |
| yqeI  | Part of T3SS PAI ETT2 remnant, ToxR homolog                                  | -1.067694        |

### 6730 one-carbon metabolic process

| Gene  | Description                                                                 | Log2 Fold Change |
|-------|------------------------------------------------------------------------------|------------------|
| 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  | DNA adenine methyltransferase, SAM-dependent                                  | 1.1538243        |
| yhdJ  | DNA adenine methyltransferase, SAM-dependent                                  | 1.0355549        |

### 6082 organic acid metabolic process

| Gene  | Description                                                                 | Log2 Fold Change |
|-------|------------------------------------------------------------------------------|------------------|
| accD  | Acetyl-CoA carboxylase, carboxyltransferase beta subunit                      | -1.0916588       |
| acpS  | Acyl carrier protein; ACP-CoA phosphopantetheinytransferase; Holo-ACP synthase | 0.020738638      |
| 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        |
| argB  | N-acetylglutamate kinase                                                      | 1.044384         |
| argC  | N-acetyl-gamma-glutamyl-phosphate reductase                                  | 1.7869039        |

### Additional information

- **6730 one-carbon metabolic process** includes genes involved in GTP cyclohydrolase I, serine hydroxymethyltransferase, DNA methyltransferase M, and DNA adenine methyltransferase.
- **6082 organic acid metabolic process** includes genes involved in acetyl-CoA carboxylase, acyl carrier protein, arginine decarboxylase, and N-acetylglutamate synthase.

### Gene Functions
- **yahA**: c-di-GMP-specific phosphodiesterase, PDE-A.
- **yahB**: LysR family of transcriptional regulators, function unknown.
- **ybaO**: Function unknown, Lrp family; putative transcriptional regulator.
- **ybaX**: Putative LysR-family transcriptional regulator, function unknown.
- **ybeF**: Putative LysR-family transcriptional regulator, function unknown.
- **ybhD**: Putative LysR-family transcriptional regulator, function unknown.
- **ydT**: Function unknown.
- **yedF**: Function unknown.
- **yegE**: Putative c-di-GMP dual activity enzyme, function unknown.
- **yfaX**: Putative transcriptional regulator, function unknown.
- **yfeG**: Predicted transcriptional regulator.
- **yfeR**: Putative methyltransferase, function unknown.
- **ygfI**: Putative LysR-family transcriptional regulator, function unknown.
- **yhiF**: Function unknown.
- **yjIR**: Putative HTH transcriptional regulator with aminotransferase domain, function unknown.
- **yqeI**: Part of T3SS PAI ETT2 remnant, ToxR homolog.

### Additional Genes
- **folE**: GTP cyclohydrolase I.
- **glyA**: Serine hydroxymethyltransferase.
- **hsdM**: DNA methyltransferase M, host modification of foreign DNA.
- **rrmJ**: DNA adenine methyltransferase, SAM-dependent.
- **yhdJ**: DNA adenine methyltransferase, SAM-dependent.

### Additional Processes
- **6730 one-carbon metabolic process** encompasses genes related to one-carbon metabolism.
- **6082 organic acid metabolic process** includes genes involved in organic acid metabolism.

### Additional Remarks
- **argA**: N-acetylglutamate synthase; first step in arginine biosynthesis; amino-acid acetyltransferase; growth on acetylornithine.
- **argB**: N-acetylglutamate kinase.
- **argC**: N-acetyl-gamma-glutamyl-phosphate reductase.
| Gene | Function | Expression Ratio |
|------|----------|-----------------|
| argD | Acetylylornithine aminotransferase; succinylcarnitine aminotransferase, PLP-dependent | 2.58062465 1.749457164 0.831167486 |
| argF | Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase; CP4-6 putative phage remnant | 2.345750989 0.780893261 1.564857729 |
| argG | Argininosuccinate synthase | 2.6295392 1.468532017 |
| argH | Argininosuccinate lyase | 1.2643517 2.489928442 1.442275936 1.047652506 |
| argI | Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase | 2.843746333 1.517740469 |
| argJ | Argininosuccinate synthase | 2.6295392 1.468532017 |
| argK | Ornithine carbamoyltransferase; ornithine transcarbamylase; OTCase | 2.0875133 0.783608438 |
| cysB | Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase | 0.442750627 1.32534585 |
| dadA | D-amino acid dehydrogenase | 0.368920809 1.625476173 1.256555364 |
| dadX | Alanine racemase; homodimeric | 0.155438273 1.291326758 |
| dapB | Dihydrodipicolinate reductase | 1.2919754 -0.563659431 -2.013465644 |
| dapC | Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulfhydrase | 1.0075407 1.32534585 |
| eutB | Ethanolamine ammonia lyase, large subunit, adenosylcobalamine-dependent; concerted induction requires both B12 and ethanolamine | 1.7656298 |
| fabB | Beta-Ketoacyl-ACP synthase I; KAS I; homodimeric | 1.148054475 2.149240165 1.449806213 |
| fabI | Enoyl-ACP reductase, NADH-dependent | -1.0237877 |
| gdhA | Glutamate dehydrogenase | -0.965960622 2.004323596 1.038362974 |
| glnA | Glutamine synthase | 1.2727609 |
| gldA | Glutamate decarboxylase A | 1.1232334 |
| gldB | Glutamate decarboxylase B, vitamin B6-dependent; hexameric | 1.0481529 |
| gldC | Glyoxylate carboligase, glyoxylate-inducible | 1.2727609 |
| gldH | Glutamate dehydrogenase | 1.0619159 |
| gldI | Glutamine synthase | -1.2570169 |
| gldJ | Glutamate decarboxylase A, vitamin B6-dependent; hexameric | -1.1524415 |
| hisH | Histidine--tRNA ligase | -1.0382023 |
| ilvC | Ketol-acid reductoisomerase | -0.2033388 0.607095095 2.038941914 1.43103601 |
| ilvN | Ketol-acid reductoisomerase | 1.33800575 -0.51491624 1.85292199 |
| iscS | Ketol-acid reductoisomerase | -1.2212651 |
| leuA | Alpha-Isopropylmalate synthase | -0.414798339 -1.432033122 1.017234783 |
| leuB | Beta-Isopropylmalate dehydrogenase | -0.199455562 -1.235586059 0.306109407 |
| leuC | Alpha-Isopropylmalate isomerase large subunit | -0.415228459 -1.467240246 1.051975801 |
| leuD | Alpha-Isopropylmalate isomerase small subunit | -0.1702462 -1.315692056 1.145455994 |
| oxC | Phenylacetyl-CoA decarboxylase; oxalate catabolism | -0.336075069 1.512178216 -1.840253285 |
| paaJ | Phenylacetate degradation; mutants are unable to use phenylacetate as a carbon source | 2.1441832 |
| Gene | Description | Fold Change |
|------|-------------|-------------|
| **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-methylcitrate cycle, characterized primarily in Salmonella | 1.6797161 |
| **purF** | gamma-Glutamyl-GABA hydrolase, putrescine utilization pathway; Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamylase | 1.5669665 |
| **puuD** | Gamma-Glutamyl-GABA hydrolase, putrescine utilization pathway; Aspartate carbamoyltransferase, catalytic subunit; ATCase; aspartate transcarbamylase; aspartate transcarbamylase | 1.0298939 |
| **pyrB** | D-3-Phosphoglycerate dehydrogenase | -1.0648217 |
| **serA** | Aspartokinase I and homoserine dehydrogenase I, bifunctional | -1.004643 |
| **thrA** | Aspartokinase I and homoserine dehydrogenase I, bifunctional | 1.18802236 |
| **yadB** | Glutamyl-queuosine tRNA(Asp) synthase | 1.391839 |
| **ybaS** | Glutaminase | 1.2362571 |
| **ybaX** | Function unknown | -1.101002 |
| **yjH** | Function unknown | -1.4842229 |

| **6800 oxygen and reactive oxygen species metabolic process** | **gene** | **function** | **Fold Change** |
|-----------------|--------|-------------|----------------|
| sodA             | Superoxide dismutase, Mn | 1.120604 | -0.384140377 |
| sodB             | Superoxide dismutase, Mn | 4.006849988 | 3.110075363 |
| **barA** | Sensor histidine protein kinase, pleiotropic; controls the expression 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; CheA 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 fumarate 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** | TerF, probable histidine kinase | 1.8229611 |
| **torS** | Sensor kinase for torCAD operon | 2.9209745 |
| Gene | Function and Regulation |
|------|-------------------------|
| acrR | Transcriptional repressor for acrAB; repression of aerobic genes and activation of some anerobic genes under anaerobic growth conditions; phosphorylates response regulator protein (ArcA); has responses regulator and second transmitter domains | -1.0204067 |
| arcB | Tripartite sensor/histidine protein kinase; controls the expression of csrB/C sRNAs; works in concert with UvrY response regulator | 2.5143914 |
| barA | Response regulator for chemotactic signal transduction; CheA is the cognate sensor protein | 1.6353183 |
| cheY | Transcriptional activator for csgBA and other genes | -1.2030091 |
| csgD | Stationary phase inducible protein; sigma S-dependent promoter; Positive regulator for Cys regulon, acetylserine inducer; downregulates ssuEADCB; cysteine desulphhydrase | 0.442750627 |
| dcuR | C4-dicarboxylate regulation of anaerobic fumarate respiratory system; two-component system response regulator | 1.0233135 |
| dcuS | C4-dicarboxylate regulation of anaerobic fumarate 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 deoxynucleobase-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 |
| gadE | Transcriptional regulator of the gadABC operon | -1.613297865 |
| galS | Repressor of the mgl operon and isorepressor of the gal operon; autoregulatory; homodimeric | 1.2070732 |
| glcC | Transcriptional positive regulator for gic 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 regulator 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 |
| lidR | Dual role activator/repressor for lidPRD operon | -1.022032736 |
| 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 |
| prpR | Transcriptional regulator of prp operon; propionate catabolism via 2-methylcitrate cycle, characterized primarily in Salmonella | 1.6797161 |
| purR | Purine regulon repressor | -1.0262108 |
| Gene  | Description                                                                 | Log2 Ratio |
|-------|-----------------------------------------------------------------------------|------------|
| rcsA  | Positive regulatory gene for capsule (colanic acid) synthesis; two regulatory proteins are derived from the same gene | 0.300528606 |
| rcsC  | TerF; probable histidine kinase; positive regulatory gene for capsule (colanic acid) synthesis, controls sliminess; contains 3OS ribosomal subunit protein S4 | 1.8229611 |
| rhaR  | Transcriptional activator for rhaSR; AraC family; putative transcriptional regulator | 1.0716362 |
| rob   | Right oriC-binding protein; AraC family; putative transcriptional regulator | 1.3771441 |
| rpsD  | Antitermination factor; 30S ribosomal subunit protein S4; NusA-like; putative transcriptional regulator | -1.0738251 |
| rpsH  | 30S ribosomal subunit protein S8; putative transcriptional regulator | -1.019196 |
| sgcR  | Putative sgc cluster transcriptional regulator | 1.3975518 |
| slyA  | RNA chaperone and DNA-binding protein; suppresses T4 td mutant; modulates micF stability; forms heteromers with, and stabilized against proteolysis by, the paralogous H-NS protein; transcriptionally repressed by H-NS | 1.015482 |
| stpA  | Sensor kinase for torCAD operon | 2.9209745 |
| dreR  | Repressor of trehalose operon | 1.5542111 |
| uuxR  | Repressor for UxuR regulon; true inducer is fructuronate | 1.0230589 |
| yahA  | LysR family of transcriptional regulators, function unknown | -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  | Function unknown; predicted transcriptional regulator | 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; predicted transcriptional regulator | 1.1252446 |
| yfeR  | Required for swarming phenotype, function unknown | 1.2977767 |
| ygfF  | Putative LysR-family transcriptional regulator, function unknown | 1.4685719 |
| yhiF  | Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family | 1.2616509 |
| yhjB  | Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family | -1.6261956 |
| yjiR  | Putative HTH transcriptional regulator with aminotransferase domain, function unknown; MocR family | 0.509971635 |
| yqeI  | Putative transcriptional regulator, function unknown; MocR family | -2.13617235 |

### 6790 sulfur metabolic process

| Gene  | Description                                                                 | Log2 Ratio |
|-------|-----------------------------------------------------------------------------|------------|
| bioB  | Biotin synthase; dethiobiotin to biotin pathway; iron-sulfur enzyme | -1.5355635 |
| bioC  | Biotin synthase blocked prior to pimeloyl CoA formation; putative SAM-dependent methyltransferase | -0.360614381 |
| bioF  | 7-keto-8-amino pelargonic acid synthase | 0.797467665 |
| cysD  | Sulfate adenylyltransferase | -1.158082046 |

**Note:** Log2 ratios indicate up-regulation (positive values) or down-regulation (negative values).
| Gene  | Description                                                                 | Value 1 | Value 2 | Value 3 | Value 4 |
|-------|------------------------------------------------------------------------------|---------|---------|---------|---------|
| 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 adenyltransferase, NAD(P) biosynthesis 2-hydroxyacid dehydrogenase involved in pyridoxine biosynthesis upstream of 4-phospho-hydroxy-threonine; isoniazid resistance | 1.1660845 |         |         |         |
| pdxB  | GTP cyclohydrolase II, riboflavin biosynthesis | 1.6453347 |         |         |         |
| ribA  | 3,4-dihydroxy-2-butano 4-phosphate synthase; riboflavin biosynthesis; acid-inducible; homodimeric | 1.9398031 | 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 ($R^2 = 29\%$, $Q^2 = 16\%$) and 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) | 37°C (Control)              | 16°C (Cold shock)           |                                 |
| **Amino Acids**           |                                          |                                          |                             |                             |                                 |
| Alanine                   | Nc                                       | +                                        | +                           | +                           | +                               |
| Amino-butyric acid        | -                                        | -                                        | Nc                          | Nc                          | -                               |
| Betaine                   | +                                        | -                                        | -                           | -                           | -                               |
| Glutamate                 | -                                        | -                                        | Nc                          | Nc                          | Nc                              |
| 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                              |
| Metabolite          | +   | +   | Nc  | Nc  | -   |
|---------------------|-----|-----|-----|-----|-----|
| Threonine           |     |     |     |     |     |
| Tryptophan          | +   | +   | Nc  | +   | Nc  |
| Tyrosine            | -   | Nc  | Nc  | Nc  | Nc  |
| Valine              | -   | -   | Nc  | -   | Nc  |

**Glycolysis**

| Metabolite          | +   | +   | Nc  | Nc  | +   | +   |
|---------------------|-----|-----|-----|-----|-----|-----|
| Glucose             | -   | Nc  | -   | +   | +   | +   |
| Glyceraldehyde      | Nc  | +   | Nc  | Nc  | Nc  | Nc  |
| Lactate             | +   | +   | +   | +   | +   | +   |
| Pyruvate            | +   | Nc  | Nc  | Nc  | Nc  | Nc  |

**Krebs Cycle**

| Metabolite          | +   | +   | Nc  | Nc  | +   |
|---------------------|-----|-----|-----|-----|-----|
| Fumarate            | +   | +   | Nc  | Nc  | +   |
| Malate              | +   | +   | Nc  | Nc  | Nc  |
| Succinate           | +   | +   | +   | +   | +   |
| Acetate*            | -   | +/- | Nc  | Nc  | -   |

**Lipid Metabolites**

| Metabolite          | +   | +   | Nc  | Nc  | Nc  |
|---------------------|-----|-----|-----|-----|-----|
| Pentanoic acid      | -   | -   | Nc  | Nc  | Nc  |
| Pentandioic acid    | +   | +   | Nc  | +   | Nc  |

**Secondary**

| Metabolite          | +   | +   | Nc  | Nc  | +   |
|---------------------|-----|-----|-----|-----|-----|
| A-hydroxyisobutyric | -   | -   | Nc  | Nc  | -   |
| Putrescine          | -   | +   | Nc  | Nc  | +   |
| Cadaverine          | Nc  | +   | Nc  | Nc  | +   |
| Inositol            | -   | -   | Nc  | -   | Nc  |
| Phosphate           | Nc  | -   | Nc  | Nc  | Nc  |

**Urea Cycle**

| Metabolite | +   | +   | Nc  | Nc  | Nc  | Nc  |
|------------|-----|-----|-----|-----|-----|-----|
| 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).*
Figure S1

Unstressed condition

Increase:  
18) Betaine  
27) Phenylalanine  
14) Succinate  
26) Tryptophan  
13) Pyruvate  
2) Lactate

Decrease:  
24) α-glucose  
9) Methionine  
11) Proline

Phosphosugar Stress

Increase:  
11) Proline

Decrease:  
18) Betaine
Figure S2
Figure S4 (a)

Figure S4 (b)
Figure S5

Bar chart showing the % RNA degraded at different citrate concentrations (mM).

- For a citrate concentration of 0 mM, the % RNA degraded is approximately 75%.
- For a citrate concentration of 10 mM, the % RNA degraded is approximately 50%.

Vertical axis: % RNA degraded
Horizontal axis: Citrate concentration (mM)
Figure S6
Polynucleotide Phosphorylase Activity May Be Modulated by Metabolites in
Escherichia coli
Salima Nurmohamed, Helen A. Vincent, Christopher M. Titman, Vidya Chandran,
Michael R. Pears, Dijun Du, Julian L. Griffin, Anastasia J. Callaghan and Ben F. Luisi

J. Biol. Chem. 2011, 286:14315-14323.
doi: 10.1074/jbc.M110.200741 originally published online February 14, 2011

Access the most updated version of this article at doi: 10.1074/jbc.M110.200741

Alerts:
• When this article is cited
• When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

Supplemental material:
http://www.jbc.org/content/suppl/2011/02/14/M110.200741.DC1.html

Read an Author Profile for this article at
http://www.jbc.org/content/suppl/2011/04/08/M110.200741.DCAuthor_profile.html

This article cites 50 references, 23 of which can be accessed free at
http://www.jbc.org/content/286/16/14315.full.html#ref-list-1