Proteomic Analysis of the Reduction and Resistance Mechanisms of *Shewanella oneidensis* MR-1 under Long-term Hexavalent Chromium Stress

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Abstract: Hexavalent chromium [Cr(VI)] is a priority heavy metal pollutant causing a series of environmental issues, and bio-reduction of Cr(VI) to trivalent chromium can remarkably decrease the environmental risk of Cr(VI). The reduction and resistance abilities of microorganisms to Cr(VI) can be dramatically improved by acclimatization. In the present study, we collected *Shewanella oneidensis* MR-1 from a 120-day acclimatization by increasing Cr(VI) concentration in the culture media to investigate its adaptation mechanisms under long-term Cr(VI) stress at the proteome level. Tandem mass tag-based quantitative proteomic analysis was performed to study the differences between 9 collected samples. A total of 2500 proteins were quantified from 2723 identified protein groups. Bioinformatics analysis showed that the differentially expressed proteins after the 120-day Cr(VI) acclimatization were mostly related to flagellar assembly, ribosomes, transport, sulfur metabolism, and energy metabolism. The findings of this study present novel insights into the molecular mechanisms for the reduction and resistance of *S. oneidensis* MR-1 responding to long-term Cr(VI) stress at the proteome level.

Keywords: *Shewanella oneidensis* MR-1, Hexavalent chromium, Long-term acclimatization, Permanent effect, Short-term stimulus

1. Introduction

Chromium, an important heavy metal, has been widely used in industry, such as electroplating, wood preservation, production of steel and alloy, leather tanning, and pigmentation (Dhal et al., 2013). Hexavalent chromium [Cr(VI)] causes many serious environmental issues and remarkably threatens all kinds of lives, including the lives of animals, plants, microorganisms and humans, due to its high toxicity, mutagenicity and carcinogenicity. Therefore, it is essential to address Cr(VI) contamination by efficient, economical and ecological methods. At present, the most efficient way to treat Cr(VI) contamination is by converting Cr(VI) into a much less toxic trivalent chromium [Cr(Ⅲ)]. Some studies have focused on Cr(VI) reduction and detoxication by employing various chemical or biological approaches, and microbiological reduction is a more promising strategy for the remediation of various Cr(VI)-contaminated environments (Alencar et al., 2017; Chai et al., 2018; Cheung and Gu, 2007; Dhal et al., 2013; Pradhan et al., 2017). Wang et al. (Wang et al., 2016) used microbial fuel cells for the remediation of Cr(VI)-contaminated soils.

Microorganisms' capacities for reduction and/or resistance to pollutants can be achieved by long-term acclimatization. For example, the removal efficiency of a high concentration of sulfamethazine antibiotics could be promoted by acclimatizing activated sludge in reactors fed with increasing sulfamethazine antibiotics (Yang et al., 2015). Chen et al. (Chen et al., 2006) investigated the effect of microorganism acclimatization on enhanced phosphorus biological removal from wastewater. The reduction and resistance abilities of microorganisms to Cr(VI) can also be dramatically improved by long-term acclimatization.

Shewanella oneidensis MR-1, a model strain of dissimilatory metal reduction bacteria, is capable of reducing Cr(VI) to Cr(Ⅲ) aerobically or anaerobically (Belchik et al., 2011; Meng et al., 2018). The mechanisms of *S. oneidensis* MR-1 for resisting or reducing Cr(VI) have been reported extensively (Bencheikh-Latmani et al., 2005; Brown et al., 2006; Wang et al., 2014). *S. oneidensis* MR-1 reduces Cr(VI) aerobically using a soluble reductase of NADH or endogenous electron reserves as electron donor, while the anaerobic reduction of Cr(VI) relates to the electron transport system involving membrane cytochromes (Wang and Shen, 1995). However, these findings are mostly based on short-term exposure of *S. oneidensis* MR-1 to low-concentration Cr(VI), and no study has focused on the adaptation mechanisms of bacteria in the Cr(VI) environment aiming at an engineering application. Therefore, the molecular mechanisms for reduction and resistance of bacteria responding to the stress from long-term high-concentration Cr(VI), i.e., the acclimation process, have never been clarified.

Proteomics is quite a powerful tool to explore the cellular molecular mechanism of organisms responding to environmental stress by analyzing differentially expressed proteins (DEPs). In the present study, we analyzed the proteome of *S. oneidensis* MR-1 after 120-day Cr(VI) exposure to determine the response mechanism of MR-1 against long-term Cr(VI) exposure. The DEPs were identified by high-resolution liquid chromatography-tandem mass spectrometry (LC-MS/MS). The results will further shed light on the molecular mechanism for resistance and reduction in MR-1 under long-term Cr(VI) exposure at the proteomic level, which can help us to make effective bioremediation and environmental risk assessments through long-term acclimatization.

2. Materials and methods

2.1. Bacterial strains and Cr(VI) treatment

The strain used in this study was the *S. oneidensis* strain MR-1, which was cultured in Luria-Bertani (LB) broth without and with Cr(VI) for 120 days and was designated D120N and D120Cr, respectively. The LB medium contains tryptone (10 g/L), yeast extract (5 g/L) and NaCl (10 g/L) (pH 7.0). The experimental strains were aerobically grown at 30 °C in 250-mL Erlenmeyer flasks containing a 100-mL LB medium by shaking at 150 rpm. The inoculation ratio was 1.0%. Cr(VI) stock solution was 100 mM K_2CrO_4 solution. The final concentration of Cr(VI) was 312 mg/L in D120Cr(+), and no Cr(VI) was added in D120N and D120Cr(-) (Fig. S1). The cell samples of D120Cr(+), D120N and D120Cr(-) were collected for protein processing after 8, 5 and 6 hours, respectively. Each treatment was prepared in triplicate.

2.2. Protein extraction and digestion

The extraction and digestion of proteins were based on the published method (Wang et al., 2017). Samples were sonicated three times on ice using a high-intensity ultrasonic processor (JY92-ⅡN, Scientz, China) in four volumes of lysis buffer (8 M urea, 1% v/v Triton-100, 10 mM dithiothreitol, 1% v/v protease inhibitor cocktail and 2 mM ethylene diamine tetraacetic acid). The remaining debris was removed by centrifugation at 20,000 *g* at 4 °C for 10 min. Finally, the supernatant was collected, and the protein was precipitated with cold 20% w/v trichloroacetic acid for 2 h at 4 °C. After centrifugation at 12,000 *g* at 4 °C for 3 min, the supernatant was discarded.

The remaining precipitate was washed three times with cold acetone. The protein was re-dissolved in 8 M urea, and the protein concentration was determined with a BCA kit (Beyotime, China) according to the manufacturer's instructions.

For digestion, the protein solution was reduced with 5 mM dithiothreitol for 30 min at 56 °C and alkylated with 11 mM iodoacetamide for 15 min at room temperature in darkness. The protein sample was then diluted by adding 100 mM TEAB to urea concentration less than 2 M. Finally, trypsin (Promega, USA) was added at a 1:50 trypsin-to-protein mass ratio for the first digestion overnight at 37 °C and 1:100 trypsin-to-protein mass ratio for a second 4 h-digestion.

2.3. TMT labeling and HPLC fractionation

The digested samples were desalted by the Strata X C18 SPE column (Phenomenex, USA) and vacuum freeze-dried. Peptides were reconstituted in 0.5 M TEAB and labeled using the TMT-10plex Kit (Thermo Fisher Scientific) according to the manufacturer’s instructions. All samples were pooled and vacuum freeze-dried. The labeled peptide mixtures were fractionated into fractions by high pH reverse-phase HPLC using the Agilent 300Extend C18 column (5 μm particles, 4.6 mm ID, 250 mm length). The peptides were combined into 18 fractions and vacuum freeze-dried.

2.4. LC-MS/MS analysis

LC−MS/MS analysis was performed using the EASY-nLC 1000 UPLC system (Thermo Fisher Scientific) coupled with a Q-Exactive Hybrid Quadrupole-Orbitrap mass spectrometer (Thermo Fisher Scientific) with a nanospray ionization (NSI) source. A data-dependent procedure that alternated between one MS scan (70000 resolving power) and 20 MS/MS (30000 resolving power) scans with 30 s dynamic exclusion.

2.5. Database search and bioinformatic analysis

The resulting MS/MS data were processed using the Maxquant search engine (v.1.5.2.8). The obtained peptide sequences were searched against the UniProt *Shewanella oneidensis* (strain MR-1) (4068 sequences) database concatenated with a reverse decoy database. The false discovery rate (FDR) was adjusted to < 0.01. The DEPs were identified only if the normalized fold change was higher than 2.0

(upregulated) or less than 0.5 (downregulated). The DEPs were annotated into three categories based on gene ontology (GO) terms, i.e., biological process, cellular component and molecular function. The protein pathway was annotated using the Kyoto Encyclopedia of Genes and Genomes (KEGG) database. The protein domain function was defined by InterProScan based on the protein sequence alignment method (http://www.ebi.ac.uk/interpro/). We used WoLF PSORT (a subcellular localization predication software) to predict subcellular localization. Enrichment analysis was conducted for the GO terms, the KEGG pathway and the protein domain using the Database for Annotation, Visualization and Integrated Discovery. The statistically significant enrichments were identified using Fisher's exact test with Benjamini-Hochberg's corrected P value <0.05. Hierarchical clustering analysis was conducted for the DEPs based on the significant enrichments using the "heatmap.2" function from the "gplots" R package.

3. Results

3.1. Protein identification and comparison

Up to 2723 proteins were identified by proteomics analysis, of which 2500 proteins were quantified in all samples, the mass error of the whole identified peptides and the repeatability of samples are shown in Figs. S2 and S3. A quantitative ratio of higher than 2 was considered to be an upregulation, whereas that less than 0.5 was considered to be a downregulation. All quantifiable proteins with increased (≥2-fold) and decreased (≤0.5-fold) expression levels are listed in Table S1 and S2 (P <0.05).

As shown in Fig. 1A, compared with D120N, 239 DEPs were induced in D120Cr(-), including 63 upregulated proteins, such as the MSHA major pilin subunit MshA, and 176 downregulated proteins, such as the extracellular iron oxide respiratory system outer membrane component MtrB; 509 DEPs were identified from D120Cr(+), including 315 upregulated proteins, such as the FMN-binding heme iron utilization protein HmuZ and the ABC-type hemin uptake system substrate-binding component HmuB, and 194 downregulated proteins, such as the extracellular iron oxide respiratory system outer membrane component MtrB. Compared with D120Cr(-), D120Cr(+) induced 447 DEPs: 397 upregulated expressed proteins and 50 downregulated expressed proteins. The Venn diagrams showed the number of common and unique upregulated/downregulated or all expressed proteins in all cases

(Figs. 1B, C and S4).

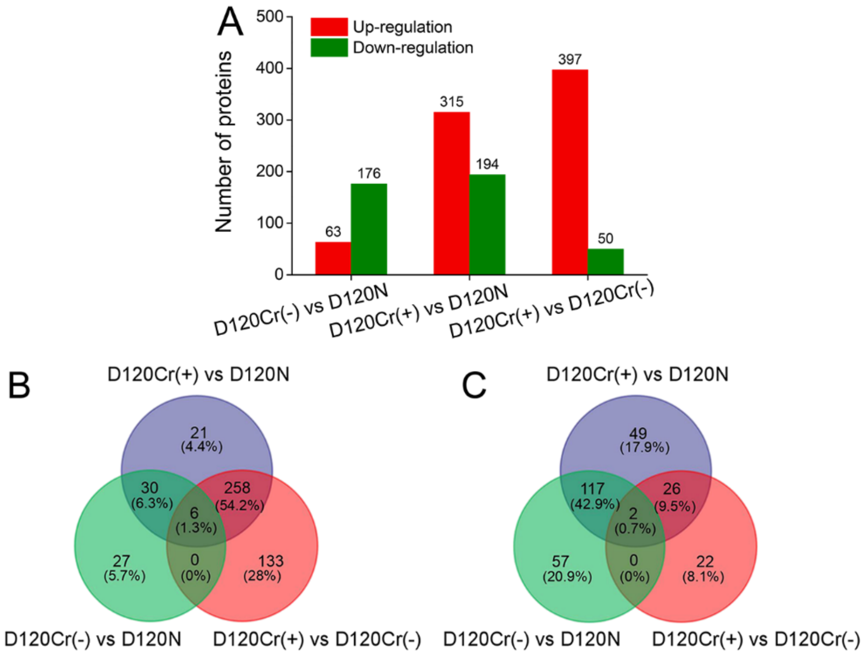


Fig. 1. Number of differentially expressed proteins (A) and Venn diagram showing the common and unique upregulated (B) or downregulated (C) expressed proteins.

3.2. Functional characterization of differentially expressed proteins

These DEPs were classified according to their subcellular location (Fig. 2). For D120Cr(-) versus D120N, 48%, 24% and 14% of DEPs were located in the cytoplasm, periplasmic and outer membrane, respectively. For D120Cr(+) versus D120N, 52% of DEPs were located in the cytoplasm, 27% were located in the periplasmic, and 10% were in the outer membrane. For D120Cr(+) versus D120Cr(-), 54% of DEPs were located in the cytoplasm, 28% were located in the periplasmic, and 8% were located in the outer membrane. The DEPs mainly were located in the cytoplasm, periplasmic and outer membrane in three cases, meaning that Cr(VI) resistance and the reduction of *S. oneidensis* MR-1 were mainly induced by changes in the cytoplasm, periplasmic and outer membrane.

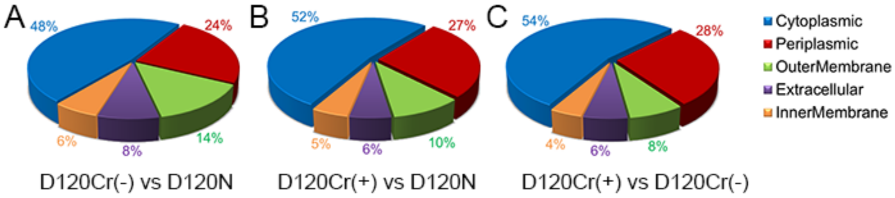


Fig. 2. Subcellular location of differentially expressed proteins.

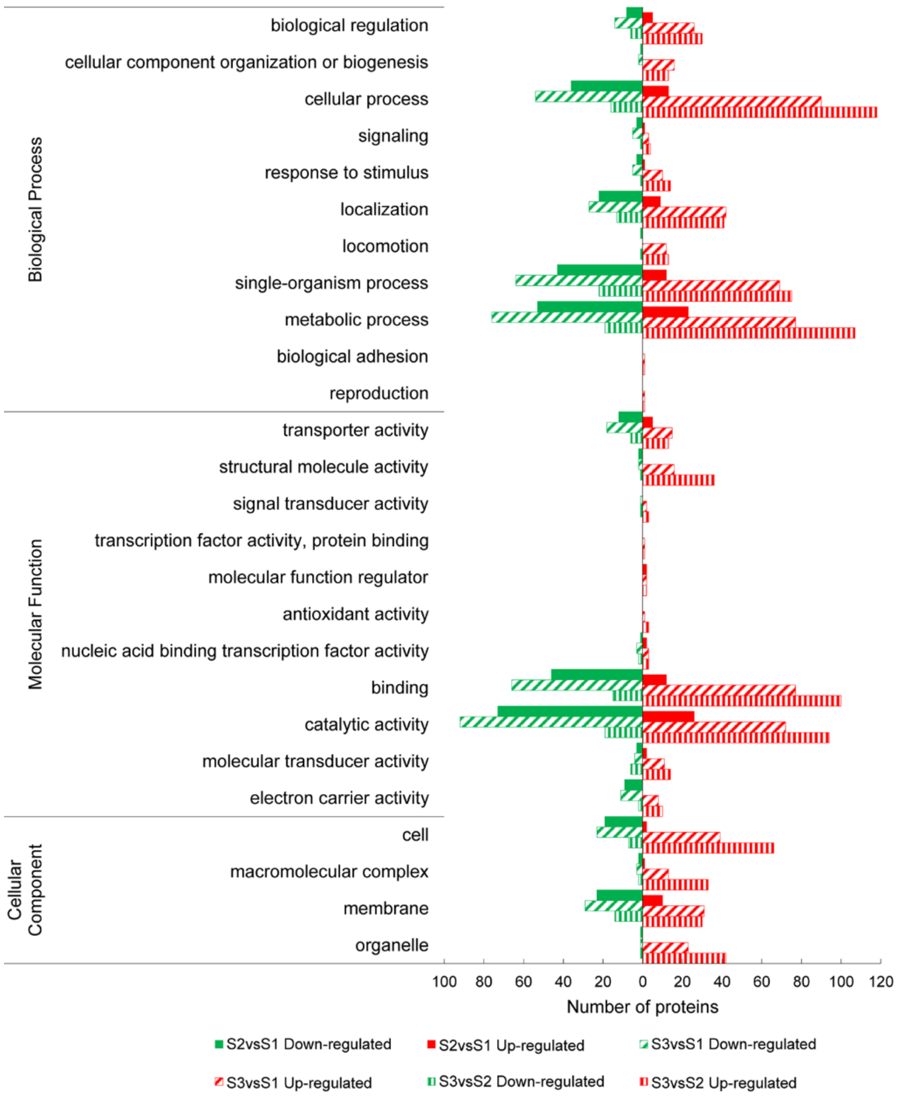


Fig. 3. Functional category distribution of differentially expressed proteins. S1, D120N; S2, D120Cr(-); S3, D120Cr(+).

Based on the GO analysis tool, the biological functions affected by DEPs were classified to the cellular component, molecular function, and biological process. The affected biological functions and the number of proteins in D120Cr(-) and D120N, D120Cr(+) and D120N and in D120Cr(+) and D120Cr(-) were analyzed and compared. The mainly affected biological functions and the amount of related proteins in all comparison groups are summarized in Table 1 and Fig. 3. The results show that these DEPs were mainly involved in the organelle, membrane, cell, catalytic activity, binding, transporter activity, structural molecule activity, metabolic process, single-organism process, localization and cellular process. Almost all DEPs have certain direct or indirect interactions with other proteins in each case (Figs. 4 and S5). Moreover, some proteins associated with streptomycin biosynthesis, beta-lactam resistance, flagellar assembly, and ribosomes were found to be especially highly clustered among the intensive interaction networks (Fig. S6).

Table 1 Gene ontology (GO) distribution of differentially expressed proteins.

GO Terms Level 1	GO Terms Level 2	No. proteins (%)		
		D120Cr(-) vs D120N	D120Cr(+) vs D120N	D120Cr(+) vs D120Cr(-)
Cellular Component	organelle	1 (2%)	24 (15%)	43 (22%)
	membrane	33 (57%)	60 (37%)	44 (23%)
	macromolecular complex	3 (5%)	16 (10%)	35 (18%)
	cell	21 (36%)	62 (38%)	73 (37%)
Molecular Function	catalytic activity	99 (51%)	164 (41%)	113 (34%)
	binding	58 (30%)	143 (35%)	115 (35%)
	structural molecule activity	2 (1%)	18 (4%)	37 (11%)
	transporter activity	17 (9%)	33 (8%)	19 (6%)
Biological Process	metabolic process	76 (32%)	153 (26%)	126 (25%)
	single-organism process	55 (23%)	133 (22%)	97 (20%)
	localization	31 (13%)	69 (12%)	54 (11%)
	cellular process	49 (21%)	144 (24%)	134 (27%)

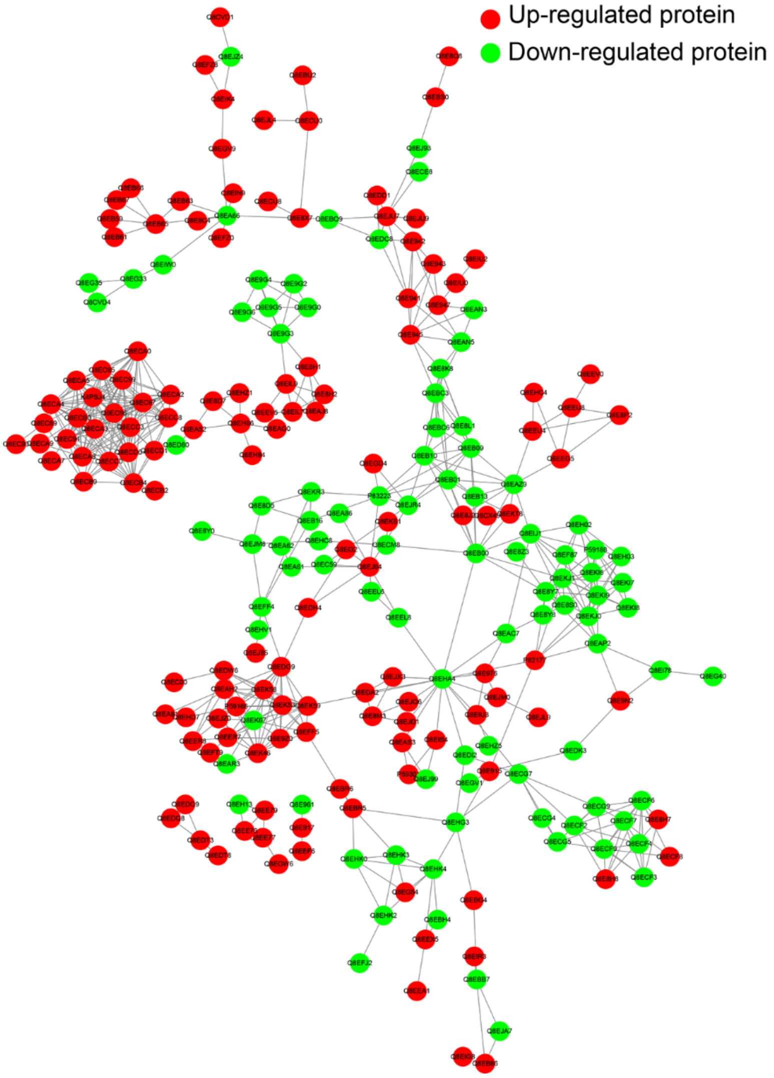


Fig. 4. The protein and protein interaction networks of all differentially expressed proteins in D120Cr(+) vs D120N.

3.3. Functional enrichment of differentially quantified proteins and clustering for protein groups

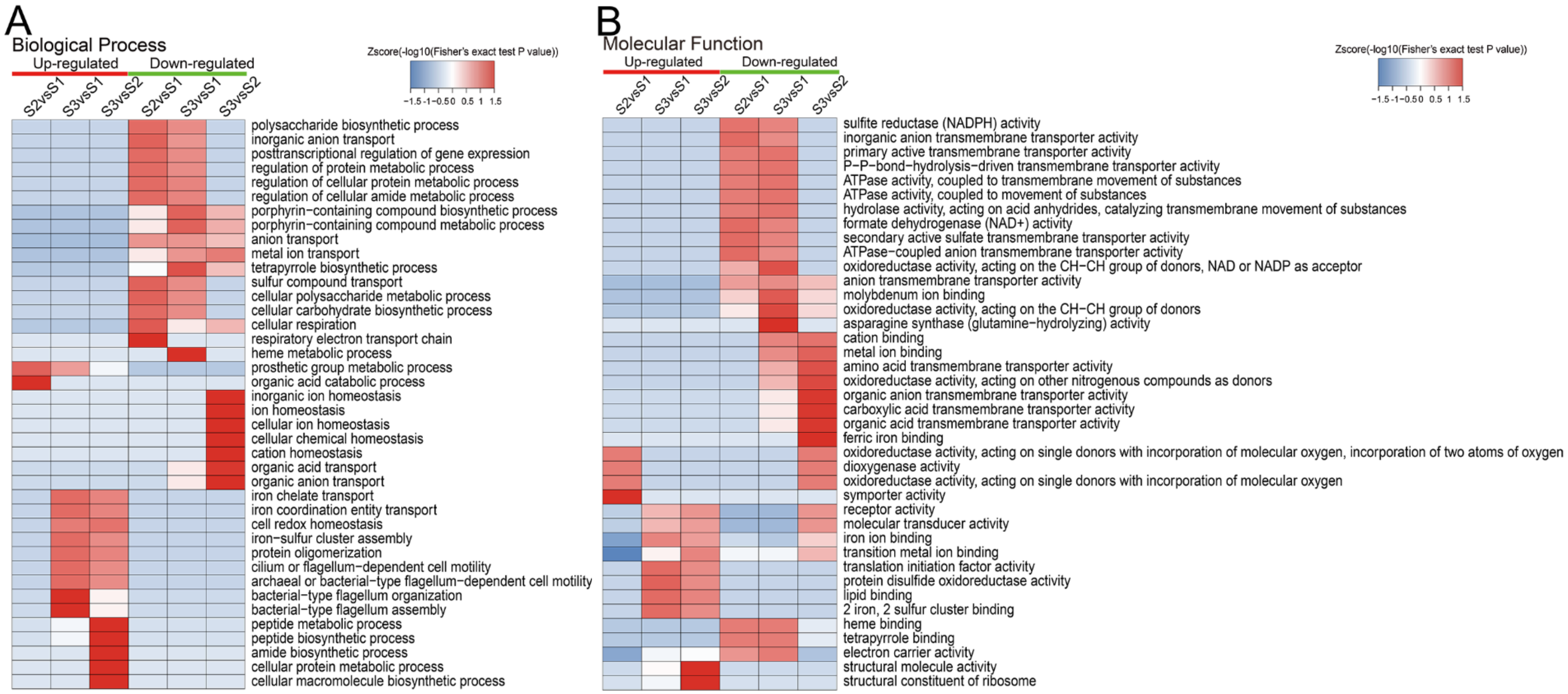
To investigate the functional differences in upregulated and downregulated proteins, the quantified proteins were analyzed separately for GO terms (molecular function, cellular component, and biological process), the protein KEGG pathway and domain enrichment as well as for enrichment-based clustering (Figs. 5, S7, S8 and S9). The proteins were significantly enriched to indicate the nature of the DEPs in each comparison group.

GO enrichment analysis of the DEPs was performed to classify the biological processes, molecular functions, and cellular components in Figs. 5 (A, B and C) and S7. For D120Cr(-) vs. D120N, the 63 upregulated proteins were mainly enriched in oxidoreductase activity (GO:0016702), dioxygenase activity (GO: 0051213), and organic acid catabolic process (GO: 0016054); meanwhile, the 176 downregulated proteins were mainly related to sulfate assimilation (GO: 0000103) and transport (GO: 0006810). For D120Cr(+) vs. D120N, the upregulated proteins were mainly involved in the structural molecule activity (GO: 0005198), 2 iron-2 sulfur cluster binding (GO: 0051537) and cell motility (GO: 0048870); meanwhile the downregulated proteins were mainly significantly enriched in the oxidation-reduction process (GO: 0055114), sulfate assimilation (GO: 0000103) and transport (GO: 0006810). For D120Cr(+) vs. D120Cr(-), the upregulated proteins were mainly associated with structural molecule activity (GO: 0005198), iron ion binding (GO: 0005506), peptide metabolic process (GO: 0006518), translation (GO: 0006412) and cell motility (GO: 0048870); the downregulation proteins were mainly enriched in transport (GO: 0006810), organic acid transport (GO: 0015849) and metal ion homeostasis (GO: 0055065).

The KEGG pathway enrichment results are shown in Figs. 5D and S8. For D120Cr(-) vs. D120N, the upregulated expressed proteins were significantly enriched in beta−lactam resistance (ko01501), cationic antimicrobial peptide (CAMP) resistance (ko01503), phenylalanine metabolism (ko00360) and tyrosine metabolism (ko00350); the downregulated expressed proteins were mainly enriched in sulfur metabolism (ko00920) and ATP-binding cassette (ABC) transporters (ko02010). For D120Cr(+) vs. D120N, the upregulated DEPs were enriched in flagellar assembly (ko02040), CAMP resistance (ko01503), and ribosomes (ko03010); the downregulated DEPs were mainly enriched in sulfur metabolism (ko00920), ABC transporters (ko02010), pyruvate metabolism (ko00620) and the pentose phosphate pathway (ko00030). For D120Cr(+) vs. D120Cr(-), the upregulated DEPs were significantly enriched in ribosome (ko03010) and flagellar assembly (ko02040); the downregulated expressed proteins were mainly enriched in tyrosine metabolism (ko00350) and oxidative phosphorylation (ko00190).

The DEPs in all cases were also examined using protein domain enrichment analysis (Figs. 5E and S9). For D120Cr(-) vs. D120N, the DEPs were mainly enriched in RND efflux pump, membrane fusion protein, barrel-sandwich domain; multidrug efflux transporter AcrB TolC docking domain, DN/DC subdomains; and outer membrane protein OmpA-like, transmembrane domain. For D120Cr(+) vs. D120N, the DEPs were significantly enriched in the flagellar basal body rod protein N−terminal and the TonB-dependent receptor plug domain. For D120Cr(+) vs. D120Cr(-), the DEPs were mainly enriched in the TonB-dependent receptor plug domain, the flagellar basal body rod protein N-terminal, and the TonB-dependent receptor beta-barrel.

The results indicated that the DEPs covered a large range with functions that were categorized into the cellular component, molecular function and biological process. The relevant metabolic pathways were mainly associated with ribosome, flagellar assembly, efflux pump, oxidation resistance, sulfur metabolism, ABC transporters, and energy metabolism. The relevant protein domains were mainly involved in the efflux pump, flagellar, TonB-dependent receptor, and thioredoxin. Furthermore, the enrichment results of upregulation DEPs for D120Cr(+) vs. D120N are similar to that of D120Cr(+) vs. D120Cr(-), while the enrichment results of the downregulated DEPs are similar to that of D120Cr(-) vs. D120N.


A
Biological Process
Up-regulated
Down-regulated
S2vsS1
S3vsS1
S3vsS2
S2vsS1
S3vsS1
S3vsS2
Zscore(-log10(Fisher's exact test P value))
−1.5 −1 −0.5 0 0.5 1 1.5
polysaccharide biosynthetic process
inorganic anion transport
posttranscriptional regulation of gene expression
regulation of protein metabolic process
regulation of cellular protein metabolic process
regulation of cellular amide metabolic process
porphyrin−containing compound biosynthetic process
porphyrin−containing compound metabolic process
anion transport
metal ion transport
tetrapyrrole biosynthetic process
sulfur compound transport
cellular polysaccharide metabolic process
cellular carbohydrate biosynthetic process
cellular respiration
respiratory electron transport chain
heme metabolic process
prosthetic group metabolic process
organic acid catabolic process
inorganic ion homeostasis
ion homeostasis
cellular ion homeostasis
cellular chemical homeostasis
cation homeostasis
organic acid transport
organic anion transport
iron chelate transport
iron coordination entity transport
cell redox homeostasis
iron−sulfur cluster assembly
protein oligomerization
cilium or flagellum−dependent cell motility
archaeal or bacterial−type flagellum−dependent cell motility
bacterial−type flagellum organization
bacterial−type flagellum assembly
peptide metabolic process
peptide biosynthetic process
amide biosynthetic process
cellular protein metabolic process
cellular macromolecule biosynthetic process
B
Molecular Function
Up-regulated
Down-regulated
S2vsS1
S3vsS1
S3vsS2
S2vsS1
S3vsS1
S3vsS2
Zscore(-log10(Fisher's exact test P value))
−1.5 −1 −0.5 0 0.5 1 1.5
sulfite reductase (NADPH) activity
inorganic anion transmembrane transporter activity
primary active transmembrane transporter activity
P−P−bond−hydrolysis−driven transmembrane transporter activity
ATPase activity, coupled to transmembrane movement of substances
ATPase activity, coupled to movement of substances
hydrolase activity, acting on acid anhydrides, catalyzing transmembrane movement of substances
formate dehydrogenase (NAD+) activity
secondary active sulfate transmembrane transporter activity
ATPase−coupled anion transmembrane transporter activity
oxidoreductase activity, acting on the CH−CH group of donors, NAD or NADP as acceptor
anion transmembrane transporter activity
molybdenum ion binding
oxidoreductase activity, acting on the CH−CH group of donors
asparagine synthase (glutamine−hydrolyzing) activity
cation binding
metal ion binding
amino acid transmembrane transporter activity
oxidoreductase activity, acting on other nitrogenous compounds as donors
organic anion transmembrane transporter activity
carboxylic acid transmembrane transporter activity
organic acid transmembrane transporter activity
ferric iron binding
oxidoreductase activity, acting on single donors with incorporation of molecular oxygen, incorporation of two atoms of oxygen
dioxygenase activity
oxidoreductase activity, acting on single donors with incorporation of molecular oxygen
symporter activity
receptor activity
molecular transducer activity
iron ion binding
transition metal ion binding
translation initiation factor activity
protein disulfide oxidoreductase activity
lipid binding
2 iron, 2 sulfur cluster binding
heme binding
tetrapyrrole binding
electron carrier activity
structural molecule activity
structural constituent of ribosome

1

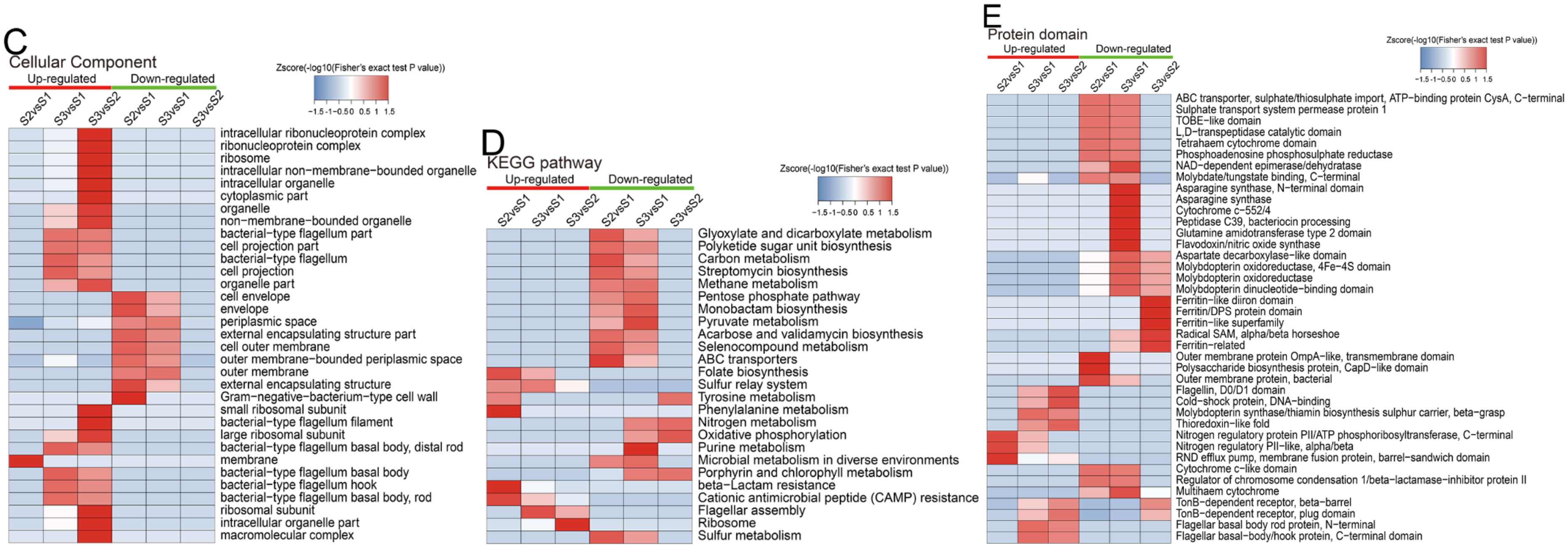


Fig. 5. Hierarchical clustering analysis was conducted for the differentially expressed proteins according to biological process (A), cellular component (B), molecular function (C), protein domain (D) and KEGG pathway (E) -based enrichment. The *P* values were transformed into Z-scores for hierarchical clustering analysis. The Z-score is shown in the color legend, and the red color represents significant enrichments. S1, D120N; S2, D120Cr(-); S2, D120Cr(+).

4 Discussion

4.1. Proteome responses to long-term acclimatization under Cr(VI) stress

After a 120-day acclimatization in media with an increasing Cr(VI) concentration, the reduction and resistance capacities of *S. oneidensis* MR-1 to Cr(VI) have been apparently improved (Fig. S10). We investigated the reduction and resistance mechanisms of MR-1 after long-term Cr(VI) exposure at the proteome level by the DEPs for D120Cr(+) versus D120N. The results showed that the long-term Cr(VI) exposure has a remarkable effect on many important biological processes, but proteome could be regulated in response to environmental stress, to some extent.

In contrast to D120N, the abundance of proteins related to structural molecule activity and cell motility, such as the 50S ribosomal protein L31 RpmE, the 30S ribosomal protein S21 RpsU, the flagellar hook-associated protein FlgL, the flagellar hook-filament junction protein FlgK, and flagellin FliC, were dramatically increased in D120Cr(+). These proteins, which involve the structural molecule activity, contribute to the structural integrity of a complex or its assembly within or outside a cell, especially ribosome. Moreover, the KEGG pathway showed that ribosome at significant enrichment level was the important pathway. Flagellar motility is very important to allow bacteria to move toward favorable conditions, form biofilms and acquire nutrients (Qin et al., 2011). Wang et al. (Wang et al., 2015) found that the flagellar assembly pathway was sensitive to environmental stresses. *S. oneidensis* MR-1 could be benefit-tending and harm-avoiding through the flagellum and motility under long-term Cr(VI) stress. The morphology analysis results also showed that microorganisms tended to aggregate together and occurred in abnormal cell morphologies under Cr(VI) exposure (Fig. S11).

We observed that the thioredoxin-like fold, thioredoxin and glutaredoxin domains involved in the oxidative stress response were increased. When chromate enters a bacterial cell, it leads to the generation of reactive oxygen species and may damage many cellular components (e.g., DNA and proteins) (Cervantes et al., 2001; Singh et al., 1998). And and Storz (And and Storz, 2000) proposed that the thioredoxin-dependent reduction systems that were found to be responsible for maintaining the reduction environment of the *Escherichia coli* and *Saccharomyces cerevisiae* cytosol acts as a defense against oxidative stress.

S. oneidensis MR-1 genes/proteins with functions in iron acquisition and homeostasis were up-regulation under acute chromate exposure (Brown et al., 2006; Thompson et al., 2007). Hu et al. (Hu et al., 2005) also observed similar results in *Caulobacter crescentus*. Similarly, our result is consistent with the fact that five domains in connection with iron transport and homeostasis were significantly enriched with upregulated proteins for adapting to the chromate stress environment, namely, the TonB-dependent receptor plug domain, the TonB-dependent receptor beta-barrel, the ferric iron reductase FhuF domain, FeS cluster biogenesis, and the 2Fe-2S ferredoxin-type iron-sulfur binding domain. The TonB-dependent hemoglobin/transferrin/lactoferrin family receptor plays an important role in the cellular adaptation of *Pseudomonas putida* F1 to chromate stress (Thompson et al., 2010). More similar results were reported, *tonB* mutants of *E. coli* K-12 was sensitive to chromium salt, which could be relieved by adding iron to the growth medium (Pugsley and Reeves, 1976; Wang and Newton, 1969). *Pseudomonas stutzeri* KC siderophore pyridine-2,6-bis(thiocarboxylic acid) (pdtc) has been shown to reduce and precipitate Cr(VI), suggesting that a novel role of pdtc was detoxification of extracellular metal toxicity (Zawadzka et al., 2007).

Cr(VI) enters the cells through the sulfate transport system because of the structural similarity of chromate (CrO_4^{2-}) and sulfate(SO_4^{2-}) (Cervantes et al., 2001; Cheung et al., 2006; Nies et al., 1989). Chromate as a competitive inhibitor of sulfate uptake results in low intracellular levels of sulfur (Ohtake et al., 1987). As was expected, the downregulated proteins related to sulfate assimilation and the sulfur metabolism process were significantly enriched in D120Cr(+) in our study. It is a protection strategy that could prevent cells from chromate damage by reducing the absorption to Cr(VI). We have observed that these upregulated proteins that are involved in the sulfur relay system were markedly enriched in D120Cr(+). It may be a compensation mechanism for sulfur absorption to keep enough of the sulfur element for cellular metabolism and normal physiological activities. Thompson et al. (Thompson et al., 2010) found that the increased uptake of cysteine and cysteine-containing compounds could compensate for the reduced sulfate uptake by other optional transporter systems. In addition, the KEGG pathway showed that CAMP resistance related to the efflux pump at a significant enrichment level was an important pathway for reducing intracellular Cr(VI).

Meanwhile, these downregulated proteins that are associated with pyruvate metabolism and the pentose phosphate pathway were significantly enriched in D120Cr(+); for example, the fumarate reductase FAD-binding subunit FrdA, acetyl-coenzyme A synthetase, the NAD-dependent malic enzyme, D-xylulose 5-phosphate/D-fructose 6-phosphate phosphoketolase Xfp, phosphopentomutase, deoxyribose-phosphate aldolase, and so on. As a consequence, pyruvate metabolism and the pentose phosphate pathway were inhibited in long-term Cr(VI)-treated *S. oneidensis* MR-1, which may be one of the Cr(VI) toxicity mechanisms, and pyruvate and the pentose phosphate pathway may be an important target of Cr(VI) toxicity. Wang et al. (Wang et al., 2014) previously reported that Cr(VI) exposure decreased the abundance of proteins that is involved in pyruvate metabolism.

ABC transporters are transmembrane proteins that utilize energy to carry substrates into the cells (Bulut et al., 2012). Our result showed that these proteins related to ABC transporters were decreased and were significantly enriched in D120Cr(+), including the ABC-type sulfate/thiosulfate uptake system substrate-binding subunit Sbp, sulfate/thiosulfate import ATP-binding protein CysA1, sulfate/thiosulfate import ATP-binding protein CysA2, ABC-type sulfate/thiosulfate uptake system substrate-binding component CysP, molybdenum import ATP-binding protein ModC, ABC-type molybdate uptake system substrate-binding component ModA, etc. Karpus et al. revealed that the *E. coli* molybdate-binding protein ModA could bind chromate tightly and was capable of removing chromate (Karpus et al., 2017). These results suggested that the organism could defend Cr(VI) stress by reducing sulfate uptake, and Cr(VI) toxicity has a serious effect on the molybdate transport of MR-1 under long-term Cr(VI) stress.

In summary, D120Cr(+) could better reduce and tolerate long-term Cr(VI) stress in the following aspects: (1) to enhance cell motility and structural integrity, particularly ribosome and flagellar; (2) to promote the oxidative stress response by the thioredoxin-dependent reduction systems; (3) to maintain iron acquisition and homeostasis for adapting to the chromate stress environment; (4) to enhance efflux by CAMP resistance, and to decrease Cr(VI) uptake by changing sulfate transport system and ABC transporters; (5) to increase the sulfur relay system as a compensation mechanism for sulfur absorption; (6) to weaken energy metabolism, mainly in pyruvate metabolism and the pentose phosphate pathway.

4.2. The permanent effect under long-term Cr(VI) pressure

We could find the permanent changes of MR-1 proteome under long-term Cr(VI) pressure based on the DEPs for D120Cr(-) versus D120N. In the absence of Cr(VI), the D120Cr(-) proteome still had striking changes in some respects; specifically, the efflux pump, amino acid catabolic/metabolic process, dioxygenase activity, oxidoreductase activity, sulfate uptake and reduction, and transport, etc.

Compared with D120N, two key proteins with the function in antioxidant activity have upregulated expressions, namely, homogentisate 1,2-dioxygenase HmgA and 4-hydroxyphenylpyruvate dioxygenase HppD. One of the strategies for detoxifying chromate toxicity is to rapidly extrude it by using the chromate efflux pump from the cytoplasm (Baaziz et al., 2017). These upregulated proteins that are associated with the efflux pump are significantly enriched in beta-lactam resistance, CAMP resistance, the RND efflux pump, the membrane fusion protein, the barrel-sandwich domain and the multidrug efflux transporter AcrB TolC docking domain, and DN/DC subdomains. Specifically, the RND-type multidrug/detergent efflux system MFP component VexB, the RND-type multidrug/detergent efflux system permease component VexA, the efflux pump membrane transporter VmeB, and the proton-coupled multidrug efflux pump MFP component VmeA. Those proteins related to the amino acid catabolic/metabolic processes are also upregulated in D120Cr(-), which could supply more energy for hexavalent chromium reduction and cell growth. It is noteworthy that the phenylalanine metabolic process and tyrosine metabolism are closely related to the synthesis of important neurotransmitters and hormones.

The main biological functions of downregulated proteins for D120Cr(-) versus D120N are similar to that of D120Cr(+) versus D120N, specifically, in transport, sulfur metabolism, and so on. It was indicated that the long-term Cr(VI) treatment could bring about more repressed changes in the above respects, which are permanent in spite of the loss of Cr(VI) stress.

4.3. The proteome responses to short-term Cr(VI) stimulus

Based on the DEPs for D120Cr(+) versus D120Cr(-), we discovered the proteome responses of D120Cr to short-term Cr(VI) stimulus. The enrichment results of the upregulated proteins are similar to that of D120Cr(+) versus D120N, which demonstrates once more that the cellular motility, iron ions and the Fe-S cluster, ribosomes and translation, and antioxidant activity are key factors in the immediate response to Cr(VI) stress. These functions and processes, which are related to the iron ion and the Fe-S cluster, were enhanced, which may be a compensation mechanism for iron ion absorption and Fe-S cluster formation to defend against Cr(VI) stress. The abundance of proteins involved in ribosomes and translation were increased due to Cr(VI) stress. These ribosome-relevant proteins take part in the translation, protein metabolism and RNA process. As a consequence, more proteins are synthesized to maintain the cellular structure and function, to repair damaged proteins and to produce new proteins against Cr(VI) stress. The GO enrichment analysis showed that peptide biosynthetic and metabolic process at significant enrichment levels were enriched by up-regulated proteins. It seems to that the short-term Cr(VI) stimulus is more likely to give rise to the upregulated expression of proteins in the above respects.

Wang et al.(Wang et al., 2017) observed that Hg treatment inhibited transition metal binding, iron ion homeostasis and cellular homeostasis. Our study found that both transport and cellular homeostasis were inhibited and significantly enriched with a majority of downregulated DEPs in D120Cr(+). Specifically, organic acid transport, organic anion transport, iron ion transport and homeostasis, and transition metal ion transport homeostasis were inhibited. Two bacterioferritins coded by *brf1* and *brf2*, respectively, were common in all homeostasis processes. It was found that these domains, including the ferritin-like diiron domain, the ferritin/DPS protein domain, the ferritin-like superfamily and the TonB-dependent receptor plug domain, etc., were enriched with downregulated proteins. Hence, it is likely that ferritin is an important target of Cr(VI) toxicity. As previously reported, ferritin exists ubiquitously among living microorganisms; as an iron storage and release protein, it is an important intracellular protein that plays a part in iron metabolism, immune defense, stress response, and so on (Aguilera et al., 2016; Wang et al., 2017). In addition, the inhibition of the transmembrane transporter activity inevitably impacts homeostasis.

Furthermore, two other important pathways were also inhibited; namely, tyrosine metabolism and oxidative phosphorylation. Reactive oxygen species can interact with numerous targets in a microbial cell, including thiols, metal centers, protein tyrosines, nucleotide bases and lipids (Fang, 2004). Moreover, cells could need less ATP to maintain a normal metabolism process under Cr(VI) stress. Therefore, the remarkable depression of those processes suggested that Cr(VI) toxicity leads to dysfunction in the transport and homeostasis of D120Cr(+) due to the damage of several crucial proteins and enzymes.

5. Conclusion

Our study investigated the molecular mechanisms for reduction and resistance of *S. oneidensis* MR-1 under long-term exposure to Cr(VI) by proteomics analysis. In reality, the proteomic changes of *S. oneidensis* MR-1 effected by long-term Cr(VI) acclimatization can be considered to be derived from two aspects: long-term natural growth and Cr(VI) stress. The reduction capacity of *S. oneidensis* MR-1 to Cr(VI) was enhanced mainly in electron transport systems and energy metabolism. The resistance capacity to Cr(VI) was promoted mainly in cellular motility, efflux systems, sulfate transport, sulfur metabolism, oxidative stress protection, and energy metabolism. We summarized the proteins or pathways involved in the Cr(VI) reduction and resistance in bacterial cells (Fig. 6). The Cr(VI) reduction was carried out by intracellular and extracellular reduction. The Cr(VI) resistance was mainly in uptake, efflux, antioxidant and repair systems. The findings will further shed light on the molecular mechanisms for resistance and reduction in MR-1 under long-term Cr(VI) exposure at the proteomic level, which could help us to make effective bioremediation and environmental risk assessments through long-term acclimatization. Further studies can be conducted for Cr(VI) bioremediation: (1) to investigate deeply certain key proteins/genes and their interaction networks; (2) to optimize or develop environmental microbial technologies, e.g. strain modification and the change of domestication strategy; (3) to prevent and control the harmful microorganisms from Cr(VI)-contaminated environments.

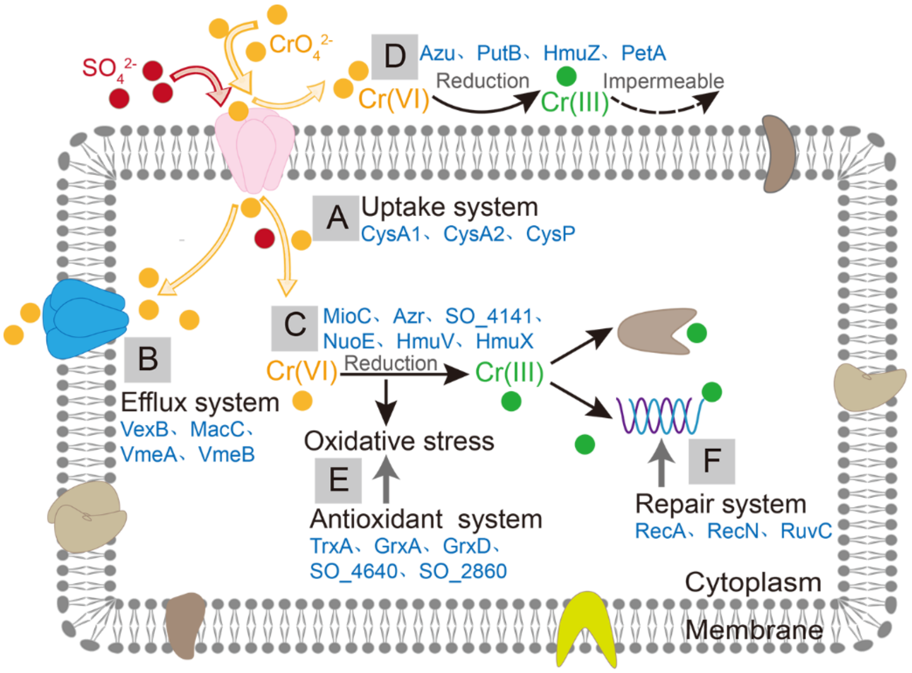


Fig. 6. Mechanisms of chromate resistance and reduction in *S. oneidensis* MR-1 cells. (A) sulfate uptake pathway which is also used by chromate. (B) Efflux of chromate from the cytoplasm. (C) Intracellular reduction of Cr(VI) by chromate reductases. (D) Extracellular reduction of Cr(VI) to Cr(III). (E) Detoxifying enzymes are involved in protection against oxidative stress. (F) DNA repair systems participate in the protection from the damage.

Acknowledgements

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Supporting Information

Proteomic Analysis of the Reduction and Resistance Mechanisms of *Shewanella oneidensis* MR-1 under Long-term Hexavalent Chromium Stress

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The Supporting Information includes Supplemental Materials, 11 figures and 2 tables as following:

Supplemental Materials

Fig. S1. The growth curves of the tested strains.

Fig. S2. The mass error of the whole identified peptides.

Fig. S3. The repeatability of samples. S1, D120N; S2, D120Cr(-); S2, D120Cr(+).

Fig. S4. Venn diagram showing common and unique differentially expressed proteins.

Fig. S5. The protein and protein interaction networks of all differentially expressed proteins in D120Cr(-) vs D120N (A) and D120Cr(+) vs D120Cr(-) (B).

Fig. S6. Clustering interaction network of upregulated (red) and downregulated (green) proteins in three cases. A and B, D120Cr(-) vs D120N; C and D, D120Cr(+) vs D120N; E and F, D120Cr(+) vs D120Cr(-).

Fig. S7. GO-based enrichment analysis of up-regulation (red) and down-regulation (green) expressed proteins. A and B, D120Cr(-) vs D120N; C and D, D120Cr(+) vs D120N; E and F, D120Cr(+) vs D120Cr(-).

Fig. S8. KEGG-based enrichment analysis of up-regulation (red) and down-regulation (green) expressed proteins. A and B, D120Cr(-) vs D120N; C and D, D120Cr(+) vs D120N; E and F, D120Cr(+) vs D120Cr(-).

Fig. S9. Protein domain-based enrichment analysis of up-regulation (red) and down-regulation (green) expressed proteins. A and B, D120Cr(-) vs D120N; C and D, D120Cr(+) vs D120N; E and F, D120Cr(+) vs D120Cr(-).

Fig. S10. The changes of total Cr, Cr(VI) and Cr(III) concentrations. (a), (b) and (c) represent 100 mg/L, 200 mg/L and 300 mg/L initial Cr(VI) concentrations, respectively.

Fig. S11. The scanning electron microscope (SEM) images of the tested strains.

Table S1 All the identified quantifiable upregulated proteins.

Table S2 All the identified quantifiable downregulated proteins.

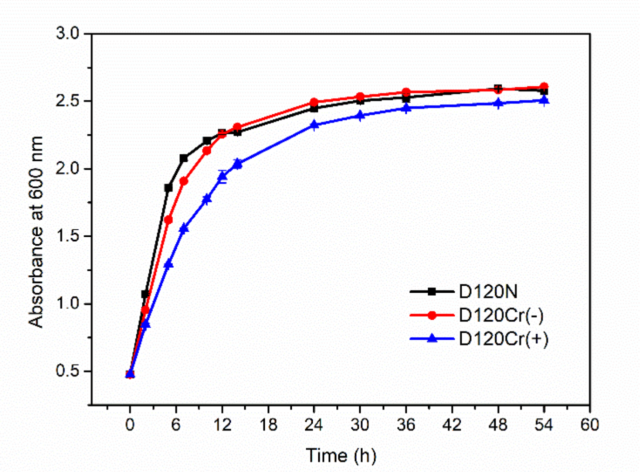


Fig. S1. The growth curves of the tested strains.

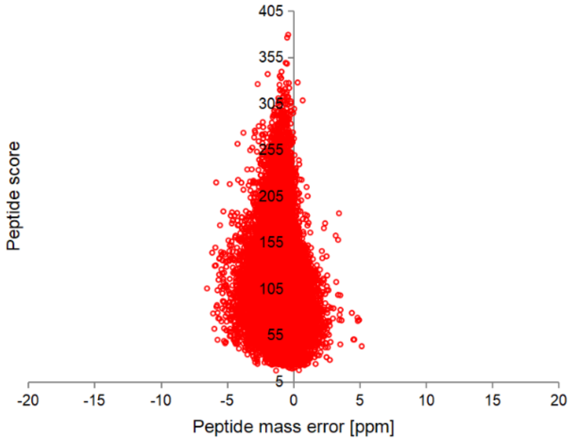
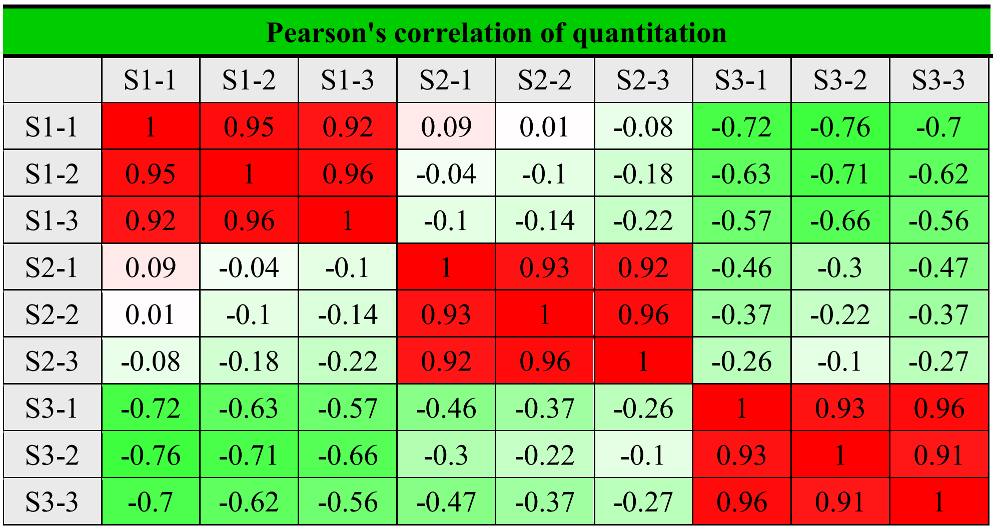


Fig. S2. The mass error of the whole identified peptides.



Pearson's correlation of quantitation

	S1-1	S1-2	S1-3	S2-1	S2-2	S2-3	S3-1	S3-2	S3-3
S1-1	1	0.95	0.92	0.09	0.01	-0.08	-0.72	-0.76	-0.7
S1-2	0.95	1	0.96	-0.04	-0.1	-0.18	-0.63	-0.71	-0.62
S1-3	0.92	0.96	1	-0.1	-0.14	-0.22	-0.57	-0.66	-0.56
S2-1	0.09	-0.04	-0.1	1	0.93	0.92	-0.46	-0.3	-0.47
S2-2	0.01	-0.1	-0.14	0.93	1	0.96	-0.37	-0.22	-0.37
S2-3	-0.08	-0.18	-0.22	0.92	0.96	1	-0.26	-0.1	-0.27
S3-1	-0.72	-0.63	-0.57	-0.46	-0.37	-0.26	1	0.93	0.96
S3-2	-0.76	-0.71	-0.66	-0.3	-0.22	-0.1	0.93	1	0.91
S3-3	-0.7	-0.62	-0.56	-0.47	-0.37	-0.27	0.96	0.91	1

Fig. S3. The repeatability of samples. S1, D120N; S2, D120Cr(-); S2, D120Cr(+).

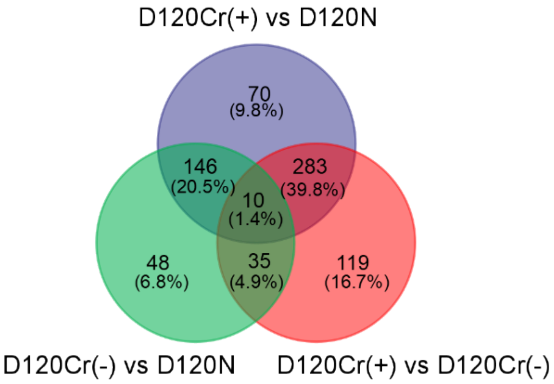
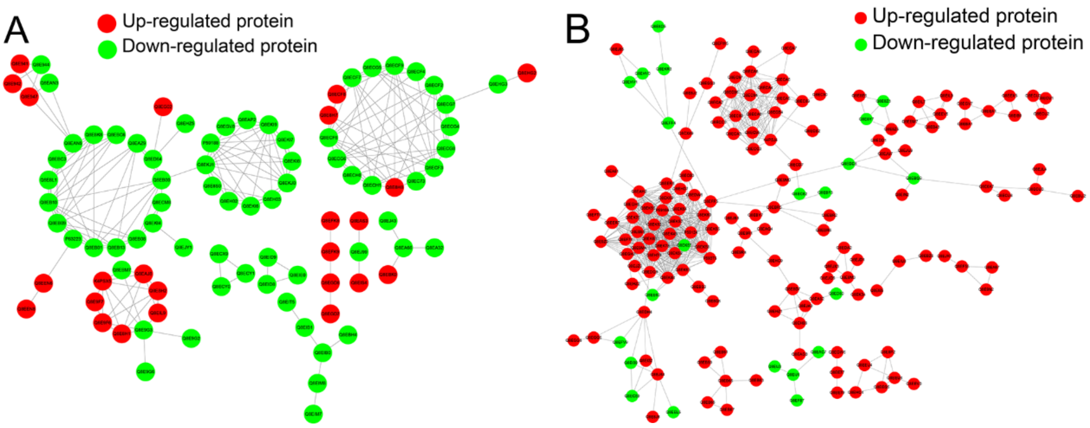


Fig. S4. Venn diagram showing common and unique differentially expressed proteins.



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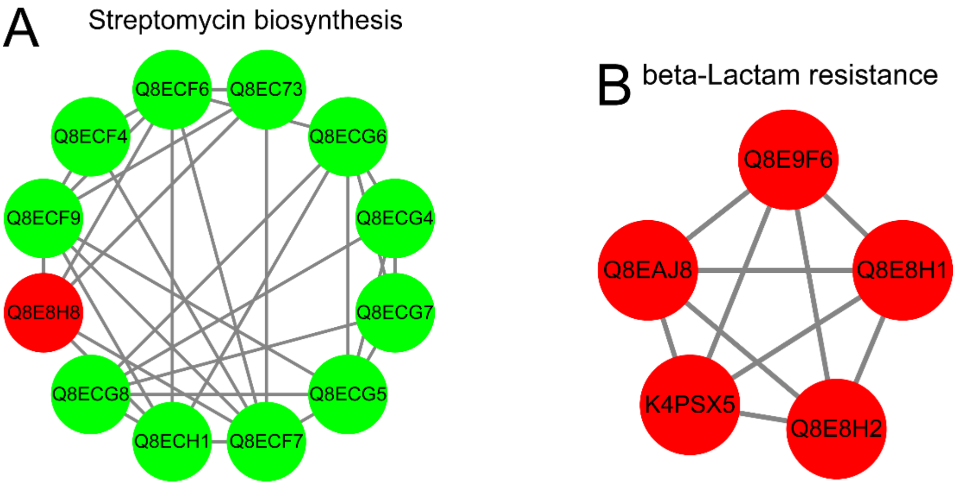


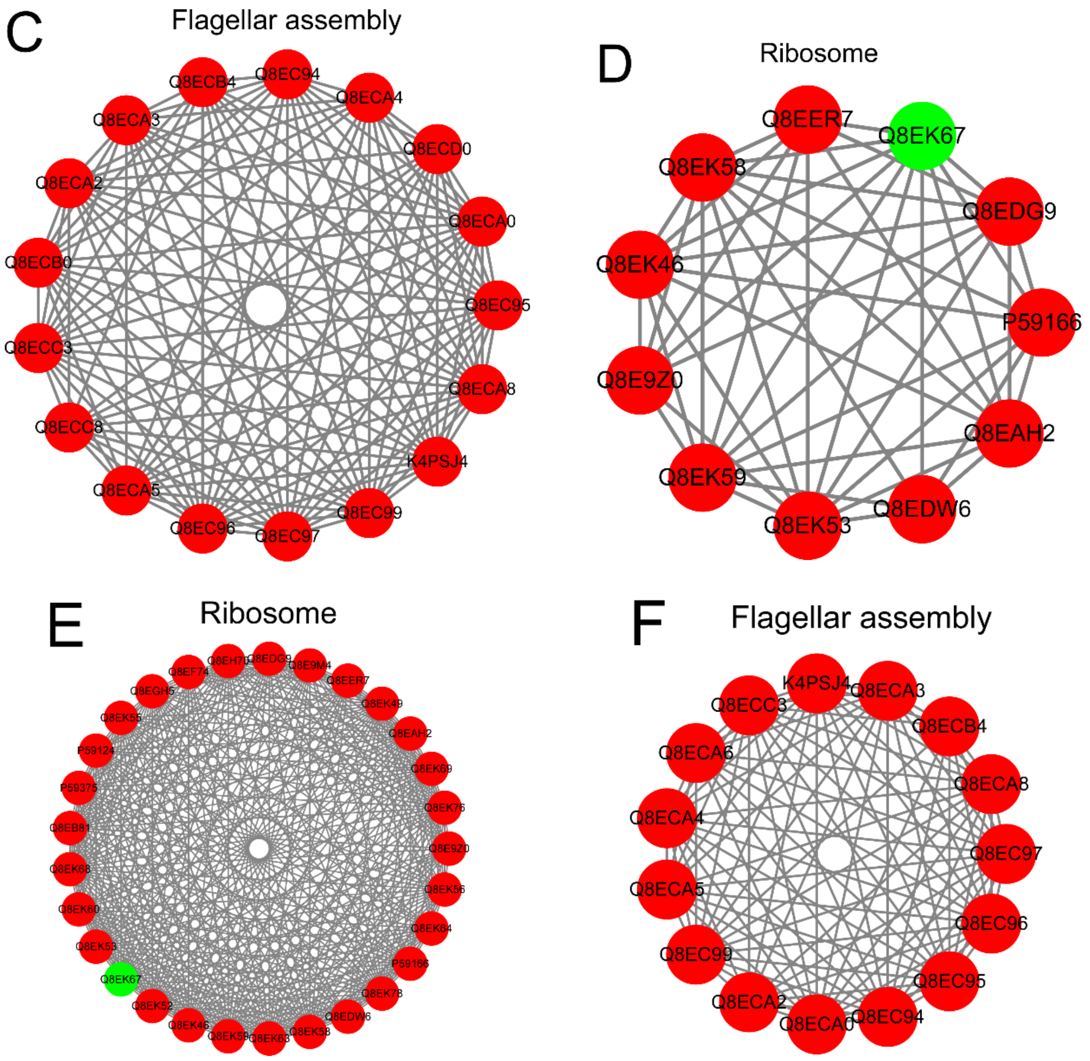
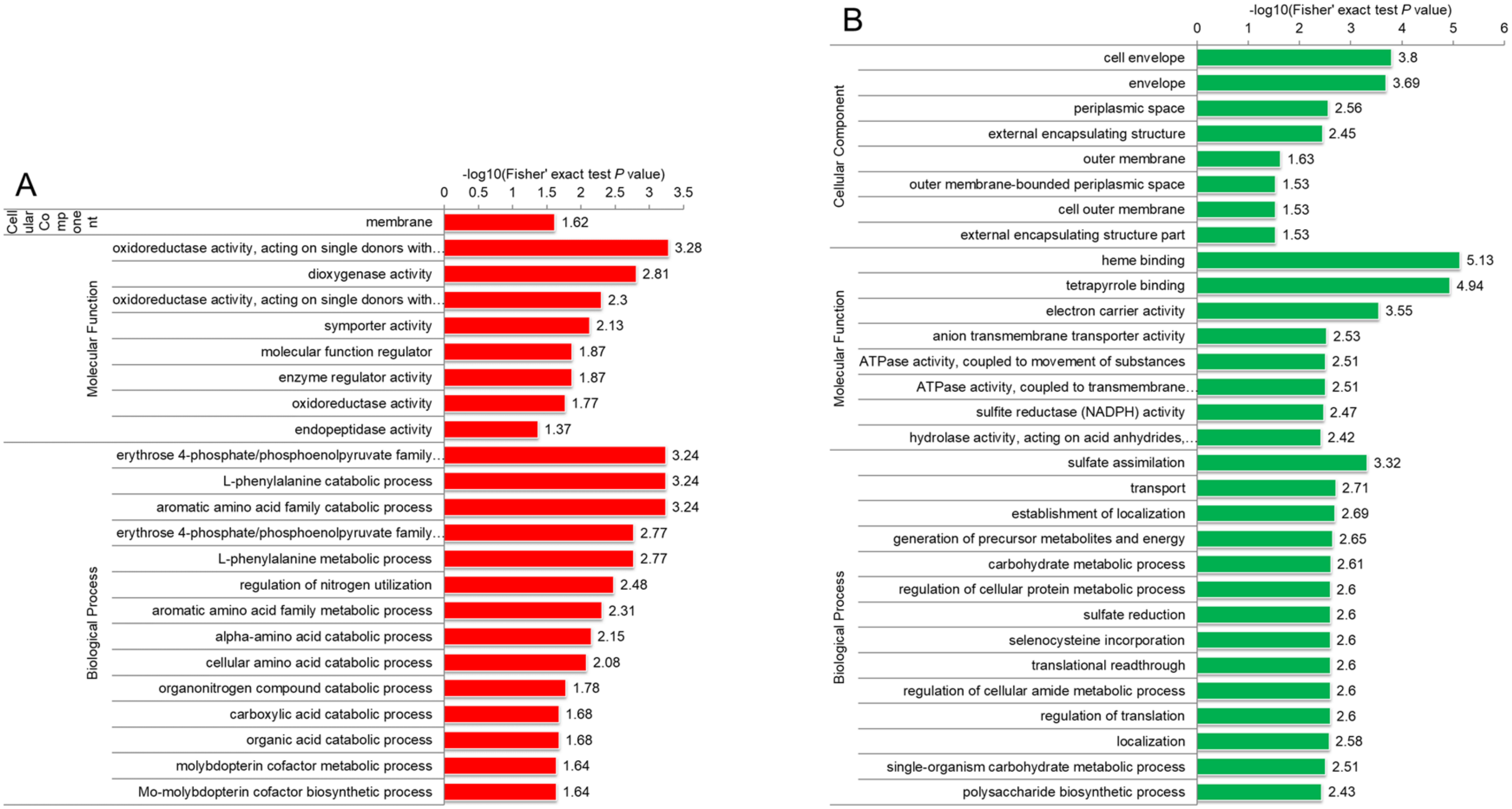
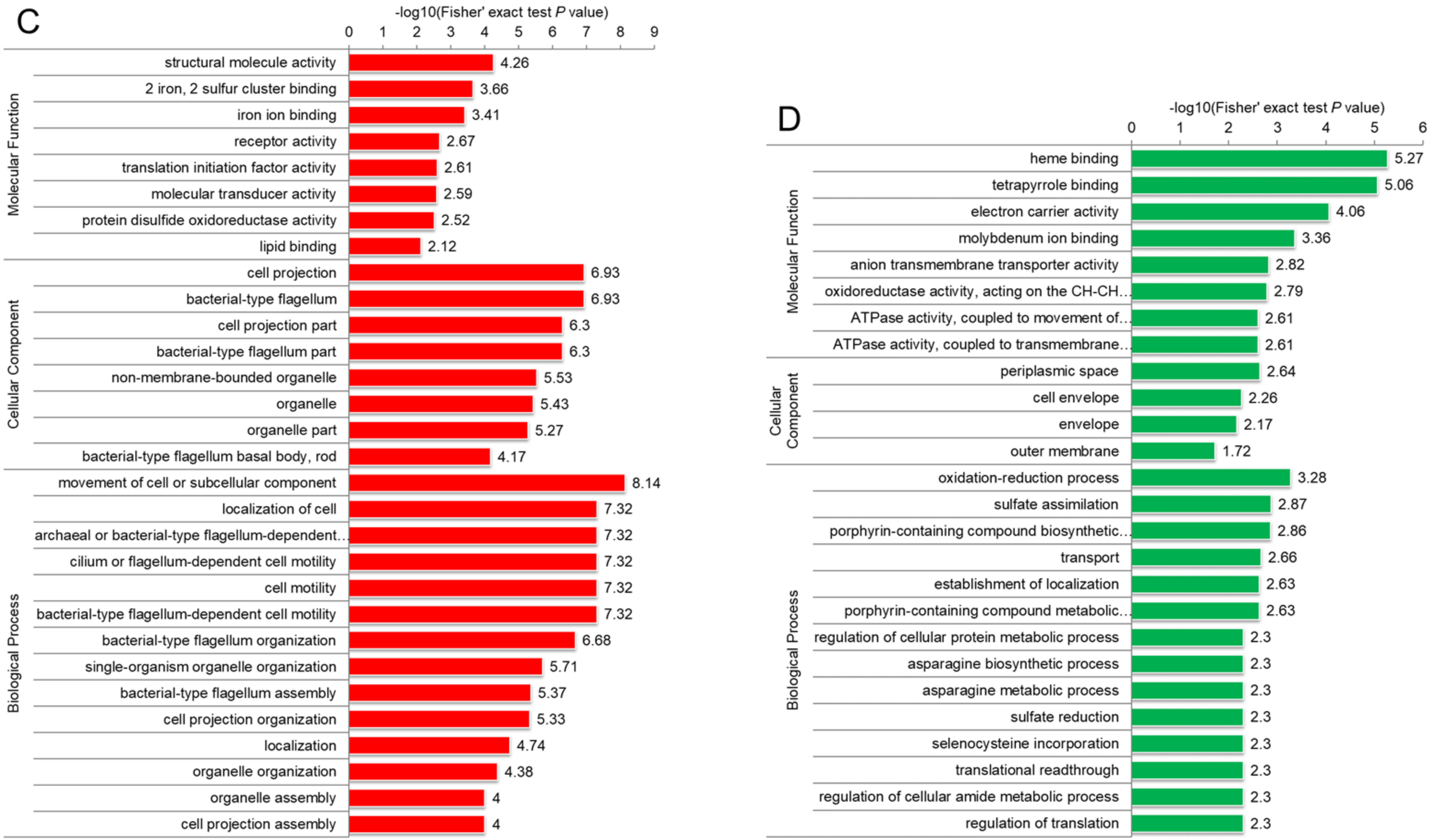
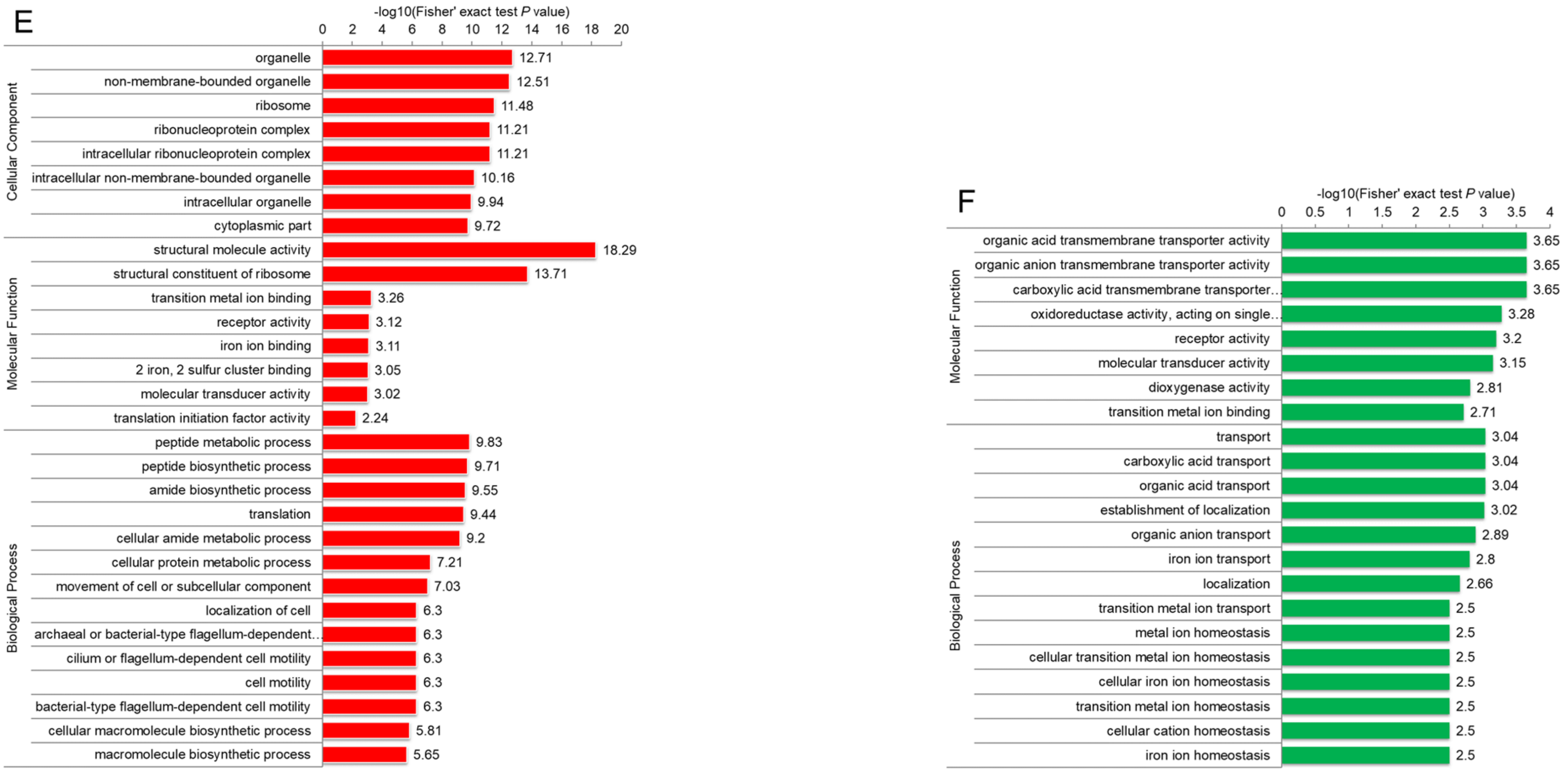


Fig. S6. Clustering interaction network of upregulated (red) and downregulated (green) proteins in three cases. A and B, D120Cr(-) vs D120N; C and D, D120Cr(+) vs D120N; E and F, D120Cr(+) vs D120Cr(-).


A
-log10(Fisher' exact test P value)
0
0.5
1
1.5
2
2.5
3
3.5
Cellular Component
membrane 1.62
Molecular Function
oxidoreductase activity, acting on single donors with… 3.28
dioxygenase activity 2.81
oxidoreductase activity, acting on single donors with… 2.3
symporter activity 2.13
molecular function regulator 1.87
enzyme regulator activity 1.87
oxidoreductase activity 1.77
endopeptidase activity 1.37
Biological Process
erythrose 4-phosphate/phosphoenolpyruvate family… 3.24
L-phenylalanine catabolic process 3.24
aromatic amino acid family catabolic process 3.24
erythrose 4-phosphate/phosphoenolpyruvate family… 2.77
L-phenylalanine metabolic process 2.77
regulation of nitrogen utilization 2.48
aromatic amino acid family metabolic process 2.31
alpha-amino acid catabolic process 2.15
cellular amino acid catabolic process 2.08
organonitrogen compound catabolic process 1.78
carboxylic acid catabolic process 1.68
organic acid catabolic process 1.68
molybdopterin cofactor metabolic process 1.64
Mo-molybdopterin cofactor biosynthetic process 1.64
B
-log10(Fisher' exact test P value)
0
1
2
3
4
5
6
Cellular Component
cell envelope 3.8
envelope 3.69
periplasmic space 2.56
external encapsulating structure 2.45
outer membrane 1.63
outer membrane-bounded periplasmic space 1.53
cell outer membrane 1.53
external encapsulating structure part 1.53
Molecular Function
heme binding 5.13
tetrapyrrole binding 4.94
electron carrier activity 3.55
anion transmembrane transporter activity 2.53
ATPase activity, coupled to movement of substances 2.51
ATPase activity, coupled to transmembrane… 2.51
sulfite reductase (NADPH) activity 2.47
hydrolase activity, acting on acid anhydrides,… 2.42
Biological Process
sulfate assimilation 3.32
transport 2.71
establishment of localization 2.69
generation of precursor metabolites and energy 2.65
carbohydrate metabolic process 2.61
regulation of cellular protein metabolic process 2.6
sulfate reduction 2.6
selenocysteine incorporation 2.6
translational readthrough 2.6
regulation of cellular amide metabolic process 2.6
regulation of translation 2.6
localization 2.58
single-organism carbohydrate metabolic process 2.51
polysaccharide biosynthetic process 2.43


C
-log10(Fisher' exact test P value)
0 1 2 3 4 5 6 7 8 9
Molecular Function
structural molecule activity 4.26
2 iron, 2 sulfur cluster binding 3.66
iron ion binding 3.41
receptor activity 2.67
translation initiation factor activity 2.61
molecular transducer activity 2.59
protein disulfide oxidoreductase activity 2.52
lipid binding 2.12
Cellular Component
cell projection 6.93
bacterial-type flagellum 6.93
cell projection part 6.3
bacterial-type flagellum part 6.3
non-membrane-bounded organelle 5.53
organelle 5.43
organelle part 5.27
bacterial-type flagellum basal body, rod 4.17
Biological Process
movement of cell or subcellular component 8.14
localization of cell 7.32
archaeal or bacterial-type flagellum-dependent… 7.32
cilium or flagellum-dependent cell motility 7.32
cell motility 7.32
bacterial-type flagellum-dependent cell motility 7.32
bacterial-type flagellum organization 6.68
single-organism organelle organization 5.71
bacterial-type flagellum assembly 5.37
cell projection organization 5.33
localization 4.74
organelle organization 4.38
organelle assembly 4
cell projection assembly 4
D
-log10(Fisher' exact test P value)
0 1 2 3 4 5 6
Molecular Function
heme binding 5.27
tetrapyrrole binding 5.06
electron carrier activity 4.06
molybdenum ion binding 3.36
anion transmembrane transporter activity 2.82
oxidoreductase activity, acting on the CH-CH… 2.79
ATPase activity, coupled to movement of… 2.61
ATPase activity, coupled to transmembrane… 2.61
Cellular Component
periplasmic space 2.64
cell envelope 2.26
envelope 2.17
outer membrane 1.72
Biological Process
oxidation-reduction process 3.28
sulfate assimilation 2.87
porphyrin-containing compound biosynthetic… 2.86
transport 2.66
establishment of localization 2.63
porphyrin-containing compound metabolic… 2.63
regulation of cellular protein metabolic process 2.3
asparagine biosynthetic process 2.3
asparagine metabolic process 2.3
sulfate reduction 2.3
selenocysteine incorporation 2.3
translational readthrough 2.3
regulation of cellular amide metabolic process 2.3
regulation of translation 2.3



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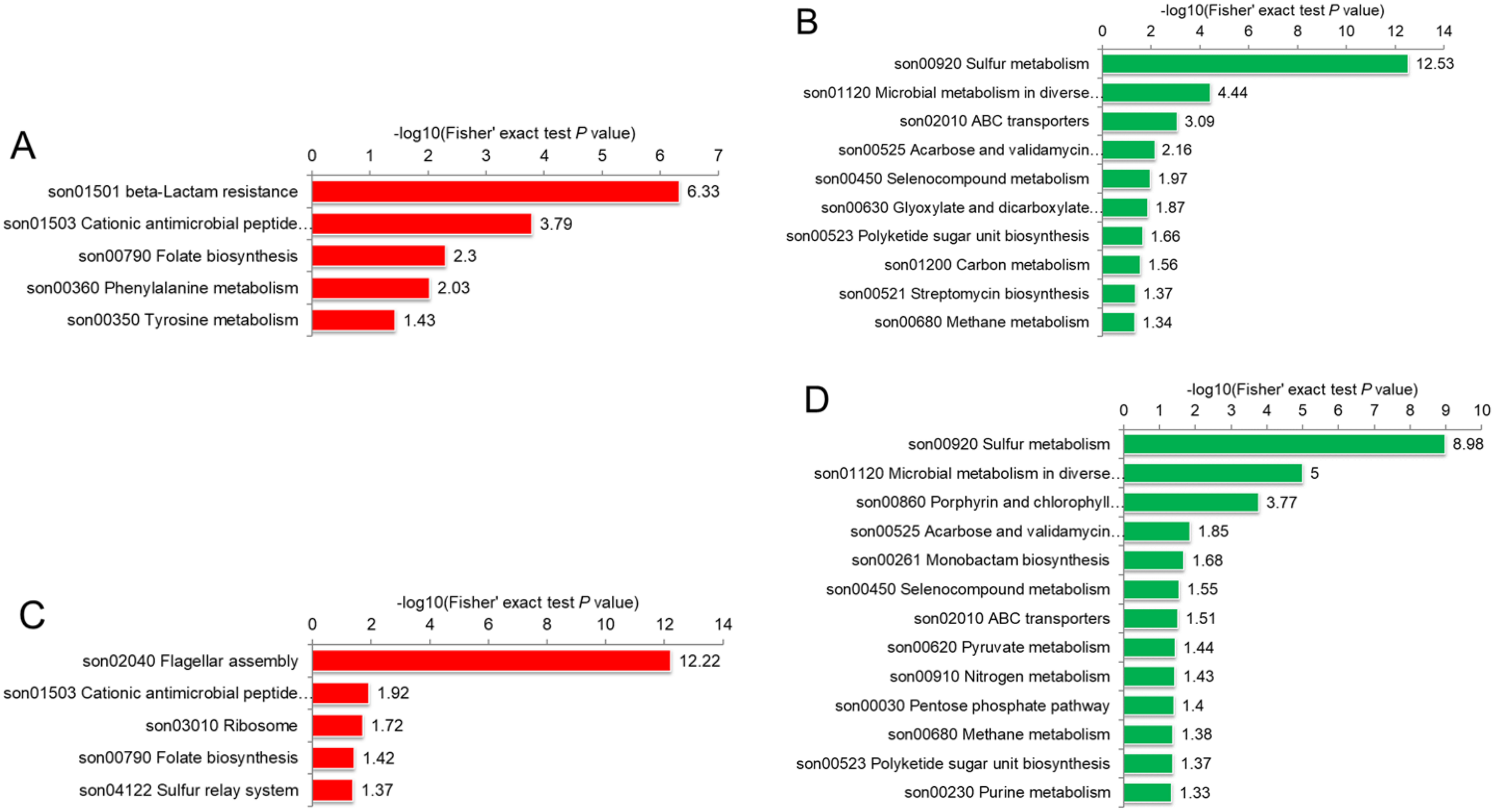

A
-log10(Fisher' exact test P value)
0
1
2
3
4
5
6
7
son01501 beta-Lactam resistance
6.33
son01503 Cationic antimicrobial peptide…
3.79
son00790 Folate biosynthesis
2.3
son00360 Phenylalanine metabolism
2.03
son00350 Tyrosine metabolism
1.43
B
-log10(Fisher' exact test P value)
0
2
4
6
8
10
12
14
son00920 Sulfur metabolism
12.53
son01120 Microbial metabolism in diverse…
4.44
son02010 ABC transporters
3.09
son00525 Acarbose and validamycin…
2.16
son00450 Selenocompound metabolism
1.97
son00630 Glyoxylate and dicarboxylate…
1.87
son00523 Polyketide sugar unit biosynthesis
1.66
son01200 Carbon metabolism
1.56
son00521 Streptomycin biosynthesis
1.37
son00680 Methane metabolism
1.34
C
-log10(Fisher' exact test P value)
0
2
4
6
8
10
12
14
son02040 Flagellar assembly
12.22
son01503 Cationic antimicrobial peptide…
1.92
son03010 Ribosome
1.72
son00790 Folate biosynthesis
1.42
son04122 Sulfur relay system
1.37
D
-log10(Fisher' exact test P value)
0
1
2
3
4
5
6
7
8
9
10
son00920 Sulfur metabolism
8.98
son01120 Microbial metabolism in diverse…
5
son00860 Porphyrin and chlorophyll…
3.77
son00525 Acarbose and validamycin…
1.85
son00261 Monobactam biosynthesis
1.68
son00450 Selenocompound metabolism
1.55
son02010 ABC transporters
1.51
son00620 Pyruvate metabolism
1.44
son00910 Nitrogen metabolism
1.43
son00030 Pentose phosphate pathway
1.4
son00680 Methane metabolism
1.38
son00523 Polyketide sugar unit biosynthesis
1.37
son00230 Purine metabolism
1.33

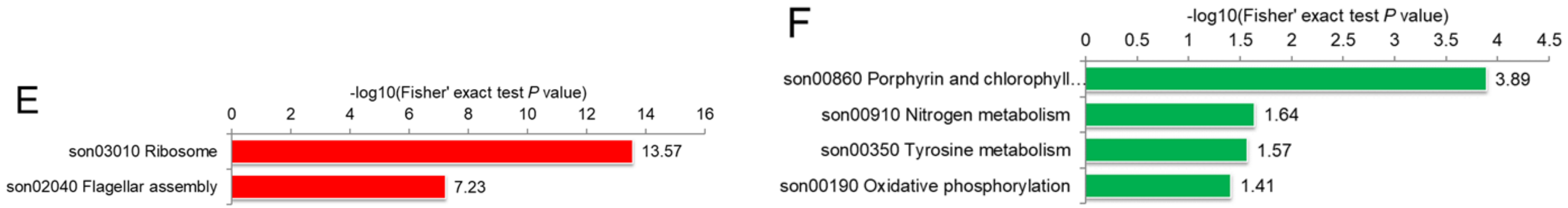
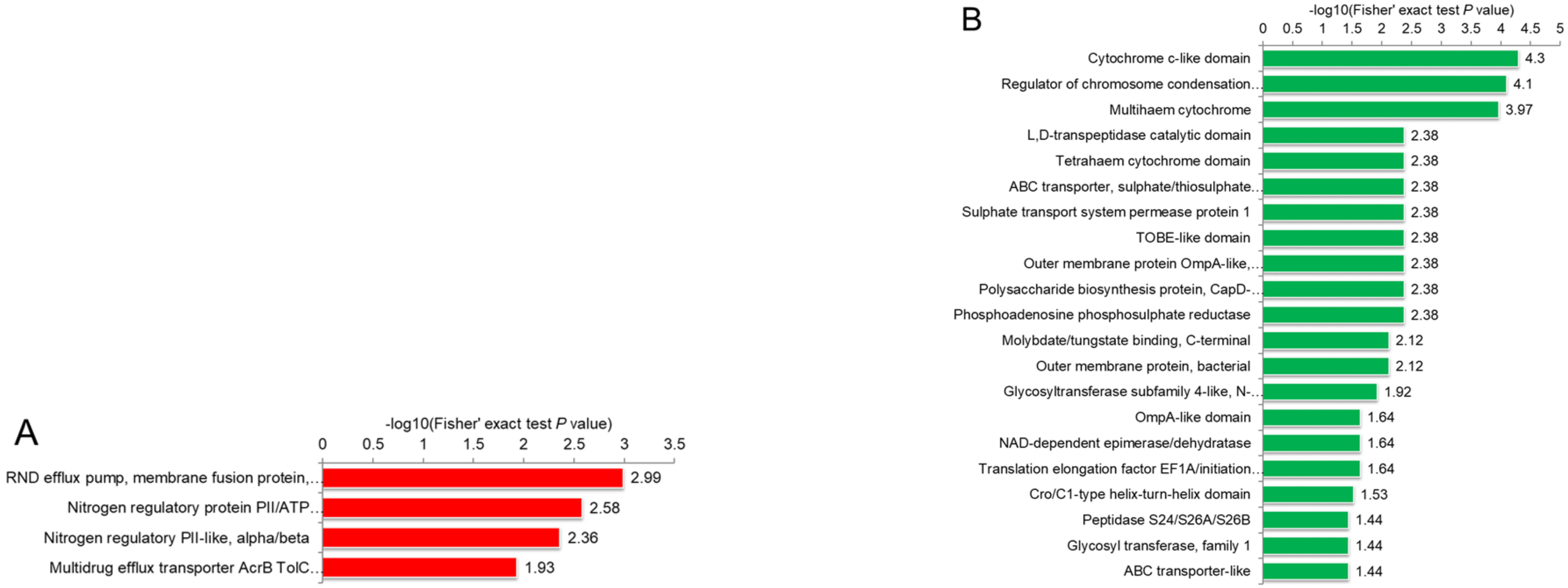
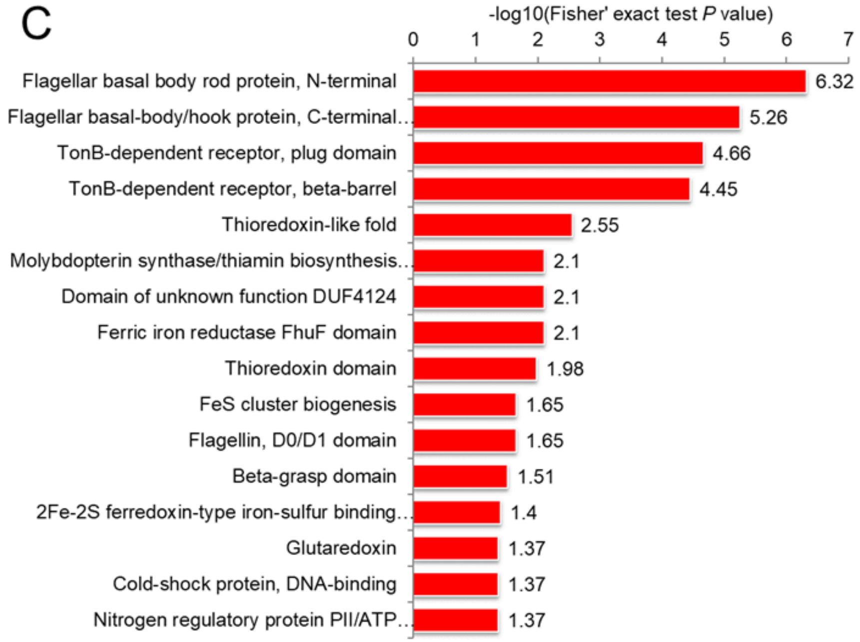


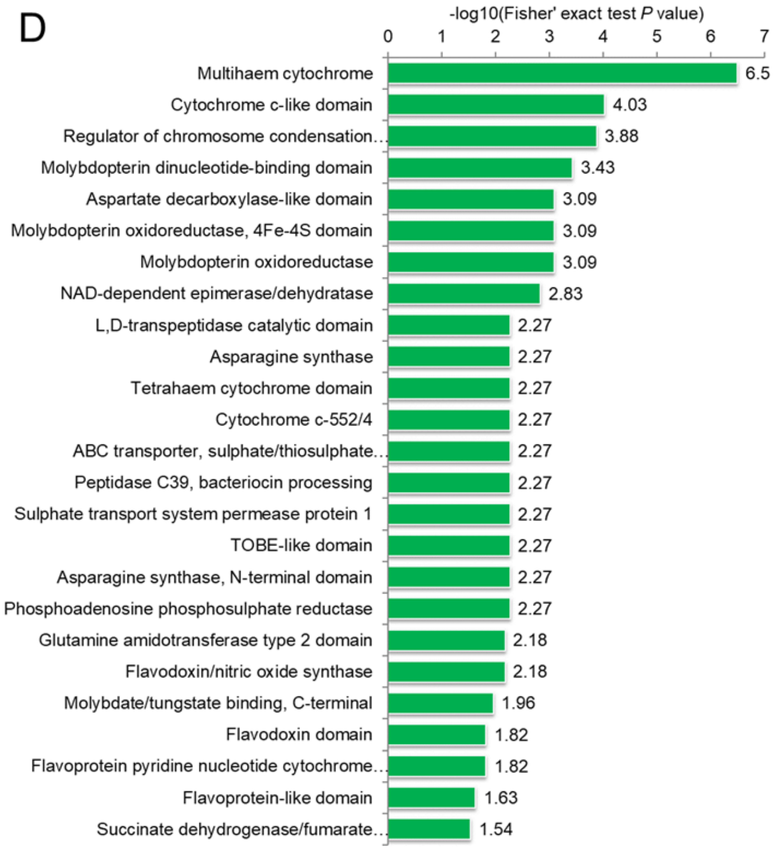
Fig. S8. KEGG-based enrichment analysis of up-regulation (red) and down-regulation (green) expressed proteins. A and B, D120Cr(-) vs D120N; C and D, D120Cr(+) vs D120N; E and F, D120Cr(+) vs D120Cr(-).


A
-log10(Fisher' exact test P value)
0
0.5
1
1.5
2
2.5
3
3.5
RND efflux pump, membrane fusion protein,…
2.99
Nitrogen regulatory protein PII/ATP…
2.58
Nitrogen regulatory PII-like, alpha/beta
2.36
Multidrug efflux transporter AcrB TolC…
1.93
B
-log10(Fisher' exact test P value)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
Cytochrome c-like domain
4.3
Regulator of chromosome condensation…
4.1
Multihaem cytochrome
3.97
L,D-transpeptidase catalytic domain
2.38
Tetrahaem cytochrome domain
2.38
ABC transporter, sulphate/thiosulphate…
2.38
Sulphate transport system permease protein 1
2.38
TOBE-like domain
2.38
Outer membrane protein OmpA-like,…
2.38
Polysaccharide biosynthesis protein, CapD-…
2.38
Phosphoadenosine phosphosulphate reductase
2.38
Molybdate/tungstate binding, C-terminal
2.12
Outer membrane protein, bacterial
2.12
Glycosyltransferase subfamily 4-like, N-…
1.92
OmpA-like domain
1.64
NAD-dependent epimerase/dehydratase
1.64
Translation elongation factor EF1A/initiation…
1.64
Cro/C1-type helix-turn-helix domain
1.53
Peptidase S24/S26A/S26B
1.44
Glycosyl transferase, family 1
1.44
ABC transporter-like
1.44

C


-log10(Fisher' exact test *P* value)
0
1
2
3
4
5
6
7
Flagellar basal body rod protein, N-terminal
6.32
Flagellar basal-body/hook protein, C-terminal…
5.26
TonB-dependent receptor, plug domain
4.66
TonB-dependent receptor, beta-barrel
4.45
Thioredoxin-like fold
2.55
Molybdopterin synthase/thiamin biosynthesis…
2.1
Domain of unknown function DUF4124
2.1
Ferric iron reductase FhuF domain
2.1
Thioredoxin domain
1.98
FeS cluster biogenesis
1.65
Flagellin, D0/D1 domain
1.65
Beta-grasp domain
1.51
2Fe-2S ferredoxin-type iron-sulfur binding…
1.4
Glutaredoxin
1.37
Cold-shock protein, DNA-binding
1.37
Nitrogen regulatory protein PII/ATP…
1.37

D


-log10(Fisher' exact test *P* value)
0
1
2
3
4
5
6
7
Multihaem cytochrome
6.5
Cytochrome c-like domain
4.03
Regulator of chromosome condensation…
3.88
Molybdopterin dinucleotide-binding domain
3.43
Aspartate decarboxylase-like domain
3.09
Molybdopterin oxidoreductase, 4Fe-4S domain
3.09
Molybdopterin oxidoreductase
3.09
NAD-dependent epimerase/dehydratase
2.83
L,D-transpeptidase catalytic domain
2.27
Asparagine synthase
2.27
Tetrahaem cytochrome domain
2.27
Cytochrome c-552/4
2.27
ABC transporter, sulphate/thiosulphate…
2.27
Peptidase C39, bacteriocin processing
2.27
Sulphate transport system permease protein 1
2.27
TOBE-like domain
2.27
Asparagine synthase, N-terminal domain
2.27
Phosphoadenosine phosphosulphate reductase
2.27
Glutamine amidotransferase type 2 domain
2.18
Flavodoxin/nitric oxide synthase
2.18
Molybdate/tungstate binding, C-terminal
1.96
Flavodoxin domain
1.82
Flavoprotein pyridine nucleotide cytochrome…
1.82
Flavoprotein-like domain
1.63
Succinate dehydrogenase/fumarate…
1.54

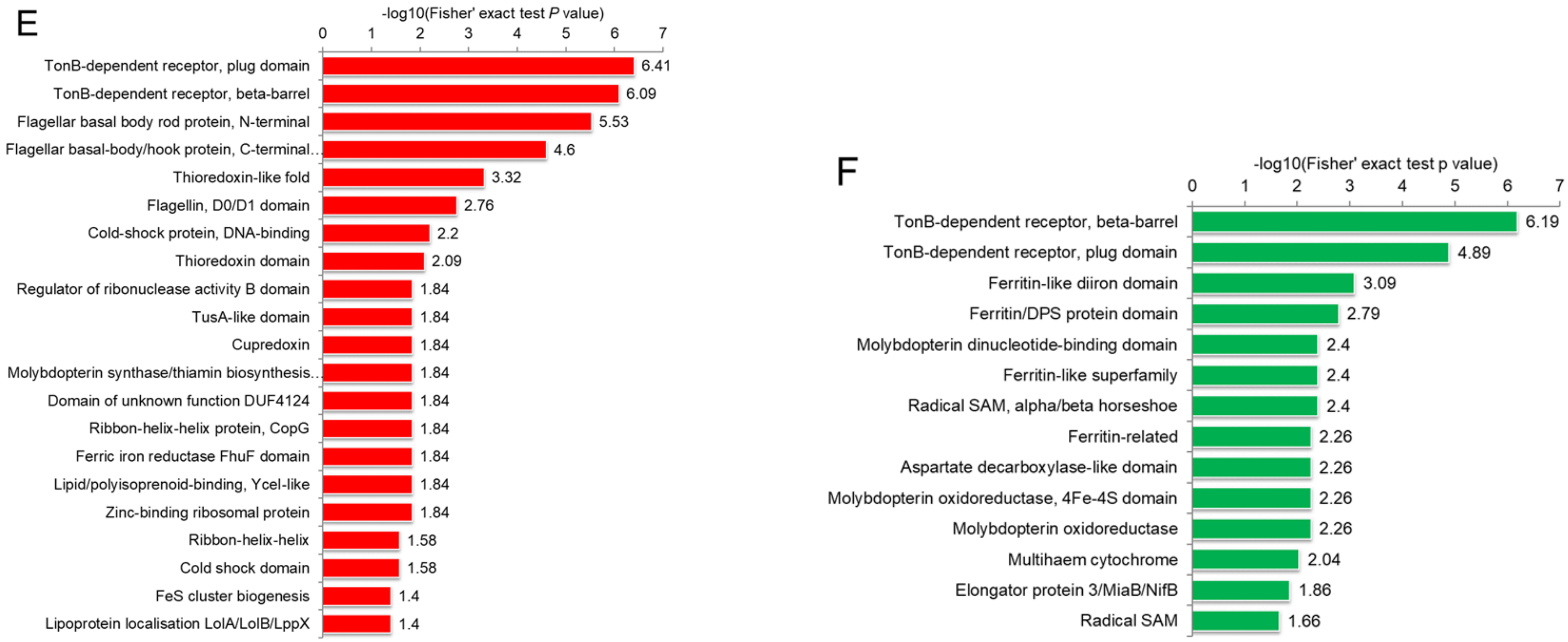


Fig. S9. Protein domain-based enrichment analysis of up-regulation (red) and down-regulation (green) expressed proteins. A and B, D120Cr(-) vs D120N; C and D, D120Cr(+) vs D120N; E and F, D120Cr(+) vs D120Cr(-).

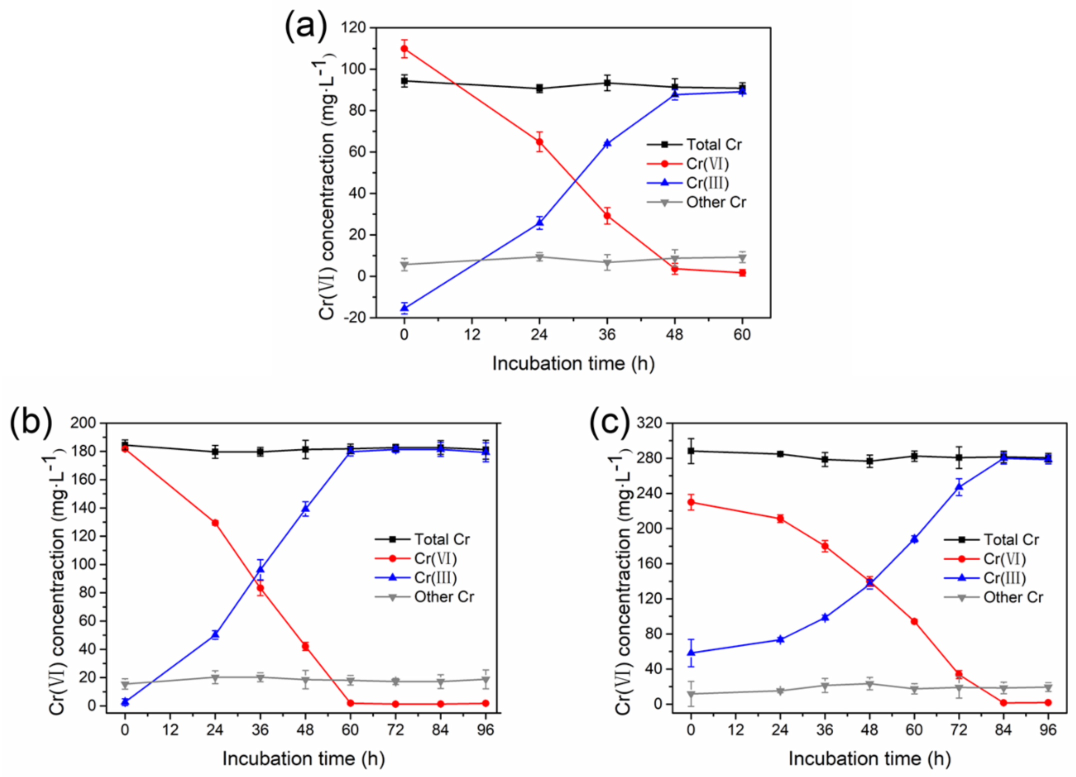


Fig. S10. The changes of total Cr, Cr(VI) and Cr(III) concentrations. (a), (b) and (c) represent 100 mg/L, 200 mg/L and 300 mg/L initial Cr(VI) concentrations, respectively.

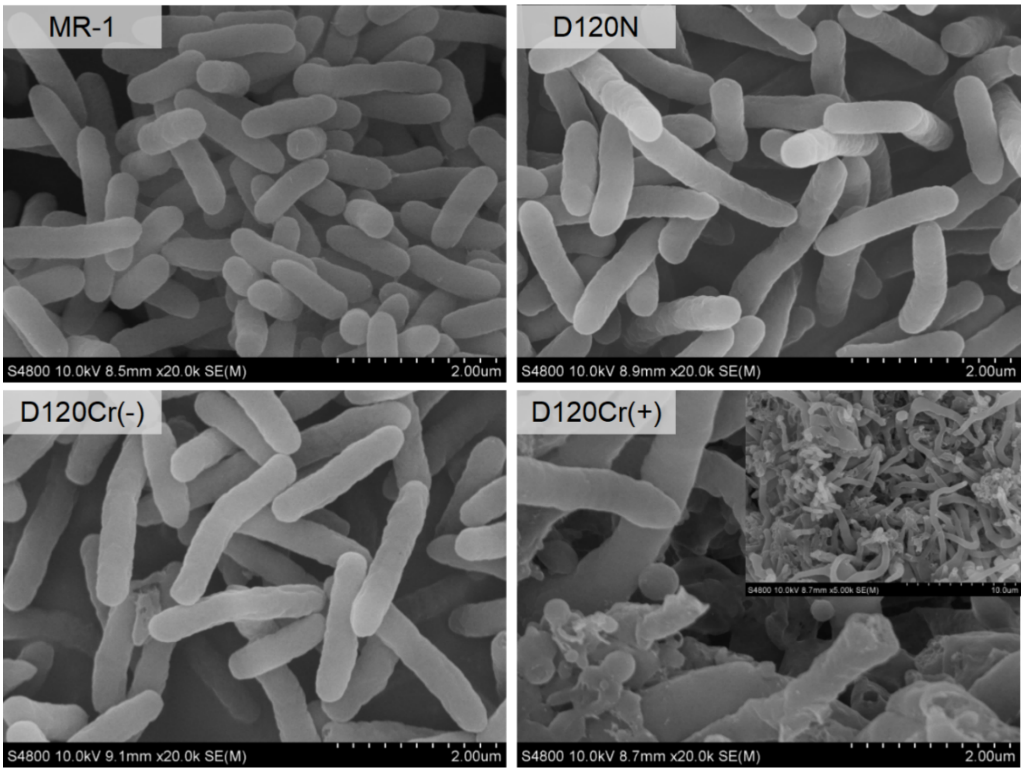


Fig. S11. The scanning electron microscope (SEM) images of the tested strains.

Table S1 All the identified quantifiable upregulated proteins (D120Cr(-) vs D120N)

Protein accession	Protein description	Gene name	Ratio
K4PSX5	RND-type multidrug/detergent efflux system permease component VexA	vexA	2.072
K4PU16	Alanine dehydrogenase	ald	2.493
P59192	UPF0225 protein SO_2497	SO_2497	2.202
Q8CM09	ISSod14 transposase TnpA_ISSod14	tnpA	2.799
Q8E7Z5	Uncharacterized protein	SO_A0173	2.638
Q8E7Z6	Site-specific recombinase resolvase family	SO_A0172	2.012
Q8E898	Uncharacterized protein	SO_A0011	3.365
Q8E8A3	ParA family protein	SO_A0006	6.751
Q8E8A4	Uncharacterized protein	SO_A0005	5.753
Q8E8A5	Type II restriction-modification system N4-cytosine or N6-adenine DNA methyltransferase	SO_A0004	8.414
Q8E8A6	Type II restriction-modication system restriction endonuclease	SO_A0003	6.961
Q8E8A7	Type II restriction-modification system activator	SO_A0002	4.234
Q8E8H1	Proton-coupled multidrug efflux pump MFP component VmeA	vmeA	2.065
Q8E8H2	Efflux pump membrane transporter	vmeB	2.077
Q8E8H7	UDP-glucose dehydrogenase WcvB	wcvB	2.96
Q8E8H8	UDP-glucuronate 4-epimerase WcvA	wcvA	3.641
Q8E8T6	Transcriptional regulator LysR family	SO_4571	4.218
Q8E8W6	Serine peptidase family S9	SO_4537	2.78
Q8E915	NAD+-dependent acetaldehyde dehydrogenase ExaC	exaC	2.198
Q8E941	"GTP 3',8-cyclase	moaA	3.42
Q8E942	Cyclic pyranopterin monophosphate synthase	moaC	2.774
Q8E947	ABC-type molybdate uptake system ATPase component ModC	modC	2.534
Q8E976	Glutamine synthetase	glnA	4.012
Q8E9F6	RND-type multidrug/detergent efflux system MFP component VexB	vexB	2.105
Q8E9F7	Transcriptional repressor of multidrug/detergent efflux pump VexR	vexR	2.118
Q8EA04	MSHA major pilin subunit MshA	mshA	11.045
Q8EAJ8	Global secretion system secretin TolC	tolC	2.649
Q8EAS3	Regulatory protein for nitrogen assimilation GlnK	glnK	4.612
Q8EB18	Thiol:disulfide interchange protein DsbA family	SO_3718	2.388
Q8EBH5	Alanine/glycine:cation symporter (AGCS) family protein	SO_3541	2.399
Q8EBK0	TonB-dependent chitooligosaccharide receptor	SO_3514	2.153
Q8EBT8	Tricorn protease homolog	SO_3411	2.074
Q8EBV9	Uncharacterized protein	SO_3386	6.52
Q8EBW4	Amine oxidase	SO_3381	2.28

Q8ECB3	Two component signal transduction system controlling flagella biosynthesis Sigma54-dependent response regulator FlrC	flrC	2.017
Q8ECF8	Putative glycine transferase in O-antigen biosynthesis cluster WbqC	wbqC	4.526
Q8ECJ9	Dipepidyl carboxypeptidase II Dcp	dcp	3.508
Q8ECL7	Alpha-N-acetylgalactosaminidase	nagA	2.087
Q8ECM4	SecDF preprotein translocase-associated protein YajC	yajC	2.201
Q8EDI3	Peptidase M28A family	SO_2766	2.652
Q8EDJ1	Putative histidine porter YuiF	yuiF	2.11
Q8EDL0	Uncharacterized protein	SO_2736	4.458
Q8EDL5	Protease HtpX	htpX	2.066
Q8EE20	DUF885 family lipoprotein	SO_2570	2.195
Q8EEB8	TonB-dependent receptor	SO_2469	4.238
Q8EEH5	Glycine radical enzyme YjjI family	SO_2407	3.199
Q8EEN6	Dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase complex	bkdB	2.005
Q8EEN8	3-methyl-2-oxobutanoate dehydrogenase complex E1 component alpha subunit BkdA1	bkdA1	2.064
Q8EFK8	"Homogentisate 1,2-dioxygenase HmgA	hmgA	4.392
Q8EFK9	4-hydroxyphenylpyruvate dioxygenase HppD	hppD	4.442
Q8EFS8	Uncharacterized protein	SO_1888	3.43
Q8EG02	Methionine gamma-lyase MdeA	mdeA	2.142
Q8EGD7	Putative pterin-4-alpha-carbinolamine dehydratase	SO_1667	2.076
Q8EGD8	Phenylalanine-4-hydroxylase PhhA	phhA	2.684
Q8EGJ7	Lipoprotein	SO_1605	5.142
Q8EH39	Short chain fatty acids transporter AtoE	atoE	3.601
Q8EHG2	Transcriptional regulator LysR family	SO_1259	2.092
Q8EI39	NADH-ubiquinone oxidoreductase subunit L NuoL	nuoL	2.121
Q8EIL9	ABC-type macrolide export systemMFP component MacA	macA	2.193
Q8EIS4	Regulatory protein for nitrogen assimilation GlnK	glnK	3.02
Q8EIT0	Uncharacterized protein	SO_0755	2.119
Q8EJV1	AMP-dependent synthetase and ligase family protein	SO_0355	2.662
Q8EJY5	Uncharacterized protein	SO_0321	2.372

(D120Cr(+) vs D120N)

Protein accession	**Protein description**	**Gene name**	**Ratio**
K4PSJ4	Flagellar hook-filament junction protein FlgK	flgK	3.524
K4PTY3	Exodeoxyribonuclease 7 small subunit	xseB	3.074
K4PTZ4	Predicted extracytoplasmic protein	SO_4783	2.207
K4PU16	Alanine dehydrogenase	ald	3.027

K4PW09	Protein with c-terminal DUF1078 domain	SO_4782	12.761
K4PW11	Mu phage uncharacterized protein	SO_4789	2.291
K4PW20	TonB-dependent ferric achromobactin receptor	SO_4422	3.073
P59166	30S ribosomal protein S12	rpsL	2.278
P59301	Acetylglutamate kinase	argB	2.056
P82177	Malate dehydrogenase	mdh	2.022
Q8CVD1	Periplasmic stress adaptor protein CpxP	cpxP	15.718
Q8CVD5	Azurin	azu	15.834
Q8CX49	10 kDa chaperonin	groS	2.248
Q8E7Z5	Uncharacterized protein	SO_A0173	15.628
Q8E7Z6	Site-specific recombinase resolvase family	SO_A0172	2.251
Q8E827	Plasmid-encoded periplasmic BOF domain protein YgiW	ygiW	3.101
Q8E869	Plasmid protein	SO_A0056	2.853
Q8E883	Antitoxin module of toxin-antitoxin system PemI	pemI	2.211
Q8E887	Uncharacterized protein	SO_A0033	2.325
Q8E898	Uncharacterized protein	SO_A0011	7.644
Q8E8A3	ParA family protein	SO_A0006	7.31
Q8E8A4	Uncharacterized protein	SO_A0005	9.203
Q8E8A5	Type II restriction-modification system N4-cytosine or N6-adenine DNA methyltransferase	SO_A0004	5.273
Q8E8A6	Type II restriction-modication system restriction endonuclease	SO_A0003	4.045
Q8E8A7	Type II restriction-modification system activator	SO_A0002	8.567
Q8E8C4	TonB-dependent siderophore receptor	SO_4743	8.64
Q8E8D7	Der GTPase-activating protein YihI	yihI	4.724
Q8E8H1	Proton-coupled multidrug efflux pump MFP component VmeA	vmeA	3.189
Q8E8H2	Efflux pump membrane transporter	vmeB	2.413
Q8E8H7	UDP-glucose dehydrogenase WcvB	wcvB	3.723
Q8E8H8	UDP-glucuronate 4-epimerase WcvA	wcvA	3.455
Q8E8J2	Thiosulfate sulfurtransferase GlpE	glpE	3.089
Q8E8L7	Propeptide PepSY amd peptidase M4 domain protein	SO_4646	3.262
Q8E8M3	Antioxidant AhpC/Tsa family	SO_4640	3.88
Q8E8P2	Fe/S biogenesis protein NfuA	nfuA	4.499
Q8E8Q8	LexA repressor	lexA	3.151
Q8E8T6	Transcriptional regulator LysR family	SO_4571	2.909
Q8E8U5	Uncharacterized protein	SO_4561	2.767
Q8E8V5	Predicted periplasmic protein	SO_4551	4.526
Q8E8W6	Serine peptidase family S9	SO_4537	2.498
Q8E8X7	Iron-responsive TonB-dependent enterobactin receptor IrgA	irgA	11.727
Q8E8Y4	TonB-dependent siderophore receptor	SO_4516	3.455
Q8E915	NAD+-dependent acetaldehyde dehydrogenase ExaC	exaC	3.355

Q8E917	Periplasmic stress-responsive two component signal transduction system histidine kinase CpxA	cpxA	2.934
Q8E924	Predicted periplasmic protein	SO_4470	2.165
Q8E932	Uncharacterized protein	SO_4462	2.981
Q8E941	"GTP 3',8-cyclase	moaA	2.214
Q8E942	Cyclic pyranopterin monophosphate synthase	moaC	2.553
Q8E943	Molybdopterin synthase sulfur carrier subunit	moaD	5.084
Q8E945	ABC-type molybdate uptake system substrate-binding component ModA	modA	2.659
Q8E947	ABC-type molybdate uptake system ATPase component ModC	modC	2.089
Q8E976	Glutamine synthetase	glnA	4.919
Q8E992	Cytoplasmic rhodanese domain protein	SO_4394	2.242
Q8E9F5	Uncharacterized protein	SO_4329	4.055
Q8E9H3	Putative lipoprotein	SO_4310	2.131
Q8E9H5	Diaminopimelate epimerase	dapF	2.381
Q8E9N2	2-isopropylmalate synthase	leuA	3.704
Q8E9R4	Sec-independent protein translocase protein TatA	tatA	2.473
Q8E9T6	Periplasmic protein of expolysaccharide biosynthesis cluster MxdD	mxdD	2.14
Q8E9X1	Oxidoreductase short-chain dehydrogenase/reductase family	SO_4141	2.683
Q8E9X8	Uncharacterized protein	SO_4134	2.871
Q8E9Z0	50S ribosomal protein L31	rpmE	3.455
Q8EA04	MSHA major pilin subunit MshA	mshA	10.301
Q8EA30	UPF0307 protein SO_4079	SO_4079	2.888
Q8EA39	Periplasmic protein associated with oxidative stress YggE	yggE	2.052
Q8EA52	Met repressor	metJ	2.658
Q8EA55	Methylenetetrahydrofolate reductase	metF	2.155
Q8EA81	Single-stranded DNA-binding protein	ssb	2.88
Q8EA90	Putative lipoprotein	SO_4018	3
Q8EAE3	Phosphotransferase system (PTS) sugar-specific IIA component PtsN	ptsN	2.211
Q8EAE7	Lipopolysaccharide export system protein LptA	lptA	2.607
Q8EAG0	Periplasmic serine endoprotease DegP-like	degQ	2.163
Q8EAH2	30S ribosomal protein S6	rpsF	2.141
Q8EAI8	TonB-dependent siderophore receptor	SO_3914	7.159
Q8EAI9	PKHD-type hydroxylase SO_3913	SO_3913	3.011
Q8EAJ5	Cytochrome oxidase copper metallochaperone	SO_3907	2.504
Q8EAJ8	Global secretion system secretin TolC	tolC	3.034
Q8EAS3	Regulatory protein for nitrogen assimilation GlnK	glnK	6.302
Q8EAW4	DNA binding domain-containing protein	SO_3777	5.9
Q8EB31	Uncharacterized protein	SO_3704	9.265
Q8EB37	Putative periplasmic protein	SO_3698	2.556
Q8EB58	Uncharacterized protein	SO_3676	3.055

Q8EB59	Hemin import ATP-binding protein HmuV	hmuV	13.159
Q8EB61	ABC-type hemin uptake system substrate-binding component HmuB	hmuB	20.755
Q8EB63	TonB1 energy transduction system for heme uptake inner membrane component ExbB	exbB	7.169
Q8EB65	TonB-dependent heme/hemoglobin receptor HmuA	hmuA	14.402
Q8EB66	Heme iron utilization protein HmuX	hmuX	16.963
Q8EB67	FMN binding heme iron utilization protein HmuZ	hmuZ	23.017
Q8EB76	Uncharacterized protein	SO_3656	2.628
Q8EB86	Dihydrofolate reductase	folA	2.156
Q8EB87	Uncharacterized protein	SO_3645	2.336
Q8EBA8	Periplasmic RmlC-type Cupin domain family protein	SO_3622	2.896
Q8EBC9	Uncharacterized protein	SO_3596	2.145
Q8EBD4	Predicted periplasmic protein	SO_3591	3.559
Q8EBE0	NADPH-dependent azoreductase Azr	azr	2.206
Q8EBE7	Predicted periplasmic protein	SO_3576	2.139
Q8EBG4	N5-carboxyaminoimidazole ribonucleotide mutase	purE	2.295
Q8EBJ3	Type IV pilin system protein	SO_3523	2.402
Q8EBP7	DNA repair protein RecN	recN	2.74
Q8EBR5	5'-nucleotidase SurE	surE	2.202
Q8EBR6	Protein-L-isoaspartate O-methyltransferase	pcm	2.114
Q8EBS0	Protein RecA	recA	3.088
Q8EBS7	Ribosomal associated cold shock response protein YfiA	yfiA	2.316
Q8EBU2	Putative siderophore transporter component 2	SO_3407	7.03
Q8EBV8	Uncharacterized protein	SO_3387	3.829
Q8EBV9	Uncharacterized protein	SO_3386	4.286
Q8EBX5	UPF0312 protein SO_3370	SO_3370	2.899
Q8EBX6	Probable Fe(2+)-trafficking protein	SO_3369	2.468
Q8EBY9	UPF0235 protein SO_3356	SO_3356	2.58
Q8EBZ0	Inner membrane osmoregulator protein YggT	yggT	2.609
Q8EBZ9	UPF0301 protein SO_3346	SO_3346	3.942
Q8EC00	Translation initiation factor protein YciH	yciH	2.88
Q8EC89	Secretion chaperone for FlgK and FlgL FlgN	flgN	3.115
Q8EC90	Flagellar biosynthesis anti-sigma factor FlgM	flgM	3.936
Q8EC94	Flagellar basal body rod protein FlgB	flgB	2.2
Q8EC95	Flagellar basal-body rod protein FlgC	flgC	3.115
Q8EC96	Basal-body rod modification protein FlgD	flgD	3.306
Q8EC97	Flagellar hook protein FlgE	flgE	4.634
Q8EC99	Flagellar basal-body rod protein FlgF	flgF	5.158
Q8ECA0	Flagellar basal-body rod protein FlgG	flgG	4.469
Q8ECA2	Flagellar P-ring protein	flgI	2.626

Q8ECA3	Flagellar rod cap protein and peptidoglycan hydrolase FlgJ	flgJ	3.262
Q8ECA4	Flagellar hook-associated protein FlgL	flgL	6.113
Q8ECA5	Flagellin	fliC	3.79
Q8ECA7	Uncharacterized flagella locus protein FlaG	flaG	3.758
Q8ECA8	Flagellar hook-associated protein 2	fliD	3.512
Q8ECA9	Flagella biosynthesis chaperone for FliD FliT	fliT	2.346
Q8ECB0	Flagellar secretion chaperone FliS	fliS	2.393
Q8ECB2	Two component signal transduction system controlling flagellar biosynthesis histidine kinase with PAS sensory domain FlrB	flrB	4.412
Q8ECB4	Flagellar hook-basal body complex protein FliE	fliE	2.315
Q8ECB9	Flagellar chaperone escort protein FliJ	fliJ	2.031
Q8ECC0	Flagellar hook-length control protein FliK	fliK	4.417
Q8ECC3	Flagellar motor switch protein FliN	fliN	2.241
Q8ECC8	Flagellar biosynthetic protein FlhB	flhB	2.065
Q8ECD0	Flagellar biosynthesis protein FlhA	flhA	2.04
Q8ECD1	Flagellar polar localization control system flagellar assembly determinant GTPase FlhF	flhF	2.025
Q8ECF8	Putative glycine transferase in O-antigen biosynthesis cluster WbqC	wbqC	2.478
Q8ECH6	Toxin-antitoxin system toxin HepN family	SO_3166	2.997
Q8ECJ9	Dipepidyl carboxypeptidase II Dcp	dcp	2.046
Q8ECL8	Uncharacterized protein	SO_3119	3.008
Q8ECP1	TPR domain protein in aerotolerance operon BatB	batB	5.486
Q8ECQ0	Predicted periplasmic protein	SO_3085	3.364
Q8ECS1	DNA topoisomerase 3	topB	2.303
Q8ECT3	Aldehyde oxidase / xanthine dehydrogenase family FeS subunit	SO_3049	3.191
Q8ECT8	Uncharacterized protein	yciL	3.864
Q8ECT9	Ferric putrebactin reductase PutB	putB	6.18
Q8ECU0	TonB-dependent ferric putrebactin siderophore receptor PutA	putA	7.436
Q8ECU1	NTP-dependent putrebactin synthetase PubC	pubC	11.83
Q8ECU2	N-hydroxyputrescine-succinyl CoA transferase PubB	pubB	16.026
Q8ECU3	Putrescine monooxygenase PubA	pubA	8.997
Q8ECU8	Periplasmic siderophore cleavage esterase IroE family	SO_3025	7.71
Q8ED42	Multifunctional thioesterase/protease/lysophospholipase L1 TesA	tesA	3.006
Q8ED43	Putative ABC-type fatty acid export system ATPase component YbbA	ybbA	2.102
Q8ED84	Glutaredoxin	grxD	2.881
Q8EDA2	Thiol:disulfide interchange protein	SO_2860	2.516
Q8EDB4	Putative periplasmic protein	SO_2848	4.563
Q8EDC7	Uncharacterized protein	SO_2835	5.676
Q8EDD1	GTP cyclohydrolase-2	ribA	2.062
Q8EDF2	UPF0434 protein SO_2800	SO_2800	3.092

Q8EDG5	Cold shock protein CspA	cspA	2.396
Q8EDG9	50S ribosomal protein L32	rpmF	2.32
Q8EDH4	Acyl carrier protein	acpP	2.212
Q8EDI3	Peptidase M28A family	SO_2766	2.066
Q8EDI6	Haloacid dehalogenase subfamily IIA associated with N-acetylglucosamine degradation NagD	nagD	3.159
Q8EDK0	Cell division coordinator CpoB	ybgF	2.672
Q8EDK1	Glutaredoxin GrxA	grxA	2.262
Q8EDL0	Uncharacterized protein	SO_2736	3.27
Q8EDM0	Purine nucleoside phosphoramidase HinT	hinT	3.491
Q8EDP9	Mu phage tail tube protein GpM	gpM	4.325
Q8EDQ5	Mu phage uncharacterized protein	SO_2688	4.278
Q8EDQ8	Mu phage major head subunit GpT	gpT	7.709
Q8EDQ9	Mu phage protease GpI	gpI	8.297
Q8EDR0	Mu phage uncharacterized protein	SO_2683	5.071
Q8EDR1	Mu phage uncharacterized protein	SO_2682	2.495
Q8EDS7	Mu phage uncharacterized protein	SO_2666	3.206
Q8EDT3	Uncharacterized protein	SO_2660	2.407
Q8EDT8	Mu phage transposase OrfB TnpB_MuSo2	tnpB	2.099
Q8EDV6	Uncharacterized protein	SO_2637	3.338
Q8EDW6	Translation initiation factor IF-1	infA	2.506
Q8EDY6	UV induced SOS regulon protein YebG	yebG	4.282
Q8EE07	Methyltransferase	SO_2583	2.063
Q8EE30	Ribonuclease HI	rnhA	2.323
Q8EE76	Electron transport complex subunit E	rnfE	2.251
Q8EE77	Electron transport complex subunit G	rnfG	2.594
Q8EE79	Electron transport complex subunit C	rnfC	3.282
Q8EEA1	Bifunctional 4-hydroxy-2-oxoglutarate aldolase/2-dehydro-3-deoxy-phosphogluconate aldolase Eda	eda	2.544
Q8EEA8	Uncharacterized protein	SO_2479	2.073
Q8EEF1	Crossover junction endodeoxyribonuclease RuvC	ruvC	2.624
Q8EEF6	Two component signal transduction system response regulator	SO_2426	9.235
Q8EEG0	Uncharacterized protein	SO_2422	2.674
Q8EEG5	Ferredoxin cofactor maintenance protein YfaE	yfaE	3.882
Q8EEM5	Uncharacterized protein	SO_2353	2.395
Q8EEP6	Ribbon-helix-helix protein repressor CopG family YbfE	ybfE	2.424
Q8EER2	Outer-membrane lipoprotein carrier protein	lolA	2.789
Q8EER7	50S ribosomal protein L35	rpmI	2.132
Q8EER8	Translation initiation factor IF-3	infC	2.604
Q8EEU4	Ferredoxin 2Fe-2S type ISC system Fdx	fdx	2.069

Q8EEU8	Iron-sulfur cluster assembly scaffold protein IscU	iscU	4.518
Q8EEV0	HTH-type transcriptional regulator IscR	iscR	2.287
Q8EEV5	Lipoprotein-releasing system ATP-binding protein LolD	lolD	2.121
Q8EEX5	Phosphotransferase system (PTS) glucose-specific IIA component Crr	crr	2.786
Q8EF04	Uncharacterized protein	SO_2201	4.87
Q8EF22	Periplasmic metalloprotease M23B family	SO_2180	3.145
Q8EF98	Integration host factor subunit alpha	ihfA	2.083
Q8EFC0	Outer membrane lipoprotein	SO_2063	2.134
Q8EFC1	Uncharacterized protein	SO_2062	4.46
Q8EFF5	Adenylate kinase	adk	2.028
Q8EFK3	Putative periplasmic protein	SO_1968	2.828
Q8EFP9	Uncharacterized protein	SO_1921	3.093
Q8EFS8	Uncharacterized protein	SO_1888	2.58
Q8EFT9	Thioredoxin-dependent thiol peroxidase Bcp	bcp	2.131
Q8EFV2	Histone-like DNA-binding protein	SO_1863	2.468
Q8EFW0	Ribosome modulation factor	rmf	6.644
Q8EFW5	DnaJ domain protein	SO_1850	3.796
Q8EFX9	Uncharacterized protein	SO_1836	2.757
Q8EFY0	S4 RNA-binding domain protein	SO_1835	2.954
Q8EFY2	Peptidyl-prolyl cis-trans isomerase PpiC	ppiC	3.586
Q8EFZ0	TonB2 energy transduction system periplasmic component	SO_1824	2.271
Q8EFZ8	UPF0319 protein SO_1816	SO_1816	2.198
Q8EG28	Ferrous iron transport protein B	feoB	3.492
Q8EG29	Ferrous iron transport protein A FeoA	feoA	8.368
Q8EG52	Transcription activator-like effector binding domain protein	SO_1757	5.105
Q8EG53	Glyoxalase family protein	SO_1756	14.345
Q8EG54	Phosphoglucomutase/phosphomannomutase family protein	SO_1755	2.516
Q8EG70	HNH endonuclease	SO_1738	2.346
Q8EGA4	Uncharacterized protein	SO_1701	2.288
Q8EGA5	Putative lipoprotein	SO_1700	4.779
Q8EGD4	Fumarylacetoacetate hydrolase FahA	fahA	2.034
Q8EGD8	Phenylalanine-4-hydroxylase PhhA	phhA	2.013
Q8EGE2	Uncharacterized protein	SO_1662	2.878
Q8EGF6	Cold shock protein Csp family	SO_1648	3.143
Q8EGG6	Periplasmic chaperone for outer membrane proteins Skp	skp	2.66
Q8EGJ1	Uncharacterized protein	SO_1611	2.686
Q8EGJ7	Lipoprotein	SO_1605	5.662
Q8EGL3	Uncharacterized protein	SO_1588	4.836
Q8EGM8	Small highly charged protein	SO_1572	5.894
Q8EGN2	Outer membrane protein YfaZ	yfaZ	2.126

Q8EGV9	TonB-dependent receptor	SO_1482	12.255
Q8EGW2	Uncharacterized protein	SO_1479	3.004
Q8EGW6	UPF0125 protein SO_1475	SO_1475	2.69
Q8EH24	Hg(II) uptake system substrate-binding component MerP family	SO_1407	2.156
Q8EH52	Peptidase family 56	SO_1378	6.33
Q8EH84	Sigma E factor positive regulatory protein RseC	rseC	2.333
Q8EH86	Anti-sigma-E factor RseA	rseA	2.44
Q8EHB2	Predicted periplasmic protein	SO_1317	2.917
Q8EHC2	Uncharacterized protein	SO_1306	2.312
Q8EHC4	Iron-sulfur cluster insertion protein ErpA	erpA	4.532
Q8EHD7	30S ribosomal protein S21	rpsU	4.103
Q8EHM9	Putative periplasmic CbiK superfamily protein	SO_1190	17.349
Q8EHN0	Uncharacterized protein	SO_1189	4.566
Q8EHN1	Inner membrane protein with PepSY TM helix	SO_1188	5.625
Q8EHY2	GlcNAc-binding protein A	gbpA	8.976
Q8EHZ1	Protein SlyX homolog	slyX	3.288
Q8EI32	NADH-ubiquinone oxidoreductase subunit E NuoE	nuoE	3.186
Q8EIF2	Putative agmatine deiminase	aguA	2.024
Q8EIF3	Uncharacterized protein	SO_0886	2.076
Q8EIG0	Uncharacterized protein	SO_0879	2.279
Q8EIG8	2-amino-4-hydroxy-6-hydroxymethyldihydropteridine pyrophosphokinase FolK	folK	2.092
Q8EIK4	Putative periplasmic peptidase C15 superfamily	SO_0835	2.422
Q8EIL5	Uncharacterized protein	SO_0824	2.749
Q8EIL7	ABC-type macrolide export system secretin component MacC	macC	3.737
Q8EIL9	ABC-type macrolide export systemMFP component MacA	macA	4.636
Q8EIM9	Uncharacterized protein	SO_0808	2.566
Q8EIN9	TonB-dependent receptor	SO_0798	3.392
Q8EIR3	5-formyltetrahydrofolate cyclo-ligase	ygfA	2.08
Q8EIR7	NAD dependent epimerase/dehydratase family protein	SO_0768	3.379
Q8EIS4	Regulatory protein for nitrogen assimilation GlnK	glnK	4.803
Q8EIS7	Predicted periplasmic protein	SO_0758	2.459
Q8EIT0	Uncharacterized protein	SO_0755	7.977
Q8EIT2	Uncharacterized protein	SO_0753	3.631
Q8EIT3	Uncharacterized protein	SO_0752	2.147
Q8EIU0	ABC-type Fe3+ uptake system substrate-binding component FbpA	fbpA	7.28
Q8EIU2	ABC-type Fe3+ uptake system ATPase component FbpC	fbpC	4.698
Q8EIU3	Gamma-glutamyltransferase GgtB	ggtB	3.914
Q8EIW1	Predicted secreted protein	SO_0718	2.143
Q8EJ36	Toxin-antitoxin system antidote Rhh family	SO_0637	4.055

Q8EJ64	Ubiquinol-cytochrome c reductase iron-sulfur subunit	petA	2.082
Q8EJ69	RNA-binding protein Hfq	hfq	2.436
Q8EJ85	Bacterioferritin-associated ferredoxin Bfd	bfd	11.508
Q8EJ92	Predicted ATPase PhoH family	SO_0576	2.108
Q8EJ95	Uncharacterized protein	SO_0573	2.99
Q8EJB3	Uncharacterized protein	SO_0554	4.601
Q8EJC4	Uncharacterized protein	SO_0543	3.957
Q8EJD1	Redox-active disulfide protein 2	SO_0536	2.628
Q8EJF2	DUF3012 domain-containing lipoprotein	SO_0515	4.034
Q8EJG6	Uncharacterized protein	SO_0501	2.005
Q8EJK7	Alpha-ketoglutarate uptake system substrate-binding component	SO_0456	2.109
Q8EJL4	Iron-regulated inner membrane protein	SO_0449	2.932
Q8EJL9	Zinc/cadmium-responsive efflux pump	SO_0444	2.283
Q8EJM0	Zinc and cadmium (II) responsive transcriptional activator ZntR	zntR	2.356
Q8EJM4	Uncharacterized protein	SO_0439	2.892
Q8EJN3	Uncharacterized protein	SO_0430	4.584
Q8EJQ1	DNA gyrase inhibitor YacG	yacG	3.442
Q8EJQ6	Thioredoxin	trxA	2.301
Q8EJR1	Zinc-type alcohol dehydrogenase-like protein	SO_0401	3.542
Q8EJU7	DNA-directed RNA polymerase subunit omega	rpoZ	2.38
Q8EJU9	Endoribonuclease L-PSP	SO_0358	2.054
Q8EJV1	AMP-dependent synthetase and ligase family protein	SO_0355	2.277
Q8EJW4	2-methyl-aconitate isomerase	prpF	2.327
Q8EJX1	Cell division protein ZapB	zapB	2.781
Q8EJX3	Thiol:disulfide interchange protein	dsbA	2.305
Q8EJY5	Uncharacterized protein OS=Shewanella	SO_0321	8.964
Q8EJZ0	Phosphatidylethanolamine-binding protein YbcL	ybcL	2.882
Q8EK46	50S ribosomal protein L17	rplQ	2.354
Q8EK53	50S ribosomal protein L18	rplR	2.065
Q8EK58	50S ribosomal protein L24	rplX	2.745
Q8EK59	50S ribosomal protein L14	rplN	2.055
Q8EKF4	Ferritin	ftn	3.059
Q8EKH4	Uncharacterized protein	SO_0119	4.459
Q8EKI1	Inhibitor of invertebrate-type lysozyme PliI-like family	SO_0112	2.023
Q8EKP0	Protein-export protein SecB	secB	2.8
Q8EKQ4	Putative DNA topoisomerase YrdD	yrdD	2.384
Q8EKS1	Sulfur carrier protein TusA	tusA	2.293
Q8EKT5	Putative membrane protein insertion efficiency factor	SO_0005	2.229
Q8EKT8	Flavodoxin protein MioC	mioC	3.937

(D120Cr(+) vs D120Cr(-))

Protein accession	**Protein description**	**Gene name**	**Ratio**
K4PSJ4	Flagellar hook-filament junction protein FlgK	flgK	2.631
K4PTY3	Exodeoxyribonuclease 7 small subunit	xseB	2.714
K4PW09	Protein with c-terminal DUF1078 domain	SO_4782	7.288
K4PW11	Mu phage uncharacterized protein	SO_4789	2.158
K4PW20	TonB-dependent ferric achromobactin receptor	SO_4422	3.265
P59124	30S ribosomal protein S5	rpsE	2.558
P59166	30S ribosomal protein S12	rpsL	3.446
P59301	Acetylglutamate kinase	argB	2.223
P59375	30S ribosomal protein S11	rpsK	2.593
Q8CM39	ISSod2 transposase TnpA_ISSod2	tnpA	2.286
Q8CVD1	Periplasmic stress adaptor protein CpxP	cpxP	11.735
Q8CVD5	Azurin	azu	8.739
Q8CX49	10 kDa chaperonin	groS	3.026
Q8E7Z5	Uncharacterized protein	SO_A0173	5.924
Q8E827	Plasmid-encoded periplasmic BOF domain protein YgiW	ygiW	5.05
Q8E840	Periplasmic metal-dependent aminohydrolase family protein	SO_A0100	2.296
Q8E847	Antitoxin	SO_A0087	3.243
Q8E860	Toxin-antitoxin system antidote transcriptional repressor Xre family	SO_A0068	2.09
Q8E863	Putative plasmid stability/partitioning determinant RepB	repB	2.127
Q8E869	Plasmid protein	SO_A0056	4.813
Q8E883	Antitoxin module of toxin-antitoxin system PemI	pemI	4.005
Q8E887	Uncharacterized protein	SO_A0033	2.686
Q8E892	Toxin-antitoxin system antidote component HigA family	SO_A0023	2.186
Q8E898	Uncharacterized protein	SO_A0011	2.272
Q8E8A7	Type II restriction-modification system activator	SO_A0002	2.024
Q8E8C4	TonB-dependent siderophore receptor	SO_4743	16.154
Q8E8D7	Der GTPase-activating protein YihI	yihI	6.859
Q8E8E6	ABC-type tungstate uptake system substrate-binding component TupA	tupA	2.509
Q8E8J2	Thiosulfate sulfurtransferase GlpE	glpE	4.032
Q8E8J8	Diheme cytochrome c4 CytcB	cytcB	2.066
Q8E8L7	Propeptide PepSY amd peptidase M4 domain protein	SO_4646	4.884
Q8E8M3	Antioxidant AhpC/Tsa family	SO_4640	5.054
Q8E8P2	Fe/S biogenesis protein NfuA	nfuA	5.761
Q8E8Q8	LexA repressor	lexA	3.515
Q8E8U5	Uncharacterized protein	SO_4561	4.593
Q8E8V5	Predicted periplasmic protein	SO_4551	5.902
Q8E8X7	Iron-responsive TonB-dependent enterobactin receptor IrgA	irgA	15.29

Q8E8Y4	TonB-dependent siderophore receptor	SO_4516	5.536
Q8E8Z5	Uncharacterized protein	SO_4505	3.09
Q8E917	Periplasmic stress-responsive two component signal transduction system histidine kinase CpxA	cpxA	2.608
Q8E924	Predicted periplasmic protein	SO_4470	4.191
Q8E932	Uncharacterized protein	SO_4462	3.851
Q8E943	Molybdopterin synthase sulfur carrier subunit	moaD	2.684
Q8E992	Cytoplasmic rhodanese domain protein	SO_4394	3.647
Q8E9A0	Uncharacterized protein	SO_4384	3.005
Q8E9A8	Uncharacterized protein	SO_4376	2.434
Q8E9E3	Uncharacterized protein	SO_4341	2.106
Q8E9F5	Uncharacterized protein	SO_4329	3.321
Q8E9H3	Putative lipoprotein	SO_4310	2.517
Q8E9H5	Diaminopimelate epimerase	dapF	2.835
Q8E9M0	Deoxyuridine 5'-triphosphate nucleotidohydrolase	dut	3.566
Q8E9M4	50S ribosomal protein L33	rpmG	2.671
Q8E9N2	2-isopropylmalate synthase	leuA	3.88
Q8E9Q1	Cell division protein FtsZ	ftsZ	2.411
Q8E9R1	Putative periplasmic protein in twin arginine protein translocase system locus	SO_4205	2.359
Q8E9R4	Sec-independent protein translocase protein TatA	tatA	2.083
Q8E9R9	Regulator of ribonuclease activity A	rraA	2.454
Q8E9X1	Oxidoreductase short-chain dehydrogenase/reductase family	SO_4141	2.621
Q8E9X4	Putative periplasmic protein	SO_4138	2.139
Q8E9X8	Uncharacterized protein	SO_4134	5.139
Q8E9Z0	50S ribosomal protein L31	rpmE	4.648
Q8E9Z6	MSHA biogenesis protein MshK	mshK	2.289
Q8EA14	Maf-like protein SO_4095	SO_4095	2.192
Q8EA30	UPF0307 protein SO_4079	SO_4079	3.672
Q8EA32	TonB-dependent receptor	SO_4077	3.435
Q8EA39	Periplasmic protein associated with oxidative stress YggE	yggE	2.705
Q8EA52	Met repressor	metJ	3.877
Q8EA67	Hydratase/decarboxylase family protein	SO_4042	2.443
Q8EA81	Single-stranded DNA-binding protein	ssb	3.761
Q8EA90	Putative lipoprotein	SO_4018	2.499
Q8EA93	HAE1 family effllux pump MFP component	SO_4015	2.668
Q8EAE3	Phosphotransferase system (PTS) sugar-specific IIA component PtsN	ptsN	2.576
Q8EAE7	Lipopolysaccharide export system protein LptA	lptA	4.034
Q8EAG0	Periplasmic serine endoprotease DegP-like	degQ	4.011
Q8EAH2	30S ribosomal protein S6	rpsF	3.15

Q8EAI8	TonB-dependent siderophore receptor	SO_3914	11.222
Q8EAI9	PKHD-type hydroxylase SO_3913	SO_3913	2.992
Q8EAJ5	Cytochrome oxidase copper metallochaperone	SO_3907	3.93
Q8EAL4	UPF0339 protein SO_3888	SO_3888	2.051
Q8EAQ4	Secreted low complexity protein	SO_3842	3.075
Q8EAT0	Peptidyl-prolyl cis-trans isomerase	ppiA	2.008
Q8EAW4	DNA binding domain-containing protein	SO_3777	8.054
Q8EAX4	Uncharacterized protein	SO_3767	2.284
Q8EAX6	PspA/IM30 family protein	SO_3765	2.822
Q8EB31	Uncharacterized protein	SO_3704	7.57
Q8EB37	Putative periplasmic protein	SO_3698	4.572
Q8EB43	ABC-type macrolide family export system ATPase component	SO_3692	2.592
Q8EB58	Uncharacterized protein	SO_3676	3.334
Q8EB59	Hemin import ATP-binding protein HmuV	hmuV	10.833
Q8EB61	ABC-type hemin uptake system substrate-binding component HmuB	hmuB	17.014
Q8EB63	TonB1 energy transduction system for heme uptake inner membrane component ExbB	exbB	8.129
Q8EB65	TonB-dependent heme/hemoglobin receptor HmuA	hmuA	14.243
Q8EB66	Heme iron utilization protein HmuX	hmuX	17.735
Q8EB67	FMN binding heme iron utilization protein HmuZ	hmuZ	22.592
Q8EB76	Uncharacterized protein	SO_3656	3.369
Q8EB81	50S ribosomal protein L27	rpmA	2.562
Q8EB86	Dihydrofolate reductase	folA	2.82
Q8EB87	Uncharacterized protein	SO_3645	2.763
Q8EBA1	NADH-dependent hydroxypyruvate reductase HprA	hprA	2.249
Q8EBA8	Periplasmic RmlC-type Cupin domain family protein	SO_3622	4.396
Q8EBC9	Uncharacterized protein	SO_3596	2.609
Q8EBD4	Predicted periplasmic protein	SO_3591	3.28
Q8EBE0	NADPH-dependent azoreductase Azr	azr	2.38
Q8EBE7	Predicted periplasmic protein	SO_3576	4.068
Q8EBG4	N5-carboxyaminoimidazole ribonucleotide mutase	purE	3.215
Q8EBH3	Outer membrane porin	SO_3545	2.523
Q8EBJ1	Type IV pili system adhesin PilY	pilY	2.236
Q8EBJ3	Type IV pilin system protein	SO_3523	3.168
Q8EBM7	HAE1 family efflux pump MFP component	SO_3483	2.303
Q8EBR2	2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase	ispD	2.233
Q8EBR5	5'-nucleotidase SurE	surE	3.035
Q8EBR6	Protein-L-isoaspartate O-methyltransferase	pcm	2.524
Q8EBS0	Protein RecA	recA	2.805
Q8EBS7	Ribosomal associated cold shock response protein YfiA	yfiA	3.265

Q8EBS9	Monoheme cytochrome c	SO_3420	2.692
Q8EBU2	Putative siderophore transporter component 2	SO_3407	8.198
Q8EBV0	Uncharacterized protein	SO_3395	2.723
Q8EBV8	Uncharacterized protein	SO_3387	4.362
Q8EBX5	UPF0312 protein SO_3370	SO_3370	3.074
Q8EBX6	Probable Fe(2+)-trafficking protein	SO_3369	2.737
Q8EBY7	dITP/XTP pyrophosphatase	SO_3358	2.521
Q8EBY9	UPF0235 protein SO_3356	SO_3356	3.511
Q8EBZ6	Glutathione peroxidase	SO_3349	2.758
Q8EBZ9	UPF0301 protein SO_3346	SO_3346	5.141
Q8EC00	Translation initiation factor protein YciH	yciH	3.789
Q8EC34	Membrane anchored protein with DUF2133 domain	SO_3310	2.304
Q8EC53	tRNA-specific adenosine deaminase	tadA	2.071
Q8EC89	Secretion chaperone for FlgK and FlgL FlgN	flgN	3.554
Q8EC90	Flagellar biosynthesis anti-sigma factor FlgM	flgM	4.727
Q8EC94	Flagellar basal body rod protein FlgB	flgB	2.368
Q8EC95	Flagellar basal-body rod protein FlgC	flgC	2.962
Q8EC96	Basal-body rod modification protein FlgD	flgD	3.876
Q8EC97	Flagellar hook protein FlgE	flgE	4.981
Q8EC99	Flagellar basal-body rod protein FlgF	flgF	4.269
Q8ECA0	Flagellar basal-body rod protein FlgG	flgG	4.097
Q8ECA2	Flagellar P-ring protein	flgI	2.081
Q8ECA3	Flagellar rod cap protein and peptidoglycan hydrolase FlgJ	flgJ	2.614
Q8ECA4	Flagellar hook-associated protein FlgL	flgL	4.002
Q8ECA5	Flagellin	fliC	5.229
Q8ECA6	Flagellin	fliC	4.272
Q8ECA7	Uncharacterized flagella locus protein FlaG	flaG	5.691
Q8ECA8	Flagellar hook-associated protein 2	fliD	3.449
Q8ECA9	Flagella biosynthesis chaperone for FliD FliT	fliT	2.559
Q8ECB2	Two component signal transduction system controlling flagellar biosynthesis histidine kinase with PAS sensory domain FlrB	flrB	2.856
Q8ECB4	Flagellar hook-basal body complex protein FliE	fliE	2.193
Q8ECC0	Flagellar hook-length control protein FliK	fliK	4.404
Q8ECC3	Flagellar motor switch protein FliN	fliN	2.349
Q8ECD7	Chemotaxis response regulator protein-glutamate methylesterase of group 1 operon	cheB1	2.088
Q8ECH6	Toxin-antitoxin system toxin HepN family	SO_3166	3.633
Q8ECI4	Uncharacterized protein	wbfC	2.039
Q8ECL1	Methylated-DNA--protein-cysteine methyltransferase	ogt	2.262
Q8ECL8	Uncharacterized protein	SO_3119	2.859

Q8ECN1	Periplasmic rhodanese domain protein	SO_3105	2.288
Q8ECP1	TPR domain protein in aerotolerance operon BatB	batB	8.363
Q8ECQ0	Predicted periplasmic protein	SO_3085	2.493
Q8ECQ8	RNA methyltransferase TrmH family	SO_3075	2.007
Q8ECS1	DNA topoisomerase 3	topB	2.294
Q8ECT3	Aldehyde oxidase / xanthine dehydrogenase family FeS subunit	SO_3049	4.253
Q8ECT7	Exodeoxyribonuclease III Xth	xth	2.01
Q8ECT8	Uncharacterized protein	yciL	5.18
Q8ECT9	Ferric putrebactin reductase PutB	putB	7.957
Q8ECU0	TonB-dependent ferric putrebactin siderophore receptor PutA	putA	8.767
Q8ECU1	NTP-dependent putrebactin synthetase PubC	pubC	13.753
Q8ECU2	N-hydroxyputrescine-succinyl CoA transferase PubB	pubB	14.99
Q8ECU3	Putrescine monooxygenase PubA	pubA	9.605
Q8ECU8	Periplasmic siderophore cleavage esterase IroE family	SO_3025	13.018
Q8ECV7	RNA binding protein YciO	yciO	2.169
Q8ED42	Multifunctional thioesterase/protease/lysophospholipase L1 TesA	tesA	3.413
Q8ED43	Putative ABC-type fatty acid export system ATPase component YbbA	ybbA	2.362
Q8ED72	UPF0178 protein SO_2894	SO_2894	2.834
Q8ED73	Base-induced periplasmic protein YceI	yceI	2.316
Q8ED84	Glutaredoxin	grxD	3.532
Q8EDA2	Thiol:disulfide interchange protein	SO_2860	3.537
Q8EDB4	Putative periplasmic protein	SO_2848	5.475
Q8EDC7	Uncharacterized protein	SO_2835	5.186
Q8EDD0	Uncharacterized protein	SO_2832	2.286
Q8EDD1	GTP cyclohydrolase-2	ribA	2.342
Q8EDF2	UPF0434 protein SO_2800	SO_2800	4.438
Q8EDG5	Cold shock protein CspA	cspA	4.024
Q8EDG9	50S ribosomal protein L32	rpmF	3.495
Q8EDH4	Acyl carrier protein	acpP	2.909
Q8EDI6	Haloacid dehalogenase subfamily IIA associated with N-acetylglucosamine degradation NagD	nagD	3.02
Q8EDK0	Cell division coordinator CpoB	ybgF	3.366
Q8EDK1	Glutaredoxin GrxA	grxA	2.835
Q8EDK6	Biotin synthase	bioB	2.343
Q8EDK8	Malonyl-[acyl-carrier protein] O-methyltransferase	bioC	2.27
Q8EDM0	Purine nucleoside phosphoramidase HinT	hinT	5.382
Q8EDP9	Mu phage tail tube protein GpM	gpM	4.471
Q8EDQ5	Mu phage uncharacterized protein	SO_2688	4.241
Q8EDQ8	Mu phage major head subunit GpT	gpT	6.017
Q8EDQ9	Mu phage protease GpI	gpI	6.701

Q8EDR0	Mu phage uncharacterized protein	SO_2683	5.724
Q8EDR1	Mu phage uncharacterized protein	SO_2682	3.789
Q8EDS7	Mu phage uncharacterized protein	SO_2666	2.884
Q8EDU1	Mu phage transcriptional regulator Cro/CI family C	C	2.059
Q8EDV6	Uncharacterized protein	SO_2637	2.789
Q8EDW3	DNA-binding cold shock protein CspD	cspD	2.096
Q8EDW6	Translation initiation factor IF-1	infA	3.136
Q8EDW9	Outer membrane protein SlyB-like protein	SO_2622	2.107
Q8EDY6	UV induced SOS regulon protein YebG	yebG	4.508
Q8EE07	Methyltransferase	SO_2583	2.435
Q8EE12	Cell division topological specificity factor	minE	2.644
Q8EE15	YcgL domain-containing protein SO_2575	SO_2575	2.215
Q8EE30	Ribonuclease HI	rnhA	2.805
Q8EE77	Electron transport complex subunit G	rnfG	2.038
Q8EE79	Electron transport complex subunit C	rnfC	3.348
Q8EEA1	Bifunctional 4-hydroxy-2-oxoglutarate aldolase/2-dehydro-3-deoxy-phosphogluconate aldolase Eda	eda	3.086
Q8EEA8	Uncharacterized protein	SO_2479	2.435
Q8EEF0	Probable transcriptional regulatory protein SO_2432	SO_2432	2.073
Q8EEF1	Crossover junction endodeoxyribonuclease RuvC	ruvC	3.539
Q8EEF6	Two component signal transduction system response regulator	SO_2426	9.812
Q8EEG0	Uncharacterized protein	SO_2422	3.381
Q8EEG5	Ferredoxin cofactor maintenance protein YfaE	yfaE	4.078
Q8EEJ3	Beta-lactamase	ampC	3.237
Q8EEM5	Uncharacterized protein	SO_2353	2.533
Q8EEP6	Ribbon-helix-helix protein repressor CopG family YbfE	ybfE	2.541
Q8EER2	Outer-membrane lipoprotein carrier protein	lolA	4.065
Q8EER7	50S ribosomal protein L35	rpmI	2.93
Q8EER8	Translation initiation factor IF-3	infC	3.15
Q8EES1	Uncharacterized protein	SO_2297	2.351
Q8EEU4	Ferredoxin 2Fe-2S type ISC system Fdx	fdx	2.574
Q8EEU8	Iron-sulfur cluster assembly scaffold protein IscU	iscU	5.848
Q8EEV0	HTH-type transcriptional regulator IscR	iscR	2.484
Q8EEV5	Lipoprotein-releasing system ATP-binding protein LolD	lolD	2.349
Q8EEX5	Phosphotransferase system (PTS) glucose-specific IIA component Crr	crr	3.251
Q8EF04	Uncharacterized protein	SO_2201	4.418
Q8EF22	Periplasmic metalloprotease M23B family	SO_2180	5.019
Q8EF55	Aldehyde-alcohol dehydrogenase	adhE	2.156
Q8EF71	Bifunctional isoaspartyl dipeptidase / l-asparaginase IaaA	iaaA	2.21
Q8EF74	50S ribosomal protein L25	rplY	2.072

Q8EFB5	1-(5-phosphoribosyl)-5-[(5-phosphoribosylamino)methylideneamino] imidazole-4-carboxamide isomerase	hisA	2.31
Q8EFC0	Outer membrane lipoprotein	SO_2063	2.641
Q8EFC1	Uncharacterized protein	SO_2062	8.022
Q8EFF5	Adenylate kinase	adk	3.034
Q8EFK3	Putative periplasmic protein	SO_1968	3.55
Q8EFL0	Maltose O-acetyltransferase Maa	maa	3.447
Q8EFP9	Uncharacterized protein	SO_1921	4.708
Q8EFT9	Thioredoxin-dependent thiol peroxidase Bcp	bcp	2.884
Q8EFV2	Histone-like DNA-binding protein	SO_1863	3.651
Q8EFW0	Ribosome modulation factor	rmf	7.22
Q8EFW5	DnaJ domain protein	SO_1850	4.667
Q8EFW6	Uncharacterized protein	SO_1849	2.153
Q8EFX9	Uncharacterized protein	SO_1836	3.83
Q8EFY0	S4 RNA-binding domain protein	SO_1835	4.165
Q8EFY2	Peptidyl-prolyl cis-trans isomerase PpiC	ppiC	4.829
Q8EFZ0	TonB2 energy transduction system periplasmic component	SO_1824	2.004
Q8EFZ8	UPF0319 protein SO_1816	SO_1816	2.776
Q8EG16	Histone-like DNA-binding protein HupB	hupB	2.41
Q8EG28	Ferrous iron transport protein B	feoB	4.213
Q8EG29	Ferrous iron transport protein A FeoA	feoA	11.336
Q8EG52	Transcription activator-like effector binding domain protein	SO_1757	5.282
Q8EG53	Glyoxalase family protein	SO_1756	12.463
Q8EG54	Phosphoglucomutase/phosphomannomutase family protein	SO_1755	3.29
Q8EG70	HNH endonuclease	SO_1738	2.519
Q8EGA4	Uncharacterized protein	SO_1701	2.122
Q8EGA5	Putative lipoprotein	SO_1700	4.706
Q8EGA7	Autocatalytic aspartic peptidase	SO_1698	4.053
Q8EGE2	Uncharacterized protein	SO_1662	2.565
Q8EGF6	Cold shock protein Csp family	SO_1648	4.627
Q8EGG5	UDP-3-O-acylglucosamine N-acyltransferase	lpxD	2.108
Q8EGG6	Periplasmic chaperone for outer membrane proteins Skp	skp	3.887
Q8EGH2	Ribosome-recycling factor	frr	2.678
Q8EGH5	30S ribosomal protein S2	rpsB	2.326
Q8EGJ1	Uncharacterized protein	SO_1611	2.368
Q8EGL1	Uncharacterized protein	SO_1590	2.122
Q8EGL3	Uncharacterized protein	SO_1588	6.331
Q8EGM0	TonB-dependent haem/haemoglobin receptor	SO_1580	2.373
Q8EGM8	Small highly charged protein	SO_1572	7.895
Q8EGN2	Outer membrane protein YfaZ	yfaZ	2.772

Q8EGN9	ABC-type phosphate uptake system substrate-binding component PstS	pstS	2.309
Q8EGS0	Protein GrpE	grpE	2.619
Q8EGV7	Isocitrate lyase AceA	aceA	2.131
Q8EGV9	TonB-dependent receptor	SO_1482	13.102
Q8EGW2	Uncharacterized protein	SO_1479	3.932
Q8EGW6	UPF0125 protein SO_1475	SO_1475	3.216
Q8EGZ2	Transcriptional regulator CopG family	SO_1445	2.377
Q8EH21	Periplasmic RmlC-type Cupin domain family protein	SO_1410	2.482
Q8EH24	Hg(II) uptake system substrate-binding component MerP family	SO_1407	3.231
Q8EH34	Cytosine deaminase	SO_1397	3.502
Q8EH52	Peptidase family 56	SO_1378	7.236
Q8EH70	50S ribosomal protein L19	rplS	2.842
Q8EH86	Anti-sigma-E factor RseA	rseA	2.456
Q8EH92	Predicted periplasmic protein	SO_1337	3.028
Q8EHB2	Predicted periplasmic protein	SO_1317	3.473
Q8EHC2	Uncharacterized protein	SO_1306	3.171
Q8EHC4	Iron-sulfur cluster insertion protein ErpA	erpA	7.297
Q8EHC9	T2aSS secretion system protein B GspB	gspB	2.332
Q8EHD7	30S ribosomal protein S21	rpsU	4.6
Q8EHM8	Transcription elongation factor GreA	greA	2.448
Q8EHM9	Putative periplasmic CbiK superfamily protein	SO_1190	21.269
Q8EHN0	Uncharacterized protein	SO_1189	5.843
Q8EHN1	Inner membrane protein with PepSY TM helix	SO_1188	10.219
Q8EHT9	Cys-tRNA(Pro)/Cys-tRNA(Cys) deacylase	ybaK	2.095
Q8EHY2	GlcNAc-binding protein A	gbpA	8.63
Q8EHZ1	Protein SlyX homolog	slyX	3.23
Q8EHZ2	Peptide deformylase 2	def2	2.203
Q8EI32	NADH-ubiquinone oxidoreductase subunit E NuoE	nuoE	3.24
Q8EI44	Dienelactone hydrolase family protein YghX	yghX	2.108
Q8EI85	Probable cytosol aminopeptidase 1	pepA1	2.292
Q8EI93	Thiol:disulfide interchange protein	dsbC	2.502
Q8EIB0	Fructose-bisphosphate aldolase class II Calvin cycle subtype Fba	fba	2.096
Q8EIC7	Bifunctional MarR family transcriptional regulator/acteyltransferase GNAT family	SO_0916	2.317
Q8EIE7	Pirin family protein	SO_0895	2.852
Q8EIF2	Putative agmatine deiminase	aguA	2.489
Q8EIF3	Uncharacterized protein	SO_0886	3.058
Q8EIG0	Uncharacterized protein	SO_0879	2.882
Q8EIG8	2-amino-4-hydroxy-6-hydroxymethyldihydropteridine pyrophosphokinase FolK	folK	2.316

Q8EIK6	Endonuclease I EndA	endA	2.057
Q8EIL5	Uncharacterized protein	SO_0824	4.657
Q8EIL7	ABC-type macrolide export system secretin component MacC	macC	3.112
Q8EIL9	ABC-type macrolide export systemMFP component MacA	macA	2.115
Q8EIM9	Uncharacterized protein	SO_0808	3.791
Q8EIN2	CBS domain containing protein	SO_0805	2.788
Q8EIN9	TonB-dependent receptor	SO_0798	4.607
Q8EIQ7	Glycine cleavage system H protein	gcvH	2.743
Q8EIR3	5-formyltetrahydrofolate cyclo-ligase	ygfA	2.364
Q8EIR7	NAD dependent epimerase/dehydratase family protein	SO_0768	3.415
Q8EIS7	Predicted periplasmic protein	SO_0758	3.36
Q8EIT0	Uncharacterized protein	SO_0755	3.765
Q8EIT2	Uncharacterized protein	SO_0753	2.691
Q8EIT3	Uncharacterized protein	SO_0752	2.372
Q8EIT5	Phosphoglycerate mutase family protein	SO_0749	3.178
Q8EIT6	Uncharacterized protein	SO_0748	2.192
Q8EIU0	ABC-type Fe3+ uptake system substrate-binding component FbpA	fbpA	6.684
Q8EIU2	ABC-type Fe3+ uptake system ATPase component FbpC	fbpC	2.483
Q8EIU3	Gamma-glutamyltransferase GgtB	ggtB	3.065
Q8EIW1	Predicted secreted protein	SO_0718	2.797
Q8EIY6	Uncharacterized protein	SO_0691	2.375
Q8EJ27	Mu Lambda phage repressor-like DNA binding protein	SO_0646	2.062
Q8EJ36	Toxin-antitoxin system antidote Rhh family	SO_0637	2.415
Q8EJ38	Peptidylprolyl isomerase	ppiC	2.4
Q8EJ43	TonB-dependent copper receptor NosA	nosA	2.183
Q8EJ46	"RNA 2',3'-cyclic phosphodiesterase	ligT	2.541
Q8EJ64	Ubiquinol-cytochrome c reductase iron-sulfur subunit	petA	2.742
Q8EJ69	RNA-binding protein Hfq	hfq	2.514
Q8EJ72	ATPase YjeE	yjeE	2.352
Q8EJ85	Bacterioferritin-associated ferredoxin Bfd	bfd	12.846
Q8EJ86	Thiopurine S-methyltransferase	tpm	2.07
Q8EJ92	Predicted ATPase PhoH family	SO_0576	4.763
Q8EJ95	Uncharacterized protein	SO_0573	4.682
Q8EJA0	Regulator of ribonuclease activity B	rraB	2.726
Q8EJB3	Uncharacterized protein	SO_0554	7.267
Q8EJC4	Uncharacterized protein	SO_0543	4.641
Q8EJD1	Redox-active disulfide protein 2	SO_0536	3.153
Q8EJF2	DUF3012 domain-containing lipoprotein	SO_0515	5.49
Q8EJK7	Alpha-ketoglutarate uptake system substrate-binding component	SO_0456	3.778
Q8EJL4	Iron-regulated inner membrane protein	SO_0449	4.923

Q8EJL9	Zinc/cadmium-responsive efflux pump	SO_0444	2.023
Q8EJM0	Zinc and cadmium (II) responsive transcriptional activator ZntR	zntR	2.393
Q8EJM4	Uncharacterized protein	SO_0439	3.552
Q8EJN3	Uncharacterized protein	SO_0430	7.11
Q8EJQ1	DNA gyrase inhibitor YacG	yacG	5.737
Q8EJQ6	Thioredoxin	trxA	3.13
Q8EJR1	Zinc-type alcohol dehydrogenase-like protein	SO_0401	3.432
Q8EJU7	DNA-directed RNA polymerase subunit omega	rpoZ	3.326
Q8EJU9	Endoribonuclease L-PSP	SO_0358	2.616
Q8EJX1	Cell division protein ZapB	zapB	2.73
Q8EJX3	Thiol:disulfide interchange protein	dsbA	3.336
Q8EJY4	Uncharacterized protein	SO_0322	2.293
Q8EJY5	Uncharacterized protein	SO_0321	3.78
Q8EJZ0	Phosphatidylethanolamine-binding protein YbcL	ybcL	4.457
Q8EK05	Ribosomal RNA small subunit methyltransferase I	rsmI	2.259
Q8EK08	Phosphoheptose isomerase	gmhA	2.101
Q8EK34	Cytochrome c-type biogenesis thioredoxin	SO_0269	2.76
Q8EK46	50S ribosomal protein L17	rplQ	3.783
Q8EK49	50S ribosomal protein L36	rpmJ	2.628
Q8EK52	50S ribosomal protein L30	rpmD	2.104
Q8EK53	50S ribosomal protein L18	rplR	2.964
Q8EK55	30S ribosomal protein S8	rpsH	2.212
Q8EK56	30S ribosomal protein S14	rpsN	2.44
Q8EK58	50S ribosomal protein L24	rplX	4.392
Q8EK59	50S ribosomal protein L14	rplN	2.817
Q8EK60	30S ribosomal protein S17	rpsQ	2.53
Q8EK63	50S ribosomal protein L22	rplV	2.65
Q8EK64	30S ribosomal protein S19	rpsS	2.278
Q8EK68	50S ribosomal protein L3	rplC	2.116
Q8EK69	30S ribosomal protein S10	rpsJ	2.329
Q8EK76	50S ribosomal protein L10	rplJ	2.232
Q8EK78	50S ribosomal protein L11	rplK	2.739
Q8EK99	"Selenide, water dikinase	selD	2.048
Q8EKE8	Predicted periplasmic protein	SO_0147	3.427
Q8EKF4	Ferritin	ftn	3.612
Q8EKF8	Uncharacterized protein	SO_0135	2.022
Q8EKH4	Uncharacterized protein	SO_0119	5.785
Q8EKI1	Inhibitor of invertebrate-type lysozyme PliI-like family	SO_0112	3.073
Q8EKI4	SirA family protein YedF	yedF	2.143
Q8EKM7	Molybdenum cofactor biosynthesis protein MogA	mogA	2.762

Q8EKN0	Toxin-antitoxin system antidote	SO_0062	2.906
Q8EKN9	Glycerol-3-phosphate dehydrogenase [NAD(P)+]	gpsA	2.219
Q8EKP0	Protein-export protein SecB	secB	3.754
Q8EKP8	Trimeric LpxA-like enzyme YrdA	yrdA	3.023
Q8EKQ4	Putative DNA topoisomerase YrdD	yrdD	3.252
Q8EKS1	Sulfur carrier protein TusA	tusA	3.372
Q8EKS2	MOSC domain protein	SO_0018	2.455
Q8EKT3	50S ribosomal protein L34	rpmH	3.047
Q8EKT5	Putative membrane protein insertion efficiency factor	SO_0005	2.562
Q8EKT8	Flavodoxin protein MioC	mioC	4.401

Table S2 All the identified quantifiable downregulated proteins (D120Cr(-) vs D120N)

Protein accession	Protein description	Gene name	Ratio
K4PST7	Lambda phage type II DNA modification methyltransferase	SO_2993	0.23
K4PU04	Lambda phage conserved protein	SO_4791	0.167
K4PW17	Uncharacterized protein	SO_4805	0.438
P59188	Protein FdhE homolog	fdhE	0.205
P83223	Fumarate reductase flavoprotein subunit	SO_0970	0.171
Q8CMC8	ISSod9 nucleotidyltransferase domain protein	SO_A0017	0.394
Q8CMJ0	Putative surface lipoprotein	SO_A0112	0.156
Q8CVD4	Extracellular iron oxide respiratory system outer membrane component MtrB	mtrB	0.11
Q8E815	Outer membrane morn variant repeat-containing protein	SO_A0141	0.475
Q8E817	Uncharacterized protein	SO_A0139	0.123
Q8E832	Outer membrane protein OmpA family	SO_A0114	0.179
Q8E833	Putative surface lipoprotein	SO_A0110	0.233
Q8E840	Periplasmic metal-dependent aminohydrolase family protein	SO_A0100	0.358
Q8E874	ABC-type bacteriocin export system multifunctional permease/ATPase/protease component	SO_A0049	0.281
Q8E875	Periplasmic prolyl oligopeptidase family protein	SO_A0048	0.183
Q8E881	Uncharacterized protein	SO_A0042	0.094
Q8E8J8	Diheme cytochrome c4 CytcB	cytcB	0.417
Q8E8K8	Sulfate/thiosulfate import ATP-binding protein CysA 2	cysA2	0.202
Q8E8L1	ABC-type sulfate/thiosulfate uptakesystem substrate-binding subunit Sbp	sbp	0.157
Q8E8S0	Cytochrome c-type protein	cymA	0.329
Q8E8T2	o-succinylbenzoate synthase	menC	0.439
Q8E944	Molybdenum cofactor biosynthesis protein E MoaE	moaE	0.303

Q8E961	Two component signal transduction system response regulator OmpR family	SO_4428	0.261
Q8E966	Subfamily M23B unassigned peptidase	SO_4420	0.425
Q8E9A0	Uncharacterized protein	SO_4384	0.283
Q8E9A6	FAD-binding protein	SO_4378	0.488
Q8E9F1	Uncharacterized protein	SO_4333	0.334
Q8E9G2	Pal-like T1SS-linked outer membrane lipoprotein	SO_4321	0.274
Q8E9G3	Type I protein secretion system secretin component AggA	aggA	0.193
Q8E9G6	Biofilm-promoting protein BpfA	bpfA	0.316
Q8E9L8	Subfamily S9C unassigned peptidase	SO_4252	0.19
Q8E9R1	Putative periplasmic protein in twin arginine protein translocase system locus	SO_4205	0.482
Q8E9X3	TPR repeat protein	SO_4139	0.173
Q8E9X4	Putative periplasmic protein	SO_4138	0.438
Q8E9Z6	MSHA biogenesis protein MshK	mshK	0.45
Q8EA32	TonB-dependent receptor	SO_4077	0.432
Q8EA61	Diheme cytochrome c4	SO_4048	0.191
Q8EA62	SoxA-like diheme cytochrome c	SO_4047	0.279
Q8EA66	TonB mediated energy transduction system energy transducer component TonB	tonB	0.31
Q8EAA5	Metal dependent phosphohydrolase with response regulator receiver modulation	SO_4003	0.444
Q8EAL4	UPF0339 protein SO_3888	SO_3888	0.428
Q8EAN3	Molybdenum import ATP-binding protein ModC	modC	0.153
Q8EAN5	ABC-type molybdate uptake system substrate-binding component ModA	modA	0.134
Q8EAP1	Uncharacterized protein	SO_3856	0.157
Q8EAP2	NAD-dependent malic enzyme	maeA	0.135
Q8EAQ4	Secreted low complexity protein	SO_3842	0.363
Q8EAV5	Uncharacterized protein	SO_3786	0.155
Q8EAW6	Uncharacterized protein	SO_3775	0.463
Q8EAX6	PspA/IM30 family protein	SO_3765	0.479
Q8EAY9	LD-transpeptidase YbiS	ybiS	0.233
Q8EAZ9	Sulfite reductase [NADPH] flavoprotein alpha-component	cysJ	0.214
Q8EB00	Sulfite reductase [NADPH] hemoprotein beta-component	cysI	0.198
Q8EB01	Phosphoadenosine phosphosulfate reductase	cysH	0.258
Q8EB04	Putative periplasmic protein	SO_3733	0.452
Q8EB08	Uroporphyrin-III C-methyltransferase CysG	cysG	0.474
Q8EB09	Sulfate adenylyltransferase subunit 2	cysD	0.303
Q8EB10	Sulfate adenylyltransferase subunit 1	cysN	0.292
Q8EB13	Adenylyl-sulfate kinase	cysC	0.252
Q8EB39	Predicted periplasmic protein	SO_3696	0.432

Q8EBC3	Sulfate/thiosulfate import ATP-binding protein CysA 1	cysA1	0.165
Q8EBC6	ABC-type sulfate/thiosulfate uptake system substrate-binding component CysP	cysP	0.159
Q8EBH3	Outer membrane porin	SO_3545	0.498
Q8EBH4	D-xylulose 5-phosphate/D-fructose 6-phosphate phosphoketolase Xfp	xfp	0.115
Q8EBM7	HAE1 family efflux pump MFP component	SO_3483	0.329
Q8EBS9	Monoheme cytochrome c	SO_3420	0.167
Q8EBV0	Uncharacterized protein	SO_3395	0.448
Q8EC45	Phenylalanine/histidine ammonia-lyase family protein	SO_3299	0.247
Q8EC73	Bifunctional UDP GlcNAc C6 dehydratase/C5 epimerase PseB	pseB	0.466
Q8ECA6	Flagellin	fliC	0.383
Q8ECE8	Transcription antitermination protein RfaH	rfaH	0.313
Q8ECE9	Outer membrane polysaccharide export channel protein Wza	wza	0.446
Q8ECF1	Polysaccharide chain length determinant Wzz	wzz	0.317
Q8ECF2	UDP-N-acetyl-d-glucosamine 6-dehydrogenase WbpA	wbpA	0.329
Q8ECF3	UDP-GlkcNAc C4 epimerase WbpP	wbpP	0.323
Q8ECF4	"dTDP-glucose-4,6-dehydratase RfbB	rfbB	0.284
Q8ECF6	Glucose-1-phosphate thymidylyltransferase	rmlA	0.239
Q8ECF7	Enzyme for biosynthesis of dTDP-Qui4N	SO_3185	0.269
Q8ECF9	Perosamine synthetase-related protein	SO_3183	0.49
Q8ECG4	Polysaccharide deacetylase	SO_3178	0.229
Q8ECG5	Formyltransferase domain protein	SO_3177	0.295
Q8ECG6	O-antigen biosynthesis glycosyl transferase family 4	SO_3176	0.41
Q8ECG7	Asparagine synthase glutamine-hydrolyzing WbpQ	wbpQ	0.367
Q8ECG8	O-antigen biosynthesis glycosyl transferase family 4	SO_3174	0.373
Q8ECH0	Galactosyl transferase WbfU	wbfU	0.429
Q8ECH1	Polysaccharide biosynthesis protein epimerase/dehydratase-like WbfY	wbfY	0.43
Q8ECM8	Bifunctional 13-dimethyluroporphyrinogen III dehydrogenase/siroheme ferrochelatase	SO_3108	0.409
Q8ECX1	Lambda phage uncharacterized protein	SO_3001	0.339
Q8ECX9	Uncharacterized protein	SO_2992	0.137
Q8ECY0	Lambda phage lipoprotein	SO_2991	0.106
Q8ECY1	Lambda phage lytic gene repressor CI	cI	0.179
Q8ECY2	Lambda phage transcriptional repressor of early genes Cro	cro	0.267
Q8ECY3	Lambda phage phage regulatory protein CII	cII	0.19
Q8ED08	Lambda phage major capsid protein	SO_2963	0.278
Q8ED29	Lambda phage transcriptional regulator	SO_2942	0.218
Q8ED33	Lambda phage encoded lipoprotein	SO_2938	0.152
Q8ED64	Cysteine synthase	cysK	0.336
Q8EDC0	Subfamily M23B unassigned peptidase	SO_2842	0.294

Q8EDI5	Nucleotide-binding protein with a TIR-like domain	SO_2763	0.434
Q8EDL6	Periplasmic tetraheme cytochrome c CctA	cctA	0.308
Q8EDL8	Transcriptional regulator LuxR family	SO_2725	0.272
Q8EDU1	Mu phage transcriptional regulator Cro/CI family C	C	0.471
Q8EDZ4	Uncharacterized protein	SO_2596	0.281
Q8EE29	Transcriptional regulator LysR family	SO_2561	0.411
Q8EE61	Predicted rhombotail lipoprotein	SO_2529	0.471
Q8EF19	LD-transpeptidase ErfK/YbiS/YcfS/YnhG family	SO_2183	0.317
Q8EF24	Diheme cytochrome c5 peroxidase CcpA	ccpA	0.343
Q8EFK0	AMP-dependent synthetase and ligase family protein	SO_1971	0.379
Q8EFL0	Maltose O-acetyltransferase Maa	maa	0.351
Q8EFV0	ABC-type export system ATPase component	SO_1865	0.278
Q8EFX1	Extracellular nuclease ExeS	exeS	0.363
Q8EG34	Extracellular iron oxide respiratory system surface decaheme cytochrome c component MtrC	mtrC	0.255
Q8EG35	Extracelllular iron oxide respiratory system periplasmic decaheme cytochrome c component MtrA	mtrA	0.335
Q8EG40	Glycerate kinase GarK	garK	0.236
Q8EG46	Streptogramin A acetyl transferase SatA	satA	0.334
Q8EGA7	Autocatalytic aspartic peptidase	SO_1698	0.177
Q8EGM9	Bifunctional DNA-binding protein / oxidoreductase	SO_1571	0.384
Q8EGN9	ABC-type phosphate uptake system substrate-binding component PstS	pstS	0.414
Q8EGV1	Alcohol dehydrogenase II AdhB	adhB	0.145
Q8EGV8	Malate synthase A AceB	aceB	0.469
Q8EGZ6	Putative cytoplasmic protein	SO_1441	0.426
Q8EH02	Extracellular dimethyl sulfoxide/manganese oxide reductase ferredoxin subunit DmsB	dmsB	0.407
Q8EH03	Extracellular dimethyl sulfoxide/manganese oxide reductase molybdopterin-binding subunit DmsA	dmsA	0.473
Q8EH21	Periplasmic RmlC-type Cupin domain family protein	SO_1410	0.451
Q8EH30	RCC1/BLIP-II superfamily protein	SO_1401	0.181
Q8EH34	Cytosine deaminase	SO_1397	0.41
Q8EH53	Putative negative regulator of univalent cation permeability	SO_1377	0.144
Q8EHG3	Adenylosuccinate synthetase	purA	0.482
Q8EHT9	Cys-tRNA(Pro)/Cys-tRNA(Cys) deacylase	ybaK	0.498
Q8EHZ5	Periplasmic alanyl aminopeptidase	SO_1059	0.45
Q8EI48	Outer membrane morn variant repeat-containing protein	SO_1002	0.359
Q8EI56	Uncharacterized protein	SO_0994	0.25
Q8EI90	Acteyltransferase GNAT family	SO_0954	0.295
Q8EIB0	Fructose-bisphosphate aldolase class II Calvin cycle subtype Fba	fba	0.475
Q8EIB1	Phosphoglycerate kinase	pgk	0.382

Q8EIC0	Uncharacterized protein	SO_0923	0.494
Q8EIC5	Acyl-homoserine lactone acylase AaiD	aaiD	0.463
Q8EIC8	Ankyrin domain protein	SO_0915	0.279
Q8EID8	Na(+)-translocating NADH-quinone reductase subunit C	nqrC	0.474
Q8EID9	Na(+)-translocating NADH-quinone reductase subunit B	nqrB	0.37
Q8EIE0	Na(+)-translocating NADH-quinone reductase subunit A	nqrA	0.323
Q8EIH9	Two component signal transduction system response regulator with HD domain	SO_0860	0.467
Q8EIK2	Beta-lactamase	blaA	0.423
Q8EIM5	RCC1/BLIP-II superfamily lipoprotein	SO_0813	0.396
Q8EIM7	Pyrimidine-specific ribonucleoside hydrolase RihA	rihA	0.373
Q8EIM8	Ribokinase	rbsK	0.396
Q8EIS1	Putative periplasmic protein	SO_0764	0.383
Q8EIT5	Phosphoglycerate mutase family protein	SO_0749	0.458
Q8EJ18	Mu phage protein	SO_0655	0.353
Q8EJ43	TonB-dependent copper receptor NosA	nosA	0.335
Q8EJ92	Predicted ATPase PhoH family	SO_0576	0.443
Q8EJ99	Diguanylate cyclase with PAS sensory domain	SO_0569	0.45
Q8EJL8	Putative negative regulator of univalent cation permeability	SO_0445	0.433
Q8EJM5	Oxidoreductase short chain dehydrogenase/reductase family	SO_0438	0.388
Q8EJQ8	Zinc dependent metalloprotease domain lipoprotein	SO_0404	0.467
Q8EJV6	Uncharacterized protein	SO_0350	0.387
Q8EJY1	Protein YchN	ychN	0.491
Q8EJY4	Uncharacterized protein	SO_0322	0.494
Q8EJZ2	Ornithine decarboxylase SpeF	speF	0.154
Q8EJZ3	Putrescine transporter PotE	potE	0.147
Q8EJZ4	Outer membrane porin	SO_0312	0.121
Q8EK21	Type IV pilus secretin PilQ	pilQ	0.31
Q8EK39	Periplasmic monoheme cytochrome c5 ScyA	scyA	0.274
Q8EKB0	Microcystin dependent MdpB family protein	SO_0185	0.481
Q8EKD6	Uncharacterized protein	SO_0159	0.243
Q8EKI3	Zn-dependent protease with chaperone function	SO_0110	0.442
Q8EKI4	SirA family protein YedF	yedF	0.42
Q8EKI6	Sulfur carrier protein FdhD	fdhD	0.416
Q8EKI7	Selenocysteine-specific translation elongation factor SelB	selB	0.407
Q8EKI8	L-seryl-tRNA(Sec) selenium transferase	selA	0.292
Q8EKI9	Nitrate-inducible formate dehydrogenase cytochrome b subunit FdnI	fdnI	0.096
Q8EKJ0	Nitrate-inducible formate dehydrogenase iron-sulfur subunit FdnH	fdnH	0.102
Q8EKJ1	Nitrate-inducible formate dehydrogenase molybdopterin-binding subunit FdnG	fdnG	0.162

Q8EKK2	Uncharacterized protein	SO_0090	0.409
Q8EKL6	Outer membrane morn variant repeat-containing protein	SO_0076	0.415
Q8EKM2	ABC-type sodium efflux system ATPase component NatA	natA	0.494
Q8EKQ7	Peptidoglycan-binding protein	SO_0033	0.346

(D120Cr(+) vs D120N)

Protein accession	Protein description	Gene name	Ratio
K4PST7	Lambda phage type II DNA modification methyltransferase	SO_2993	0.249
K4PU04	Lambda phage conserved protein	SO_4791	0.18
P59188	Protein FdhE homolog	fdhE	0.196
P83223	Fumarate reductase flavoprotein subunit	SO_0970	0.135
Q8CMJ0	Putative surface lipoprotein	SO_A0112	0.197
Q8CVD4	Extracellular iron oxide respiratory system outer membrane component MtrB	mtrB	0.052
Q8E817	Uncharacterized protein	SO_A0139	0.265
Q8E832	Outer membrane protein OmpA family	SO_A0114	0.175
Q8E833	Putative surface lipoprotein	SO_A0110	0.175
Q8E874	ABC-type bacteriocin export system multifunctional permease/ATPase/protease component	SO_A0049	0.297
Q8E875	Periplasmic prolyl oligopeptidase family protein	SO_A0048	0.178
Q8E881	Uncharacterized protein	SO_A0042	0.064
Q8E8D5	Coproporphyrinogen-III oxidase	hemN	0.474
Q8E8K8	Sulfate/thiosulfate import ATP-binding protein CysA 2	cysA2	0.162
Q8E8L1	ABC-type sulfate/thiosulfate uptakesystem substrate-binding subunit Sbp	sbp	0.171
Q8E8S0	Cytochrome c-type protein	cymA	0.172
Q8E8T2	o-succinylbenzoate synthase	menC	0.393
Q8E8Y0	Coproporphyrinogen III oxidase oxygen-independent	SO_4520	0.239
Q8E8Y7	Fnr-inducilble formate dehydrogenase molybdopterin-binding subunit FdhA	fdhA	0.311
Q8E8Y8	Fnr-inducible formate dehydrogenase accessory protein FdhX	fdhX	0.401
Q8E8Z3	Formate dehydrogenase chaperone FdhT	fdhT	0.491
Q8E961	Two component signal transduction system response regulator OmpR family	SO_4428	0.277
Q8E966	Subfamily M23B unassigned peptidase	SO_4420	0.372
Q8E9A6	FAD-binding protein	SO_4378	0.357
Q8E9E4	Putative transport protein with Tim44-like domain	SO_4340	0.445
Q8E9F1	Uncharacterized protein	SO_4333	0.258
Q8E9G0	Bifunctional diguanylate cyclase/phosphodiesterase LasD-like protein	SO_4323	0.488

Q8E9G2	Pal-like T1SS-linked outer membrane lipoprotein	SO_4321	0.17
Q8E9G3	Type I protein secretion system secretin component AggA	aggA	0.146
Q8E9G4	Type I protein secretion system MFP component AggB	aggB	0.495
Q8E9G5	Type I protein secretion system bifunctional ATPase and permease component AggC	aggC	0.453
Q8E9G6	Biofilm-promoting protein BpfA	bpfA	0.21
Q8E9L8	Subfamily S9C unassigned peptidase	SO_4252	0.206
Q8E9X3	TPR repeat protein	SO_4139	0.183
Q8EA61	Diheme cytochrome c4	SO_4048	0.261
Q8EA62	SoxA-like diheme cytochrome c	SO_4047	0.356
Q8EA66	TonB mediated energy transduction system energy transducer component TonB	tonB	0.338
Q8EA86	Periplasmic peptidase family M16B	SO_4022	0.454
Q8EA95	TPR repeat domain protein	SO_4013	0.481
Q8EAA5	Metal dependent phosphohydrolase with response regulator receiver modulation	SO_4003	0.356
Q8EAC7	Cytochrome c-552	nrfA	0.391
Q8EAI4	Periplasmic peptidase subfamily S1B	SO_3918	0.348
Q8EAL0	Uncharacterized protein	SO_3892	0.462
Q8EAN3	Molybdenum import ATP-binding protein ModC	modC	0.184
Q8EAN5	ABC-type molybdate uptake system substrate-binding component ModA	modA	0.115
Q8EAP1	Uncharacterized protein	SO_3856	0.143
Q8EAP2	NAD-dependent malic enzyme	maeA	0.132
Q8EAR3	Peptide chain release factor 1	prfA	0.424
Q8EAV5	Uncharacterized protein	SO_3786	0.153
Q8EAW6	Uncharacterized protein	SO_3775	0.373
Q8EAY9	LD-transpeptidase YbiS	ybiS	0.386
Q8EAZ9	Sulfite reductase [NADPH] flavoprotein alpha-component	cysJ	0.151
Q8EB00	Sulfite reductase [NADPH] hemoprotein beta-component	cysI	0.144
Q8EB01	Phosphoadenosine phosphosulfate reductase	cysH	0.194
Q8EB04	Putative periplasmic protein	SO_3733	0.442
Q8EB09	Sulfate adenylyltransferase subunit 2	cysD	0.246
Q8EB10	Sulfate adenylyltransferase subunit 1	cysN	0.245
Q8EB13	Adenylyl-sulfate kinase	cysC	0.212
Q8EB16	Oxygen-independent protoporphyrinogen oxidase HemG	hemG	0.467
Q8EB30	5-methylthioadenosine nucleosidase/S-adenosylhomocysteine nucleosidase	SO_3705	0.449
Q8EB52	Uncharacterized protein	SO_3682	0.358
Q8EBB7	Formate-dependent phosphoribosylglycinamide formyltransferase	purT	0.46
Q8EBC3	Sulfate/thiosulfate import ATP-binding protein CysA 1	cysA1	0.128

Q8EBC6	ABC-type sulfate/thiosulfate uptake system substrate-binding component CysP	cysP	0.133
Q8EBH4	D-xylulose 5-phosphate/D-fructose 6-phosphate phosphoketolase Xfp	xfp	0.085
Q8EBQ9	CTP synthase	pyrG	0.477
Q8EBS9	Monoheme cytochrome c	SO_3420	0.449
Q8EC05	Small conductance mechanosensitive ion channel protein MscS	mscS	0.428
Q8EC45	Phenylalanine/histidine ammonia-lyase family protein	SO_3299	0.175
Q8EC59	Cytochrome d ubiquinol oxidase subunit II CydB	cydB	0.365
Q8ECE8	Transcription antitermination protein RfaH	rfaH	0.285
Q8ECE9	Outer membrane polysaccharide export channel protein Wza	wza	0.427
Q8ECF1	Polysaccharide chain length determinant Wzz	wzz	0.225
Q8ECF2	UDP-N-acetyl-d-glucosamine 6-dehydrogenase WbpA	wbpA	0.229
Q8ECF3	UDP-GlkcNAc C4 epimerase WbpP	wbpP	0.234
Q8ECF4	"dTDP-glucose-4,6-dehydratase RfbB	rfbB	0.226
Q8ECF6	Glucose-1-phosphate thymidylyltransferase	rmlA	0.14
Q8ECF7	Enzyme for biosynthesis of dTDP-Qui4N	SO_3185	0.268
Q8ECF9	Perosamine synthetase-related protein	SO_3183	0.369
Q8ECG4	Polysaccharide deacetylase	SO_3178	0.207
Q8ECG5	Formyltransferase domain protein	SO_3177	0.279
Q8ECG7	Asparagine synthase glutamine-hydrolyzing WbpQ	wbpQ	0.369
Q8ECG9	NAD-dependent epimerase/dehydratase family protein	SO_3173	0.425
Q8ECM8	Bifunctional 13-dimethyluroporphyrinogen III dehydrogenase/siroheme ferrochelatase	SO_3108	0.409
Q8ECM9	Uncharacterized protein	yaeQ	0.462
Q8ECX1	Lambda phage uncharacterized protein	SO_3001	0.224
Q8ECX9	Uncharacterized protein	SO_2992	0.085
Q8ECY0	Lambda phage lipoprotein	SO_2991	0.118
Q8ECY1	Lambda phage lytic gene repressor CI	cI	0.259
Q8ECY2	Lambda phage transcriptional repressor of early genes Cro	cro	0.327
Q8ECY3	Lambda phage phage regulatory protein CII	cII	0.223
Q8ED08	Lambda phage major capsid protein	SO_2963	0.399
Q8ED29	Lambda phage transcriptional regulator	SO_2942	0.179
Q8ED33	Lambda phage encoded lipoprotein	SO_2938	0.135
Q8ED60	ArgR-regulated TonB-dependent receptor	SO_2907	0.43
Q8ED80	Fatty acid metabolism regulator protein	fadR	0.397
Q8EDC0	Subfamily M23B unassigned peptidase	SO_2842	0.472
Q8EDC8	Anaerobic ribonucleoside-triphosphate reductase NrdD	nrdD	0.26
Q8EDI2	Asparagine synthase glutamine-hydrolyzing AsnB	asnB	0.475
Q8EDK3	Acetyl-coenzyme A synthetase	acsA	0.434
Q8EDL6	Periplasmic tetraheme cytochrome c CctA	cctA	0.273

Q8EDL8	Transcriptional regulator LuxR family	SO_2725	0.331
Q8EDU5	Two component signal transduction system response regulator activating acetyl-CoA synthase LuxR family	SO_2648	0.489
Q8EDZ4	Uncharacterized protein	SO_2596	0.403
Q8EE29	Transcriptional regulator LysR family	SO_2561	0.329
Q8EE61	Predicted rhombotail lipoprotein	SO_2529	0.473
Q8EE92	Smr domain protein	SO_2495	0.423
Q8EEL6	Cbb3-type cytochrome c oxidase subunit II CcoO	ccoO	0.463
Q8EEL8	Cbb3-type cytochrome c oxidase subunit	ccoP	0.402
Q8EF19	LD-transpeptidase ErfK/YbiS/YcfS/YnhG family	SO_2183	0.415
Q8EF24	Diheme cytochrome c5 peroxidase CcpA	ccpA	0.208
Q8EF87	Periplasmic [Ni-Fe] hydrogenase large subunit HyaB	hyaB	0.449
Q8EFF4	Ferrochelatase 1	hemH1	0.256
Q8EFJ2	Ribose phosphate pyrophosphokinase NadR	nadR	0.498
Q8EFK0	AMP-dependent synthetase and ligase family protein	SO_1971	0.344
Q8EFV0	ABC-type export system ATPase component	SO_1865	0.348
Q8EFX1	Extracellular nuclease ExeS	exeS	0.486
Q8EG33	Extracelllular iron oxide respiratory system surface decaheme cytochrome c component OmcA	omcA	0.21
Q8EG34	Extracellular iron oxide respiratory system surface decaheme cytochrome c component MtrC	mtrC	0.152
Q8EG35	Extracelllular iron oxide respiratory system periplasmic decaheme cytochrome c component MtrA	mtrA	0.231
Q8EG40	Glycerate kinase GarK	garK	0.311
Q8EG46	Streptogramin A acetyl transferase SatA	satA	0.385
Q8EG58	ABC-type transport system bifunctional permease and peptidase M1 family component	SO_1751	0.427
Q8EGV1	Alcohol dehydrogenase II AdhB	adhB	0.159
Q8EH02	Extracellular dimethyl sulfoxide/manganese oxide reductase ferredoxin subunit DmsB	dmsB	0.271
Q8EH03	Extracellular dimethyl sulfoxide/manganese oxide reductase molybdopterin-binding subunit DmsA	dmsA	0.259
Q8EH07	Predicted outer membrane lipoprotein	SO_1424	0.483
Q8EH13	FAD:protein FMN transferase	SO_1418	0.367
Q8EH19	Outer membrane beta barrel protein	SO_1412	0.457
Q8EH30	RCC1/BLIP-II superfamily protein	SO_1401	0.194
Q8EH42	Aminopeptidase P AmpP	ampP	0.412
Q8EH53	Putative negative regulator of univalent cation permeability	SO_1377	0.137
Q8EHA4	NADPH-dependent glutamate synthase large subunit GltB	gltB	0.429
Q8EHB9	TonB-dependent receptor	SO_1309	0.395
Q8EHC8	"Glutamate-1-semialdehyde 2,1-aminomutase	hemL	0.487

Q8EHG3	Adenylosuccinate synthetase	purA	0.37
Q8EHH2	Peptidase U32 family YhbU	SO_1249	0.337
Q8EHH3	Peptidase U32 family YhbV	SO_1248	0.417
Q8EHI5	Purine transporter AzgA family	SO_1236	0.319
Q8EHK0	Purine nucleoside phosphorylase DeoD-type 2	deoD2	0.46
Q8EHK2	Phosphopentomutase	deoB	0.287
Q8EHK3	Thymidine phosphorylase	deoA	0.327
Q8EHK4	Deoxyribose-phosphate aldolase	deoC	0.415
Q8EHK6	Nucleoside-specific outer membrane porin OmpK	ompK	0.412
Q8EHS7	4-hydroxy-tetrahydrodipicolinate reductase	dapB	0.429
Q8EHV1	Bacterioferritin	brf2	0.336
Q8EHZ5	Periplasmic alanyl aminopeptidase	SO_1059	0.388
Q8EI56	Uncharacterized protein	SO_0994	0.204
Q8EI78	Fermentative lactate dehydrogenase NADH dependent LdhA	ldhA	0.353
Q8EI90	Acteyltransferase GNAT family	SO_0954	0.32
Q8EI94	Branched-chain amino acid transport system carrier protein	brnQ	0.309
Q8EIA9	Uncharacterized protein	SO_0934	0.448
Q8EIC4	Serine uptake transporter SdaC	sdaC	0.498
Q8EIC8	Ankyrin domain protein	SO_0915	0.219
Q8EID5	Na(+)-translocating NADH-quinone reductase subunit F	nqrF	0.399
Q8EID8	Na(+)-translocating NADH-quinone reductase subunit C	nqrC	0.479
Q8EIE0	Na(+)-translocating NADH-quinone reductase subunit A	nqrA	0.357
Q8EIE2	Oxidoreductase aldo/keto reductase family	SO_0900	0.458
Q8EIH9	Two component signal transduction system response regulator with HD domain	SO_0860	0.396
Q8EIJ1	Periplasmic nitrate reductase	napA	0.348
Q8EIJ6	Transcriptional regulator LysR family	SO_0843	0.348
Q8EIK2	Beta-lactamase	blaA	0.419
Q8EIM5	RCC1/BLIP-II superfamily lipoprotein	SO_0813	0.344
Q8EIN3	Uncharacterized protein	SO_0804	0.491
Q8EIS1	Putative periplasmic protein	SO_0764	0.455
Q8EIW0	TonB-dependent hemoprotein receptor	SO_0719	0.457
Q8EJ18	Mu phage protein	SO_0655	0.334
Q8EJ75	Uncharacterized protein	SO_0595	0.3
Q8EJ87	Zn-binding protein	SO_0581	0.373
Q8EJ93	RNA polymerase-associated protein RapA	rapA	0.477
Q8EJ99	Diguanylate cyclase with PAS sensory domain	SO_0569	0.371
Q8EJA7	Formate--tetrahydrofolate ligase	fhs	0.265
Q8EJM8	Uroporphyrinogen decarboxylase	hemE	0.483
Q8EJQ8	Zinc dependent metalloprotease domain lipoprotein	SO_0404	0.177

Q8EJQ9	Predicted outer membrane protein	SO_0403	0.214
Q8EJR4	Quinol:fumarate reductase FAD-binding subunit FrdA	frdA	0.454
Q8EJV6	Uncharacterized protein	SO_0350	0.278
Q8EJY1	Protein YchN	ychN	0.317
Q8EJZ2	Ornithine decarboxylase SpeF	speF	0.128
Q8EJZ3	Putrescine transporter PotE	potE	0.082
Q8EJZ4	Outer membrane porin	SO_0312	0.072
Q8EK21	Type IV pilus secretin PilQ	pilQ	0.318
Q8EK67	50S ribosomal protein L4	rplD	0.407
Q8EKD6	Uncharacterized protein	SO_0159	0.26
Q8EKI3	Zn-dependent protease with chaperone function	SO_0110	0.469
Q8EKI6	Sulfur carrier protein FdhD	fdhD	0.371
Q8EKI7	Selenocysteine-specific translation elongation factor SelB	selB	0.323
Q8EKI8	L-seryl-tRNA(Sec) selenium transferase	selA	0.373
Q8EKI9	Nitrate-inducible formate dehydrogenase cytochrome b subunit FdnI	fdnI	0.06
Q8EKJ0	Nitrate-inducible formate dehydrogenase iron-sulfur subunit FdnH	fdnH	0.103
Q8EKJ1	Nitrate-inducible formate dehydrogenase molybdopterin-binding subunit FdnG	fdnG	0.141
Q8EKJ7	Imidazolonepropionase	hutI	0.481
Q8EKK2	Uncharacterized protein	SO_0090	0.274
Q8EKR3	Oxygen-independent protoporphyrinogen oxidase HemG	hemG	0.333

(D120Cr(+) vs D120Cr(-))

Protein accession	**Protein description**	**Gene name**	**Ratio**
Q8CVD4	Extracellular iron oxide respiratory system outer membrane component MtrB	mtrB	0.475
Q8E8D5	Coproporphyrinogen-III oxidase	hemN	0.465
Q8E8Y0	Coproporphyrinogen III oxidase oxygen-independent	SO_4520	0.466
Q8E8Y7	Fnr-inducilble formate dehydrogenase molybdopterin-binding subunit FdhA	fdhA	0.432
Q8E8Z3	Formate dehydrogenase chaperone FdhT	fdhT	0.44
Q8E9F7	Transcriptional repressor of multidrug/detergent efflux pump VexR	vexR	0.491
Q8EAC7	Cytochrome c-552	nrfA	0.35
Q8EBF3	"Bifunctional 2',3'-cyclic-nucleotide 2'-phosphodiesterase/3`-nucleotidase CpdB	cpdB	0.437
Q8EBH5	Alanine/glycine:cation symporter (AGCS) family protein	SO_3541	0.385
Q8EBK0	TonB-dependent chitooligosaccharide receptor	SO_3514	0.407
Q8EBK2	SapC family protein	SO_3512	0.466
Q8EBQ9	CTP synthase	pyrG	0.495

Q8EC59	Cytochrome d ubiquinol oxidase subunit II CydB	cydB	0.399
Q8EC62	Energy taxis modulating methyl accepting sensory transducer	SO_3282	0.486
Q8ED60	ArgR-regulated TonB-dependent receptor	SO_2907	0.223
Q8ED80	Fatty acid metabolism regulator protein	fadR	0.323
Q8EDC8	Anaerobic ribonucleoside-triphosphate reductase NrdD	nrdD	0.385
Q8EE60	Peptide deformylase 3	def3	0.479
Q8EEB8	TonB-dependent receptor	SO_2469	0.349
Q8EEF5	ArgR-regulated TonB-dependent receptor	SO_2427	0.453
Q8EEH5	Glycine radical enzyme YjjI family	SO_2407	0.477
Q8EEL5	Cbb3-type cytochrome c oxidase subunit I CcoN	ccoN	0.415
Q8EEW8	Transcriptional repressor of maltodextrose utilization MalR	malR	0.409
Q8EF87	Periplasmic [Ni-Fe] hydrogenase large subunit HyaB	hyaB	0.382
Q8EFE8	Uncharacterized protein	SO_2027	0.442
Q8EFF4	Ferrochelatase 1	hemH1	0.365
Q8EFK8	"Homogentisate 1,2-dioxygenase HmgA	hmgA	0.369
Q8EFK9	4-hydroxyphenylpyruvate dioxygenase HppD	hppD	0.323
Q8EFV9	3-hydroxydecanoyl-[acyl-carrier-protein] dehydratase	fabA	0.482
Q8EG33	Extracelllular iron oxide respiratory system surface decaheme cytochrome c component OmcA	omcA	0.344
Q8EGS2	Lactate transport protein LctP family	SO_1522	0.476
Q8EH39	Short chain fatty acids transporter AtoE	atoE	0.44
Q8EHB9	TonB-dependent receptor	SO_1309	0.21
Q8EHE6	Proton:oligopeptide symporter POT family	SO_1277	0.467
Q8EHH2	Peptidase U32 family YhbU	SO_1249	0.355
Q8EHH3	Peptidase U32 family YhbV	SO_1248	0.38
Q8EHI5	Purine transporter AzgA family	SO_1236	0.431
Q8EHS7	4-hydroxy-tetrahydrodipicolinate reductase	dapB	0.469
Q8EHV0	Bacterioferritin	brf1	0.359
Q8EHV1	Bacterioferritin	brf2	0.174
Q8EI39	NADH-ubiquinone oxidoreductase subunit L NuoL	nuoL	0.492
Q8EI94	Branched-chain amino acid transport system carrier protein	brnQ	0.392
Q8EIC4	Serine uptake transporter SdaC	sdaC	0.352
Q8EIJ1	Periplasmic nitrate reductase	napA	0.265
Q8EIJ3	Quinol dehydrogenase ferredoxin subunit NapH	napH	0.33
Q8EIJ6	Transcriptional regulator LysR family	SO_0843	0.453
Q8EJQ8	Zinc dependent metalloprotease domain lipoprotein	SO_0404	0.38
Q8EJQ9	Predicted outer membrane protein	SO_0403	0.285
Q8EK67	50S ribosomal protein L4	rplD	0.483
Q8EKR3	Oxygen-independent protoporphyrinogen oxidase HemG	hemG	0.496