The Acquisition of Resistance to Carbapenem and Macrolide-mediated Quorum Sensing Inhibition by *Pseudomonas aeruginosa* via a Novel Integrative and Conjugative Element ICE$_{Tn43716385}$

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Abstract

*Pseudomonas aeruginosa* can cause persistant and life-threatening infections in immunocompromised patients. Carbapenems are the first-line agents to treat *P. aeruginosa* infections; therefore, the emergence of carbapenem-resistant *P. aeruginosa* strains has greatly challenged effective antibiotic therapy. In this study, we characterised the full-length genomes of two carbapenem resistant *P. aeruginosa* clinical isolates that produce the carbapebemase New Delhi metallo-β-lactamase-1 (NDM-1). We found that the *blaNDM-1* gene is encoded by a novel intergrative and conjugative element (ICE) ICE*Tn4371*6385, which also carries the macrolide resistance gene *msr(E)* and the florfenicol resistance gene *floR*. The *msr(E)* gene has rarely been described in *P. aeruginosa* genomes. To investigate the functional roles of *msr(E)* in *P. aeruginosa*, we exogeneously expressed this gene in *P. aeruginosa* laboratory strains and found that the acquisition of *msr(E)* could abolish the azithromycin-mediated quorum sensing inhibition *in vitro* and the anti-Pseudomonas effect of azithromycin *in vivo*. In addition, the expression of *msr(E)* almost completely restored the azithromycin-affected *P. aeruginosa* transcriptome, as shown by our RNA sequencing analysis. We present the first evidence of *blaNDM-1* to be carried by intergrative and conjugative elements, and the first evidence of co-transfer of carbapenem resistance and the resistance to macrolide-mediated quorum sensing inhibition into *P. aeruginosa* genomes.

Importance

Carbapenem resistant *P. aeruginosa* has recently been listed as the top three most dangerous superbugs by World Health Organisation. The transmission of *blaNDM-1* gene into *P. aeruginosa* can cause extreme resistance to carbapenems and fourth generation cephalosporins, which greatly compromises the effectiveness of these antibiotics against *Pseudomonas* infections. However, the lack of complete genome sequence of NDM-1-
producing *P. aeruginosa* has limited our understanding of the transmisibility of *blanDM-1* in this organism. Here we showed the co-transfer of *blanDM-1* and *msr(E)* into *P. aeruginosa* genome by a novel integrative and conjugative element (ICE). The acquisition of these two genes confers *P. aeruginosa* with resistance to carbapenem and macrolide-mediated quorum sensing inhibition, both of which are important treatment strategies for *P. aeruginosa* infections. Our findings highlight the potential of ICEs in transmitting carbapenem resistance, and that the anti-virulence treatment of *P. aeruginosa* infections by macrolides can be challenged by horizontal gene transfer.
Introduction

*Pseudomonas aeruginosa* is an opportunistic pathogen which can cause life-threatening infections in immunocompromised patients (1). It is also responsible for nosocomial infections such as chronic wound infections and ventilator-associated pneumonia, and chronic airway infections in cystic fibrosis and chronic obstructive pulmonary disease patients (2-5). These infections are usually very difficult to eradicate and associated with high mortality rates (3, 6). Worse still, *P. aeruginosa* is also notorious for its ability to develop multidrug resistance, which leaves only a handful of antibiotics remain effective to treat its infections in clinical practice (7).

Carbapenems such as imipenem and meropenem are the first-line agents for treating *P. aeruginosa* infections and the last-ressort drugs in severe infections caused by Gram-negative bacteria (8). However, the clinical efficacy of carbapenems has been greatly compromised by the spreading of the carbapebemase New Delhi metallo-β-lactamase-1 (NDM-1), which is usually encoded and transmitted by broad-host self-conjugative plasmids in Enterobacteriacea spp. and *Acinetobacter baumannii* (9). The *blaNDM-1* gene was first described in *P. aeruginosa* in 2011 and has ever since been identified in *P. aeruginosa* isolated from North America, Europe and Asia (10-16). The NDM-1-producing *P. aeruginosa* strains usually have extremely high resistance to carbapenems and many other classes of antibiotics, which makes infections caused by these superbugs even more difficult to treat (10-16). Therefore, it is important to develop novel treatment strategies for *P. aeruginosa* infections.

One alternative strategy for treating *P. aeruginosa* infections is to inhibit the production of virulence factors, which are essential for the pathogenesis of this bacterium. For instance, the type III secretion system and the secreted products such as elastase and exotoxin A have been shown to play important roles during the colonization of *P. aeruginosa* in human airways (17,
In particular the secreted detergent rhamnolipid causes rapid necrosis of the host immune cells and protects bacterial cells from immune attack and facilitate the establishment of infections (19). In *P. aeruginosa*, the expression of many virulence factors is under tight control of its quorum sensing (QS) systems, which can be potential targets for the design of anti-virulence drugs (20, 21). However, although several anti-QS compounds have been identified in the past, none of them has so far entered clinical trial (21-23). On the other hand, the macrolide antibiotics such as erythromycin, azithromycin (AZM) and clarithromycin were shown to have a promising anti-QS activity, which makes them ideal anti-virulence drugs for treating *P. aeruginosa* infections (21). It was suggested that macrolides repress the synthesis of QS signaling molecules by interfering with the signaling pathways of RsmZ and RsmY through yet-to-be identified targets, resulting in the downregulation of the QS-regulated virulence products such as rhamnolipids and elastase in *P. aeruginosa* (24). The use of macrolides as QS inhibitor may therefore expand our antimicrobial arsenal against *P. aeruginosa* infections until new and more efficient anti-virulence drugs become clinically available.

Although NDM-1-producing *P. aeruginosa* strains have been prevalent worldwide, the complete genome information and transmission mechanisms is still lacking (10-16). To improve the understanding of the transmission of *blanDM-1* among *P. aeruginosa* strains, we sequenced the complete genomes of two local clinical NDM-producing *P. aeruginosa* isolates (14). Comparative genomic analysis showed that the *blanDM-1* gene is encoded by a novel Tn4371 family integrative and conjugative element (ICE), which is a class of mobile genetic element present in the genomes of a broad range of β- and γ-proteobacteria (25). In addition to *blanDM-1*, this element also carries the macrolide resistance gene *msr(E)* and the florfenicol resistance gene *floR*. We found that the acquisition of *msr(E)* by *P. aeruginosa* abolished the AZM-mediated QS inhibition *in vitro* and the anti-Pseudomonas effect of AZM
in vivo. To our knowledge, this is the first description of *blaNDM-1* encoded by ICEs and the first evidence on the co-acquisition of carbapenem resistance and the resistance to AZM-mediated QS inhibition by *P. aeruginosa*.

**Results**

**Identification of a novel NDM-1-producing *P. aeruginosa* group**

A nosocomial outbreak of NDM-1-producing *P. aeruginosa* was previously reported in a local Singapore hospital and was the first case report of NDM-1-producing *P. aeruginosa* in Southeast Asia (14). The strains isolated during this outbreak exhibited multidrug resistance to carbapenems, cephalosporins, aminoglycosides, and fluoroquinolones, whereas remained sensitive to polymyxin B (Table S1). To identify the origin of these NDM-1-producing *P. aeruginosa* isolates, we sequenced the draft genomes of 11 isolated strains on an Illumina MiSeq platform and found that all these isolates belong to multilocus sequence type ST308 and have harbored the same sets of antibiotic resistance genes (Fig. S1). In addition, the 12 genomes are highly similar to each other as shown by multiple genome alignment using Progressive Mauve (26) (Fig. S2). These results suggested that the 12 NDM-1-producing *P. aeruginosa* strains isolated in this outbreak belong to the same phylogenetic group. Therefore, we named this closely related *P. aeruginosa* group PASGNDM and selected two representative isolates, PASGNDM345 and PASGNDM699 for further investigation.

To better understand the detailed features of the PASGNDM genomes and the transmission of *blaNDM-1* into *P. aeruginosa* genome, we further sequenced PASGNDM345 and PASGNDM699 genomes on a Pacific Biosciences RSII platform. The PacBio sequencing reads have achieved 163- and 161-fold coverage for PASGNDM345 and PASGNDM699 genomes, respectively, and were successfully assembled into two full-length genomes. Construction of a phylogenetic tree using PASGNDM345 and PASGNDM699 genomes
together with other 21 *P. aeruginosa* full-length genomes showed that the two PASGNDM strains formed a monophyletic group (Fig. 1). Interestingly, the closest genome to the PASGNDM group in the phylogenetic tree is PA_D1 (NZ_CP012585.1), which is an endemic *P. aeruginosa* strain causing ventilator-associated pneumonia in China as identified in previous work by us (manuscript submitted).

**Characterisation of PASGNDM345 and PASGNDM699 genomes**

The genome of PASGNDM345 consists of a circular chromosome of 6,893,164 bp with an average GC content of 66.1%, whereas the PASGNDM699 genome is 6,985,102 bp with an average GC content of 66.0%. In total, 6,503 and 6,589 genes were predicted from PASGNDM345 and PASGNDM699 genomes, respectively. General features of these predicted genes can be found in Table S2.

To identify the strain specific genomic regions in the PASGNDM genomes, the complete genomes of PASGNDM699 and PASGNDM345 were compared with six other strains clustered in the same clade in the phylogenetic tree (Fig. 1). Genome alignment result showed that the two PASGNDM genomes possess several regions with low sequence identity to the other six strains (Fig. 2). Furthermore, we also predicted the genomic islands (GIs) in the two PASGNDM genomes using Island Viewer 3 server (27). A total of 41 and 47 GIs were predicted from the PASGNDM345 and PASGNDM699 genomes, respectively, which correlate well with the strain specific regions in the PASGNDM genome (Fig. 2 and Table S3, S4). The genes located in the GIs are mostly enriched in generating transposons, efflux pumps and multidrug resistance (Table S3, S4), which may be important for the survival and nosocomial spread of the PASGNDM strains. In addition, eight acquired antibiotic resistance genes including *bla*\_NDM-1 are embedded in the GIs of PASGNDM699 and PASGNDM345 genomes (Fig. 2), suggesting the importance of mobile genetic elements in the acquisition of antibiotic resistance by the PASGNDM isolates.
Identification of a novel ICE\textsubscript{Tn4371}6385 encoding \textit{bla\textsubscript{NDM-1}}, \textit{msr(E)} and \textit{floR}

It was noted that the \textit{bla\textsubscript{NDM-1}} is clustered together with \textit{msr(E)} and \textit{floR} in a GI region, suggesting the three antibiotic resistance genes might be co-transferred into the PASGNDM genomes (Fig. 2). Further sequence analysis revealed that the three genes are embedded in a 74.2 kb ICE-like element located between the \textit{exoY} (PA2191) and \textit{henA} (PA2193) genes in the PASGNDM345 and PASGNDM699 genomes (Fig. 3). Both ends of this element are flanked by a 5’-TTTTTTGT-3’ sequence, which resembles the conserved \textit{attB} site of almost all Tn4371 family ICEs (25). It also contains the core genes conserved among the Tn4371 family ICEs, including a \textit{int} integrase gene, the \textit{parB}, \textit{repA} and \textit{parA} genes of the ICE stabilisation system, and homologues to the DNA conjugative transfer machineries such as \textit{traI} and \textit{traG} (25) (Fig. 3). In addition, the integrase encoded by the \textit{int} gene shared 71% identity with Int\textsubscript{Tn4371} (AJ536756), which further proved that the ICE identified here should be considered as a member of the Tn4371 family, as suggested by a previous study (25). We therefore named this element ICE\textsubscript{Tn4371}6385 following the nomenclature system proposed by Roberts \textit{et al.} (28).

To track the origin of ICE\textsubscript{Tn4371}6385, we searched its entire sequence against Genbank and found that ICE\textsubscript{Tn4371}6385 is similar to a 56.4 kb ICE-like element present in \textit{Pseudomonas fluorescens} UK4 genome (CP008896.1). Comparative sequence analysis between the two elements showed that they shared a common Tn4371 ICE core gene scaffolds (25), whereas their major differences are the unique accessory gene cluster downstream of the \textit{int} gene, and a 13.7 kb segment encoding the three antibiotic resistance genes harbored by ICE\textsubscript{Tn4371}6385 (Fig. 3). This 13.7 kb segment is immediately flanked by 695 bp direct repeats (termed DR), which share 99.87% identity (694/695) (Fig. 3). Interestingly, only a single copy of this DR sequence was present in the ICE-like element of the \textit{P. fluorescens} UK4 genome (Fig. 3). It is
possible that the duplicated DR sequences in ICE\textsubscript{Tn4371}6385 were the result of homologous recombination, which might lead to the acquisition of the 13.7 kb segment by ICE\textsubscript{Tn4371}6385. Therefore, we present a novel ICE\textsubscript{Tn4371}6385 element identified from PASGNDM genomes, which have acquired three antibiotic resistance genes namely \textit{bla\textsubscript{NDM-1}}, \textit{msr(E)} and \textit{floR}. The acquisition of the \textit{bla\textsubscript{NDM-1}} gene by PASGNDM699 is probably responsible for its extreme resistance to carbapenems (Table S1), whereas \textit{msr(E)} and \textit{floR} are associated with macrolides and flornenicol resistance, respectively (29, 30).

**Acquisition of \textit{msr(E)} protects \textit{P. aeruginosa} from AZM-mediated QS inhibition**

Previous studies have reported that sub-MIC concentrations of AZM could suppress the expression of several QS-regulated virulence factors such as elastase and rhamnolipids and the swarming motility of \textit{P. aeruginosa}, probably by inhibiting its QS systems (24, 31, 32). We therefore hypothesized that the acquisition of \textit{msr(E)} by \textit{P. aeruginosa} could counteract the QS-inhibition effect of AZM. However, the investigation on the functions of \textit{msr(E)} gene in the PASGNMD strains by a reductionist approach is difficult due to their multidrug resistance; hence, an alternative approach by exogenously expressing \textit{msr(E)} gene in laboratory strains of \textit{P. aeruginosa} was adopted for this purpose. We first amplified the \textit{msr(E)} gene together with its putative promoter from PASGNDM699 genome and have the entire fragment inserted into a \textit{pUCP18} vector to construct \textit{pUCP18::msr(E)} plasmid, in which the expression of \textit{msr(E)} gene is solely controlled under its putative promoter. Transformation of \textit{pUCP18::msr(E)} into the \textit{P. aeruginosa} strains PAO1 and PA14 increased their MICs to the AZM by more than 8 fold (from 256 μg/ml to >2048 μg/ml), indicating that the acquired \textit{msr(E)} in PASGNNDM genomes can be expressed from its own promoter to enhance resistance to AZM in \textit{P. aeruginosa}. Both the PASGNNDM699 and PASGNNDM345 have comparable AZM resistance levels to the two transformed strains, suggesting that the encoded \textit{msr(E)} is expressed in the PASGNNDM strains.
We then performed elastase and rhamnolipid quantification and swarming motility assays with PA01/pUCP18::msr(E) and PA14/pUCP18::msr(E) strains. The results showed that 8 μg/ml of AZM (1/32 of the MICs of PAO1 and PAO1/pUCP18) have reduced elastase production in both wildtype PA01 and vector-carrying strain PAO1/pUCP18 by at-least 40%, whereas the elastase produced by PAO1/pUCP18::msr(E) was not significantly affected upon AZM treatment (Fig. 4a). We also found that AZM have reduced the amount of rhamnolipid in the supernatant of both PAO1 and PAO1/pUCP18 overnight culture by at-least 60%, whereas PAO1/pUCP18::msr(E) produced similar levels of rhamnolipid in the presence and absence of AZM (Fig. 4b). In addition, the swarming motilities of PA01 and PAO1/pUCP18 were significantly inhibited by 8 μg/ml of AZM, under which PAO1/pUCP18::msr(E) exhibited a normal swarming phenotype (Fig. 5). Similar results were also obtained using the PA14 strains (Fig. 4c and 4d, Fig. 5), suggesting that the anti-AZM-mediated QS-inhibition effect of Msr(E) is not strain-specific. Taken together, these results clearly showed that the acquisition of msr(E) could protect *P. aeruginosa* from AZM-mediated QS inhibition.

**Expression of msr(E) in *P. aeruginosa* restores AZM-affected transcriptome**

AZM was previously reported to affect the transcriptome of *P. aeruginosa* in a microarray analysis (32). To better illustrate the effect of Msr(E) on the AZM-affected transcriptome of *P. aeruginosa*, we compared the gene expression profiles of PAO1/pUCP18::msr(E) in the presence and absence of 8 μg/ml AZM by total RNA sequencing. In PAO1, a total of 550 genes (~10% of PAO1 genome) were differentially expressed upon AZM treatment, of which 305 were upregulated and 245 were downregulated (Table S4, Fig. 6). We found that the upregulated genes are enriched in genes encoding, the type III secretion pathway apparatus, and other possible defense mechanisms against AZM (*infA* and *efp*) (Table S5). Whereas the downregulated genes include *rsmY* and *rsmZ*, the non-coding RNA products of which positively regulates QS by sequestering the translational inhibitor RsmA, *pslE-I* of the Psl
synthesis operon, \textit{lasI} of the LasI/LasR QS system, and the \textit{flK} gene the expression of which is essential for swarming motility (Table S5). These results are consistent with findings in previous studies (21, 24, 31-33) and could explain the QS-inhibition effect of AZM on PAO1 as shown in this study (Fig. 4, Fig.5, and Fig.6). Surprisingly, the transcriptome of PAO1\textit{pUCP18::msr(E)} was almost not affected by AZM, for which only 6 genes were differentially expressed upon AZM treatment (Table S6, Fig. 6). Therefore, Msr(E) probably protected \textit{P. aeruginosa} from AZM-mediated QS inhibition by restoring AZM-affected transcriptome.

**Msr(E) abolished anti-Pseudomonas effect of AZM in vivo**

Previous studies showed that macrolide antibiotics such as erythromycin and clarithromycin could enhance the clearance of \textit{P. aeruginosa} at the infection sites in a murine implant infection model and a murine lung infection model (34, 35). To investigate if the acquisition of \textit{msr(E)} by \textit{P. aeruginosa} can affect the anti-Pseudomonas activity of AZM in vivo, we used the murine implant model to compare the effectiveness of AZM treatment on PAO1 and PAO1\textit{pUCP18::msr(E)} infections. Briefly, silicone implants pre-colonized with PAO1 or PAO1\textit{pUCP18::msr(E)} strains were inserted into the peritoneal cavity of mice. After 12 hours of incubation, mice were treated with AZM by injecting AZM solution into the peritoneal cavity, whereas the control mice were injected with the same amount of saline. The silicone implants and mice spleens were harvested at 24-hour post infection to enumerate colony forming units (CFU) of \textit{P. aeruginosa}, which were used to indicate the clearance of bacterial at infection site and the spreading of infection to other organs according to previous studies (35, 36). We found that AZM treatment could reduce the CFU of PAO1 residing in the silicone implants and the mice spleens by 2.0-log and 3.8-log, respectively (Fig. 7). By contrast, AZM treatment did not significantly affect the CFU of PAO1\textit{pUCP18::msr(E)} recovered from either the silicone implants or the mice spleens, as compared to the saline-
treated control group (Fig. 7). These results indicated that Msr(E) could confer *P. aeruginosa* resistance against the anti-Pseudomonas activity of AZM *in vivo*.

**Discussion**

Tn4371 family ICEs have been previously described in a broad range of β- and γ-proteobacteria isolated from both environmental and clinical settings, which could confer their hosts adaptive functions such as multidrug/heavy metal resistance and the ability to metabolize specific carbon sources (25). Furthermore, a Tn4371-like element from *P. aeruginosa* genomes has recently been characterized to carry *bla*<sub>SPM-1</sub> and *bcr1*, suggesting that the Tn4371 family ICEs is an important source for the acquisition of carbapenem resistance by *P. aeruginosa* (37). In the current work, we identified a novel ICE<sub>Tn4371</sub>6385 from PASGNDM699 isolated from clinical sources. This element carries three antibiotic resistance genes including *bla*<sub>NDM-1</sub>, *msr*(E) and *flo*<sub>R</sub>, and retains the intact machinery for conjugative transfer (Fig. 3), suggesting that it is responsible for the transmission of these resistance genes into the PASGNDM genomes (25, 38). However, the conjugative transfer of ICE<sub>Tn4371</sub>6385 was not observed in mating experiments between PASGNDM699 and several recipient *P. aeruginosa* strains under laboratory conditions (data not shown). It is possible that the conjugation has extremely low efficiencies that is below our detection limit or requires specific inductive conditions (38, 39). Our findings provide the first evidence that *bla*<sub>NDM-1</sub> is encoded and potentially disseminated by ICEs, together with *msr*(E) and *flo*<sub>R</sub>. The macrolide resistance gene *msr*(E) and its variants were mainly identified from Gram-positive bacteria and several Gram-negative bacterial species such as Enterobacteriaceae spp., *Pasteurella multocida* and *A. baumannii*, but has been rarely described in *P. aeruginosa* (29, 40-42). Hence, the transmission of *msr*(E) by ICE<sub>Tn4371</sub>6385 into the clinical isolates characterized in this study has led us to investigate its possible functional roles in *P.*
aeruginosa. Our *in vitro* assays clearly showed that the exogenous expression of *msr(E)* in *P. aeruginosa* could abolish the QS inhibition activity of AZM *in vitro*, which in turn rescued the inhibition of elastase production, rhamnolipid production and swarming motility by AZM treatment (Fig. 4, 5). In addition, the acquisition of *msr(E)* by PAO1 almost completely restored the AZM-affected transcriptome and abolished the anti-Pseudomonas activity of AZM in a murine infection model (Fig. 6, Fig. 7, Table S5, Table S6). These results demonstrate that Msr(E) could confer *P. aeruginosa* with resistance to AZM-mediated QS inhibition and that the transmission of *msr(E)* into this organism will greatly challenge the use of AZM in treating infections caused by *P. aeruginosa*.

The third antibiotic resistance gene carried by ICE*_{Tn4371}6385* is *floR*, which encodes an efflux pump and is the determinant for florfenicol resistance (43). This gene was first identified in *Salmonella typhimurium* DT104 in 1999, and has ever since been detected in *E. coli* and *P. multocida* isolated from livestock and aquaculture settings (44-47). It is possible that the emergence and spreading of *floR* is due to the selection by florfenicol, since this antibiotic has been extensively used in veterinary medicine, especially in aquaculture settings (46, 48). Therefore, the carriage of *floR* by ICE*_{Tn4371}6385* may confer its hosts with advantages under environmental conditions where florfenicol may be present (48, 49), and hence facilitate the transmission and dissemination of *bla*NDM-1 and *msr(E)*.

In conclusion, we have characterized the full-length genomes of two NDM-1-producing *P. aeruginosa* clinical isolates, from which we identified a novel ICE*_{Tn4371}6385* element encoding three antibiotic resistance genes. Among them, the *bla*NDM-1 gene is responsible for extreme resistance to anti-Pseudomonal carbapenems, whereas *msr(E)* can quench AZM-mediated QS inhibition, and *floR* may enhance the survival of host bacteria under florfenicol exposure. We present the first evidence of *bla*NDM-1 to be carried by ICEs, and the first evidence of co-transfer of carbapenem resistance and the resistance to macrolide-mediated
QS inhibition into *P. aeruginosa*. Our findings highlight the importance of ICEs in transmitting antibiotic resistance, and that anti-virulence treatment of *P. aeruginosa* infections by targeting QS can be challenged by horizontal transfer of resistance mechanisms.
Materials and Methods

Bacterial strains and plasmids All the strains were routinely grown in Lysogeny broth (LB) or on LB plates with 1.5% agar at 37°C. The \textit{msr(E)} gene with its putative promoter were amplified from PASGNDM699 genome using primers 5’ACCGGCCAAGATAGTGACG3’ and 5’AGGAAGTCAACCGCCTTT3’ and ligated into the smal site of \textit{pUCP18} vector (50) to construct \textit{pUCP18::msr(E)} plasmid, where the \textit{msr(E)} gene is upstream to the \textit{lac} promoter. Both \textit{pUCP18} and \textit{pUCP18::msr(E)} were transformed into PAO1 and PA14 by electroporation, and the strains carrying these two plasmids were grown in LB supplemented with 300 μg/ml of carbenicillin (MP Bio) to maintain the plasmids.

Sequencing, assembly, and annotation Genomic DNA was purified using Blood and Cell Culture DNA Midi Kit (Qiagen) and sequenced on an Illumina MiSeq platform or a PacBio RS II system. The full-length genomes of PASGNDM345 and PASGNDM699 were assembled from long reads obtained from the PacBio RS II system using HGAP2 pipeline assisted with manual curation. The \textit{ICE\textsubscript{Tn4371}}6385 sequence and ICE-like element from \textit{P. fluorescens} UK4 were uploaded to the Rapid Annotations using Subsystem Technology (RAST) server for gene prediction and annotation, assisted with manual curation (51). Comparison of the two elements was done using EasyFig v2.2.2 (52).

Phylogenetic and comparative genomic analysis Phylogenetic analysis was carried out using Parsnp v1.1.2 (53). The phylogenetic tree was constructed using the approximate maximum likelihood algorithm based on core genome alignment, with filtration of recombination sites. Genomic islands of PASGNDM699 and PASGNDM345 genomes were predicted by the IslandViewer 3 server (54), and the encoded antibiotic resistance genes were predicted using the ResFinder 2.1 server (55). Comparison of PASGNDM699 and PASGNDM345 genomes with six other full-length \textit{P. aeruginosa} genomes was done by
BLASTn search using BLAST Ring Image Generator v0.95 (56), with genomic islands and antibiotic resistance genes plotted in the same image.

**Quantification of elastase, rhamnolipid and swarming motility**

Bacterial strains were grown in ABT minimal medium supplemented with 5 g l⁻¹ glucose and 2 g l⁻¹ casamino acids (ABTGC), with or without addition of 8 μg/ml AZM (Spectrum). The supernatants of overnight culture were filter sterilised before quantification of elastase and rhamnolipid production. Elastase activity was measured using EnzCheck Elastase Assay Kit (Thermo Fisher Scientific) as instructed by the manual. The quantification of rhamnolipid was performed as previously described with modifications (57). Briefly, rhamnolipid was extracted from supernatants with diethyl esther and dissolved in deionised water. The solution was added with 0.19% (w/v) orcinol dissolved in 50% H₂SO₄, followed by heating at 80°C for 30 min. The elastase activity and rhamnolipid were quantified by measuring emission at 530 nm and absorbance at 460 nm by using an Infinite 200 PRO system (Tecan), respectively. Both experiments were performed in at least triplicates, and the results were normalised with optical density at 600 nm (OD₆₀₀) and shown as mean ± standard deviation in the figures. The swarming motility of each strain was measured on 0.5% agar plates containing 8 g/L nutrient broth (Oxoid) and 5 g/L glucose (58). One μl of bacterial overnight culture (adjusted to OD₆₀₀ = 1) was inoculated to the center of the plate, followed by incubation at 37°C for 12 hours. The images were taken by a Gel Doc XR+ System (Bio-Rad).

**Transcriptomic analysis** Strains were grown in ABTGC medium at 37°C with 200 rpm shaking. Cells were harvested at mid-log phase (OD₆₀₀ = 0.6), and the total RNA was extracted using RNeasy Mini Kit (Qiagen). RNA sequencing was performed on an Illumina HiSeq 2000 platform to generate paired-end reads of 100 nt, which were mapped to PAO1 genome (NC_002516.2) by using CLC Genomics Workbench 9.0 (Qiagen). The transcript count table was analysed by DESeq 2 package of the R/Bioconductor by performing negative
binomial test (59). Hierarchical clustering analysis was performed to produce the heatmap for the differentially expressed genes with statistical significance (fold change > 4, P <0.05) using heatmap.2 package of the R/Bioconductor (60).

**Animal model** A murine silicone implant model was used to evaluate effects of AZM treatment *in vivo* on the two strains as previously described with modifications (36). Briefly, washed bacterial cells were re-suspended in 0.9% NaCl to an OD₆₀₀ of 0.01. Bacteria cells were allowed to attach onto sterile silicone tubes (length, 3 mm; inner diameter, 4 mm; outer diameter, 6 mm; Ole Dich) by incubation at 37°C, with 110 rpm shaking for 18 hours, after which the silicone tubes coated with bacteria were implanted into mouse peritoneal cavity by surgery. Treatment with AZM (10 mg per mouse, dissolved in 0.2 ml of 0.9% saline) or saline was performed by injection into the mouse peritoneal cavity 12 hours after surgery. Mice were sacrificed 24 after surgery and the bacterial cells residing on the silicone tube and in the mouse spleen were dispersed into the 0.9% NaCl solution by sonication using an Elmasonic P120H (Elma, Germany; power=50% and frequency=37 KHz) and homogenisation using a Bio-Gen PRO200 Homogenizer (Pro Scientific), respectively. The CFU was quantified by serial dilution and plating on LB agar plates, and the results were shown in log CFU with mean ± standard deviation.

**Ethics** The use of clinical specimen samples was approved by Department of Laboratory Medicine, National University Hospital, Singapore, registered under the reference 2016/00856. The animal model protocols were approved by the Institutional Animal Care and Use Committee (IACUC) of Nanyang Technological University, under the permit number A-0191 AZ. Animal experiments were performed in accordance to the NACLAR Guidelines of Animal and Birds (Care and Use of Animals for Scientific Purposes) Rules by Agri-Food & Authority of Singapore (AVA).
**Accession numbers** The genome sequencing data and RNA-Seq data have been deposited in the NCBI Short Read Archive database with the accession codes SRP103165 and SRP103155. The complete and draft genome sequences have been submitted to NCBI registered under BioProject PRJNA381838.

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Y.D. and L.Y. designed the experiments; J.T. collected clinical samples and conducted sample identification; D.I.D. did RNA sequencing; Y.D. analyzed sequencing data, carried out laboratory experiments, animal work, interpreted results and wrote the manuscript; All authors read and commented on the manuscript.
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Figure 1 Phylogenetic tree of PASGNDM345 and PASGNDM699 with 21 *P. aeruginosa* genomes

P. aeruginosa PASGNDM345 and PASGNDM699 genomes sequenced in this study (indicated with *) was compared with 21 other *P. aeruginosa* genomes. Phylogenetic tree was constructed based on 64,240 variant sites using the approximate maximum likelihood algorithm, with clade confidence estimated with SH-like support values. Accession numbers of strains in the phylogenetic tree are listed in Table S7.
Figure 2 Sequence conservation between PA_D1 and 5 other *P. aeruginosa* genomes.

From the innermost to outermost: Circle 1, PASGNDM699; Circle 2, PASGNDM345; Circle 3, PA_D1; Circle 4, PA14; Circle 5, DK2, NCGM2.S1; Circle 6, MTB-1; Circle 7, B136-33; Circle 8, VRFPNA04. Circle 9, GIs present in PASGNDM699 and PASGNDM345 predicted by the Island Viewer3 server (27). Blocks in black indicate GIs present in both PASGNDM699 and PASGNDM345, whereas blocks in grey indicate GIs present only in PASGNDM699. Circle 10, predicted antibiotic resistance genes present in PASGNDM699 and PASGNDM345 genomes with the ResFinder 2.1 server (55). Accession numbers of the strains are listed in Table S5, and GIs are listed in Table S3 and S4.
Figure 3 Comparison between ICE\textsubscript{Tn4371}\textsubscript{6385} and the ICE-like element from \textit{P. fluorescens} UK4 genome (CP008896.1). The 74 genes encoded by ICE\textsubscript{Tn4371}\textsubscript{6385} are represented by arrows with different colors representing their functional classes. The length of each arrow is to the scale of the gene size, whereas the arrow direction indicates the transcriptional direction of the gene. The 13.7 kb segments containing three antibiotic resistance genes are between two DRs (thin green arrows) in ICE\textsubscript{Tn4371}\textsubscript{6385}, possibly due to a homologous recombination event. The shades between the two elements indicate the sequence identity of the linked regions. 

Figure 4 Impact of exogenous expression of Msr(E) on
The production of elastase and rhamnolipid was inhibited in wildtype strains and vector-carrying strains of PAO1 (a), (b) and PA14 (c), (d) under the treatment of 8 µg/ml AZM, whereas no inhibition was observed in the strains expressing Msr(E).
Figure 5 Impact of exogenous expression of Msr(E) on the swarming motilities of PAO1 and PA14 under 8 μg/ml of AZM. The swarming motility of wildtype strains and vector-carrying strains of PAO1 and PA14 were inhibited by the addition of 4 μg/ml of AZM, whereas the exogenous expression of Msr(E) in both strains restored the AZM-mediated inhibition on swarming motilities. No swarming inhibition by AZM was observed in PASGNDM699 strain with msr(E) encoded in the genome.
Figure 6 Heat map of 550 genes with significant changes between the AZM-treated and non-treated PAO1, including their behaviors in the AZM-treated and non-treated PAO1/pUCP18::msr(E). The differentially expressed genes (fold-change $> 4$, P value $< 0.05$) between the AZM-treated and non-treated PAO1 cells were identified by performing a negative binomial test using the DESeq 2 package of R/Bioconductor. Whereas similar change in the gene expression profile was not observed in PAO1/pUCP18::msr(E) cells when treated and not treated with AZM. The full lists of genes that were differentially expressed between AZM-treated and non-treated PAO1 and between AZM-treated and non-treated PAO1/pUCP18::msr(E) can be found in Table S4 and Table S5.
Figure 7 The effect of AZM treatment on PAO1 and PAO1/pUCP18::msr(E) in a murine silicone implant model. The silicone implants attached by PAO1 and PAO1/pUCP18::msr(E) were inserted into the peritoneal cavity of mice by surgery. AZM treatment at 10 mg per mouse significantly reduced the CFU of PAO1 recovered from (a) the silicone implants by 2.0-log and (b) the mice spleens by 3.8-log, whereas it had no effect on the CFU of PAO1/pUCP18::msr(E) recovered from either the silicone implants (a) or the mice spleens (b). Results are shown as log CFU per silicone implant and log CFU per mouse spleen, respectively (n = 6, ns P > 0.05, ** P < 0.01, **** P < 0.0001, Student’s t-test)
Figure S1 Antibiotic resistance genes present in 11 PASGNDM genomes. Presence of antibiotic resistance genes in genomes were predict by ResFinder 2.1 server (55). Multilocus sequencing type (MLST) of each strain was determined using DTU MLST server 1.8 (61).

|             | Aminoglycoside | Beta-lactam | Fluoroquinolone | Fosfomycin | Macrolide | Phenicol | Sulphonamide | Trimethoprim | MLST |
|-------------|----------------|-------------|-----------------|------------|-----------|----------|--------------|--------------|------|
| PASGNDM345  | aac(3)-Id      | strA        | blaOXA-51       | QnrC1      | msr(3)    | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM544  | aph(3’)-Ile   | strB        | blaPAO         | fosA       | cot97     | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM571  | aac(3)-Id      | strA        | blaOXA-51       | QnrC1      | msr(3)    | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM583  | aph(3’)-Ile   | strB        | blaPAO         | fosA       | cot97     | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM586  | aac(3)-Id      | strA        | blaOXA-51       | QnrC1      | msr(3)    | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM587  | aph(3’)-Ile   | strB        | blaPAO         | fosA       | cot97     | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM590  | aac(3)-Id      | strA        | blaOXA-51       | QnrC1      | msr(3)    | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM591  | aph(3’)-Ile   | strB        | blaPAO         | fosA       | cot97     | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM592  | aac(3)-Id      | strA        | blaOXA-51       | QnrC1      | msr(3)    | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM593  | aph(3’)-Ile   | strB        | blaPAO         | fosA       | cot97     | floR     | sul2         | dfr65        | ST-308 |
| PASGNDM699  | aac(3)-Id      | strA        | blaOXA-51       | QnrC1      | msr(3)    | floR     | sul2         | dfr65        | ST-308 |
Figure S2 Alignment of the 11 PASGNDM genomes. Complete genomes of PASGNDM345 and PASGNDM699 were aligned with draft genomes of the other 9 PASGNDM strains using Progressive Mauve (26). Alignment results showed the 11 strains are highly similar.
Table S1 The MICs of PASGNMD strains to various antibiotics. The strains only remain sensitive to polymyxin B. Clinical specimens from which the strains were isolated are also shown in the table.

| Strain        | Specimen       | Ceftazidime | Cefepime | Imipenem | Meropenem | Gentamicin | Amikacin | Ciprofloxacin | Levofloxacin | Ertapenem | Polymyxin B |
|---------------|----------------|-------------|----------|----------|-----------|------------|----------|---------------|--------------|------------|-------------|
| PASGNMD544    | ETT aspirate   | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 1.5         |
| PASGNMD699    | Sputum         | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 1.5         |
| PASGNMD345    | Sputum         | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 2           |
| PASGNMD571    | Urine          | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 1           |
| PASGNMD583    | Urine          | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 1           |
| PASGNMD586    | Urine          | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 0.5         |
| PASGNMD587    | Wound swab     | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 0.5         |
| PASGNMD590    | Urine          | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 0.75        |
| PASGNMD591    | Urine          | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 2           |
| PASGNMD592    | Urine          | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 2           |
| PASGNMD593    | Urine          | >64         | >64      | >16      | >16       | >64        | >4       | >8            | >8           | >8         | 0.75        |
Table S2 Genome features of PASGNDM699 and PASGNDM345.

|                  | Length (bp) | G+C content | Genes | Protein-coding genes | tRNA | rRNA |
|------------------|-------------|-------------|-------|----------------------|------|------|
| PASGNDM345       | 6,893,164   | 66.1%       | 6503  | 6427                 | 64   | 12   |
| PASGNDM699       | 6,985,102   | 66.0%       | 6589  | 6513                 | 64   | 12   |
Table S3 Predicted genomic islands from the full-length genome of PASGNDM699. Fonts in bold indicate the GI only present in PASGNDM699 but not PASGNDM345 genome.

| Island start | Island end | Length | Method | Gene start | Gene end | Product |
|--------------|------------|--------|--------|------------|----------|---------|
| 692910       | 699692     | 6782   | Predicted by at least one method | 692780     | 693475   | Phage minor tail protein |
| 692910       | 699692     | 6782   | Predicted by at least one method | 693478     | 694248   | Phage tail assembly protein |
| 692910       | 699692     | 6782   | Predicted by at least one method | 694303     | 694905   | Phage tail assembly protein I |
| 692910       | 699692     | 6782   | Predicted by at least one method | 694964     | 698617   | Phage tail fiber protein |
| 692910       | 699692     | 6782   | Predicted by at least one method | 699603     | 700703   | FIG00966085: hypothetical protein |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1060868    | 1061077  | FIG00954142: hypothetical protein |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1061279    | 1061758  | Transcriptional regulator, AsnC family |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1062236    | 1062919  | FIG00954854: hypothetical protein |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1063897    | 1064313  | Cobalt-zinc-cadmium resistance protein |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1064455    | 1066968  | ATP-dependent helicase HrpB |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1067024    | 1068490  | site-specific recombinase, phage integrase family |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1068487    | 1070415  | hypothetical protein |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1070412    | 1072460  | Phage Integrase |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1073024    | 1073206  | Transcriptional regulator, XRE family |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1073925    | 1075325  | FOG: GGDEF domain |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1076625    | 1076921  | Mobile element protein |
| 1060767      | 1077432    | 16665  | Predicted by at least one method | 1076944    | 1077324  | Mobile element protein |
| 1250067      | 1256766    | 6699   | Predicted by at least one method | 1250412    | 1251239  | Integrase |
| 1250067      | 1256766    | 6699   | Predicted by at least one method | 1251864    | 1252256  | Rossmann fold nucleotide-binding protein |
| 1250067      | 1256766    | 6699   | Predicted by at least one method | 1252789    | 1252905  | Smf possibly involved in DNA uptake |
| 1250067      | 1256766    | 6699   | Predicted by at least one method | 1252954    | 1253256  | hypothetical protein |
| 1250067      | 1256766    | 6699   | Predicted by at least one method | 1253253    | 1253594  | hypothetical protein |
| Start Position | End Position | Length | Description                           |
|----------------|--------------|--------|---------------------------------------|
| 1250067        | 1256766      | 6699   | Predicted by at least one method      |
| 1253599        | 1254288      |        | Phage protein                         |
| 12554461       | 1254652      |        | Phage protein                         |
| 1254652        | 1254768      |        | Phage protein                         |
| 1255424        | 1255759      |        | Phage protein                         |
| 1255762        | 1255992      |        | Phage protein                         |
| 1255762        | 1256090      |        | Phage protein                         |
| 1256090        | 1256323      |        | hypothetical protein                  |
| 1256326        | 1256712      |        | Transcriptional regulator, LuxR family|
| 1260441        | 1260728      |        | hypothetical protein                  |
| 1260725        | 1261033      |        | hypothetical protein                  |
| 1261301        | 1261534      |        | hypothetical protein                  |
| 1261780        | 1262301      |        | hypothetical protein                  |
| 1262298        | 1262528      |        | FIG00964051: hypothetical protein     |
| 1262697        | 1263698      |        | Primosomal protein I                  |
| 1263695        | 1264483      |        | DNA replication protein DnaC          |
| 1264480        | 1265910      |        | Replicative DNA helicase              |
| 1265943        | 1266191      |        | FIG00956875: hypothetical protein     |
| 1266852        | 1268860      |        | phage holin, lambda family            |
| 1268857        | 1269474      |        | Lytic enzyme                          |
| 1269549        | 1269713      |        | hypothetical protein                  |
| 1269665        | 1269907      |        | hypothetical protein                  |
| 1271731        | 1273506      |        | Phage terminase, large subunit        |
| 1273506        | 1273709      |        | hypothetical protein                  |
| 1273711        | 1275237      |        | Phage portal protein                  |
| 1275245        | 1277200      |        | ATP-dependent Clp protease proteolytic|
| 1277272        | 1277634      |        | hypothetical protein                  |
| 1277953        | 1278426      |        | Phage protein                         |
| 1278430        | 1278624      |        | FIG00964642: hypothetical protein     |
| 1278626        | 1279378      |        | hypothetical protein                  |
| 1280513        | 1282996      |        | FIG00954405: hypothetical protein     |
| Gene ID     | Description                                      | Predicted by at least one method | PE-PGRS virulence associated protein | FIG00956273: hypothetical protein | FIG00964183: hypothetical protein | FIG00963969: hypothetical protein | COG1156: Archaeal/vacuolar-type H+-ATPase subunit B | FIG00967075: hypothetical protein | FIG00965686: hypothetical protein | FIG00958463: hypothetical protein | Phage protein | Phage protein | hypothetical protein |
|-------------|--------------------------------------------------|----------------------------------|-------------------------------------|-----------------------------------|------------------------------------|------------------------------------|-------------------------------------|-----------------------------------|------------------------------------|-----------------------------------|----------------|----------------|---------------------|
| 1259039     | Predicted by at least one method                 | 1283420                         | 1283557                             |                                   |                                    |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1283557                         | 1285254                             |                                   | FIG00956273: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1285257                         | 1285667                             |                                   | FIG00964183: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1286223                         | 1286627                             |                                   | FIG00963969: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1286624                         | 1288282                             |                                   | COG1156: Archaeal/vacuolar-type H+-ATPase subunit B |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1288312                         | 1288899                             |                                   | FIG00967075: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1289055                         | 1289648                             |                                   | FIG00965686: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1289654                         | 1289929                             |                                   | FIG00956286: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1290524                         | 1290826                             |                                   | FIG00958463: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1291219                         | 1291356                             |                                   | Phage protein                      |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1291710                         | 1291863                             |                                   | Phage protein                      |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1259039     | Predicted by at least one method                 | 1293130                         | 1293331                             |                                   | hypothetical protein               |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1351730     | Predicted by at least one method                 | 1351730                         | 1351993                             |                                   | Transcriptional regulator in PFGI-1-like cluster |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1351730     | Predicted by at least one method                 | 1352073                         | 1352834                             |                                   | FIG00642059: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1351730     | Predicted by at least one method                 | 1353145                         | 1353378                             |                                   | FIG01214592: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1351730     | Predicted by at least one method                 | 1353712                         | 1354257                             |                                   | RecA-family ATPase                 |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1351730     | Predicted by at least one method                 | 1354304                         | 1355116                             |                                   | Phage replication protein          |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1351730     | Predicted by at least one method                 | 1355848                         | 1356126                             |                                   | IncP-type oriT binding protein TraK |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1351730     | Predicted by at least one method                 | 1356446                         | 1356817                             |                                   | IncP-type oriT binding protein TraJ |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1356446     | Predicted by at least one method                 | 1356446                         | 1356817                             |                                   | IncP-type oriT binding protein TraJ |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1356446     | Predicted by at least one method                 | 1357083                         | 1357868                             |                                   | Conjugative transfer protein TrbJ  |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1356446     | Predicted by at least one method                 | 1357884                         | 1358153                             |                                   | Conjugative transfer entry exclusion protein TrbK |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1356446     | Predicted by at least one method                 | 1358150                         | 1359739                             |                                   | Conjugative transfer protein TrbL  |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1356446     | Predicted by at least one method                 | 1360077                         | 1360307                             |                                   | FIG01213713: hypothetical protein |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1356446     | Predicted by at least one method                 | 1360552                         | 1361100                             |                                   | hypothetical protein               |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1356446     | Predicted by at least one method                 | 1361271                         | 1361489                             |                                   | Mercuric transport protein, MerE   |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| 1356446     | Predicted by at least one method                 | 1361486                         | 1361851                             |                                   | Mercuric resistance operon coregulator |                                    |                                    |                                   |                                    |                                   |                |                |                     |
| Accession | Start POS | End POS | Description |
|-----------|-----------|---------|-------------|
| 1356446   | 1376081   | 19635   | Mercuric ion reductase |
| 1356446   | 1376081   | 19635   | Periplasmic mercury(+2) binding protein |
| 1356446   | 1376081   | 19635   | Mercuric transport protein, MerT |
| 1356446   | 1376081   | 19635   | Mercuric resistance operon regulatory protein |
| 1356446   | 1376081   | 19635   | Aminoglycoside 3'-phosphotransferase 2 |
| 1356446   | 1376081   | 19635   | Mobile element protein |
| 1356446   | 1376081   | 19635   | Mobile element protein |
| 1356446   | 1376081   | 19635   | Type IV secretory pathway, VirD2 components (relaxase) |
| 1356446   | 1376081   | 19635   | Mobile element protein |
| 1370666   | 1375516   | 4850    | Mobile element protein |
| 1370666   | 1375516   | 4850    | Mobile element protein |
| 1824170   | 1828537   | 4367    | NADH oxidase |
| 1824170   | 1828537   | 4367    | Mobile element protein |
| 1824170   | 1828537   | 4367    | Mobile element protein |
| 1824170   | 1828537   | 4367    | Type III restriction-modification system methylation subunit |
| 1996654   | 2001263   | 4609    | Glycine cleavage system H protein |
| 1996654   | 2001263   | 4609    | Hypothetical protein |
| 1996654   | 2001263   | 4609    | Hypothetical protein |
| 1996654   | 2001263   | 4609    | Hypothetical protein |
| 1996654   | 2001263   | 4609    | Hypothetical protein |
| 1996654   | 2001263   | 4609    | Glutathione S-transferase |
| 1996654   | 2001263   | 4609    | Multimeric flavodoxin WrbA |
| 1996654   | 2001263   | 4609    | Putative LysR-family transcriptional regulator |
| 2057249   | 2078394   | 21145   | Chorismate mutase I / Prephenate dehydratase |
| Gene ID   | Start Position | End Position | Predicted by | Start Position | End Position | Description                              |
|----------|----------------|--------------|--------------|----------------|--------------|------------------------------------------|
| 2057249  | 2078394        | 21145        | Predicted by | 2058415        | 2059524      | Biosynthetic Aromatic amino acid         |
|          |                |              | at least one |                |              | aminotransferase beta                    |
| 2057249  | 2078394        | 21145        | Predicted by | 2059517        | 2061757      | Cyclohexadienyl dehydrogenase(EC 1.3.1.43) / 5-Enolpyruvylshikimate-3-phosphate synthase |
| 2057249  | 2078394        | 21145        | Predicted by | 2062714        | 2064393      | SSU ribosomal protein S1p                 |
| 2057249  | 2078394        | 21145        | Predicted by | 2064530        | 2064814      | Integration host factor beta subunit      |
| 2057249  | 2078394        | 21145        | Predicted by | 2070388        | 2070660      | UDP-N-acetylglucosamine 4,6-dehydratase  |
| 2057249  | 2078394        | 21145        | Predicted by | 2070675        | 2070827      | UDP-N-acetylglucosamine 4,6-dehydratase  |
| 2057249  | 2078394        | 21145        | Predicted by | 2070831        | 2071949      | WbjC                                     |
| 2057249  | 2078394        | 21145        | Predicted by | 2072270        | 2073097      | UDP-N-acetylglucosamine 2-epimerase      |
| 2057249  | 2078394        | 21145        | Predicted by | 2073409        | 2074317      | Putative glycosyltransferase             |
| 2057249  | 2078394        | 21145        | Predicted by | 2074575        | 2075258      | UDP-glucose 4-epimerase                  |
|          |                |              | at least one |                |              | nucleotide sugar epimerase/dehydratase   |
|          |                |              |              |                |              | WbpM                                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2457819        | 2458094      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2458094        | 2458213      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2458198        | 2458410      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2458407        | 2460287      | C-5 cytosine-specific DNA methylase      |
|          |                |              | at least one |                |              | family protein                           |
| 2457987  | 2469377        | 11390        | Predicted by | 2460284        | 2460466      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2460773        | 2461012      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2461009        | 2461635      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2461685        | 2462002      | transcriptional regulator, putative      |
| 2457987  | 2469377        | 11390        | Predicted by | 2461999        | 2462229      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2462380        | 2462664      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2462683        | 2462994      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2464587        | 2464835      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2465325        | 2465609      | hypothetical protein                     |
| 2457987  | 2469377        | 11390        | Predicted by | 2465613        | 2465843      | hypothetical protein                     |
| Gene ID   | Description                        | Predicted by at least one method | Annotation                                                                 |
|-----------|------------------------------------|----------------------------------|-----------------------------------------------------------------------------|
| 2457987   | Predicted by at least one method   | 2466057                          | DNA primase, phage associated                                               |
| 2533316   | Predicted by at least one method   | 2533619                          | Hemoglobin-like protein HbO                                                 |
| 2533316   | Predicted by at least one method   | 2534625                          | hypothetical protein                                                        |
| 2533316   | Predicted by at least one method   | 2539299                          | hypothetical protein                                                        |
| 2541257   | Predicted by at least one method   | 2541452                          | hypothetical protein                                                        |
| 2541257   | Predicted by at least one method   | 2544784                          | hypothetical protein                                                        |
| 2541257   | Predicted by at least one method   | 2546125                          | hypothetical protein                                                        |
| 2541257   | Predicted by at least one method   | 2546419                          | hypothetical protein                                                        |
| 2541257   | Predicted by at least one method   | 2546504                          | hypothetical protein                                                        |
| 2541257   | Predicted by at least one method   | 2547578                          | hypothetical protein                                                        |
| 2541257   | Predicted by at least one method   | 2551380                          | autotransporter, putative                                                   |
| 2541257   | Predicted by at least one method   | 2553240                          | hypothetical protein                                                        |
| 2541257   | Predicted by at least one method   | 2553249                          | hypothetical protein                                                        |
| 2544797   | Predicted by at least one method   | 2554110                          | VrlI protein                                                                |
| 2546504   | Predicted by at least one method   | 2554666                          | Type I restriction-modification system, DNA-methyltransferase subunit M     |
| 2546504   | Predicted by at least one method   | 2556084                          | Putative deoxyribonuclease similar to YcfH, type 4                          |
| 2546504   | Predicted by at least one method   | 2562386                          | Phage integrase                                                             |
| 2546504   | Predicted by at least one method   | 2564162                          | ATP-dependent DNA helicase RecQ                                             |
| 2546504   | Predicted by at least one method   | 2569944                          | VrlII protein                                                               |
| 2546504   | Predicted by at least one method   | 2571979                          | Type I restriction-modification system, DNA-methyltransferase subunit M     |
| 2546504   | Predicted by at least one method   | 2571979                          | DNA-methyltransferase subunit M                                             |
| Accession | Description | Start Position | Stop Position | Predicted by | Function |
|-----------|-------------|----------------|---------------|--------------|----------|
| 2660496   | General secretion pathway protein I | 2660496 | 2660921 | Predicted by at least one method | protein secretion pathway |
| 2660496   | Type II secretory pathway, pseudopilin PulG | 2660918 | 2661508 | Predicted by at least one method | protein secretion pathway, pseudopilin PulG |
| 2660496   | Type II secretory pathway, component PulK | 2661564 | 2662577 | Predicted by at least one method | protein secretion pathway, component PulK |
| 2764602   | Integrase | 2764681 | 2765685 | Predicted by at least one method | enzyme |
| 2764602   | Hypothetical protein | 2766142 | 2766264 | Predicted by at least one method | protein |
| 2764602   | Phage protein | 2766257 | 2766736 | Predicted by at least one method | protein |
| 2764602   | Phage-related protein | 2769536 | 2770162 | Predicted by at least one method | protein |
| 3282382   | Uncharacterized protein conserved in bacteria | 3281822 | 3282541 | Predicted by at least one method | protein |
| 3282382   | Elements of external origin; transposon-related functions | 3289853 | 3290875 | Predicted by at least one method | protein |
| 3282382   | Hypothetical protein | 3291562 | 3291912 | Predicted by at least one method | protein |
| 3282541   | Cointegrate resolution protein T | 3289853 | 3290875 | Predicted by at least one method | protein |
| 3282541   | Tn4652, cointegrate resolution protein S | 3291562 | 3291912 | Predicted by at least one method | protein |
| 3282541   | Bacteriophage protein gp37 | 3292986 | 3293207 | Predicted by at least one method | protein |
| 3282541   | Hypothetical protein | 3293246 | 3294247 | Predicted by at least one method | protein |
| 3296194   | Homospermidine synthase | 3297922 | 3299331 | Predicted by at least one method | protein |
| 3296194   | Homospermidine synthase | 3305099 | 3299331 | Predicted by at least one method | protein |
| Accession | Description                                           |
|-----------|-------------------------------------------------------|
| 3296194   | Mobile element protein                                 |
| 3296194   | Heavy metal RND efflux outer membrane protein, CzcC family |
| 3296194   | Cobalt/zinc/cadmium efflux RND transporter, membrane fusion protein, CzcB family |
| 3309732   | CzcA; Cation efflux system CusA                         |
| 3309732   | Bacteriophage protein gp37                             |
| 3309732   | Tn4652, cointegrate resolution protein S                |
| 3309732   | Tn21 protein of unknown function Urf2                  |
| 3309732   | Transposon Tn21 resolvase                              |
| Protein ID | Description                                                                 | Predicted by methods          | Accession | Description |
|------------|------------------------------------------------------------------------------|-------------------------------|-----------|-------------|
| 3309732    | Mobile element protein                                                       | Predicted by at least one method | 3325971   | 3328937     |
| 3309979    | hypothetical protein                                                          | Predicted by at least one method | 3309732   | 3310088     |
| 3309979    | BNR repeat domain protein                                                    | Predicted by at least one method | 3310514   | 3311200     |
| 3309979    | hypothetic protein                                                            | Predicted by at least one method | 3310514   | 3311200     |
| 3309979    | hypothetical protein                                                          | Predicted by at least one method | 3311295   | 3312114     |
| 3309979    | hypothetical protein                                                          | Predicted by at least one method | 3311295   | 3312114     |
| 3309979    | FIG00960741: hypothetical protein                                            | Predicted by at least one method | 3314027   | 3314245     |
| 3309979    | Tn4652, cointegrate resolution protein S                                      | Predicted by at least one method | 3316550   | 3317521     |
| 3309979    | Tn4652, cointegrate resolution protein S                                      | Predicted by at least one method | 3316550   | 3317521     |
| 3309979    | Cointegrate resolution protein T                                             | Predicted by at least one method | 3318786   | 3319382     |
| 3309979    | Bacteriophage protein gp37                                                    | Predicted by at least one method | 3319471   | 3319842     |
| 3309979    | Mercuric resistance operon regulatory protein                                 | Predicted by at least one method | 3320774   | 3321208     |
| 3309979    | Mercuric transport protein, MerT                                              | Predicted by at least one method | 3321280   | 3321630     |
| 3309979    | Periplasmic mercury(+2) binding protein                                       | Predicted by at least one method | 3321643   | 3321918     |
| 3309979    | Mercuric ion reductase                                                        | Predicted by at least one method | 3321990   | 3323675     |
| 3309979    | Mercuric resistance operon coregulator                                       | Predicted by at least one method | 3323693   | 3324058     |
| 3309979    | Mercuric transport protein, MerE                                              | Predicted by at least one method | 3324055   | 3324291     |
| 3309979    | Tn21 protein of unknown function Urf2                                          | Predicted by at least one method | 3324288   | 3325277     |
| 3309979    | Transposon Tn21 resolvase                                                     | Predicted by at least one method | 3325408   | 3325968     |
| 3309979    | Mobile element protein                                                        | Predicted by at least one method | 3325971   | 3328937     |
| 3309979    | Phage replication initiation protein                                          | Predicted by at least one method | 3330769   | 3332055     |
| 3309979    | Mobile element protein                                                        | Predicted by at least one method | 3332403   | 3332753     |
| 3309979    | hypothetical protein                                                          | Predicted by at least one method | 3332965   | 3333171     |
| 3309979    | Probable coat protein A precursor                                            | Predicted by at least one method | 3333322   | 3334776     |
| 3415786    | Copper chaperone                                                              | Predicted by at least one method | 3415786   | 3415980     |
| Gene ID  | Accessory ID | Predicted by at least one method | Accessory ID 1 | Accessory ID 2 | Protein Description |
|---------|--------------|----------------------------------|----------------|----------------|---------------------|
| 3415786 | 3442204      | Predicted by at least one method | 3416055        | 3416813        | hypothetical protein |
| 3415786 | 3442204      | Predicted by at least one method | 3417031        | 3417369        | Ferredoxin, 2Fe-2S  |
| 3415786 | 3442204      | Predicted by at least one method | 3417386        | 3417865        | HTH-type transcriptional regulator |
| 3415786 | 3442204      | Predicted by at least one method | 3417881        | 3420310        | Lead, cadmium, zinc and mercury |
| 3415786 | 3442204      | Predicted by at least one method | 3420690        | 3420971        | copper translocating P-type ATPase |
| 3415786 | 3442204      | Predicted by at least one method | 3421010        | 3422320        | Transcriptional regulator, ArsR family |
| 3415786 | 3442204      | Predicted by at least one method | 3422330        | 3422587        | Probable NreB protein |
| 3415786 | 3442204      | Predicted by at least one method | 3422678        | 3422884        | LysR family transcriptional regulator |
| 3415786 | 3442204      | Predicted by at least one method | 3422994        | 3424154        | STM3121 |
| 3415786 | 3442204      | Predicted by at least one method | 3424440        | 3426302        | Type IV secretory pathway, VirD2 |
| 3415786 | 3442204      | Predicted by at least one method | 3426725        | 3427684        | components (relaxase) |
| 3415786 | 3442204      | Predicted by at least one method | 3428169        | 3429644        | transposase InsA |
| 3415786 | 3442204      | Predicted by at least one method | 3429926        | 3431455        | COG0488: ATPase components of ABC |
| 3415786 | 3442204      | Predicted by at least one method | 3431913        | 3432725        | transposase InsA |
| 3415786 | 3442204      | Predicted by at least one method | 3433164        | 3434693        | Beta-lactamase |
| 3415786 | 3442204      | Predicted by at least one method | 3433164        | 3434693        | transposase InsA |
| Accession | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
|-----------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |
| 3415786   | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method | Predicted by at least one method |

**Method:** Predicted by at least one method. **Heat shock protein 60 family chaperone GroEL**

**NreA-like protein**

**Cobalt-zinc-cadmium resistance protein CzcD**

**Transcriptional regulator, ArsR family**

**Probable Co/Zn/Cd efflux system membrane fusion protein / Multidrug efflux membrane fusion protein M**

**RND multidrug efflux transporter; Acriflavin resistance protein**

**Adenylylsulfate kinase**

**Probable glycosyl transferase**

**Twin-arginine translocation protein TatC**

**Adenylylsulfate kinase**

**Probable glycosyl transferase**

**Twin-arginine translocation protein TatC**

**Twin-arginine translocation protein TatC**

**Probable SN-glycerol-3-phosphate transport ATP-binding protein UgPC (TC 3.A.1.1.3)**

**Lipid carrier : UDP-N-acetylgalactosaminyltransferase / Alpha-1,3-N-acetylgalactosamine transferase**
| Gene ID | Description | Prediction Method | Predicted by at least one method | Additional Information |
|---------|-------------|------------------|----------------------------------|------------------------|
| 4368021 | Predicted by at least one method | 4380320 | 4380436 | hypothetical protein |
| 4368021 | Predicted by at least one method | 4380704 | 4382338 | hypothetical protein |
| 4368021 | Predicted by at least one method | 4383028 | 438537 | General secretion pathway protein D |
| 4368021 | Predicted by at least one method | 4385291 | 4385578 | hypothetical protein |
| 4368021 | Predicted by at least one method | 4386143 | 4387054 | Transcriptional regulator, AraC family |
| 4368021 | Predicted by at least one method | 4387201 | 4388034 | Short-chain dehydrogenase/reductase SDR |
| 4824516 | Predicted by at least one method | 4825034 | 4825393 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4826135 | 4826602 | Phage protein |
| 4824516 | Predicted by at least one method | 4826604 | 4826822 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4827221 | 4827844 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4828037 | 4828307 | Phage protein |
| 4824516 | Predicted by at least one method | 4828641 | 4828757 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4828854 | 4829042 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4829081 | 4829422 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4829424 | 4830590 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4830590 | 4831233 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4831233 | 4832072 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4832072 | 4832715 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4832715 | 4833458 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4833458 | 4834101 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4834101 | 4834747 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4834747 | 4835393 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4835393 | 4836039 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4836039 | 4836683 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4836683 | 4837329 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4837329 | 4837975 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4837975 | 4838622 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4838622 | 4839268 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4839268 | 4839914 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4839914 | 4840560 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4840560 | 4841206 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4841206 | 4841852 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4841852 | 4842498 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4842498 | 4843144 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4843144 | 4843790 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4843790 | 4844436 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4844436 | 4845082 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4845082 | 4845728 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4845728 | 4846374 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4846374 | 4847020 | hypothetical protein |
| 4824516 | Predicted by at least one method | 4847020 | 4847666 | hypothetical protein |
| StartPosition | EndPosition | Description | Predicted by at least one method | StartPosition | EndPosition | Description |
|---------------|-------------|-------------|----------------------------------|---------------|-------------|-------------|
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4847611       | 4848126     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4848123       | 4848575     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4848572       | 4848775     | hypothetical protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4848782       | 4849522     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4849624       | 4850007     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4850261       | 4853893     | Phage tail length tape-measure protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4853893       | 4854852     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4855814       | 4857484     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4857738       | 4858289     | Phage FAD/FMN-containing dehydrogenase |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4858299       | 4858529     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4858830       | 4860953     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4860950       | 4862098     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4862095       | 4862382     | Phage protein |
| 4838194       | 4862792     | 24598       | Predicted by at least one method | 4862543       | 4862680     | Phage protein |
| 4877189       | 4881287     | 4098        | Predicted by at least one method | 4877189       | 4877437     | FIG00960798: hypothetical protein |
| 4877189       | 4881287     | 4098        | Predicted by at least one method | 4877440       | 4879170     | Protein with ParB-like nuclease domain in PFGI-1-like cluster |
| 4877189       | 4881287     | 4098        | Predicted by at least one method | 4879198       | 4879965     | FIG004780: hypothetical protein in PFGI-1-like cluster |
| 4877189       | 4881287     | 4098        | Predicted by at least one method | 4879962       | 4881287     | FIG141751: hypothetical protein in PFGI-1-like cluster |
| 4888002       | 4892800     | 4798        | Predicted by at least one method | 4888002       | 4888154     | Haemophilus-specific protein, uncharacterized |
| 4888002       | 4892800     | 4798        | Predicted by at least one method | 4888188       | 4888754     | Haemophilus-specific protein, uncharacterized |
| 4888002       | 4892800     | 4798        | Predicted by at least one method | 4888712       | 4890467     | Homoserine/homoserine lactone efflux protein |
| 4888002       | 4892800     | 4798        | Predicted by at least one method | 4890911       | 4892800     | Transcriptional regulator, LysR family |
| 4888002       | 4892800     | 4798        | Predicted by at least one method | 4892797       | 4894770     | DNA/RNA helicase in PFGI-1-like cluster |
| Accession | Accession | Length | Methodology | Accession | Accession |
|-----------|-----------|--------|-------------|-----------|-----------|
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4925894   | 4926934   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4926918   | 4928954   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4929370   | 4929969   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4929930   | 4930046   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4930205   | 4930657   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4932274   | 4933722   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4933810   | 4934277   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4935008   | 4936465   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4937342   | 4937803   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4940332   | 4941912   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4942286   | 4943233   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4943362   | 4944042   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4944053   | 4944808   |
| 4926918   | 4944808   | 17890  | Predicted by at least one method | 4944793   | 4945374   |
| 4929252   | 4942176   | 12924  | Predicted by at least one method | 4929370   | 4929969   |
| 4929252   | 4942176   | 12924  | Predicted by at least one method | 4929930   | 4930046   |
| 4929252   | 4942176   | 12924  | Predicted by at least one method | 4930205   | 4930657   |
| 4929252   | 4942176   | 12924  | Predicted by at least one method | 4932274   | 4933722   |
| 4929252   | 4942176   | 12924  | Predicted by at least one method | 4933810   | 4934277   |
| 4929252   | 4942176   | 12924  | Predicted by at least one method | 4935008   | 4936465   |
| 4929252   | 4942176   | 12924  | Predicted by at least one method | 4937342   | 4937803   |
| 4929252   | 4942176   | 12924  | Predicted by at least one method | 4940332   | 4941912   |
| 5146667   | 5151453   | 4786   | Predicted by at least one method | 5145495   | 5146751   |

**Predicted by at least one method**

- Inner membrane component of tripartite multidrug resistance system
- Membrane fusion component of tripartite multidrug resistance system
- Transcriptional regulator, LysR family
- Hypothetical protein
- PrnC
- Multidrug resistance protein B
- Outer membrane component of tripartite multidrug resistance system
- Multidrug resistance protein B
- Membrane fusion component of tripartite multidrug resistance system
- Outer membrane component of tripartite multidrug resistance system
- Pirin
- Catalase
- Mobile element protein
- Methyl-accepting chemotaxis protein
- Probable exported protein STY4558
- Soluble lytic murein transglycosylase and related regulatory proteins (some contain LysM/invasin dom)
- Multidrug resistance protein B
- Membrane fusion component of tripartite multidrug resistance system
- Outer membrane component of tripartite multidrug resistance system
- Pirin
- Catalase
- Phage integrase
| Gene ID     | Accession   | Start | End   | Description                                                       |
|------------|-------------|-------|-------|------------------------------------------------------------------|
| 5146667    | 5151453     | 4786  | 5147106 | DEAD/DEAH box helicase domain protein                           |
| 5146667    | 5151453     | 4786  | 5149706 | bll2187; hypothetical protein                                    |
| 5146667    | 5151453     | 4786  | 5150951 | FIG00957676: hypothetical protein                               |
| 5146667    | 5151453     | 4786  | 5151318 | Mycobacteriophage Barnyard protein gp56                         |
| 5286995    | 5294366     | 7371  | 5286983 | hypothetical protein                                              |
| 5286995    | 5294366     | 7371  | 5288289 | hypothetical protein                                              |
| 6237355    | 6243264     | 5909  | 6236450 | TniB NTP-binding protein                                         |
| 6237355    | 6243264     | 5909  | 6237355 | TniQ                                                             |
| 6237355    | 6243264     | 5909  | 6242509 | Phage terminase, large subunit (P2-like 5' - extended COS ends) |
| 6237355    | 6243264     | 5909  | 6243264 | Phage head completion-stabilization protein                     |
| 6403449    | 6413362     | 9913  | 6402981 | Phage capsid scaffolding protein                                 |
| 6403449    | 6413362     | 9913  | 6405754 | Phage major capsid protein                                       |
| 6403449    | 6413362     | 9913  | 6406776 | Phage terminase, small subunit                                   |
| 6403449    | 6413362     | 9913  | 6407581 | Phage tail X                                                     |
| 6403449    | 6413362     | 9913  | 6408279 | hypothetical protein                                              |
| 6403449    | 6413362     | 9913  | 6408634 | Phage major tail sheath protein                                  |
| 6403449    | 6413362     | 9913  | 6408906 | Putative phage-encoded peptidoglycan binding protein             |
| 6403449    | 6413362     | 9913  | 6409709 | Phage endolysin                                                  |
| 6403449    | 6413362     | 9913  | 6409706 | Phage tail completion protein                                    |
| 6403449    | 6413362     | 9913  | 6410245 | Phage tail completion protein                                    |
| 6403449    | 6413362     | 9913  | 6410245 | Phage tail completion protein                                    |
| 6403449    | 6413362     | 9913  | 6412086 | Baseplate assembly protein V                                     |
| 6403449    | 6413362     | 9913  | 6412086 | Baseplate assembly protein V                                     |
| 6403449    | 6413362     | 9913  | 6412655 | Phage baseplate assembly protein                                 |
| 6403449    | 6413362     | 9913  | 6412655 | Phage baseplate assembly protein                                 |
| 6414976    | 6431666     | 16690 | 6414524 | Phage tail fiber protein                                         |
| 6414976    | 6431666     | 16690 | 6414524 | Phage tail fiber protein                                         |
| 6414976    | 6431666     | 16690 | 6416351 | Phage major tail sheath protein                                  |
| 6414976    | 6431666     | 16690 | 6416886 | Phage major tail sheath protein                                  |
| 6414976    | 6431666     | 16690 | 6418118 | Phage major tail tube protein                                    |
| Start Position | End Position | Length | Identification          | Description                                      |
|---------------|--------------|--------|-------------------------|--------------------------------------------------|
| 6414976       | 6418688      | 1690   | Predicted by at least one method | Phage tail fibers                                |
| 6419026       | 6419145      | 1690   | Predicted by at least one method | hypothetical protein                             |
| 6419135       | 6425488      | 1690   | Predicted by at least one method | Phage tail length tape-measure protein            |
| 6421900       | 6422340      | 1690   | Predicted by at least one method | Phage tail protein                               |
| 6425085       | 6425435      | 1690   | Predicted by at least one method | Phage protein                                    |
| 6425488       | 6425604      | 1690   | Predicted by at least one method | Phage protein                                    |
| 6426181       | 6426393      | 1690   | Predicted by at least one method | hypothetical protein                             |
| 6426456       | 6426893      | 1690   | Predicted by at least one method | Orf33                                            |
| 6427180       | 6427530      | 1690   | Predicted by at least one method | hypothetical protein                             |
| 6427607       | 6427840      | 1690   | Predicted by at least one method | Phage protein                                    |
| 6430602       | 6430955      | 1690   | Predicted by at least one method | hypothetical protein                             |
| 6430967       | 6431173      | 1690   | Predicted by at least one method | FIG00957497: hypothetical protein                |
| 6431477       | 6433387      | 1690   | Predicted by at least one method | C-5 cytosine-specific DNA methylase              |
| 6431477       | 6433387      | 1690   | Predicted by at least one method | C-5 cytosine-specific DNA methylase              |
| 6433384       | 6434616      | 1690   | Predicted by at least one method | 3'-phosphoadenosine 5'-phosphosulfate sulfurtransferase DndC |
| 6435021       | 6436169      | 1690   | Predicted by at least one method | Mobile element protein                           |
| 6436288       | 6436485      | 1690   | Predicted by at least one method | hypothetical protein                             |
| Island start | Island end | Length | Method | Gene start | Gene end | Strand | Product |
|--------------|------------|--------|--------|------------|----------|--------|---------|
| 692912       | 699694     | 6782   | Predicted by at least one method | 692782     | 693477   | 1      | Phage minor tail protein |
| 692912       | 699694     | 6782   | Predicted by at least one method | 693480     | 694250   | 1      | Phage tail assembly protein |
| 692912       | 699694     | 6782   | Predicted by at least one method | 694305     | 694907   | 1      | Phage tail assembly protein I |
| 692912       | 699694     | 6782   | Predicted by at least one method | 694966     | 698619   | 1      | Phage tail fiber protein |
| 692912       | 699694     | 6782   | Predicted by at least one method | 699605     | 700705   | 1      | FIG00966085: hypothetical protein |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1062239    | 1062922  | 1      | FIG00954854: hypothetical protein |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1062915    | 1063811  | -1     | Cobalt-zinc-cadmium resistance protein |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1063900    | 1064316  | -1     | Polyribonucleotide nucleotidylyltransferase (polynucleotide phosphorylase) |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1064458    | 1066971  | 1      | ATP-dependent helicase HrpB |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1067027    | 1068493  | 1      | site-specific recombinase, phage integrase family |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1068490    | 1070418  | 1      | hypothetical protein |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1070415    | 1072463  | 1      | Phage Integrase |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1073027    | 1073209  | -1     | Transcriptional regulator, XRE family |
| 1062239      | 1077435    | 15196  | Predicted by at least one method | 1074042    | 1075328  | 1      | FIG: GGDEF domain |
| Accession | Start | End | Description | Prediction | Method | Notes |
|-----------|-------|-----|-------------|------------|--------|-------|
| 1062239   | 1077435 | 15196 | Mobile element protein | Predicted by at least one method | 1076628 | 1076924 | Mobile element protein |
| 1250070   | 1256769 | 6699  | Integrase   | Predicted by at least one method | 1250415 | 1251242 | Integrase |
| 1250070   | 1256769 | 6699  | Rossmann fold nucleotide-binding protein Smf possibly involved in DNA uptake | Predicted by at least one method | 1251867 | 1252259 | Rossmann fold nucleotide-binding protein Smf possibly involved in DNA uptake |
| 1250070   | 1256769 | 6699  | hypothetical protein | Predicted by at least one method | 1252792 | 1252908 | hypothetical protein |
| 1250070   | 1256769 | 6699  | hypothetical protein | Predicted by at least one method | 1252957 | 1253259 | hypothetical protein |
| 1250070   | 1256769 | 6699  | hypothetical protein | Predicted by at least one method | 1253256 | 1253597 | hypothetical protein |
| 1250070   | 1256769 | 6699  | Phage protein | Predicted by at least one method | 1253602 | 1254291 | Phage protein |
| 1250070   | 1256769 | 6699  | Phage protein | Predicted by at least one method | 1254464 | 1254655 | Phage protein |
| 1250070   | 1256769 | 6699  | Phage protein | Predicted by at least one method | 1254655 | 1254771 | Phage protein |
| 1250070   | 1256769 | 6699  | Phage protein | Predicted by at least one method | 1254768 | 1255430 | Phage protein |
| 1250070   | 1256769 | 6699  | Phage protein | Predicted by at least one method | 1255427 | 1255762 | Phage protein |
| 1250070   | 1256769 | 6699  | Phage protein | Predicted by at least one method | 1255765 | 1255995 | Phage protein |
| 1250070   | 1256769 | 6699  | hypothetical protein | Predicted by at least one method | 1256093 | 1256326 | hypothetical protein |
| 1250070   | 1256769 | 6699  | Transcriptional regulator, LuxR family | Predicted by at least one method | 1256329 | 1256715 | Transcriptional regulator, LuxR family |
| 1259042   | 1294050 | 35008 | hypothetical protein | Predicted by at least one method | 1260444 | 1260731 | hypothetical protein |
| #   | Gene ID | Start | Stop | Method | Prediction | Product                                    |
|-----|---------|-------|------|--------|------------|---------------------------------------------|
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1260728 | 1261036 | hypothesised protein |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1261304 | 1261537 | hypothesised protein |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1261783 | 1262304 | hypothesised protein |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1262301 | 1262531 | FIG00964051: hypothesised protein |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1262700 | 1263701 | Primosomal protein I |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1263698 | 1264486 | DNA replication protein DnaC |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1264483 | 1265913 | Replicative DNA helicase |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1265946 | 1266194 | FIG00956875: hypothesised protein |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1268531 | 1268863 | phage holin, lambda family |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1268860 | 1269477 | Lytic enzyme |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1269552 | 1269716 | hypothesised protein |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1271734 | 1273509 | Phage terminase, large subunit |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1273509 | 1273712 | hypothesised protein |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1274014 | 1275240 | Phage portal protein |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1275248 | 1277203 | ATP-dependent Clp protease proteolytic subunit |
| 1259042 | 1294050 | 35008 |      | Predicted by at least one method | 1277275 | 1277637 | hypothesised protein |
|     |     |     | Predicted by at least one method |     |     |     |
|-----|-----|-----|---------------------------------|-----|-----|-----|
| 1259042 | 1294050 | 35008 | Phage protein                   |     |     |     |
| 1259042 | 1294050 | 35008 | FIG00964642: hypothetical protein |     |     |     |
| 1259042 | 1294050 | 35008 | PE-PGRS virulence associated protein |     |     |     |
| 1259042 | 1294050 | 35008 | COG1156: Archaeal/vacuolar-type H+-ATPase subunit B |     |     |     |
| 1259042 | 1294050 | 35008 | FIG00956273: hypothetical protein |     |     |     |
| 1259042 | 1294050 | 35008 | FIG00964183: hypothetical protein |     |     |     |
| 1259042 | 1294050 | 35008 | FIG00965686: hypothetical protein |     |     |     |
| 1259042 | 1294050 | 35008 | Phage protein                   |     |     |     |
| 1259042 | 1294050 | 35008 | Phage protein                   |     |     |     |
| 1259042 | 1294050 | 35008 | Phage protein                   |     |     |     |
| Accession | Start | Stop | Predicted | Start | Stop | Method | Protein Description |
|-----------|-------|------|-----------|-------|------|--------|---------------------|
| 1259042   | 1294050 | 35008 | Predicted by at least one method | 1291717 | 1291866 | 1 | hypothetical protein |
| 1280516   | 1285257 | 4741  | Predicted by at least one method | 1280516 | 1282999 | 1 | FIG00954405: hypothetical protein |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1351733 | 1351996 | -1 | Transcriptional regulator in PFGI-1-like cluster |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1352076 | 1352837 | -1 | FIG00642059: hypothetical protein |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1353148 | 1353381 | 1 | FIG01214592: hypothetical protein |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1353715 | 1354260 | 1 | RecA-family ATPase |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1354307 | 1355119 | 1 | Phage replication protein |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1355851 | 1356129 | 1 | IncP-type oriT binding protein TraK |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1356449 | 1356820 | 1 | IncP-type oriT binding protein TraJ |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1357086 | 1357871 | 1 | Conjugative transfer protein TrbJ |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1357887 | 1358156 | 1 | Conjugative transfer entry exclusion protein TrbK |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1358153 | 1359742 | 1 | Conjugative transfer protein TrbL |
| 1351733   | 1360310 | 8577  | Predicted by at least one method | 1360080 | 1360310 | 1 | FIG01213713: hypothetical protein |
| Gene ID   | Accession | Start | Predicted by at least one method | Predicted by at least one method 1356820 | 1 | Description |
|-----------|-----------|-------|----------------------------------|------------------------------------------|---|-------------|
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1356449                                  | 1 | IncP-type oriT binding protein TraJ |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1357086                                  | 1 | Conjugative transfer protein TrbJ |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1357887                                  | 1 | Conjugative transfer entry exclusion protein TrbK |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1358153                                  | 1 | Conjugative transfer protein TrbL |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1360080                                  | 1 | FIG01213713: hypothetical protein |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1360555                                  | -1| hypothetical protein |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1361274                                  | -1| Mercuric transport protein, MerE |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1361489                                  | -1| Mercuric resistance operon coregulator |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1362619                                  | -1| Mercuric ion reductase |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1364318                                  | -1| Periplasmic mercury(+2) binding protein |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1364610                                  | -1| Mercuric transport protein, MerT |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1365032                                  | 1 | Mercuric resistance operon regulatory protein |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1365260                                  | -1| Aminoglycoside 3'- phosphotransferase 2 @ Streptomyacin 3'-kinase StrB |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1367705                                  | 1 | Mobile element protein |
| 1356449   | 1376084   | 19635 | Predicted by at least one method | 1370669                                  | 1 | Mobile element protein |
| 1356449 | 1376084 | 19635 | Predicted by at least one method | 1371515 | 1372150 | 1 | Type IV secretory pathway, VirD2 components (relaxase) |
| 1356449 | 1376084 | 19635 | Predicted by at least one method | 1374026 | 1375519 | 1 | Mobile element protein |
| 1370669 | 1375519 | 4850 | Predicted by at least one method | 1370669 | 1371235 | 1 | Mobile element protein |
| 1370669 | 1375519 | 4850 | Predicted by at least one method | 1371515 | 1372150 | 1 | Type IV secretory pathway, VirD2 components (relaxase) |
| 1370669 | 1375519 | 4850 | Predicted by at least one method | 1374026 | 1375519 | 1 | Mobile element protein |
| 1824172 | 1828539 | 4367 | Predicted by at least one method | 1824172 | 1824573 | -1 | hypothetical protein |
| 1824172 | 1828539 | 4367 | Predicted by at least one method | 1824763 | 1825953 | -1 | NADH oxidase |
| 1824172 | 1828539 | 4367 | Predicted by at least one method | 1825934 | 1826539 | -1 | hypothetical protein |
| 1824172 | 1828539 | 4367 | Predicted by at least one method | 1827043 | 1828539 | -1 | Type III restriction-modification system methylation subunit |
| 1996656 | 2001267 | 4611 | Predicted by at least one method | 1996656 | 1997390 | -1 | FIG01219979: hypothetical protein |
| 1996656 | 2001267 | 4611 | Predicted by at least one method | 1997484 | 1997870 | -1 | Glycine cleavage system H protein |
| 1996656 | 2001267 | 4611 | Predicted by at least one method | 1997982 | 1998158 | -1 | hypothetical protein |
| 1996656 | 2001267 | 4611 | Predicted by at least one method | 1998209 | 1998820 | -1 | FIG00984683: hypothetical protein |
| 1996656 | 2001267 | 4611 | Predicted by at least one method | 1998965 | 1999582 | -1 | Glutathione S-transferase |
| 1996656 | 2001267 | 4611 | Predicted by at least one method | 1999658 | 2000212 | -1 | Multimeric flavodoxin WrbA |
| 1996656 | 2001267 | 4611 | Predicted by at least one method | 2000314 | 2001267 | 1 | putative LysR-family transcriptional regulator |
| Gene ID | Accession | Predicted by at least one method | Start | End | Length | Function |
|--------|-----------|----------------------------------|-------|-----|--------|----------|
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2059528 | 1 | Biosynthetic Aromatic amino acid aminotransferase beta |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2061761 | 1 | Cyclohexadienyl dehydrogenase(EC 1.3.1.43) / 5-Enolpyruvylshikimate-3-phosphate synthase |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2062450 | 1 | Cytidylate kinase |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2064397 | 1 | SSU ribosomal protein S1p |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2064818 | 1 | Integration host factor beta subunit |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2070394 | 1 | UDP-N-acetylglucosamine 4,6-dehydratase |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2070834 | 1 | WbjC |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2071974 | 1 | UDP-N-acetylglucosamine 2-epimerase |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2073416 | 1 | Putative glycosyltransferase |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2074324 | 1 | UDP-glucose 4-epimerase |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2076539 | 1 | Nucleotide sugar epimerase/dehydratase WbpM |
| 2058383 | 2078921   | Predicted by at least one method | 20538 | 2078921 | 1 | DNA uptake protein and related DNA-binding proteins |
| 2457992 | 2469382   | Predicted by at least one method | 11390 | 2458203 | 1 | Hypothetical protein |
| 2457992 | 2469382   | Predicted by at least one method | 11390 | 2458218 | 1 | Hypothetical protein |
| 2457992 | 2469382   | Predicted by at least one method | 11390 | 2458412 | 1 | C-5 cytosine-specific DNA methylase |
| Accession | Start | Stop | Description                                   | Predicted by at least one method | Length | Family Protein |
|-----------|-------|------|----------------------------------------------|----------------------------------|--------|----------------|
| 2457992   | 2469382 | 11390 | family protein                               | 2460289 2460471 -1               |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2460778 2461017 -1               |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2461014 2461640 -1               |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2461690 2462007 -1               |        | transcriptional regulator, putative |
| 2457992   | 2469382 | 11390 | family protein                               | 2462004 2462234 -1               |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2462385 2462669 -1               |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2462688 2462999 -1               |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2464592 2464840 -1               |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2465330 2465614 1                |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2465618 2465848 1                |        |                |
| 2457992   | 2469382 | 11390 | family protein                               | 2466062 2467183 1                |        | DNA primase, phage associated |
| 2533321   | 2539616 | 6295  | family protein                               | 2533624 2534043 -1               |        | Hemoglobin-like protein HbO    |
| 2533321   | 2539616 | 6295  | family protein                               | 2539304 2541457 1                |        |                |
| 2541262   | 2554957 | 13695 | family protein                               | 2539304 2541457 1                |        |                |
| 2541262   | 2554957 | 13695 | family protein                               | 2541586 2544789 -1               |        |                |
| Method     | Predicted by at least one method | Gene ID | P-value | Score 1 | Score 2 | Hypothetical Protein |
|------------|----------------------------------|---------|---------|---------|---------|----------------------|
| 2541262    | Predicted by at least one method | 2546130 | -1      | 2544802 |         | hypothetical protein |
| 2541262    | Predicted by at least one method | 2546424 | -1      | 2546260 |         | hypothetical protein |
| 2541262    | Predicted by at least one method | 2546715 | 1       | 2546509 |         | hypothetical protein |
| 2541262    | Predicted by at least one method | 2547583 | -1      | 2547464 |         | hypothetical protein |
| 2541262    | Predicted by at least one method | 2551385 | -1      | 2548824 |         | autotransporter, putative |
| 2541262    | Predicted by at least one method | 2552029 | -1      | 2551583 |         | hypothetical protein |
| 2541262    | Predicted by at least one method | 2552515 | 1       | 2552168 |         | Transcriptional regulator, XRE family |
| 2541262    | Predicted by at least one method | 2552847 | -1      | 2552545 |         | hypothetical protein |
| 2541262    | Predicted by at least one method | 2553148 | -1      | 2552966 |         | hypothetical protein |
| 2541262    | Predicted by at least one method | 2554115 | 1       | 2553195 |         | FIG00957676: hypothetical protein |
| 2541262    | Predicted by at least one method | 2555199 | -1      | 2554195 |         | Phage-related protein |
| 2557079    | Predicted by at least one method | 2557216 | -1      | 2556944 |         | FIG00957676: hypothetical protein |
| 2557079    | Predicted by at least one method | 2559361 | 1       | 2557415 |         | Phage T7 exclusion protein |
| 2557079    | Predicted by at least one method | 2560256 | 1       | 2559726 |         | Phage T7 exclusion protein associated hypothetical protein |
| 2557079    | Predicted by at least one method | 2561623 | 1       | 2560253 |         | FIG014574: hypothetical protein |
| 2557079    | Predicted by at least one method | 2562392 | 1       | 2561964 |         | Putative deoxyribonuclease similar to |
| Method                              | Type                                  | Predicted by at least one method | Predicted by at least two methods | Predicted by at least three methods | Predicted by at least four methods |
|------------------------------------|---------------------------------------|---------------------------------|----------------------------------|-----------------------------------|----------------------------------|
| YcfH, type 4                       |                                       |                                 |                                  |                                   |                                  |
| 2557079 2586926 29847              | Predicted by at least one method      | 2563842                         | 2564168                          | -1                                | Phage integrase                  |
| 2557079 2586926 29847              | Predicted by at least one method      | 2564507                         | 2569636                          | 1                                 | ATP-dependent DNA helicase RecQ  |
| 2557079 2586926 29847              | Predicted by at least one method      | 2569735                         | 2569950                          | 1                                 | VrII protein                     |
| 2557079 2586926 29847              | Predicted by at least one method      | 2569979                         | 2571985                          | 1                                 | Type I restriction-modification system, DNA-methyltransferase subunit M |
| 2557079 2586926 29847              | Predicted by at least one method      | 2571982                         | 2573319                          | 1                                 | hypothetical protein             |
| 2557079 2586926 29847              | Predicted by at least one method      | 2573822                         | 2575360                          | 1                                 | type I restriction-modification system, S subunit, putative |
| 2557079 2586926 29847              | Predicted by at least one method      | 2575362                         | 2579522                          | 1                                 | protein kinase, putative         |
| 2557079 2586926 29847              | Predicted by at least one method      | 2579522                         | 2581195                          | 1                                 | hypothetical protein             |
| 2557079 2586926 29847              | Predicted by at least one method      | 2581192                         | 2586756                          | 1                                 | hypothetical protein             |
| 2557079 2586926 29847              | Predicted by at least one method      | 2586874                         | 2588265                          | -1                                | Phage-related integrase          |
| 2660502 2664757 4255               | Predicted by at least one method      | 2660502                         | 2660927                          | 1                                 | General secretion pathway protein I |
| 2660502 2664757 4255               | Predicted by at least one method      | 2660924                         | 2661514                          | 1                                 | Type II secretory pathway, pseudopilin PuG |
| 2660502 2664757 4255               | Predicted by at least one method      | 2661570                         | 2662583                          | 1                                 | Type II secretory pathway, component PuK |
| 2660502 2664757 4255               | Predicted by at least one method      | 2663230                         | 2663613                          | 1                                 | hypothetical protein             |
| 2660502 2664757 4255               | Predicted by at least one method      | 2663613                         | 2664197                          | 1                                 | FIG00959371: hypothetical protein |
| Start | End | Length | Description | Predicted by at least one method | Score | Ref | Notes |
|-------|-----|--------|-------------|---------------------------------|-------|-----|-------|
| 2660502 | 2664757 | 4255 | Predicted by at least one method | 2664440 2664757 | 1 | FIG00956760: hypothetical protein |
| 2764609 | 2769544 | 4935 | Predicted by at least one method | 2764688 2765692 | -1 | Integrase |
| 2764609 | 2769544 | 4935 | Predicted by at least one method | 2766149 2766271 | -1 | hypothetical protein |
| 2764609 | 2769544 | 4935 | Predicted by at least one method | 2766264 2766743 | -1 | Phage protein |
| 2764609 | 2769544 | 4935 | Predicted by at least one method | 2766743 2768023 | -1 | Phage protein |
| 2764609 | 2769544 | 4935 | Predicted by at least one method | 2768121 2768627 | -1 | hypothetical protein |
| 2764609 | 2769544 | 4935 | Predicted by at least one method | 2768986 2769546 | -1 | Phage protein |
| 2764609 | 2769544 | 4935 | Predicted by at least one method | 2769543 2770169 | -1 | Phage-related protein |
| 3282390 | 3292432 | 10042 | Predicted by at least one method | 3281830 3282549 | -1 | Uncharacterized protein conserved in bacteria |
| 3282390 | 3292432 | 10042 | Predicted by at least one method | 3289861 3290883 | -1 | elements of external origin; transposon-related functions |
| 3282390 | 3292432 | 10042 | Predicted by at least one method | 3291570 3291920 | 1 | hypothetical protein |
| 3282549 | 3299339 | 16790 | Predicted by at least one method | 3289861 3290883 | -1 | elements of external origin; transposon-related functions |
| 3282549 | 3299339 | 16790 | Predicted by at least one method | 3291570 3291920 | 1 | hypothetical protein |
| 3282549 | 3299339 | 16790 | Predicted by at least one method | 3292994 3293215 | -1 | hypothetical protein |
| 3282549 | 3299339 | 16790 | Predicted by at least one method | 3293254 3294255 | -1 | Cointegrate resolution protein Tn4652, cointegrate resolution protein S |
| 3282549 | 3299339 | 16790 | Predicted by at least one method | 3294436 3295407 | 1 | |
| Accession  | Start | End   | Description                                         |
|-----------|-------|-------|-----------------------------------------------------|
| 3282549   | 3299339 | 16790 | Predicted by at least one method                    |
| 3282549   | 3299339 | 16790 | Predicted by at least one method                    | Bacteriophage protein gp37
| 3282549   | 3299339 | 16790 | Predicted by at least one method                    | hypothetical protein
| 3295437   | 3305107 | 9670  | Predicted by at least one method                    | Homospermidine synthase
| 3295437   | 3305107 | 9670  | Predicted by at least one method                    | hypothetical protein
| 3295437   | 3305107 | 9670  | Predicted by at least one method                    | Homospermidine synthase
| 3295437   | 3305107 | 9670  | Predicted by at least one method                    | Mobile element protein
| 3295437   | 3305107 | 9670  | Predicted by at least one method                    | Heavy metal RND efflux outer membrane protein, CzcC family
| 3295437   | 3305107 | 9670  | Predicted by at least one method                    | Cobalt/zinc/cadmium efflux RND transporter, membrane fusion protein, CzcB family
| 3309987   | 3316647 | 6660  | Predicted by at least one method                    | hypothetical protein
| 3309987   | 3316647 | 6660  | Predicted by at least one method                    | BNR repeat domain protein
| 3309987   | 3316647 | 6660  | Predicted by at least one method                    | Putative protein-S-isoprenylcysteine methyltransferase
| 3309987   | 3316647 | 6660  | Predicted by at least one method                    | hypothetical protein
| 3309987   | 3316647 | 6660  | Predicted by at least one method                    | hypothetical protein
| 3309987   | 3316647 | 6660  | Predicted by at least one method                    | hypothetical protein
| FIG00954364 |       |       | FIG00954364: hypothetical protein
|    |    |    | method                        |    |    |          |          |          |          |          |          |
|----|----|----|------------------------------|----|----|----------|----------|----------|----------|----------|----------|
| 3309987 | 3316647 | 6660 | Predicted by at least one method | 3314443 | 3315762 | -1 | hypothetical protein |
| 3309987 | 3316647 | 6660 | Predicted by at least one method | 3315785 | 3316528 | -1 | Bacteriophage protein gp37 |
| 3309987 | 3316647 | 6660 | Predicted by at least one method | 3316558 | 3317529 | -1 | Tn4652, cointegrate resolution protein S |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3310522 | 3311208 | 1 | BNR repeat domain protein |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3311303 | 3311965 | -1 | Putative protein-S-isoprenylcysteine methyltransferase |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3312122 | 3312286 | -1 | hypothetical protein |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3312390 | 3312674 | -1 | hypothetical protein |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3312866 | 3312979 | 1 | hypothetical protein |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3314035 | 3314253 | 1 | FIG00954364: hypothetical protein |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3314443 | 3315762 | -1 | hypothetical protein |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3315785 | 3316528 | -1 | Bacteriophage protein gp37 |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3316558 | 3317529 | -1 | Tn4652, cointegrate resolution protein S |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3317709 | 3318707 | 1 | Cointegrate resolution protein T |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3318794 | 3319390 | 1 | hypothetical protein |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3319479 | 3319850 | 1 | FIG00960741: hypothetical protein |
| 3310522 | 3328945 | 18423 | Predicted by at least one method | 3320782 | 3321216 | -1 | Mercuric resistance operon regulatory |
| Accession  | Accession  | Start | Method                                             | Predicted      | Protein                                                                 |
|-----------|-----------|-------|---------------------------------------------------|----------------|--------------------------------------------------------------------------|
| 3310522   | 3328945   | 18423 | Predicted by at least one method                  | 3321288        | Mercuric transport protein, MerT                                          |
| 3310522   | 3328945   | 18423 | Predicted by at least one method                  | 3321651        | Periplasmic mercury(+2) binding protein                                   |
| 3310522   | 3328945   | 18423 | Predicted by at least one method                  | 3321998        | Mercuric ion reductase                                                   |
| 3310522   | 3328945   | 18423 | Predicted by at least one method                  | 3323701        | Mercuric resistance operon coregulator                                    |
| 3310522   | 3328945   | 18423 | Predicted by at least one method                  | 3324063        | Mercuric transport protein, MerE                                          |
| 3310522   | 3328945   | 18423 | Predicted by at least one method                  | 3324296        | Tn21 protein of unknown function Urf2                                     |
| 3310522   | 3328945   | 18423 | Predicted by at least one method                  | 3325416        | Transposon Tn21 resolvase                                                |
| 3310522   | 3328945   | 18423 | Predicted by at least one method                  | 3325979        | Mobile element protein                                                   |
| 3317497   | 3336299   | 18802 | Predicted by at least one method                  | 3316558        | Tn4652, cointegrate resolution protein S                                  |
| 3317497   | 3336299   | 18802 | Predicted by at least one method                  | 3317709        | Cointegrate resolution protein T                                          |
| 3317497   | 3336299   | 18802 | Predicted by at least one method                  | 3318794        | hypothetical protein                                                     |
| 3317497   | 3336299   | 18802 | Predicted by at least one method                  | 3319479        | FIG00960741: hypothetical protein                                        |
| 3317497   | 3336299   | 18802 | Predicted by at least one method                  | 3320782        | Mercuric resistance operon regulatory protein                             |
| 3317497   | 3336299   | 18802 | Predicted by at least one method                  | 3320782        | Mercuric transport protein, MerT                                          |
| 3317497   | 3336299   | 18802 | Predicted by at least one method                  | 3321651        | Periplasmic mercury(+2) binding protein                                  |
| 3317497   | 3336299   | 18802 | Predicted by at least one method                  | 3321998        | Mercuric ion reductase                                                   |
| ID       | Type                          | Predicted by at least one method | GenBank ID | ENSMUSG00000012092 ID | Gene          |
|----------|-------------------------------|----------------------------------|------------|-----------------------|---------------|
| 3317497  | Mercuric resistance operon coregulator | Predicted by at least one method | 3323701    | 3324066               | 1             |
| 3317497  | Mercuric transport protein, MerE | Predicted by at least one method | 3324063    | 3324299               | 1             |
| 3317497  | Tn21 protein of unknown function Urf2 | Predicted by at least one method | 3324296    | 3325285               | 1             |
| 3317497  | Transposon Tn21 resolvase     | Predicted by at least one method | 3325416    | 3325976               | 1             |
| 3317497  | Mobile element protein        | Predicted by at least one method | 3325979    | 3328945               | 1             |
| 3317497  | Phage replication initiation protein | Predicted by at least one method | 3330777    | 3332063               | 1             |
| 3317497  | hypothetical protein          | Predicted by at least one method | 3332411    | 3332761               | 1             |
| 3317497  | hypothetical protein          | Predicted by at least one method | 3332973    | 3333179               | 1             |
| 3317497  | Probable coat protein A precursor | Predicted by at least one method | 3333330    | 3334784               | 1             |
| 3415794  | Copper chaperone              | Predicted by at least one method | 3415794    | 3415988               | 1             |
| 3415794  | hypothetical protein          | Predicted by at least one method | 3416063    | 3416821               | -1            |
| 3415794  | Ferredoxin, 2Fe-2S            | Predicted by at least one method | 3417039    | 3417377               | -1            |
| 3415794  | HTH-type transcriptional regulator cueR | Predicted by at least one method | 3417394    | 3417873               | -1            |
| 3415794  | Lead, cadmium, zinc and mercury transporting ATPase; Copper-translocating P-type ATPase | Predicted by at least one method | 3417889    | 3420318               | -1            |
| 3415794  | Transcriptional regulator, ArsR family | Predicted by at least one method | 3420698    | 3420979               | 1             |
| Start | End | Gene | Predicted by | Start | End | COG | Description |
|-------|-----|------|-------------|-------|-----|-------|-------------|
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3421018 | 3422328 | -1 | Probable NreB protein |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3422338 | 3422595 | -1 | hypothetical protein |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3422687 | 3422893 | -1 | LysR family transcriptional regulator STM3121 |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3423003 | 3424163 | -1 | Bicyclomycin resistance protein |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3424449 | 3426311 | -1 | Type IV secretory pathway, VirD2 components (relaxase) |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3426734 | 3427693 | -1 | transposase InsA |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3428178 | 3429653 | 1 | COG0488: ATPase components of ABC transporters with duplicated ATPase domains |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3429935 | 3431464 | -1 | transposase InsA |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3431922 | 3432734 | -1 | Beta-lactamase |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3432792 | 3432908 | 1 | Microsomal dipeptidase |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3433173 | 3434702 | -1 | transposase InsA |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3434929 | 3435075 | -1 | Heat shock protein 60 family chaperone GroEL |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3435377 | 3435634 | -1 | NreA-like protein |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3435924 | 3436955 | 1 | Cobalt-zinc-cadmium resistance protein CzcD |
| 3415794 | 3442212 | 26418 | Predicted by at least one method | 3436999 | 3437376 | 1 | Transcriptional regulator, ArsR family |
| Accession | Accession | Length | Description | Score 1 | Score 2  |
|-----------|-----------|--------|-------------|---------|---------|
| 3415794   | 3442212   | 26418  | Predicted by at least one method | 3437801 | 3439039 |
| 3415794   | 3442212   | 26418  | Predicted by at least one method | 3439036 | 3442212 |
| 4367448   | 4374573   | 7125   | Predicted by at least one method | 4367448 | 4367714 |
| 4367448   | 4374573   | 7125   | Predicted by at least one method | 4368208 | 4368798 |
| 4367448   | 4374573   | 7125   | Predicted by at least one method | 4370100 | 4370444 |
| 4367448   | 4374573   | 7125   | Predicted by at least one method | 4370517 | 4371980 |
| 4368032   | 4387238   | 19206  | Predicted by at least one method | 4370100 | 4370444 |
| 4368032   | 4387238   | 19206  | Predicted by at least one method | 4370517 | 4371980 |
| 4368032   | 4387238   | 19206  | Predicted by at least one method | 4373089 | 4374573 |
| 4368032   | 4387238   | 19206  | Predicted by at least one method | 4373089 | 4374573 |
| 4368032   | 4387238   | 19206  | Predicted by at least one method | 4374670 | 4375398 |
| 4368032   | 4387238   | 19206  | Predicted by at least one method | 4375415 | 4377106 |
| 4368032   | 4387238   | 19206  | Predicted by at least one method | 4377118 | 4378101 |

**Probable Co/Zn/Cd efflux system membrane fusion protein / Multidrug efflux membrane fusion protein M**

**RND multidrug efflux transporter; Acriflavin resistance protein**

**FIG00953120: hypothetical protein**

**Adenylylsulfate kinase**

**probable glycosyl transferase**

**hypothetical protein**

**Twin-arginine translocation protein TatC**

**SN-glycerol-3-phosphate transport ATP-binding protein UgpC (TC 3.A.1.1.3)**
| Gene ID   | Start Position | Length | Function Description                                                                 |
|----------|----------------|--------|--------------------------------------------------------------------------------------|
| 4368032  | 437238         | 19206  | Predicted by at least one method                                                      |
| 4368032  | 437238         | 19206  | Predicted by at least one method                                                      |
| 4368032  | 437238         | 19206  | Predicted by at least one method                                                      |
| 4368032  | 437238         | 19206  | Predicted by at least one method                                                      |
| 4368032  | 437238         | 19206  | Predicted by at least one method                                                      |
| 4368032  | 437238         | 19206  | Predicted by at least one method                                                      |
| 4368032  | 437238         | 19206  | Predicted by at least one method                                                      |
| 4403905  | 4408549        | 4644   | Predicted by at least one method                                                      |
| 4403905  | 4408549        | 4644   | Predicted by at least one method                                                      |
| 4403905  | 4408549        | 4644   | Predicted by at least one method                                                      |
| 4403905  | 4408549        | 4644   | Predicted by at least one method                                                      |
| 4403905  | 4408549        | 4644   | Predicted by at least one method                                                      |
| 4403905  | 4408549        | 4644   | Predicted by at least one method                                                      |
| 4403905  | 4408549        | 4644   | Predicted by at least one method                                                      |
| 4838207  | 4851391        | 13184  | Predicted by at least one method                                                      |

- **Lipid carrier**: UDP-N-acetyl-N-acetylgalactosamine transferase / Alpha-1,3-N-acetyl-N-galactosamine transferase
- **3-oxoacyl-acyl-carrier protein reductase**
- **Putative protein-S-isoprenylcysteine methyltransferase**
- **Thioredoxin reductase**
- **Phenazine biosynthesis protein PhzF like**
- **Lipoprotein, phage-associated**
| GeneID | EnsemblID | Status | Description |
|--------|-----------|--------|-------------|
| 4838207 | 4851391  | 13184  | Predicted by at least one method |
| 4838207 | 4851391  | 13184  | Predicted by at least one method |
| 4838207 | 4851391  | 13184  | Predicted by at least one method |
| 4838207 | 4851391  | 13184  | Predicted by at least one method |
| 4838207 | 4851391  | 13184  | Predicted by at least one method |
| 4838207 | 4851391  | 13184  | Predicted by at least one method |
| 4838207 | 4851391  | 13184  | Predicted by at least one method |
| 4838207 | 4851391  | 13184  | Predicted by at least one method |

- Hypothetical protein
- Phage terminase, small subunit
- Phage terminase, large subunit
- Phage (Mu-like) virion morphogenesis protein
- Possible bacteriophage Mu G-like protein
- Mu-like prophage FluMu protein gp29
- Mu-like prophage FluMu I protein
- Phage major capsid protein
- Phage protein
- Phage protein
- Phage protein
- Phage protein
- Hypothetical protein
- Phage protein
- Phage protein
- Phage protein
| GenBank Accession | Start Position | Length | Description                                                                 |
|-------------------|----------------|--------|------------------------------------------------------------------------------|
| 4838207 4851391  | 13184          |        | Predicted by at least one method                                               |
|                  |                |        | 4850035 4850178 1 hypothetical protein                                          |
| 4838207 4851391  | 13184          |        | Predicted by at least one method                                               |
|                  |                |        | 4850274 4853906 1 Phage tail length tape-measure protein                      |
| 4856326 4862805  | 6479           |        | Predicted by at least one method                                               |
|                  |                |        | 4855827 4857497 1 Phage protein                                               |
| 4856326 4862805  | 6479           |        | Predicted by at least one method                                               |
|                  |                |        | 4857751 4858302 1 Phage FAD/FMN-containing dehydrogenase                      |
| 4856326 4862805  | 6479           |        | Predicted by at least one method                                               |
|                  |                |        | 4858312 4858542 1 Phage protein                                               |
| 4856326 4862805  | 6479           |        | Predicted by at least one method                                               |
|                  |                |        | 4858843 4860966 1 Phage protein                                               |
| 4856326 4862805  | 6479           |        | Predicted by at least one method                                               |
|                  |                |        | 4860963 4862111 1 Phage protein                                               |
| 4856326 4862805  | 6479           |        | Predicted by at least one method                                               |
|                  |                |        | 4862108 4862395 1 Phage protein                                               |
| 4856326 4862805  | 6479           |        | Predicted by at least one method                                               |
|                  |                |        | 4862556 4862693 1 Phage protein                                               |
| 4877202 4881300  | 4098           |        | Predicted by at least one method                                               |
|                  |                |        | 4877202 4877450 1 FIG00960798: hypothetical protein                           |
| 4877202 4881300  | 4098           |        | Predicted by at least one method                                               |
|                  |                |        | 4877453 4879183 1 Protein with ParB-like nuclease domain in PFGI-1-like cluster|
| 4877202 4881300  | 4098           |        | Predicted by at least one method                                               |
|                  |                |        | 4879211 4879978 1 FIG004780: hypothetical protein in PFGI-1-like cluster       |
| 4877202 4881300  | 4098           |        | Predicted by at least one method                                               |
|                  |                |        | 4879975 4881300 1 FIG141751: hypothetical protein in PFGI-1-like cluster       |
| 4888015 4892813  | 4798           |        | Predicted by at least one method                                               |
|                  |                |        | 4888015 4888167 1 Haemophilus-specific protein, uncharacterized                |
| 4888015 4892813  | 4798           |        | Predicted by at least one method                                               |
|                  |                |        | 4888189 4888767 1 Haemophilus-specific protein, uncharacterized                |
| 4888015 4892813  | 4798           |        | Predicted by at least one method                                               |
|                  |                |        | 4888884 4889489 -1 Homoserine/homoserine lactone efflux protein                |
| Gene ID 1 | Gene ID 2 | Gene ID 3 | Description                                                                                     |
|----------|-----------|-----------|------------------------------------------------------------------------------------------------|
| 4888015 | 4892813   | 4798      | Predicted by at least one method                                                                 |
| 4888015 | 4892813   | 4798      | Predicted by at least one method                                                                 |
| 4888015 | 4892813   | 4798      | Predicted by at least one method                                                                 |
| 4908449 | 4913491   | 5042      | Predicted by at least one method                                                                 |
| 4908449 | 4913491   | 5042      | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| FIG00963899 |         |           | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |
| 4926932 | 4944056   | 17124     | Predicted by at least one method                                                                 |

**Description:**
- Transcriptional regulator, LysR family
- Hypothetical protein in PFGI-1-like cluster
- DNA/RNA helicase in PFGI-1-like cluster
- Hypothetical protein
- FIG00963899: hypothetical protein
- Inner membrane component of tripartite multidrug resistance system
- Membrane fusion component of tripartite multidrug resistance system
- Transcriptional regulator, LysR family
- Hypothetical protein
- PrnC
- Multidrug resistance protein B
- Outer membrane component of tripartite multidrug resistance system
- Pirin
- Catalase
- Mobile element protein
- Methyl-accepting chemotaxis protein
| Accession | Accession | Length | Status | Description |
|-----------|-----------|--------|--------|-------------|
| 4929266   | 4941323   | 12057  | Predicted by at least one method | Transcriptional regulator, LysR family |
| 4929266   | 4941323   | 12057  | Predicted by at least one method | hypothetical protein |
| 4929266   | 4941323   | 12057  | Predicted by at least one method | PrnC |
| 4929266   | 4941323   | 12057  | Predicted by at least one method | Multidrug resistance protein B |
| 4929266   | 4941323   | 12057  | Predicted by at least one method | Outer membrane component of tripartite multidrug resistance system |
| 4929266   | 4941323   | 12057  | Predicted by at least one method | Pirin |
| 4929266   | 4941323   | 12057  | Predicted by at least one method | Catalase |
| 4982171   | 4987382   | 5211   | Predicted by at least one method | hypothetical protein |
| 4982171   | 4987382   | 5211   | Predicted by at least one method | Pyruvate/2-oxoglutarate dehydrogenase complex, dihydrolipoamide acyltransferase (E2) component, and |
| 4982171   | 4987382   | 5211   | Predicted by at least one method | Integrase |
| 4982171   | 4987382   | 5211   | Predicted by at least one method | Chromosome (plasmid) partitioning protein ParA |
| 4988621   | 4992964   | 4343   | Predicted by at least one method | FIG00954566: hypothetical protein |
| 4988621   | 4992964   | 4343   | Predicted by at least one method | FIG004780: hypothetical protein in PFGI-1-like cluster |
| 4988621   | 4992964   | 4343   | Predicted by at least one method | Phage protein |
| 4988621   | 4992964   | 4343   | Predicted by at least one method | FIG00953473: hypothetical protein |
| 4988621 | 4992964 | 4343 | Predicted by at least one method | 4990944 | 4992287 | 1 | Replicative DNA helicase |
| 4988621 | 4992964 | 4343 | Predicted by at least one method | 4992344 | 4992964 | 1 | hypothetical protein |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 4996138 | 4997160 | 1 | Nucleoid-associated protein |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 4997157 | 4998047 | 1 | DNA methyl transferase, phage-associated |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 4998068 | 4998340 | 1 | FIG00960798: hypothetical protein |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 4998340 | 5000067 | 1 | Protein with ParB-like nuclease domain in PFGI-1-like cluster |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 5000095 | 5000850 | 1 | FIG004780: hypothetical protein in PFGI-1-like cluster |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 5000847 | 5002178 | 1 | FIG141751: hypothetical protein in PFGI-1-like cluster |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 5002199 | 5003065 | 1 | Protein-L-isoaspartate O-methyltransferase |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 5003331 | 5004059 | 1 | FIG141694: hypothetical protein in PFGI-1-like cluster |
| 4997157 | 5004613 | 7456 | Predicted by at least one method | 5004065 | 5004613 | 1 | Integrase regulator R |
| 5023128 | 5028585 | 5457 | Predicted by at least one method | 5022601 | 5023131 | 1 | Conjugative transfer protein PilS in PFGI-1-like cluster |
| 5023128 | 5028585 | 5457 | Predicted by at least one method | 5023128 | 5024084 | 1 | Conjugative transfer ATPase PilU in PFGI-1-like cluster |
| 5023128 | 5028585 | 5457 | Predicted by at least one method | 5024077 | 5025456 | 1 | Conjugative transfer pilus-tip adhesin protein PilV in PFGI-1-like cluster |
| 5023128 | 5028585 | 5457 | Predicted by at least one method | 5025474 | 5025911 | 1 | Conjugative transfer protein PilM in PFGI-1-like cluster |
| 5023128 | 5028585 | 5457 | Predicted by at least one method | 5026910 | 5027884 | 1 | putative transposase |
|     |     |     | Predicted by at least one method |     |     |     |
|-----|-----|-----|---------------------------------|-----|-----|-----|
| 5023128 | 5028585 | 5457 | Predicted by at least one method | 5028196 | 5028585 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5025474 | 5025911 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5026910 | 5027884 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5028196 | 5028585 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5029297 | 5029785 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5030144 | 5030776 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5030773 | 5031048 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5031118 | 5031480 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5031548 | 5031808 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5031901 | 5032506 | 1 |
| 5025474 | 5033981 | 8507 | Predicted by at least one method | 5032536 | 5033981 | 1 |
| 5070115 | 5077947 | 7832 | Predicted by at least one method | 5070115 | 5070462 | 1 |
| 5070115 | 5077947 | 7832 | Predicted by at least one method | 5070459 | 5071970 | 1 |
| 5070115 | 5077947 | 7832 | Predicted by at least one method | 5072476 | 5072748 | 1 |

- FIG00963899: hypothetical protein
- Conjugative transfer protein PilM in PFGI-1-like cluster
- FIG051360: Periplasmic protein TonB, links inner and outer membranes
- Predicted transcriptional regulators containing the CopG/Arc/MetJ DNA-binding domain

- Predicted by at least one method

- FIG00963899: hypothetical protein
- Conjugative transfer protein PilM in PFGI-1-like cluster
- FIG051360: Periplasmic protein TonB, links inner and outer membranes
- Predicted transcriptional regulators containing the CopG/Arc/MetJ DNA-binding domain
| Accession | Start | Stop | Description                                                                 |
|-----------|-------|------|-----------------------------------------------------------------------------|
| 5070115   | 5077947 | 7832 | Predicted by at least one method | putative plasmid stabilization protein |
| 5072752   | 5073105 | 1    | Pyruvate/2-oxoglutarate dehydrogenase complex, dihydrolipoamide acyltransferase (E2) component, and |
| 5074844   | 5076670 | 1    | Integrase                                                                    |
| 5237432   | 5241643 | 4211 | Predicted by at least one method | Phage integrase |
| 5237432   | 5241643 | 4211 | Predicted by at least one method | DEAD/DEAH box helicase domain protein |
| 5239043   | 5241643 | 1    | DEAD/DEAH box helicase domain protein |
| 5238604   | 5243390 | 4786 | Predicted by at least one method | Phage integrase |
| 5239043   | 5241643 | 1    | DEAD/DEAH box helicase domain protein |
| 5238604   | 5243390 | 4786 | Predicted by at least one method | bll2187; hypothetical protein |
| 5238604   | 5243390 | 4786 | Predicted by at least one method | FIG00957676: hypothetical protein |
| 5238604   | 5243390 | 4786 | Predicted by at least one method | Mycobacteriophage Barnyard protein gp56 |
| 5378932   | 5386303 | 7371 | Predicted by at least one method | Phage protein |
| 5378932   | 5386303 | 7371 | Predicted by at least one method | hypothetical protein |
| 6329293   | 6335202 | 5909 | Predicted by at least one method | TniB NTP-binding protein |
| 6329293   | 6335202 | 5909 | Predicted by at least one method | TniQ |
| 6329293   | 6335202 | 5909 | Predicted by at least one method | TniQ |
| ID     | Start | Length | Classification                                                                 |
|--------|-------|--------|---------------------------------------------------------------------------------|
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage terminase, large subunit (P2-like 5'-extended COS ends)                    |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage capsid scaffolding protein                                                 |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage major capsid protein                                                       |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage terminase, small subunit                                                  |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage head completion-stabilization protein                                     |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage tail X                                                                     |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | hypothetical protein                                                             |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage protein                                                                    |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Putative phage-encoded peptidoglycan binding protein                            |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage endolysin                                                                  |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage tail completion protein                                                    |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage tail completion protein                                                    |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Baseplate assembly protein V                                                      |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Phage baseplate assembly protein                                                 |
| 6495387| 6505300| 9913   | Predicted by at least one method                                                |
|        |       |        | Baseplate assembly protein J                                                      |
| 6506914| 6523604| 16690  | Predicted by at least one method                                                |
|        |       |        | Phage tail fiber protein                                                          |
| Gene ID   | Start   | End   | Description                                                      |
|----------|---------|-------|-----------------------------------------------------------------|
| 6506914  | 6523604 | 16690 | Phage tail fiber assembly protein                               |
| 6506914  | 6523604 | 16690 | Phage major tail sheath protein                                 |
| 6506914  | 6523604 | 16690 | Phage major tail tube protein                                   |
| 6506914  | 6523604 | 16690 | Phage tail tube protein                                          |
| 6506914  | 6523604 | 16690 | Phage tail length tape-measure protein                          |
| 6506914  | 6523604 | 16690 | Phage tail protein                                              |
| 6506914  | 6523604 | 16690 | Phage protein D                                                 |
| 6506914  | 6523604 | 16690 | Phage protein                                                   |
| 6506914  | 6523604 | 16690 | Phage-related protein                                           |
| 6506914  | 6523604 | 16690 | Hypothetical protein                                            |
| Accession | Start Position | Length | Prediction Method | Annotation |
|-----------|----------------|--------|-------------------|------------|
| 6506914   | 6523604        | 16690  | Predicted by at least one method | FIG00957497: hypothetical protein |
| 6506914   | 6523604        | 16690  | Predicted by at least one method | C-5 cytosine-specific DNA methylase |
| 6523832   | 6528267        | 4435   | Predicted by at least one method | C-5 cytosine-specific DNA methylase |
| 6523832   | 6528267        | 4435   | Predicted by at least one method | 3'-phosphoadenosine 5'-phosphosulfate sulfurtransferase DndC |
| 6523832   | 6528267        | 4435   | Predicted by at least one method | Mobile element protein |
| 6523832   | 6528267        | 4435   | Predicted by at least one method | hypothetical protein |
Table S5 The 550 genes that are differentially expressed between AZM-treated and non-treated PAO1. Gene names, fold change, P value and functional annotations are shown in the table. Cut-off: fold-change > 4, P value < 0.05.

| Gene name | Fold change | P value | Functional annotation                                      |
|-----------|-------------|---------|----------------------------------------------------------|
| PA1914    | -43.99      | 0.00    |                                                          |
| rmf       | -40.52      | 0.00    | ribosome modulation factor                                |
| PA0111    | -31.65      | 0.00    |                                                          |
| PA3568    | -29.15      | 0.00    | probable acetyl-coa synthetase                           |
| PA3415    | -22.72      | 0.00    | probable dihydrolipoamide acetyltransferase              |
| PA5096    | -21.86      | 0.00    | probable binding protein component of ABC transporter    |
| PA1877    | -20.83      | 0.00    | probable secretion protein                               |
| PA0112    | -20.75      | 0.00    | hypothetical protein                                     |
| hutG      | -20.36      | 0.00    | N-formylglutamate amidohydrolase                         |
| PA4298    | -20.35      | 0.00    |                                                          |
| coxA      | -19.52      | 0.00    | cytochrome c oxidase, subunit I                          |
| PA5099    | -19.39      | 0.00    | probable transporter                                     |
| hutU      | -19.26      | 0.00    | urocanase                                               |
| PA1874    | -18.91      | 0.00    |                                                          |
| PA4377    | -18.78      | 0.00    |                                                          |
| hutH      | -18.25      | 0.00    | histidine ammonia-lyase                                  |
| PA3416    | -18.23      | 0.00    | probable pyruvate dehydrogenase E1 component, beta chain |
| PA4637a   | -17.13      | 0.00    |                                                          |
| mmsA      | -16.95      | 0.00    | methylmalonate-semialdehyde dehydrogenase                |
| PA1876    | -16.84      | 0.00    | probable ATP-binding/permease fusion ABC transporter     |
| PA0113    | -16.09      | 0.00    | probable cytochrome c oxidase assembly factor            |
| PA3919    | -16.00      | 0.00    | conserved hypothetical protein                          |
| tadA      | -15.89      | 0.00    | TadA ATPase                                            |
| PA1875    | -15.80      | 0.00    | probable outer membrane protein precursor               |
| cpo       | -15.74      | 0.00    | chloroperoxidase precursor                             |
| PA4651    | -15.42      | 0.00    |                                                          |
| PA5093    | -14.99      | 0.00    | probable histidine/phenylalanine ammonia-lyase          |
| tadD      | -14.94      | 0.00    | TadD                                                   |
| PA5094    | -14.94      | 0.00    | probable ATP-binding component of ABC transporter       |
| PA3709    | -14.82      | 0.00    | probable major facilitator superfamily (MFS) transporter |
| hutI      | -14.67      | 0.00    | imidazolone-5-propionate hydrolase HutI                 |
| PA4648    | -14.29      | 0.00    |                                                          |
| PA3417    | -14.20      | 0.00    | probable pyruvate dehydrogenase E1 component, alpha subunit |
| PA4294    | -14.14      | 0.00    |                                                          |
| Gene   | Log2 Fold Change | p-value | Function                                      |
|--------|------------------|---------|-----------------------------------------------|
| PA5097 | -13.84           | 0.00    | probable amino acid permease                  |
| flp    | -13.62           | 0.00    |                                               |
| mmsB   | -13.56           | 0.00    | 3-hydroxyisobutyrate dehydrogenase            |
| coxB   | -13.41           | 0.00    | cytochrome c oxidase, subunit II              |
| PA3710 | -13.08           | 0.00    | probable GMC-type oxidoreductase              |
| PA0110 | -12.97           | 0.00    | hypothetical protein                          |
| aprA   | -12.95           | 0.00    | alkaline metalloproteinase precursor          |
| PA5095 | -12.84           | 0.00    | probable permease of ABC transporter          |
| pprA   | -12.34           | 0.00    | two-component sensor PprA                     |
| PA2167 | -11.61           | 0.00    |                                               |
| PA0107 | -11.56           | 0.00    | conserved hypothetical protein                 |
| PA4573 | -11.50           | 0.00    |                                               |
| PA1190 | -11.46           | 0.00    |                                               |
| PA0586 | -11.44           | 0.00    |                                               |
| arcC   | -11.29           | 0.00    | carbamate kinase                              |
| PA4652 | -10.69           | 0.00    |                                               |
| PA2168 | -10.56           | 0.00    | hypothetical protein                          |
| tadC   | -10.33           | 0.00    |                                               |
| PA2699 | -10.19           | 0.00    | hypothetical protein                          |
| lecA   | -10.13           | 0.00    | LecA                                         |
| PA2433 | -10.06           | 0.00    |                                               |
| PA1930 | -9.98            | 0.00    | probable chemotaxis transducer                |
| PA4649 | -9.56            | 0.00    |                                               |
| PA1216 | -9.55            | 0.00    |                                               |
| PA0175 | -9.40            | 0.00    | probable chemotaxis protein methyltransferase |
| tadZ   | -9.20            | 0.00    |                                               |
| PA0587 | -9.05            | 0.00    |                                               |
| PA3723 | -8.99            | 0.00    | probable FMN oxidoreductase                   |
| PA4650 | -8.82            | 0.00    |                                               |
| PA5181 | -8.77            | 0.00    | probable oxidoreductase                       |
| tadG   | -8.57            | 0.00    |                                               |
| PA3451 | -8.31            | 0.00    |                                               |
| PA2161 | -8.20            | 0.00    |                                               |
| exaC   | -7.94            | 0.00    | NAD+ dependent aldehyde dehydrogenase ExaC    |
| PA3461 | -7.71            | 0.00    |                                               |
| PA1215 | -7.62            | 0.00    | hypothetical protein                          |
| PA1244 | -7.60            | 0.00    |                                               |
| PA2939 | -7.29            | 0.00    | probable aminopeptidase                       |
| PA2021 | -7.23            | 0.00    |                                               |
| PA1213 | -7.21            | 0.00    | hypothetical protein                          |
| PA5106 | -7.17            | 0.00    | conserved hypothetical protein                 |
| PA4607 | -7.17            | 0.00    |                                               |
| Gene     | Score | Province | Description                                                |
|----------|-------|----------|------------------------------------------------------------|
| PA0744   | -7.05 | 0.00     | probable enoyl-CoA hydratase/isomerase                    |
| coIII    | -7.00 | 0.00     | cytochrome c oxidase, subunit III                         |
| PA1212   | -7.00 | 0.00     | probable major facilitator superfamily (MFS) transporter  |
| PA1878   | -6.94 | 0.00     |                                                           |
| rsmY     | -6.91 | 0.00     | regulatory RNA RsmY                                        |
| PA0788   | -6.78 | 0.00     | hypothetical protein                                       |
| PA1728   | -6.76 | 0.00     |                                                           |
| PA2918   | -6.68 | 0.00     | probable short-chain dehydrogenase                        |
| PA3231   | -6.66 | 0.00     |                                                           |
| xdhB     | -6.52 | 0.00     | xanthine dehydrogenase                                    |
| PA1289   | -6.52 | 0.00     |                                                           |
| PA1135   | -6.51 | 0.00     | conserved hypothetical protein                             |
| pslF     | -6.49 | 0.00     | PsIF                                                      |
| PA0174   | -6.48 | 0.00     | conserved hypothetical protein                             |
| PA5527   | -6.44 | 0.00     |                                                           |
| rcpA     | -6.43 | 0.00     | RcpA                                                      |
| arcB     | -6.41 | 0.00     | ornithine carbamoyltransferase, catabolic                  |
| PA1214   | -6.38 | 0.00     | hypothetical protein                                       |
| PA2171   | -6.35 | 0.00     |                                                           |
| glgB     | -6.34 | 0.00     | 1,4-alpha-glucan branching enzyme                          |
| PA4653   | -6.29 | 0.00     |                                                           |
| PA1404   | -6.28 | 0.00     |                                                           |
| PA0588   | -6.18 | 0.00     | conserved hypothetical protein                             |
| PA1217   | -6.13 | 0.00     | probable 2-isopropylmalate synthase                       |
| pslL     | -6.13 | 0.00     | hypothetical protein                                       |
| gcvP1    | -6.10 | 0.00     | glycine cleavage system protein P1                        |
| PA4925   | -6.09 | 0.00     | conserved hypothetical protein                             |
| PA3234   | -6.07 | 0.00     | probable sodium:solute symporter                          |
| PA2377   | -6.07 | 0.00     |                                                           |
| tadB     | -6.05 | 0.00     |                                                           |
| PA2150   | -6.03 | 0.00     | conserved hypothetical protein                             |
| PA0173   | -6.03 | 0.00     | probable methylesterase                                   |
| xdhA     | -6.02 | 0.00     | xanthine dehydrogenase                                    |
| PA2486   | -6.02 | 0.00     |                                                           |
| PA2919   | -5.99 | 0.00     |                                                           |
| PA2370   | -5.99 | 0.00     |                                                           |
| PA3273   | -5.96 | 0.00     |                                                           |
| PA2174   | -5.95 | 0.00     |                                                           |
| PA1323   | -5.92 | 0.00     |                                                           |
| PA1888   | -5.90 | 0.00     |                                                           |
| PA2571   | -5.85 | 0.00     | probable two-component sensor                             |
| PA4877   | -5.84 | 0.00     | hypothetical protein                                       |
| Protein ID  | Score | Description                                      |
|------------|-------|--------------------------------------------------|
| PA1887     | -5.83 | 0.00                                             |
| PA2371     | -5.82 | 0.00                                             |
| PA3315     | -5.77 | 0.00 probable permease of ABC transporter        |
| PA2152     | -5.74 | 0.00 probable trehalose synthase                 |
| PA4680     | -5.74 | 0.00                                             |
| PA2149     | -5.73 | 0.00                                             |
| PA3460     | -5.71 | 0.00 probable acetyltransferase                  |
| PA1218     | -5.67 | 0.00                                             |
| PA3688     | -5.65 | 0.00                                             |
| PA2222     | -5.64 | 0.00                                             |
| PA2162     | -5.64 | 0.00 probable glycosyl hydrolase                 |
| PA2937     | -5.61 | 0.00                                             |
| napE       | -5.58 | 0.00 periplasmic nitrate reductase protein NapE   |
| PA2223     | -5.57 | 0.00 hypothetical protein                        |
| PA2160     | -5.52 | 0.00 probable glycosyl hydrolase                 |
| PA2169     | -5.50 | 0.00                                             |
| PA2618     | -5.50 | 0.00 hypothetical protein                        |
| PA4702     | -5.49 | 0.00                                             |
| PA1879     | -5.49 | 0.00 hypothetical protein                        |
| aer2       | -5.47 | 0.00 aerotaxis transducer Aer2                   |
| PA2151     | -5.47 | 0.00 conserved hypothetical protein               |
| PA5546     | -5.46 | 0.00 conserved hypothetical protein               |
| PA4608     | -5.45 | 0.00 hypothetical protein                        |
| PA2178     | -5.44 | 0.00 hypothetical protein                        |
| PA2148     | -5.43 | 0.00 conserved hypothetical protein               |
| PA0745     | -5.40 | 0.00 probable enoyl-CoA hydratase/isomerase      |
| flgK       | -5.35 | 0.00 flagellar hook-associated protein 1 FlgK    |
| hutC       | -5.34 | 0.00 histidine utilization repressor HutC         |
| PA1041     | -5.34 | 0.00 probable outer membrane protein precursor   |
| PA2155     | -5.33 | 0.00 probable phospholipase                      |
| PA3567     | -5.33 | 0.00 probable oxidoreductase                     |
| PA0052     | -5.30 | 0.00                                             |
| PA1340     | -5.29 | 0.00                                             |
| PA2180     | -5.28 | 0.00                                             |
| pslE       | -5.25 | 0.00 PsIE                                        |
| PA1837a    | -5.22 | 0.00                                             |
| PA2938     | -5.22 | 0.00 probable transporter                        |
| PA1324     | -5.19 | 0.00                                             |
| nosF       | -5.19 | 0.00 NosF protein                                |
| PA2754     | -5.17 | 0.00                                             |
| PA4611     | -5.12 | 0.00                                             |
| PA1870     | -5.09 | 0.00                                             |
| Gene  | Log2 Fold Change | p-value | Description                                                |
|-------|------------------|---------|------------------------------------------------------------|
| liuE  | -5.07            | 0.00    | 3-hydroxy-3-methylglutaryl-CoA lyase                      |
| pslI  | -5.06            | 0.00    | PsII                                                      |
| PA2777| -5.06            | 0.00    | conserved hypothetical protein                            |
| lipA  | -5.05            | 0.00    | lactonizing lipase precursor                              |
| PA0880| -5.03            | 0.00    |                                                           |
| pslH  | -5.02            | 0.00    | PsIH                                                     |
| cupB3 | -4.90            | 0.00    | usher CupB3                                               |
| PA2173| -4.89            | 0.00    |                                                           |
| PA4781| -4.88            | 0.00    | cyclic di-GMP phosphodiesterase                          |
| PA1327| -4.88            | 0.00    | probable protease                                        |
| PA2572| -4.84            | 0.00    | probable two-component response regulator                 |
| PA2154| -4.82            | 0.00    |                                                           |
| arcA  | -4.80            | 0.00    | arginine deiminase                                        |
| PA0656| -4.80            | 0.00    | probable HIT family protein                               |
| PA1341| -4.76            | 0.00    |                                                           |
| PA5169| -4.76            | 0.00    |                                                           |
| PA2024| -4.75            | 0.00    |                                                           |
| PA5435| -4.74            | 0.00    | probable transcarboxylase subunit                         |
| exaB  | -4.74            | 0.00    | cytochrome c550                                           |
| PA3311| -4.74            | 0.00    |                                                           |
| PA2173a| -4.69           | 0.00    |                                                           |
| fusA2 | -4.67            | 0.00    | elongation factor G                                       |
| PA2779| -4.67            | 0.00    |                                                           |
| PA2422| -4.65            | 0.00    |                                                           |
| PA1339| -4.63            | 0.00    |                                                           |
| PA3923| -4.60            | 0.00    |                                                           |
| pra   | -4.60            | 0.00    | protein activator                                         |
| PA5104| -4.58            | 0.00    |                                                           |
| PA1784| -4.57            | 0.00    |                                                           |
| PA0038| -4.56            | 0.00    |                                                           |
| PA4041| -4.54            | 0.00    |                                                           |
| PA2140| -4.53            | 0.00    | probable metallothionein                                 |
| PA1324.1| -4.50         | 0.00    |                                                           |
| ggt   | -4.50            | 0.00    | gamma-glutamyltranspeptidase precursor                   |
| PA5180| -4.50            | 0.00    | conserved hypothetical protein                            |
| PA4880| -4.50            | 0.00    | probable bacterioferritin                                |
| PA1118| -4.49            | 0.00    |                                                           |
| ldh   | -4.49            | 0.00    | leucine dehydrogenase                                    |
| PA2177| -4.48            | 0.00    | probable sensor/response regulator hybrid                 |
| PA3986| -4.48            | 0.00    |                                                           |
| PA3040| -4.48            | 0.00    |                                                           |
| Protein ID | Score | Description |
|------------|-------|-------------|
| PA4139     | -4.46 |             |
| PA0451     | -4.44 |             |
| PA1088     | -4.44 |             |
| PA4682     | -4.41 |             |
| PA3274     | -4.40 |             |
| PA2142     | -4.39 | probable short-chain dehydrogenase |
| PA0565     | -4.38 | conserved hypothetical protein |
| ansB       | -4.37 | glutaminase-asparaginase |
| PA3235     | -4.35 |             |
| PA0329     | -4.34 |             |
| PA2146     | -4.34 |             |
| bkdB       | -4.33 | branched-chain alpha-keto acid dehydrogenase (lipoamide component) |
| PA3023     | -4.33 | conserved hypothetical protein |
| PA3233     | -4.31 | hypothetical protein |
| PA2164     | -4.31 | probable glycosyl hydrolase |
| PA3089     | -4.28 |             |
| PA2573     | -4.26 | probable chemotaxis transducer |
| PA3957     | -4.22 | probable short-chain dehydrogenase |
| PA4025     | -4.22 | probable ethanolamine ammonia-lyase light chain |
| coaB       | -4.21 |             |
| PA0747     | -4.20 | probable aldehyde dehydrogenase |
| PA2172     | -4.20 |             |
| pslG       | -4.19 | PslG |
| PA1617     | -4.18 | probable AMP-binding enzyme |
| PA2179     | -4.17 | hypothetical protein |
| napA       | -4.17 | periplasmic nitrate reductase protein NapA |
| PA2165     | -4.17 | probable glycogen synthase |
| polB       | -4.17 | DNA polymerase II |
| lasI       | -4.17 | autoinducer synthesis protein LasI |
| PA5101     | -4.16 |             |
| PA3459     | -4.15 | probable glutamine amidotransferase |
| PA2170     | -4.13 |             |
| PA4915     | -4.12 | probable chemotaxis transducer |
| PA2564     | -4.09 | hypothetical protein |
| PA2142a    | -4.07 |             |
| PA0256     | -4.07 |             |
| PA2708     | -4.07 |             |
| PA0742     | -4.06 |             |
| PA2031     | -4.05 |             |
| PA3041     | -4.04 |             |
| napF       | -4.04 | ferredoxin protein NapF |
| Gene   | Log2 Fold Change | P-value | Description                                      |
|--------|-----------------|---------|--------------------------------------------------|
| PA4341 | -4.04           | 0.00    | probable transcriptional regulator               |
| fumC2  | -4.02           | 0.00    | fumarate hydratase                               |
| PA1220 | -4.01           | 0.00    |                                                  |
| pscE   | 4.00            | 0.00    | type III export protein PscE                     |
| PA4675 | 4.01            | 0.00    |                                                  |
| hcnB   | 4.01            | 0.00    | hydrogen cyanide synthase HcnB                   |
| pscH   | 4.01            | 0.00    | type III export protein PscH                     |
| PA2792 | 4.01            | 0.00    |                                                  |
| PA3331 | 4.02            | 0.00    | cytochrome P450                                  |
| PA0925 | 4.02            | 0.00    |                                                  |
| PA2774 | 4.03            | 0.00    |                                                  |
| PA5273 | 4.05            | 0.00    |                                                  |
| PA4789 | 4.05            | 0.00    |                                                  |
| pcrG   | 4.06            | 0.00    | regulator in type III secretion                  |
| pscG   | 4.06            | 0.00    | type III export protein PscG                     |
| dapA   | 4.08            | 0.00    | dihydrodipicolinate synthase                     |
| PA0563 | 4.09            | 0.00    | conserved hypothetical protein                   |
| PA4046 | 4.10            | 0.00    |                                                  |
| PA5503 | 4.10            | 0.00    | probable ATP-binding component of ABC transporter|
| rimM   | 4.11            | 0.00    | 16S rRNA processing protein                      |
| PA4837 | 4.12            | 0.00    | probable outer membrane protein precursor        |
| PA4387 | 4.12            | 0.00    | conserved hypothetical protein                   |
| trkH   | 4.12            | 0.00    | potassium uptake protein TrkH                    |
| PA4524 | 4.15            | 0.00    |                                                  |
| pscL   | 4.15            | 0.00    | type III export protein PscL                     |
| rplO   | 4.16            | 0.00    | 50S ribosomal protein L15                        |
| PA0359 | 4.16            | 0.00    |                                                  |
| PA3388 | 4.18            | 0.00    |                                                  |
| PA0801 | 4.18            | 0.00    |                                                  |
| PA1964 | 4.20            | 0.00    | probable ATP-binding component of ABC transporter|
| atpH   | 4.20            | 0.00    | ATP synthase delta chain                         |
| prfA   | 4.20            | 0.00    | peptide chain release factor 1                   |
| PA1644 | 4.24            | 0.00    | conserved hypothetical protein                   |
| PA0818 | 4.24            | 0.00    |                                                  |
| rplE   | 4.24            | 0.00    | 50S ribosomal protein L5                         |
| rpsO   | 4.24            | 0.00    | 30S ribosomal protein S15                        |
| minD   | 4.25            | 0.00    | cell division inhibitor MinD                     |
| rpmD   | 4.25            | 0.00    | 50S ribosomal protein L30                        |
| rplF   | 4.27            | 0.00    | 50S ribosomal protein L6                         |
| PA3129 | 4.27            | 0.00    | conserved hypothetical protein                   |
| PA0320 | 4.27            | 0.00    |                                                  |
| Gene   | Score | Type                      |
|--------|-------|---------------------------|
| PA1158 | 4.29  | probable two-component sensor |
| dipZ   | 4.30  | thiol:disulfide interchange protein DipZ |
| PA4065 | 4.31  | hypothetical protein      |
| PA1116 | 4.34  |                           |
| rpsJ   | 4.35  | 30S ribosomal protein S10 |
| PA1656 | 4.35  |                           |
| queA   | 4.35  | S-adenosylmethionine:trna ribosyltransferase-isomerase |
| thiI   | 4.35  | thiazole biosynthesis protein ThiI |
| hisC2  | 4.35  | histidinol-phosphate aminotransferase |
| PA3268 | 4.37  | probable TonB-dependent receptor |
| PA4456 | 4.39  | probable ATP-binding component of ABC transporter |
| rplS   | 4.40  | 50S ribosomal protein L19 |
| mreB   | 4.40  | rod shape-determining protein MreB |
| phrS   | 4.41  | PhrS                      |
| ispA   | 4.42  | geranyltrantransferase    |
| PA0541 | 4.42  | hypothetical protein      |
| PA3988 | 4.42  |                           |
| atpF   | 4.44  | ATP synthase B chain      |
| PA3665 | 4.45  | hypothetical protein      |
| pyrD   | 4.45  | dihydroorotate dehydrogenase |
| lpxB   | 4.46  | lipid A-disaccharide synthase |
| pcrR   | 4.46  | transcriptional regulator protein PcrR |
| infA   | 4.46  | initiation factor         |
| nirM   | 4.47  | cytochrome c-551 precursor |
| PA4404 | 4.48  |                           |
| PA3838 | 4.49  | probable ATP-binding component of ABC transporter |
| rpsT   | 4.50  | 30S ribosomal protein S20 |
| PA3093 | 4.50  | hypothetical protein      |
| PA5343 | 4.50  |                           |
| PA3842 | 4.51  |                           |
| PA4896 | 4.53  | probable sigma-70 factor, ECF subfamily |
| PA3762 | 4.53  |                           |
| rplM   | 4.54  | 50S ribosomal protein L13 |
| PA2010 | 4.54  | probable transcriptional regulator |
| hemA   | 4.54  | glutamyl-tRNA reductase   |
| cycH   | 4.54  | cytochrome c-type biogenesis protein |
| PA3335 | 4.55  |                           |
| PA3985 | 4.57  |                           |
| rpsM   | 4.57  | 30S ribosomal protein S13 |
| guaB   | 4.57  | inosine-5'-monophosphate dehydrogenase |
| PA1825 | 4.59  |                           |
| PA5467 | 4.59  |                           |
| Gene   | E-value | Description                                      |
|--------|---------|--------------------------------------------------|
| PA3586 | 4.61    | 0.00 hypothetical protein                         |
| PA4371 | 4.61    | 0.00 hypothetical protein                         |
| rpsP   | 4.62    | 0.00 30S ribosomal protein S16                    |
| tig    | 4.63    | 0.00 trigger factor                                |
| rplX   | 4.63    | 0.00 50S ribosomal protein L24                    |
| PA4685 | 4.66    | 0.00 hypothetical protein                         |
| PA1741 | 4.67    | 0.00 hypothetical protein                         |
| PA0456 | 4.68    | 0.00 probable cold-shock protein                  |
| rpsN   | 4.68    | 0.00 30S ribosomal protein S14                    |
| PA3485 | 4.68    | 0.00 hypothetical protein                         |
| PA3262 | 4.69    | 0.00 probable peptidyl-prolyl cis-trans isomerase, FkbP-type |
| PA1478 | 4.70    | 0.00 hypothetical protein                         |
| PA2627 | 4.70    | 0.00 hypothetical protein                         |
| PA2943 | 4.72    | 0.00 phospho-2-dehydro-3-deoxyheptonate aldolase |
| PA0777 | 4.72    | 0.00 hypothetical protein                         |
| fabD   | 4.72    | 0.00 malonyl-CoA-[acyl-carrier-protein] transacylase |
| PA4029 | 4.74    | 0.00 hypothetical protein                         |
| pscJ   | 4.76    | 0.00 type III export protein PscJ                 |
| pscQ   | 4.76    | 0.00 translocation protein in type III secretion |
| rplN   | 4.77    | 0.00 50S ribosomal protein L14                    |
| fpr    | 4.81    | 0.00                                             |
| PA1548 | 4.81    | 0.00                                             |
| rpmG   | 4.81    | 0.00 50S ribosomal protein L33                    |
| purU1  | 4.82    | 0.00 formyltetrahydrofolate deformylase           |
| PA3906 | 4.82    | 0.00                                             |
| PA3336 | 4.83    | 0.00 probable major facilitator superfamily (MFS) transporter |
| PA3675 | 4.84    | 0.00                                             |
| lytB   | 4.87    | 0.00 LytB protein                                |
| folB   | 4.89    | 0.00 dihydromeopterin aldolase                   |
| PA3726 | 4.91    | 0.00                                             |
| PA2772a| 4.95    | 0.00                                             |
| PA2393 | 4.98    | 0.00 putative dipeptidase                         |
| PA5357 | 5.00    | 0.00 hypothetical protein                         |
| PA2202 | 5.03    | 0.00 probable amino acid permease                |
| ureD   | 5.12    | 0.00 urease accessory protein                     |
| PA2921 | 5.13    | 0.00 probable transcriptional regulator          |
| phzG2  | 5.14    | 0.00 probable pyridoxamine 5'-phosphate oxidase  |
| sdhB   | 5.15    | 0.00 succinate dehydrogenase (B subunit)         |
| proA   | 5.15    | 0.00 gamma-glutamyl phosphate reductase           |
| argS   | 5.16    | 0.00 arginyl-tRNA synthetase                     |
| phzC1  | 5.17    | 0.00 phenazine biosynthesis protein PhzC          |
| purD   | 5.18    | 0.00 phosphoribosylamine--glycine ligase          |
| Gene  | Log2FC | FDR  | Description                                      |
|-------|--------|------|-------------------------------------------------|
| atpB  | 5.19   | 0.00 | ATP synthase A chain                            |
| nadD  | 5.19   | 0.00 |                                                 |
| rluD  | 5.19   | 0.00 | pseudouridine synthase                          |
| purK  | 5.20   | 0.00 | phosphoribosylaminomimidazole carboxylase       |
| PA1750| 5.23   | 0.00 | phospho-2-dehydro-3-deoxyheptonate aldolase     |
| rplD  | 5.24   | 0.00 | 50S ribosomal protein L4                         |
| PA4390| 5.28   | 0.00 |                                                 |
| PA1157| 5.28   | 0.00 | probable two-component response regulator        |
| PA3139| 5.33   | 0.00 |                                                 |
| gmk   | 5.34   | 0.00 | guanylate kinase                                 |
| rnk   | 5.36   | 0.00 | nucleoside diphosphate kinase regulator          |
| PA3474| 5.36   | 0.00 | conserved hypothetical protein                   |
| PA5135| 5.36   | 0.00 | conserved hypothetical protein                   |
| gatC  | 5.37   | 0.00 | Glu-tRNA(Gln) amidotransferase subunit C         |
| rpmB  | 5.38   | 0.00 | 50S ribosomal protein L28                        |
| rbfA  | 5.38   | 0.00 | ribosome-binding factor A                        |
| hcnA  | 5.39   | 0.00 | hydrogen cyanide synthase HcnA                   |
| PA4045| 5.39   | 0.00 | conserved hypothetical protein                   |
| rplA  | 5.39   | 0.00 | 50S ribosomal protein L1                         |
| folA  | 5.46   | 0.00 | dihydrofolate reductase                          |
| rplC  | 5.46   | 0.00 | 50S ribosomal protein L3                         |
| micA  | 5.49   | 0.00 | DNA mismatch repair protein MicA                 |
| pscU  | 5.56   | 0.00 | translocation protein in type III secretion      |
| PA2204| 5.56   | 0.00 | probable binding protein component of ABC transporter |
| PA2901| 5.57   | 0.00 |                                                 |
| PA3409| 5.66   | 0.00 |                                                 |
| PA1844| 5.67   | 0.00 |                                                 |
| PA3469| 5.72   | 0.00 | conserved hypothetical protein                   |
| PA5244| 5.72   | 0.00 |                                                 |
| PA2775| 5.72   | 0.00 |                                                 |
| ccoO2 | 5.72   | 0.00 | Cytochrome c oxidase, cbb3-type, CcoO subunit    |
| pvdP  | 5.73   | 0.00 | PvdP                                            |
| pscB  | 5.74   | 0.00 | type III export apparatus protein                |
| PA3209| 5.79   | 0.00 |                                                 |
| grx   | 5.80   | 0.00 |                                                 |
| oprG  | 5.80   | 0.00 | Outer membrane protein OprG precursor            |
| PA4058| 5.83   | 0.00 |                                                 |
| PA3837| 5.86   | 0.00 | probable permease of ABC transporter             |
| PA3647| 5.89   | 0.00 | probable outer membrane protein precursor        |
| phzC2 | 5.97   | 0.00 | phenazine biosynthesis protein PhzC              |
| glyA3 | 5.97   | 0.00 | serine hydroxymethyltransferase                 |
| Gene   | Score | Unit | Description                                      |
|--------|-------|------|--------------------------------------------------|
| PA3327 | 5.98  | 0.00 | probable non-ribosomal peptide synthetase        |
| PA2436 | 6.00  | 0.00 |                                                  |
| PA4005 | 6.01  | 0.00 |                                                  |
| pscT   | 6.04  | 0.00 | translocation protein in type III secretion      |
| PA3329 | 6.04  | 0.00 |                                                  |
| PA4438 | 6.04  | 0.00 | conserved hypothetical protein                    |
| PA1790 | 6.07  | 0.00 |                                                  |
| PA3685 | 6.12  | 0.00 |                                                  |
| comL   | 6.13  | 0.00 | competence protein ComL                           |
| PA4013 | 6.17  | 0.00 |                                                  |
| PA2828 | 6.21  | 0.00 | probable aminotransferase                        |
| PA3905 | 6.23  | 0.00 | adenylate kinase                                 |
| adk    | 6.23  | 0.00 | probable transcriptional regulator               |
| PA0236 | 6.23  | 0.00 | rod shape-determining protein MreD               |
| PA0805 | 6.23  | 0.00 | ribulose-phosphate 3-epimerase                   |
| fabH2  | 6.28  | 0.00 | 3-oxoacyl-[acyl-carrier-protein] synthase III    |
| PA1595 | 6.32  | 0.00 | hypothetical protein                              |
| pcrD   | 6.34  | 0.00 | type III secretory apparatus protein PcrD         |
| nhaP   | 6.34  | 0.00 | Na+/H+ antiporter                                |
| PA0080 | 6.37  | 0.00 |                                                  |
| PA2983 | 6.42  | 0.00 | probable tolQ-type transport protein             |
| secF   | 6.48  | 0.00 | secretion protein SecF                           |
| hprA   | 6.51  | 0.00 | glycerate dehydrogenase                          |
| PA5472 | 6.53  | 0.00 | hypothetical protein                              |
| argF   | 6.53  | 0.00 | ornithine carbamoyltransferase, anabolic          |
| PA4616 | 6.54  | 0.00 | probable c4-dicarboxylate-binding protein        |
| phzB1  | 6.63  | 0.00 | probable phenazine biosynthesis protein           |
| PA3967 | 6.68  | 0.00 | hypothetical protein                              |
| phzB2  | 6.69  | 0.00 | probable phenazine biosynthesis protein           |
| htpX   | 6.75  | 0.00 | heat shock protein HtpX                           |
| PA2712 | 6.75  | 0.00 | hypothetical protein                              |
| PA1360 | 6.75  | 0.00 | conserved hypothetical protein                    |
| omlA   | 6.76  | 0.00 | Outer membrane lipoprotein OmlA precursor         |
| thiG   | 6.77  | 0.00 | thiamine biosynthesis protein, thiazole moiety   |
| PA3263 | 6.78  | 0.00 | conserved hypothetical protein                    |
| PA1692 | 6.78  | 0.00 | probable translocation protein in type III secretion |
| phhB   | 6.78  | 0.00 | pterin-4-alpha-carbinolamine dehydratase          |
| PA5138 | 6.81  | 0.00 | hypothetical protein                              |
| yrfI   | 6.85  | 0.00 | heat shock protein HSP33                          |
| PA2685 | 7.10  | 0.00 |                                                  |
| Gene   | Score | S/A | Description |
|--------|-------|-----|-------------|
| dauB   | 7.18  | 0.00|             |
| PA4724.1 | 7.21 | 0.00| 50S ribosomal protein L11 |
| rplK   | 7.23  | 0.00| probable transcriptional regulator |
| PA2115 | 7.25  | 0.00| FAD-dependent catabolic D-arginine dehydrogenase, DauA |
| dauA   | 7.25  | 0.00| conserved hypothetical protein |
| bacA   | 7.31  | 0.00| bacitracin resistance protein |
| PA3328 | 7.33  | 0.00| probable FAD-dependent monooxygenase |
| PA0802 | 7.34  | 0.00|             |
| PA1274 | 7.37  | 0.00| conserved hypothetical protein |
| aroP2  | 7.43  | 0.00| aromatic amino acid transport protein AroP2 |
| PA3330 | 7.55  | 0.00| probable short chain dehydrogenase |
| rpsl   | 7.56  | 0.00| 30S ribosomal protein S9 |
| PA4374 | 7.65  | 0.00|             |
| glyA2  | 7.66  | 0.00| serine hydroxymethyltransferase |
| PA0380 | 7.66  | 0.00|             |
| PA0046 | 7.75  | 0.00|             |
| efp    | 7.77  | 0.00| translation elongation factor P |
| phzA2  | 7.77  | 0.00| probable phenazine biosynthesis protein |
| PA5130 | 7.84  | 0.00|             |
| icp    | 7.85  | 0.00|             |
| PA0961 | 7.89  | 0.00| probable cold-shock protein |
| pscO   | 7.96  | 0.00| translocation protein in type III secretion |
| PA0789 | 8.13  | 0.00| probable amino acid permease |
| purE   | 8.14  | 0.00| phosphoribosylaminomimidazole carboxylase, catalytic subunit |
| PA1697 | 8.20  | 0.00| ATP synthase in type III secretion system |
| pvdO   | 8.35  | 0.00| PvdO |
| PA3410 | 8.46  | 0.00|             |
| PA5155 | 8.51  | 0.00|             |
| capB   | 8.52  | 0.00| cold acclimation protein B |
| PA2201 | 8.57  | 0.00|             |
| PA4270.1 | 8.65 | 0.00|             |
| rpmA   | 8.69  | 0.00| 50S ribosomal protein L27 |
| PA0775 | 8.83  | 0.00| conserved hypothetical protein |
| PA5081 | 8.89  | 0.00| hypothetical protein |
| PA2203 | 8.91  | 0.00| probable amino acid permease |
| pvdN   | 9.06  | 0.00| PvdN |
| PA5470 | 9.18  | 0.00| probable peptide chain release factor |
| PA4574 | 9.27  | 0.00| conserved hypothetical protein |
| phhC   | 9.29  | 0.00| aromatic amino acid aminotransferase |
| Gene   | Score | %ID | Description                                      |
|--------|-------|-----|--------------------------------------------------|
| PA0952 | 9.47  | 0.00| hypothetical protein                             |
| PA0045 | 9.60  | 0.00|                                                  |
| PA4963 | 9.73  | 0.00|                                                  |
| gcvP2  | 9.74  | 0.00| glycine cleavage system protein P2               |
| PA4746 | 9.80  | 0.00|                                                  |
| PA2464 | 9.82  | 0.00|                                                  |
| PA2019 | 9.85  | 0.00|                                                  |
| rplII  | 10.00 | 0.00| 50S ribosomal protein L9                         |
| rplL   | 10.04 | 0.00| 50S ribosomal protein L7 / L12                   |
| prs    | 10.12 | 0.00| ribose-phosphate pyrophosphokinase               |
| PA2463 | 10.14 | 0.00| hypothetical protein                             |
| PA4933 | 10.18 | 0.00|                                                  |
| putA   | 10.28 | 0.00| proline dehydrogenase PutA                       |
| PA1791 | 10.38 | 0.00|                                                  |
| putP   | 10.50 | 0.00| sodium/proline symporter PutP                    |
| phzA1  | 10.57 | 0.00| probable phenazine biosynthesis protein          |
| pscP   | 10.60 | 0.00| translocation protein in type III secretion      |
| thiE   | 10.60 | 0.00| thiamin-phosphate pyrophosphorylase              |
| PA3822 | 10.63 | 0.00|                                                  |
| rpsR   | 10.66 | 0.00| 30S ribosomal protein S18                        |
| PA4063 | 11.06 | 0.00|                                                  |
| PA2006 | 11.09 | 0.00| probable major facilitator superfamily (MFS) transporter |
| PA0047 | 11.29 | 0.00|                                                  |
| rpsF   | 11.55 | 0.00| 30S ribosomal protein S6                         |
| PA3332 | 11.90 | 0.00| conserved hypothetical protein                    |
| PA3483 | 12.00 | 0.00|                                                  |
| PA2900 | 12.15 | 0.00| probable outer membrane protein precursor        |
| PA1700 | 12.32 | 0.00|                                                  |
| ilvA2  | 12.39 | 0.00| threonine dehydratase, biosynthetic              |
| rplJ   | 12.84 | 0.00| 50S ribosomal protein L10                        |
| PA0422 | 12.90 | 0.00| conserved hypothetical protein                    |
| trpG   | 13.43 | 0.00| anthranilate synthase component II               |
| PA5139 | 13.60 | 0.00| hypothetical protein                             |
| PA1702 | 13.81 | 0.00|                                                  |
| rpsB   | 13.93 | 0.00| 30S ribosomal protein S2                         |
| PA4272.1| 14.12 | 0.00|                                                  |
| PA5504 | 14.12 | 0.00| D-methionine ABC transporter membrane protein    |
| PA0385 | 14.33 | 0.00|                                                  |
| PA4429 | 14.92 | 0.00| probable cytochrome c1 precursor                |
| PA4672 | 15.94 | 0.00| peptidyl-tRNA hydrolase                          |
| PA4671 | 16.23 | 0.00| probable ribosomal protein L25                   |
| Protein   | Score | E-value | Description                                           |
|-----------|-------|---------|-------------------------------------------------------|
| glycine cleavage system protein H2 | 16.45 | 0.00 | PA0800                                               |
| 50S ribosomal protein L21 | 16.80 | 0.00 | PA1052a                                              |
| type III export protein PscK | 16.82 | 0.00 | PA1701                                               |
| tyrosyl-tRNA synthetase | 18.89 | 0.00 | rplU                                                  |
| Type III secretion outer membrane protein PopN precursor | 18.90 | 0.00 | pscK                                                  |
| fumarylacetoacetase | 20.24 | 0.00 | tyrS                                                  |
| conserved hypothetical protein | 23.79 | 0.00 | popN                                                  |
| phenylalanine-4-hydroxylase | 26.06 | 0.00 | fahA                                                  |
| homogentisate 1,2-dioxygenase | 26.27 | 0.00 | phhA                                                  |
| 4-hydroxyphenylpyruvate dioxygenase | 26.56 | 0.00 | PA1428                                                |
| maleylacetoacetate isomerase | 34.09 | 0.00 | PA1325                                                |
| homogentisate 1,2-dioxygenase | 35.33 | 0.00 | hmgA                                                  |
| 4-hydroxyphenylpyruvate dioxygenase | 37.22 | 0.00 | hpd                                                   |
| maleylacetoacetate isomerase | 42.78 | 0.00 | maiA                                                  |
| PA5084 | 58.70 | 0.00 | PA5083                                                |
| PA5082 | 91.94 | 0.00 | PA5082                                                |
Table S6 The 6 genes that are differentially expressed between AZM-treated and non-treated PAO1/pUCP18::msr(E). Gene names, fold change, P value and functional annotations are shown in the table. Cut-off: fold-change > 4, P value < 0.05.

| Gene name | Fold change | P value | Function                                      |
|-----------|-------------|---------|------------------------------------------------|
| PA0781    | -4.55       | 0.00    | hypothetical protein                          |
| PA3600    | -7.49       | 0.00    | conserved hypothetical protein                |
| PA3601    | -9.54       | 0.00    | conserved hypothetical protein                |
| PA4063    | -9.51       | 0.00    |                                                 |
| PA4836    | -7.09       | 0.00    | hypothetical protein                          |
| PA4837    | -8.04       | 0.00    | probable outer membrane protein precursor     |
Table S7 Accession numbers of the genomes used to construct phylogenetic tree in Figure 1.

| Strain                      | Accession number |
|-----------------------------|------------------|
| *P. aeruginosa* DK2         | NC_018080.1      |
| *P. aeruginosa* PA14        | NC_008463.1      |
| *P. aeruginosa* PAO1        | NC_002516.2      |
| *P. aeruginosa* B136-33     | NC_020912.1      |
| *P. aeruginosa* L135b       | NC_011770.1      |
| *P. aeruginosa* M18         | NC_017548.1      |
| *P. aeruginosa* NCGM2.S1    | NC_017549.1      |
| *P. aeruginosa* RP73        | NC_021577.1      |
| *P. aeruginosa* YL84        | NZ_CP007147.1    |
| *P. aeruginosa* MTB-1       | NC_023019.1      |
| *P. aeruginosa* Carb01-63   | NZ_CP011317.1    |
| *P. aeruginosa* VRFPA04     | NZ_CP008739.1    |
| *P. aeruginosa* PA_D1       | NZ_CP012585.1    |
| *P. aeruginosa* DHS01       | NZ_CP013993.1    |
| *P. aeruginosa* SJTD-1      | NZ_CP015877.1    |
| *P. aeruginosa* AES-1R      | NZ_CP013680.1    |
| *P. aeruginosa* ATCC 27853  | NZ_CP015117.1    |
| *P. aeruginosa* USDA-ARS-USMARC-41639 | NZ_CP013989.1 |
| *P. aeruginosa* SCV20265    | NC_023149.1      |
| *P. aeruginosa* PA1         | NC_022808.2      |
| *P. aeruginosa* NCTC10332   | NZ_LN831024.1    |