

**SWARMING MOTILITY IN *PSEUDOMONAS AERUGINOSA*: A COMPLEX
ADAPTATION WITH IMPLICATIONS FOR ANTIBIOTIC RESISTANCE AND
VIRULENCE**

by

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B.Sc., The University of British Columbia, 2014

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES
(MICROBIOLOGY AND IMMUNOLOGY)

THE UNIVERSITY OF BRITISH COLUMBIA
(Vancouver)

April 2020

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Swarming motility in *Pseudomonas aeruginosa*: a complex adaptation with implications for antibiotic resistance and virulence

submitted by Shannon Coleman in partial fulfillment of the requirements for

the degree of Doctor of Philosophy

in Microbiology and Immunology

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Abstract

Pseudomonas aeruginosa is a Gram-negative opportunistic pathogen that possesses intrinsic antibiotic resistance. Highly adaptable, *P. aeruginosa* is capable of different forms of motility, including swarming, swimming, twitching and surfing. Swarming motility is a multicellular movement of cells across semisolid surfaces that is associated with complex adaptations including adaptive antibiotic resistance. Here a disc diffusion assay showed that swarming bacteria were resistant to multiple antibiotics, including aminoglycosides, β -lactams, chloramphenicol, ciprofloxacin, macrolides, tetracycline, and trimethoprim. RNA-Seq of swarming cells showed the dysregulation of 1,581 genes, including 104 regulatory factors, upregulated virulence and iron acquisition factors, and downregulated ribosomal genes. Forty-one mutants resistant to tobramycin under swarming conditions were found, including *priN*, a regulator of pyocin, and *wbpW*, involved in LPS biosynthesis. RNA-Seq of swarming cells treated with tobramycin revealed the upregulation of the multidrug efflux pump *mexXY*. To investigate the role of swarming *in vivo*, a screen for swarming-specific mutants was performed, revealing *ptsP*, a regulator of carbon and nitrogen metabolism. The $\Delta ptsP$ mutant was deficient specifically in swarming but not swimming or twitching motility. Interestingly, $\Delta ptsP$ also had greatly reduced organ invasion in a mouse infection model, suggesting a likely role for swarming *in vivo*. Besides *ptsP*, small RNAs also regulated swarming motility, typically via post-transcriptional means. A screen of sRNA overexpressing strains revealed an sRNA, PA0805.1 that influenced diverse bacterial behaviours including swarming, swimming, twitching, cytotoxicity, adherence and tobramycin resistance. RNA-Seq and proteomics uncovered a broad regulatory profile with 1,121 differentially expressed genes and 925 proteins, including 118 regulatory factors, downregulated pilus genes, upregulated adherence and virulence factors, and upregulated multidrug efflux systems including *mexXY* and *mexGHI-opmD*. Another sRNA, PA2952.1, when overexpressed influenced swarming, swimming, and tobramycin, gentamicin and trimethoprim resistance. Transcriptomics and proteomics showed differential abundance of 784 genes and 445 proteins, encompassing 82 regulatory factors, downregulated pili, dysregulated flagellar genes, upregulated *mexGHI-opmD* and the upregulated *arn* operon involved in LPS modification. Overall this thesis has shown that swarming motility is a complex adaptation conferring multiple antibiotic resistance, that is regulated by sRNAs and coupled to virulence adaptations *in vivo*.

Lay Summary

Antibiotic resistance is a rising global health threat with several contributing causes. One of these is adaptive resistance that is triggered by and dependent on specific growth conditions, such as during multicellular movement over a surface, termed swarming motility. In *Pseudomonas aeruginosa*, I showed that swarming bacteria were resistant to multiple antibiotics. More than a thousand genes were dysregulated under swarming conditions. The resistance of swarming cells to tobramycin was dependent on 41 of these genes. By generating a specific swarming-defective mutant in a regulator of carbon and nitrogen metabolism, I demonstrated reduced virulence in an infection model, indicating that swarming was important for infections. I also showed that swarming was regulated by a novel element, small RNAs that typically affect the production of proteins in cells. I showed specific elements had massive and diverse impacts on cellular behaviour, gene expression and protein abundance.

Preface

This thesis is an original intellectual product of the author, Shannon Coleman, with the guidance and mentorship of Dr. Robert (Bob) Hancock. Dr. Hancock was responsible for the original conceptualization, while I designed experiments using his advice. I performed the majority of all experiments in this thesis, with exceptions noted below. I analyzed all the data, with the exception of initial differential analyses of RNA-Seq and proteomics data, which were analyzed by the bioinformaticists and proteomics collaborators named below. I drafted all of the manuscripts, with help from collaborators for their specific sections in the Materials & Methods. Dr. Hancock and I both edited the manuscripts extensively.

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Chapter 2:

Sections of Chapter 2 were derived from the three manuscripts listed for Chapters 3, 4, and 5.

Chapter 3:

A version of Chapter 3 has been published. **Coleman SR**, Blimkie T, Falsafi R, Hancock REW. Multidrug adaptive resistance of *Pseudomonas aeruginosa* swarming cells. *Antimicrob. Agents Chemother.* 2020, **64**:e01999-19.

Reza Falsafi depleted ribosomal RNA and prepared RNA-Seq libraries for all experiments in this thesis. Travis Blimkie analyzed the RNA-Seq data in Chapter 3, uploaded it to GEO, and wrote methods for the RNA-Seq analysis.

Chapter 4:

A version of Chapter 4 is currently in revision. **Coleman SR**, Smith ML, Spicer V, Lao Y, Mookherjee N, Hancock REW. Overexpression of the small RNA PA0805.1 in *Pseudomonas aeruginosa* modulates the expression of a large set of genes and proteins, resulting in altered motility, cytotoxicity and tobramycin resistance.

Dr. Maren Smith analyzed the RNA-Seq data in Chapter 4 and helped me to upload it to GEO. Dr. Neeloffer Mookherjee assisted with experimental design for the proteomics experiments in Chapter 4 and also edited the manuscripts based on these studies. Ying Lao lysed bacterial pellets, prepared samples for proteomics, acquired mass spectrometry data, and wrote methods for the

proteomics. Victor Spicer performed the differential analysis of proteins for Chapter 4, uploaded data to MassIVE, and wrote methods for the proteomics analysis.

Chapter 5:

A version of Chapter 5 is currently being prepared for publication. **Coleman SR**, Smith ML, Spicer V, Lao Y, Taylor P, Mookherjee N, Hancock REW. The small RNAs PA2952.1 and *prhH* as regulators of virulence, motility and iron metabolism in *Pseudomonas aeruginosa*.

Dr. Maren Smith analyzed the RNA-Seq data in Chapter 5 and helped me to upload it to GEO. Dr. Neeloffer Mookherjee assisted with experimental design for the proteomics experiments in Chapter 5. Ying Lao lysed bacterial pellets, prepared samples for proteomics, acquired mass spectrometry data, and wrote methods for the proteomics. Victor Spicer performed the differential analysis of proteins for Chapter 5, and wrote methods for the proteomics analysis. Dr. Patrick Taylor was involved in experimental design and initial investigations of small RNAs.

Chapter 6:

Dr. Daniel Pletzer performed the *in vivo* work in Chapter 6, wrote methods for the *in vivo* work, and also assisted with troubleshooting and experimental design.

Other publications arising from work presented in this thesis:

1. Pletzer D, **Coleman SR**, Hancock REW. Anti-biofilm peptides as a new weapon in antimicrobial warfare. *Curr. Opin. Microbiol.* 2016, **33**:35–40.

This review was written by Dr. Daniel Pletzer and I and edited by Dr. Hancock.

Ethics statements

Animal experiments were performed in accordance with The Canadian Council on Animal Care (CCAC) guidelines and were approved by the University of British Columbia Animal Care Committee (certificate number A14-0363). Mice used in this study were female outbred CD-1. All animals were purchased from Charles River Laboratories (Wilmington, MA), were 7 weeks of age, and weighed about 25 ± 3 g at the time of the experiments. Isoflurane (1 to 3%) was used to anesthetize the mice. Mice were euthanized with carbon dioxide. The use of all bacterial strains presented in this thesis was approved by UBC Risk Management Services under the UBC Biosafety Permit Number B14-0207 and B14-0208.

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List of Abbreviations

$\Delta\Delta\text{CT}$ – comparative cycle threshold method
1D – one-dimensional
2YT – yeast extract and tryptone media
3-O-C12 – N-(3-oxododecanoyl)-L-homoserine lactone
AGC – automatic gain control
ANOVA – analysis of variance
ASM – American Society of Microbiology
BM2 – basal medium 2
bp – basepair
C4-HSL – N-butanoyl-L-homoserine lactone
CAA – Casamino acids
CCAC – Canadian Council on Animal Care
cf. – Latin: *confer/conferatur* (compare)
CF – cystic fibrosis
CFU – colony forming units
CGS – Canada Graduate Scholarship
CIHR – Canadian Institutes for Health Research
CPA – common polysaccharide antigen
CRISPR – clusters of regularly interspaced short palindromic repeats
CRP – catabolite repressor protein
DE – differentially expressed
DMEM - Dulbecco's Modified Eagle Medium
DNA – deoxyribonucleic acid
EDTA - ethylenediaminetetraacetic acid
e.g. – Latin *exempli gratia* (for example)
EPS – extracellular polymeric substance
EV – empty vector
FBS – fetal bovine serum
FC – fold change
GAF – domain found in cGMP-PDEs, adenylyl cyclases, and *E. coli* fh1A
gDNA – genomic DNA
GEO – Gene Expression Omnibus
h – hour
HBE – human bronchial epithelial cells
HEPES – 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid
HHQ – 4-hydroxy-2-heptylquinoline
IC – inhibitory concentration
i.e. – Latin: *id est* (in other words)
LB – Luria-Bertani broth
LC-MS – liquid chromatography-mass spectrometry
LC/MS/MS – liquid chromatography with tandem mass spectrometry
LDH – lactate dehydrogenase
LPS – lipopolysaccharide
Mbp – mega basepairs
MDR – multidrug resistant
MEM – Minimum Essential Medium
MGF – mascot generic format

MIC – minimal inhibitory concentration
 min – minute
 mRNA – messenger RNA
 ms – millisecond
 m/z – mass per charge number
 NPN – N-phenyl-1-naphthylamine
 OSA – O-specific antigen
 p – probability value
 padj – adjusted p value
 PBS – phosphate buffered saline
 PCR – polymerase chain reaction
 PG – peptidoglycan
 PPM – parts per million
 PQS – 2-heptyl-3,4-dihydroxyquinoline
 PTM – post-translational modification
 qRT-PCR – quantitative reverse transcriptase PCR
 QS – quorum sensing
 RF – radio frequency
 RNA – ribonucleic acid
 RND – Resistance-Nodulation-Cell Division
 RPMI – Roswell Park Memorial Institute
 rRNA – ribosomal RNA
 s – second
 SCFM – synthetic cystic fibrosis sputum media
 SD – standard deviation
 SDS – sodium dodecyl sulfate
 SP3 – single-pot solid-phase-enhanced sample preparation
 sRNA – small RNA
 T1SS – type I secretion system
 T2SS – type II secretion system
 T3SS – type III secretion system
 T5SS – type V secretion system
 T6SS – type VI secretion system
 TE – Tris-EDTA
 TMT – tandem mass tag
 Tn – transposon
 TOB – tobramycin
 Tris – tris (hydroxymethyl) aminomethane
 tRNA – transfer RNA
 UNTR – untreated
 vs. – versus
 WT – wild type
 WT EV – wild type empty vector

Acknowledgements

I thank my supervisor Dr. Robert Hancock for his advice, patience and support throughout my degree. My thesis committee was also supportive and encouraging and included Drs. J. Thomas Beatty, Michael Murphy, and Charles Thompson.

Research reported in this thesis was supported by a grant from the Canadian Institutes for Health Research FDN-154287 and the Cystic Fibrosis (CF) Canada Award Number 3177. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Canadian Institutes for Health Research. I was the recipient of CIHR Frederick Banting and Charles Best Canada Graduate Scholarship Master's (CGS-M, 141534) and Doctoral Awards (CGS-D, 146221), and a Four Year Fellowship for PhD students from UBC. My supervisor Dr. Robert Hancock holds a Canada Research Chair in Health and Genomics and a UBC Killam Professorship.

I also thank all lab members for their help throughout the years, particularly Dr. Susan Farmer, Manjeet Bains and Reza Falsafi for lab management, Drs. Mike Trimble, Daniel Pletzer, Evan Haney and Amy Lee for scholarly discussions, and other residents of room 235 for assistance with daily tasks and troubleshooting, including Dr. Evelyn Sun, Lauren Wilkinson, Corrie Belanger, Melanie Dostert, Noushin Akhoundsadegh and Morgan Alford. Dr. Amy Lee and Reza Falsafi were also very helpful in coordinating and executing RNA-Seq projects in the lab. Special thanks to Dr. Daniel Pletzer for performing *in vivo* work in Chapter 6 and for advice about the project.

In addition I also thank collaborators for assistance with proteomics: Dr. Neeloffer Mookherjee, Ying Lao and Victor Spicer. I also enjoyed collaborating with Martha Liu from the Gaynor lab on the *Bacillus* project.

Special thanks are owed to my parents, Chris and Judy Coleman, who have provided moral and nutritional support throughout my years of education, and my brothers Jonathan and Daniel.

Chapter 1: Introduction

1.1 *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is a Gram-negative rod-shaped γ -proteobacterium. As a facultative anaerobe with a large (5-7 Mbp) genome, *P. aeruginosa* thrives in a variety of environments, including soil, freshwater ecosystems, and is an opportunistic pathogen of plants and animals (Chatterjee et al., 2017; Curran et al., 2018; Moradali et al., 2017).

1.1.1 A diverse opportunistic pathogen

P. aeruginosa infects a wide range of living organisms, including plants such as lettuce, *Arabidopsis* and sweet basil (Starkey & Rahme, 2019; Walker et al., 2004). In animals, *P. aeruginosa* is a pathogen of invertebrates, including *Drosophila* (D'Argenio et al., 2001) and *Caenorhabditis elegans* (An et al., 1999), as well as vertebrates such as dogs, cats, cattle (Haenni et al., 2017), fish (Clatworthy et al., 2009) and mice (Pletzer et al., 2018). Importantly, *P. aeruginosa* is also an opportunistic pathogen of humans, and able to colonize numerous niches within the host, contributing to a variety of diseases including cystic fibrosis (CF), pneumonia, burn wound infections, bloodstream infections, keratitis, nosocomial infections, urinary tract infections, ear infections and more (Davies, 2002; Mittal et al., 2009; Moore & Flaws, 2011). Patients at increased risk of infection with *P. aeruginosa* include those who have CF, burn wounds, or use mechanical ventilators (Moore & Flaws, 2011). *P. aeruginosa* is particularly problematic in the human lung, where it causes major complications in diseases such as CF and pneumonia. *P. aeruginosa* is one of the most common CF pathogens, and up to 60% of patients are colonized by *Pseudomonas* by age 30 (Surette, 2014; Davies, 2002; Murray et al., 2007; Marshall et al., 2016). Despite the aggressive use of antibiotics, *P. aeruginosa* infections in CF are difficult to clear and almost always become chronic (Davies, 2002; Murray et al., 2007).

1.1.2 An arsenal of virulence factors

P. aeruginosa possesses numerous virulence factors that enable the bacterium to colonize and invade its host. Alkaline protease and heme acquisition factor are secreted by type I secretion systems (T1SS); the two type II secretion systems (T2SS) (Xcp and Hxc) secrete a variety of toxins, and hydrolytic enzymes including proteases, lipases, phospholipases, and alkaline phosphatases, etc.; the T3SS injects the four strain-dependent toxins ExoS, ExoT, ExoU and ExoY directly into the eukaryotic cell; the type V secretion system (T5SS) secretes a few lipases and proteases that each have an autotransporter domain for their own individual secretion; and the type VI secretion systems (T6SS) are thought to be more involved in interspecies competition (Filloux,

2011), although they can also function to inhibit eukaryotic cell function (Berni et al., 2019).

In addition to secretion systems, *P. aeruginosa* also employs extracellular appendages for both motility and attachment, allowing for dissemination and virulence in the host. These include a single polar flagellum per cell (a long, flexible filament that rotates to propel the bacterium), multiple pili (contractile rods that are major adherence factors and drag the cell over surfaces in a process termed twitching) and several other adherence factors that aid in colonization and biofilm formation. Biofilms are surface-associated aggregates of bacteria held together by an extracellular matrix comprised of polysaccharides, proteins and DNA. They represent a complex adaptive growth state, are associated with major transcriptional reprogramming, and are adaptively resistant (10- to 1000-fold) to multiple antibiotics (Jefferson, 2004). Biofilms are the major cause of infections (65%) and are associated with chronic infections throughout the body and on implanted medical devices and prosthetics.

QS systems also play a role in bacterial virulence. *P. aeruginosa* synthesizes the auto-inducer molecules N-butanoyl-L-homoserine lactone (C4-HSL) and N-(3-oxododecanoyl)-L-homoserine lactone (3-O-C12), and the quinolones 4-hydroxy-2-alkylquinoline (HAQ), 4-hydroxy-2-heptylquinoline (HHQ) and 2-heptyl-3,4-dihydroxyquinoline (PQS) (Kim et al., 2010). As bacterial density increases, the levels of these auto-inducers build, so that they can be used to sense the surrounding population. Each auto-inducer binds to a global transcriptional regulator (RhIR, LasR or PqsR/MvfR), so that specific programs can be initiated once sufficient density (and concentration of autoinducer) is reached. The QS systems are interconnected with LasR at the top of the hierarchy (Lee & Zhang, 2014).

In order to survive *in vivo*, bacteria must also be able to extract iron, which is tightly sequestered by the host. *P. aeruginosa* produces several siderophores for this purpose, including pyoverdine and pyochelin. Its genome also encodes receptors to reuptake the siderophores once they have bound iron. The siderophore pyoverdine and the phenazine pyocyanin give *Pseudomonas* cultures their distinctive blue-green colour. In addition, pyocyanin and pyochelin also have redox activity and can modulate host functions including cilia movement (Britigan et al., 1992; Kanthakumar et al., 1993).

Once bacteria establish an infection, they are able to form a biofilm to enable them to persist in the host and resist antimicrobial treatment. Adherence factors such as the type IV pili and flagella are involved in surface sensing and initial attachment. *P. aeruginosa* produces three exopolysaccharides that aid in biofilm formation and protection from the host, pel, psl and alginate,

and the latter two are the major components of biofilm matrix in this organism. Additionally, *P. aeruginosa* also synthesizes lipopolysaccharide (LPS), which forms the outer monolayer of the outer membrane, is a major antigen, and through the membrane-proximal lipid A portion can elicit a strong inflammatory response in the host by interacting with Toll-like receptor 4.

1.1.3 Progression of chronic CF lung infections

CF is an autosomal recessive genetic disease resulting from mutations in the CF transmembrane conductance regulator (CFTR) gene (Bhagirath et al., 2016). CFTR is an important protein involved in both ion transport and signaling, and mutations in CFTR cause the accumulation of thick mucus in the lung, and also affect other organs such as the pancreas (Bhagirath et al., 2016). The CF lung is susceptible to polymicrobial infection and patients continually struggle in this regard. CF epithelial cells have decreased phagocytosis of *P. aeruginosa*, and the thick mucus impairs ciliary beating (Bhagirath et al., 2016). Infections with *P. aeruginosa* are especially concerning since progression of *P. aeruginosa* infections is associated with poor patient outcomes and disease severity (Lee et al., 2003; Sanders, 2014). The presence of *P. aeruginosa* is associated with increased morbidity: the risk of death was 2.6 times higher in those infected with *P. aeruginosa* than those without (Bhagirath et al., 2016).

Research has shown that as *P. aeruginosa* lung infections progress over time, clinical isolates in chronic, cf. acute, infections tend to lose motility and lipopolysaccharide O-antigen as well as certain virulence factors such as type III secretion system (T3SS) and quorum sensing (QS), while overproducing the polysaccharide alginate and undergoing hypermutation (Figure 1-1) (Hancock et al., 1983; Winstanley et al., 2016). Overall, in chronic infections bacteria become more senescent, evade the immune system and resist antibiotic treatment (Bhagirath et al., 2016); whereas motility is thought to be more important for initial colonization in acute infections and is associated with the production of virulence factors (Overhage et al., 2008). Eventually, the *P. aeruginosa* bacterial burden increases to a point of no return and biofilm formation genes are expressed while the host produces antibodies against *P. aeruginosa* and more polymorphonuclear leukocytes are recruited (Bhagirath et al., 2016). Chronic inflammation eventually leads to irreversible loss of lung function (Bhagirath et al., 2016).

Current therapies for CF largely rely on antibiotic treatment, which is ineffective in the long term due to mechanisms of antibiotic resistance. Other therapies also include oxygen therapy, bronchodilation, airway clearance, anti-inflammatory medication and CFTR modulation (Bhagirath et al., 2016). Gene therapies are being developed but thus far showed little efficacy in

clinical trials (Yan et al., 2019). Life expectancy of CF patients has increased over the years and is about 40-50 years, depending on factors such as location, sex and CFTR genotype (Keogh et al., 2018; Stephenson et al., 2018).

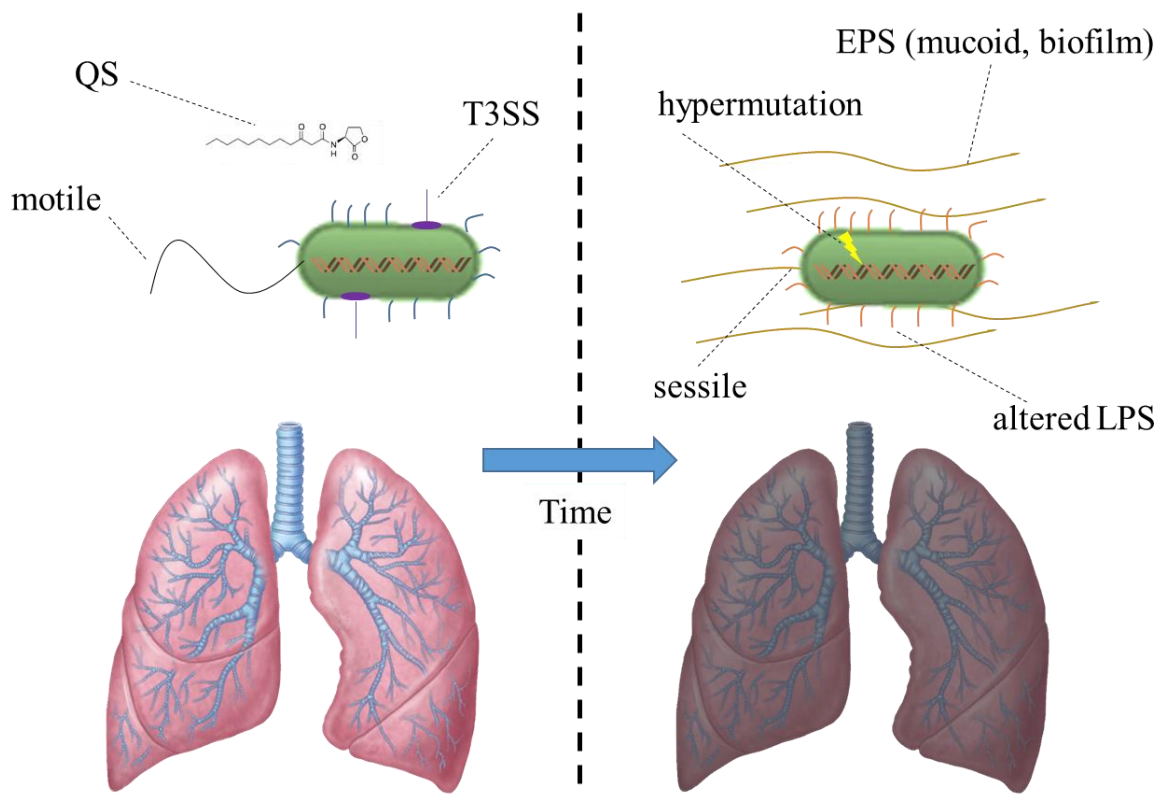


Figure 1-1. Characteristic features of the progression from acute (left) to chronic (right) lung infections. EPS, extracellular polymeric substance.

1.2 Bacterial motility

Motility is a critical behaviour for many bacteria, such as *P. aeruginosa*, as a means to seek out and rapidly colonize new niches, both in the environment and *in vivo*. Motility takes on many different forms, and can be observed at both macroscopic (Figure 1-2) and microscopic levels.

1.2.1 Swarming motility

Swarming motility is a complex and multicellular adaptation used for surface translocation. Many rod-shaped bacteria such as *Bacillus*, *Escherichia coli*, *Salmonella*, *Serratia*, *Proteus mirabilis*, *Vibrio* and *Pseudomonas* can swarm, as can the spiral-shaped *Rhodospirillum* (Kearns, 2010). General features of swarming motility include a requirement for flagella, production of a surfactant and elongation of the cells undergoing swarming. These features vary from species to species, since some species are peritrichously flagellated; whereas *P. aeruginosa* can acquire an extra polar flagellum (Kearns, 2010). The degree of cellular elongation also varies, as well as the specific surfactant produced. Soft agar, representing decreased medium viscosity (compared to

standard solid plates with 1.5 or 2% agar), is usually required for swarming, although some species, such as *P. mirabilis* and *Vibrio parahaemolyticus*, can swarm even on hard agar (Verstraeten et al., 2008). Lastly, the macroscopic pattern produced by swarming colonies varies considerably depending on the strain and ranges from dendritic to terraced to circular or vortex-shaped (Kearns, 2010).

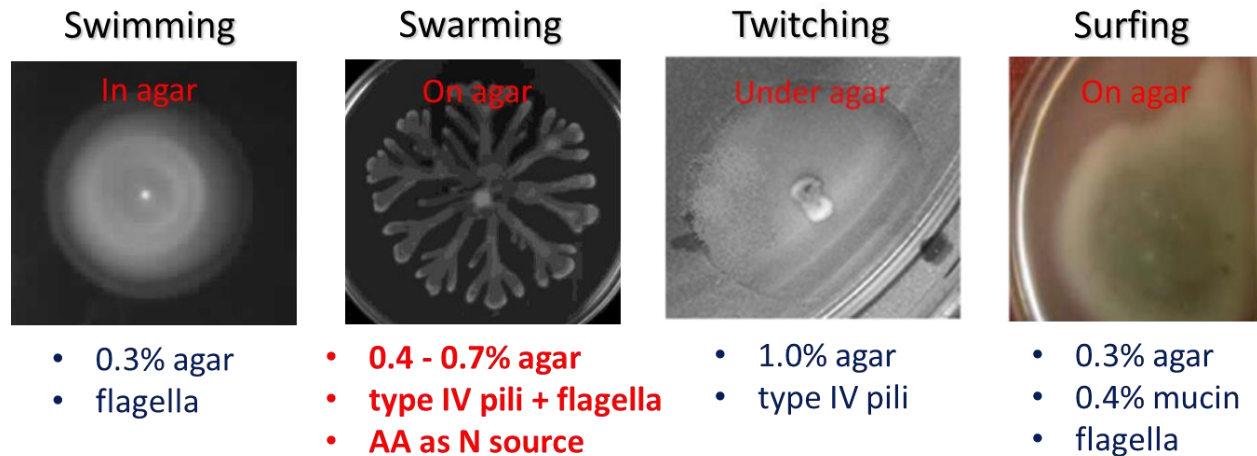


Figure 1-2. Different forms of motility in *P. aeruginosa*.

In *P. aeruginosa*, swarming occurs on lower-viscosity surfaces (0.4-0.7% agar) with amino acids as the nitrogen source. Interestingly, ammonium as a nitrogen source inhibits swarming in *P. aeruginosa*. It is a collective (so-called social) behaviour and cells inoculated onto a swarming plate can take at least several hours to build up sufficient density to initiate swarming, depending on the medium and inoculum. Prior to tendrill formation, a clear layer can be seen expanding from the colony, representing the surfactant rhamnolipid (product of *rhlABC*), which is used to help the bacteria spread. Once swarming initiates, bacteria raft together and move rapidly, propelling the swarm front forward. On a macroscopic level, tendrils bud from the central colony, branching occasionally, and can fill a 10 cm dish overnight. Tendrils commonly avoid touching one another, a phenomenon known as contact inhibition that is mediated in part by rhamnolipids (Caiazza et al., 2016). Pattern formation is strain-dependent, with PA14 typically forming large, well-separated tendrils, and PAO1 forming solar flare patterns, or thinner, closely-spaced tendrils, depending on the medium.

In *P. aeruginosa*, swarming is unusual in that it relies on both flagella and type IV pili (Köhler et al., 2000). Mutants in pili and related genes have deficiencies in swarming motility (Köhler et al., 2000; Yeung et al., 2009), although the basis for this is unclear. It is possible that the pilus is involved in surface sensing (Köhler et al., 2000), or possibly in intercellular rafting

and/or branching (Anyan et al., 2014).

Swarming in *P. aeruginosa* is dependent on QS, with mutants in *rhlIR* being completely deficient for swarming, and mutants in *lasIR* showing partial reductions in swarming (Köhler et al., 2000). RhlR and LasR are global transcriptional regulators, and in addition to *rhlABC* and *lasAB* regulate many other virulence factors and biofilm formation (Medina et al., 2003; Mukherjee et al., 2017; Ueda et al., 2009). A screen of the strain PA14 transposon insertion mutant library (Liberati et al., 2006) revealed 233 mutants with altered swarming, including 35 mutants in transcriptional regulators (Yeung et al., 2009). Of the 233 mutants, only 4 were hyperswarmers; the rest had either complete or partial defects in swarming motility (Yeung et al., 2009).

1.2.2 Other forms of motility

Unlike most other forms of motility, swimming is not associated with surfaces but rather occurs in liquid or low viscosity (e.g. 0.25-0.3% agar) environments. Bacteria use the flagellum and chemotactic machinery to move toward attractants or away from repellants. A widespread paradigm in *E. coli* is that rotation of the flagellum is occasionally reversed, causing the bacterium to tumble and allowing for reorientation (run-and-tumble). However, given that *P. aeruginosa* usually only has a single polar flagellum, cells reorient during a “pause” phase, or a “run-reverse-turn” paradigm by Brownian motion, and the polar flagellum spends equal time in the clockwise and counterclockwise phases (Qian et al., 2013). The pause phase allows time for the cells to turn, and pause duration is positively correlated with angle size (Qian et al., 2013). Free-swimming cells can exhibit different trajectories, including helical behaviour, which is rare in bacteria (Vater et al., 2014).

Twitching motility occurs on surfaces or at interfaces such as between a layer of agar and a Petri dish. Extension and retraction of the type IV pilus allows the cell to slowly drag itself forward. Interestingly, like swarming, twitching cells also form rafts that migrate *en masse* and form concentric rings (Semmler et al., 1999), suggesting that these two forms of motility may share some commonalities. Bacteria are normally oriented horizontal to the surface, but interestingly the type IV pilus can also mediate “walking motility,” where the cells can be seen moving in an upright vertical position (Conrad et al., 2011).

Surfing motility is another complex adaptive surface motility unique in its dependence on the presence of surface-wetting agents such as mucin (Yeung et al., 2012). It is also dependent on the presence of flagella, QS systems, and confers adaptive resistance to multiple antibiotics (Yeung et al., 2012; Sun et al., 2018a). Multiple studies have shown it to be largely distinct from swarming

both in transcriptional changes and genes required for surfing (Sun et al., 2018a; Sun et al., 2019; Yeung et al., 2012). Surfing motility was demonstrated in species other than *P. aeruginosa* although the dependence on QS varied in different species (Sun et al., 2018b).

Sliding motility is a passive surface motility that relies on colony expansion and surfactant production to propagate cells across a surface (Murray & Kazmierczak, 2008). Neither flagella nor type IV pili are required for this motility, in fact the presence of pili inhibits sliding motility, suggesting that cellular appendages can, under certain circumstances, create drag and slow down motility (Murray & Kazmierczak, 2008).

1.3 Antibiotic resistance

Antibiotic resistance is a growing global threat to public health. Bacterial populations are highly capable of acquiring drug resistance over time due to a number of different factors. First, their short generation time enables resistant subpopulations to rapidly dominate in the face of selective pressure (such as treatment of patients with antibiotics). Second, bacteria possess multiple systems for the uptake and exchange of foreign DNA, such as conjugation and transduction. Third, free-living bacteria are extremely versatile and can respond to different environmental stresses with massive changes in gene expression leading to adaptive resistance.

All of these factors combined with the overuse of antibiotics, particularly as a growth-promoting agent in livestock, and the lack of development of new drug classes, has led to a crisis whereby simple infections are now once again life-threatening in the case of multidrug-resistant (MDR) bacteria. The Centre for Disease Control and Prevention declared in 2013 that we are now in a “post-antibiotic era” (Ventola, 2015). *P. aeruginosa*, specifically, is on the World Health Organization’s list for critical development of new antibiotics (WHO, 2017), and 13% of *P. aeruginosa* infections in 2014 were MDR (Ventola, 2015). It is therefore critical to learn more about antibiotic resistance as well as develop new antimicrobial drugs.

1.3.1 Mechanism of resistance to specific antibiotics

Two mechanisms that confer resistance to multiple antibiotic classes are multidrug efflux and decreased membrane permeability. *P. aeruginosa* possesses a suite of multidrug efflux pumps that export from the cell many small molecules (often with diverse chemical natures and including multiple antibiotic classes and other toxic chemicals). *P. aeruginosa* is also known for its low outer membrane permeability, which is 12-100 times less than that of *E. coli* (Breidenstein et al., 2011; Fernández & Hancock, 2012).

Many antibiotics target the bacterial ribosome, including aminoglycosides, tetracycline,

macrolides and chloramphenicol. Chloramphenicol inhibits peptidyl transferase activity; macrolides bind to 23S RNA; tetracyclines inhibit binding of aminoacyl-transfer (t)RNA to the bacterial ribosomal A-site; and aminoglycosides bind to the 30S subunit causing mismatches (Lambert, 2012). Specific mechanisms of resistance to ribosome-targeting antibiotics include plasmid-borne or chromosomal enzymes that modify aminoglycosides by adenylation, phosphorylation or acetylation (Walsh & Wencewicz, 2016). The bacterial ribosome may also be modified either by mutation or methylation of rRNA to reduce affinity to antibiotics (Walsh & Wencewicz, 2016).

β -lactams target the cell wall, specifically peptidoglycan (PG) synthesis. β -lactams possess a reactive four-member ring that inhibits transpeptidation. A common mechanism of resistance to β -lactams is the production of β -lactamases, enzymes that inactivate the antibiotic. Penicillin binding proteins including transpeptidases can also be mutated or replaced by drug-insensitive forms (Walsh & Wencewicz, 2016).

Fluoroquinolones, such as ciprofloxacin or norfloxacin, target DNA gyrase and topoisomerase IV, enzymes that regulate the supercoiled state of DNA (Redgrave et al., 2014). Besides efflux, bacteria commonly become resistant to fluoroquinolones as a result of point mutations in topoisomerases that decrease the fluoroquinolone-binding affinity of the target protein (Redgrave et al., 2014).

Trimethoprim inhibits dihydrofolate reductase, depleting the cell of tetrahydrofolate, a one-carbon donor for a number of important metabolites in the cell including the nucleotide thymidylate (Sangurdekar et al., 2011). Structural gene mutations (i.e. in dihydrofolate reductase) are a common mechanism of trimethoprim resistance (Walsh & Wencewicz, 2016).

Polymyxin B is a nonribosomal lipopeptide with positive charge. It binds to the negatively charged LPS and disrupts the bacterial outer membrane although its specific mechanism against cells has not been clearly demonstrated (Breidenstein et al., 2011). Mechanisms of resistance include modification of LPS to a less negative form by addition of 4-amino-4-deoxyarabinose or phosphatidylethanolamine (Walsh & Wencewicz, 2016). In *P. aeruginosa*, the *arnBCADTEF* operon is involved in aminoarabinylation of LPS and is regulated by several different two-component systems, including PhoPQ, PmrAB, ParRS and CprRS (Barrow & Kwon, 2009; Fernández et al., 2010, 2012). The *arnBCADTEF* operon also confers resistance to cationic peptides and aminoglycosides (Breidenstein et al., 2011).

1.3.2 Acquired resistance

Antibiotic resistance can be acquired either horizontally or vertically. Resistance genes acquired vertically (mutationally) may emerge slowly, but the existence of hypermutator strains can speed the process (Breidenstein et al., 2011). In contrast, horizontal acquisition is rapid and can occur by diverse means, including conjugation, transduction, or transformation. Mobile DNA elements include plasmids, transposons, integrons, prophages and resistance islands (Breidenstein et al., 2011).

1.3.3 Adaptive resistance

Environmental conditions, specific growth states and/or antibiotics or other stresses can reversibly induce the differential expression of many genes, leading to adaptive antibiotic resistance. Conditions known to induce adaptive resistance include anaerobiosis, altered pH or temperature, low concentrations of divalent cations, and subinhibitory concentrations of antibiotics or other toxic compounds (Breidenstein et al., 2011; Fernández et al., 2010). Additionally, adaptive resistance also results from defined growth states such as biofilm formation and swarming and surfing motility. When the conditions that trigger adaptive resistance no longer exist, bacteria revert to a susceptible state.

1.3.4 Antibiotics used to treat *P. aeruginosa* infections

Clinically relevant antibiotic classes for *P. aeruginosa* infections include amnioglycosides, β -lactams, fluoroquinolones and lipopeptides (Tümmler, 2019). Some of the more toxic drugs such as polymyxin B and colistin are reserved for last resort (Tümmler, 2019). Two antibiotics from different classes are often prescribed for severe cases, such as piperacillin or ceftazidime and an aminoglycoside (Tümmler, 2019). To overcome β -lactam resistance, cephalosporin- β -lactamase inhibitor combinations are sometimes used, such as ceftazidime-avibactam and ceftolozane-tazobactam (Tümmler, 2019). For CF infections, aerosolized antibiotics may be used, such as tobramycin, colistin, liposomal amikacin, or liposomal ciprofloxacin (Tümmler, 2019). Drugs such as ciprofloxacin, meropenem, tobramycin, gentamicin and amikacin can be encapsulated into liposomes or loaded into nanoparticles in order to improve penetration of antimicrobials in burn wounds or chronic lung infections (Tümmler, 2019). The macrolide azithromycin has also proved useful in treating chronic lung infections, and even helps to reduce neutrophilic inflammation and improve lung function (Bhagirath et al., 2016; Tümmler, 2019).

1.4 Small RNAs

In bacteria, small inhibitory RNAs (sRNA) are short (40-500 bp) untranslated sequences

that are distinct from other forms of RNA such as mRNA, tRNA and rRNA. The purpose of sRNAs is to provide post-transcriptional regulation in order to alter protein abundance as needed. sRNAs may be intergenic or overlapping with other genes. In addition, sRNAs are also characterized as cis or trans. Cis-encoded sRNAs overlap with their target mRNA and have high sequence similarity; whereas trans-encoded sRNAs are encoded distant from their targets and utilize imperfect base-pairing (Li et al., 2012).

1.4.1 Mechanisms of regulation by sRNAs

There are several different ways that sRNAs can regulate a target. First, sRNAs can bind to mRNAs and block the ribosome binding site, leading to inhibition of translation (Waters & Storz, 2009). Second, sRNAs can bind to a different region of the mRNA, causing unmasking of the ribosome binding site, leading to increased translation (Li et al., 2012; Storz et al., 2004). Third, sRNAs can interact directly with proteins in order to sequester or alter their activity (Gottesman & Storz, 2011; Li et al., 2012; Pita et al., 2018). Last, sRNA binding to an mRNA can also initiate degradation of the mRNA, or alternatively stabilize mRNA (Pita et al., 2018; Prévost et al., 2011). sRNA-mRNA interactions often require the chaperone Hfq for stabilization (Gottesman & Storz, 2011). Additionally, *Pseudomonas* possesses other more selective RNA-binding proteins such as RsmA and Crc.

1.4.2 Known sRNAs in *P. aeruginosa*

The global transcriptional regulator GacA, part of the two-component system GacAS, induces the expression of two sRNAs, *rsmY* and *rsmZ* (Figure 1-3) (Pita et al., 2018). *rsmY* and *rsmZ*, in turn, sequester the post-transcriptional regulator RsmA from its target mRNA (Janssen et al., 2018; Pita et al., 2018). RsmA has diverse downstream effects, since it directly inhibits the translation of regulons involved in chronic infection, including T6SS, QS, biofilm formation and iron homeostasis; whereas it indirectly and positively regulates genes involved in acute lifestyles, such as T3SS, type IV pili, and virulence programs regulated by Vfr (Pita et al., 2018). Interestingly, *rsmY* and *rsmZ* can be indirectly regulated by alternative regulators such as HptB, AlgR and BfiSR; whereas the polynucleotide phosphorylase PNPase directly regulates *rsmY* and *rsmZ* by increasing their stability (Pita et al., 2018).

The two tandem and highly homologous *prfF* sRNAs, *prfF1* and *prfF2*, are involved in iron homeostasis and virulence *in vivo*, and use the RNA-binding protein Hfq (Djapgne et al., 2018; Pita et al., 2018; Wilderman et al., 2004). The entire region can also be transcribed as a whole, referred to as *prfH* (Djapgne et al., 2018; Pita et al., 2018). In iron-replete conditions, the

repressor Fur binds iron and represses *prrH*; whereas *prrH* represses or spares the use of iron under iron-limiting conditions (Pita et al., 2018). Interestingly, *prrH* also represses the expression of AntR, a positive regulator of genes that convert anthranilate into catechol (Djapgne et al., 2018; Pita et al., 2018). When AntR is repressed, then anthranilate is instead channeled into the PQS system, resulting in the increased expression of virulence factors (Pita et al., 2018). The sRNA *crcZ* competes with *prrH* for binding to Hfq, and can act as a sponge to sequester Hfq, since *crcZ* has a higher affinity for Hfq than does *prrH* (Pita et al., 2018; Sonnleitner et al., 2017).

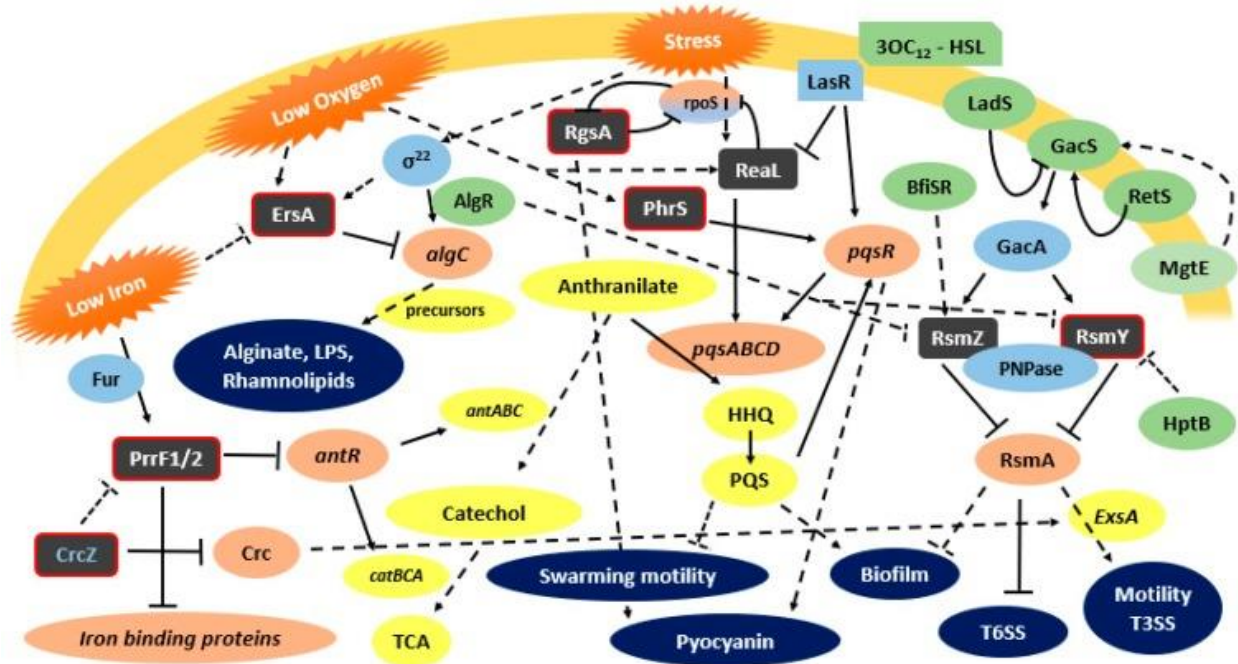


Figure 1-3. Known sRNAs and their involvement in the regulation of virulence factors. Reproduced from reference (Pita et al., 2018), this figure is licensed under CC BY 4.0 (<http://creativecommons.org/licenses/by/4.0/>).

The *crcZ* sRNA is expressed under the control of the global two-component regulatory CbrAB system (Sonnleitner et al., 2009), involved in carbon and nitrogen metabolism, antibiotic resistance and virulence (Yeung et al., 2011). Initially, *crcZ* was thought to bind to Crc to influence carbon catabolite repression (Sonnleitner et al., 2009), but a subsequent study showed that Crc had no RNA binding activity, whereas *crcZ* bound to Hfq with high affinity (Sonnleitner & Bläsi, 2014). Instead, Crc acts in concert with Hfq by stabilizing Hfq-RNA interactions by a mechanism that is not currently fully understood (Kavita et al., 2018).

The sRNA *phrS* activates PqsR and downstream QS pathways by an unusual mechanism (Sonnleitner et al., 2011). The *pqsR* mRNA has secondary structure that restricts translation to a moderate level under aerobic conditions (Sonnleitner et al., 2011). Under anaerobic conditions, an

oxygen-responsive regulator Anr is activated and increases levels of *phrS*. Then *phrS* binds to *pqsR* mRNA, and its secondary structure is rearranged, enhancing transcription from an upstream open reading frame which contributes to increased translation of *pqsR* (Sonnleitner et al., 2011). In turn, this leads to increased levels of PQS and pyocyanin (Sonnleitner et al., 2011). Interestingly, *phrS* was recently identified as a regulator of the CRISPR-Cas system (Lin et al., 2019).

The *ersA* sRNA is Hfq-dependent and involved in envelope stress response, repressing translation of the bifunctional enzyme AlgC (Pita et al., 2018). AlgC is involved in the synthesis of polysaccharides including alginate, psl, pel, LPS and rhamnolipids (Pita et al., 2018). The porin OprD, involved in the uptake of peptides and carbapenems, is also repressed by *ersA*, leading to an additional role in antibiotic resistance (Pita et al., 2018).

The sRNA *nrsZ* is induced upon nitrogen-limitation by the two-component system NtrBC in concert with RpoN (Wenner et al., 2014). Subsequently *nrsZ* post-transcriptionally activates RhlA, which is required for rhamnolipid production (Wenner et al., 2014). A mutant in *nrsZ* was unable to produce rhamnolipids or swarm (Wenner et al., 2014). This is interesting since nitrogen limitation is a feature known to enhance swarming motility in *P. aeruginosa* (Köhler et al., 2000).

In contrast, a deletion mutant in the sRNA *rgsA* led to an increase in swarming motility (Lu et al., 2016). It was found that *rgsA* directly regulates the global transcriptional regulator Fis and the acyl carrier protein AcpP (Lu et al., 2016). This sRNA is under direct control of RpoS, and indirect control of GacAS (Lu et al., 2016); however, *rgsA* also negatively regulates RpoS in an intricate regulatory loop (Lu et al., 2018).

Other recently characterized sRNAs include *srbA*, *real*, *pesA* and *phrD*. sRNA *srbA* is involved in biofilm formation and pathogenicity in a *C. elegans* infection model (Taylor et al., 2017). sRNA *real* is involved in pathogenicity in a *Galleria mellonella* infection model and links the Las and PQS QS systems (Pita et al., 2018). Interestingly, *real* also negatively regulates swarming motility and influences biofilm formation and pyocyanin production (Carloni et al., 2017). sRNA *pesA* is encoded on a pathogenicity island and present in strain PA14 but not PAO1 (Pita et al., 2018), and involved in pathogenicity against CF bronchial cells and also in regulating the expression of S-type pyocins (Pita et al., 2018). sRNA *phrD* was shown to positively influence the QS regulator RhlR (Malgaonkar & Nair, 2019). Overexpression of *phrD* results in increased production of rhamnolipids and pyocyanin (Malgaonkar & Nair, 2019).

1.4.3 Uncharacterized sRNAs in *P. aeruginosa*

Several studies have investigated the transcription of sRNAs on a genome-wide scale in *P.*

aeruginosa. A study in 2012 on strain PAO1 identified more than 500 novel intergenic sRNAs (Gómez-Lozano et al., 2012). Strain PA14 was also studied, revealing 165 intergenic sRNAs as well as 380 *cis*-antisense RNAs (Wurtzel et al., 2012). In another study, the expression of 31 intergenic sRNAs was confirmed by qRT-PCR and expression was shown to be differential during swarming and/or biofilm formation (Gill et al., 2018). Another 2012 study looked for sRNAs in strains PA14 and PAO1, identifying 150 novel sRNA candidates, and validating expression of 52 sRNAs by Northern blot (Ferrara et al., 2012). Of these, 13 sRNAs showed strain specificity, with 11 unique to PA14 and 2 unique to PAO1 (Ferrara et al., 2012). This supports the idea that sRNAs are rapidly evolving (Gómez-Lozano et al., 2015). Lastly, a study in 2014 identified 232 antisense RNAs, and comparison of their results with two other studies revealed little overlap, suggesting that expression of some sRNAs may be strongly dependent on specific conditions (Gómez-Lozano et al., 2014).

Hundreds of sRNAs have therefore been identified and await further characterization. This represents a large field awaiting further exploration.

1.5 Hypothesis and Objectives

I hypothesize that swarming motility is a complex adaptation regulated by sRNAs that is coupled to antibiotic resistance and virulence in acute *in vivo* infections.

1.5.1 Objectives

1. Investigate the antibiotic resistance of swarming cells by determining wild type (WT) susceptibility to different antibiotics under swarming conditions, as well as screening selected mutants to uncover mechanistic detail.
 - a. Approach: The antibiotic susceptibility of PA14 WT was compared between three growth conditions: swimming, swarming and spread plates using the disc diffusion assay with various antibiotics. Next, resistome mutants in genes dysregulated under swarming conditions (from RNA-Seq and qRT-PCR data) were screened for differential susceptibility vs. WT under swarming conditions. I expected that PA14 would be more resistant under swarming conditions to at least some antibiotics, and that specific mutants would reveal the underlying mechanism(s) behind this phenomenon.
2. Examine the role of sRNA species in the regulation of swarming motility by creating overexpression strains and screening for relevant phenotypes.
 - a. Approach: Fifteen sRNA species dysregulated under swarming conditions (Gill et al., 2018) were cloned and overexpressed in PAO1 WT and screened in relevant assays such

as motility, adherence and cytotoxicity. Two sRNAs with interesting phenotypes in the overexpression strains were selected to identify targets by RNA-Seq and proteomics, make deletion mutants and study in further detail.

3. Study the interconnection of swarming motility with other behaviours such as biofilm formation, other forms of motility, and cytotoxicity to discover a swarming-specific mutant to enable investigation of the role of swarming *in vivo*.
 - a. Approach: Previously identified swarming-deficient mutants (Yeung et al., 2009) were screened for swimming, twitching, biofilm formation, cytotoxicity and growth. The mutant with minimal effects on phenotypes other than swarming was selected to test in an acute *in vivo* mouse model and was expected to show reduced virulence.

Chapter 2: Materials and Methods

2.1 Bacterial strains and growth conditions

P. aeruginosa strains UCBPP-PA14 and PAO1 H103 and transposon mutants from the PA14 Harvard library (Liberati et al., 2006) were routinely grown in Luria-Bertani broth (LB) and BM2 minimal medium (62 mM potassium phosphate buffer, pH 7, 0.5 mM MgSO₄, 10 µM FeSO₄, carbon and nitrogen sources as indicated). The deletion mutant $\Delta prrH$ ($\Delta prrF1-2$) was obtained from reference (Wilderman et al., 2004). Gentamicin at 30 µg/ml was included in streak plates for PA14 transposon mutants. LB overnight cultures were diluted 1/50 and grown to mid-log phase (OD_{600nm} of 0.3 to 0.6) to initiate motility studies.

2.1.1 Growth curves

Overnight cultures were diluted to a final OD_{600nm} of 0.05 in the indicated medium and seeded in 96 well round-bottom plates at 100 µl/well. They were incubated at 37°C with shaking at frequency 567 cpm (3 mm) in the synergy H1 microplate reader and the OD_{600nm} was read every 30 min. Media recipes used were:

1. Synthetic cystic fibrosis sputum media (SCFM) without NH₄Cl modified from (Palmer et al., 2007) as follows: 1.3 mM NaH₂PO₄, 1.25 mM Na₂HPO₄, 0.348 mM KNO₃, 1.114 g/L KCl, 3.03 g/L NaCl, 10 mM MOPS, 0.827 mM L-aspartate, 1.072 mM L-threonine, 1.446 mM L-serine, 1.549 mM L-glutamate HCl, 1.661 mM L-proline, 1.203 mM L-glycine, 1.78 mM L-alanine, 0.16 mM L-cysteine HCl, 1.117 mM L-valine, 0.633 mM L-methionine, 1.12 mM L-isoleucine, 1.609 mM L-leucine, 0.802 mM L-tyrosine, 0.53 mM L-phenylalanine, 0.676 mM L-ornithine HCl, 2.128 mM L-lysine, 0.519 mM L-histidine, 0.013 mM L-tryptophan, 0.306 mM L-arginine, 1.754 mM CaCl₂, 0.606 mM MgCl₂, 3.6 µM FeSO₄, 3 mM D-glucose, 9.3 mM L-lactate (sodium lactate).
2. RPMI supplemented with 5% Mueller-Hinton Broth.
3. BM2 glycerol (no (NH₄)₂SO₄, 0.4% glycerol (wt/vol), 0.1% Casamino acids (CAA) (wt/vol), and 1% arabinose (wt/vol)).
4. BM2 glucose (no (NH₄)₂SO₄, 0.4% glucose (wt/vol), 0.1% CAA (wt/vol)).
5. LB.

2.2 Motility assays

For direct comparisons between swarming, swimming and spread plate conditions, all plates were composed of the same medium, excepting agar concentration. All plates were stab

(swim and twitch) or spot (swarm) inoculated with 1.5 µl of mid-log phase bacteria, except for spread plates, which were spread with 10^6 cfu per plate (final OD_{600nm} 1.3×10^{-3}). Bacteria were always inoculated at the same distance from the disc or another spot inoculum by using a stencil pattern drawn on the bottom of all plates. After inoculation, plates were incubated 15-20 h at 37°C and imaged on the ChemiDoc™ Touch Imaging System (Biorad).

2.2.1 Swarming

Swarming was generally assayed on BM2 with 0.4% glucose, 0.1% CAA and 0.5% agar (wt/vol), unless otherwise indicated. For strains overexpressing sRNAs on the plasmid pHERD20T, 0.4% glycerol was often substituted as the carbon source (unless otherwise indicated), since glucose represses expression from the P_{BAD} promoter (Qiu et al., 2008). Plates were poured to contain 25 ml medium each, and solidified and dried for 1 h prior to use.

2.2.2 Swimming

Swimming was generally assayed in BM2 glucose with 0.25 or 0.3% agar (wt/vol), using 0.4% glucose and 0.1% CAA as the nitrogen source for direct comparisons with swarming (as indicated). For strains overexpressing sRNAs on the plasmid pHERD20T, 20 mM potassium succinate pH 7.0 was substituted as the carbon source and 7 mM (NH₄)₂SO₄ as the nitrogen source (unless otherwise indicated). Plates were poured to contain 25 ml medium each, and solidified for 1 h prior to use.

2.2.3 Twitching

Twitching plates were composed of 10 ml of LB with 1% agar and dried overnight. Bacteria were stab inoculated to the bottom of the plate, incubated overnight at 37°C, and one extra day at room temperature before visualization on the ChemiDoc™ Touch Imaging System (Biorad).

2.2.4 Disc diffusion assay

Discs were impregnated with the amount of antibiotic indicated in Table 2-1 and allowed to dry briefly before being placed in the centre of a BM2 glucose agar plate with 0.3, 0.4, 0.5 or 1.5% agar. For swarming and swimming, bacteria were spot inoculated at a distance of 19 mm from the edge of the disc; for the 1.5% agar plates, bacteria (10^6 cfu) were spread onto the surface of the plate prior to adding the disc. After overnight incubation, the zone of inhibition, representing the closest distance between the edge of the disc and visible bacterial growth, was measured using a ruler. Statistically significant differences were determined by ANOVA using GraphPad Prism.

Table 2-1. Amount of antibiotic used in the disc diffusion assay.

Antibiotic	Amount (µg)
Amikacin	125

Antibiotic	Amount (µg)
Azithromycin	300
Chloramphenicol	300
Ciprofloxacin	1
Erythromycin	4000
Gentamicin	80
Meropenem	0.7
Piperacillin	32
Polymyxin B	400
Tetracycline	80
Tobramycin	80
Trimethoprim	250

2.2.5 Agar dilution assay

Antibiotics were incorporated into BM2 swarming agar (0.5% agar) at varying concentrations. After overnight incubation, the minimal concentration that completely inhibited swarming tendril formation was reported as the swarming inhibitory concentration (IC).

2.2.6 Six well plate assays

Motility assays performed using 10 cm dishes were modified to a six well format for Figure 6-1 with the following specifications: swarming (BM2 glucose, 0.1% CAA, 0.5% agar at 4 ml/well), swimming (BM2 glucose, 7 mM (NH₄)₂SO₄, 0.25% agar at 4 ml/well) and twitching (LB, 1% agar at 1.5 ml/well).

2.3 Other phenotypic assays

2.3.1 Biofilm formation

Overnight cultures were diluted 1/100 in ¼ LB (5 g/L) and seeded at 100 µl/well in 96 well polystyrene round-bottom plates. After incubating for 24 h at 37°C, the media was discarded and plates were rinsed three times with dH₂O. Crystal violet (105 µl of 0.1%) was added and incubated with shaking for 20 min at room temperature, then the plates were rinsed three times with dH₂O and the crystal violet was solubilized by adding 110 µl 70% (vol/vol) ethanol and shaking for 20 min at room temperature. Then the absorbance at 595 nm was read in an Epoch plate reader (BioTek).

2.3.2 Adherence

Overnight cultures were diluted to a final OD_{600nm} of 0.03 in 90% LB supplemented with 5% arabinose (wt/vol) and seeded at 100 µl/well in 96 well flat-bottom polystyrene plates. After incubating for 4 h at 37°C, unattached cells were removed by discarding the media and rinsing three times with dH₂O. Crystal violet (105 µl of 0.1%) was added and incubated with shaking for

20 min at room temperature, then the plates were rinsed three times with dH₂O and the crystal violet was solubilized by adding 110 µl 70% (vol/vol) ethanol and shaking for 20 min at room temperature. Then the absorbance at 595 nm was read in an Epoch plate reader (BioTek).

2.3.3 Cytotoxicity

Human bronchial epithelial 16HBE14o- cells (HBE) between passage 14 and 40 were grown in Minimum Essential Medium with Earle's Salts (1X) (MEM) (Gibco) supplemented with 10% fetal bovine serum (FBS) (Gibco), 2 mM L-glutamine (Gibco) and 1% penicillin-streptomycin (Gibco). After cells reached 80-100% confluency, they were washed once with phosphate buffered saline pH 7.4 (1X) (PBS) (Gibco), trypsinized with 0.25% Trypsin-EDTA (Gibco) and diluted in medium before counting. HBE were seeded at 2×10^4 cells/well at 200 µl/well in a 96 well plate and grown again to confluency (2-3 days). Then the medium was changed to MEM or DMEM (Gibco), as indicated in Table 2-2, 1-2 h prior to infection. Next, bacterial cultures were prepared by pelleting overnight cultures, washing once with PBS and resuspending in the medium indicated in Table 2-2. Bacteria were diluted in the same medium. Next, the medium of the HBEs was removed and replaced with a suspension containing the bacterial inoculum described in Table 2-2. The coculture was incubated at 37°C with 5% CO₂ for the amount of time indicated in Table 2-2, followed by monitoring the release of lactate dehydrogenase (LDH) as an indicator of cytotoxicity as described below. Cells treated with 2% Triton®-X-100 (vol/vol) (Fisher Scientific) in the respective media were used as a positive control for the LDH assay.

Table 2-2. Parameters for cocultures optimized for the PA14 and PAO1 strains.

Strain	Medium	Inoculum (cfu/ml)	MOI	Time (h)
PA14	MEM, 1% FBS, 2 mM L-glutamine	7.5×10^5	7.5	4
PAO1	DMEM, no glucose, 1% FBS, 1% sodium pyruvate, ± 1% arabinose	3×10^5	3	16

Plates were centrifuged for 5 min at 1000 rpm in the Eppendorf centrifuge 5810 R (15 amp version) and 50 µl supernatant were removed and mixed with 50 µl solution as indicated in the Cytotoxicity Detection Kit (Roche) assessing release of LDH (1/100 catalyst/reaction mixture), and incubated for 10 min at room temperature in the dark. Then the absorbance at 492 and 900 nm was read in the Epoch plate reader (BioTek). Next, the absorbance at 900 nm was subtracted from the absorbance at 492 nm. % cytotoxicity was calculated by subtracting bacteria and HBE alone controls from coculture values, and then normalizing to the Triton-X control.

2.3.4 Outer membrane permeabilization assay

Outer membrane permeability was assessed using the fluorescent dye N-phenyl-1-naphthylamine (NPN) as described previously (Schurek et al., 2008) with minor modifications. Briefly, cells were harvested from antibiotic-free BM2 glucose swarm plates (0.5% agar) and resuspended in 5 mM HEPES pH 7.0 supplemented with 5 μ M carbonyl cyanide *m*-chlorophenyl hydrazone, then diluted to an OD_{600nm} of 0.5. Fluorescence was monitored in the PerkinElmer Fluorescence Spectrometer LS 55 at an excitation wavelength of 350 nm and emission wavelength of 420 nm. NPN was added at a final concentration of 10 μ M, then tobramycin was added at a final concentration of 40 μ g/ml.

2.3.5 Pyoverdine assay

Bacteria were grown overnight in Casamino acid medium (0.5% CAA, 0.1 mM MgSO₄, 7 mM potassium phosphate buffer, pH 7.0). Turbid cultures were pelleted and the supernatant collected in a fresh tube. Next, 5 μ l of supernatant was mixed with 995 μ l 10 mM Tris pH 6.8. Then the fluorescence was monitored on the PerkinElmer Fluorescence Spectrometer 168 LS 55 with excitation wavelength 405 nm and scanning the emission spectrum from 400-700 nm. The fluorescence emission was corrected by subtracting the values for a blank buffer control.

2.4 Antibiotic susceptibility assays

2.4.1 Minimal inhibitory concentration (MIC)

Bacteria were seeded at 5×10^5 cfu/ml (final OD_{600nm} 6.7×10^{-5}) in a twofold concentration gradient of antibiotic in either LB or BM2 0.1% CAA, no (NH₄)₂SO₄, with glucose or glycerol as indicated, at 100 μ l/well in 96 well polystyrene round-bottom plates. After incubating for 24 h at 37°C, the minimal concentration to inhibit visible bacterial growth was reported as the MIC.

2.4.2 Kill curves

Bacteria were harvested from antibiotic-free swim (0.3% agar) and swarm (0.5% agar) BM2 glucose plates and resuspended in 62 mM potassium phosphate buffer, pH 7.0 and diluted to a final OD_{600nm} of 0.025 in 10 ml 62 mM potassium phosphate buffer. Cells were then treated with 20 μ g/ml tobramycin with aeration at room temperature, and aliquots were periodically taken for serial dilution in PBS pH 7.4 for colony enumeration on LB plates.

2.5 RNA-Seq

2.5.1 Conditions used

Bacteria were harvested from the edge (2-3 mm) of swarm fronts or from colonies swimming within agar using the conditions as follows. Swarm (0.5% agar) vs. swim (0.25% agar)

RNA-Seq was performed using PA14 WT in BM2 glucose 0.1% CAA supplemented with 1.4 mM (NH₄)₂SO₄ to inhibit swarming in swim plates. Tobramycin vs. untreated RNA-Seq was done using PA14 WT swarming in BM2 glucose 0.5% agar ± 0.5 µg/ml tobramycin. Both PA0805.1 and PA2952.1 RNA-Seq and proteomics were performed at the same time under swarming conditions using overexpression strains compared to EV in BM2 glycerol 0.5% agar and 1% arabinose to induce expression.

2.5.2 RNA isolation

Harvested bacteria were transferred to RNeasy Protect Bacteria Reagent (Qiagen), pelleted and stored at -80°C. For the swim samples, most of the agar was removed from the pellets by pipetting. Swim pellets were lysed by resuspension in 6 mg/ml lysozyme dissolved in Tris-EDTA (TE) buffer pH 8.0 (Thermo Fisher), supplemented with 5 U β-agarase I (NEB) to digest remaining agar in the swim pellets. Swarm pellets were resuspended in lysozyme-TE without agarase. RNA isolation then proceeded according to the manufacturer's instructions using the RNeasy Mini Kit (Qiagen). Eluted RNA was further purified with the TURBO DNA-free kit (Thermo Fisher). The quality and quantity of RNA was confirmed using the Bioanalyzer instrument. The number of biological replicates for each experiment are indicated in Table 2-1.

Table 2-3. Number of biological replicates per RNA-Seq experiment.

Experiment	No. replicates		No. independent RNA-Seq runs
	Test condition	Control condition	
Swarm vs. swim	5	6	2
TOB vs. UNTR	3	3	1
PA0805.1 vs. EV	5	5	2
PA2952.1 vs. EV	5	5	2

2.5.3 RNA-Seq and identification of differentially expressed (DE) genes

RNA samples were depleted of rRNA using the RiboZero Bacteria Kit (Illumina), and libraries were prepared using the KAPA Stranded Total RNA Kit (KAPA Biosystems). Sequencing was done on an Illumina HiSeq2500 by the University of British Columbia Sequencing and Bioinformatics Consortium. Sequence quality was determined using FastQC v0.11.8 and MultiQC v1.7. Reads were mapped to the *P. aeruginosa* UCBPP-PA14 or PAO1 reference genome obtained from the Pseudomonas Genome Database (www.pseudomonas.com) using the alignment program STAR v2.6.1a. Counts were generated using v0.11.2 of the HTSeq count function.

For the experiment involving a subinhibitory concentration of tobramycin, in addition to the 3 untreated swarming controls specifically obtained for this experiment, the swarming samples

from the “swarm vs. swim” experiment described herein were also included when performing all downstream analyses for the subinhibitory-tobramycin experiment, bringing the total number of samples for this experiment to 11, 8 untreated swarming controls and 3 tobramycin-treated swarming samples.

Experiment date was included in the design formula to control for any potential batch effects. DE genes were determined using the package DESeq2 v1.20.0, in R v3.5.3, with thresholds of adjusted p-value ≤ 0.05 and absolute fold change ≥ 1.5 . All lists of DE genes are available in Tables A1 and A2.

2.6 Proteomics

2.6.1 Protein digestion and quantification

Bacteria harvested in Section 2.5.1 were washed three times with PBS pH 7.4 and stored as a pellet at -80°C . Bacterial cell pellets were resuspended in lysis buffer (100 mM HEPES (pH 8.5), 4% SDS, 1X Halt protease inhibitor cocktail (Thermo Fisher Scientific)). The cells were sonicated three times for 15 s per cycle with 1 min cooling on ice between each cycle. The insoluble cellular debris was removed by centrifugation at 17,000 g for 10 min. Protein concentration was determined using the Pierce detergent compatible Bradford assay kit (Thermo Fisher Scientific). All protein samples were processed and handled using single-pot solid-phase-enhanced sample preparation (SP3) protocol described below. Prior to SP3 treatment, two types of carboxylate-modified SeraMag Speed beads (GE Life Sciences) were combined in a ratio of 1:1 (vol/vol), rinsed, and reconstituted in water at a concentration of 20 μg solids per μl . Initially, 200 μg of lysate was reduced with 10 mM (final concentration) dithiothreitol for 30 min at 60°C followed by alkylation using 50 mM (final concentration) iodoacetamide for 45 min in the dark at room temperature. After that, 20 μl of the prepared bead mix was added to the lysate and samples were adjusted to pH 7 using HEPES buffer. To promote protein binding to the beads, acetonitrile was added to a final concentration of 70% (vol/vol) and samples were incubated at room temperature on a tube rotator for 18 min. Subsequently, beads were immobilized on a magnetic rack for 1 min. The supernatant was discarded and the pellet was rinsed twice with 200 μl of 70% ethanol and once with 200 μl of 100% acetonitrile while on the magnetic rack. Rinsed beads were resuspended in 65 μl of 50 mM HEPES buffer (pH 8) supplemented with trypsin/Lys-C mix (Promega) at an enzyme-to-protein ratio of 1:25 (wt/wt) and incubated for 16 h at 37°C . After overnight digestion, supernatant containing peptides was transferred into a fresh tube and subsequently measured for peptide yield using Pierce Quantitative Fluorometric Peptide Assay (Thermo Fisher Scientific).

2.6.2 Tandem mass tag (TMT) labeling

Representative samples containing 85 µg of peptides were adjusted to the same concentration using 50 mM HEPES (pH 8) and labeled with 10-plex TMT reagents (Thermo Fisher Scientific). The TMT10 reporter channels were sequentially assigned in increasing reporter mass as TMT0-TMT9. Four TMT10 channels (TMT0-TMT3) were assigned to samples from the EV strain, three channels (TMT4-TMT6) to the PA2952.1 strain, and three channels (TMT7-TMT9) to the PA0805.1 strain. In short, 0.8 mg of each TMT channel was first dissolved in 41 µl of DMSO before adding to the corresponding peptide digests. The labeling reaction was incubated at room temperature for 60 min. Following incubation, samples were quenched for 15 min with the addition of 8 µl of 5% hydroxylamine. Finally, labeled samples were mixed at equal volume and desalted using SOLA HRP SPE cartridge (Thermo Fisher Scientific) prior to LC/MS/MS.

2.6.3 Mass spectrometry data acquisition

Analysis of TMT labeled peptide digests was carried out on an Orbitrap Q Exactive HF-X instrument (Thermo Fisher Scientific, Bremen, Germany). The peptide mixture was resuspended in 0.1% formic acid prior to injection. The sample was introduced using an Easy-nLC 1000 system (Thermo Fisher Scientific) at 2 µg per injection. Mobile phase A was 0.1% (vol/vol) formic acid and mobile phase B was 0.1% (vol/vol) formic acid in 80% acetonitrile (LC-MS grade). Gradient separation of peptides was performed on a C18 (Luna C18(2), 3 µm particle size (Phenomenex, Torrance, CA)) column packed in-house in Pico-Frit (100 µm X 30 cm) capillaries (New Objective, Woburn, MA). Peptide separation used the following gradient: 3 – 5 % increase of phase B over 4 min, 5 – 7 % over 3 min, 7 – 25 % over 197 min, 25 – 60 % over 25 min, 60 – 90% over 1 min, with final elution of 90% B for 10 min at a flow rate of 300 nL/min.

Data acquisition on the Orbitrap Q Exactive HF-X instrument was configured for data-dependent method using the full MS/DD–MS/MS setup in a positive mode. Spray voltage was set to 1.85 kV, funnel RF level at 40, and heated capillary at 275°C. Survey scans covering the mass range of 350–1500 m/z were acquired at a resolution of 120,000 (at m/z 200), with a maximum ion injection time of 60 ms, and an automatic gain control (AGC) target value of 3e6. For MS2 scan triggering, up to 20 most abundant ions were selected for fragmentation at 32% normalized collision energy, with intensity threshold kept at 5.7e4. AGC target value for fragment spectra was set at 1E5, which were acquired at a resolution of 45,000, with a maximum ion injection time of 88 ms and an isolation width set at 0.7 m/z. Dynamic exclusion of previously selected masses was enabled for 30 s, charge state filtering was limited to 2–6, peptide match was set to preferred, and

isotope exclusion was on.

2.6.4 Identification and differential analysis of proteins

A January 2019 reference database of *P. aeruginosa* PAO1 (taxon 208964) was downloaded from uniprot (www.uniprot.org). The 1D LC-MS run was converted into an MGF file using the Proteome Discoverer bundled tool, and was searched against the PAO1 database using X!tandem (cyclone 2012.10.01.1). Peptide identification settings were standard for the instrument: single missed cleavage tryptic peptides were permitted, with a parent and fragment mass tolerance of 10 PPM. A fixed post-translational modification of C+57.021 was applied, and variable PTMs including N-terminal acetylation, deamidation, phosphorylation and oxidation were permitted. Peptide assignment into source proteins was managed by X!tandem.

Peptide level TMT10 reporter tags intensities were integrated across window of ± 3 mDa each, and corrected for isotopic overlap between channels using the supplied batch-specific correction matrix. Protein level quantitation required at least two unique peptides of expectation values $\log(e) \leq -1.5$ each, yielding highly confident protein assignments of at least $\log(e) \leq -3$. The sum of peptide level TMT10 reporter tag intensities for each protein was converted into a \log_2 scale for simplified differential analysis. Protein expression values across each TMT10 reporter channel were normalized into a common scale (mean=0, SD=1).

Differential analyses between normalized sample populations (PA0805.1 vs. EV and PA2952.1 vs. EV) were conducted using the Welch T-test function in Excel between population averages. The p-scores were not subjected to multiple-testing corrections, and any differences with $p < 0.05$ were considered candidates for biological exploration. Differences between normalized population means were scaled back into a \log_2 scale by multiplying them by an average system-wide SD of 2.26.

2.7 Murine infection abscess model

Bacterial strains were tested *in vivo* by injecting bacteria subdermally to form a cutaneous abscess (Pletzer et al., 2017). *P. aeruginosa* PA14 was grown to an OD_{600nm} of 1.0 in 2YT broth, subsequently washed twice with sterile PBS, and further adjusted to 5×10^8 CFU/ml. A 50 μ l bacterial suspension was injected subdermally into the right side of the dorsum. One hour post infection, mice were either treated with 14 mg/kg 1018 (dissolved in 5% dextrose), or dextrose alone. After 16-18 h, mice were euthanized, organs harvested, and homogenized in 1 ml sterile PBS using a Mini-Beadbeater-96 (Biospec products) for 5 min. Bacterial counts were determined by serial dilution and experiments were performed at least 3 times independently with 3 to 5

animals per group. These studies were performed in collaboration with Dr. Daniel Pletzer at UBC.

2.8 qRT-PCR

Cells were harvested from a variety of conditions as described in Table 2-4. For cultures grown in BM2, (NH₄)₂SO₄ was omitted and 0.1% CAA was used as the nitrogen source. RNA was isolated and DNase digested as described in the RNA-Seq section, but omitting the use of agarase, and quantified on a NanoDrop® Spectrophotometer ND-1000. RNA was then diluted to 1 ng/μl and 5 μl were used in a total reaction volume of 25 μl. The qScript One-Step SYBR Green RT-qPCR (Quantabio) was used and samples were run on the LightCycler® 96 (Roche). Cq values were normalized to the housekeeping gene *rpoD* using the $\Delta\Delta CT$ method. *rpoD* routinely served as an appropriate housekeeping gene, except in the swarm vs. swim experiment (Section 4.10), where 16S was used instead. Primers used for qRT-PCR are described in Table 2-5.

Table 2-4. Comparisons and media used for qRT-PCR experiments.

Comparison	Medium	Section
Swarm vs. planktonic (Overhage et al., 2008)	BM2 glucose, ± 0.5% agar	Chapter 3
Swarm vs. swim	BM2 glucose, 0.5 vs. 0.3% agar	4.10
PA0805.1 vs. EV	BM2 glycerol, 1% arabinose, 0.5% agar	4.5
PA0805.1 induced vs. uninduced	BM2 glycerol, 0.5% agar ± 0.5% arabinose	4.2
PA2952.1 vs. EV	BM2 glycerol, 1% arabinose, 0.5% agar	Chapter 5
<i>ΔptsP</i> EV vs. WT EV <i>ΔptsP</i> ⁺ vs. WT EV	LB planktonic	Chapter 6

Table 2-5. Primers used for qRT-PCR.

Name	Sequence (5' -> 3')
16S F	GGCAGGCCTAACACATGCAA
16S R	TTATCCCCCACTACCAGGCA
<i>aprA</i> F	TCCAAGCTGGTGTCTCGGT
<i>aprA</i> R	AGCGCCTTCTCGTTGAGGTT
<i>gmd</i> F	GAGATGTTTCGGCCTGATCCA
<i>gmd</i> R	ACGGTGATCCAGTGGCCATA
<i>lasA</i> F	GACGAACTGTTCTCTACGGTC
<i>lasA</i> R	CCAGGTATTCGCTCTTGTCG
<i>mexG</i> F	ACTCGCTCGAAAGCAACTGG
<i>mexG</i> R	AGGCTGGCCTGATAGTCGAA
<i>mexH</i> F	ATCCGTCTCAAGGCGCAGTT
<i>mexH</i> R	TTGTCCAGCTGTTCTGCGA
<i>mexI</i> F	ATCACCGTCACCACCGAGTA
<i>mexI</i> R	AAAGGTAGTCGATGCCCTCC

Name	Sequence (5' -> 3')
<i>opmD</i> F	TACAGCCGCAGCATCGAACA
<i>opmD</i> R	CCGAACAGGTCGATTTCCCA
PA0805.1 qF	TGGTATTGCGGGACGCC
PA0805.1 qR	ACTCTTCTGAAGCAATCCCCTG
PA3670 F	AGGATTCGCCTGCAGGTGAT
PA3670 R	CTGCTGCAGGGGAATTCCTT
PA3836 F	GGCTACGAAGACGGCAAGAA
PA3836 R	CTTGTCGCCGATGAACTTGC
PA5542 F	GCCGCCGATCTCTATGAACT
PA5542 R	TGGTCCCCTTGTGGATAACC
<i>pchF</i> F	GATGACTGCGTACTGCACTGCT
<i>pchF</i> R	CCATTGCGGATCGAGATAGC
<i>pcrG</i> F	AATACACCGAAGACACCCTGCG
<i>pcrG</i> R	TTGCCACATTTCCGCCAGCA
<i>prtN</i> F	CGTGGAATTGGTCTACCGCA
<i>prtN</i> R	CCAGGGCCTTGCTGAAGTTT
<i>ptsP</i> qF	CTCAACACGCTGCGCAAGAT
<i>ptsP</i> qR	TGGGTACCCATGGCTTCCTT
<i>rhlR</i> F	CGCGTCGAACTTCTTCTGGAT
<i>rhlR</i> R	GCAAGAGTTCCGGGGAAATC
<i>rmd</i> F	CTCTCCGGTTTTCGTAGGCAA
<i>rmd</i> R	CAGCAGATCGTAACGATGCG
<i>rpoD</i> F	TCACGCACGCAGAGTTGCAT
<i>rpoD</i> R	AAGCTGGTGCCCAAGCAGTT
<i>vfr</i> F	TAGACAAGCTGCTCGCACAC
<i>vfr</i> R	GAAATCACCGCTGTTGAGGT
<i>wbpW</i> F	CGAGAAACCCGATGAGGAAACC
<i>wbpW</i> R	GTCGAGGCCGTGAAACAGAA
<i>wbpX</i> F	GACCAACTGGTCTTGCTGGA
<i>wbpX</i> R	TAGATCACCGAGACGATGCC
<i>wbpZ</i> F	CGGTTTTTCCCTGAGCGTGT
<i>wbpZ</i> R	GGAAATGCACCAGGTCCATG
<i>wzm</i> F	GGCTATCGTGGCTTCGTTCT
<i>wzm</i> R	ATCGACAGCGGATTGAGCAC
<i>wzt</i> F	GAGGAAATCCAGGCGCTGAT
<i>wzt</i> R	ATCTGCATGCCGCTGGAGTA

2.9 DNA manipulation

2.9.1 Deletion mutants

Deletion mutants of PA0805.1 and *ptsP* were constructed using previously described methods with minor modifications (Pletzer et al., 2014). Briefly, PAO1 WT genomic DNA was PCR-amplified using the primers PA0805.1 A1 and A2, and PA0805.1 B1 and B2 described in Table 2-6. PA14 WT gDNA was amplified with primers *ptsP* A1 and A2, and *ptsP* B1 and B2 (Table 2-6). After gel extraction of the fragments, a fusion PCR was performed using primers PA0805.1 A1 and B2, and *ptsP* A1 and B2. The PCR products were then TOPO cloned as described in Section 2.9.2, digested with *Bam*HI and *Xba*I, cloned into the vector pEX18Gm, transformed into the *E. coli* donor strain ST18 (an auxotroph for 5-aminolevulinic acid) and conjugated into PAO1 or PA14 WT using LB agar plates with 50 µg/ml 5-aminolevulinic acid. After, *P. aeruginosa* conjugants were selected on gentamicin 30 µg/ml and then counterselected at least three times with LB 5% sucrose. The deletion mutants were confirmed by lack of growth on gentamicin and PCR of the deleted region.

Table 2-6. Primers used for cloning.

Name	Sequence (5' -> 3')
PA0730.1 F	GACTCTAGACGATGGGAACGCGGCGA
PA0730.1 R	CTCGGTACCGTCCCTTTCCTTCCCGGCAT
PA0805.1 A1	CTCGGATCCTCTGAGTGGAGTACGGGAGA
PA0805.1 A2	CGAAAGATATACAATCCGGGAAAGCGTGAAAGTAAAGGAACAT
PA0805.1 B1	ATG TTCCTTTACTTTCACGCTTTCCTCCGGATTGTATATCTTTCG
PA0805.1 B2	GACTCTAGAGAAGGATGGGAACAGGTCTG
PA0805.1 F	GACTCTAGAATGGAGCAGCGTATATTGC
PA0805.1 R	CTCGGTACCCTGCGTACCAAAGTAAAGTC
PA0958.1 F	GACTCTAGACTTGCGGATAGTTGAGGTTCC
PA0958.1 R	CTCGGTACCGTTTGCTTTCAAACAGAATAGCCT
PA1091.1 F	CTCGGTACCAACTTCCACCCTCTGCCG
PA1091.1 R	GACTCTAGAGGTGATTTCTTCCAAAGGACC
PA14sr120 F	CTCGGTACCATGGAGCAGCGTATATTGC
PA14sr120 R	GACTCTAGATAGTACCTGAACTGCCAGC
PA2461.1 F	GACTCTAGATCTTCAGCTCAGACACAGGTT
PA2461.1 R	CTCGGTACCCTTAGAGGAAGGTCCATTCAAACA
PA2461.3 F	GACTCTAGACTGTACCGCGAGCCCC
PA2461.3 R	CTCGGTACCCAACGCTGGAGTATCATCCACT
PA2952.1 F	CTCGGTACCGCCCGTATCTTGACCGGAT
PA2952.1 R	GACTCTAGATAGCTGCATGGGCAGGTC
PA2952.1W F	CTCGGTACCATAAGGATGTCGCCAGACAGG

Name	Sequence (5' -> 3')
PA2952.1W R	GACTCTAGAGAGCGGGCGCATTAT
PA3159.1 F	CTCGGTACCCACCCCGCGATTGCC
PA3159.1 R	GACTCTAGATAGTTATTGAAGTGGTGATGCGT
PA4539.1 F	GACTCTAGAGCCGCCAGACCGAACG
PA4539.1 R	CTCGGTACCGCGGAAAAGCTGGATGCATGG
PA4656.1 F	CTCGGTACCATTCGGGCGTTATCCTGTGA
PA4656.1 R	GACTCTAGACCTCTCTGGTTGTGTAGCGT
PA5078.1 F	GACTCTAGACGTCCGTGAACATGAATTACT
PA5078.1 R	CTCGGTACCCTGTACAGGACAGGCCG
PA5304.1 F	GACTCTAGACAGTATAGGAAGAGGCAGGCA
PA5304.1 R	CTCGGTACCAGGCTCCGCGAGCGCTCTGG
<i>prhH</i> F	GGATCCAACCTGGTCGCGAGAT
<i>prhH</i> R	TCTAGAAGGAAGGGCGCGAGG
<i>prtN</i> F	GGATCCATGCAGCCAACCATCGCC
<i>prtN</i> R	TCTAGATCAGGATGCGATGCTGTCC,
<i>ptsP</i> A1	CTCGGATCCCGATGGTTTTTCGCCCCGAATG
<i>ptsP</i> A2	TCCGGCGCGCGGGAAAGCTCGGGGCGCTTGTCTCCGTGTT
<i>ptsP</i> B1	AACACGGAGACAAGGCCCGAGCTTTCCCGCGCGCCGGA
<i>ptsP</i> B2	GACTCTAGACCTCGCAGTATTCCGGGCTT
<i>ptsP</i> F	GGATCCATGCTCAACACGCTGCGCAAGA
<i>ptsP</i> R	TCTAGATCAGGGCTGGACGGTAGC
<i>rsmY</i> F	CTCGGTACCGTCAGGACATTGCGCAGGAA
<i>rsmY</i> R	GACTCTAGAAAAACCCCGCCTTTTGGGC
<i>srbA</i> F	CTCGGTACCATCAGGGGCTCTGAAACGAC
<i>srbA</i> R	GACTCTAGATCAAGAAATGTATTGGTTGAGCACC
<i>wbpW</i> F	GGATCCATGCTGATTCCCGTGGTGC
<i>wbpW</i> R	TCTAGATCAGACCACCCTGCCGTA.

2.9.2 Complementation and overexpression strains

PA14 and PAO1 WT gDNA was isolated as specified in the Qiagen DNeasy Blood and Tissue kit protocol. 80-300 ng was PCR amplified using the primers described in Table 2-6. PCR products were then cloned using one of two cloning strategies as described in Table 2-7. PCR products cloned via the TOPO strategy were gel-extracted with the GeneJet Gel Extraction Kit (Thermo Fisher) and TOPO cloned (Invitrogen). TOPO reactions were transformed into TOP10 *E. coli* and selected with 50 µg/ml kanamycin (TOPO). Plasmid was subsequently isolated according to the Thermo Fisher kit and digested with the restriction endonucleases indicated in Table 2-7. This allowed the sRNAs to be cloned in two different orientations, termed a and b, and

other constructs to be cloned in one specific orientation. After the fragments were gel-extracted, they were ligated into similarly digested vectors with T4 DNA ligase (Thermo Scientific), transformed into TOP10 *E. coli*, and selected with antibiotic as indicated. PCR products cloned via the direct strategy were PCR purified using the PCR purification kit (Thermo), then digested with the restriction enzymes indicated in Table 2-7. Next, digested fragments were gel extracted and ligated as described above, then transformed into TOP10 *E. coli* and selected with antibiotic as indicated in Table 2-7. Plasmid sequences were confirmed by Sanger sequencing at the Sequencing and Bioinformatics Consortium at UBC.

Table 2-7. Cloning strategies and restriction enzymes used.

PCR product	Cloning strategy	Enzymes used	Final product	Vector	Antibiotic (µg/ml)
PA0730.1	Direct	<i>KpnI XbaI</i>	PA0730.1	pHERD20T	Ampicillin 100
PA0805.1	TOPO	<i>KpnI XbaI</i>	PA0805.1a	pHERD20T	Ampicillin 100
		<i>EcoRI KpnI</i>	PA0805.1	pHERD20T	Ampicillin 100
				pUC18miniTn7Tp	Trimethoprim 50
ΔPA0805.1	TOPO	<i>BamHI XbaI</i>	ΔPA0805.1	pEX18Gm	Gentamicin 15
PA0958.1	Direct	<i>KpnI XbaI</i>	PA0958.1	pHERD20T	Ampicillin 100
PA1091.1	TOPO	<i>KpnI XbaI</i>	PA1091.1a	pHERD20T	Ampicillin 100
		<i>HindIII XbaI</i>	PA1091.1b	pHERD20T	Ampicillin 100
PA2461.1	Direct	<i>KpnI XbaI</i>	PA2461.1	pHERD20T	Ampicillin 100
PA2461.3	Direct	<i>KpnI XbaI</i>	PA2461.3	pHERD20T	Ampicillin 100
PA2952.1	Direct	<i>KpnI XbaI</i>	PA2952.1	pHERD20T	Ampicillin 100
PA2952.1W	Direct	<i>KpnI XbaI</i>	PA2952.1W	pHERD20T	Ampicillin 100
PA3159.1	TOPO	<i>KpnI XbaI</i>	PA3159.1a	pHERD20T	Ampicillin 100
		<i>EcoRI KpnI</i>	PA3159.1b	pHERD20T	Ampicillin 100
PA4539.1	Direct	<i>KpnI XbaI</i>	PA4539.1	pHERD20T	Ampicillin 100
PA4656.1	TOPO	<i>KpnI XbaI</i>	PA4656.1a	pHERD20T	Ampicillin 100
		<i>EcoRI KpnI</i>	PA4656.1b	pHERD20T	Ampicillin 100
PA5078.1	Direct	<i>KpnI XbaI</i>	PA5078.1	pHERD20T	Ampicillin 100
PA5304.1	Direct	<i>KpnI XbaI</i>	PA5304.1	pHERD20T	Ampicillin 100
PA14sr120	Direct	<i>KpnI XbaI</i>	PA14sr120	pHERD20T	Ampicillin 100
<i>prhH</i>	TOPO	<i>EcoRI XbaI</i>	<i>prhH</i>	pHERD20T	Ampicillin 100
<i>priN</i>	TOPO	<i>SacI XbaI</i>	<i>priN</i>	pHERD20T	Ampicillin 100
<i>ptsP</i>	TOPO	<i>BamHI XbaI</i>	<i>ptsP</i>	pBBR1mcs5	Gentamicin 10
Δ <i>ptsP</i>	TOPO	<i>BamHI XbaI</i>	Δ <i>ptsP</i>	pEX18Gm	Gentamicin 15
<i>rsmY</i>	Direct	<i>KpnI XbaI</i>	<i>rsmY</i>	pHERD20T	Ampicillin 100
<i>srbA</i>	Direct	<i>KpnI XbaI</i>	<i>srbA</i>	pHERD20T	Ampicillin 100
<i>wbpW</i>	TOPO	<i>BamHI XbaI</i>	<i>wbpW</i>	pBBR1mcs2	Kanamycin 50

2.9.3 Transformation of *P. aeruginosa*

P. aeruginosa strains were transformed either by electroporation or conjugation as described in Table 2-8. This was due to the observation that certain vectors transformed more

efficiently via conjugation. Note that for comparisons between WT, mutants, complementation and overexpression strains, the same method of transformation was always used, and WT and mutants were also always transformed with EV to rule out any effect of the vector.

2.9.3.1 Electroporation

Electrocompetent *P. aeruginosa* were transformed with both EV and vector with insert according to Choi et al. (Choi et al., 2006). Transformants were selected with antibiotic as indicated in Table 2-8 and confirmed to carry the correct plasmid.

2.9.3.2 Conjugation

Strains were transformed by conjugation using previously described methods with minor modifications (Pletzer et al., 2014). The plasmid of interest was transformed into the *E. coli* donor strain ST18 (an auxotroph for 5-aminolevulinic acid) and conjugated into the *P. aeruginosa* strain of interest using LB agar plates with 50 µg/ml 5-aminolevulinic acid. After, conjugants were selected with antibiotic as indicated in Table 2-8 and confirmed to carry the correct plasmid.

Table 2-8. Methods of transformation used in this thesis, including vectors and antibiotic concentrations.

Strain	Mutant	Method	Vector	Antibiotic (µg/ml)
PA14	WT	Electroporation	pBBR1mcs2	Kanamycin 250
PA14	WT	Electroporation	pHERD20T	Carbenicillin 300
PA14	WT	Conjugation	pBBR1mcs5	Gentamicin 30
PA14	<i>priN</i>	Electroporation	pHERD20T	Carbenicillin 300
PA14	<i>wbpW</i>	Electroporation	pBBR1mcs2	Kanamycin 250
PA14	<i>ΔptsP</i>	Conjugation	pBBR1mcs5	Gentamicin 30
PAO1	WT	Electroporation	pHERD20T	Carbenicillin 300
PAO1	ΔPA0805.1	Conjugation	pUC18miniTn7Tp pTNS3	Trimethoprim 250
PAO1	<i>ΔprhH</i>	Electroporation	pHERD20T	Carbenicillin 300

2.10 In silico sRNA target prediction

sRNA targets were predicted using three tools: IntaRNA2 (Busch et al., 2008), RNAPredator (Eggenhofer et al., 2011), and TargetRNA2 (Tjaden et al., 2006). For IntaRNA2 and TargetRNA2, input parameters were adjusted to 75 nucleotides up and downstream, and a minimum of 7 basepairs in the seed sequence was used. Cutoffs used were top 100 and $p \leq 0.05$ for IntaRNA2, $p \leq 0.05$ for TargetRNA2, and top 100 for RNAPredator. Only targets predicted by more than one tool were considered.

2.11 Statistical analysis

All experiments were repeated independently with at least three biological replicates.

Experiments performed in 96 well plates additionally used at least two technical replicates per biological replicate. Unless otherwise specified, mean \pm standard error was reported or depicted in graphs. Statistical tests (Student's t-test or ANOVA) were performed in GraphPad Prism, with a p value of 0.05 being considered significant and the p values are indicated by * ($0.01 < p \leq 0.05$), ** ($0.001 < p \leq 0.01$), *** ($0.0001 < p \leq 0.001$), and **** ($p \leq 0.0001$).

2.12 Data availability

RNA-Seq data was deposited in Gene Expression Omnibus (GEO) under accession numbers GSE121504 (swarm vs. swim), GSE137676 (tobramycin vs. untreated), GSE137738 (PA0805.1 vs. EV), and GSE146765 (PA2952.1 vs. EV). Proteomics data was deposited in MassIVE under the index number MSV000084373 (PA0805.1 vs. EV).

Chapter 3: Swarming motility and antibiotic resistance

3.1 Introduction

When *P. aeruginosa* undergoes swarming motility, adaptive antibiotic resistance is triggered (Lai et al. 2009; Overhage et al. 2008). To date this has only been investigated in a limited fashion; research presented in this chapter provides an in-depth investigation of this phenomenon.

Swarming motility in *P. aeruginosa* is a rapid, coordinated, surface-associated movement that occurs under semi-viscous, nitrogen-limiting conditions (Overhage et al., 2008). Importantly, these conditions have some similarities with the mucosal surfaces of the human lung (Yeung et al., 2009); therefore, understanding how swarming in *P. aeruginosa* leads to multiple-antibiotic adaptive resistance is relevant to our understanding of lung infections and the limitations of antibiotic therapy in this situation. Features of the lung environment that are likely to support swarming include increased glucose levels in the diseased lung (Baker et al., 2007; Gill et al., 2016), amino acids as the main nitrogen source, sufficient levels of magnesium (Palmer et al., 2007), and a humid and viscous environment. Swarming is thought to have clinical relevance particularly in the acute or initial infection of lungs, since strains isolated from chronic infections tend to lose motility over time (Winstanley et al., 2016). Thus swarming can allow for rapid colonization in the lung and the establishment of infection, and is also important in the initial formation of biofilms (O'May & Tufenkji, 2011), which are a common problem in infections due to their ability to persist and resist antimicrobial treatment.

In the swarm state, *P. aeruginosa* conditionally increases its resistance to several antibiotics (Lai et al., 2009; Overhage et al., 2008). This resistance is not dependent on prior antibiotic exposure and also occurs in other swarming species such as *Salmonella* sp. (Butler et al., 2010), *E. coli* and *Bacillus subtilis* (Lai et al., 2009).

Little is known about the genetic mechanisms that result in adaptive antibiotic resistance in *P. aeruginosa* swarming motility. Therefore, after confirming and extending the observation that *P. aeruginosa* exhibits resistance in the swarm state, RNA-Seq and qRT-PCR were performed on swarming cells and swarming cells treated with tobramycin, and mutants in genes dysregulated under swarming conditions were selected and tested for altered antibiotic susceptibility under swarming conditions.

3.2 Swarming cells were resistant to multiple antibiotic classes

To confirm and extend the observation that *P. aeruginosa* exhibits resistance in the swarming state (Lai et al., 2009; Overhage et al., 2008), BM2 glucose agar plates solidified with

varying concentrations of agar (allowing for different modes of growth) were inoculated with mid-log phase *P. aeruginosa* PA14 (Figure 3-1, Figure A1). After overnight incubation, the zone of inhibition around antibiotic discs (i.e. the closest approach of motile cells to the antibiotic disc) was measured as an indicator of resistance. PA14 swarming cells on 0.4% agar were significantly more resistant to aminoglycosides (amikacin, gentamicin, kanamycin, and tobramycin) and β -lactams (ceftazidime, meropenem, and piperacillin) when compared to the control swim and spread plates (Figure 3-1, top panels). Swarming cells were also significantly more resistant to chloramphenicol, ciprofloxacin, tetracycline and trimethoprim. For the macrolides, erythromycin and azithromycin, swarming cells were significantly more resistant than swimming cells but not bacteria on 1.5% agar spread plates. Swarming cells were not resistant to polymyxin B (Figure 3-1, top panels). Resistance of swarming cells was more readily observable at 0.4% agar since this condition permitted better swarming (Figure 3-1). However, similar trends were observed for swarming at 0.5% agar (Figure A1).

To confirm these results by a different method, cells were harvested from antibiotic-free swimming and swarming plates and subjected to tobramycin treatment. Swarming cells were killed more slowly, showing approximately 100-fold better survival than swimming cells after 300 min (Figure 3-2).

3.3 Swarming motility is a complex adaptation accompanied by many changes in the expression of resistome genes

Due to the complexity of these resistance data and to enable an understanding of the global changes accompanying swarming motility, I first characterized the global gene expression changes accompanying swarming motility. Previous studies analyzing global gene expression changes were performed using microarrays with planktonic (broth culture grown cells) as a control; this had identified the dysregulation of 417 genes including 18 regulators (Overhage et al., 2008). Here I improved this analysis by comparing swarming to swimming cells taken from plate cultures (varying only in the agar concentration), and utilizing the more accurate method of RNA-Seq.

The comparison of swarming vs. swimming by RNA-Seq resulted in the differential expression of 1,581 genes (753 downregulated and 828 upregulated) (Table A1). This was a substantial portion, 28%, of the *P. aeruginosa* genome, showing that swarming is a distinct and complex adaptation.

The dysregulated genes included 104 transcriptional regulators, two-component systems and sigma factors (Table 3-1). There were several regulators of nitrogen metabolism such as *nirQ*,

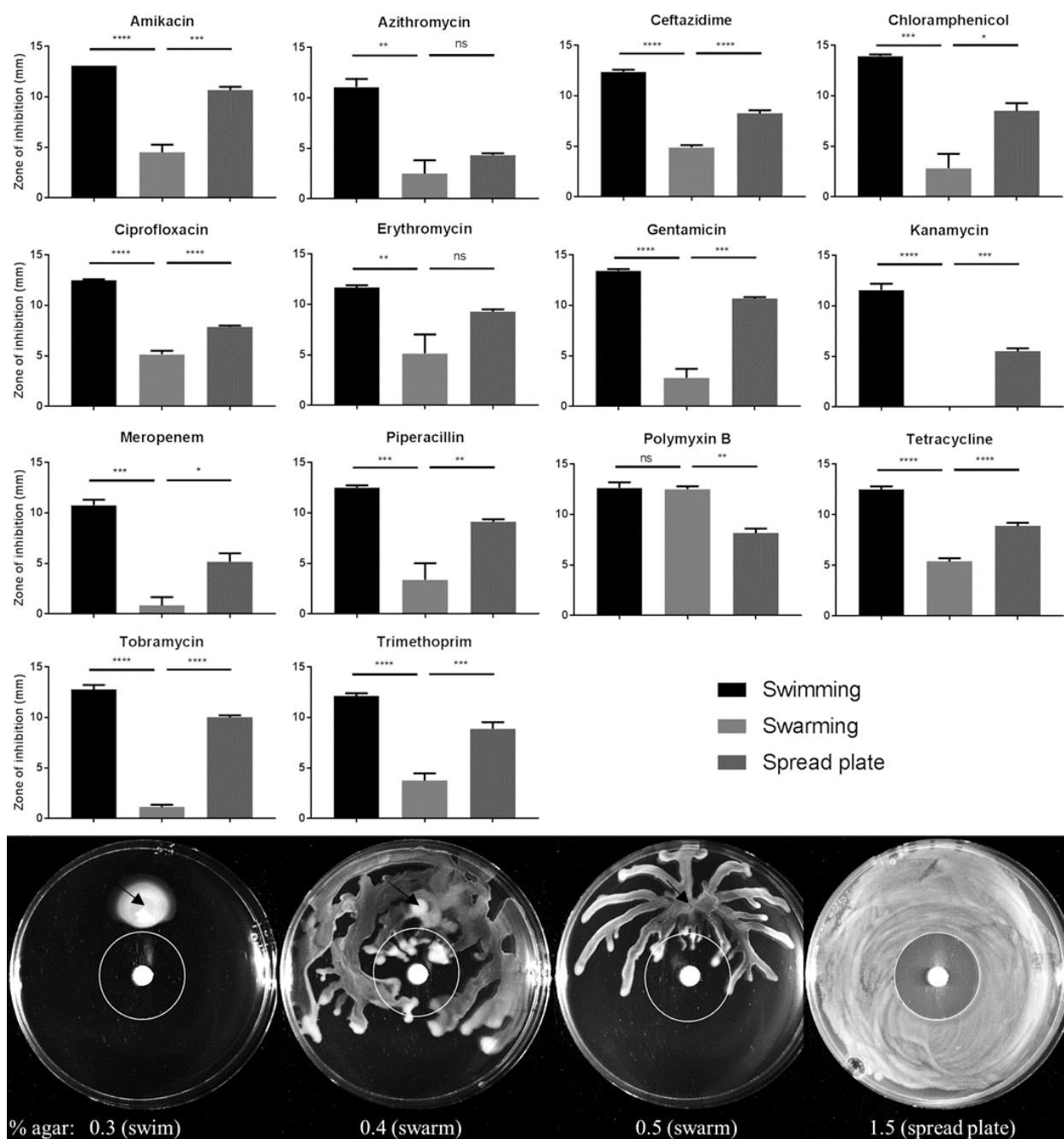


Figure 3-1. Swarming bacteria exhibited heightened resistance to most antibiotic classes. Top panels: Zone of inhibition assay using 0.3% agar for swimming, 0.4% for swarming and 1.5% for spread plate with different antibiotics. Statistically significant differences were determined by ANOVA. **Lower panels:** Zone of inhibition assay for PA14 WT using tobramycin discs. Arrows indicate position of inoculation. p values (*) are described in Section 2.11. $n \geq 3$.

nirG, *nosR*, and *hutR*. Other interesting regulators included BfiS, a two-component sensor involved in biofilm formation (Petrova & Sauer, 2010), PchR, a regulator of ferripyochelin receptor gene (Heinrichs & Poole, 1996), VqsR, a global regulator of QS and virulence (Liang et al., 2012a), and AlgR, which is involved in coordinating alginate and rhamnolipid production, and

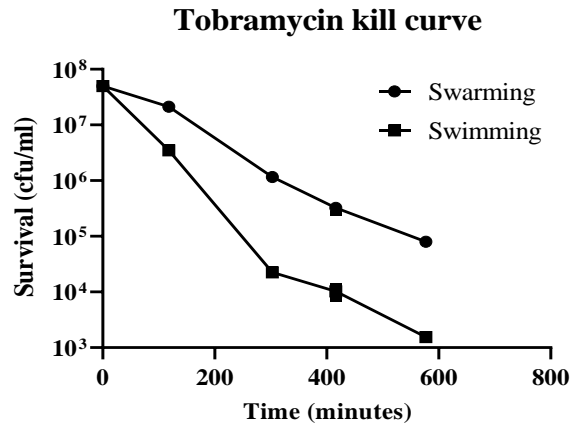


Figure 3-2. Tobramycin kill curve showing that swarming cells survived better than swimming cells in the presence of tobramycin. $n = 3$.

swarming and twitching motilities (Okkotsu et al., 2013). The dysregulated sigma factors included *hasI*, *femI*, *fiuI*, *foxI*, *fpvI*, *pvdS*, *rpoS*, *vreI*, PA1351, PA2050, PA2093, and PA4896.

Table 3-1. Selected results from swarm vs. swim RNA-Seq comparisons. These revealed 104 dysregulated transcriptional regulators, and dysregulated efflux and β -lactamase genes. Cutoffs used were fold change (FC) ≥ 1.5 and adjusted p value (padj) ≤ 0.05 .

Locus Tag	PAO1	Name	Product Name	padj	FC
Transcriptional regulators, two-component systems and sigma factors					
PA14_00600	PA0048		transcriptional regulator	9.1E-06	1.7
PA14_00680	PA0056		LysR family transcriptional regulator	2.0E-03	1.5
PA14_02250	PA0178		two-component sensor	5.2E-09	1.6
PA14_02260	PA0179		two-component response regulator	4.4E-07	1.5
PA14_02390	PA0191		transcriptional regulator	3.4E-08	-2.0
PA14_02870	PA0233		transcriptional regulator	1.9E-08	1.5
PA14_03070	PA0248		transcriptional regulator	9.0E-06	1.6
PA14_03580	PA0275		transcriptional regulator	9.8E-07	1.5
PA14_04820	PA0367	<i>laoR</i>	TetR family transcriptional regulator	4.4E-14	1.6
PA14_06170	PA0471	<i>fiuR</i>	transmembrane sensor	1.0E-04	1.7
PA14_06180	PA0472	<i>fiuI</i>	RNA polymerase sigma factor	3.0E-05	1.5
PA14_06690	PA0513	<i>nirG</i>	transcriptional regulator	1.8E-13	-3.2
PA14_06710	PA0515		transcriptional regulator	5.4E-13	-3.4
PA14_06770	PA0520	<i>nirQ</i>	regulatory protein	4.6E-21	-2.9
PA14_06970	PA0535		Cro/CI family transcriptional regulator	2.5E-09	-1.6
PA14_07110	PA0547		ArsR family transcriptional regulator	8.7E-27	1.7
PA14_09260	PA4227	<i>pchR</i>	transcriptional regulator	5.6E-28	3.8
PA14_09680	PA4197	<i>bfiS</i>	two-component sensor	5.4E-09	-1.7
PA14_09790	PA4182		transcriptional regulator	1.3E-13	-1.5
PA14_10530	PA4132		GntR family transcriptional regulator	2.0E-28	-1.5
PA14_10660	PA4120		transcriptional regulator	7.9E-05	1.9
PA14_10940	PA4094		AraC family transcriptional regulator	2.0E-06	1.6

Locus Tag	PAO1	Name	Product Name	padj	FC
PA14_11120	PA4080		response regulator	6.9E-08	1.5
PA14_12140	PA3995		transcriptional regulator	1.3E-09	1.7
PA14_13000	PA3932		transcriptional regulator	1.2E-14	-2.7
PA14_13150	PA3921		transcriptional regulator	1.6E-14	1.5
PA14_15240	PA3776		LysR family transcriptional regulator	1.3E-03	-1.6
PA14_15290	PA3771		transcriptional regulator	7.9E-06	1.9
PA14_15830	PA3757	<i>nagR</i>	GntR family transcriptional regulator	2.9E-05	-1.5
PA14_16790	PA3678	<i>mexL</i>	TetR family transcriptional regulator	6.8E-15	1.5
PA14_17380	PA3630	<i>gfnR</i>	glutathione-dependent formaldehyde neutralization regulator	7.1E-11	1.8
PA14_17480	PA3622	<i>rpoS</i>	RNA polymerase sigma factor	1.9E-11	1.6
PA14_17540	PA3616		recombination regulator RecX	6.3E-10	-1.6
PA14_19380	PA3458		transcriptional regulator	3.8E-08	1.8
PA14_19990	PA3410	<i>hasI</i>	RNA polymerase ECF-subfamily sigma-70 factor	3.6E-06	-2.0
PA14_20230	PA3391	<i>nosR</i>	regulatory protein	2.1E-37	-17.2
PA14_20780	PA3346	<i>hsbR</i>	two-component response regulator	2.6E-20	1.6
PA14_23190	PA3174	<i>hutR</i>	transcriptional regulator	1.1E-12	-2.2
PA14_23590	PA3133	<i>sawR</i>	transcriptional regulator	5.2E-11	-2.1
PA14_24710	PA3045	<i>rocA2</i>	two-component response regulator	9.1E-11	-2.5
PA14_24720	PA3044	<i>rocsS2</i>	two-component sensor	5.2E-14	-2.1
PA14_25800	PA2957		TetR family transcriptional regulator	3.5E-13	-1.5
PA14_26330	PA2917		AraC family transcriptional regulator	4.4E-18	-2.3
PA14_26860	PA2879		LysR family transcriptional regulator	3.2E-19	2.0
PA14_30580	PA2591	<i>vqsR</i>	LuxR family transcriptional regulator	2.5E-21	1.6
PA14_30840	PA2571		signal transduction histidine kinase	7.2E-09	1.5
PA14_32060	PA2519	<i>xylS</i>	transcriptional regulator	3.6E-08	1.8
PA14_32460	PA2488		transcriptional regulator	7.7E-04	1.5
PA14_32710	PA2468	<i>foxI</i>	ECF subfamily RNA polymerase sigma-70 factor	5.8E-05	1.8
PA14_32720	PA2467	<i>foxR</i>	transmembrane sensor	1.7E-04	1.5
PA14_33260	PA2426	<i>pvdS</i>	extracytoplasmic-function sigma-70 factor	9.7E-07	2.0
PA14_33440	PA2417		LysR family transcriptional regulator	3.5E-09	1.6
PA14_33800	PA2387	<i>fpvI</i>	RNA polymerase sigma factor	1.8E-33	2.2
PA14_33840	PA2383		transcriptional regulator	4.3E-17	2.9
PA14_34440	PA2337	<i>mtlR</i>	transcriptional regulator	1.7E-04	1.5
PA14_34660	PA2320	<i>gntR</i>	transcriptional regulator	1.3E-19	1.6
PA14_34730	PA2312		XRE family transcriptional regulator	3.5E-15	-3.0
PA14_34820	PA2304	<i>ambC</i>	regulatory protein	2.7E-20	3.5
PA14_34830	PA2303	<i>ambD</i>	regulatory protein	1.2E-30	3.6
PA14_34880	PA2299		GntR family transcriptional regulator	7.2E-14	2.0
PA14_35250	PA2267		LysR family transcriptional regulator	1.5E-06	1.6
PA14_35370	PA2259	<i>ptxS</i>	transcriptional regulator	1.3E-08	-2.1

Locus Tag	PAO1	Name	Product Name	padj	FC
PA14_35380	PA2258	<i>ptxR</i>	transcriptional regulator	1.7E-13	2.4
PA14_36300	PA2196		TetR family transcriptional regulator	5.0E-10	1.6
PA14_36420	PA2177		sensor/response regulator hybrid	3.7E-18	2.3
PA14_36990	PA2133		cyclic-guanylate-specific phosphodiesterase	4.8E-03	-1.9
PA14_37140	PA2121		LysR family transcriptional regulator	4.0E-03	1.6
PA14_37420	PA2094		transmembrane sensor protein	7.9E-13	3.7
PA14_37430	PA2093		RNA polymerase sigma factor	2.4E-07	2.5
PA14_37580	PA2082	<i>kynR</i>	leucine-responsive regulatory protein	1.6E-04	1.5
PA14_37980	PA2051		Fe ²⁺ -dicitrate sensor, membrane protein	5.8E-08	-3.3
PA14_37990	PA2050		RNA polymerase sigma factor	1.5E-13	-4.5
PA14_38250	PA2032		transcriptional regulator	8.7E-18	1.6
PA14_39800	PA1912	<i>femI</i>	ECF subfamily RNA polymerase sigma-70 factor	2.6E-03	-1.6
PA14_39980	PA1898	<i>qscR</i>	transcriptional regulator	2.7E-07	1.7
PA14_42390	PA1713	<i>exsA</i>	transcriptional regulator	1.3E-24	2.7
PA14_45250	PA1484		transcriptional regulator	5.6E-05	1.5
PA14_45950	PA1431	<i>rsaL</i>	regulatory protein	2.1E-74	3.0
PA14_46290	PA1403		TetR family transcriptional regulator	4.2E-07	2.0
PA14_46810	PA1351		RNA polymerase ECF-subfamily sigma-70 factor	1.7E-10	1.9
PA14_47390	PA1301		transmembrane sensor	2.4E-03	1.6
PA14_48160	PA1243		sensor/response regulator hybrid	1.4E-40	3.2
PA14_48830	PA1196	<i>ddaR</i>	transcriptional regulator	2.7E-07	1.6
PA14_49170	PA1180	<i>phoQ</i>	two-component sensor	4.7E-16	-2.0
PA14_49180	PA1179	<i>phoP</i>	two-component response regulator	5.5E-14	-1.8
PA14_49790	PA1128		transcriptional regulator	1.9E-05	1.7
PA14_53410	PA0839		transcriptional regulator	2.7E-04	-1.5
PA14_53720	PA0816		transcriptional regulator	2.1E-10	1.8
PA14_55160	PA0707	<i>toxR</i>	transcriptional regulator	2.4E-17	5.5
PA14_55550	PA0675	<i>vreI</i>	ECF subfamily RNA polymerase sigma-70 factor	8.4E-10	-2.6
PA14_55780	PA4293	<i>pprA</i>	two-component sensor	8.6E-18	2.5
PA14_57140	PA4396		two-component response regulator	1.5E-17	1.6
PA14_58380	PA4499	<i>psdR</i>	transcriptional regulator	7.2E-10	-1.6
PA14_58510	PA4508		AsnC family transcriptional regulator	7.7E-06	-1.6
PA14_61620	PA4659		MerR family transcriptional regulator	2.0E-11	-1.9
PA14_63280	PA4787		transcriptional regulator	1.6E-13	1.6
PA14_64050	PA4843	<i>gcbA</i>	two-component response regulator	2.1E-48	-1.9
PA14_64500	PA4878	<i>brlR</i>	transcriptional regulator	1.6E-13	-1.8
PA14_64690	PA4895		transmembrane sensor	3.3E-06	-1.8
PA14_64700	PA4896		RNA polymerase sigma factor	1.3E-05	-1.9
PA14_66850	PA5059		TetR family transcriptional regulator	1.1E-09	1.7
PA14_69470	PA5261	<i>algR</i>	alginate biosynthesis regulatory protein	2.3E-12	1.6

Locus Tag	PAO1	Name	Product Name	padj	FC
PA14_71170	PA5389	<i>cdhR</i>	AraC family transcriptional regulator	1.1E-03	1.6
PA14_71750	PA5437		LysR family transcriptional regulator	2.5E-79	-3.3
PA14_72380	PA5483	<i>algB</i>	two-component response regulator	2.3E-11	1.9
PA14_72390	PA5484	<i>kinB</i>	two-component sensor	1.4E-16	1.9
Multidrug efflux and β-lactamases					
PA14_01940	PA0156	<i>triA</i>	Resistance-Nodulation-Cell Division (RND) efflux membrane fusion protein	6.6E-12	1.6
PA14_09500	PA4208	<i>opmD</i>	outer membrane protein	1.3E-22	1.8
PA14_09520	PA4207	<i>mexI</i>	RND efflux transporter	2.0E-23	1.6
PA14_18760	PA3523	<i>mexP</i>	RND efflux membrane fusion protein	3.1E-10	-4.0
PA14_18780	PA3522	<i>mexQ</i>	RND efflux transporter	1.5E-31	-3.4
PA14_18790	PA3521	<i>opmE</i>	outer membrane efflux protein	1.2E-12	-3.3
PA14_32390	PA2494	<i>mexF</i>	RND multidrug efflux transporter	3.6E-14	-2.0
PA14_32400	PA2493	<i>mexE</i>	RND multidrug efflux membrane fusion protein	4.2E-11	-1.9
PA14_38395	PA2019	<i>mexX</i>	periplasmic multidrug efflux lipoprotein	3.4E-07	-1.8
PA14_38410	PA2018	<i>mexY</i>	multidrug efflux protein	2.1E-06	-1.6
PA14_41280	PA1797		beta-lactamase	2.8E-11	2.0
PA14_44520	PA1541		drug efflux transporter	1.5E-10	-5.6
PA14_44530	PA1540		multidrug efflux system protein MdtI	6.7E-05	-2.4
PA14_45910	PA1435		RND efflux membrane fusion protein	1.1E-02	-1.6
PA14_48240	PA1238		outer membrane component of multidrug efflux pump	4.3E-02	1.7
PA14_54700	PA0740	<i>sdsAI</i>	beta-lactamase	1.5E-03	-1.5

RNA-Seq of swarm vs. swim cells also revealed the downregulation of 55 ribosomal genes and other related translation factors (Table A1). This was of interest since the ribosome is the target of tobramycin. Interestingly, these genes included *fusAI* and *rplU*, which are involved in tobramycin resistance of CF clinical isolates (López-Causapé et al., 2018). The ribosome modulation factor *rmf*, which induces the dimerization of 70S subunits into an inactive form (Izutsu et al., 2001), was upregulated 1.8-fold.

A search was made for multidrug efflux transporters and β -lactamases, and 16 genes were found, both up and downregulated (Table 3-1). Since the upregulated genes were not strongly induced, it seems unlikely that efflux or β -lactamase production is a major mechanism of the resistance intrinsic to swarm cells, although I show below that multidrug efflux could be induced upon tobramycin treatment.

RNA-Seq also revealed the upregulation of several pilus-related genes and rhamnosyltransferase 2 *rhIC* (Table A1). This is consistent with the requirement of pili and rhamnolipids for swarming motility in *P. aeruginosa*, and the observation that a mutant in *rcpA*

was unable to swarm (Yeung et al., 2009).

Swarm cells also upregulated numerous genes in the type I, II and III secretion systems (Table A1) including genes encoding virulence factors such as exotoxin A, exoenzyme S and Y, phospholipase PlcB and elastases LasA and LasB. Many T6SS genes were also upregulated although certain T6SS genes were downregulated (*hcpC* and *vgrG4a,b*) (Table A1). Lastly, many pyoverdine, pyochelin and phenazine genes were also upregulated under swarming conditions (Table A1). This confirms previous studies indicating that swarming cells exhibit broad enhancement of virulence potential (Overhage et al., 2008).

3.4 Multiple factors contributed to swarming-mediated antibiotic resistance

Having confirmed that swarming cells were resistant to multiple antibiotics, I sought to elucidate the mechanism(s) of swarming-mediated antibiotic resistance by testing mutants for swarming in the presence of antibiotic. Tobramycin was selected as the antibiotic of interest since swarming cells were strongly resistant (Figure 3-1). RNA-Seq data were analyzed to identify genes corresponding to the resistome (i.e. those genes that affect antibiotic resistance under standard growth conditions) (Alvarez-Ortega et al., 2010; Brazas et al., 2007; Breidenstein et al., 2008; Dötsch et al., 2009; Fajardo et al., 2008; Schurek et al., 2008) that were dysregulated under swarming conditions. Mutants in these genes, as well as some in operons of interest that did not initially appear in the list of dysregulated genes, were screened for altered tobramycin susceptibility under swarming conditions using the agar dilution method. A gene was considered to potentially contribute to swarming-mediated antibiotic resistance if it was downregulated and the corresponding mutant was resistant under swarming conditions (i.e. decreased expression of the gene in question led to resistance). Conversely if the gene was upregulated, and the corresponding mutant was supersusceptible under swarming conditions this might also indicate a role in adaptive resistance, but this did not occur here (Table 3-2, Table A3). Mutants showing

Table 3-2. Genes dysregulated under swarming conditions that matched with the known resistome revealed 26 tobramycin resistance mutants. PA14 transposon mutants in selected genes were tested for altered tobramycin susceptibility under swarming conditions using the agar dilution method (inhibitory concentrations shown in µg/ml of tobramycin, along with images of swarming colonies at 1 µg/ml). Evidence of dysregulation came from swarm vs. swim RNA-Seq (superscript 1) or tobramycin RNA-Seq (superscript 2). Selected genes were also confirmed by qRT-PCR from (Overhage et al., 2008) (superscript 3), Additional mutants in genes showing no evidence of dysregulation (*gmd* and *rmd*) but belonging to operons containing dysregulated genes were also tested. 17 additional mutants are described in Table A3.

LocusTag	PAO1	Name	Product Name	Fold change	Swarming inhibitory concentration	
PA14 WT					1	
PA14_00830 ²	PA0071	<i>tagR1</i>	hypothetical protein	-1.8	≥2	
PA14_07950 ³	PA0610	<i>priN</i>	transcriptional regulator PriN	-2.6	2	
PA14_08070 ¹	PA0622	<i>gpFI</i>	phage tail sheath protein	-8.1	2	
PA14_08220 ¹	PA0634		phage tail assembly chaperone-like	-6.1	2	
PA14_08300 ¹	PA0641	<i>JF1</i>	phage-related protein, tail component	-5.0	2	
PA14_44380 ¹	PA1553	<i>ccoO</i>	cbb3-type cytochrome c oxidase subunit II	-1.7	1-2 ^a	
PA14_37060 ¹	PA2128	<i>cupA1</i>	fimbrial subunit	-4.6	2	
PA14_37040 ¹	PA2129	<i>cupA2</i>	chaperone	-4.7	2	
PA14_37030 ¹	PA2130	<i>cupA3</i>	usher	-3.5	2	
PA14_36990 ¹	PA2133		cyclic-guanylate-specific phosphodiesterase	-1.9	2	
PA14_33630 ²	PA2400	<i>pvdJ</i>	peptide synthetase	-8.9	≥2	
PA14_20200 ¹	PA3392	<i>nosZ</i>	nitrous-oxide reductase	-16.5	1-2 ^a	
PA14_20190 ¹	PA3393	<i>nosD</i>	copper ABC transporter periplasmic substrate-binding protein	-16.0	2	
PA14_20180 ¹	PA3394	<i>nosF</i>	ATP/GTP binding protein	-18.6	2	
PA14_16890 ³	PA3670		auxiliary component of ABC transporter	-1.9	2	
PA14_14390 ³	PA3836		ABC-type transport protein, periplasmic c	-2.5	2	
PA14_66950 ²	PA5067	<i>hisE</i>	phosphoribosyl-ATP pyrophosphatase	-1.8	≥2	
PA14_71910 ³	PA5447	<i>wbpZ</i>	glycosyltransferase	-1.8	2	
PA14_71930 ³	PA5449	<i>wbpX</i>	glycosyltransferase	-2.4	2	
PA14_71940 ³	PA5450	<i>wzt</i>	ABC subunit of A-band LPS efflux transporter	-2.0	2	
PA14_71960 ³	PA5451	<i>wzm</i>	membrane subunit of A-band LPS efflux transporter	-1.9	2	
PA14_71970 ³	PA5452	<i>wbpW</i>	phosphomannose isomerase/GDP-mannose	-7.4	2	
PA14_71990 ³	PA5453	<i>gmd</i>	GDP-mannose 4,6-dehydratase	-1.4	2	
PA14_72000 ³	PA5454	<i>rmd</i>	oxidoreductase	-1.3	2	
PA14_72960 ¹	PA5530		MFS dicarboxylate transporter	-11.7	2	
PA14_73090 ³	PA5542		<i>Pseudomonas</i> imipenem beta-lactamase PIB-1	-14.2	2	

^a Two mutants showed minimal swarming at tobramycin 1 µg/ml but grew better than WT at 2 µg/ml.

deficiencies in swarming motility in the absence of antibiotic were excluded from testing as they would appear supersusceptible due to their lack of swarming ability, rather than true susceptibility.

A comprehensive description of the resistome under planktonic conditions has been published, with mutations in 135 genes leading to adaptive resistance to tobramycin (Schurek et al., 2008). Interestingly, there were a moderate number of overlaps with the genes identified here as being likely involved in adaptive resistance, prominently including genes involved in membrane energization (*ccoO*, cytochrome c oxidase), LPS biosynthesis genes (*wbpW* and its operon *wbpZ-rmd*), nitrous oxide metabolism where the *nosZDF* genes were 16.0 to 18.6 fold downregulated, and a major facilitator superfamily transporter, PA5530, that mediates α -ketoglutarate transport (Lundgren et al., 2014). In addition to these there were some novel resistome genes previously described as being involved in susceptibility/resistance to other antibiotics including a large phage/pyocin operon (PA0613-PA0641), which has been implicated in susceptibility to ciprofloxacin (Brazas & Hancock, 2005). Similarly a cup fimbriae biosynthesis operon (*cupA1-3*) was identified that includes a cyclic-GMP phosphodiesterase previously implicated in regulation of flagella, chemotaxis, type III secretion, and a TolC-like efflux protein (PA2133/*fcsR*; (Rossello et al., 2017)). CupA1 (implicated in ceftazidime susceptibility) was identified from the resistome study (Alvarez-Ortega et al., 2010); whereas CupA3 (β -lactam and ciprofloxacin resistance) was identified in other studies (Dötsch et al., 2009). Other genes included PA3670, a component of an ABC transport system, that was implicated in susceptibility to β -lactams, levofloxacin and trimethoprim-sulfamethoxazole (identified from (Dötsch et al., 2009)). PA3836, another ABC transport protein involved in ciprofloxacin resistance was identified in (Breidenstein et al., 2008). Lastly, a carbapenemase-expressing gene (PA5542 (Fajardo et al., 2014)), the mutant in which was supersusceptible to β -lactams, was identified from (Fajardo et al., 2008). Thus resistance under swarming conditions involved both canonical/known tobramycin resistance genes, as well as novel genes.

Two mutants *prtN* and *wbpW* were selected for study in greater detail, since they represented larger gene groups (the pyocins and LPS biosynthetic operon) with a uniform direction of regulation and phenotype. PrtN was of particular interest since it is a regulator and could potentially affect the expression of many genes. The antibiotic susceptibility phenotypes of *prtN* and *wbpW* were confirmed using both the disc diffusion and agar dilution methods (Figure 3-3, Figure 3-4) and their appropriate dysregulation of gene expression under swarming conditions was confirmed using qRT-PCR (*i.e.* *prtN* and *wbpW* were downregulated by 2.6 ± 0.8 and 7.4 ± 2.8 fold).

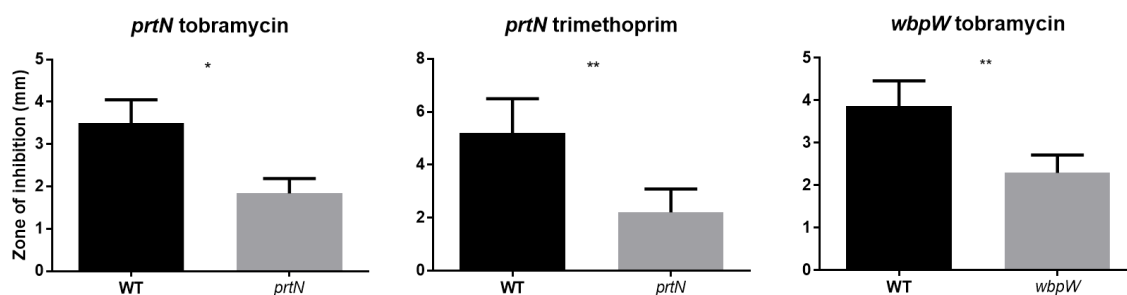


Figure 3-3. Antibiotic susceptibility of PA14 mutants under swarming conditions using the disc diffusion method at 0.5% agar. Statistically significant differences were determined by paired t test. $n \geq 4$.

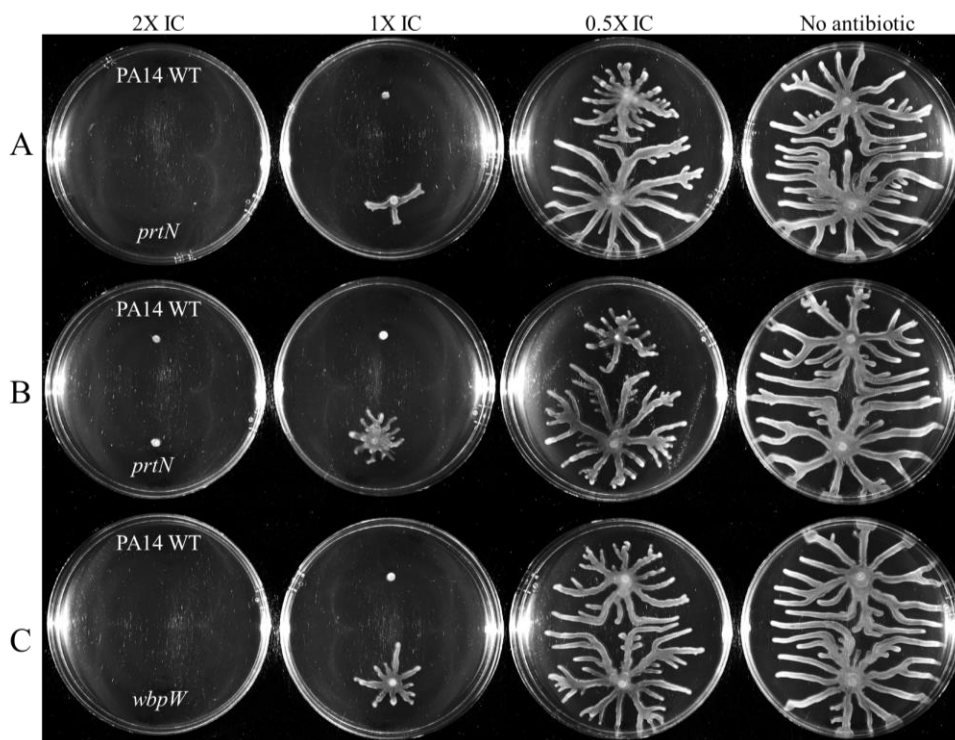


Figure 3-4. Agar dilution method for determining the swarming inhibitory concentration (IC) of PA14 mutants at 0.5% agar. A) tobramycin swarming IC = 1 $\mu\text{g/ml}$ B) trimethoprim IC = 10 $\mu\text{g/ml}$ C) tobramycin. $n \geq 3$.

3.5 A mutant in *wbpW* was resistant to tobramycin and had decreased membrane permeability

Under swarming conditions, a mutant in *wbpW*, GDP-mannose pyrophosphorylase, an enzyme involved in common polysaccharide antigen (CPA) synthesis, was twofold more resistant to tobramycin (Figure 3-3, Figure 3-4, Table 3-2, Table A4). There are two forms of O antigen in *P. aeruginosa* LPS termed CPA and O-specific antigen (OSA). The mutant in *wbpW* was complemented to normal susceptibility by reintroducing *wbpW* in a low copy plasmid (Figure 3-5B). We have previously shown in *P. aeruginosa* that polycationic aminoglycosides, such as

tobramycin, are taken up across the outer membrane via the self-promoted uptake system (Hancock et al., 1981). The concept of self-promoted uptake is that polycationic antibiotics interact with divalent cation binding sites on outer membrane surface LPS, causing disruption of these sites (since they are more bulky than the native divalent cations Mg^{2+} and Ca^{2+}) and thus promote the uptake of the polycationic antibiotic. This membrane disruption can be probed using the fluorophor 1-N-phenyl-naphthylamine (NPN). NPN is a dye that is normally excluded by wild type *P. aeruginosa* and is weakly fluorescent in aqueous media but fluoresces strongly when it enters the hydrophobic interior of the outer membrane (Schurek et al., 2008); thus its uptake into bacterial membranes is an indicator of membrane permeabilization by tobramycin. In the NPN assay, after addition of tobramycin, the *wbpW* mutant had decreased membrane permeabilization, consistent with its reduced susceptibility, and this was complemented in the *wbpW*⁺ strain (Figure 3-6) and is thus the likely cause of tobramycin resistance.

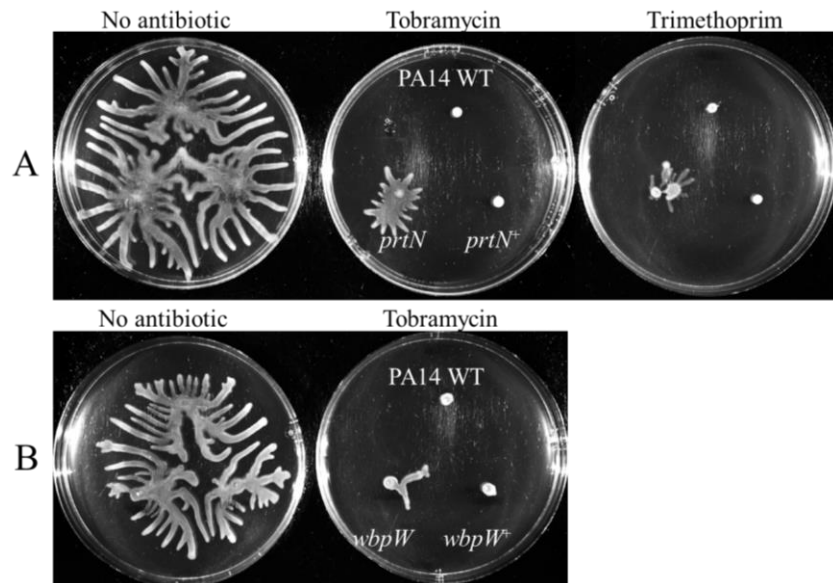


Figure 3-5. Complementation of swarming antibiotic susceptibility phenotypes for A) *prtN* B) *wbpW*. All strains were transformed with either the respective empty vector (WT and mutants) or a vector with insert (complemented (+) strains). $n \geq 3$.

3.6 Mutation of *prtN* induced resistance to tobramycin and trimethoprim

The mutant in the gene *prtN*, the positive regulator of pyocin, showed partial resistance to both tobramycin and trimethoprim under swarming conditions (Figure 3-3, Figure 3-4, Table 3-2, Table A4). Antibiotic susceptibility was restored by reintroducing *prtN* in an arabinose-inducible construct (pHERD20T) (Figure 3-5A). Success with other vectors was limited due to lack of plasmid stability when *prtN* was constitutively expressed (data not shown). These results indicated that swarming cells might increase antibiotic resistance by downregulating a process regulated by

PrtN, such as the biologically costly production of pyocins, also termed genotoxic stress (Penterman et al., 2014). Consistent with the latter explanation, mutants in several genes downstream of, and regulated by PrtN, namely PA0613-PA0641, were also tested for antibiotic susceptibility under swarming conditions and found to be resistant to tobramycin, although unlike *prtN* no significant differences were observed in trimethoprim susceptibility (Table 3-2, Table A3 and data not shown).

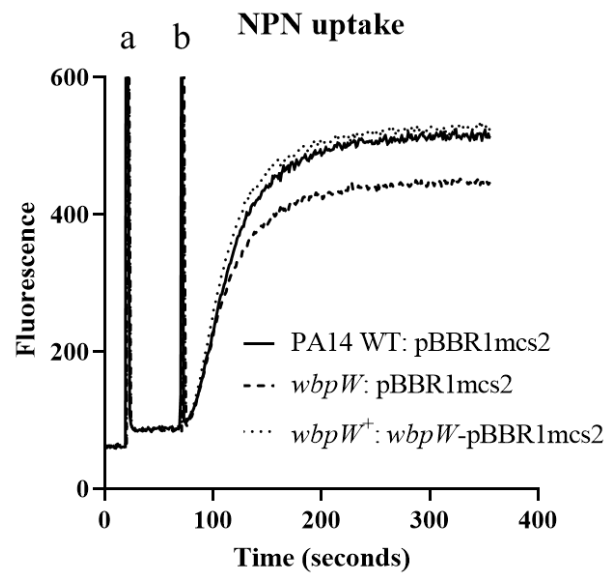


Figure 3-6. A *wbpW* mutant had reduced membrane permeabilization. Swarm cells were harvested and treated where indicated with a) NPN and b) tobramycin. $n = 3$.

3.7 Antibiotic susceptibility was affected by growth conditions

The mutants were also assayed under standard broth dilution MIC conditions in the rich medium LB and the minimal medium BM2 glucose (Table A5). In contrast to their effect on susceptibility under swarming conditions, the mutants showed little difference in MIC compared to wild type, with the exception of *prtN* that was two-fold more resistant to trimethoprim in LB. This indicated that growth conditions had an important effect on antibiotic resistance and suggests that standard screening methods might miss such phenotypes.

The tobramycin resistance phenotype was much more pronounced under swarming conditions (Table 3-2, Figure 3-3, Figure 3-4) compared to standard MICs (Table A5). When tested in a standard MIC, the *prtN* and *wbpW* mutants showed no increase in MIC (Table A5). Other representative mutants were also tested but showed no difference under standard MIC conditions (Table A6). Nevertheless, some of the genes in Table 3-2 likely do play a role beyond the swarming condition, since they were previously shown to be part of the tobramycin resistome (including *ccoO*, *wbpW* and its operon *wbpZ-rmd*, *nosZDF* and PA5530) (Schurek et al., 2008). It seems

possible that some genes may confer resistance specifically under swarming conditions, whereas others may confer resistance under multiple conditions.

3.8 Subinhibitory tobramycin treatment under swarming conditions

Swarming bacteria treated with the subinhibitory tobramycin dose of 0.5 µg/ml were compared to untreated swarm cells by RNA-Seq, since this was relevant to the increased resistance of cells swarming in the presence of tobramycin. Differential expression analysis revealed 224 genes, 186 of which were downregulated (Table A1). The downregulated genes included many virulence factors, particularly in T3SS and pyoverdine genes (Table A1), indicating a secondary benefit of tobramycin treatment, even in the absence of killing. Amongst the upregulated genes was the efflux pump *mexXY*, a known mechanism of aminoglycoside resistance (Table 3-3) (Aires et al., 1999). Eight ribosomal proteins and translation factors were also downregulated (*efp*, *infA*, *infC*, *rplU*, *rpmB*, *rpsG*, *rpsS*, and PA5492), as well as four genes in an LPS biosynthetic operon (*wzz*, *wbpA*, *wbpI*, and *wbpL*) (Table 3-3). Since pyocins were already implicated in swarming-mediated antibiotic resistance, it was interesting that the genes *tolAR*, which are involved in the uptake of pyocin AR41, were downregulated (Table 3-3) (Dennis et al., 1996).

Table 3-3. Selected genes that were differentially expressed upon tobramycin treatment under swarming conditions.

LocusTag	PAO1	Name	Product Name	padj	FC
PA14_08810	PA4267	<i>rpsG</i>	30S ribosomal protein S7	2.1E-02	-1.7
PA14_08890	PA4259	<i>rpsS</i>	30S ribosomal protein S19	2.8E-02	-1.8
PA14_23360	PA3160	<i>wzz</i>	O-antigen chain length regulator	6.9E-03	-1.8
PA14_23370	PA3148	<i>wbpI</i>	putative UDP-N-acetylglucosamine 2-epimerase	2.6E-02	-1.7
PA14_23380	PA3159	<i>wbpA</i>	UDP-N-acetyl-D-mannosaminuronate dehydrogenase	1.8E-02	-2.1
PA14_23460	PA3145	<i>wbpL</i>	putative group 4 glycosyl transferase	2.7E-02	-1.8
PA14_27210	PA2851	<i>efp</i>	elongation factor P	2.0E-02	-1.6
PA14_28660	PA2743	<i>infC</i>	translation initiation factor IF-3	1.3E-02	-1.9
PA14_30240	PA2619	<i>infA</i>	translation initiation factor IF-1	3.5E-03	-1.5
PA14_38380	PA2020	<i>mexZ</i>	putative transcriptional regulator	2.8E-02	1.6
PA14_38395	PA2019	<i>mexX</i>	periplasmic multidrug efflux lipoprotein precursor	3.5E-22	8.5
PA14_38410	PA2018	<i>mexY</i>	multidrug efflux protein	1.3E-36	8.0
PA14_38430	PA2016	<i>liuR</i>	regulatory gene of gnyRDBHAL cluster, GnyR	7.8E-03	-2.3
PA14_41575	PA1776	<i>sigX</i>	RNA polymerase sigma factor	1.4E-02	-1.6
PA14_42390	PA1713	<i>exsA</i>	transcriptional regulator	1.5E-07	-2.4
PA14_42460	PA1707	<i>pcrH</i>	regulatory protein	2.7E-02	-1.8
PA14_45950	PA1431	<i>rsaL</i>	regulatory protein	1.7E-02	-1.8
PA14_51730	PA0971	<i>tolA</i>	membrane transport protein	2.4E-03	-1.6
PA14_51740	PA0970	<i>tolR</i>	membrane transport protein	1.8E-02	-1.5

LocusTag	PAO1	Name	Product Name	padj	FC
PA14_52570	PA0905	<i>rsmA</i>	carbon storage regulator	8.8E-03	-1.9
PA14_55160	PA0707	<i>toxR</i>	transcriptional regulator	5.8E-05	-4.4
PA14_56070	PA4315	<i>mvaT</i>	transcriptional regulator, P16 subunit	2.6E-02	-1.5
PA14_60460	PA4568	<i>rplU</i>	50S ribosomal protein L21	4.0E-02	-1.6
PA14_70190	PA5316	<i>rpmB</i>	50S ribosomal protein L28	1.6E-02	-1.6
PA14_72210	PA5471	<i>armZ</i>	hypothetical protein	2.3E-19	3.4
PA14_72480	PA5492		ribosome biogenesis GTP-binding protein YsxC	3.9E-02	-1.6

Dysregulated transcriptional regulators included two regulators of virulence factor production (*exsA* and *toxR*), *mexZ*, the repressor of *mexXY* (Matsuo et al., 2004), *liuR*, a regulator of the leucine/isovalerate utilization pathway (Díaz-Pérez et al., 2018), *sigX*, an extracytoplasmic function sigma factor involved in the regulation of the major porin OprF, antibiotic resistance, T3SS, swarming motility, biofilm formation and carbon catabolite repression (Blanka et al., 2014; Fléhard et al., 2018; Gicquel et al., 2013), *rsaL*, a repressor of virulence gene expression and QS (De Kievit et al., 1999; Rampioni et al., 2006), *mvaT*, a global regulator of QS, virulence and swarming motility (Diggle et al., 2002), and *rsmA*, a post-transcriptional regulator of multidrug efflux, motility, QS, T6SS and virulence (Allsopp et al., 2017; Burrowes et al., 2006; Mulcahy et al., 2008) (Table 3-3). Interestingly, the *mexXY* operon has been shown to be upregulated in a SigX mutant, along with the repressor *mexZ*, providing more evidence that upregulation of *mexXY* can be independent of *mexZ* (Blanka et al., 2014).

Resistome mutants were also tested from the tobramycin vs. untreated RNA-Seq. Although some mutants could not be tested due to deficiencies in swarming motility, it was shown that mutants in *tagRI* (a type VI secretion protein (HSI-I) with a sulfatase-modifying domain associated with the outer membrane (Casabona et al., 2013; Winsor et al., 2011)), *pvdJ* (peptide synthetase of pyoverdine) and *hisE* (involved in histidine biosynthesis (Winsor et al., 2011)) were resistant to tobramycin under swarming conditions and downregulated upon tobramycin treatment (Table 3-2). Interestingly, PvdQ, an acylase of the QS molecule 3-oxo-C12-HSL, also involved in pyoverdine synthesis, has already been shown to play a role in the antibiotic resistance of swarming cells (Wang et al., 2013). The mechanism of PvdQ-mediated resistance is via decreased membrane permeability (Wang et al., 2013).

3.9 Comparison of RNA-Seq experiments

The two RNA-Seq experiments were also compared to determine what degree of overlap existed. Ninety genes were found in common between the two experiments (Figure A2). While this represented a substantial portion of the total genes dysregulated upon tobramycin treatment,

the majority of the 90 genes were oppositely regulated (Figure A3), with 51 genes that were downregulated upon tobramycin treatment but upregulated in swarm vs. swim. These 51 genes included iron acquisition factors (pyoverdine and phenazine) as well as T3SS genes. This indicates that the response to subinhibitory tobramycin was distinct from the swarm vs. swim comparison.

3.10 Discussion

In this study, 41 mutants were characterized as tobramycin resistant under swarming conditions. This lends support to a previous study that showed that the tobramycin resistome is quite large (135 genes) with many mutants (including 57 in energy metabolism) showing low level resistance (Schurek et al., 2008). Not all genes overlapped between this prior study and the current investigation, indicating that there may be distinct mechanisms of resistance in swarm cells as compared to broth-grown cells.

One mutant demonstrating complementable tobramycin and trimethoprim resistance and equivalent downregulation in the wild type under swarming conditions was in the *prtN* gene, that encodes a positive regulator of pyocin production under control of the *prtR* repressor. Under UV stress, RecA causes the autocleavage of PrtR, leading to the expression of *prtN* and production of pyocins (Matsui et al., 1993). A lysis cassette is also induced, including holin-like and lysozyme-like genes that cause cell lysis and the release of pyocin (Penterman et al., 2014). Interestingly, a mutation inactivating the catalytic activity of PrtR resulted in increased resistance to aminoglycosides, ciprofloxacin, and UV stress (Penterman et al., 2014), which was attributed to effects on genotoxic stress, while mutants in the phage tail-like bacteriocins regulated by *prtRN* were resistant to ciprofloxacin (Brazas & Hancock, 2005; Breidenstein et al., 2008). In other studies, a mutant in *prtN* was found to be resistant to piperacillin, cefotaxime and trimethoprim-sulfamethoxazole (Dötsch et al., 2009).

Overall, the downregulation of the phage-tail like bacteriocins in the cluster of genes from PA0613-PA0641 was a striking feature observed in the transcriptome of swarming cells ((Overhage et al., 2008) and the RNA-Seq study reported here). Mutating the positive regulator for these genes, *prtN*, resulted in resistance to both tobramycin and trimethoprim under swarming conditions, an effect consistent with the multiple resistance of the catalytically inactive (autocleavage-resistant) repressor *prtR* mutant (Penterman et al., 2014). Though pyocins play a role in intra- and interspecies competition, activation of these genes clearly incurs negative consequences for the cell. Furthermore, self-killing activity in a portion of the community with damaged DNA may be beneficial to the population as a whole (Chang et al., 2005).

Trimethoprim inhibits dihydrofolate reductase, depleting the cell of tetrahydrofolate, a one-carbon donor for a number of important metabolites in the cell including the nucleotide thymidylate (Sangurdekar et al., 2011). Therefore, as a consequence of trimethoprim treatment, DNA synthesis is inhibited and the DNA damage response is induced (Sangurdekar et al., 2011). Since the DNA damage response also leads to the activation of *PrtN* and induction of pyocin genes (Matsui et al., 1993; Penterman et al., 2014), it would seem reasonable that a mutant in *prtN* is resistant to trimethoprim. An association between aminoglycoside resistance and the regulation of pyocins has previously been shown (Penterman et al., 2014), although the mechanism for this is less clear. It is also possible that other genes regulated by *prtN* might be responsible.

Another interesting mutant was in the gene encoding *WbpW*, which catalyzes the conversion of mannose-1-phosphate to GDP-D-mannose (Byrd et al., 2015). Interestingly, GDP-D-mannose can be used in the synthesis of alginate, but is also utilized by *Rmd* for the synthesis of CPA LPS (Byrd et al., 2015). Mutants in genes involved in the synthesis of LPS have previously been shown to lead to tobramycin resistance, due to the reduced ability of tobramycin to cross the outer membrane via self-promoted uptake (Schurek et al., 2008). The resistance of the *wbpW* mutant was complemented by reintroducing *wbpW* in a low copy number plasmid (Figure 3-5B), and furthermore the *wbpW* mutant had reduced membrane permeability (Figure 3-6).

While *wbpW* was downregulated, low levels of expression could allow for a reduced amount of CPA LPS, rather than a complete deficiency. Mutants in *wbpW* also have reduced but not completely absent CPA LPS due to the presence of two *wbpW* homologs that are bifunctional enzymes (*algA* and *pslB*) (King et al., 2009). Over time, strains unable to produce O antigen come to predominate in the lungs of cystic fibrosis patients (Hancock et al., 1983), suggesting that LPS alterations might be one mechanism by which *P. aeruginosa* evades host recognition and adaptive immune responses. In addition, it has been shown that lipid A modifications are common and constitute a mechanism of immune evasion (Cigana et al., 2009). In another study, the loss of OSA was associated with increased T3SS activity (facilitating acute infections), while loss of any O antigen resulted in increased lung damage *in vivo* (Augustin et al., 2007). Together these studies suggest that a reduction in CPA LPS might be beneficial to *P. aeruginosa* persistence *in vivo*.

The two RNA-Seq experiments (swarm vs. swim and tobramycin vs. untreated) also showed that there is an important distinction between the inherent resistance of swarm cells and the inducible response of swarm cells to the antibiotic tobramycin. In the absence of antibiotic, more than 1,500 genes were dysregulated, and antibiotic resistance is likely a cumulative effect of

many different genes, although multidrug efflux did not appear to play a major role, as found in another study (Lai et al., 2009). In contrast, in the presence of tobramycin, fewer genes were dysregulated but an obvious mechanism of tobramycin resistance emerged in the overexpression of *mexXY*. Thus it appears there are genetic factors that enable swarming cells to resist antibiotics in the native swarming state, but also specific and distinct mechanisms of resistance that are induced upon antibiotic exposure. Perhaps a key role of swarming-mediated resistance genes is to allow sufficient time for more established mechanisms, such as multidrug efflux, to take effect.

Upon tobramycin treatment, downregulation of the genes *wzz*, *wbpA*, *wbpI*, and *wbpL* (Table 3-3) could also contribute to tobramycin resistance, although these genes were not identified in resistome studies (Schurek et al., 2008). As these genes, like *wbpW*, are involved in LPS biosynthesis, the resulting alterations in LPS could potentially result in tobramycin resistance. However, the mutant in *wzz* was not resistant to tobramycin, and mutants in *wbpAIL* were either not available or deficient for swarming motility (data not shown), therefore firm conclusions could not be drawn.

In both the absence and presence of tobramycin, ribosomal proteins and translation factors were downregulated under swarming conditions (Table 3-3, Table A1). Since aminoglycosides, as well as many other antibiotic classes including macrolides, chloramphenicol and tetracycline, target the bacterial ribosome, a decrease in translational activity could confer some level of resistance. However, since ribosomes are encoded by essential genes, this hypothesis is difficult to test.

During swarming motility, many genes are dysregulated, resulting in a hardy, multiple antibiotic-resistant phenotype associated with increased virulence factor production and iron scavenging. Downregulation of pyocin genes could allow swarming cells to circumvent harmful agents, leading to greater resilience in the face of antibiotic treatment. Downregulation of *wbpW* could result in reduced uptake of tobramycin. Upon treatment with tobramycin, the multidrug efflux pump MexXY was strongly upregulated. The combination of these factors, plus other as-yet-undetermined resistance factors, results in a state of (reversible) multiple antibiotic resistance during swarming motility in *P. aeruginosa*.

Chapter 4: Influence of the sRNA PA0805.1 on motility and virulence

4.1 Introduction

Swarming motility is a highly regulated process and previous studies have shown that 18 regulators are dysregulated under swarming conditions (Overhage et al., 2008), while mutants in 35 regulators have alterations in swarming motility (Yeung et al., 2009). However, alternative means of regulation have not been well investigated, including post-transcriptional and translational regulation, and the modification or degradation of proteins.

sRNAs are non-coding RNA species involved in post-transcriptional regulation, and are rapidly evolving (Gómez-Lozano et al., 2015). sRNAs can be classified in two categories: cis and trans-encoded. In many bacterial species, the RNA chaperone Hfq is required to stabilize sRNA-mRNA interactions (Gottesman & Storz, 2011), although *Pseudomonas* exhibits other more selective RNA-binding proteins such as Crc and RsmA. Interestingly, prior to 2012 only 44 sRNAs had been identified in *P. aeruginosa* (Gómez-Lozano et al., 2015), but subsequent RNA-Seq studies have identified hundreds of potential intergenic sRNAs (Gómez-Lozano et al., 2012; Wurtzel et al., 2012). Nevertheless, few of these novel sRNAs have been characterized, leaving a large field to be explored.

Prior research in our lab identified 20 sRNA species that were dysregulated under swarming conditions (Gill et al., 2018). One of these, sRNA PA0805.1, overlapping previously-identified sRNAs pant89 (Gómez-Lozano et al., 2012) and PA14sr119/120 (Wurtzel et al., 2012), was studied here in detail by genetic manipulation, phenotypic screens and omic comparisons.

4.2 Overexpression of PA0805.1 resulted in decreased motility

Specific qRT-PCR analysis demonstrated that the transcript for PA0805.1 was upregulated in swarming motility clones, cf. swimming cells by 5.0 ± 1.7 fold. In contrast, it was downregulated in biofilm cells by -4.8 ± -3.8 fold (Gill et al., 2018). Since biofilms are considered a sedentary lifestyle typical of chronic infections while swarming is considered more typical of acute infections, this ~25-fold difference in expression levels indicated that sRNA PA0805.1 had the potential to discriminate or even act as a switch between chronic and acute modes of infection. To investigate this further I overexpressed sRNA PA0805.1, since sRNAs often act in a suppressive manner. The PA0805.1 gene was cloned and inserted after the *araC* promoter in the arabinose-inducible pHERD20T vector, and transformed into PAO1 H103 WT. PA0805.1 was overexpressed after induction with arabinose by 28.1 ± 1.9 fold under swarming conditions (BM2 glycerol).

At the time of the assay, arabinose was added to induce expression. Motility assays showed that PA0805.1 overexpression had anti-motility effects resulting in partial reductions in each of swarming (reduced to $59 \pm 6\%$ of EV), swimming ($51 \pm 10\%$) and twitching ($61 \pm 3\%$) motility (Figure 4-1).

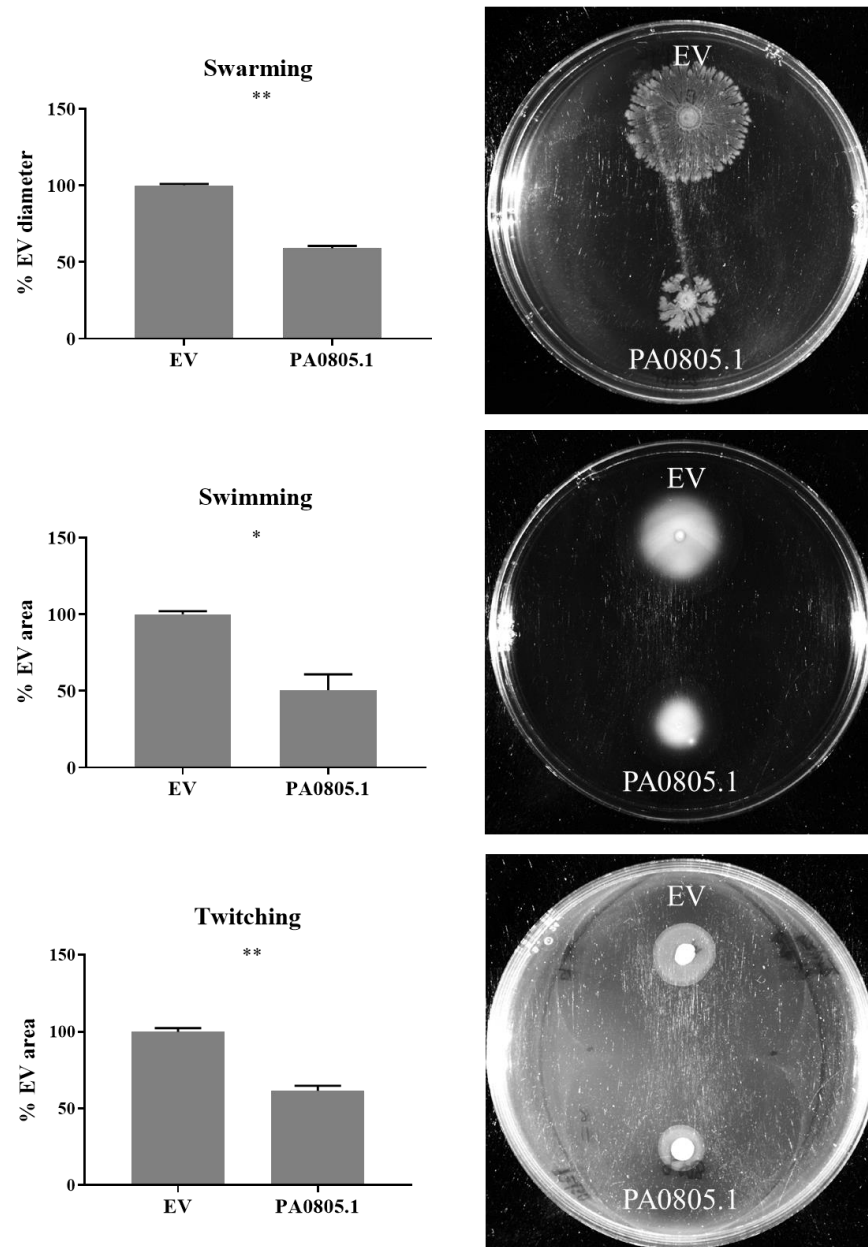


Figure 4-1. Motility assays revealed that overexpression of PA0805.1 was generally anti-motility. 1% arabinose was used to induce expression and statistically significant differences were determined using paired Student's t test. $n \geq 3$.

4.3 Overexpression of PA0805.1 resulted in increased cytotoxicity against HBE cells and increased tobramycin resistance

The PA0805.1 overexpression strain was also tested for cytotoxicity against HBE cells

(Figure 4-2). Similar to the motility assays, overexpression of PA0805.1 resulted in a consistent and statistically significant phenotype, with an increase of 15% in cytotoxicity as compared to the EV strain. Growth curves performed in BM2 glycerol with 1% arabinose showed little difference between strains (Figure A4). Interestingly the PA0805.1 overexpression strain was resistant to tobramycin even in the absence of arabinose under swarming conditions (Figure 4-3). In the presence of arabinose, the anti-motility effect of PA0805.1 made it difficult to assess any antibiotic phenotypes under swarming conditions. MIC assays performed in the equivalent medium in microtitre trays showed little difference (Table A7).

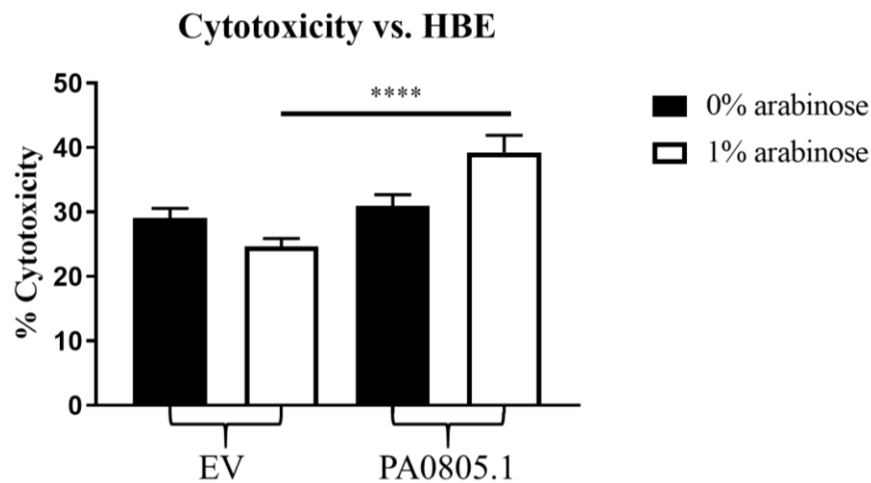


Figure 4-2. Cytotoxicity assay of the PA0805.1 overexpression strain revealed that induction of PA0805.1 led to increased cytotoxicity against HBE cells. Statistically significant differences were determined using paired Student's t test. $n \geq 3$.

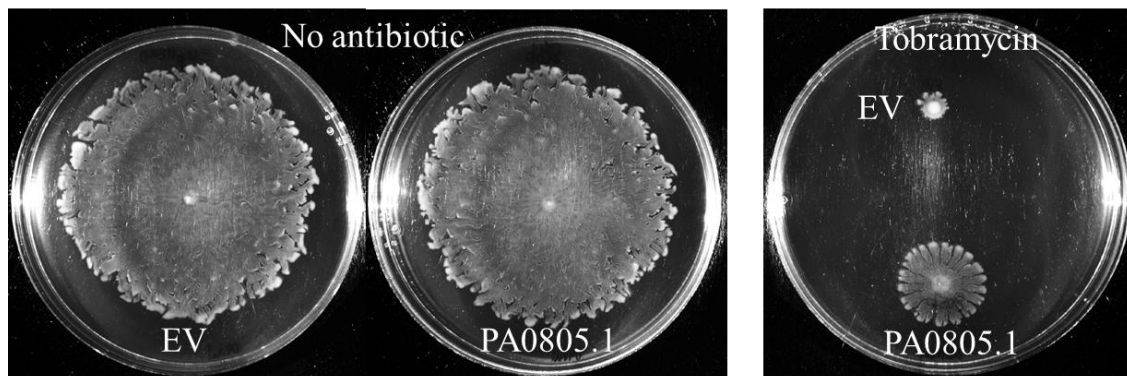


Figure 4-3. PA0805.1 overexpression led to swarming-dependent tobramycin resistance as assessed in BM2 glucose swarm plates with no arabinose and supplemented where indicated with tobramycin at 1 $\mu\text{g/ml}$. $n = 3$.

4.4 Overexpression of PA0805.1 resulted in broad protein and transcriptional changes including 118 regulatory factors

To investigate these phenotypes further, I performed proteomics and RNA-Seq under

swarming conditions in the presence of arabinose compared to the EV control. Proteomics identified 925 proteins with significantly different abundance in the PA0805.1 overexpression strain vs. EV, including 435 with increased abundance, and 490 with decreased abundance (Table A2). In addition, there were 1121 DE genes revealed by RNA-Seq, with 401 downregulated and 720 upregulated. Amongst the DE genes and proteins with differential abundance, 118 transcriptional regulators, two-component systems, sigma and anti-sigma factors were found (Table 4-1). Of these, 42 were found uniquely in the proteome and the equivalent genes did not demonstrate a change in transcription (shown with **bold** locus tag in Table 4-1). These changes thus might explain in part the rather substantial transcriptional dysregulation observed. These regulators were of particular interest since the mechanism of sRNA regulation is post-transcriptional, and therefore they would provide candidates for direct sRNA regulation. Many important regulators involved in diverse processes such as virulence, antimicrobial resistance, QS, and carbon metabolism were represented on the list of regulators dysregulated at the level of protein expression, including CbrB, LasR, MvaT, ParS, PsrA, RpoN, and Vfr. Other regulators with altered protein expression that were upstream of the widespread changes in motility, adherence and virulence factors described below, included FleQ, PilS, AlgU, and AlgB (Figure 4-4). Interestingly there were also three amino acid biosynthetic regulators, ArgR, BkdR and CysB.

Table 4-1. Selected genes of interest with differential expression in the PA0805.1 overexpression strain as compared to EV by RNA-Seq and/or proteomics. Categories of interest include regulators, multidrug efflux, motility, LPS biosynthesis, type VI secretion and other virulence factors. Cutoffs used were $p/\text{padj} \leq 0.05$ and for RNA-Seq, $\text{FC} \geq 1.5$.

Locus Tag	Name	Product Name	RNA-Seq		Proteomics	
			FC	padj	FC	p
Transcriptional regulators, two-component systems, sigma and anti-sigma factors						
PA0150		anti-sigma factor	-1.71	2.9E-02		
PA0178		probable two-component sensor	1.83	8.5E-06		
PA0179		probable two-component response regulator	2.02	2.0E-06		
PA0268		probable transcriptional regulator	1.52	3.0E-03		
PA0416	chpD	probable transcriptional regulator	-1.96	9.0E-07		
PA0471	fiuR	regulatory protein	-1.80	4.6E-04		
PA0472	fiuI	regulatory protein	-2.03	4.2E-04		
PA0479		probable transcriptional regulator	1.57	2.5E-04		
PA0535		probable transcriptional regulator	-1.69	1.2E-03		
PA0612	ptrB	repressor	2.52	6.3E-04		
PA0652	vfr	transcriptional regulator			-1.17	3.9E-04
PA0757		probable two-component sensor	-1.53	9.9E-04		
PA0762	algU	sigma factor			1.23	9.5E-03
PA0763	mucA	anti-sigma factor	1.68	5.7E-05		

Locus Tag	Name	Product Name	RNA-Seq		Proteomics	
			FC	padj	FC	p
PA0893	<i>argR</i>	transcriptional regulator			1.17	3.8E-03
PA0929		two-component response regulator	-1.68	1.9E-03		
PA0930		two-component sensor	-1.61	1.5E-02		
PA0942		probable transcriptional regulator	1.54	1.2E-03		
PA0964	<i>pmpR</i>	pqsR-mediated PQS regulator	-1.64	8.6E-08	-1.18	3.2E-04
PA1097	<i>fleQ</i>	transcriptional regulator			1.18	5.0E-03
PA1099	<i>fleR</i>	two-component response regulator	1.52	3.9E-08		
PA1136		probable transcriptional regulator	1.75	1.4E-04		
PA1157		probable two-component response regulator			1.17	5.5E-04
PA1315		probable transcriptional regulator			1.08	2.5E-02
PA1363		ECF sigma factor	-1.69	2.4E-03		
PA1397		probable two-component response regulator	-1.68	5.3E-05		
PA1430	<i>lasR</i>	transcriptional regulator			-1.28	4.9E-02
PA1431	<i>rsaL</i>	regulatory protein	1.70	6.8E-04	1.25	8.3E-03
PA1490		probable transcriptional regulator			1.16	2.3E-02
PA1504		probable transcriptional regulator			-1.15	1.7E-03
PA1619		probable transcriptional regulator	-1.50	1.8E-03		
PA1705	<i>pcrG</i>	regulator in type III secretion	-9.28	5.4E-12		
PA1707	<i>pcrH</i>	regulatory protein	-8.60	4.9E-26		
PA1713	<i>exsA</i>	transcriptional regulator	-4.77	6.3E-62		
PA1754	<i>cysB</i>	transcriptional regulator			1.21	3.2E-02
PA1785	<i>nasT</i>	regulatory protein	1.76	3.3E-02	-1.26	1.3E-04
PA1798	<i>parS</i>	two-component sensor			1.17	2.3E-02
PA1859		probable transcriptional regulator	1.55	5.8E-04		
PA1945		probable transcriptional regulator	1.53	3.6E-03		
PA2082	<i>kynR</i>	regulatory protein			1.18	5.2E-03
PA2126	<i>cgrC</i>	CupA gene regulator C	2.18	1.2E-05		
PA2126.1	<i>cgrB</i>	CupA gene regulator B	1.78	7.6E-03		
PA2127	<i>cgrA</i>	CupA gene regulator A	1.80	4.3E-06		
PA2177		probable sensor/response regulator hybrid	1.77	2.5E-04		
PA2227	<i>vqsM</i>	AraC-type transcriptional regulator	1.77	3.3E-06		
PA2246	<i>bkdR</i>	transcriptional regulator			1.06	2.1E-02
PA2258	<i>ptxR</i>	transcriptional regulator	2.15	1.2E-05		
PA2259	<i>ptxS</i>	transcriptional regulator	1.82	1.6E-04		
PA2273	<i>soxR</i>	regulatory protein	2.38	1.5E-09		
PA2276		probable transcriptional regulator	3.41	2.8E-38	1.27	9.3E-04
PA2277	<i>arsR</i>	regulatory protein	2.28	1.9E-06		
PA2376		probable transcriptional regulator	1.56	1.4E-03		
PA2388	<i>fpvR</i>	regulatory protein			-1.30	1.2E-02
PA2467	<i>foxR</i>	anti-sigma factor	-1.62	1.3E-02		
PA2523	<i>czcR</i>	regulatory protein	2.32	4.9E-08		
PA2524	<i>czcS</i>	regulatory protein	2.24	1.2E-04		
PA2571		probable two-component sensor	2.02	3.1E-06		
PA2572		probable two-component response regulator	1.86	8.1E-06	1.29	1.4E-02
PA2577		probable transcriptional regulator	1.70	3.4E-05		

Locus Tag	Name	Product Name	RNA-Seq		Proteomics	
			FC	padj	FC	p
PA2696		probable transcriptional regulator	1.53	4.5E-03		
PA2846		probable transcriptional regulator	1.64	7.3E-03		
PA2849	<i>ohrR</i>	regulatory protein	1.63	2.2E-05	1.11	2.8E-02
PA2889	<i>atvR</i>	atypical virulence-related response regulator	1.55	7.7E-04		
PA3006	<i>psrA</i>	transcriptional regulator			1.09	3.4E-02
PA3007	<i>lexA</i>	repressor protein	1.84	5.6E-23	1.10	6.1E-03
PA3034		probable transcriptional regulator			-1.10	1.8E-02
PA3122		probable transcriptional regulator			1.17	3.0E-03
PA3174	<i>hutR</i>	regulatory protein	-1.66	1.8E-02		
PA3225		transcriptional regulator			1.14	1.6E-02
PA3271		probable two-component sensor			1.09	1.9E-02
PA3341		probable transcriptional regulator			1.23	4.2E-03
PA3346	<i>hsbR</i>	HptB-dependent secretion and biofilm regulator	1.78	3.6E-09	1.22	1.2E-02
PA3347	<i>hsbA</i>	HptB-dependent secretion and biofilm anti anti-sigma factor	1.66	4.9E-05		
PA3477	<i>rhlR</i>	transcriptional regulator	1.77	1.9E-05	1.17	1.9E-02
PA3622	<i>rpoS</i>	sigma factor	1.75	1.4E-09	1.17	5.1E-03
PA3689		probable transcriptional regulator			1.06	2.4E-02
PA3702	<i>wspR</i>	regulatory protein			-1.08	1.4E-02
PA3899	<i>fecI</i>	regulatory protein	-1.73	1.3E-02		
PA3946	<i>rocSI</i>	two-component sensor	1.74	4.3E-07		
PA3947	<i>rocR</i>	regulatory protein	1.57	7.5E-06		
PA4070		probable transcriptional regulator	1.52	3.3E-02		
PA4074		probable transcriptional regulator	2.20	2.7E-03		
PA4080		probable response regulator	1.54	5.3E-04		
PA4101	<i>bfmR</i>	regulatory protein			-1.16	5.8E-03
PA4157		probable transcriptional regulator			1.06	4.5E-02
PA4203	<i>nmoR</i>	regulatory protein	1.50	4.6E-02		
PA4288		probable transcriptional regulator	2.20	1.9E-07		
PA4293	<i>pprA</i>	two-component sensor	2.22	5.0E-16	1.31	3.8E-03
PA4296	<i>pprB</i>	two-component response regulator	1.82	6.4E-07	1.12	1.1E-03
PA4315	<i>mvaT</i>	transcriptional regulator MvaT, P16 subunit			1.26	2.6E-02
PA4367	<i>bifA</i>	regulatory protein			-1.10	2.6E-02
PA4396		two-component response regulator	-2.15	4.8E-11		
PA4462	<i>rpoN</i>	RNA polymerase sigma-54 factor			1.16	3.2E-02
PA4464	<i>ptsN</i>	nitrogen regulatory IIA protein	1.74	1.6E-10		
PA4493	<i>roxR</i>	regulatory protein			1.26	2.5E-02
PA4546	<i>pilS</i>	two-component sensor			1.28	3.1E-03
PA4600	<i>nfxB</i>	transcriptional regulator			1.25	4.7E-02
PA4601	<i>morA</i>	motility regulator	-1.54	1.2E-12		
PA4659		probable transcriptional regulator			1.13	1.8E-02
PA4726	<i>cbrB</i>	two-component response regulator			-1.24	2.5E-04
PA4769		probable transcriptional regulator			1.35	2.8E-02
PA4778	<i>cueR</i>	regulatory protein			-1.17	6.5E-03

Locus Tag	Name	Product Name	RNA-Seq		Proteomics	
			FC	padj	FC	p
PA4787		probable transcriptional regulator			-1.11	8.5E-03
PA4843	<i>gcbA</i>	regulatory protein	-1.97	4.4E-18		
PA4886		probable two-component sensor	-1.65	2.3E-02		
PA4916	<i>nrtR</i>	Nudix-related transcriptional regulator	1.60	1.8E-08	1.18	4.6E-03
PA5117	<i>typA</i>	regulatory protein	-1.56	2.3E-05		
PA5199	<i>amgS</i>	regulatory protein			-1.08	9.3E-03
PA5200	<i>amgR</i>	regulatory protein			-1.22	1.8E-02
PA5261	<i>algR</i>	alginate biosynthesis regulatory protein	1.57	1.4E-05		
PA5274	<i>rnk</i>	nucleoside diphosphate kinase regulator	-1.53	1.5E-05	-1.26	3.5E-02
PA5293		probable transcriptional regulator			1.05	3.7E-02
PA5301	<i>pauR</i>	regulatory protein			-1.22	1.7E-02
PA5344	<i>oxyR</i>	regulatory protein			-1.04	4.5E-02
PA5356	<i>glcC</i>	transcriptional regulator	1.74	7.2E-07		
PA5380	<i>gbdR</i>	regulatory protein	1.58	2.5E-02		
PA5483	<i>algB</i>	two-component response regulator			1.17	1.4E-02
PA5484	<i>kinB</i>	regulatory protein			1.23	2.6E-03
Multidrug efflux systems						
PA0426	<i>mexB</i>	RND multidrug efflux transporter			1.15	1.4E-02
PA2018	<i>mexY</i>	RND multidrug efflux transporter	1.79	6.5E-04		
PA2019	<i>mexX</i>	RND multidrug efflux membrane fusion protein	1.91	4.9E-07	1.53	5.4E-04
PA2020	<i>mexZ</i>	negative transcriptional regulator			1.13	4.3E-02
PA2491	<i>mexS</i>	probable transcriptional regulator			-1.25	2.0E-03
PA2493	<i>mexE</i>	RND multidrug efflux membrane fusion protein precursor			1.11	1.2E-02
PA3677	<i>mexJ</i>	efflux transporter			1.15	3.7E-02
PA4205	<i>mexG</i>	hypothetical protein	1.76	2.0E-14	1.59	9.1E-05
PA4206	<i>mexH</i>	probable RND efflux membrane fusion protein	1.71	7.2E-13	1.11	2.8E-02
PA4207	<i>mexI</i>	probable RND efflux transporter			1.16	1.3E-03
PA4208	<i>opmD</i>	probable outer membrane protein precursor			1.14	4.4E-02
PA4374	<i>mexV</i>	RND multidrug efflux membrane fusion protein			1.16	1.1E-02
Motility and related genes						
PA0020	<i>tsaP</i>	T4P secretin-associated protein	-1.97	6.8E-11	-1.35	1.0E-03
PA0395	<i>pilT</i>	twitching motility protein			-1.13	1.4E-03
PA0396	<i>pilU</i>	twitching motility protein			-1.15	3.9E-04
PA0408	<i>pilG</i>	twitching motility protein	-2.09	2.8E-17	-1.52	2.5E-03
PA0409	<i>pilH</i>	twitching motility protein	-2.42	2.2E-29	-1.64	1.2E-02
PA0410	<i>pilI</i>	twitching motility protein	-2.37	1.1E-16	-1.48	6.8E-04
PA0411	<i>pilJ</i>	twitching motility protein	-2.76	4.3E-24	-1.49	4.8E-05
PA0412	<i>pilK</i>	methyltransferase	-2.40	2.3E-19		
PA0413	<i>chpA</i>	pilus related chemotactic signal transduction system component	-2.44	1.9E-33	-1.24	3.8E-06
PA0414	<i>chpB</i>	probable methylesterase	-2.31	3.1E-24		

Locus Tag	Name	Product Name	RNA-Seq		Proteomics	
			FC	padj	FC	p
PA0415	<i>chpC</i>	probable chemotaxis protein	-2.18	2.0E-13		
PA0417	<i>chpE</i>	probable chemotaxis protein	-2.77	7.8E-04		
PA0499		probable pili assembly chaperone	1.87	3.1E-03		
PA1077	<i>flgB</i>	flagellar basal-body rod protein	1.66	5.3E-11		
PA1078	<i>flgC</i>	flagellar basal-body rod protein	1.70	5.1E-10		
PA1079	<i>flgD</i>	flagellar basal-body rod modification protein	1.56	8.1E-09		
PA1080	<i>flgE</i>	flagellar hook protein	1.58	9.5E-11		
PA1081	<i>flgF</i>	flagellar basal-body rod protein	1.65	5.1E-11		
PA1082	<i>flgG</i>	flagellar basal-body rod protein	1.57	4.5E-07		
PA1083	<i>flgH</i>	flagellar L-ring protein precursor			1.15	2.5E-02
PA1084	<i>flgI</i>	flagellar P-ring protein precursor	1.53	1.6E-08		
PA1085	<i>flgJ</i>	flagellar protein	1.54	2.4E-06		
PA1092	<i>fliC</i>	flagellin type B	1.55	4.7E-06		
PA1094	<i>fliD</i>	flagellar capping protein	1.53	4.9E-06		
PA1100	<i>fliE</i>	flagellar hook-basal body complex protein	1.76	6.3E-08		
PA1101	<i>fliF</i>	flagella M-ring outer membrane protein precursor	1.52	3.5E-11		
PA1103		probable flagellar assembly protein			1.22	2.8E-02
PA1130	<i>rhlC</i>	rhamnosyltransferase 2	1.56	5.8E-04		
PA1452	<i>flhA</i>	flagellar biosynthesis protein			1.28	1.3E-02
PA1461	<i>motD</i>	flagellar motor protein			1.12	6.9E-03
PA1822	<i>fimL</i>	hypothetical protein			-1.13	1.1E-02
PA3350		hypothetical protein	1.62	3.1E-15	1.17	4.2E-03
PA3351	<i>flgM</i>	flagellar anti-sigma factor	1.52	1.2E-07		
PA3478	<i>rhlB</i>	rhamnosyltransferase chain B	2.39	3.0E-04		
PA3479	<i>rhlA</i>	rhamnosyltransferase chain A	2.55	1.1E-04		
PA3526	<i>motY</i>	flagellar motor protein	1.60	2.3E-07		
PA4085	<i>cupB2</i>	chaperone	1.52	3.7E-02		
PA4294		hypothetical protein	2.32	1.4E-20		
PA4295	<i>fppA</i>	Flp prepilin peptidase A	1.68	9.8E-05		
PA4297	<i>tadG</i>	putative Tad-like Flp pilus-assembly	1.53	1.1E-02		
PA4298		hypothetical protein	2.25	1.9E-07		
PA4299	<i>tadD</i>	Flp pilus assembly lipoprotein	1.89	1.4E-06	1.23	3.0E-03
PA4300	<i>tadC</i>	Flp pilus assembly protein TadC	1.78	1.2E-05	1.29	8.1E-03
PA4301	<i>tadB</i>	Flp pilus assembly protein	1.95	1.5E-06		
PA4302	<i>tadA</i>	ATPase	1.93	2.8E-08	1.20	5.0E-02
PA4303	<i>tadZ</i>	pilus assembly protein	2.09	5.3E-11	1.22	1.4E-02
PA4304	<i>rcpA</i>	secretin	1.97	1.3E-10		
PA4305	<i>rcpC</i>	Flp pilus assembly protein	2.12	8.4E-10		
PA4306	<i>flp</i>	type IVb pilin	1.84	1.4E-03		
PA4525	<i>pilA</i>	type 4 fimbrial precursor	-1.64	2.0E-04	-1.30	3.4E-03
PA4527	<i>pilC</i>	type 4 fimbrial biogenesis protein (put. pseudogene)			-1.21	7.2E-04
PA4528	<i>pilD</i>	type 4 prepilin peptidase	-1.84	1.1E-08		
PA4550	<i>fimU</i>	type 4 fimbrial biogenesis protein	-1.74	2.0E-06	-1.11	4.9E-02

Locus Tag	Name	Product Name	RNA-Seq		Proteomics	
			FC	padj	FC	p
PA4551	<i>pilV</i>	type 4 fimbrial biogenesis protein	-1.99	9.3E-07	-1.10	1.7E-02
PA4552	<i>pilW</i>	type 4 fimbrial biogenesis protein	-1.72	9.2E-08	-1.22	2.4E-03
PA4553	<i>pilX</i>	type 4 fimbrial biogenesis protein	-1.63	1.4E-04		
PA4554	<i>pilY1</i>	type 4 fimbrial biogenesis protein	-1.59	9.6E-08		
PA4555	<i>pilY2</i>	type 4 fimbrial biogenesis protein	-1.51	6.9E-05	-1.34	7.3E-03
PA4556	<i>pilE</i>	type 4 fimbrial biogenesis protein			-1.64	9.4E-03
PA4648	<i>cupE1</i>	pilin subunit	2.56	2.7E-16		
PA4649	<i>cupE2</i>	pilin subunit	2.06	1.8E-12		
PA4650	<i>cupE3</i>	pilin subunit	1.91	1.9E-06		
PA4651	<i>cupE4</i>	pilin assembly chaperone	2.00	5.2E-20	1.28	1.3E-03
PA4652	<i>cupE5</i>	fimbrial usher protein	1.66	1.7E-07		
PA4653	<i>cupE6</i>	adhesin-like protein	1.69	1.1E-06		
PA4953	<i>motB</i>	chemotaxis protein			-1.20	3.2E-03
PA4959	<i>fimX</i>	diguanylate cyclase/phosphodiesterase	-1.54	2.7E-07		
PA5040	<i>pilQ</i>	type 4 fimbrial biogenesis outer membrane protein	-1.63	8.0E-11	-1.38	4.7E-03
PA5041	<i>pilP</i>	type 4 fimbrial biogenesis protein	-1.70	1.2E-08		
PA5042	<i>pilO</i>	type 4 fimbrial biogenesis protein	-1.67	2.6E-12	-1.26	9.0E-04
PA5043	<i>pilN</i>	type 4 fimbrial biogenesis protein	-1.70	2.1E-10	1.77	6.6E-04
PA5044	<i>pilM</i>	type 4 fimbrial biogenesis protein	-1.53	1.5E-10	-1.27	5.6E-03
LPS biosynthesis						
PA3141	<i>wbpM</i>	nucleotide sugar epimerase/dehydratase			1.25	8.3E-03
PA3145	<i>wbpL</i>	glycosyltransferase			1.17	5.7E-03
PA3147	<i>wbpJ</i>	probable glycosyl transferase			1.14	1.8E-03
PA3148	<i>wbpI</i>	UDP-N-acetylglucosamine 2-epimerase			1.23	7.0E-04
PA3150	<i>wbpG</i>	LPS biosynthesis protein			1.13	2.0E-02
PA3151	<i>hisF2</i>	imidazoleglycerol-phosphate synthase, cyclase subunit			1.13	1.1E-02
PA3152	<i>hisH2</i>	glutamine amidotransferase			1.08	1.8E-02
PA3155	<i>wbpE</i>	UDP-2-acetamido-2-dideoxy-d-ribo-hex-3-uluronic acid transaminase	1.53	4.8E-11		
PA3156	<i>wbpD</i>	UDP-2-acetamido-3-amino-2,3-dideoxy-d-glucuronic acid N-acetyltransferase			1.18	4.3E-04
PA3158	<i>wbpB</i>	UDP-2-acetamido-2-deoxy-d-glucuronic acid 3-dehydrogenase			1.14	5.7E-04
PA3159	<i>wbpA</i>	UDP-N-acetyl-d-glucosamine 6-Dehydrogenase			1.21	6.2E-05
PA3160	<i>wzz</i>	O-antigen chain length regulator			1.27	2.3E-02
PA4378	<i>warB</i>	lipopolysaccharide kinase	1.94	5.4E-04		
PA5448	<i>wbpY</i>	glycosyltransferase	-1.56	1.2E-03		
PA5449	<i>wbpX</i>	glycosyltransferase	-1.62	3.8E-09		
PA5452	<i>wbpW</i>	phosphomannose isomerase/GDP-mannose			-1.13	3.0E-02
PA5453	<i>gmd</i>	GDP-mannose 4,6-dehydratase			-1.12	3.1E-02
PA5454	<i>rmd</i>	oxidoreductase			-1.25	4.1E-03
Type VI secretion system						

Locus Tag	Name	Product Name	RNA-Seq		Proteomics	
			FC	padj	FC	p
PA0070	<i>tagQ1</i>	type VI secretion-associated lipoprotein			1.22	2.2E-02
PA0071	<i>tagR1</i>	FGE-sulfatase domain-containing protein			1.37	1.8E-03
PA0075	<i>pppA</i>	serine/threonine protein phosphatase			1.45	1.1E-02
PA0076	<i>tagF1</i>	type VI secretion-associated protein	1.56	1.5E-02		
PA0077	<i>icmF1</i>	type VI secretion protein			1.37	4.7E-04
PA0078	<i>tssL1</i>	type VI secretion system protein	1.59	1.3E-03	1.31	5.6E-03
PA0079	<i>tssK1</i>	type VI secretion protein	1.58	1.4E-04	1.40	3.1E-03
PA0080	<i>tssJ1</i>	type VI secretion protein	1.51	1.7E-07		
PA0082	<i>tssA1</i>	type VI secretion protein	1.52	4.1E-05	1.48	2.7E-03
PA0083	<i>tssB1</i>	type VI secretion protein	1.72	2.8E-06		
PA0084	<i>tssC1</i>	type VI secretion protein	1.58	5.7E-04	1.52	4.7E-03
PA0085	<i>hcp1</i>	type VI secretion system effector	1.74	3.9E-05	2.14	4.5E-04
PA0086	<i>tagJ1</i>	type VI secretion system	1.74	1.6E-04		
PA0087	<i>tssE1</i>	type VI secretion system lysozyme-like protein	1.92	1.7E-04		
PA0088	<i>tssF1</i>	type VI secretion protein	1.58	3.7E-03		
PA0090	<i>clpV1</i>	chaperone	1.59	1.5E-03	1.54	3.4E-03
PA0091	<i>vgrG1</i>	type VI secretion system tip protein	1.52	6.0E-03	1.23	2.4E-04
PA0094	<i>eagT6</i>	chaperone			1.38	4.7E-04
PA0095		type VI secretion protein	1.57	4.4E-09		
PA0096		hypothetical protein	2.11	1.4E-06		
PA0097		hypothetical protein	1.63	2.0E-07		
PA0098		hypothetical protein	1.67	6.2E-04		
PA0099		type VI effector protein	1.57	6.4E-06		
PA0100		hypothetical protein	1.52	2.0E-06	1.29	4.4E-04
PA1659	<i>hsiF2</i>	type VI secretion system lysozyme-like protein	1.61	1.3E-04		
PA1661	<i>hsiH2</i>	type VI secretion protein	1.53	8.1E-03		
PA1666	<i>lip2</i>	type VI secretion system lipoprotein			1.33	1.8E-04
PA2361	<i>icmF3</i>	type VI secretion protein	1.52	1.6E-05		
PA2362	<i>dotU3</i>	type VI secretion protein	1.89	1.1E-05		
PA2363	<i>hsiJ3</i>	type VI secretion protein	1.71	1.8E-09		
PA2364	<i>lip3</i>	type VI secretion protein	1.55	7.4E-05		
PA2365	<i>hsiB3</i>	type VI secretion protein	1.86	7.4E-09		
PA2366	<i>hsiC3</i>	type VI secretion protein	1.88	1.8E-07		
PA2367	<i>hcp3</i>	type VI secretion system effector	1.76	2.2E-06		
PA2368	<i>hsiF3</i>	type VI secretion protein	1.68	3.1E-03		
PA2369	<i>hsiG3</i>	type VI secretion protein	1.92	3.2E-11		
PA2370	<i>hsiH3</i>	type VI secretion protein	2.20	1.9E-06		
PA2371	<i>clpV3</i>	type VI secretion system ATPase	1.65	9.5E-07		
PA2372		hypothetical protein	1.69	1.4E-05		
PA2373	<i>vgrG3</i>	type VI secretion protein	1.68	4.7E-07		
PA3486	<i>vgrG4b</i>	type VI secretion protein	1.69	6.9E-04		
PA5266	<i>vgrG6</i>	type VI secretion protein	1.89	7.3E-04		

Locus Tag	Name	Product Name	RNA-Seq		Proteomics	
			FC	padj	FC	p
Other virulence factors						
PA0051	<i>phzH</i>	potential phenazine-modifying enzyme	2.53	9.4E-13		
PA0122	<i>rahU</i>	hemolysin	2.30	3.0E-07	2.04	1.4E-02
PA1871	<i>lasA</i>	LasA protease precursor	1.68	2.0E-04		
PA1899	<i>phzA2</i>	probable phenazine biosynthesis protein	1.70	2.6E-08		
PA1900	<i>phzB2</i>	probable phenazine biosynthesis protein	1.95	3.0E-10	1.25	4.3E-02
PA1901	<i>phzC2</i>	phenazine biosynthesis protein	1.85	2.2E-06	1.44	4.5E-03
PA1903	<i>phzE2</i>	phenazine biosynthesis protein	1.24	7.2E-04		
PA1905	<i>phzG2</i>	probable pyridoxamine 5'-phosphate oxidase	1.53	2.7E-05	1.16	9.7E-03
PA2231	<i>pslA</i>	undecaprenyl-phosphate glucose phosphotransferase	1.85	1.3E-09	1.29	2.2E-03
PA2232	<i>pslB</i>	mannose-1-phosphate guanylyltransferase/mannose-6-phosphate isomerase	1.80	8.7E-12	1.34	6.5E-03
PA2233	<i>pslC</i>	putative glycosyl transferase	1.58	5.4E-09	1.14	4.5E-02
PA2234	<i>pslD</i>	polysaccharide export protein	1.71	4.9E-18	1.29	5.6E-03
PA2235	<i>pslE</i>	psl exopolysaccharide biosynthesis	1.68	2.6E-09	1.19	4.8E-03
PA2236	<i>pslF</i>	glycosyl transferase	1.62	1.4E-07		
PA2237	<i>pslG</i>	beta-xylosidase	1.52	1.4E-14	1.19	4.1E-03
PA2238	<i>pslH</i>	glycosyl transferase	1.71	1.1E-06	1.28	1.8E-03
PA2239	<i>pslI</i>	psl exopolysaccharide biosynthesis	1.55	7.4E-05	1.13	4.6E-02
PA2243	<i>pslM</i>	hypothetical protein	1.73	5.1E-03		
PA2244	<i>pslN</i>	hypothetical protein	1.88	8.2E-03		
PA2570	<i>lecA</i>	galactose-binding lectin	7.32	2.4E-08	2.41	3.4E-03
PA3361	<i>lecB</i>	fucose-binding lectin PA-IIL	2.86	1,2E-07		
PA3540	<i>algD</i>	GDP-mannose 6-dehydrogenase	7.13	2.9E-09		
PA3541	<i>alg8</i>	alginate biosynthesis protein	2.79	4.7E-05		
PA3542	<i>alg44</i>	alginate biosynthesis protein	2.11	2.7E-02		
PA3544	<i>algE</i>	alginate production outer membrane protein	2.73	1.8E-04		
PA3545	<i>algG</i>	alginate-c5-mannuronan-epimerase	2.41	9.7E-05		
PA3547	<i>algL</i>	poly(beta-d-mannuronate) lyase precursor	2.03	3.5E-02		
PA3548	<i>algI</i>	alginate o-acetyltransferase	1.80	3.9E-02		
PA3550	<i>algF</i>	alginate o-acetyltransferase	1.74	4.7E-02		
PA3551	<i>algA</i>	phosphomannose isomerase / GDP-D-mannose pyrophosphorylase	1.82	1.3E-03		
PA3724	<i>lasB</i>	elastase	1.64	1.7E-07		
PA4175	<i>piv</i>	protease IV	1.86	1.7E-05		
PA4212	<i>phzCI</i>	phenazine biosynthesis protein			1.44	4.5E-03
PA4213	<i>phzDI</i>	phenazine biosynthesis protein	1.20	1.4E-03		
PA4214	<i>phzEI</i>	phenazine biosynthesis protein	1.24	7.2E-04		

4.5 The multidrug efflux genes *mexXY* and *mexGHI-opmD* were upregulated in the PA0805.1 overexpression strain

Related to the tobramycin phenotype, the multidrug efflux pump *mexXY*, a known efflux

pump mediating resistance to aminoglycosides (Aires et al., 1999), was upregulated (Table 4-1). Interestingly, the repressor of *mexXY*, *mexZ* (Matsuo et al., 2004), was also upregulated in the proteomics dataset, yet clearly this was not sufficient to repress production of *mexXY* (Table 4-1). In addition, the multidrug efflux genes *mexGH* were upregulated by 1.7-1.8 fold in the RNA-Seq data, which could contribute to tobramycin resistance, since aminoglycosides are a substrate of the MexGHI-OpmD pump (Table 4-1) (Aendekerk et al., 2005). Proteomics and qRT-PCR indeed showed that the whole *mexGHI-opmD* operon was upregulated (Table 4-1, Table 4-2). Additionally, there were several other upregulated efflux genes, including *mexB*, *mexE*, *mexJ* and *mexV* (Table 4-1). MexS, a negative regulator of *mexEF-oprN* (Uwate et al., 2013), was downregulated in the proteomics (Table 4-1). Furthermore, *czcR*, a response regulator involved in heavy metal resistance, was also upregulated by 2.3 fold (Table 4-1). Moreover, genes in the *wbp* (PA5448-PA5454) LPS biosynthetic operon were downregulated, and in other studies we showed these can also lead to tobramycin resistance (Table 4-1) (Schurek et al., 2008). In contrast, genes in a different LPS biosynthetic operon (PA3141-PA3160) were upregulated (Table 4-1).

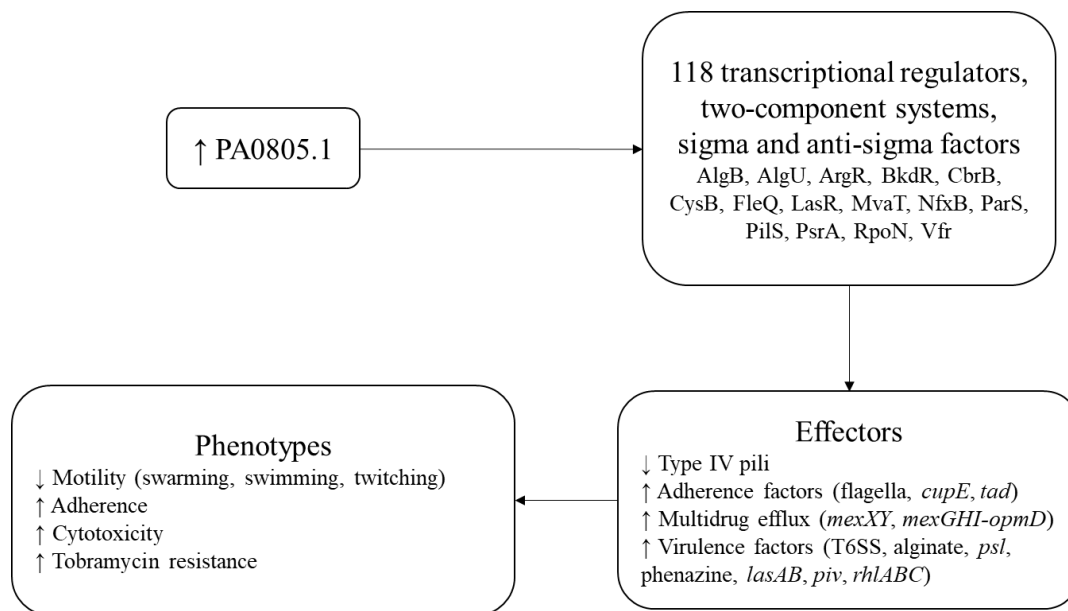


Figure 4-4. Proposed model for how the overexpression of PA0805.1 dysregulated many genes, resulting in altered phenotypes. Connecting arrows represent direct or indirect regulation.

Table 4-2. The MexGHI-OpmD operon was upregulated in the PA0805.1 overexpression strain when compared to EV strain by qRT-PCR. Bacteria were harvested from BM2 glycerol swarm plates with 1% arabinose and 0.1% CAA. $n = 3$.

Gene	Fold change
<i>mexG</i>	2.1 ± 0.1
<i>mexH</i>	2.0 ± 0.2

Gene	Fold change
<i>mexI</i>	1.9 ± 0.1
<i>opmD</i>	2.1 ± 0.4

4.6 Adherence factors were dysregulated in the PA0805.1 overexpression strain

Amongst the DE genes were a number of genes that could explain the anti-motility effect. Downregulation of the diguanylate cyclase FimX and PilGH could cause the downregulation of twitching motility proteins PilIJKTU and the type 4 fimbrial biogenesis proteins PilACD, PilMNOPQ, PilEVWX, and PilY1-2 (Table 4-1) (Jain et al., 2017). Downregulation of these genes could lead to reductions in twitching and/or swarming motility (Figure 4-1, Table 4-1) (Yeung et al., 2009). Aside from pilus-related genes, all other adherence factors were upregulated, including the *cupA* gene regulators *cgrABC*, but not the *cupA* operon (Table 4-1). Regulators *rocSI* and *rocR* were also upregulated (Table 4-1), which can lead to the production of CupB and CupC fimbriae (Kulasekara et al., 2005). The upregulated genes also included *cupE1-6*, *cupB2*, *tadABCDGZ*, and *flp* (Table 4-1). Lastly, the transcriptional regulator FleQ was also upregulated, along with downstream genes *flgBCDEFGHIJ*, *fliCDEF* and *flhA*. Consistent with this, an adherence assay was performed showing that the overexpression strain PA0805.1 had increased adherence (Figure 4-5). Collectively the overexpression of these adherence factors and their regulators could influence the reduced motility seen for this strain.

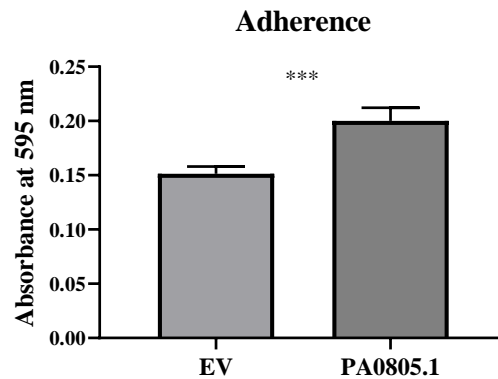


Figure 4-5. The PA0805.1 overexpression strain demonstrated increased adherence to polystyrene plates in 90% LB with 5% arabinose. Statistically significant differences were determined using Student's paired t test. $n \geq 3$.

4.7 Additional virulence factors were upregulated in the PA0805.1 overexpression strain

PA0805.1 also had an increased cytotoxicity against HBE cells (Figure 4-2). Amongst the upregulated DE genes were *lasAB* and *piv* which are cytotoxic proteases. Other upregulated virulence factors were T6SS genes, *rahU*, alginate and phenazine biosynthetic genes, *pslABCDEFGHIMN*, and *rhlABC* (Table 4-1, Table A2). In contrast, certain pyochelin, T1SS and

T3SS genes were downregulated (Table A2). Several global regulators implicated in virulence could account for these changes, such as CbrB, LasR, MvaT, and Vfr, but specifically the sigma factor AlgU, the two-component response regulator AlgB, and the transcriptional regulators PcrGH and ExsA are likely to be involved in regulating alginate and T3SS genes.

4.8 Comparison of RNA-Seq and proteomics

Comparison of the transcriptional and proteomic response revealed considerable overlap, with 243 genes and the encoded proteins identified to be differentially expressed by both methods (Figure A2). Of the 243 common gene and protein candidates, there was a good correlation in the direction of fold change (Figure A3, $R^2 = 0.73$), with 233 genes similarly down- (quadrant III, 90 genes), or up- (quadrant I, 143 genes) regulated, while 10 were regulated in opposite fashions (quadrants II and IV). This might relate in part to the differing abilities of the two methods since RNA-Seq was more sensitive and identified transcription from 5194 genes while proteomics identified only 2366 proteins. It is worth noting that transcripts for extracellular proteins were more likely detected in the RNA-Seq data since wash steps were employed prior to proteomics. Conversely, since sRNAs act by post-transcriptional regulation, it was expected that there would be changes in protein abundance with no corresponding difference in RNA transcript levels, while a single translationally dysregulated regulatory protein might control the expression of hundreds of genes.

4.9 *In silico* sRNA target prediction

Three *in silico* sRNA target prediction tools, IntaRNA2, RNAPredator and TargetRNA2 were used to predict sRNA targets for PA0805.1 (Table A8). Of the fourteen predicted targets, four were validated *in vitro*, in showing changes in either RNA or protein abundance (Table 4-3). These genes included *aprF*, the first gene in the operon encoding the T1SS for alkaline protease; *mep72*, a metzincin protease; PA3840, a putative rRNA methyl transferase; and PA5187, a probable acyl-CoA dehydrogenase (Table 4-3).

Table 4-3. sRNA targets predicted *in silico* that were confirmed for PA0805.1 by RNA-Seq or proteomics as well as their FC, p-values (padj/p) and predictive methods.

Locus Tag	Name	Product Name	RNA-Seq		Proteomics		Predicted by
			FC	padj	FC	p	
PA1248	<i>aprF</i>	alkaline protease secretion outer membrane protein AprF precursor			-1.18	4.6E-03	RNAPredator, IntaRNA2
PA2783	<i>mep72</i>	Mep72	-2.45	9.2E-05			RNAPredator, IntaRNA2
PA3840		conserved hypothetical protein	-1.87	2.6E-07			RNAPredator, IntaRNA2

Locus Tag	Name	Product Name	RNA-Seq		Proteomics		Predicted by
			FC	padj	FC	p	
PA5187		probable acyl-CoA dehydrogenase			1.11	3.5E-03	TargetRNA2, IntaRNA2

4.10 In its native state, PA0805.1 contributed to tobramycin susceptibility under swarming conditions

As mentioned above, PA0805.1 was upregulated by 5.0 ± 1.7 fold under swarming vs. swimming conditions (BM2 glucose). A deletion mutant of PA0805.1 was constructed, and showed no dramatic motility phenotype, but was supersusceptible to tobramycin under swarming conditions, and when complemented substantially restored tobramycin resistance (Figure 4-6). These data were consistent with the positive regulation of tobramycin resistance but negative regulation of motility.

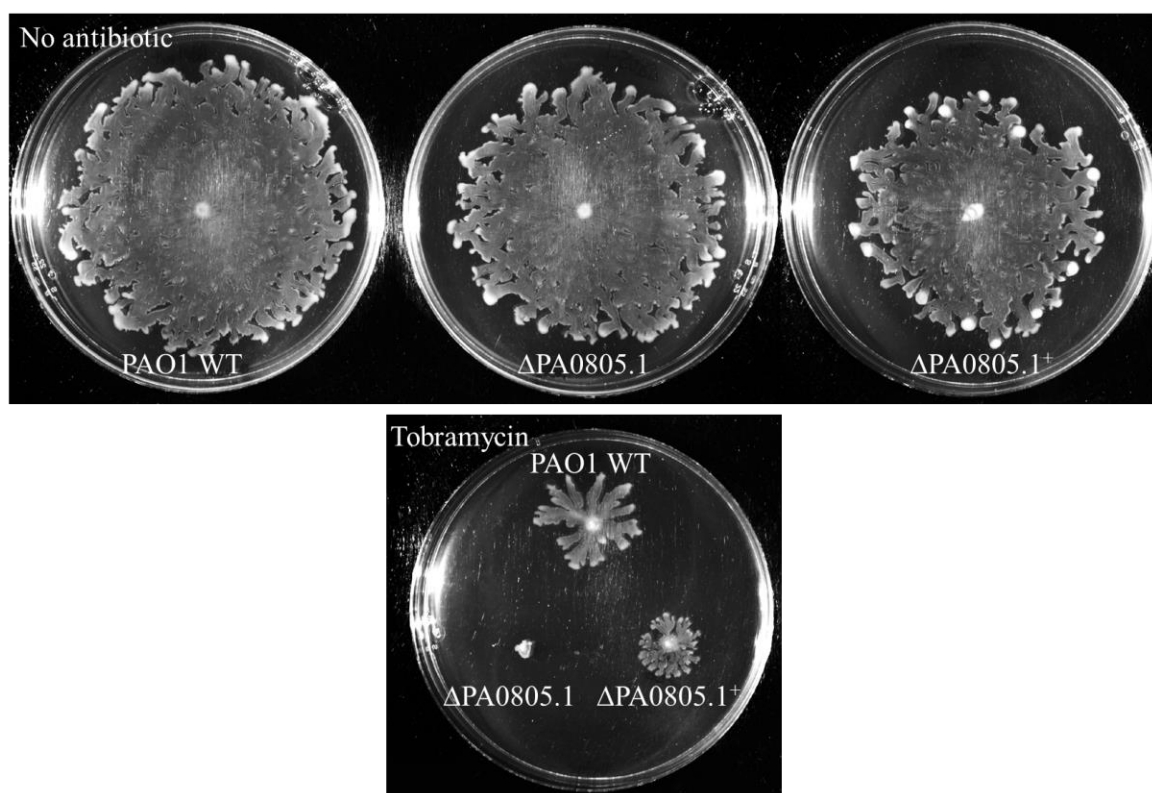


Figure 4-6. A deletion mutant of PA0805.1 was supersusceptible to tobramycin as assessed in BM2 glucose swarming agar with no arabinose. The deletion mutant was complemented with a chromosomal insertion of the sRNA PA0805.1. Tobramycin was incorporated into the agar where indicated at 1 μ g/ml. $n = 3$.

4.11 Discussion

Here I demonstrated that the overexpression of sRNA PA0805.1 led to a wide range of phenotypic changes including reduced swarming, swimming and twitching motility, as well as

increased adherence, cytotoxicity, and tobramycin resistance. In contrast to this situation, few phenotypes were observed for the deletion mutant Δ PA0805.1. This was likely due to the fact that sRNAs usually act by inhibiting translation of target mRNA; hence overexpression is more likely to have an effect than deletion. As expected, the tobramycin phenotype of the deletion mutant (TOB supersusceptible, Figure 4-6) was the opposite of that of the overexpression strain (TOB resistant) under conditions of low expression (using glucose to inhibit expression from the P_{BAD} promoter of pHERD20T) (Figure 4-3). The tobramycin phenotype was difficult to observe in the overexpression strain at higher levels of expression (*i.e.* with arabinose) due to the inhibition of swarming motility.

The differential expression of many global transcriptional regulators in the proteomics data was intriguing and suggests a prospective key global regulatory role for the sRNA PA0805.1 in influencing other regulators (Figure 4-4). For example, regulators with altered expression when this sRNA was overexpressed included LasR, a global regulator in *P. aeruginosa* that controls QS, virulence factor production, and motility (Kiratisin et al., 2002; Köhler et al., 2000), RpoN, an alternative sigma factor σ 54 that regulates virulence factors and pathogenicity in plants and animals as well as nitrogen metabolism (Hendrickson et al., 2001), MvaT, another global regulator of virulence that influences swarming motility and QS (Diggle et al., 2002), Vfr, a homolog of the *E. coli* catabolite repressor protein (CRP) that regulates virulence factor production (Fuchs et al., 2010; Rojo, 2010; Suh et al., 2015), and CbrB, a global response regulator, part of the two-component system CbrAB that regulates carbon and nitrogen metabolism, as well as antibiotic resistance, virulence, biofilm formation and swarming motility (Abdou et al., 2011; Yeung et al., 2011).

Here it was shown that overexpressing the sRNA PA0805.1 resulted in broad transcriptional and proteomic changes, most likely through a hierarchical regulatory cascade (Figure 4-4). Forty-two transcriptional regulators, two-component systems, sigma and anti-sigma factors were dysregulated at the proteomic level and 118 overall, likely explaining the extensive downstream effects. For example, type IV pili and its equivalent chemosensory system (ChpA-E) were downregulated, which would lead to decreased swarming and twitching motility, although certain other adherence factors were upregulated. Conversely, many flagellar genes were mildly upregulated but the decreased expression of particular regulators such as *lasR* and *cbrB* might explain decreased swimming and swarming. Furthermore, there is a connection between swimming and twitching, since the two-component PilRS system controls flagellar genes and

swimming motility (Kilmury & Burrows, 2018). Since PilS had altered protein abundance (Table 4-1), PilS may have affected swimming motility. In addition, many virulence factors, including the genes encoding the cytotoxic proteases *lasAB* and *piv* were upregulated, likely resulting in the observed increased cytotoxicity. Lastly, several multidrug efflux systems were upregulated, importantly including *mexXY* and *mexGHI-opmD*, which might contribute to tobramycin resistance. The sRNA PA0805.1 thus modulates important adaptations in *P. aeruginosa*, including motility, virulence and antibiotic resistance.

Chapter 5: The sRNAs PA2952.1 and *prhH* as regulators of virulence, motility and iron metabolism

5.1 Introduction

Coupling a large genome with a high percentage of transcriptional regulators (roughly 10%), *P. aeruginosa* has considerable potential to adapt to different conditions such as surface motility and antibiotic treatment. In addition, hundreds of regulatory sRNAs have been predicted, interspersed throughout the genome (Gómez-Lozano et al., 2012; Wurtzel et al., 2012). These non-coding regulatory elements allow for rapid regulation typically through post-transcriptional modification (Kavita et al., 2018). An exception to this is the ability of some sRNAs to influence degradation or increase stability of mRNAs (Pita et al., 2018; Prévost et al., 2011).

A 2018 study examined the expression of intergenic sRNAs and found 31 species to be differentially expressed under swarming and/or biofilm conditions (Gill et al., 2018). Most of the 20 sRNAs dysregulated under swarming conditions were previously uncharacterized, except for *prhH*, *rsmY* and *srbA*. A previous study showed that deleting *srbA* had an effect on biofilm formation and virulence in a *C. elegans* infection model (Taylor et al., 2017).

The sRNAs *rsmY* and *rsmZ* are induced by GacA, a global transcriptional regulator part of the two-component system GacAS, and partially redundant (Kay et al., 2006; Pita et al., 2018). After induction, *rsmY* and *rsmZ* sequester the post-transcriptional regulator RsmA from its target mRNA, causing diverse downstream effects on chronic and acute lifestyles (Janssen et al., 2018; Pita et al., 2018). Both *rsmY* and *rsmZ* can also be (in)directly regulated by AlgR, BfiSR, HptB, and PNPase.

sRNA *prhH* has also been shown to be dysregulated under swarming conditions (Gill et al., 2018). As mentioned in the Introduction, *prhH* is regulated by Fur and controls iron metabolism and virulence traits. It also competes with *crcZ* for binding to Hfq, since *crcZ* has higher affinity for Hfq than does *prhH* (Pita et al., 2018; Sonnleitner et al., 2017).

Here we probed the role of sRNAs in adaptive behaviours in *P. aeruginosa*, by cloning and overexpressing sRNAs dysregulated under swarming conditions. The overexpressing strains were examined in phenotypic assays for differences in motility, cytotoxicity and adherence. Next, RNA-Seq and proteomics were performed to investigate the effects mediated by the sRNA PA2952.1.

5.2 Phenotypic screens of sRNA overexpression strains

sRNA species previously show to be dysregulated under swarming conditions (Gill et al., 2018) were cloned to enable overexpression since sRNAs often have inhibitory functions. To

determine which region or orientation might result in a phenotype, some of these sRNAs were cloned in two orientations (PA0805.1 and PA0805.1a; PA1091.1a and b; PA3159.1a and b; and PA4656.1a and b), or different regions were cloned (PA2952.1W, overlapping version of PA2952.1; and PA14sr120, shorter version of PA0805.1) (Gill et al., 2018; Gómez-Lozano et al., 2012; Wurtzel et al., 2012). PA14sr120 was predicted from the PA14 genome (Wurtzel et al., 2012) in the same relative orientation as the construct for PA0805.1, but shorter than predicted in PAO1. A total of 21 constructs were made in the arabinose-inducible pHERD20T vector and transformed into PAO1 H103 WT by electroporation. One of these, PA0805.1, was described previously in Chapter 4.

At the time of the assay, arabinose was added to induce sRNA expression. Overexpression strains were confirmed to have no growth defects (Figure A4 and data not shown). Next, overexpression strains were screened for swarming, swimming, and twitching (Figure 5-1). Strains were also screened for adherence to polystyrene, but showed little difference in this assay (Figure A5).

Swarming and swimming motilities correlated well for some strains in these experiments (Figure 5-1). The overexpression strain PA14sr120 showed swarming and swimming motility that was reduced to $81\pm6\%$ and $65\pm2\%$ of the wild type (WT) containing the empty cloning vector (EV). The PA2952.1 overexpressing strain had motility reduced to 69 ± 3 and $43\pm4\%$ for swarming and swimming respectively. The PA1091.1b overexpressing strain showed a reduction to $80\pm2\%$ in swarming motility. Interestingly, overexpression of *prhH* resulted in substantially reduced swimming (to $28\pm3\%$ of the WT EV control) but no change in swarming motility (Figure 5-1). Overexpression strains were also screened for twitching motility but showed no significant differences (Figure 5-1). Sample colonies showing partial reductions in motility are shown in Figure 5-2.

The sRNA overexpression strains were also screened for cytotoxicity against human bronchial epithelial cells (HBE), with and without arabinose. Few significant differences were found amongst the strains (data not shown), except for PA2952.1 and *prhH*. In the absence of arabinose, PA2952.1 had cytotoxicity reduced by 36.4% of WT levels; however the PA2952.1 overexpressing strain when compared to WT EV with 1% arabinose was not significantly different (Figure 5-3A, Figure A6a).

5.3 sRNA *prhH* played a role in cytotoxicity and pyoverdine production

The sRNA *prhH*, encompassing the two adjacent and highly homologous sRNAs *prhF1*

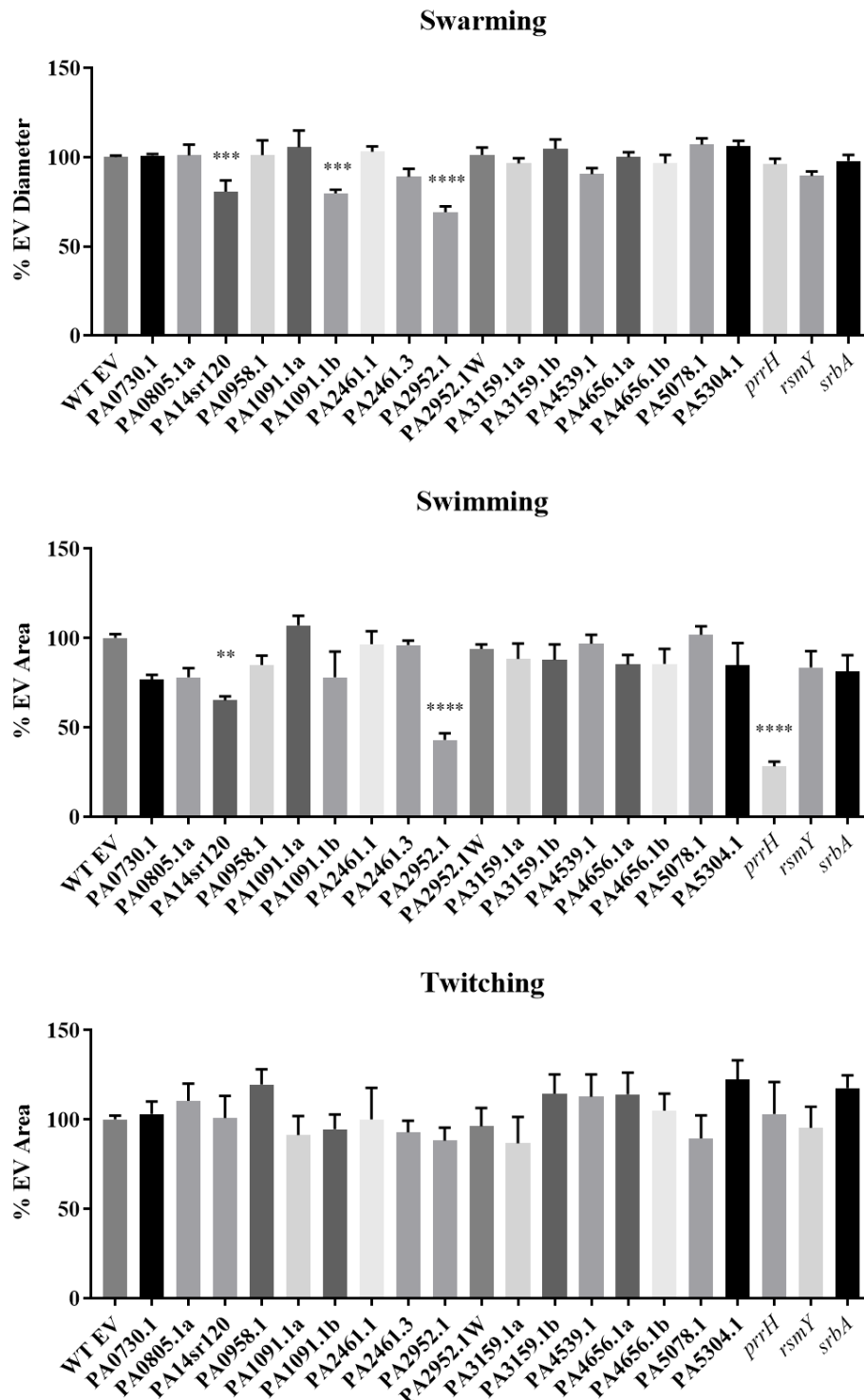


Figure 5-1. Motility screen of sRNA overexpression strains revealed that overexpression of certain sRNAs altered motility. 1% Arabinose was used to induce expression and statistically significant differences from WT EV were determined using one-way ANOVA. $n \geq 3$.

and *prrF2* (Wilderman et al., 2004), also played a role in cytotoxicity (Figure 5-3B). When *prrH* was overexpressed at low levels (0% arabinose), the cytotoxicity of WT +*prrH* was reduced by 40.2% of WT levels. In the absence of arabinose, a deletion mutant Δ *prrH* had even lower levels

of cytotoxicity (reduced by 68.9%), which was partially complemented (to 53.7% of WT levels) when the sRNA was reintroduced on the uninduced pHERD20T plasmid (Figure 5-3B). Interestingly, in the presence of arabinose, these phenotypes were minimized. With arabinose, only the change in cytotoxicity due to deletion in $\Delta prrH$ was significantly different and could not be complemented by overexpression of *prrH* (Figure A6b).

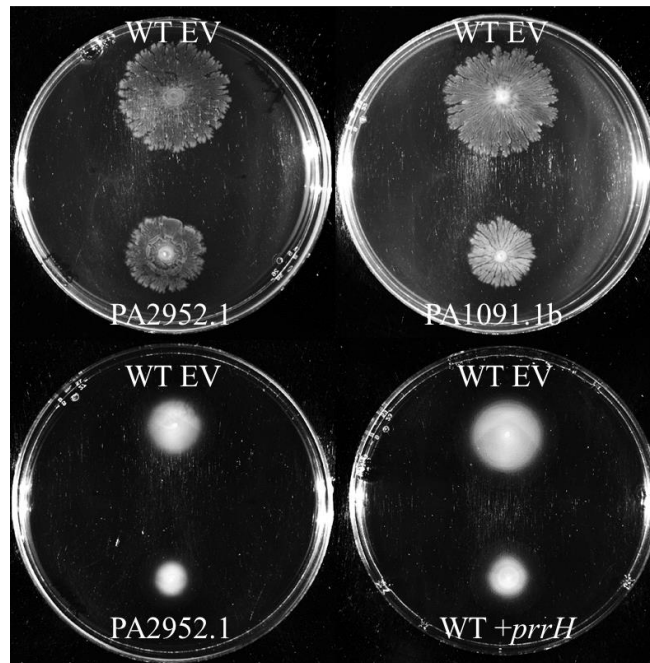


Figure 5-2. Overexpression of certain sRNAs led to partial reductions in swarming (top row) and swimming (bottom row) motilities. $n \geq 3$.

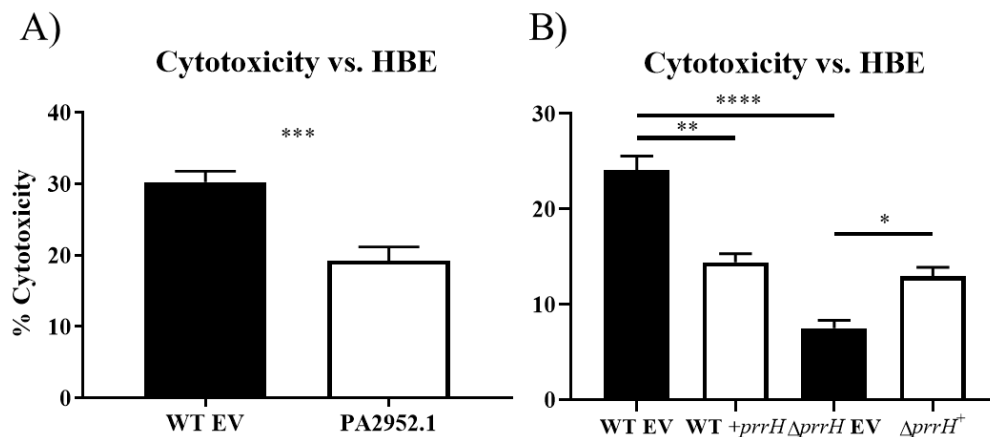


Figure 5-3. Cytotoxicity phenotypes of sRNA overexpression strains in the absence of arabinose. A) overexpression of PA2952.1 compared to WT EV. B) deletion and overexpression of *prrH*. Statistically significant differences were determined by unpaired t test (A) or one-way ANOVA (B). $n \geq 3$.

The deletion mutant $\Delta prrH$ also produced >2-fold increased levels of pyoverdine (Figure

5-4). This phenotype was restored to WT levels by complementation. The strain overexpressing *prhH* however showed no difference from the WT EV isolate (Figure 5-4).

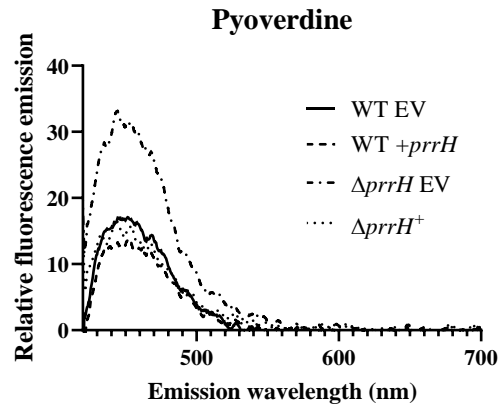


Figure 5-4. A deletion mutant Δ *prhH* had increased production of pyoverdine. $n = 3$.

5.4 Overexpression of sRNAs altered antibiotic susceptibility under swarming conditions

The sRNA PA2952.1, which inhibited swarming and swimming (Figure 5-2), also showed altered antibiotic susceptibility under swarming conditions. PA2952.1 overexpression at low levels led to resistance to both tobramycin and gentamicin (Figure 5-5A). This modest resistance phenotype could not be observed at higher levels of expression, in part due to the inhibitory effect of PA2952.1 on swarming motility. In contrast, at higher levels of expression, increased susceptibility to trimethoprim was observed under swarming conditions (Figure 5-5B). No major differences in MIC to either antibiotic were observed in standard microdilution assays (Table A9), however, subinhibitory concentrations of trimethoprim specifically inhibited the growth of the PA2952.1 overexpression strain in the presence of 1% arabinose (Figure A7).

Overexpression of the sRNA PA14sr120 at low levels resulted in resistance to tobramycin under swarming conditions (Figure 5-5C). Similar to the observations made for PA2952.1, overexpression of PA1091.1b at high levels resulted in increased trimethoprim susceptibility under swarming conditions (Figure 5-5D).

5.5 Overexpression of PA2952.1 resulted in broad transcriptional changes including altered expression of 82 regulatory factors

The sRNA PA2952.1 was selected for study in greater detail due to its broad phenotypic effects and lack of prior studies. To determine which genes or proteins caused the above-described phenotypic changes, RNA-Seq and proteomics were performed on the WT strain overexpressing PA2952.1 compared to that with the WT EV control, by harvesting bacteria from the edges of swarming colonies grown with 1% arabinose. Substantial transcriptional and proteomic changes

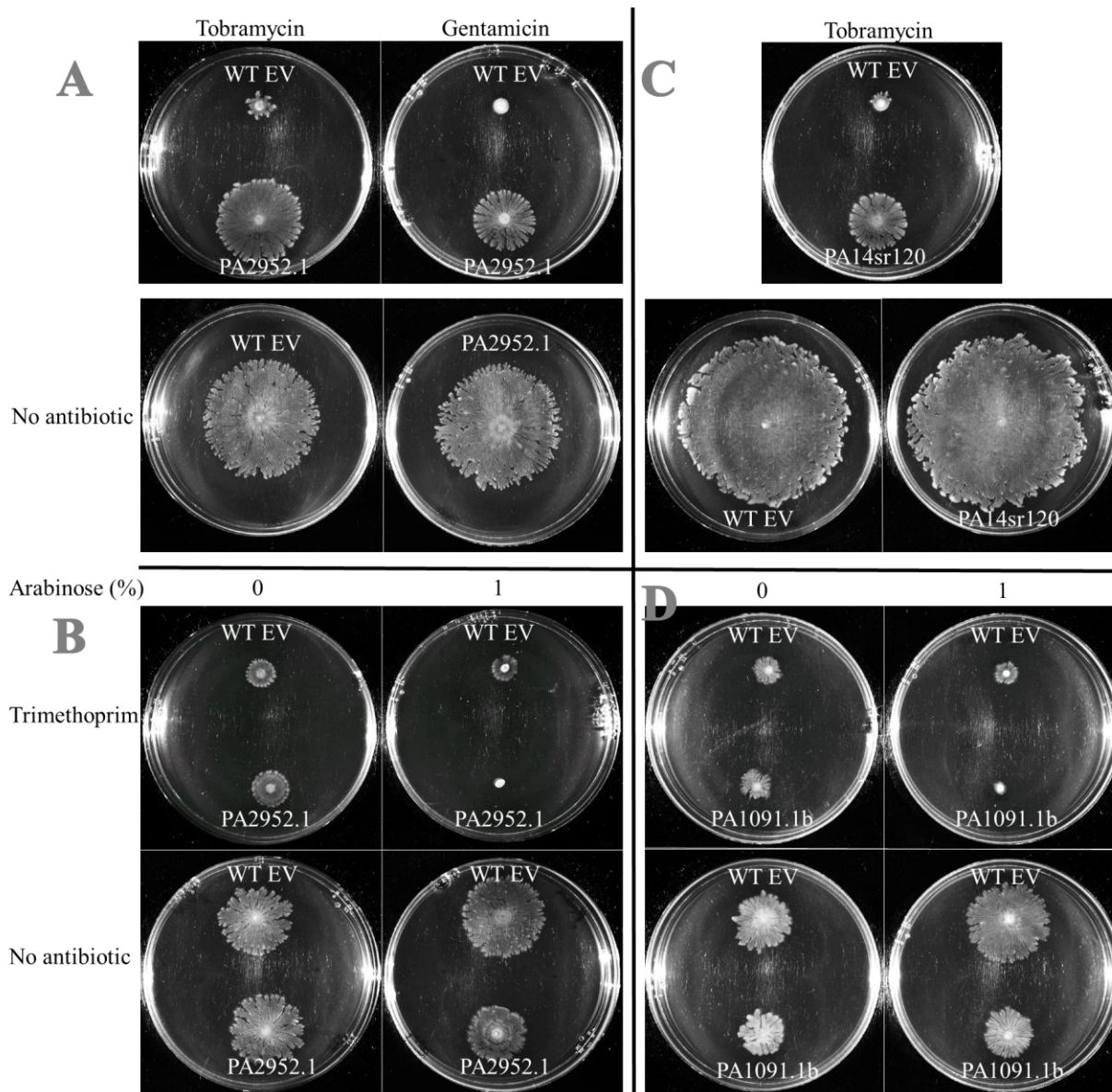


Figure 5-5. Antibiotic susceptibility phenotypes were affected by sRNAs under swarming conditions. **A.** The strain overexpressing PA2952.1 showed resistance to tobramycin and gentamicin in BM2 glucose swarm plates with no arabinose, supplemented where indicated with 1 μ g/ml antibiotic. $n = 3$. **B.** Overexpression of PA2952.1 induced susceptibility to trimethoprim in BM2 glycerol swarm plates. Trimethoprim is included where indicated at 10 μ g/ml. $n \geq 3$. **C.** The PA14sr120 overexpression strain was resistant to tobramycin in BM2 glucose swarm plates with no arabinose. Tobramycin is included where indicated at 1 μ g/ml. $n \geq 3$. **D.** Overexpression of PA1091.1b increased susceptibility to trimethoprim in BM2 glycerol swarm plates. Trimethoprim is included where indicated at 10 μ g/ml. $n \geq 3$.

were observed, encompassing 446 proteins with differential abundance and 784 DE genes in the RNA-Seq (Table A2). Of these, 339 genes were downregulated and 445 were upregulated; while

221 proteins had decreased abundance and 225 were increased (Table A2). There was a large number (82 genes/proteins) of regulatory factors (transcriptional regulators, two-component systems, sigma and anti-sigma factors) found amongst these genes, which might have accounted for the large transcriptional changes observed (Table 5-1). Amongst the 82 regulatory factors, 27 factors showed changes only in the proteomics dataset (shown with **bold** locus tag in Table 5-1) and thus might represent potential post-transcriptional sRNA targets.

Table 5-1. Selected differential expressed genes/proteins in the PA2952.1 overexpression strain as compared to WT EV by RNA-Seq and/or proteomics. Loci shown in **bold** showed differences uniquely in the proteome. Cutoffs used were $p/\text{padj} \leq 0.05$ and for RNA-Seq, $\text{FC} \geq 1.5$.

Locus Tag	Name	Product Name	RNA Seq		Proteomics	
			FC	padj	FC	p
Transcriptional regulators, two-component systems and sigma factors						
PA0048		probable transcriptional regulator	-1.56	2.0E-02		
PA0155	<i>pcaR</i>	transcriptional regulator	1.84	5.5E-14		
PA0217		probable transcriptional regulator	1.57	1.8E-03		
PA0243		probable transcriptional regulator			1.10	1.1E-02
PA0403	<i>pyrR</i>	transcriptional regulator	1.59	1.8E-04		
PA0463	<i>creB</i>	two-component response regulator	1.81	2.4E-13		
PA0472	<i>fiuI</i>	probable sigma-70 factor, ECF subfamily	1.94	5.0E-05		
PA0528		probable transcriptional regulator	1.78	1.9E-08		
PA0652	<i>vfr</i>	transcriptional regulator			-1.11	2.2E-03
PA0828		probable transcriptional regulator	-2.01	2.0E-02		
PA0877		probable transcriptional regulator	-1.51	2.6E-02		
PA0964	<i>pmpR</i>	pqsR-mediated PQS regulator			-1.08	2.7E-02
PA1157		probable two-component response regulator			1.10	6.5E-03
PA1179	<i>phoP</i>	two-component response regulator	-1.51	6.1E-21		
PA1223		probable transcriptional regulator	-1.56	3.7E-03		
PA1261	<i>lhpR</i>	transcriptional regulator	1.96	2.3E-03		
PA1285		probable transcriptional regulator	1.66	5.1E-07		
PA1290		probable transcriptional regulator			1.30	1.1E-02
PA1315		probable transcriptional regulator			1.09	3.3E-02
PA1328		probable transcriptional regulator	1.65	5.1E-06		
PA1399		probable transcriptional regulator	1.62	7.5E-03		
PA1431	<i>rsaL</i>	regulatory protein	1.98	8.0E-08		
PA1627		probable transcriptional regulator	2.21	1.4E-08		
PA1707	<i>pcrH</i>	regulatory protein	-1.88	1.7E-04		
PA1714	<i>exsD</i>	probable transcriptional regulator			-1.29	3.2E-02
PA1785	<i>nasT</i>	regulatory protein			-1.11	7.0E-03
PA1836		probable transcriptional regulator	-1.51	2.5E-03		
PA1911	<i>femR</i>	sigma factor regulator	1.93	1.5E-02		
PA1912	<i>femI</i>	ECF sigma factor	1.88	1.5E-03		

Locus Tag	Name	Product Name	RNA Seq		Proteomics	
			FC	padj	FC	p
PA1949	<i>rbsR</i>	ribose operon repressor			1.07	1.6E-02
PA1980	<i>eraR</i>	response regulator	-1.81	1.1E-02		
PA2082	<i>kynR</i>	probable transcriptional regulator			1.12	8.0E-03
PA2126	<i>cgrC</i>	cupA gene regulator C	1.74	8.5E-05		
PA2126.1	<i>cgrB</i>	cupA gene regulator B	2.33	2.4E-07		
PA2276		probable transcriptional regulator			1.13	4.3E-03
PA2337	<i>mtlR</i>	transcriptional regulator	1.60	9.3E-04		
PA2426	<i>pvdS</i>	sigma factor	2.07	2.0E-02		
PA2467	<i>foxR</i>	anti-sigma factor	2.11	6.2E-07		
PA2486	<i>ptrC</i>	<i>Pseudomonas</i> type III repressor gene C	2.89	2.6E-13		
PA2491	<i>mexS</i>	Transcriptional regulator			-1.18	5.9E-03
PA2511	<i>antR</i>	Transcriptional regulator	1.67	2.7E-03		
PA2663	<i>ppyR</i>	psl and pyoverdine operon regulator	2.14	1.5E-04		
PA2665	<i>fhpR</i>	transcriptional activator of <i>P. aeruginosa</i> flavohemoglobin			1.07	1.7E-02
PA2848		probable transcriptional regulator	1.56	1.3E-02		
PA2882		probable two-component sensor	2.31	5.0E-03		
PA2895	<i>sbrR</i>	anti-sigma factor	1.52	2.2E-05		
PA2896	<i>sbrI</i>	probable sigma-70 factor, ECF subfamily	1.50	1.6E-06		
PA2917		probable transcriptional regulator	1.65	1.0E-06		
PA2931	<i>cifR</i>	putative transcriptional regulator	-1.59	1.9E-03		
PA3006	<i>psrA</i>	transcriptional regulator			1.14	1.6E-02
PA3122		probable transcriptional regulator			1.11	7.9E-03
PA3220		probable transcriptional regulator	1.54	2.2E-04		
PA3341		probable transcriptional regulator			1.13	2.0E-03
PA3458		probable transcriptional regulator	-1.50	6.2E-03		
PA3583	<i>glpR</i>	glycerol-3-phosphate regulon repressor			1.06	1.3E-03
PA3622	<i>rpoS</i>	sigma factor			1.13	1.1E-02
PA3689		probable transcriptional regulator			1.10	3.0E-04
PA3757	<i>nagR</i>	transcriptional regulator of N-acetylglucosamine catabolism operon	1.52	2.6E-03		
PA3878	<i>narX</i>	two-component sensor	1.57	1.1E-07		
PA3899	<i>fecI</i>	probable sigma-70 factor, ECF subfamily	1.62	7.4E-03		
PA4057	<i>nrdR</i>	transcriptional repressor	-1.54	2.6E-06		
PA4070		probable transcriptional regulator	1.98	1.1E-05		
PA4293	<i>pprA</i>	two-component sensor			1.18	2.5E-02
PA4296	<i>pprB</i>	two-component response regulator			1.08	2.0E-02
PA4493	<i>roxR</i>	response regulator			1.17	2.8E-02
PA4546	<i>pilS</i>	two-component sensor			1.09	3.5E-02
PA4726	<i>cbrB</i>	two-component response regulator	1.51	4.4E-25	-1.13	8.9E-04
PA4764	<i>fur</i>	ferric uptake regulation protein			1.08	3.1E-02

Locus Tag	Name	Product Name	RNA Seq		Proteomics	
			FC	padj	FC	p
PA4777	<i>pmrB</i>	two-component regulator system signal sensor kinase	1.54	5.4E-03		
PA4778	<i>cueR</i>	probable transcriptional regulator			-1.14	3.1E-02
PA4784		probable transcriptional regulator	1.53	2.0E-05		
PA4914	<i>amaR</i>	transcriptional regulator	1.62	1.5E-05		
PA5029		probable transcriptional regulator	1.54	2.5E-05		
PA5124	<i>ntrB</i>	two-component sensor	1.72	6.6E-06		
PA5189		probable transcriptional regulator	1.59	3.6E-05		
PA5261	<i>algR</i>	alginate biosynthesis regulatory protein	1.58	5.2E-08		
PA5288	<i>glnK</i>	nitrogen regulatory protein P-II 2	1.58	4.5E-04		
PA5293		probable transcriptional regulator			1.07	4.5E-02
PA5356	<i>glcC</i>	transcriptional regulator	2.19	1.1E-18		
PA5403		probable transcriptional regulator	1.70	1.1E-03		
PA5484	<i>kinB</i>	two-component sensor			1.10	6.5E-03
PA5499	<i>zur</i>	zinc uptake regulator	2.27	6.3E-06		
Motility and related genes						
PA0396	<i>pilU</i>	twitching motility protein			-1.12	3.6E-03
PA0408	<i>pilG</i>	twitching motility protein			-1.33	4.9E-02
PA0411	<i>pilJ</i>	twitching motility protein			-1.32	1.6E-04
PA0413	<i>chpA</i>	component of chemotactic signal transduction system			-1.17	2.3E-05
PA0415	<i>chpC</i>	probable chemotaxis protein	-1.56	3.3E-06		
PA1083	<i>flgH</i>	flagellar L-ring protein precursor			1.12	4.9E-02
PA1088		hypothetical protein			1.09	1.9E-02
PA1100	<i>fliE</i>	flagellar hook-basal body complex protein	-1.55	1.6E-06		
PA1442		conserved hypothetical protein	-1.52	1.0E-09		
PA1445	<i>fliO</i>	flagellar protein			-1.05	3.6E-02
PA1461	<i>motD</i>	flagellar motor protein			1.11	1.3E-02
PA4525	<i>pilA</i>	type 4 fimbrial precursor	-2.86	7.2E-24		
PA4527	<i>pilC</i>	still frameshift type 4 fimbrial biogenesis protein (putative pseudogene)			-1.09	6.1E-03
PA4552	<i>pilW</i>	type 4 fimbrial biogenesis protein			-1.09	4.8E-02
PA4554	<i>pilY1</i>	type 4 fimbrial biogenesis protein			-1.15	4.9E-02
PA5043	<i>pilN</i>	type 4 fimbrial biogenesis protein			1.38	9.1E-03
Multidrug efflux and LPS modification						
PA2494	<i>mexF</i>	RND multidrug efflux transporter	1.66	2.7E-02		
PA2525	<i>opmB</i>	outer membrane efflux protein			1.67	3.0E-02
PA2528	<i>muxA</i>	probable RND efflux membrane fusion protein			-1.10	6.5E-03
PA3522	<i>mexQ</i>	efflux pump membrane transporter	-1.63	1.8E-02		
PA3676	<i>mexK</i>	probable RND efflux transporter			1.12	4.6E-02
PA4205	<i>mexG</i>	hypothetical protein			1.24	1.2E-03
PA4206	<i>mexH</i>	probable RND efflux membrane fusion protein			1.07	3.4E-02

Locus Tag	Name	Product Name	RNA Seq		Proteomics	
			FC	padj	FC	p
		precursor				
PA4374	<i>mexV</i>	RND multidrug efflux membrane fusion protein	2.89	2.2E-18	1.11	2.8E-02
PA3552	<i>arnB</i>	UDP-4-amino-4-deoxy-L-arabinose--oxoglutarate aminotransferase	2.06	1.8E-04		
PA3553	<i>arnC</i>	undecaprenyl-phosphate 4-deoxy-4-formamido-L-arabinose transferase	2.48	3.1E-08		
PA3554	<i>arnA</i>	bifunctional polymyxin resistance protein	1.61	9.4E-03		
PA3556	<i>arnT</i>	inner membrane L-Ara4N transferase	1.71	1.5E-03		
PA3558	<i>arnF</i>	probable 4-amino-4-deoxy-L-arabinose-phosphoundecaprenol flippase subunit	2.45	1.0E-05		
PA3559		probable nucleotide sugar dehydrogenase	1.97	3.8E-04		
DNA synthesis						
PA0143	<i>nuh</i>	purine nucleosidase			-1.09	5.9E-03
PA0196	<i>pntB</i>	pyridine nucleotide transhydrogenase, beta subunit			1.10	4.8E-02
PA0342	<i>thyA</i>	thymidylate synthase			-1.05	3.5E-02
PA0357	<i>mutM</i>	formamidopyrimidine-DNA glycosylase			-1.11	1.5E-02
PA0441	<i>dht</i>	dihydropyrimidinase	2.10	1.9E-02		
PA0582	<i>folB</i>	dihydroneopterin aldolase	-2.32	5.3E-13		
PA3438	<i>folE1</i>	GTP cyclohydrolase I precursor			-1.20	4.3E-03
PA3640	<i>dnaE</i>	DNA polymerase III, alpha chain			-1.08	3.0E-02
PA4645		probable purine/pyrimidine phosphoribosyl transferase			-1.11	6.1E-04
PA4946	<i>mutL</i>	DNA mismatch repair protein			-1.07	2.9E-02
PA4964	<i>parC</i>	topoisomerase IV subunit A			-1.12	2.8E-03
PA4967	<i>parE</i>	topoisomerase IV subunit B			-1.10	7.9E-04
PA5345	<i>recG</i>	ATP-dependent DNA helicase			-1.14	2.4E-03
PA5443	<i>uvrD</i>	DNA helicase II			-1.11	2.3E-02
PA5493	<i>polA</i>	DNA polymerase I			-1.08	1.5E-03
PA5541	<i>pyrQ</i>	dihydroorotase	6.74	7.7E-04		
Virulence factors						
PA0071	<i>tagR1</i>	FGE-sulfatase domain-containing protein			1.13	4.6E-02
PA0075	<i>pppA</i>	serine/threonine protein phosphatase			1.17	1.8E-02
PA0077	<i>icmF1</i>	type VI secretion protein			1.15	2.2E-02
PA0078	<i>tssL1</i>	type VI secretion system protein			1.19	1.6E-02
PA0079	<i>tssK1</i>	type VI secretion protein			1.18	2.4E-02
PA0081	<i>fha1</i>	type VI secretion protein	1.51	9.1E-11		
PA0082	<i>tssA1</i>	type VI secretion protein			1.39	6.8E-03
PA1694	<i>pscQ</i>	translocation protein in type III secretion	-2.28	1.2E-03		
PA1700	<i>pcr2</i>	type III secretion chaperone	-3.32	9.0E-03		
PA1703	<i>pcrD</i>	type III secretory apparatus protein	-1.59	2.0E-06		
PA1706	<i>pcrV</i>	type III secretion protein	-1.61	9.4E-04		

Locus Tag	Name	Product Name	RNA Seq		Proteomics	
			FC	padj	FC	p
PA1708	<i>popB</i>	translocator protein	-2.16	8.9E-11		
PA1709	<i>popD</i>	translocator outer membrane protein precursor	-1.79	1.5E-06		
PA1710	<i>exsC</i>	exoenzyme S synthesis protein C precursor.	-1.73	2.4E-08		
PA1712	<i>exsB</i>	exoenzyme S synthesis protein B	-1.76	3.1E-10		
PA1715	<i>pscB</i>	type III export apparatus protein	-2.41	3.2E-04		
PA1717	<i>pscD</i>	type III export protein	-2.22	9.0E-05		
PA1719	<i>pscF</i>	type III export protein	-1.59	3.0E-03		
PA1720	<i>pscG</i>	type III export protein	-1.71	6.4E-03		
PA1722	<i>pscI</i>	type III export protein	-2.15	3.5E-04		
PA1723	<i>pscJ</i>	type III export protein	-1.74	4.1E-06		
PA2191	<i>exoY</i>	adenylate cyclase	-2.04	6.6E-07		
PA2231	<i>pslA</i>	undecaprenyl-phosphate glucose phosphotransferase			1.21	3.2E-02
PA2232	<i>pslB</i>	mannose-1-phosphate guanylyltransferase/mannose-6-phosphate isomerase			1.19	3.2E-02
PA2238	<i>pslH</i>	glycosyl transferase			1.12	4.0E-02
PA2244	<i>pslN</i>	hypothetical protein	1.68	8.8E-03		
PA3841	<i>exoS</i>	exoenzyme S	-1.53	5.3E-06		
Cell division						
PA0373	<i>ftsY</i>	signal recognition particle receptor			-1.07	2.0E-02
PA1528	<i>zipA</i>	cell division protein			1.07	3.3E-02
PA3243	<i>minC</i>	cell division inhibitor			-1.05	1.9E-02
PA3245	<i>minE</i>	cell division topological specificity factor	-1.73	3.9E-20		
PA4003	<i>pbpA</i>	penicillin-binding protein 2			-1.04	5.0E-02
PA4020	<i>mpl</i>	UDP-N-acetylmuramate:L-alanyl-gamma-D-glutamyl-meso-diaminopimelate ligase			-1.11	3.2E-03
PA4407	<i>ftsZ</i>	cell division protein			1.14	2.0E-02
PA4408	<i>ftsA</i>	cell division protein			1.10	7.4E-03
PA4411	<i>murC</i>	UDP-N-acetylmuramate--alanine ligase			1.12	9.2E-04
PA4414	<i>murD</i>	UDP-N-acetylmuramoylalanine--D-glutamate ligase			1.08	1.4E-02
PA4416	<i>murF</i>	UDP-N-acetylmuramoylalanine-D-glutamyl-2, 6-diaminopimelate--D-alanyl-D-alanyl ligase			1.11	2.8E-02
PA4417	<i>murE</i>	UDP-N-acetylmuramoylalanine-D-glutamyl-2, 6-diaminopimelate ligase			1.09	1.1E-02
PA4418	<i>ftsI</i>	penicillin-binding protein 3			1.12	4.3E-02
PA5538	<i>amiA</i>	N-acetylmuramoyl-L-alanine amidase	4.63	4.7E-04		
PA5562	<i>spoOJ</i>	chromosome partitioning protein			1.08	6.2E-03
PA5563	<i>soj</i>	chromosome partitioning protein			1.08	3.9E-02
Iron and zinc uptake						
PA0470	<i>fliuA</i>	ferrichrome receptor	4.33	2.3E-23		

Locus Tag	Name	Product Name	RNA Seq		Proteomics	
			FC	padj	FC	p
PA3621	<i>fdxA</i>	ferredoxin I	-2.13	3.1E-09		
PA3812	<i>iscA</i>	probable iron-binding protein	-1.56	1.0E-08		
PA4235	<i>ftnA</i>	bacterial ferritin			1.11	7.1E-03
PA4358	<i>feoB</i>	ferrous iron transport protein B	1.59	1.8E-02		
PA4655	<i>hemH</i>	ferrochelataase	1.57	8.1E-12		
PA4688	<i>hitB</i>	iron (III)-transport system permease			-1.07	2.7E-02
PA4880		probable bacterioferritin	2.72	1.1E-10		
PA5500	<i>znuC</i>	zinc transport protein	2.34	9.5E-08		

These 27 regulatory factors that were altered only at the proteomic level included several global regulators including Fur, that regulates iron acquisition, metabolism, virulence and the response to toxic oxygen radicals (Hassett et al., 1996; Pasqua et al., 2017), RpoS, a stationary sigma factor involved in the stress response and antibiotic tolerance (Murakami et al., 2005; Suh et al., 1999), the two-component system PprAB, that regulates biofilm formation, drug susceptibility and virulence (de Bentzmann et al., 2012), PmpR, a regulator of the PQS QS system, T3SS, swarming and biofilm formation (Liang et al., 2008; Liang et al., 2012b), PsrA, a regulator of PQS, T3SS, antimicrobial peptide resistance, swarming and biofilm formation (Gooderham et al., 2008; Kojic et al., 2005; Shen et al., 2006; Wells et al., 2017), Vfr, a regulator of virulence factors and homolog of the *E. coli* catabolite repressor protein (Fuchs et al., 2010; Rojo, 2010; Suh et al., 2015), PilS, a two-component sensor that regulates both twitching and swimming motilities (Kilmury & Burrows, 2018), and KinB, a two-component sensor that regulates alginate production, virulence, and motility (Chand et al., 2012; Damron et al., 2012; Damron et al., 2009). Other regulators not unique to the proteome included *algR*, *cbrB*, *glnK*, *ntrB*, *phoP*, *pmrB*, *pvdS*, *rsaL* and *sbrIR* (Table 5-1).

Comparison of the RNA-Seq and proteomics data revealed an overlap of 50 genes/proteins (Figure A2), indicative of significant post-transcriptional modulation. Nevertheless, genes within the same operon were often regulated in the same direction in both RNA-Seq and proteomics (Table 5-1), suggesting there may be more similarities between the two data sets than immediately evident.

5.6 Pili and flagellar genes were dysregulated in the PA2952.1 overexpression strain

Overexpression of PA2952.1 led to partial reductions in both swarming and swimming motilities (Figure 5-2). Motility genes dysregulated in the RNA-Seq and proteomics could explain this effect (Table 5-1). Pili genes were generally downregulated, including *pilAC*, *pilW*, *pilYI*,

pilUGJ and the accompanying chemotactic genes *chpAC* (Table 5-1). The type IV pilus plays a role in swarming motility in *P. aeruginosa* (Köhler et al., 2000), and mutants in *pilC*, *pilJ*, *pilW* and *pilYI* all have deficient swarming ability (Yeung et al., 2009). Flagellar genes were also dysregulated, and the downregulated *fliE*, *fliO* and PA1442 could contribute to decreases in both swarming and swimming motilities (Table 5-1). Other genes required for swarming that were downregulated in the PA2952.1 overexpression strain, were PA0591, PA0837 (*slyD*), PA0894, PA1827, PA2023 (*galU*), PA2445, PA2630, PA3091, PA3386, PA4005, PA4505, PA4616, PA4775 (*greA*), PA4778 (*cueR*), PA4851, PA5078 (*opgG*), PA5134 (*ctpA*), PA5232, PA5315 (*rpmG*), and PA5345 (*recG*); collectively these could have exerted a multigenic influence to decrease swarming.

5.7 Upregulation of *mexGHI-opmD* and the *arn* operon might lead to aminoglycoside resistance in the PA2952.1 overexpression strain

Related to the aminoglycoside resistance phenotype (Figure 5-5A), efflux proteins MexGH demonstrated increased abundance in the proteome (Table 5-1), while qRT-PCR revealed a modest upregulation of the entire operon (Table 5-2). The *mexGHI-opmD* efflux pump was previously shown to be involved in aminoglycoside efflux (Aendekerk et al., 2005). Similarly, MexS, a negative regulator of efflux (Uwate et al., 2013), had decreased abundance in the proteome (Table 5-2).

Table 5-2. The *mexGHI-opmD* operon was modestly upregulated in the PA2952.1 overexpression strain when compared to WT EV by qRT-PCR. Bacteria were harvested from BM2 glycerol swarm plates with 1% arabinose and 0.1% CAA. *n* = 3.

Gene	Fold change
<i>mexG</i>	1.7 ± 0.2
<i>mexH</i>	1.7 ± 0.2
<i>mexI</i>	1.8 ± 0.3
<i>opmD</i>	1.8 ± 0.5

A dysregulation of LPS biosynthetic genes was also observed (Table A2), and this might be important due to the role of LPS in self-promoted uptake of aminoglycosides and swarming-dependent adaptive resistance to tobramycin (Chapter 3). In addition, *arnBCATF* were upregulated (Table 5-1). These genes are involved in the aminoarabinylation of LPS to a more positively charged form, resulting in resistance to both aminoglycosides and cationic antimicrobial peptides (Breidenstein et al., 2011). The *arn* operon is regulated by several different two-component systems; in this case the PmrAB system may be implicated (Barrow & Kwon, 2009), since *pmrB*

was also upregulated (Table 5-1). Furthermore, 40 ribosomal and related genes were modestly downregulated (Table A2), which may also be a contributing factor, since the ribosome is the target of aminoglycosides.

5.8 DNA biosynthetic pathways were dysregulated

Genes involved in DNA synthesis, including those involved in pyrimidine metabolism, were dysregulated (Table 5-1). These genes were generally mildly downregulated, with the exception of *pntB*, *dht*, and *pyrQ* that were upregulated (Table 5-1). This could contribute to the increased susceptibility to trimethoprim observed in the PA2952.1 overexpression strain (Figure 5-5B), since trimethoprim inhibits the enzyme dihydrofolate reductase, causing a decrease in the levels of tetrahydrofolate (Sangurdekar et al., 2011). Tetrahydrofolate plays a role as a carbon donor in nucleic acid and amino acid biosynthesis, importantly also enabling production of the nucleotide thymidylate (Sangurdekar et al., 2011). Therefore if DNA synthesis was already partly inhibited (Table 5-1), adding trimethoprim could further sensitize the cells.

5.9 Virulence, cell division, and metal uptake pathways were dysregulated

Although significant differences were only observed in cytotoxicity of the overexpression strain in the absence of arabinose (Figure 5-3A), numerous virulence factors were dysregulated. Genes in T6SS and T1SS were dysregulated, while the T3SS, including its regulators, *exsD* and *pcrH*, and effectors, *exoY* and *exoS*, were all downregulated (Table 5-1 and Table A2). Similarly a repressor of T3SS, *ptrC*, was upregulated (Table 5-1) (Jin et al., 2011). Additionally, phenazine, *psl* and pyoverdine genes were generally upregulated, except for *phzG1*, and three alginate biosynthetic genes were dysregulated (Table 5-1 and Table A2). Interestingly, *algR*, *pvdS* and *ppyR*, regulators of alginate, pyoverdine and *psl*, were also upregulated (Attila et al., 2008; Hunt et al., 2002; Okkotsu et al., 2013).

Genes involved in cell division also showed a mild dysregulation, particularly at the protein level (Table 5-1). Interestingly, genes involved in iron, zinc and copper acquisition were also dysregulated, including the regulators *fur*, *zur* and *cueR* (Table 5-1).

5.10 In silico sRNA target prediction

The three tools IntaRNA2, RNAPredator and TargetRNA2 were used to predict sRNA targets (Table A10). Of the fourteen predicted targets, four were validated *in vitro*, showing changes in either transcript or protein abundance (Table 5-3). This included the methionine aminopeptidase *map*, the tRNA methyltransferase *trmU*, the probable TetR type transcriptional regulator PA0828 and PA2459 (Table 5-3).

Table 5-3. sRNA targets predicted *in silico* that were confirmed for PA2952.1 by RNA-Seq or proteomics as well as their FC, p-values (padj/p) and predictive methods.

Locus Tag	Name	Product Name	RNA-Seq		Proteomics		Predicted by
			FC	padj	FC	p	
PA0828		probable transcriptional regulator	-2.01	2.0E-02			RNAPredator, TargetRNA2
PA2459		hypothetical protein	-1.87	6.2E-04			RNAPredator, TargetRNA2
PA2626	<i>trmU</i>	tRNA methyltransferase			-1.05	2.4E-02	IntaRNA2, RNAPredator
PA3657	<i>map</i>	methionine aminopeptidase			1.12	3.6E-03	IntaRNA2, RNAPredator

5.11 Comparison of PA2952.1 omics data with previous datasets

To look for consistent themes, the differentially expressed RNA-Seq and proteomics datasets from the PA2952.1 overexpressing strain compared to those for the empty vector were compared with the above-described datasets.

5.11.1 Comparison with swarm vs. swim RNA-Seq

Comparison of RNA-Seq from swarm vs. swim with differentially expressed genes from the PA2952.1 overexpressing strain, showed an overlap of 288 genes (Figure A2). There were some similarities in the datasets, since 220 genes were regulated in the same direction in both datasets; whereas only 68 genes were oppositely regulated (Figure A3). Similarly-regulated genes included those encoding ribosomal proteins, pyoverdine biosynthesis enzymes, and regulators such as AlgR, FoxR, PhoP, PtrC, PpyR, PvdS, and SbrR.

5.11.2 Comparison of RNA-Seq and proteomics data for the PA0805.1 and PA2952.1 overexpressing strains

Although dozens to hundreds of unique genes and proteins were identified, comparison of the PA0805.1 and PA2952.1 overexpression strains omics datasets revealed striking commonalities (Figure A2, Figure A3). The PA0805.1-overexpression vs. PA2952.1-overexpression proteomics comparison was the most similar, with all of the common 363 commonly dysregulated proteins showing the same direction of regulation. Comparison of the two RNA-Seq experiments for the PA0805.1 and PA2952.1 overexpression strains also revealed considerable similarities, with 220 of the 258 commonly dysregulated genes showing the same direction of regulation. This indicates that while there were many unique genes and proteins, there were also prominent commonalities between PA0805.1 and PA2952.1, suggesting there was a relationship between the effects mediated by the two sRNAs.

5.12 Discussion

Here I probed the role of sRNAs in motility and other adaptive processes. A total of 21 constructs were made featuring sRNAs dysregulated during swarming or biofilm formation and functions were identified for five of these (including PA0805.1) when cloned to enable overexpression, since this enhances the known inhibitory functions of sRNAs. In contrast, in this study, no phenotypes were observed for the overexpression of *rsmY*. This may be due to redundancy with *rsmZ*; for instance, when *rsmY* was overexpressed, *rsmZ* could have been downregulated to cancel out any effects (Kay et al., 2006). I also did not observe a phenotype for *srbA*, but this may be because the sRNA was overexpressed rather than deleted.

Two of these sRNAs, *prhH* and PA2952.1, are related by an interconnection with Fur, the ferric uptake regulator, a transcriptional repressor that can also function as an activator (Wilderman et al., 2004). Under iron-depleted conditions, the expression of *prhH* is highly induced (Wilderman et al., 2004), while it is 163-fold upregulated under swarming conditions (Gill et al., 2018). Results presented here indicated that *prhH* was involved in both cytotoxicity (Figure 5-3B) and the production of pyoverdine (Figure 5-4), and that overexpression of *prhH* led to a reduction in swimming motility (Figure 5-2). Similarly, in the PA2952.1 overexpression strain, Fur had increased abundance in the proteome, iron acquisition and virulence factors were dysregulated, and swimming motility was decreased to a similar extent (Table 5-1, Figure 5-2).

Other interesting regulators with altered abundance in the PA2952.1 overexpression strain included AlgR, a regulator of alginate, swarming, twitching and rhamnolipid production (Okkotsu et al., 2013), GlnK and NtrB, two regulators of nitrogen metabolism, PhoP, a two-component sensor involved in antimicrobial resistance and virulence (Gellatly et al., 2012; Macfarlane et al., 2000), PvdS, a sigma factor controlled by Fur that regulates pyoverdine and exotoxin A (Hunt et al., 2002), RsaL, a regulator of QS and virulence (De Kievit et al., 1999; Lee & Zhang, 2014), and SbrIR, a sigma-anti-sigma factor pair that controls swarming motility and biofilm formation (McGuffie et al., 2016) (Table 5-1).

Upon overexpression of the sRNA PA2952.1, hundreds of genes and proteins showed significant changes in abundance (Table A2), accompanied by several phenotypic differences (Figure 5-2, Figure 5-5A and B) indicating that this has the hallmarks of a global regulatory system. A model was proposed to account for this surprisingly large amount of dysregulation (Figure 5-6). In a hierarchical fashion, overexpression of PA2952.1 directly or indirectly led to alterations in 82 regulatory factors, which then in turn influenced the expression of downstream genes (Figure 5-6).

For example, AlgR that was affected by PA2952.1 could in turn influence alginate, ExsD, PcrH and PtrC influence T3SS, Fur influence iron uptake, PilS influence type IV pili and flagella, PmrB influence the *arn* operon, and PvdS and PpyR influence pyoverdine and psl biosynthesis (Figure 5-6). This might also influence additional downstream genes without an obvious regulator, or genes with multiple potential regulators, and further experimentation would be required to determine the exact pathway. Downregulation of pili and certain flagellar genes, as well as genes required for swarming, would then lead to decreases in swarming and swimming motilities, upregulation of *mexGHI-opmD* and the *arn* operon to mediate aminoglycoside resistance, and downregulation of certain genes involved in DNA synthesis to influence trimethoprim susceptibility. Overall, this highlights a potential key role for the sRNA PA2952.1 in modulating gene expression and controlling bacterial lifestyles, and demonstrates that predictive programs that usually indicate a very modest number of target genes have the potential to dramatically underestimate actual targets.

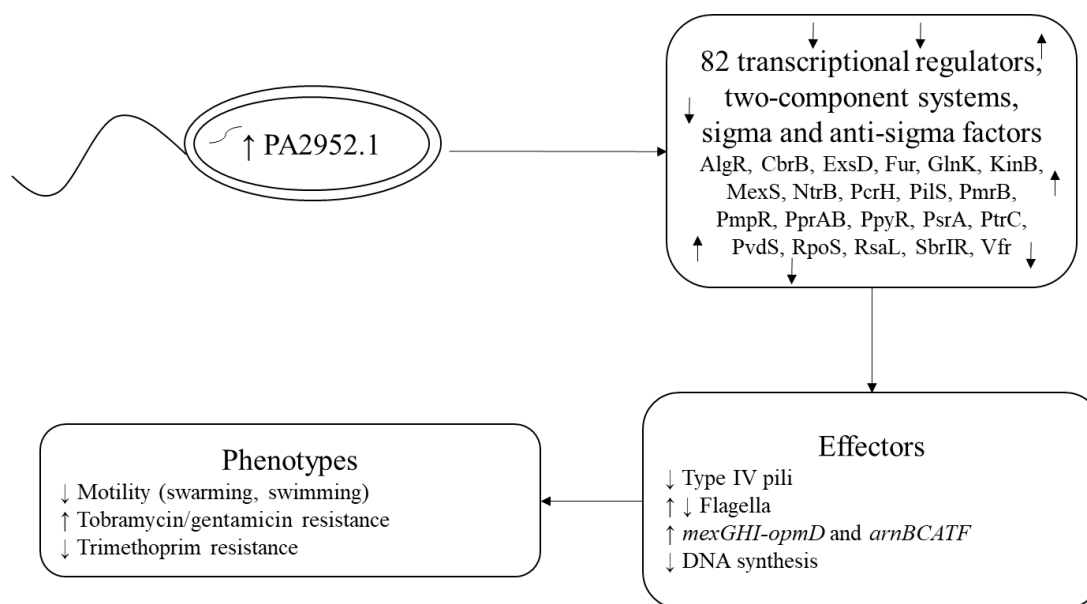


Figure 5-6. Proposed model for how the overexpression of PA2952.1 dysregulates many genes, resulting in altered phenotypes. Connecting arrows represent direct or indirect regulation.

Chapter 6: The role of swarming *in vivo*

6.1 Introduction

Standard drug testing and development is typically performed using planktonic bacterial cultures. While convenient and standardized, the planktonic, rapidly-dividing bacterium is not necessarily reflective of the growth state *in vivo*. Biofilms, for example, are associated with two-thirds of all infections (Boisvert et al., 2016). Bacteria may also exist as motile surface-associated communities within the host; therefore drug development and treatment strategies may be better informed by considering alternative growth states. Indeed, some recent research has focused on the use of peptides to specifically target biofilms (Pletzer et al., 2016), and these compounds show efficacy in treating recalcitrant abscess infections *in vivo* (Pletzer et al., 2018).

It is interesting to consider whether compounds that specifically target swarming motility (or target both swarming and biofilms) may also exist, and whether the use of such compounds could help to prevent the dissemination of bacteria *in vivo*. Peptide 1037, a derivative of the human cathelicidin LL-37, was already shown to inhibit swarming motility, as well as biofilm formation (de la Fuente-Núñez et al., 2012). Peptide 1018, a cationic peptide derived from bactenecin (de la Fuente-Núñez et al., 2016), was previously shown to act against biofilms at low concentrations (de la Fuente-Núñez et al., 2014), as well as having beneficial immunomodulatory effects (Achtman et al., 2012; Rivas-Santiago et al., 2013; Wieczorek et al., 2010). Therefore, the effect of 1018 on swarming motility was investigated in greater detail.

Swarming tends to correlate with other bacterial behaviours such as biofilm formation (Caiazza et al., 2007). In addition, the flagella also powers swimming motility, whereas the type IV pilus is also used for twitching; thus, there are also overlaps between these three forms of motility. It was therefore necessary to find a mutant specific for swarming motility so that the effects of other behaviours could be ruled out in an *in vivo* model.

6.2 The host defense peptide 1018 specifically inhibited swarming motility

In contrast to the resistance of swarming cells to most tested antibiotic classes (Chapter 3), swarming motility was inhibited at low concentrations of the host defense peptide 1018 (Figure 6-1). This effect appeared to be specific to swarming motility, since swimming and twitching were unaffected at the same concentrations of 1018 (up to 20 µg/ml).

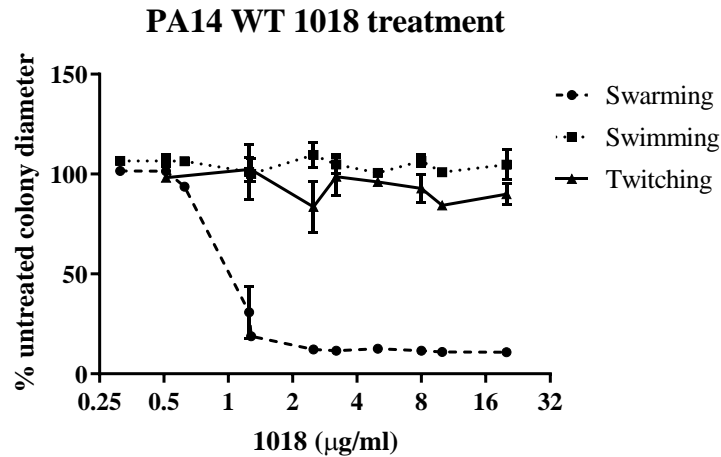


Figure 6-1. Peptide 1018 specifically inhibited swarming motility. $n \geq 3$.

6.3 Screen of swarming-deficient mutants

Next, I sought to find a mutant that would reflect the specificity of 1018 treatment (inhibited swarming but not swimming or twitching). The 233 previously-identified PA14 transposon insertion mutants (Yeung et al., 2009) were initially screened for swarming and swimming motility in BM2 glucose (swarming: 0.5% agar and 0.1% CAA; swimming: 0.25% agar and 7 mM $(\text{NH}_4)_2\text{SO}_4$). A list of initial candidates was then generated using cutoffs of less than 50% WT swarming and greater than 70% WT swimming. These mutants were then screened for other relevant phenotypes including twitching, biofilm formation, and cytotoxicity (Table 6-1).

Amongst these mutants, twitching motility generally did not vary from WT, but biofilm formation was often either decreased or increased. Cytotoxicity tended to be modestly decreased in these mutants, which may correlate with the observation that swarm cells overexpress virulence factors (Chapter 3). Moving forward, the mutant in *ptsP* was selected as the best candidate.

Table 6-1. Candidate swarming-deficient mutants. Numbers shown are percent of WT. Numbers shown in **bold** are less than 70% of WT or significantly greater than 100% of WT. The allele numbers 1553 and 1946 designate the position (bp) of the transposon insertion for the two *ptsP* mutants. $n \geq 3$.

Tn mutant	Function	Swarm	Swim	Twitch	Biofilm	Cytotox- icity
<i>dsbM</i>	protein-disulfide isomerase	2.2±0.4	78.6±5.7	83.0±11.8	285.4±19	103.3±6.5
<i>ybeB</i>	conserved hypothetical protein	2.9±1.0	82.1±8.2	34.2±2.9	22.7±3.5	49.8±5.3
<i>epd</i>	D-erythrose 4-phosphate dehydrogenase	3.1±1.7	101.3±3.3	101.0±2.0	212.5±20	78.5±11.1
<i>ampG</i>	permease for AmpC beta-lactamase expression	7.7±0.9	99.6±2.9	104.7±7.8	29.0±3.8	3.0±1.0

Tn mutant	Function	Swarm	Swim	Twitch	Biofilm	Cytotoxicity
<i>ptsP</i> (1553)	phosphoenolpyruvate-protein phosphotransferase	10.4±1.1	86.0±4.6	107.3±13.9	82.2±3.8	57.9±4.2
PA14_59060	hypothetical protein	11.1±4.0	95.7±6.2	77.6±7.1	99.1±10.3	13.1±5.3
<i>ptsP</i> (1946)	phosphoenolpyruvate-protein phosphotransferase	11.9±1.2	76.6±3.8	108.3±5.9	75.1±4.4	59.4±5.8
PA14_17160	intergenic PA14_17150-17170	18.0±2.0	97.2±2.9	79.6±1.6	30.9±8.6	63.2±4.7
<i>miaA</i>	tRNA delta(2)-isopentenylpyrophosphate transferase	28.7±1.8	92.6±2.5	53.7±6.5	73.4±6.7	13.1±5.9
<i>surE</i>	stationary phase survival protein	34.6±3.1	89.4±6.5	89.0±6.7	86.1±6.4	58.4±8.8

6.4 A mutant in *ptsP* was specifically inhibited for swarming motility

A deletion mutant $\Delta ptsP$ was generated and complemented. Motility assays confirmed that the mutant had greatly reduced swarming motility, but relatively normal levels of swimming and twitching (Figure 6-2). The complemented strain $\Delta ptsP^+$ had substantially restored swarming motility and normal levels of swimming and twitching.

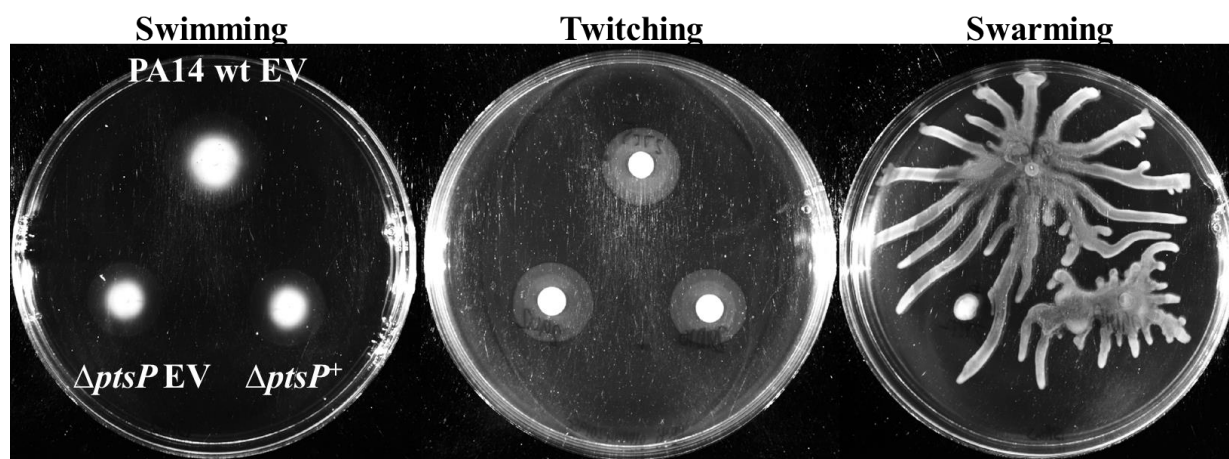


Figure 6-2. The $\Delta ptsP$ mutant had deficient swarming ability but relatively normal swimming and twitching motility. $n \geq 3$.

To confirm that the $\Delta ptsP$ mutant had no growth deficiencies, growth curves were performed in four different media: liquid swarming media (BM2 glucose), LB, and two host-like media, SCFM and RPMI. In these four media, the $\Delta ptsP$ mutant grew no differently from WT (Figure 6-3).

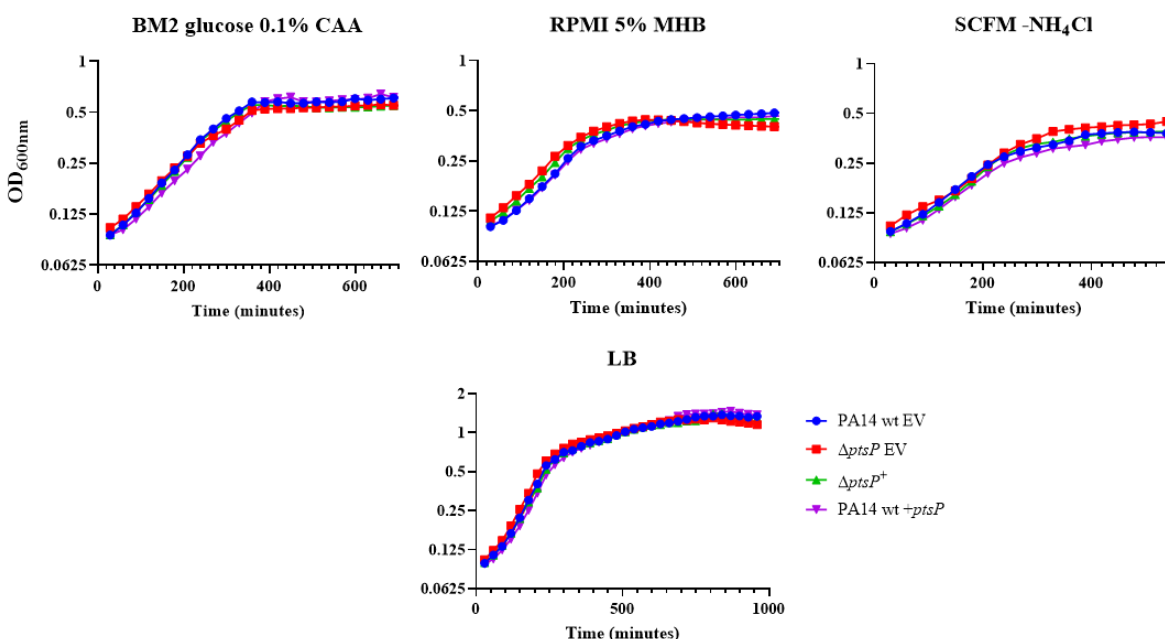


Figure 6-3. Growth curves for the $\Delta ptsP$ mutant in four different media. $n = 3$.

To confirm that *ptsP* had no effect on the production of virulence factors, qRT-PCR was performed on the $\Delta ptsP$ mutant. No significant dysregulation was observed for *aprA* (the T1SS alkaline metalloproteinase), *lasA* (T2SS cytotoxic protease), *pchF* (pyochelin synthetase), *pcrG* (a regulator in T3SS), *rhlR* (QS regulator) or *vfr* (regulator of virulence factors) (Table 6-2). As expected, *ptsP* was strongly downregulated in the $\Delta ptsP$ mutant, and somewhat overexpressed in the complemented $\Delta ptsP^+$ strain. Cytotoxicity was also investigated, and although the cytotoxicity of $\Delta ptsP$ was significantly decreased compared to WT, this amounted to a minor difference (~ 0.15 absorbance values) that was partially restored by complementation (Figure A8). In any case, the swarming phenotype (Figure 6-2) was much more dramatic than the cytotoxicity phenotype.

Table 6-2. Virulence factors were not dysregulated in the $\Delta ptsP$ mutant. $n = 3$.

Gene	$\Delta ptsP$ EV vs. WT EV	$\Delta ptsP^+$ vs. WT EV
<i>aprA</i>	-1.6 ± 0.2	1.0 ± 0.3
<i>lasA</i>	1.6 ± 1.0	3.8 ± 1.5
<i>pchF</i>	1.1 ± 0.2	1.4 ± 0.4
<i>ptsP</i>	-413.7 ± 124.0	23.6 ± 11.9
<i>pcrG</i>	1.1 ± 0.3	-1.5 ± 0.3
<i>rhlR</i>	-1.5 ± 0.1	-1.1 ± 0.1
<i>vfr</i>	-1.3 ± 0.0	-1.4 ± 0.2

6.5 The swarming-deficient mutant $\Delta ptsP$ had reduced virulence *in vivo*

Having confirmed that the mutant $\Delta ptsP$ was specifically deficient for swarming motility, we sought to test the mutant *in vivo* in the cutaneous abscess model, to determine whether the lack

of swarming had an effect on virulence. Mutant and complemented strains (2.5×10^7 CFU) were injected subdermally into the back of mice, and after incubation overnight, mice were sacrificed and internal organs were harvested and plated for CFUs. The wild type was widely disseminated amongst the organs (heart, kidney, liver, lung, and spleen) (Figure 6-4). In contrast, far fewer CFU/organ were recovered for the $\Delta ptsP$ mutant, which could be due to its deficiency in swarming motility. On average, more CFU/organ were recovered for the complemented strain $\Delta ptsP^+$ than the mutant $\Delta ptsP$, although the difference did not always reach statistical significance. Mice treated with 1018 had an intermediate level of CFU/organ recovered, showing that 1018 was able to reduce dissemination in the host.

6.6 Discussion

In this study, the $\Delta ptsP$ mutant was shown to have greatly reduced swarming ability, and organ invasion *in vivo*, while maintaining normal levels of swimming and twitching. PtsP is a phosphoenolpyruvate-protein phosphotransferase involved in the regulation of carbon and nitrogen metabolism. The equivalent of enzyme I Ntr (EI^{Ntr}), PtsP is a cytoplasmic enzyme involved in a phosphorelay that regulates carbon and nitrogen source utilization (Higa & Edelstein, 2001; Reizer et al., 1999; Velázquez et al., 2007). PtsP has an N-terminal GAF sensor domain and is thought to function primarily as a regulator rather than directly participating in the phosphorylation (or translocation) of carbohydrates (Mavrodi et al., 2006; Reizer et al., 1999). The *ptsP* mutant has been identified in several screens for virulence factors in plants (Mavrodi et al., 2006; Rahme et al., 2016, 2019), *C. elegans* (Feinbaum et al., 2012; Tan et al., 1999) and mammals (Higa & Edelstein, 2001), although little is known about why *ptsP* is a virulence factor. I suggest here it may be due to the swarming deficiency of the $\Delta ptsP$ mutant.

The $\Delta ptsP$ mutant was substantially but incompletely complemented by reintroducing *ptsP* on a plasmid. There might be valid reasons for the lack of full complementation; in this case it is possible that *ptsP* was expressed too highly in the $\Delta ptsP^+$ strain (Table 6-2), and that overexpression of this gene actually inhibits swarming. Furthermore, *ptsP* is part of a three-gene operon between *rppH* and PA0388, and the lack of the other two genes on the complementation plasmid may reflect a requirement for the complete operon for full restoration of wild type phenotype.

A question for future exploration is why *ptsP* is required for swarming. Since it is possible the $\Delta ptsP$ mutant may have deficient levels of certain metabolites, attempts were made to restore swarming of the $\Delta ptsP$ mutant by adding carbon sources such as pyruvate or citrate. Addition of

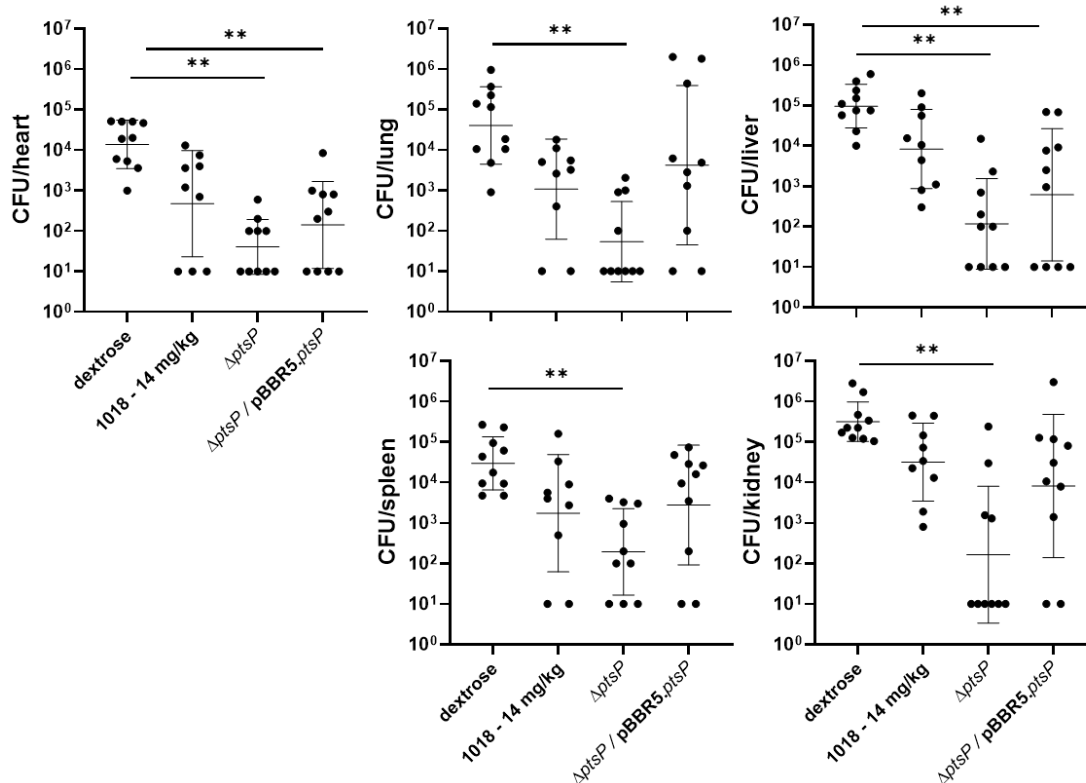


Figure 6-4. The $\Delta ptsP$ mutant had reduced organ invasion *in vivo*. CD-1 mice were injected with 2.5×10^7 CFU to form a cutaneous abscess. After 16-18 h, organs were harvested, homogenized and plated for CFU counting.

pyruvate enhanced swarming of both wild type and the mutant; whereas citrate inhibited wild type swarming at concentrations greater than 25 mM (data not shown); therefore firm conclusions could not be drawn. It may be that the strong dependency of swarming on medium components such as carbon and nitrogen sources affected the ability of the $\Delta ptsP$ mutant to swarm since its lack would impact on the sugars that can be readily metabolized by *Pseudomonas*. There may be other more subtle consequences, since e.g. *ptsP* in *P. putida* affects production of polyhydroxyalkanoates (Velázquez et al., 2007) that are precursors of rhamnolipid (Déziel et al., 2003).

In conclusion, peptide 1018 inhibited swarming motility at low concentrations that had no effect on swimming or twitching. A corresponding mutant $\Delta ptsP$ was found by phenotypic screening that was also specifically inhibited for swarming, but not swimming or twitching. Testing of $\Delta ptsP$ *in vivo* revealed a greatly reduced organ invasion by this mutant. This indicates that swarming may play a role in bacterial dissemination *in vivo*.

Chapter 7: Conclusion

7.1 Summary of thesis work

Here I have shown that swarming motility in the opportunistic pathogen *P. aeruginosa* is a distinct and complex adaptation. RNA-Seq comparing the transcriptome of swarming vs. swimming cells revealed that swarming cells overexpress numerous virulence and iron acquisition factors, while modestly downregulating ribosomal proteins (total 1,581 DE genes) (Chapter 3). Antibiotic susceptibility testing showed that swarming bacteria were also adaptively resistant to many antibiotic classes, including aminoglycosides, β -lactams, macrolides, chloramphenicol, ciprofloxacin, tetracycline and trimethoprim. An exception to this was the lipopeptide polymyxin B, to which swarming cells were not resistant. I focused on the aminoglycoside tobramycin and performed mutant screens, discovering that mutants in the LPS biosynthetic gene *wbpW* and phage-related pyocins and their regulator *priN* were resistant to tobramycin under swarming conditions. Membrane permeability assays confirmed that the mutant in *wbpW* had reduced membrane permeabilization to tobramycin. In total, I found 41 mutants that were resistant to tobramycin under swarming conditions, indicating that swarming-mediated antibiotic resistance is a multigenic phenomenon. I also treated swarming cells with subinhibitory tobramycin and used RNA-Seq to discover that the multidrug efflux pump MexXY was upregulated. To date, this is the first time that efflux has been demonstrated as a mechanism of resistance for swarming cells, since previous mutant studies failed to find an association, possibly due to the presence of redundant efflux systems (Lai et al., 2009). This study also advances the field by employing RNA-Seq to more accurately describe the transcriptome of swarming cells, including 104 dysregulated regulatory factors and the genes corresponding to the 41 mutants that were resistant to tobramycin under swarming conditions, whereas relatively little was previously known concerning specific mechanisms of antibiotic resistance in swarming cells.

Similar to polymyxin B, I found that swarm cells displayed susceptibility to the cationic peptide 1018 (Chapter 6). Tendril formation was completely inhibited at concentrations greater than 2 $\mu\text{g/ml}$, while swimming and twitching proceeded normally up to 20 $\mu\text{g/ml}$. This suggests that 1018 may have specific anti-swarming properties and could be used to target swarming cells in cases where antibiotics may be less effective. To investigate this further, I identified a swarming-specific mutant in *ptsP*. *In vivo* testing in an acute murine infection model revealed that 1018 treatment reduced bacterial dissemination in internal organs, and the $\Delta ptsP$ mutant was recovered at even lower rates from organs. This is an interesting finding in the field of swarming motility,

since to date little has been done to directly investigate the role of swarming *in vivo*.

To learn more about the regulation of swarming motility, in addition to transcriptional regulators, I studied sRNAs dysregulated under swarming conditions by overexpressing them and screening for phenotypes (Chapters 4 and 5). The screens revealed a strain overexpressing the sRNA, PA0805.1, that possessed numerous phenotypes, including reduced motility (swarming, swimming and twitching), and increased adherence, cytotoxicity and tobramycin resistance (Chapter 4). RNA-Seq and proteomics revealed broad transcriptomic and proteomic changes, including 118 regulatory factors, downregulated pilus genes, upregulated adherence and virulence factors, and upregulated multidrug efflux systems (total 1,121 DE genes and 925 DE proteins), suggestive of a hierarchical network. A deletion mutant Δ PA0805.1 was also constructed and was supersusceptible to tobramycin under swarming conditions.

Another sRNA overexpressing strain, PA2952.1, was studied and showed to have reductions in swarming and swimming but not twitching (Chapter 5). Overexpression of this sRNA also led to resistance to tobramycin and gentamicin, and supersusceptibility to trimethoprim. Transcriptomic and proteomic approaches uncovered 784 DE genes and 445 proteins with differential abundance. This included downregulated pili genes, dysregulated flagellar genes, upregulated multidrug efflux genes *mexGH*, upregulated LPS modification operon *arnBCATF*, and dysregulated DNA synthesis genes.

The large transcriptomes of the sRNAs PA0805.1 and PA2952.1 are relatively unprecedented for sRNAs (Chapters 4 and 5). The transcriptomes of mutants in the RNA-binding proteins Hfq and Rsm also indicate hundreds of differentially expressed genes (Romero et al., 2018; Sonnleitner et al., 2018), consistent with the conclusion that PA0805.1 and PA2952.1 might serve key regulatory functions in *P. aeruginosa*.

The sRNA *prrH* was also studied and shown to be involved in the production of the siderophore pyoverdine and cytotoxicity against HBE cells, a new addition to its previously described phenotypes (Chapter 5). In addition, overexpression of *prrH* led to reduced swimming motility. Two other sRNAs, PA14sr120 (a short version of PA0805.1) and PA1091.1b, were also shown to be involved in tobramycin resistance and trimethoprim susceptibility, respectively. These studies contribute to the field by providing phenotypic characterization of more than a dozen sRNAs, most of which were previously completely uncharacterized.

Therefore, swarming motility is a behaviour conferring antibiotic resistance (but inhibited by 1018) that is regulated by sRNAs and likely plays a role in invasiveness *in vivo*.

7.2 Applications

These studies provide insights into the reasons behind observations that standard antimicrobial susceptibility testing does not always accurately predict *in vivo* efficacy (Ersoy et al., 2017). It shows that bacteria may enter a state of reduced drug susceptibility due to their growth as multicellular communities, such as swarming colonies or as shown by others, biofilms. Research in this thesis shows that lipopeptides or cationic peptides may be more effective against swarming bacteria than other antimicrobial agents; in particular, peptide 1018 already shows promise as an anti-swarming agent. Efflux pump inhibitors in combination with other antimicrobial drugs (Wang et al., 2016) may be another potential venue for investigation, based on RNA-Seq results of subinhibitory tobramycin treatment, which showed that MexXY was upregulated. If swarm cells have decreased outer membrane permeability, then agents that increase membrane permeability may be useful as well (Vaara, 1992).

sRNAs also have potential applications as therapeutics, since they are relatively easy to synthesize and customize, and could be used to reverse specific drug resistance mechanisms (Chan et al., 2017; Di Noto et al., 2019). Potential delivery systems include nanoparticles, phages, extracellular vesicles, liposomes and the CRISPR-Cas system (Di Noto et al., 2019). sRNAs themselves, or a complementary RNA to silence the sRNA, may have use in modifying bacterial behaviour. Swarming and motility-inhibitory sRNAs could have benefits in acute infections, and PA2952.1 could be used in conjunction with trimethoprim, to which cells are sensitized. Conversely, an anti-sense version of PA0805.1 could be used to sequester PA0805.1, decrease expression of virulence factors, efflux pumps, and bacterial adhesion, leading to improved patient outcomes. Inhibiting *prhH* is another intriguing possibility, since bacteria may have difficulty surviving in the iron-depleted host environment without appropriate regulation of iron acquisition and utilization. In fact, mutants in *Fur* are conditionally essential (Pasqua et al., 2017), and decreased virulence could be another added benefit.

7.3 Future directions

In this study, resistome genes were mined from the literature and used in combination with RNA-Seq and qRT-PCR data to identify initial candidates. Future work could include a comprehensive mutant library screen, or a Tn-Seq (transposon sequencing) library screen, in order to determine if any other candidates may be present at a genome-wide scale. Tn-Seq would provide additional information about mutants that survived or were eliminated, and also the relative abundance or fitness of different mutants. Tn-Seq data could be compared back to data generated

in this thesis to provide additional support. This could be done on swarming colonies in the presence and absence of tobramycin. Luminescent reporter strains could also be constructed for key swarming regulators in order to assess expression *in vivo*.

Antimicrobial agents could be developed to specifically inhibit swarming motility by screening drugs in the swarming agar dilution assay, or this assay could be added as an additional step during drug screening and development to better inform on the response of bacteria grown under different conditions. The swarming assay can be modified to allow more high throughput methods, such as the 6 well format (Section 2.2.6), or a 96 well stamp on large square plates (Yeung et al., 2009). Such anti-swarming agents could then be tested alone or in combination with conventional antibiotics, to investigate potential synergistic effects.

The mechanism by which 1018 inhibits swarming motility is another question for further research. Some research has already been done to address this question, including a mutant library screen and RNA-Seq of 1018-treated swarming colonies (Wilkinson, 2018), but further in-depth characterization of mutants or Tn-Seq could provide more mechanistic detail. Likewise, the mechanism causing inhibition of swarming in the $\Delta ptsP$ mutant is unclear and could be addressed by further characterization of the mutant, possibly by RNA-Seq.

Further screening of sRNAs could be performed to find an ideal sRNA that would modify bacterial behaviour as desired. Computer modeling approaches could come into play, and predictions could be easily tested since nucleic acids are inexpensive to synthesize and easy to manipulate. In addition, combinations of sRNAs could be used to achieve a desired effect. It would be interesting to transform multiple sRNAs into one strain and overexpress them simultaneously to observe cumulative effects.

Further characterization of the sRNAs PA0805.1 and PA2952.1 could also clarify specific sRNA targets by experimental approaches such as (G)RIL-Seq (Han et al., 2016; Melamed et al., 2018), where sRNAs are ligated to target mRNAs and then sequenced. It seems likely that PA0805.1 and PA2952.1 would have many targets, given the extensive downstream effects, and it would clarify the mechanism to validate targets experimentally.

In conclusion, swarming motility in *P. aeruginosa* is intricately regulated by both transcriptional regulators and sRNAs to give rise to antibiotic resistance and virulence *in vivo*.

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Appendices

Appendix A Supplementary Figures

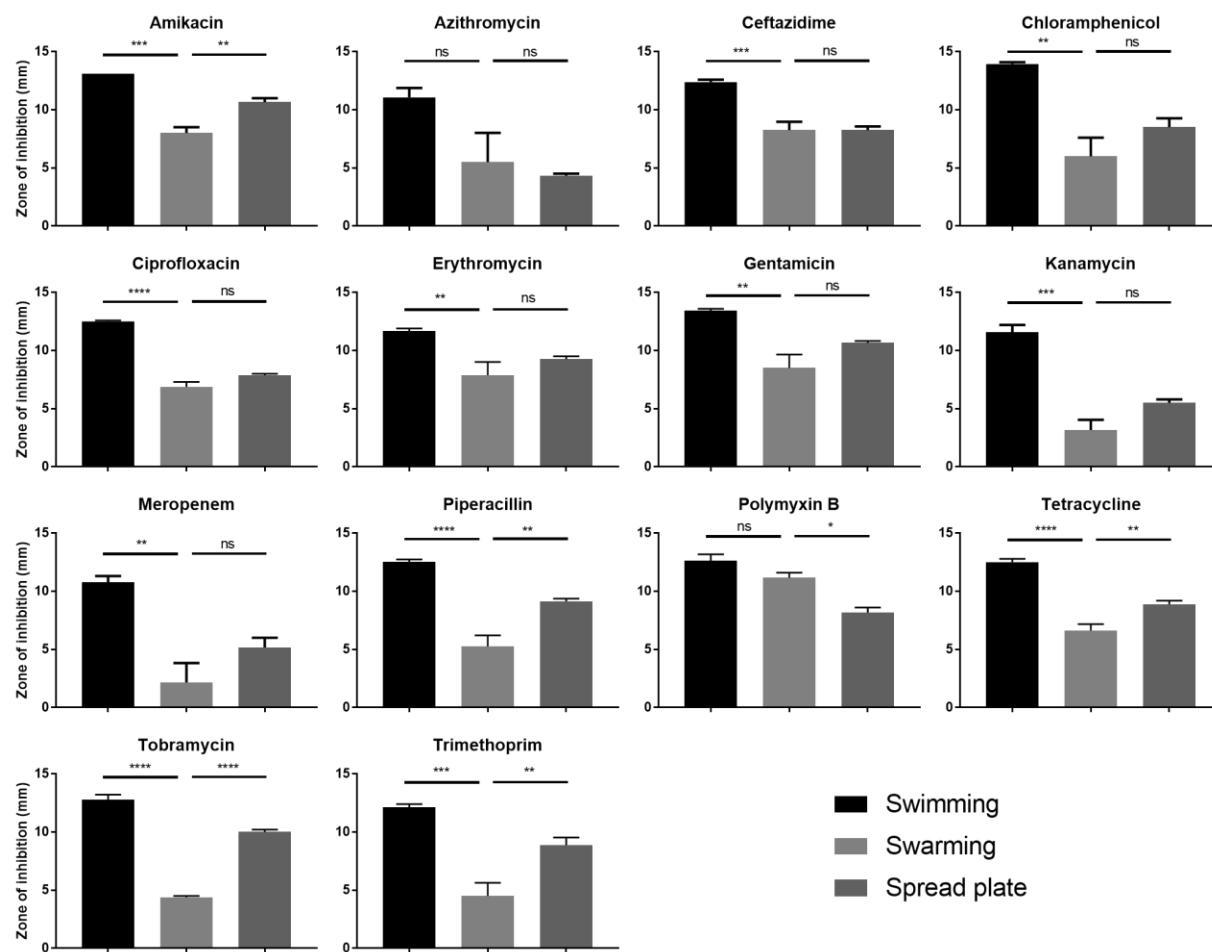


Figure A1. Disc diffusion assay for PA14 WT performed at a higher agar concentration. Agar concentrations were: 0.5% (swarming), cf. 0.3% (swimming), and 1.5% (spread plate). $n \geq 3$.

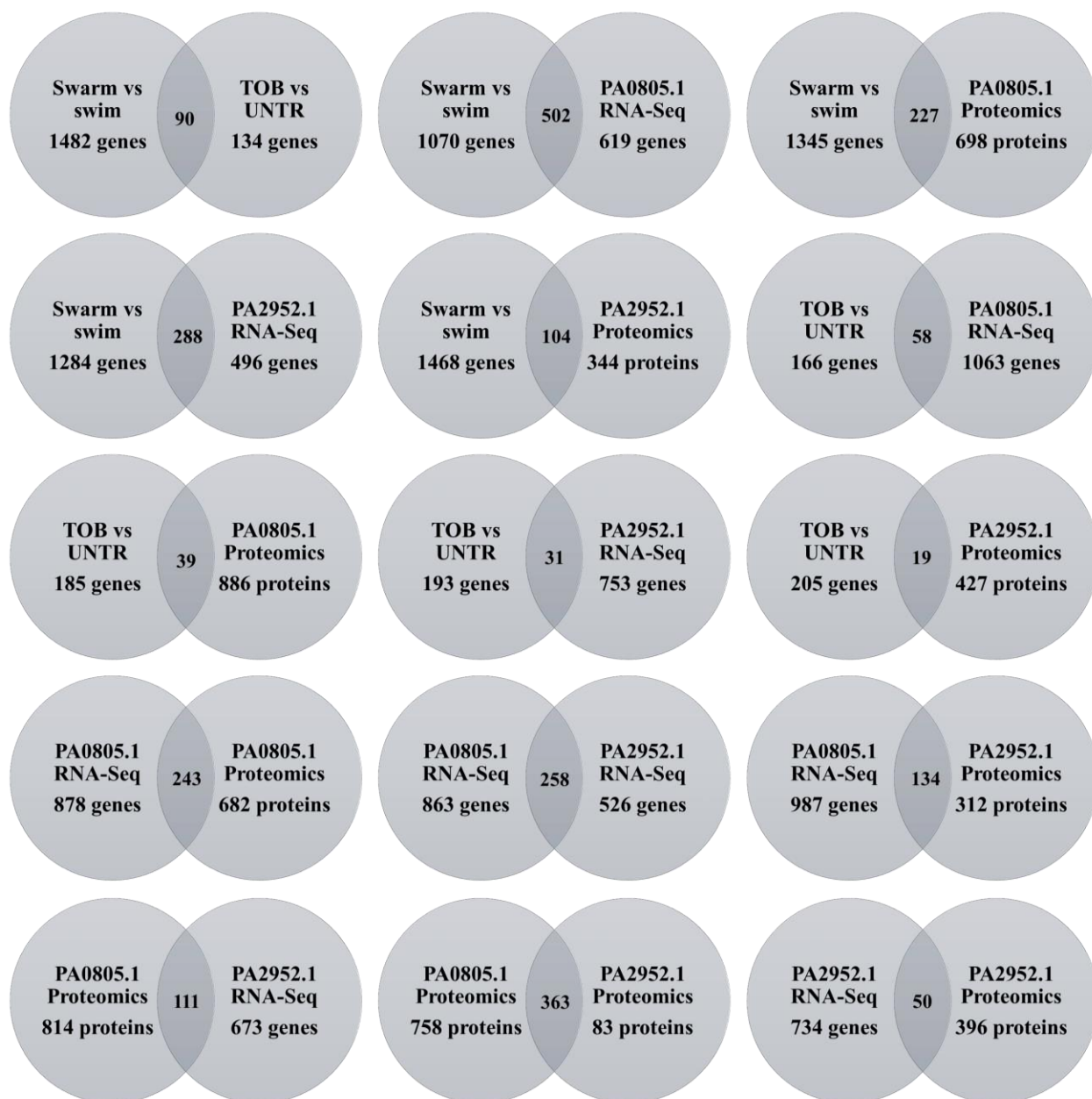


Figure A2. Venn diagrams showing common and unique genes for omic comparisons.

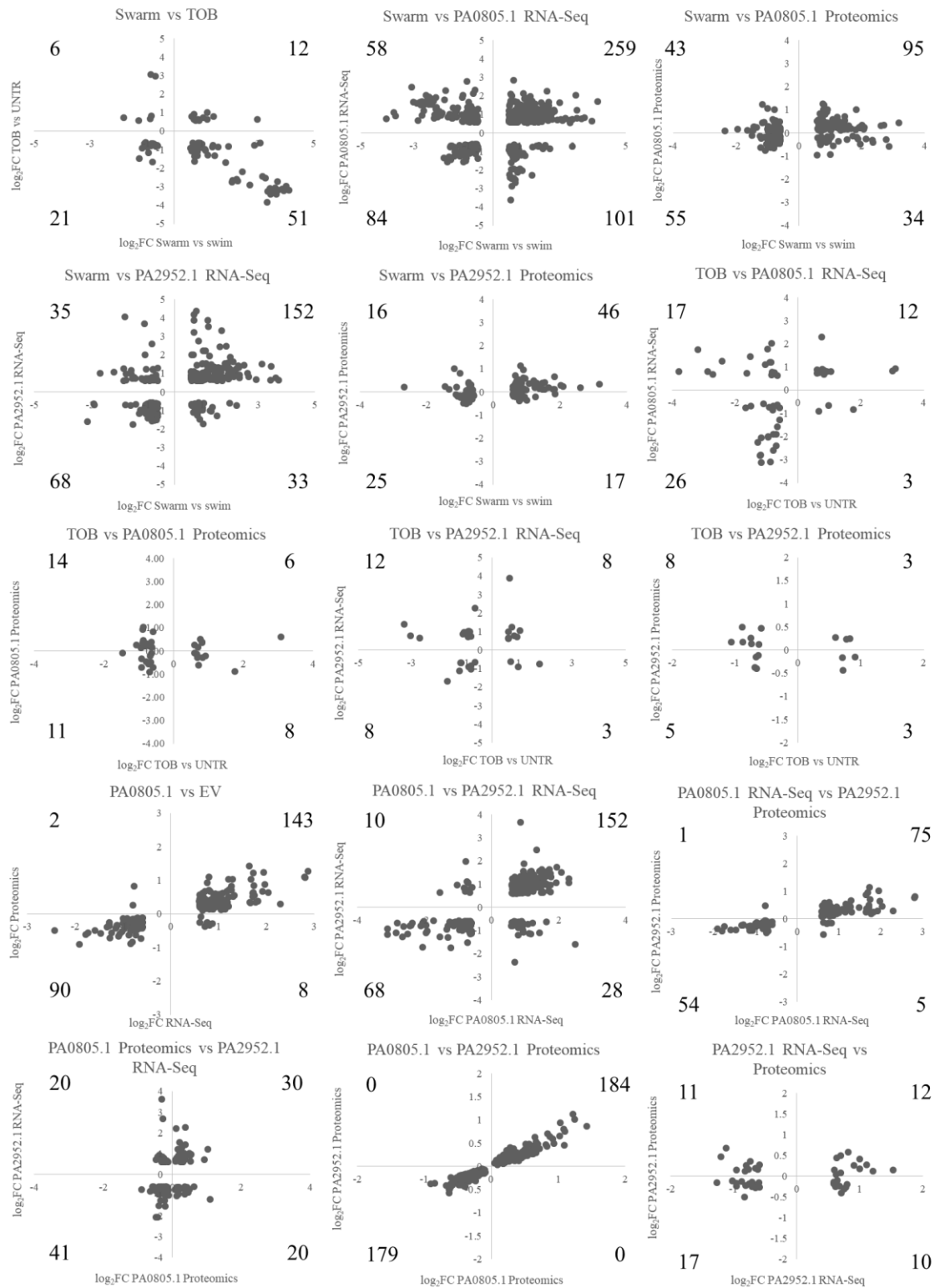


Figure A3. Scatterplots showing correlations of common genes for omic comparisons. Numbers in the four corners of each graph show the number of genes/proteins found in each quadrant.

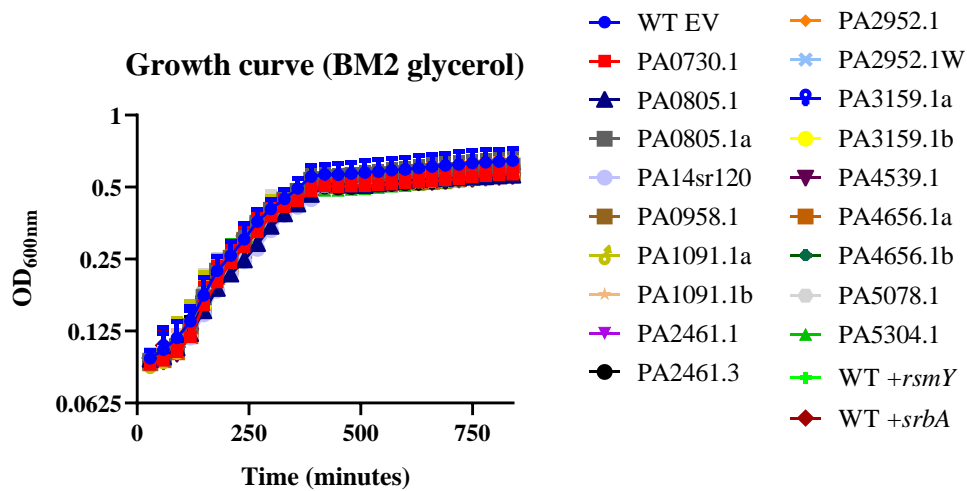


Figure A4. Growth curves of sRNA overexpression strains in BM2 glycerol with 1% arabinose showed little difference compared to EV. $n \geq 3$.

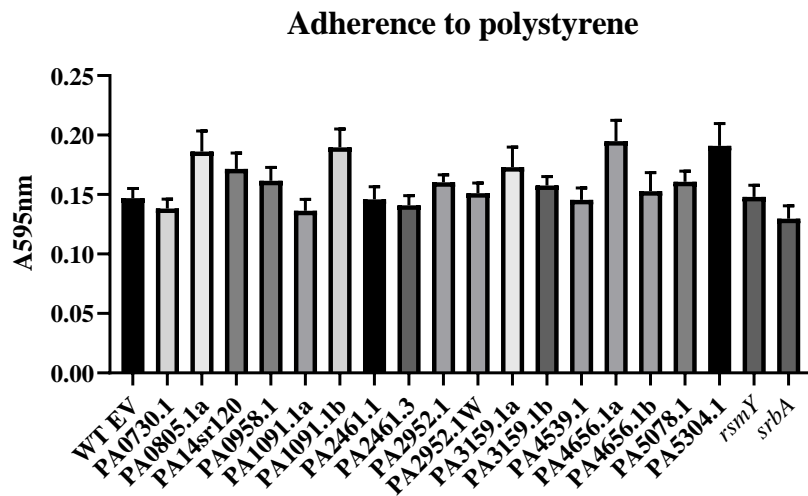


Figure A5. Adherence of sRNA overexpression strains to polystyrene plates. Statistically significant differences were determined using one-way ANOVA. $n \geq 3$.

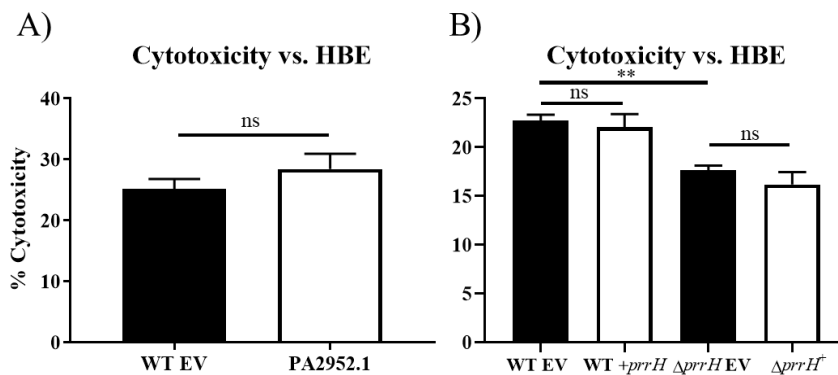


Figure A6. Cytotoxicity phenotypes of sRNA overexpression strains with 1% arabinose. a) overexpression of PA2952.1 compared to WT EV. b) deletion and overexpression of *prpH*. Statistically significant differences were determined by unpaired t test (a) or one-way ANOVA (b). $n \geq 3$.

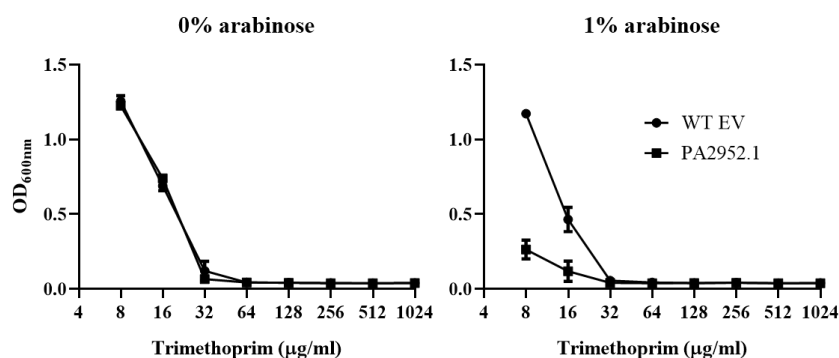


Figure A7. Subinhibitory trimethoprim inhibited the growth of the PA2952.1 overexpression strain in standard MICs in BM2 glycerol with 1% arabinose. $n = 3$.

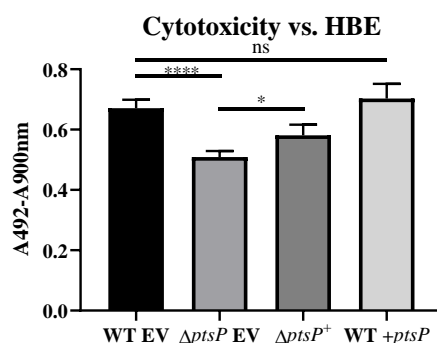


Figure A8. Cytotoxicity phenotype of the $\Delta ptsP$ mutant. Statistically significant differences were determined by ANOVA. $n \geq 3$.

Appendix B Supplementary Tables

B.1 PA14 RNA-Seq data

Table A1. Compilation of all PA14 RNA-Seq data reported in this thesis.

PAO1	PA14	Name	Product Name	Swarm vs. swim		TOB vs. UNTR	
				FC	padj	FC	padj
PA0007	PA14_00080		hypothetical protein	1.93	1.9E-22		
PA0013	PA14_00140		conserved hypothetical protein	-1.92	2.9E-22		
PA0026	PA14_00300	<i>plcB</i>	phospholipase C, PlcB	1.87	8.9E-19		
PA0027	PA14_00310		hypothetical protein	2.81	1.0E-28		
PA0028	PA14_00320		hypothetical protein	3.45	3.2E-38		
PA0038	PA14_00470		hypothetical protein	1.77	4.3E-13		
PA0039	PA14_00480		hypothetical protein	2.28	9.1E-38		
	PA14_00520		hypothetical protein			-2.11	8.5E-03
PA0044	PA14_00560	<i>exoT</i>	exoenzyme T			-1.93	4.3E-03
PA0045	PA14_00570		hypothetical protein	-2.21	5.1E-41	-1.85	1.5E-02
PA0046	PA14_00580		hypothetical protein	-2.07	7.4E-38		
PA0047	PA14_00590		hypothetical protein	-2.32	3.5E-39		
PA0048	PA14_00600		probable transcriptional regulator	1.66	9.1E-06		
PA0050	PA14_00630		hypothetical protein	-1.97	5.0E-13		
PA0051	PA14_00640	<i>phzH</i>	potential phenazine-modifying enzyme	-1.85	4.7E-05		
PA0052	PA14_00650		hypothetical protein	2.25	9.3E-16		
PA0056	PA14_00680		probable transcriptional regulator	1.53	2.0E-03		
PA0057	PA14_00690		hypothetical protein	-1.80	1.2E-09		
PA0059	PA14_00710	<i>osmC</i>	osmotically inducible protein OsmC	2.84	6.4E-22		
PA0060	PA14_00720		conserved hypothetical protein	2.41	6.7E-29		
PA0062	PA14_00740		hypothetical protein	1.52	4.1E-05		
PA0071	PA14_00830	<i>tagR1</i>	TagR1			-1.83	8.1E-03
PA0073	PA14_00860	<i>tagT1</i>	TagT1	1.81	4.2E-06		
PA0074	PA14_00875	<i>ppkA</i>	serine/threonine protein kinase PpkA	1.62	2.7E-10		
PA0075	PA14_00890	<i>pppA</i>	PppA	1.50	1.2E-05		
PA0076	PA14_00900	<i>tagF1</i>	TagF1	1.50	5.4E-08		
PA0078	PA14_00925	<i>tssL1</i>	TssL1	1.56	1.0E-09	1.77	4.1E-02
PA0098	PA14_01190		hypothetical protein	1.51	2.8E-04		
PA0099	PA14_01200		type VI effector protein	1.62	3.3E-08		
PA0100	PA14_01220		hypothetical protein	1.58	7.2E-09		
PA0101	PA14_01230		hypothetical protein	1.56	9.9E-06		
PA0105	PA14_01290	<i>coxB</i>	cytochrome c oxidase, subunit II	3.16	1.6E-33		

PA0106	PA14_01300	<i>coxA</i>	cytochrome c oxidase, subunit I	6.55	1.2E-33		
PA0107	PA14_01310		conserved hypothetical protein	8.87	1.1E-26		
PA0108	PA14_01320	<i>colIII</i>	cytochrome c oxidase, subunit III	7.91	1.7E-29	1.58	1.8E-02
PA0109	PA14_01330		hypothetical protein	1.76	5.8E-07		
PA0110	PA14_01340		hypothetical protein	6.13	2.3E-29		
PA0111	PA14_01350		hypothetical protein	6.28	2.3E-17		
PA0112	PA14_01360		hypothetical protein	7.42	2.1E-27		
PA0113	PA14_01380		probable cytochrome c oxidase assembly factor	7.52	1.2E-19		
PA0114	PA14_01390	<i>senC</i>	SenC	-1.68	2.1E-14		
PA0122	PA14_01490	<i>rahU</i>	rahU	1.71	4.4E-18	-1.82	7.8E-03
PA0128	PA14_01560		conserved hypothetical protein	-1.67	1.2E-12		
PA0132	PA14_01620	<i>bauA</i>	Beta-alanine:pyruvate transaminase	-2.26	1.1E-15		
PA0141	PA14_01730		conserved hypothetical protein	2.46	1.4E-15		
PA0142	PA14_01750		hypothetical protein	-1.87	5.6E-12		
PA0144	PA14_01780		hypothetical protein			1.65	1.8E-04
PA0151	PA14_01870		probable TonB-dependent receptor	-1.58	9.0E-05		
PA0153	PA14_01900	<i>pcaH</i>	protocatechuate 3,4-dioxygenase, beta subunit	3.01	1.1E-12		
PA0154	PA14_01910	<i>pcaG</i>	protocatechuate 3,4-dioxygenase, alpha subunit	3.56	2.9E-12		
PA0156	PA14_01940	<i>triA</i>	Resistance-Nodulation-Cell Division (RND) triclosan efflux membrane fusion protein, TriA	1.64	6.6E-12		
PA0164	PA14_02050		probable gamma-glutamyltranspeptidase	-1.60	1.9E-08		
PA0165	PA14_02060		hypothetical protein	-2.20	1.9E-22		
PA0166	PA14_02070		probable transporter	-1.84	2.9E-02		
PA0169	PA14_02110	<i>siaD</i>	SiaD	-2.53	6.3E-20		
PA0170	PA14_02130		hypothetical protein	-3.14	6.7E-20		
PA0171	PA14_02140		hypothetical protein	-2.98	1.7E-14		
PA0172	PA14_02150	<i>siaA</i>	SiaA	-2.74	4.9E-48		
PA0173	PA14_02180		probable methylesterase	2.80	1.7E-15		
PA0174	PA14_02190		conserved hypothetical protein	2.52	3.5E-13		
PA0175	PA14_02200		probable chemotaxis protein methyltransferase	1.92	3.8E-11		
PA0176	PA14_02220	<i>aer2</i>	aerotaxis transducer Aer2	1.74	1.8E-13		
PA0177	PA14_02230		probable purine-binding chemotaxis protein	1.73	7.0E-09		
PA0178	PA14_02250		probable two-component sensor	1.60	5.2E-09		
PA0179	PA14_02260		probable two-component response regulator	1.51	4.4E-07		

PA0185	PA14_02340		probable permease of ABC transporter	-1.56	5.0E-02		
PA0187	PA14_02360		hypothetical protein	-1.62	2.0E-04		
PA0191	PA14_02390		probable transcriptional regulator	-1.96	3.4E-08		
PA0193	PA14_02410		hypothetical protein	-3.63	8.6E-07		
PA0195	PA14_02450	<i>pntAA</i>	putative NAD(P) transhydrogenase, subunit alpha part 1	-1.98	5.1E-04		
PA0195.1	PA14_02470	<i>pntAB</i>	putative NAD(P) transhydrogenase, subunit alpha part 2	-1.65	2.5E-02		
PA0197	PA14_02490	<i>tonB2</i>	hypothetical protein	-2.98	3.7E-07		
PA0198	PA14_02500	<i>exbB1</i>	transport protein ExbB	-1.54	1.1E-02		
PA0200	PA14_02520		hypothetical protein	1.56	5.7E-03	-2.06	4.1E-02
PA0201	PA14_02530		hypothetical protein	-2.96	6.1E-27		
PA0209	PA14_02560		conserved hypothetical protein	2.01	1.2E-03		
PA0210	PA14_02570	<i>mdcC</i>	malonate decarboxylase subunit delta	2.46	4.5E-03		
PA0211	PA14_02580	<i>mdcD</i>	malonate decarboxylase beta subunit	2.07	2.9E-05		
PA0212	PA14_02590	<i>mdcE</i>	malonate decarboxylase gamma subunit	2.48	5.7E-07		
PA0213	PA14_02610		hypothetical protein	2.40	7.9E-05		
PA0214	PA14_02620		probable acyl transferase	2.81	1.4E-09		
PA0216	PA14_02640		malonate transporter MadM	1.90	1.4E-05		
PA0221	PA14_02700		probable aminotransferase	1.62	1.8E-02		
PA0222	PA14_02720		hypothetical protein	1.72	3.5E-02		
PA0223	PA14_02730		probable dihydrodipicolinate synthetase	1.61	1.2E-03		
PA0226	PA14_02760		probable CoA transferase, subunit A	1.74	2.8E-11		
PA0227	PA14_02770		probable CoA transferase, subunit B	2.27	1.1E-16		
PA0228	PA14_02790	<i>pcaF</i>	beta-ketoadipyl CoA thiolase PcaF	2.45	5.3E-15		
PA0229	PA14_02810	<i>pcaT</i>	dicarboxylic acid transporter PcaT	2.71	1.1E-15		
PA0230	PA14_02830	<i>pcaB</i>	3-carboxy-cis,cis-muconate cycloisomerase	2.26	2.3E-19		
PA0231	PA14_02840	<i>pcaD</i>	beta-ketoadipate enol-lactone hydrolase	2.14	3.4E-16		
PA0232	PA14_02850	<i>pcaC</i>	gamma-carboxymuconolactone decarboxylase	2.44	1.1E-19		
PA0233	PA14_02870		probable transcriptional regulator	1.51	1.9E-08		
PA0234	PA14_02890		hypothetical protein	-1.91	7.1E-05		
PA0235	PA14_02900	<i>pcaK</i>	4-hydroxybenzoate transporter PcaK	1.51	2.9E-03		
PA0240	PA14_02980		probable porin	2.19	1.1E-08		
PA0241	PA14_02990		probable major facilitator superfamily (MFS) transporter	2.19	1.3E-09		
PA0242	PA14_03000		hypothetical protein	4.08	2.6E-29		

PA0248	PA14_03070		probable transcriptional regulator	1.65	9.0E-06		
PA0263	PA14_03240	<i>hcpC</i>	secreted protein Hcp	-2.17	4.2E-04		
PA1512	PA14_03240	<i>hcpA</i>	secreted protein Hcp	-2.17	4.2E-04		
PA5267	PA14_03240	<i>hcpB</i>	secreted protein Hcp	-2.17	4.2E-04		
PA0979	PA14_03290		conserved hypothetical protein			-1.56	2.9E-02
	PA14_03390		hypothetical protein	-2.02	6.6E-08		
	PA14_03400		hypothetical protein	-4.31	1.7E-13		
PA0269	PA14_03490		conserved hypothetical protein	1.64	2.1E-05		
PA0270	PA14_03510		hypothetical protein	2.22	1.1E-18		
PA0271	PA14_03520		hypothetical protein	2.04	3.0E-13		
PA0275	PA14_03580		probable transcriptional regulator	1.52	9.8E-07		
PA0277	PA14_03610		conserved hypothetical protein	-2.66	1.1E-38		
PA0278	PA14_03620		hypothetical protein	-2.40	4.4E-08		
PA0280	PA14_03650	<i>cysA</i>	sulfate transport protein CysA	-2.23	7.2E-15		
PA0281	PA14_03670	<i>cysW</i>	sulfate transport protein CysW	-2.85	5.2E-22	-1.67	2.6E-02
PA0282	PA14_03680	<i>cysT</i>	sulfate transport protein CysT	-2.97	1.7E-21		
PA0283	PA14_03700	<i>sbp</i>	sulfate-binding protein precursor	-3.23	2.8E-23	-1.86	5.3E-03
PA0284	PA14_03710		hypothetical protein	-2.86	1.0E-15		
PA0286	PA14_03730	<i>desA</i>	delta-9 fatty acid desaturase, DesA	-1.68	5.8E-14		
PA0287	PA14_03760	<i>gpuP</i>	sodium:solute symporter	-3.14	3.4E-16		
PA0288	PA14_03770	<i>gpuA</i>	3-guanidinopropionase	-2.49	1.2E-11		
PA0291	PA14_03800	<i>oprE</i>	Anaerobically-induced outer membrane porin OprE precursor	-2.74	3.4E-69		
PA0297	PA14_03870	<i>spuA</i>	probable glutamine amidotransferase	-1.72	9.3E-10		
PA0320	PA14_04180	<i>carO</i>	calcium-regulated OB-fold protein CarO	-1.86	3.0E-11		
PA0324	PA14_04230		probable permease of ABC transporter	-1.96	4.1E-02		
PA0328	PA14_04290	<i>aaaA</i>	arginine-specific autotransporter of <i>Pseudomonas aeruginosa</i> , AaaA	-1.56	2.8E-12		
PA0340	PA14_04440		conserved hypothetical protein	-1.76	1.6E-14		
PA0341	PA14_04460	<i>lgt</i>	prolipoprotein diacylglyceryl transferase	-1.65	2.9E-21		
PA0344	PA14_04510		hypothetical protein	2.10	5.4E-18		
PA0345	PA14_04520		hypothetical protein	1.84	1.8E-16		
PA0346	PA14_04530		hypothetical protein	1.95	5.9E-09		
PA0352	PA14_04610		probable transporter	-1.67	5.6E-17		
PA0355	PA14_04650	<i>pfpI</i>	protease PfpI	3.49	1.3E-23		
	PA14_04710		hypothetical protein	-2.72	7.2E-38		
PA0364	PA14_04780	<i>laoA</i>	LaoA	2.06	5.7E-12		
PA0365	PA14_04790	<i>laoB</i>	LaoB	1.86	1.3E-14		

PA0366	PA14_04810	<i>laoC</i>	LaoC	1.99	1.9E-16		
PA0367	PA14_04820	<i>laoR</i>	LaoR	1.62	4.4E-14		
PA0383	PA14_05010		conserved hypothetical protein	-1.85	7.9E-13		
PA0385	PA14_05030		hypothetical protein	-1.55	6.0E-07		
PA0386	PA14_05040		probable oxidase	-1.53	3.0E-06		
PA0389	PA14_05070		hypothetical protein	-1.50	1.6E-14		
PA0390	PA14_05080	<i>metX</i>	homoserine O-acetyltransferase	-1.61	1.3E-21		
PA0409	PA14_05330	<i>pilH</i>	twitching motility protein PilH			-1.51	2.7E-02
PA0413	PA14_05390	<i>chpA</i>	component of chemotactic signal transduction system	1.67	3.3E-41		
PA0414	PA14_05400	<i>chpB</i>	probable methylesterase	1.71	1.1E-21		
PA0422	PA14_05500		conserved hypothetical protein	-2.73	3.3E-51		
PA0433	PA14_05630		hypothetical protein	2.72	6.0E-10		
PA0434	PA14_05640		hypothetical protein	3.27	8.2E-05		
PA0435	PA14_05650		hypothetical protein	2.46	5.5E-05		
PA0443	PA14_05790		probable transporter	-1.90	1.0E-02		
PA0450	PA14_05870		probable phosphate transporter	-1.52	2.9E-03		
PA0451	PA14_05880		conserved hypothetical protein	1.64	2.5E-06	1.90	1.4E-02
PA0459	PA14_06000		probable ClpA/B protease ATP binding subunit	1.86	2.0E-10		
PA0471	PA14_06170	<i>fiuR</i>	FiuR	1.68	1.0E-04		
PA0472	PA14_06180	<i>fiuI</i>	FiuI	1.54	3.0E-05		
PA0480	PA14_06270		hydrolase	2.49	7.5E-08		
PA0484	PA14_06310		conserved hypothetical protein	1.74	5.5E-11		
PA0485	PA14_06320		conserved hypothetical protein	-1.57	2.7E-07		
PA0490	PA14_06390		hypothetical protein	1.62	1.0E-07		
PA0506	PA14_06600		probable acyl-CoA dehydrogenase	-1.67	4.0E-20		
PA0509	PA14_06650	<i>nirN</i>	NirN	-3.32	1.2E-19		
PA0510	PA14_06660	<i>nirE</i>	NirE	-2.91	2.1E-11		
PA0511	PA14_06670	<i>nirJ</i>	heme d1 biosynthesis protein NirJ	-3.19	4.9E-18		
PA0512	PA14_06680	<i>nirH</i>	hypothetical protein	-2.69	1.2E-11		
PA0513	PA14_06690	<i>nirG</i>	transcriptional regulator	-3.19	1.8E-13		
PA0514	PA14_06700	<i>nirL</i>	heme d1 biosynthesis protein NirL	-2.92	9.1E-12		
PA0515	PA14_06710		transcriptional regulator	-3.38	5.4E-13		
PA0516	PA14_06720	<i>nirF</i>	heme d1 biosynthesis protein NirF	-3.37	2.7E-16		
PA0517	PA14_06730	<i>nirC</i>	c-type cytochrome	-3.30	5.1E-23		
PA0518	PA14_06740	<i>nirM</i>	cytochrome c-551 precursor	-4.27	1.4E-35		
PA0519	PA14_06750	<i>nirS</i>	nitrite reductase precursor	-4.52	7.5E-27		
PA0520	PA14_06770	<i>nirQ</i>	regulatory protein NirQ	-2.93	4.6E-21		
PA0521	PA14_06790		cytochrome c oxidase subunit	-5.78	1.2E-23		

PA0522	PA14_06800		hypothetical protein	-10.38	3.8E-26		
PA0523	PA14_06810	<i>norC</i>	nitric-oxide reductase subunit C	-13.47	8.4E-28		
PA0524	PA14_06830	<i>norB</i>	nitric-oxide reductase subunit B	-13.04	2.0E-32		
PA0525	PA14_06840		probable dinitrification protein NorD	-13.77	2.6E-31		
PA0526	PA14_06860		hypothetical protein	-1.52	4.1E-05		
PA0534	PA14_06960	<i>pauBI</i>	FAD-dependent oxidoreductase	-4.68	3.4E-94		
PA0535	PA14_06970		probable transcriptional regulator	-1.64	2.5E-09		
PA0543	PA14_07050		hypothetical protein	1.76	2.0E-06		
PA0546	PA14_07090	<i>metK</i>	methionine adenosyltransferase	1.78	2.3E-38		
PA0547	PA14_07110		probable transcriptional regulator	1.74	8.7E-27		
PA0553	PA14_07200		hypothetical protein	1.51	2.1E-16		
PA0561	PA14_07300		hypothetical protein	-1.58	1.6E-13		
PA0567	PA14_07370		conserved hypothetical protein	2.28	7.7E-12	2.03	4.4E-02
PA0572	PA14_07430		hypothetical protein	2.46	4.5E-23		
	PA14_07460		hypothetical protein	-2.03	1.2E-16	-1.50	2.5E-02
	PA14_07480		reverse transcriptase			-1.52	2.0E-02
PA0602	PA14_07850		probable binding protein component of ABC transporter	1.84	5.2E-19		
PA0607	PA14_07910	<i>rpe</i>	ribulose-phosphate 3-epimerase	-1.65	4.9E-13		
PA0608	PA14_07930		probable phosphoglycolate phosphatase	-1.51	5.7E-08	-1.72	4.1E-02
PA0612	PA14_07970	<i>ptrB</i>	repressor, PtrB	-4.54	6.4E-41		
PA0613	PA14_07980		hypothetical protein	-4.34	2.1E-63		
PA0614	PA14_07990		hypothetical protein	-4.50	4.8E-47		
PA0615	PA14_08000		hypothetical protein	-2.61	9.5E-48		
PA0616	PA14_08010		hypothetical protein	-3.61	1.6E-81		
PA0617	PA14_08020		probable bacteriophage protein	-4.82	1.8E-63		
PA0618	PA14_08030		probable bacteriophage protein	-5.28	1.8E-106		
PA0619	PA14_08040		probable bacteriophage protein	-5.82	3.8E-79		
PA0620	PA14_08050		probable bacteriophage protein	-4.09	1.5E-136		
PA0621	PA14_08060		conserved hypothetical protein	-3.92	1.0E-24		
PA0622	PA14_08070		probable bacteriophage protein	-8.13	1.2E-290		
PA0623	PA14_08090		probable bacteriophage protein	-7.41	6.1E-221		
PA0624	PA14_08100		hypothetical protein	-6.43	1.1E-110		
	PA14_08110		hypothetical protein	-6.95	1.8E-56		
PA0625	PA14_08120		hypothetical protein	-5.42	1.1E-133		

PA0626	PA14_08130		hypothetical protein	-4.62	2.9E-108		
PA0627	PA14_08140		conserved hypothetical protein	-4.31	6.1E-27		
PA0628	PA14_08150		conserved hypothetical protein	-5.15	4.8E-133		
PA0629	PA14_08160		conserved hypothetical protein	-6.46	7.3E-69		
PA0630	PA14_08180		hypothetical protein	-6.29	1.1E-42		
PA0631	PA14_08190		hypothetical protein	-8.11	5.8E-29		
PA0632	PA14_08200		hypothetical protein	-8.56	1.0E-41		
PA0633	PA14_08210		hypothetical protein	-6.66	2.8E-231		
PA0634	PA14_08220		hypothetical protein	-6.08	1.7E-136		
PA0635	PA14_08230		hypothetical protein	-6.78	9.9E-127		
PA0636	PA14_08240		hypothetical protein	-5.63	2.9E-172		
PA0637	PA14_08250		conserved hypothetical protein	-5.24	6.9E-46		
PA0638	PA14_08260		probable bacteriophage protein	-5.43	6.9E-104		
PA0639	PA14_08270		conserved hypothetical protein	-6.13	5.2E-122		
PA0640	PA14_08280		probable bacteriophage protein	-5.06	9.1E-84		
PA0641	PA14_08300		probable bacteriophage protein	-5.05	2.1E-284		
PA0646	PA14_08310		hypothetical protein	-1.68	2.1E-15		
PA0650	PA14_08350	<i>trpD</i>	anthranilate phosphoribosyltransferase			-1.51	4.1E-02
PA0654	PA14_08390	<i>speD</i>	S-adenosylmethionine decarboxylase proenzyme	-2.78	2.2E-86		
PA4280	PA14_08620	<i>birA</i>	BirA bifunctional protein	-1.70	2.7E-25		
PA4279	PA14_08630		pantothenate kinase	-1.68	8.7E-15		
PA4278	PA14_08640		hypothetical protein	-1.67	5.2E-11		
PA4266	PA14_08820	<i>fusA1</i>	elongation factor G	-1.62	1.0E-15		
PA4277	PA14_08680	<i>tufB</i>	elongation factor Tu	-1.60	1.6E-26		
PA4270	PA14_08760	<i>rpoB</i>	DNA-directed RNA polymerase beta chain	-1.62	7.5E-17		
PA4268	PA14_08790	<i>rpsL</i>	30S ribosomal protein S12	-1.53	3.0E-10		
PA4267	PA14_08810	<i>rpsG</i>	30S ribosomal protein S7	-1.58	8.0E-13	-1.67	2.1E-02
PA4265	PA14_08830	<i>tufA</i>	elongation factor Tu	-1.51	7.4E-16		
PA4264	PA14_08840	<i>rpsJ</i>	30S ribosomal protein S10	-1.64	2.6E-15		
PA4263	PA14_08850	<i>rplC</i>	50S ribosomal protein L3	-1.79	6.9E-20		

PA4262	PA14_08860	<i>rplD</i>	50S ribosomal protein L4	-1.91	5.0E-29		
PA4261	PA14_08870	<i>rplW</i>	50S ribosomal protein L23	-1.93	1.1E-23		
PA4260	PA14_08880	<i>rplB</i>	50S ribosomal protein L2	-1.96	2.0E-25		
PA4259	PA14_08890	<i>rpsS</i>	30S ribosomal protein S19	-1.95	5.2E-26	-1.78	2.8E-02
PA4258	PA14_08900	<i>rplV</i>	50S ribosomal protein L22	-1.88	5.2E-19		
PA4257	PA14_08910	<i>rpsC</i>	30S ribosomal protein S3	-1.88	8.1E-24		
PA4256	PA14_08920	<i>rplP</i>	50S ribosomal protein L16	-1.88	6.8E-23		
PA4255	PA14_08930	<i>rpmC</i>	50S ribosomal protein L29	-1.76	5.3E-18		
PA4254	PA14_08940	<i>rpsQ</i>	30S ribosomal protein S17	-1.88	3.6E-26		
PA4253	PA14_08950	<i>rplN</i>	50S ribosomal protein L14	-1.78	4.2E-27		
PA4252	PA14_08960	<i>rplX</i>	50S ribosomal protein L24	-1.72	8.5E-27		
PA4251	PA14_08970	<i>rplE</i>	50S ribosomal protein L5	-1.60	1.8E-28		
PA4250	PA14_08980	<i>rpsN</i>	30S ribosomal protein S14	-1.58	2.6E-30		
PA4249	PA14_08990	<i>rpsH</i>	30S ribosomal protein S8	-1.66	5.4E-12		
PA4248	PA14_09000	<i>rplF</i>	50S ribosomal protein L6	-1.73	3.4E-14		
PA4247	PA14_09010	<i>rplR</i>	50S ribosomal protein L18	-1.71	5.8E-12		
PA4246	PA14_09020	<i>rpsE</i>	30S ribosomal protein S5	-1.78	1.5E-15		
PA4245	PA14_09030	<i>rpmD</i>	50S ribosomal protein L30	-1.80	3.5E-13		
PA4244	PA14_09040	<i>rplO</i>	50S ribosomal protein L15	-1.70	1.2E-15		
PA4243	PA14_09050	<i>secY</i>	secretion protein SecY	-1.54	1.1E-08		
PA4241	PA14_09080	<i>rpsM</i>	30S ribosomal protein S13	-1.61	3.0E-12		
PA4240	PA14_09090	<i>rpsK</i>	30S ribosomal protein S11	-1.75	2.8E-26		
PA4239	PA14_09100	<i>rpsD</i>	30S ribosomal protein S4	-1.66	6.1E-17		
PA4238	PA14_09115	<i>rpoA</i>	DNA-directed RNA polymerase alpha chain	-1.56	1.8E-16		
PA4232	PA14_09200	<i>ssb</i>	single-stranded DNA-binding protein	-1.59	1.3E-30		
PA4231	PA14_09210	<i>pchA</i>	salicylate biosynthesis isochorismate synthase	8.11	8.0E-51		
PA4230	PA14_09220	<i>pchB</i>	salicylate biosynthesis protein PchB	7.32	8.6E-36	-1.65	2.3E-02
PA4229	PA14_09230	<i>pchC</i>	pyochelin biosynthetic protein PchC	5.03	5.8E-26		
PA4228	PA14_09240	<i>pchD</i>	pyochelin biosynthesis protein PchD	5.12	1.2E-29		
PA4227	PA14_09260	<i>pchR</i>	transcriptional regulator PchR	3.79	5.6E-28		
PA4226	PA14_09270	<i>pchE</i>	dihydroaeruginosic acid synthetase	5.77	2.5E-41		
PA4225	PA14_09280	<i>pchF</i>	pyochelin synthetase	6.85	1.9E-56		
PA4224	PA14_09290	<i>pchG</i>	pyochelin biosynthetic protein PchG	7.94	8.9E-55		
PA4223	PA14_09300		probable ATP-binding component of ABC transporter	7.87	3.8E-63		
PA4222	PA14_09320		probable ATP-binding component of ABC transporter	9.07	3.9E-78		
PA4221	PA14_09340	<i>fptA</i>	Fe(III)-pyochelin outer membrane receptor precursor	3.88	1.8E-25	-1.73	7.9E-03

PA4220	PA14_09350		hypothetical protein	3.90	1.7E-46		
PA4219	PA14_09370	<i>ampO</i>	AmpO	3.67	5.2E-26		
PA4218	PA14_09380	<i>ampP</i>	AmpP	4.41	2.8E-30		
PA4217	PA14_09400	<i>phzS</i>	flavin-containing monooxygenase	2.28	3.1E-16		
PA1905	PA14_09410	<i>phzG2</i>	probable pyridoxamine 5'-phosphate oxidase	2.41	9.7E-13		
PA4216	PA14_09410	<i>phzG1</i>	probable pyridoxamine 5'-phosphate oxidase	2.41	9.7E-13		
PA1903	PA14_09440	<i>phzE2</i>	phenazine biosynthesis protein PhzE	2.53	3.4E-21		
PA4214	PA14_09440	<i>phzE1</i>	phenazine biosynthesis protein PhzE	2.53	3.4E-21		
PA1902	PA14_09450	<i>phzD2</i>	phenazine biosynthesis protein PhzD	2.37	3.9E-13		
PA4213	PA14_09450	<i>phzD1</i>	phenazine biosynthesis protein PhzD	2.37	3.9E-13		
	PA14_09460	<i>phzC1</i>	phenazine biosynthesis protein PhzC	2.23	3.2E-10		
PA4211	PA14_09470	<i>phzB1</i>	probable phenazine biosynthesis protein	2.15	3.4E-08		
PA4209	PA14_09490	<i>phzM</i>	probable phenazine-specific methyltransferase	1.82	1.1E-08	-1.52	2.8E-02
PA4208	PA14_09500	<i>opmD</i>	probable outer membrane protein precursor	1.77	1.3E-22		
PA4207	PA14_09520	<i>mexI</i>	probable Resistance-Nodulation-Cell Division (RND) efflux transporter	1.59	2.0E-23		
PA4204	PA14_09550	<i>ppgL</i>	periplasmic gluconolactonase, PpgL	1.90	3.0E-12		
PA4198	PA14_09660		probable AMP-binding enzyme	-1.91	7.1E-08		
PA4197	PA14_09680	<i>bfiS</i>	BfiS	-1.71	5.4E-09		
PA4189	PA14_09710		probable aldehyde dehydrogenase	1.74	1.4E-03		
PA4187	PA14_09740		probable major facilitator superfamily (MFS) transporter	1.83	1.2E-02		
PA4182	PA14_09790		hypothetical protein	-1.54	1.3E-13		
PA4181	PA14_09810		hypothetical protein	-2.04	9.5E-19		
PA4179	PA14_09850		probable porin	-2.13	4.4E-04		
PA4178	PA14_09870	<i>eftM</i>	SAM-dependent methyltransferase , EftM	-3.07	3.0E-25		
PA4177	PA14_09880		hypothetical protein	2.37	4.6E-08		
PA4175	PA14_09900	<i>piv</i>	protease IV	2.36	1.5E-13		
PA4172	PA14_09930		probable nuclease	3.09	5.6E-27		
PA4171	PA14_09940		probable protease	2.92	4.8E-25		
PA4168	PA14_09970	<i>fpvB</i>	second ferric pyoverdine receptor FpvB			-2.35	1.4E-02
PA4167	PA14_09980		probable oxidoreductase	-2.45	1.1E-03		
PA4166	PA14_09990		probable acetyltransferase	-2.48	5.5E-11		
	PA14_10090		LysR family transcriptional regulator	1.57	3.4E-06		
PA4152	PA14_10240		probable hydrolase	2.12	3.3E-03		

PA4144	PA14_10330		probable outer membrane protein precursor	2.04	4.0E-07		
PA4143	PA14_10340		probable toxin transporter	2.10	4.0E-08		
PA4142	PA14_10350		probable secretion protein	2.68	7.3E-14		
PA4141	PA14_10360		hypothetical protein	2.33	3.8E-13	-2.38	5.0E-07
PA4140	PA14_10370		hypothetical protein	-3.81	1.7E-26		
PA4139	PA14_10380		hypothetical protein	-2.86	1.9E-39		
PA4138	PA14_10420	<i>tyrS</i>	tyrosyl-tRNA synthetase	-2.05	3.6E-14		
PA4137	PA14_10440		probable porin	-2.20	1.6E-08		
PA4134	PA14_10490		hypothetical protein	-1.89	8.3E-49		
PA4133	PA14_10500		cytochrome c oxidase subunit (cbb3-type)	-1.97	1.2E-75	-1.68	2.0E-12
PA4132	PA14_10530		conserved hypothetical protein	-1.50	2.0E-28		
PA4131	PA14_10540		probable iron-sulfur protein	-1.89	7.4E-56		
PA4120	PA14_10660		probable transcriptional regulator	1.87	7.9E-05		
PA4119	PA14_10670	<i>aph</i>	aminoglycoside 3'-phosphotransferase type IIb	-1.52	2.6E-09		
PA4116	PA14_10710	<i>bphO</i>	heme oxygenase, BphO	-1.72	1.1E-21		
PA4113	PA14_10750		probable major facilitator superfamily (MFS) transporter	-1.88	5.8E-14		
	PA14_10830		LysR family transcriptional regulator	1.77	1.3E-09		
PA4094	PA14_10940		probable transcriptional regulator	1.63	2.0E-06		
PA4086	PA14_11060	<i>cupB1</i>	probable fimbrial subunit CupB1	1.96	1.5E-06		
PA4080	PA14_11120		probable response regulator	1.55	6.9E-08		
PA4078	PA14_11140		probable nonribosomal peptide synthetase	1.79	2.0E-10		
PA4070	PA14_11240		probable transcriptional regulator	1.58	1.5E-02		
PA4063	PA14_11320		hypothetical protein	1.62	4.9E-04		
PA4061	PA14_11340		probable thioredoxin	-1.73	4.0E-34		
PA4052	PA14_11450	<i>nusB</i>	NusB protein	-1.52	8.0E-10		
PA4031	PA14_11690	<i>ppa</i>	inorganic pyrophosphatase	-1.81	9.4E-52		
PA4029	PA14_11720		conserved hypothetical protein	-1.55	2.4E-08		
PA4017	PA14_11890		conserved hypothetical protein	1.51	3.1E-09		
PA4009	PA14_11980		hypothetical protein	1.69	1.7E-04		
PA3995	PA14_12140		probable transcriptional regulator	1.66	1.3E-09		
PA3990	PA14_12180		conserved hypothetical protein	-1.79	8.0E-12		
PA3986	PA14_12260		hypothetical protein	1.69	2.0E-10		
PA3979	PA14_12360		hypothetical protein	-1.74	2.2E-10		
PA3960	PA14_12640		hypothetical protein	-1.81	6.5E-05		
PA3959	PA14_12650		hypothetical protein	-1.64	7.1E-07		
PA3957	PA14_12680		probable short-chain dehydrogenase	1.68	1.7E-09		

PA3952	PA14_12740		hypothetical protein			2.06	1.9E-02
PA3938	PA14_12920		probable periplasmic taurine-binding protein precursor	-3.89	3.6E-31	-2.40	9.4E-05
PA3937	PA14_12940		probable ATP-binding component of ABC taurine transporter	-2.34	7.0E-11		
PA3936	PA14_12960		probable permease of ABC taurine transporter	-2.48	2.6E-11		
PA3935	PA14_12970	<i>tauD</i>	taurine dioxygenase	-2.03	5.6E-08		
PA3932	PA14_13000		probable transcriptional regulator	-2.66	1.2E-14		
PA3931	PA14_13010		conserved hypothetical protein	-4.30	9.8E-34		
PA3923	PA14_13130		hypothetical protein	2.00	3.3E-11		
PA3922	PA14_13140		conserved hypothetical protein	2.25	4.5E-18		
PA3921	PA14_13150		probable transcriptional regulator	1.52	1.6E-14		
PA3920	PA14_13170		probable metal transporting P-type ATPase	-3.87	6.3E-30		
PA3915	PA14_13260	<i>moaB</i> <i>I</i>	molybdopterin biosynthetic protein B1	-2.36	1.4E-14		
PA3914	PA14_13280	<i>moaA</i> <i>I</i>	molybdenum cofactor biosynthetic protein A1	-4.00	1.0E-17		
PA3913	PA14_13290		probable protease	-1.77	2.8E-10		
PA3911	PA14_13320		conserved hypothetical protein	-1.55	3.4E-04		
PA3901	PA14_13430	<i>fecA</i>	Fe(III) dicitrate transport protein FecA	-1.55	6.0E-04		
PA3891	PA14_13580	<i>opuC</i> <i>A</i>	OpuC ABC transporter, ATP-binding protein, OpuCA	2.27	2.7E-16		
PA3890	PA14_13590	<i>opuC</i> <i>B</i>	OpuC ABC transporter, permease protein, OpuCB	2.40	1.1E-13		
PA3889	PA14_13600	<i>opuC</i> <i>C</i>	OpuC ABC transporter, periplasmic substrate-binding protein, OpuCC	2.55	1.8E-19		
PA3888	PA14_13610	<i>opuC</i> <i>D</i>	OpuC ABC transporter, permease protein, OpuCD	2.68	1.6E-15		
	PA14_13630		hypothetical protein	2.41	6.5E-14		
PA3886	PA14_13650		hypothetical protein			1.66	2.8E-02
PA3877	PA14_13750	<i>narK1</i>	nitrite extrusion protein 1	-5.91	7.1E-31		
PA3876	PA14_13770	<i>narK2</i>	nitrite extrusion protein 2	-5.68	3.0E-17		
PA3875	PA14_13780	<i>narG</i>	respiratory nitrate reductase alpha chain	-6.18	1.5E-68		
PA3874	PA14_13800	<i>narH</i>	respiratory nitrate reductase beta chain	-3.53	2.0E-24		
PA3873	PA14_13810	<i>narJ</i>	respiratory nitrate reductase delta chain	-5.30	2.7E-18		
PA3872	PA14_13830	<i>narI</i>	respiratory nitrate reductase gamma chain	-3.25	1.7E-12		

PA3871	PA14_13840		probable peptidyl-prolyl cis-trans isomerase, PpiC-type	-3.06	4.3E-17		
PA3870	PA14_13850	<i>moaA</i> <i>I</i>	molybdopterin biosynthetic protein A1	-1.78	7.8E-05		
	PA14_13920		hypothetical protein	2.11	4.9E-04		
PA3866	PA14_13940		Pyocin S4			-3.09	2.6E-05
PA3865 .1	PA14_13950		hypothetical protein			-1.92	7.8E-03
PA3865	PA14_13990		probable amino acid binding protein	-1.85	7.5E-20		
PA3863	PA14_14010	<i>dauA</i>	FAD-dependent catabolic D-arginine dehydrogenase, DauA	-1.68	5.1E-10		
PA3862	PA14_14020	<i>dauB</i>	NAD(P)H-dependent anabolic L-arginine dehydrogenase, DauB	-1.99	1.3E-14		
PA3842	PA14_14330	<i>spcS</i>	specific Pseudomonas chaperone for ExoS, SpcS	1.61	8.0E-04		
PA3840	PA14_14340		conserved hypothetical protein	-1.74	5.7E-09		
	PA14_14540		hypothetical protein	-2.41	4.1E-10		
	PA14_14550		hypothetical protein	-3.78	8.8E-81		
	PA14_14560		hypothetical protein	-2.58	3.8E-16		
PA3818	PA14_14680		extragenic suppressor protein SuhB	-1.75	1.4E-19		
PA3815	PA14_14710	<i>iscR</i>	IscR	-1.81	1.6E-20		
PA3814	PA14_14730	<i>iscS</i>	L-cysteine desulfurase (pyridoxal phosphate-dependent)	-1.89	2.6E-24		
PA3813	PA14_14740	<i>iscU</i>	probable iron-binding protein IscU	-1.73	6.6E-26		
PA3812	PA14_14750	<i>iscA</i>	probable iron-binding protein IscA	-1.63	1.1E-15		
PA3811	PA14_14770	<i>hscB</i>	heat shock protein HscB	-1.77	2.7E-15		
PA3810	PA14_14780	<i>hscA</i>	heat shock protein HscA	-1.77	7.5E-17		
PA3809	PA14_14800	<i>fdx2</i>	ferredoxin [2Fe-2S]	-1.57	3.4E-11		
PA3808	PA14_14810		conserved hypothetical protein	-1.58	1.5E-11		
PA3795	PA14_14990		probable oxidoreductase	1.98	2.5E-18		
PA3791	PA14_15050		hypothetical protein	1.53	5.3E-04		
PA3790	PA14_15070	<i>oprC</i>	Putative copper transport outer membrane porin OprC precursor	4.24	4.1E-12		
PA3789	PA14_15080		hypothetical protein	2.56	3.8E-13		
PA3788	PA14_15090		hypothetical protein	1.68	2.1E-08		
PA3783	PA14_15140		hypothetical protein	1.71	6.7E-03		
PA3776	PA14_15240		probable transcriptional regulator	-1.63	1.3E-03		
PA3775	PA14_15250		hypothetical protein	1.91	2.7E-02		
PA3771	PA14_15290		probable transcriptional regulator	1.93	7.9E-06		
	PA14_15510	<i>traJ</i>	conjugal transfer relaxosome component TraJ			-1.90	3.4E-02
	PA14_15520	<i>trbJ</i>	conjugal transfer protein TrbJ	-1.77	2.1E-11		

	PA14_15530		entry/exclusion protein TrbK	-2.20	3.2E-04		
	PA14_15560		hypothetical protein			-1.82	2.9E-02
	PA14_15570		hypothetical protein			-1.93	1.6E-02
	PA14_15580		Type II restriction enzyme, methylase subunit			-1.52	1.3E-02
PA3766	PA14_15700		probable aromatic amino acid transporter	-1.73	1.4E-08		
PA3762	PA14_15770		hypothetical protein	2.24	1.9E-16		
PA3757	PA14_15830	<i>nagR</i>	Transcriptional regulator of N- Acetylglucosamine catabolism operon	-1.50	2.9E-05		
PA3745	PA14_15970	<i>rpsP</i>	30S ribosomal protein S16	-1.51	6.3E-08		
PA3743	PA14_15990	<i>trmD</i>	tRNA (guanine-N1)- methyltransferase	-1.54	6.9E-09		
PA3742	PA14_16000	<i>rplS</i>	50S ribosomal protein L19	-1.55	4.8E-12		
PA3741	PA14_16010		hypothetical protein	-1.66	2.2E-08		
PA3734	PA14_16100		hypothetical protein	2.05	5.3E-09		
	PA14_16110		hypothetical protein	1.95	3.5E-20		
PA3726	PA14_16210		conserved hypothetical protein	-1.58	4.0E-12		
PA3725	PA14_16220	<i>recJ</i>	single-stranded-DNA-specific exonuclease RecJ	-1.57	1.7E-12		
PA3724	PA14_16250	<i>lasB</i>	elastase LasB	2.32	1.2E-29		
PA3723	PA14_16260		probable FMN oxidoreductase	1.62	1.1E-11		
PA3722	PA14_16270		hypothetical protein	-2.16	8.0E-31		
PA3719	PA14_16300	<i>armR</i>	antirepressor for MexR, ArmR	1.61	2.3E-03		
PA3716	PA14_16330		hypothetical protein	-1.78	7.4E-64		
PA3713	PA14_16360	<i>spdH</i>	spermidine dehydrogenase, SpdH	-1.96	7.1E-25		
PA3703	PA14_16480	<i>wspF</i>	probable methylesterase	1.54	3.8E-20		
PA3692	PA14_16630	<i>lptF</i>	Lipotoxon F, LptF	2.30	5.4E-23		
PA3691	PA14_16640		hypothetical protein	2.54	9.9E-31		
PA3687	PA14_16690	<i>ppc</i>	phosphoenolpyruvate carboxylase	1.58	1.7E-12		
PA3678	PA14_16790	<i>mexL</i>	MexL	1.52	6.8E-15		
PA3671	PA14_16880		probable permease of ABC transporter	1.56	7.4E-03		
PA3670	PA14_16890		hypothetical protein	1.78	7.6E-06		
PA3669	PA14_16910		hypothetical protein	1.97	4.8E-12		
PA3662	PA14_16990		hypothetical protein	-2.90	8.4E-28		
PA3656	PA14_17060	<i>rpsB</i>	30S ribosomal protein S2	-1.52	5.0E-16		
PA3655	PA14_17070	<i>tsf</i>	elongation factor Ts	-1.59	1.1E-16		
PA3654	PA14_17080	<i>pyrH</i>	uridylate kinase	-1.77	1.1E-17		
PA3653	PA14_17100	<i>frr</i>	ribosome recycling factor	-1.55	4.3E-22		

PA3641	PA14_17250		probable amino acid permease	-2.01	4.1E-32		
PA3630	PA14_17380	<i>gfnR</i>	glutathione-dependent formaldehyde neutralization regulator GfnR	1.82	7.1E-11		
PA3622	PA14_17480	<i>rpoS</i>	sigma factor RpoS	1.58	1.9E-11		
PA3617	PA14_17530	<i>recA</i>	RecA protein	-1.76	2.5E-41		
PA3616	PA14_17540		conserved hypothetical protein	-1.62	6.3E-10		
PA3615	PA14_17550		hypothetical protein	1.69	7.4E-16		
PA3614	PA14_17570		hypothetical protein	1.63	1.8E-08		
PA3613	PA14_17580		hypothetical protein	1.81	7.1E-09		
PA3612	PA14_17590		conserved hypothetical protein			-2.14	2.3E-02
PA3610	PA14_17610	<i>potD</i>	polyamine transport protein PotD	-3.65	3.1E-63		
PA3609	PA14_17620	<i>potC</i>	polyamine transport protein PotC	-3.06	6.7E-17		
PA3608	PA14_17630	<i>potB</i>	polyamine transport protein PotB	-2.40	8.0E-14		
PA3607	PA14_17640	<i>potA</i>	polyamine transport protein PotA	-3.21	3.5E-45		
PA3588	PA14_17730		probable porin	1.50	4.6E-02		
PA3598	PA14_17730		conserved hypothetical protein	2.31	1.2E-19		
PA3586	PA14_17910		probable hydrolase	1.71	1.1E-02		
PA3580	PA14_17990		conserved hypothetical protein			-1.73	2.8E-02
	PA14_18070		periplasmic metal-binding protein	-3.68	1.1E-19		
PA3567	PA14_18160		probable oxidoreductase	-1.55	3.1E-06		
PA3566	PA14_18180		conserved hypothetical protein	-2.00	4.8E-08		
PA3562	PA14_18250	<i>fruI</i>	phosphotransferase system transporter enzyme I, FruI	-1.51	2.0E-03		
PA3558	PA14_18310	<i>arnF</i>	ArnF	-1.51	7.3E-04		
PA3556	PA14_18330	<i>arnT</i>	inner membrane L-Ara4N transferase ArnT	-1.64	5.4E-11		
PA3543	PA14_18520	<i>algK</i>	alginate biosynthetic protein AlgK precursor			-3.18	4.2E-02
PA3532	PA14_18660		hypothetical protein	-1.83	8.0E-15		
PA3531	PA14_18670	<i>bfrB</i>	bacterioferritin	-2.02	1.5E-15	-1.62	3.9E-03
PA3530	PA14_18680	<i>bfd</i>	bacterioferritin-associated ferredoxin Bfd	1.97	3.9E-12	-1.83	1.5E-02
PA3526	PA14_18720	<i>motY</i>	MotY	-1.67	6.1E-22		
PA3523	PA14_18760	<i>mexP</i>	RND efflux membrane fusion protein	-4.03	3.1E-10		
PA3522	PA14_18780	<i>mexQ</i>	MexQ	-3.38	1.5E-31		
PA3521	PA14_18790	<i>opmE</i>	outer membrane efflux protein	-3.31	1.2E-12		
PA3520	PA14_18800		hypothetical protein	-2.56	6.8E-12		
PA3519	PA14_18810		hypothetical protein	-4.75	1.6E-21		
PA3518	PA14_18820		hypothetical protein	-10.19	1.1E-45		
PA3517	PA14_18830		probable lyase	-4.79	1.8E-32		

PA3516	PA14_18850		probable lyase	-5.62	8.6E-29		
PA3515	PA14_18860		hypothetical protein	-2.00	8.1E-08		
PA3488	PA14_18960	<i>tli5</i>	Tli5	-1.62	9.2E-05		
PA3487	PA14_18970	<i>tle5</i>	Tle5	-1.68	2.9E-13		
PA3486	PA14_18985	<i>vgrG4b</i>	VgrG4b	-1.71	2.2E-09		
PA3474	PA14_19150		conserved hypothetical protein	-1.77	2.5E-09		
PA3473	PA14_19160		hypothetical protein	-1.62	2.9E-08		
PA3466	PA14_19290		probable ATP-dependent RNA helicase	-1.63	3.9E-19	-1.60	3.0E-02
PA3465	PA14_19310		conserved hypothetical protein	1.97	2.9E-12		
PA3461	PA14_19350		conserved hypothetical protein	2.85	2.2E-26		
PA3460	PA14_19360		probable acetyltransferase	2.68	4.6E-24		
PA3459	PA14_19370		probable glutamine amidotransferase	2.85	1.2E-35		
PA3458	PA14_19380		probable transcriptional regulator	1.83	3.8E-08		
PA3453	PA14_19450		conserved hypothetical protein	-1.63	1.3E-20		
PA3450	PA14_19490	<i>lsfA</i>	1-Cys peroxiredoxin LsfA	-2.37	9.7E-15	-2.75	7.8E-06
PA3449	PA14_19500		conserved hypothetical protein	-6.73	2.1E-32		
PA3448	PA14_19510		probable permease of ABC transporter	-3.84	3.5E-14		
PA3447	PA14_19520		probable ATP-binding component of ABC transporter	-3.70	8.0E-10		
PA3446	PA14_19530		conserved hypothetical protein	-4.76	1.4E-31		
PA3445	PA14_19540		hypothetical protein	-4.06	2.9E-32		
PA3444	PA14_19560		alkanesulfonate monooxygenase	-3.02	3.3E-14		
PA3443	PA14_19570		probable permease of ABC transporter	-2.48	3.0E-09		
PA3442	PA14_19580		aliphatic sulfonates transport ATP-binding subunit	-2.12	1.1E-09		
PA3436	PA14_19650		hypothetical protein			2.06	1.8E-05
PA3432	PA14_19680		hypothetical protein	1.82	9.2E-06		
PA3431	PA14_19690		conserved hypothetical protein	2.22	1.2E-11		
PA3419	PA14_19860		hypothetical protein	1.64	4.6E-09	1.63	1.0E-02
PA3415	PA14_19920		probable dihydrolipoamide acetyltransferase	-1.53	3.1E-02		
	PA14_19930		hypothetical protein	-1.70	5.7E-03		
PA3414	PA14_19940		hypothetical protein	-1.94	3.2E-21		
PA3413	PA14_19950		conserved hypothetical protein	-1.59	2.0E-12		
PA3412	PA14_19960		hypothetical protein	2.39	1.6E-04		
PA3411	PA14_19970		hypothetical protein	-1.71	4.4E-03		
PA3410	PA14_19990	<i>hasI</i>	HasI	-2.00	3.6E-06		

PA3407	PA14_20020	<i>hasAp</i>	heme acquisition protein HasAp	7.33	4.6E-11		
PA3406	PA14_20030	<i>hasD</i>	transport protein HasD	1.74	1.8E-03		
PA3405	PA14_20040	<i>hasE</i>	metalloprotease secretion protein	1.76	6.0E-03		
PA3404	PA14_20050		outer membrane protein	1.63	2.0E-02		
	PA14_20060		hypothetical protein	1.71	4.7E-07		
PA3396	PA14_20150	<i>nosL</i>	NosL protein	-12.77	1.3E-29		
PA3395	PA14_20170	<i>nosY</i>	NosY protein	-15.62	1.1E-48		
PA3394	PA14_20180	<i>nosF</i>	NosF protein	-18.65	5.8E-59		
PA3393	PA14_20190	<i>nosD</i>	copper ABC transporter periplasmic substrate-binding protein	-16.02	3.4E-36		
PA3392	PA14_20200	<i>nosZ</i>	nitrous-oxide reductase precursor	-16.52	8.6E-33		
PA3391	PA14_20230	<i>nosR</i>	regulatory protein NosR	-17.19	2.1E-37		
PA3389	PA14_20240		probable ring-cleaving dioxygenase	-2.05	1.9E-04		
PA3388	PA14_20260		conserved hypothetical protein	-1.74	2.7E-08		
PA3387	PA14_20270	<i>rhlG</i>	beta-ketoacyl reductase	-1.79	3.2E-05		
PA3384	PA14_20300	<i>phnC</i>	ATP-binding component of ABC phosphonate transporter	1.96	8.8E-05		
PA3378	PA14_20380		hypothetical protein	1.57	4.2E-02		
PA3376	PA14_20400		phosphonate C-P lyase system protein PhnK	1.99	7.9E-03		
PA3371	PA14_20460		hypothetical protein	3.75	4.3E-20		
PA3370	PA14_20470		hypothetical protein	3.85	2.5E-21		
PA3369	PA14_20480		hypothetical protein	3.46	1.1E-16		
PA2457	PA14_20510		hypothetical protein			-1.88	1.2E-02
PA2458	PA14_20520		hypothetical protein			-2.26	2.9E-03
	PA14_20530		hypothetical protein	1.71	6.1E-18	-1.86	1.2E-02
PA3354	PA14_20690		hypothetical protein	1.54	3.7E-06		
PA3346	PA14_20780	<i>hsbR</i>	HptB-dependent secretion and biofilm regulator HsbR	1.60	2.6E-20		
PA3337	PA14_20890	<i>rfaD</i>	ADP-L-glycero-D-mannoheptose 6-epimerase	1.64	2.9E-06		
PA3336	PA14_20900		probable major facilitator superfamily (MFS) transporter	2.02	2.2E-07		
PA3335	PA14_20920		hypothetical protein	2.01	4.6E-09		
PA3334	PA14_20940	<i>acp3</i>	Acp3	2.04	9.0E-09		
PA3333	PA14_20950	<i>fabH2</i>	3-oxoacyl-[acyl-carrier-protein] synthase III	1.68	4.6E-05		
PA3332	PA14_20960		conserved hypothetical protein	1.58	4.6E-04		
PA3331	PA14_20970		cytochrome P450	1.76	2.7E-07		
PA3330	PA14_20980		probable short chain dehydrogenase	1.72	1.5E-08		
PA3329	PA14_21000		hypothetical protein	1.68	6.2E-06		

PA3328	PA14_21010		probable FAD-dependent monooxygenase	1.74	2.2E-06		
PA3309	PA14_21220		conserved hypothetical protein	1.63	1.6E-05		
	PA14_21260		hypothetical protein			-2.30	7.8E-03
PA3298	PA14_21380		hypothetical protein	-2.19	9.5E-06		
PA3295	PA14_21440		probable HIT family protein	-1.53	5.0E-23		
PA3294	PA14_21450	<i>vgrG4a</i>	VgrG4a	-1.63	5.2E-13		
PA3293	PA14_21460		hypothetical protein	-1.81	2.4E-08		
PA3292	PA14_21470		hypothetical protein	-1.75	3.1E-06		
PA3291	PA14_21480	<i>tliI</i>	TliI	-1.65	1.7E-04		
PA3290	PA14_21490	<i>tleI</i>	TleI			-1.64	2.5E-02
PA3284	PA14_21570		hypothetical protein	-6.08	7.9E-75		
PA3283	PA14_21580		conserved hypothetical protein	-7.25	8.8E-180		
PA3282	PA14_21590		hypothetical protein	-7.40	5.9E-80		
PA3281	PA14_21600		hypothetical protein	-7.11	5.1E-57		
PA3280	PA14_21610	<i>oprO</i>	Pyrophosphate-specific outer membrane porin OprO precursor	-5.72	2.1E-47		
PA3276	PA14_21650		hypothetical protein	-1.58	4.3E-06		
PA3275	PA14_21660		conserved hypothetical protein	-1.55	9.9E-05		
PA3274	PA14_21670		hypothetical protein	3.69	1.2E-18		
PA3268	PA14_21730		probable TonB-dependent receptor	-1.50	7.1E-03		
PA3266	PA14_21760	<i>capB</i>	cold acclimation protein B	-2.09	1.0E-06		
	PA14_21830		hypothetical protein	2.38	3.2E-48		
PA3248	PA14_21980		Uncharacterized protein	1.53	8.4E-06		
PA3246	PA14_22000	<i>rluA</i>	pseudouridine synthase RluA	-1.54	1.8E-12		
	PA14_22090		hypothetical protein			-2.30	1.9E-02
	PA14_22160		hypothetical protein	-2.23	3.5E-04		
	PA14_22190		hypothetical protein			-1.62	1.6E-02
	PA14_22250		hypothetical protein	-1.72	9.3E-03		
	PA14_22260		hypothetical protein	-2.01	2.5E-02		
	PA14_22280		pirin-related protein			-1.98	4.6E-02
PA3235	PA14_22340		conserved hypothetical protein	2.50	1.0E-05		
PA3234	PA14_22350		probable sodium:solute symporter	2.62	3.7E-04		
PA3233	PA14_22370		hypothetical protein	2.12	2.3E-10		
PA3232	PA14_22380		probable nuclease	2.13	1.3E-08		
PA3231	PA14_22400		hypothetical protein	3.46	1.9E-27		
PA3228	PA14_22440		probable ATP-binding/permease fusion ABC transporter	1.50	1.6E-10		
PA3222	PA14_22560		hypothetical protein			1.96	2.6E-02

PA3221	PA14_22570	<i>csaA</i>	CsaA protein	-1.69	9.9E-12		
PA3214	PA14_22650		hypothetical protein	1.50	3.9E-14		
PA3205	PA14_22740		hypothetical protein	-1.50	1.9E-06		
PA3195	PA14_22890	<i>gapA</i>	glyceraldehyde 3-phosphate dehydrogenase	1.83	5.8E-28		
PA3188	PA14_23000		probable permease of ABC sugar transporter	1.53	1.6E-07		
PA3187	PA14_23010		probable ATP-binding component of ABC transporter	1.67	1.8E-11		
PA3186	PA14_23030	<i>oprB</i>	Glucose/carbohydrate outer membrane porin OprB precursor	2.04	6.3E-21		
PA3182	PA14_23080	<i>pgl</i>	6-phosphogluconolactonase			1.62	7.8E-04
PA3179	PA14_23110		conserved hypothetical protein	-2.53	1.2E-56		
PA3175	PA14_23170	<i>hutE</i>	HutE	-2.14	2.4E-08		
PA3174	PA14_23190	<i>hutR</i>	HutR	-2.16	1.1E-12		
PA3160	PA14_23360	<i>wzz</i>	O-antigen chain length regulator			-1.84	6.9E-03
PA3148	PA14_23370	<i>wbpI</i>	UDP-N-acetylglucosamine 2-epimerase WbpI			-1.68	2.6E-02
PA3159	PA14_23380	<i>wbpA</i>	UDP-N-acetyl-d-glucosamine 6-Dehydrogenase			-2.08	1.8E-02
	PA14_23390	<i>orfE</i>	polysaccharide biosynthesis protein			-2.88	1.6E-02
	PA14_23400		hypothetical protein			-1.78	1.2E-02
	PA14_23410	<i>orfJ</i>	glycosyl transferase family protein			-3.45	2.0E-02
	PA14_23430	<i>hepP</i>	HepP			-1.54	2.8E-02
PA3145	PA14_23460	<i>wbpL</i>	glycosyltransferase WbpL			-1.77	2.7E-02
PA3133	PA14_23590	<i>sawR</i>	SawR	-2.06	5.2E-11		
PA3132	PA14_23610		probable hydrolase	-1.58	2.9E-06		
PA3128	PA14_23650		probable short-chain dehydrogenase	1.54	7.5E-06		
PA3126	PA14_23680	<i>ibpA</i>	heat-shock protein IbpA	-5.30	1.9E-50		
PA3121	PA14_23750	<i>leuC</i>	3-isopropylmalate dehydratase large subunit	1.67	7.9E-09		
PA3120	PA14_23760	<i>leuD</i>	3-isopropylmalate dehydratase small subunit	1.75	2.6E-12		
PA3119	PA14_23770		conserved hypothetical protein	1.54	1.1E-07		
PA3104	PA14_23980	<i>xcpP</i>	secretion protein XcpP			-1.82	7.8E-03
PA3096	PA14_24080	<i>xcpY</i>	general secretion pathway protein L	1.51	1.0E-13		
PA3095	PA14_24100	<i>xcpZ</i>	general secretion pathway protein M	1.67	2.6E-26		
PA3091	PA14_24180		hypothetical protein	1.90	5.5E-27		
PA3071	PA14_24420		hypothetical protein			1.58	2.2E-02
PA3062	PA14_24500	<i>pelC</i>	lipoprotein	-1.66	1.6E-02		
PA3060	PA14_24530	<i>pelE</i>	hypothetical protein	-1.70	1.6E-04		

PA3057	PA14_24570		hypothetical protein	2.16	2.8E-04		
PA3049	PA14_24650	<i>rmf</i>	ribosome modulation factor	1.82	8.6E-13		
PA3046	PA14_24700		conserved hypothetical protein	-1.91	1.0E-30		
PA3045	PA14_24710	<i>rocA2</i>	Two-component response regulator, RocA2	-2.45	9.1E-11		
PA3044	PA14_24720	<i>rocsS2</i>	Two-component sensor RocS2	-2.09	5.2E-14		
PA3042	PA14_24740		hypothetical protein	1.98	2.6E-14		
PA3041	PA14_24760		hypothetical protein	1.93	2.5E-12		
PA3040	PA14_24770		conserved hypothetical protein	1.89	1.3E-16		
PA3038	PA14_24790	<i>opdQ</i>	OpdQ	1.68	1.6E-02		
PA3037	PA14_24810		hypothetical protein	-2.07	1.6E-02		
PA3036	PA14_24820		hypothetical protein	-1.89	2.2E-03		
PA3035	PA14_24830		probable glutathione S-transferase	-1.51	3.0E-02		
PA3032	PA14_24860	<i>snr1</i>	cytochrome c Snr1	1.74	2.5E-06		
PA3024	PA14_24960		probable carbohydrate kinase	1.61	1.3E-12		
PA3023	PA14_24970		conserved hypothetical protein	2.20	1.9E-20		
PA3017	PA14_25040		conserved hypothetical protein			1.61	5.9E-03
PA3014	PA14_25080	<i>faoA</i>	fatty-acid oxidation complex alpha-subunit	-1.85	1.5E-77		
PA3013	PA14_25090	<i>faoB</i>	fatty-acid oxidation complex beta-subunit	-1.65	3.0E-47		
PA3008	PA14_25150		hypothetical protein	-1.94	6.1E-27		
PA3007	PA14_25160	<i>lexA</i>	repressor protein LexA	-1.81	6.9E-39		
PA3001	PA14_25250		probable glyceraldehyde-3-phosphate dehydrogenase	-1.50	1.6E-12		
PA2957	PA14_25800		probable transcriptional regulator	-1.52	3.5E-13		
PA2953	PA14_25840		electron transfer flavoprotein-ubiquinone oxidoreductase	-1.61	2.6E-45		
PA2948	PA14_25920	<i>cobM</i>	precorrin-3 methylase	1.75	1.3E-19		
PA2944	PA14_25970	<i>cobN</i>	cobalamin biosynthetic protein CobN	1.52	1.3E-24		
PA2943	PA14_25980		phospho-2-dehydro-3-deoxyheptonate aldolase	-1.60	2.0E-08		
PA2939	PA14_26020		probable aminopeptidase	1.68	5.9E-05		
PA2936	PA14_26070		hypothetical protein	-3.86	1.9E-12		
PA2934	PA14_26090	<i>cif</i>	CFTR inhibitory factor, Cif	-10.75	1.6E-38		
PA2933	PA14_26110		MFS transporter	-9.30	2.1E-27		
PA2932	PA14_26130	<i>morB</i>	morphinone reductase	-6.49	2.3E-19		
PA2929	PA14_26160		hypothetical protein	-1.69	1.0E-02		
PA2927	PA14_26190		hypothetical protein	1.54	3.1E-10		
PA2917	PA14_26330		probable transcriptional regulator	-2.27	4.4E-18		
PA2916	PA14_26340		hypothetical protein	-4.59	6.5E-15		

PA2915	PA14_26350		hypothetical protein	1.56	8.3E-09		
PA2914	PA14_26360		probable permease of ABC transporter	2.28	1.1E-13		
PA2913	PA14_26390		hypothetical protein	2.20	3.3E-14		
PA2912	PA14_26400		probable ATP-binding component of ABC transporter	2.05	1.5E-11		
PA2911	PA14_26420		probable TonB-dependent receptor	1.76	1.3E-15		
PA2906	PA14_26485		probable oxidoreductase	1.64	1.1E-21		
PA2905	PA14_26500	<i>cobH</i>	precorrin isomerase CobH	1.67	1.6E-13		
PA2904	PA14_26510	<i>cobI</i>	precorrin-2 methyltransferase CobI	1.63	3.2E-20		
PA2903	PA14_26530	<i>cobJ</i>	precorrin-3 methylase CobJ	1.72	2.4E-41		
PA2895	PA14_26610	<i>sbrR</i>	SbrR	1.54	7.2E-12		
PA2892	PA14_26650	<i>atuG</i>	GCase, alpha-subunit (biotin-containing)	1.88	3.8E-04		
PA2891	PA14_26670	<i>atuF</i>	geranyl-CoA carboxylase, alpha-subunit (biotin-containing)	1.74	5.4E-08		
PA2889	PA14_26700	<i>atvR</i>	atypical virulence-related response regulator AtvR	1.61	2.1E-04		
PA2888	PA14_26720	<i>atuC</i>	geranyl-CoA carboxylase, beta-subunit	1.72	6.5E-08		
PA2887	PA14_26730	<i>atuB</i>	putative dehydrogenase involved in catabolism of citronellol	1.52	3.6E-03		
PA2884	PA14_26770		hypothetical protein	1.50	7.8E-11		
PA2883	PA14_26780		hypothetical protein	2.55	9.5E-28		
PA2879	PA14_26860		probable transcriptional regulator	1.99	3.2E-19		
PA2874	PA14_26920		hypothetical protein	1.90	7.1E-14		
PA2873	PA14_26930	<i>tgpA</i>	transglutaminase protein A, TgpA	1.74	3.3E-16		
PA2869	PA14_26980		hypothetical protein	-1.70	1.6E-06		
PA2863	PA14_27090	<i>lipH</i>	lipase modulator protein	2.59	2.9E-07		
PA2862	PA14_27100	<i>lipA</i>	lactonizing lipase precursor	2.18	2.0E-06		
PA2855	PA14_27170		hypothetical protein	-1.53	2.3E-07		
PA2851	PA14_27210	<i>efp</i>	translation elongation factor P			-1.59	2.0E-02
PA2850	PA14_27220	<i>ohr</i>	organic hydroperoxide resistance protein	-2.23	2.7E-14		
PA2840	PA14_27370		probable ATP-dependent RNA helicase	-2.75	1.7E-13		
PA2839	PA14_27390		conserved hypothetical protein	-1.67	5.1E-05		
PA2831	PA14_27470		conserved hypothetical protein	-1.92	4.3E-51		
PA2830	PA14_27480	<i>htpX</i>	heat shock protein HtpX	-1.95	2.1E-27		
PA2829	PA14_27490		hypothetical protein	-1.60	8.5E-09		
PA2826	PA14_27520		probable glutathione peroxidase	-1.53	7.8E-07		
	PA14_27650		hypothetical protein	1.85	7.2E-03		

	PA14_27700		transcriptional regulator	-2.19	1.4E-05		
PA2817	PA14_27710		hypothetical protein	-1.65	9.8E-10		
PA2815	PA14_27730		probable acyl-CoA dehydrogenase	2.23	1.5E-24		
PA2794	PA14_27990		pseudaminidase			-2.07	2.0E-02
PA2790	PA14_28030		hypothetical protein	-1.58	1.5E-08		
PA2786	PA14_28070		hypothetical protein	-1.82	3.5E-04		
PA2779	PA14_28140		hypothetical protein	1.72	5.3E-05		
PA2778	PA14_28150		hypothetical protein	1.73	3.1E-05		
PA2777	PA14_28170		conserved hypothetical protein	3.50	1.8E-29		
PA2776	PA14_28180	<i>pauB3</i>	FAD-dependent oxidoreductase	-1.52	9.5E-08		
PA2770	PA14_28280		hypothetical protein	-1.57	1.6E-17		
PA2769	PA14_28290		hypothetical protein	-1.57	3.6E-10		
	PA14_28330		hypothetical protein	2.06	6.8E-03		
PA2762	PA14_28380		hypothetical protein	-1.67	3.0E-07		
PA2761	PA14_28390		hypothetical protein			-1.58	4.9E-02
PA2754	PA14_28490		conserved hypothetical protein	2.31	5.8E-17		
	PA14_28520		hypothetical protein	2.08	2.2E-13		
PA2751	PA14_28530		conserved hypothetical protein	2.48	4.0E-14		
PA2747	PA14_28600		hypothetical protein	2.59	2.3E-15		
PA2746	PA14_28620		hypothetical protein	1.52	1.3E-04		
PA2745	PA14_28630		probable hydrolase	1.58	3.1E-08		
PA2743	PA14_28660	<i>infC</i>	translation initiation factor IF-3			-1.91	1.3E-02
PA2740	PA14_28690	<i>pheS</i>	phenylalanyl-tRNA synthetase, alpha-subunit	-1.77	1.2E-17		
PA2739	PA14_28710	<i>pheT</i>	phenylalanyl-tRNA synthetase, beta subunit	-1.70	7.2E-23		
	PA14_28760		hypothetical protein	1.87	1.4E-08		
	PA14_28840		helicase	1.59	4.4E-15	-1.52	3.0E-02
	PA14_28850		hypothetical protein	1.77	8.0E-15		
	PA14_28870		hypothetical protein	1.69	3.0E-12		
PA2721	PA14_28960		hypothetical protein	1.56	7.8E-05		
	PA14_28980		Fe ²⁺ -dicitrate sensor	-1.94	8.7E-04		
PA2717	PA14_29020	<i>cpo</i>	chloroperoxidase precursor	1.67	3.7E-08		
PA2712	PA14_29070		hypothetical protein	-1.78	2.1E-07		
PA2708	PA14_29120		hypothetical protein	2.43	4.2E-31		
PA2701	PA14_29210		probable major facilitator superfamily (MFS) transporter	2.08	1.7E-03		
PA2700	PA14_29220	<i>opdB</i>	proline porin OpdB	1.76	1.3E-02		
PA2688	PA14_29350	<i>pfeA</i>	Ferric enterobactin receptor, outer membrane protein PfeA precursor	-2.81	3.7E-13		
PA2677	PA14_29490		probable type II secretion protein	1.52	1.1E-03		

PA2672	PA14_29540		type II secretion system protein	2.06	1.3E-02		
PA2670	PA14_29560		hypothetical protein	1.69	1.1E-03		
PA2666	PA14_29600		probable 6-pyruvoyl tetrahydrobiopterin synthase	-1.79	5.2E-10	-1.70	1.9E-02
PA2663	PA14_29650	<i>ppyR</i>	psl and pyoverdine operon regulator, PpyR	1.61	4.5E-02		
PA2653	PA14_29770		probable transporter	-2.70	3.6E-45		
PA2652	PA14_29800		methyl-accepting chemotaxis protein	-2.24	1.1E-48		
PA2650	PA14_29830		conserved hypothetical protein	-1.59	2.2E-08		
PA2630	PA14_30100		conserved hypothetical protein	-1.86	1.2E-21		
PA2629	PA14_30110	<i>purB</i>	adenylosuccinate lyase	-1.85	9.3E-17		
PA2625	PA14_30160		conserved hypothetical protein	-1.76	7.6E-09		
PA2624	PA14_30180	<i>idh</i>	isocitrate dehydrogenase	-1.70	7.2E-13		
PA2622	PA14_30200	<i>cspD</i>	cold-shock protein CspD	1.55	1.5E-08		
PA2621	PA14_30210	<i>clpS</i>	ClpS			-1.56	2.9E-02
PA2619	PA14_30240	<i>infA</i>	initiation factor			-1.54	3.5E-03
PA2600	PA14_30460		hypothetical protein	-1.57	8.9E-06		
PA2598	PA14_30490		hypothetical protein	-1.53	5.4E-04		
PA2594	PA14_30550		conserved hypothetical protein	-2.82	5.7E-17		
PA2591	PA14_30580	<i>vqsR</i>	VqsR	1.58	2.5E-21		
PA2587	PA14_30630	<i>pqsH</i>	probable FAD-dependent monooxygenase	1.72	2.9E-32		
PA2582	PA14_30710		hypothetical protein			-1.51	1.8E-02
PA2579	PA14_30750	<i>kynA</i>	L-Tryptophan:oxygen 2,3-oxidoreductase (decyclizing) KynA	-1.56	2.0E-12		
PA2575	PA14_30800		hypothetical protein	-2.06	6.4E-22		
PA2573	PA14_30820		probable chemotaxis transducer	1.94	3.4E-17		
PA2571	PA14_30840		probable two-component sensor	1.53	7.2E-09		
	PA14_30850		TrbI-like protein	1.67	1.2E-02		
	PA14_30860		TrbG-like protein	2.14	3.5E-02		
	PA14_30880		conjugal transfer protein TrbL	2.61	1.5E-02		
	PA14_30970		transcriptional regulator	1.63	7.0E-16		
	PA14_31270		hypothetical protein	2.05	2.1E-07		
PA2570	PA14_31290	<i>lecA</i>	LecA	1.69	1.2E-05		
PA2569	PA14_31300		hypothetical protein	2.07	1.5E-16		
	PA14_31340		hypothetical protein	-2.02	4.5E-02		
PA2566	PA14_31350		conserved hypothetical protein	2.41	8.1E-45		
PA2565	PA14_31360		hypothetical protein	1.89	2.3E-17		
PA2564	PA14_31370		hypothetical protein	1.55	4.4E-11		
PA2563	PA14_31380		probable sulfate transporter	-2.17	2.1E-10		
PA2562	PA14_31390		hypothetical protein	1.86	1.5E-09		

PA2561	PA14_31400	<i>ctpH</i>	CtpH	-1.77	8.0E-13		
	PA14_31430		hypothetical protein	1.70	1.8E-08		
PA2550	PA14_31580		probable acyl-CoA dehydrogenase	-1.66	1.4E-03		
PA2531	PA14_31820		probable aminotransferase	2.58	1.9E-10		
PA2519	PA14_32060	<i>xylS</i>	transcriptional regulator XylS	1.84	3.6E-08		
PA2515	PA14_32130	<i>xylL</i>	1,6-dihydroxycyclohexa-2,4-diene-1-carboxylate dehydrogenase	1.94	1.5E-02		
PA2504	PA14_32280		hypothetical protein	1.71	2.0E-15		
PA2502	PA14_32300		hypothetical protein	-1.80	4.5E-20		
PA2500	PA14_32330		probable major facilitator superfamily (MFS) transporter	1.81	8.3E-08		
PA2499	PA14_32340		probable deaminase	2.01	1.1E-02		
PA2494	PA14_32390	<i>mexF</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux transporter MexF	-2.00	3.6E-14		
PA2493	PA14_32400	<i>mexE</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux membrane fusion protein MexE precursor	-1.87	4.2E-11		
PA2488	PA14_32460		probable transcriptional regulator	1.52	7.7E-04		
PA2486	PA14_32480	<i>ptrC</i>	Pseudomonas type III repressor gene C, PtrC	2.02	6.3E-10		
PA2485	PA14_32490		hypothetical protein	1.99	3.7E-07		
PA2483	PA14_32520		conserved hypothetical protein	-1.60	1.1E-09		
PA2468	PA14_32710	<i>foxI</i>	ECF sigma factor FoxI	1.77	5.8E-05		
PA2467	PA14_32720	<i>foxR</i>	Anti-sigma factor FoxR	1.51	1.7E-04		
PA2465	PA14_32750		hypothetical protein	-2.52	4.5E-08		
PA2463	PA14_32780		hypothetical protein	-1.70	7.8E-06		
	PA14_32820		hypothetical protein			-2.29	4.1E-02
PA2458	PA14_32830		hypothetical protein			-2.08	2.0E-02
PA2453	PA14_32890		hypothetical protein	-1.82	2.0E-11		
PA2452	PA14_32905		hypothetical protein	8.95	1.9E-16	-5.32	1.2E-06
PA2451	PA14_32905		hypothetical protein	8.95	1.9E-16		
PA2448	PA14_32950		hypothetical protein	1.78	8.3E-12		
PA2441	PA14_33050		hypothetical protein	-2.27	4.3E-09		
PA2440	PA14_33060		hypothetical protein	-2.35	1.0E-11		
PA2438	PA14_33080		hypothetical protein	1.53	4.8E-06		
PA2435	PA14_33130		probable cation-transporting P-type ATPase	1.56	2.7E-14		
PA2434	PA14_33150		hypothetical protein	1.79	9.2E-13		
PA2433	PA14_33160		hypothetical protein	3.98	7.6E-49		
PA2430	PA14_33220		conserved hypothetical protein	1.56	1.7E-04		

PA2428	PA14_33240		hypothetical protein	1.55	4.1E-02		
PA2427	PA14_33250		hypothetical protein	17.56	3.4E-57		
PA2426	PA14_33260	<i>pvdS</i>	sigma factor PvdS	2.03	9.7E-07		
PA2425	PA14_33270	<i>pvdG</i>	protein PvdG	10.22	6.2E-18	-9.38	2.7E-02
PA2424	PA14_33280	<i>pvdL</i>	PvdL	14.65	5.9E-25	-8.59	4.1E-02
	PA14_33330		hypothetical protein			-1.93	1.4E-02
	PA14_33360		hypothetical protein	1.74	2.5E-02		
PA2422	PA14_33370		hypothetical protein	1.83	4.1E-02		
PA2419	PA14_33420		probable hydrolase	1.64	7.8E-03		
PA2417	PA14_33440		probable transcriptional regulator	1.63	3.5E-09		
PA2415	PA14_33460		hypothetical protein	3.43	8.0E-21		
PA2414	PA14_33480		L-sorbose dehydrogenase	3.26	4.4E-57		
PA2413	PA14_33500	<i>pvdH</i>	L-2,4-diaminobutyrate:2-ketoglutarate 4-aminotransferase, PvdH	13.14	6.1E-19	-6.51	2.9E-02
PA2412	PA14_33510		conserved hypothetical protein	10.03	1.9E-16	-13.92	1.0E-02
PA2411	PA14_33520		probable thioesterase	10.76	7.8E-19		
PA2410	PA14_33530	<i>fpvF</i>	FpvF	4.23	1.9E-18	-6.66	7.3E-04
PA2409	PA14_33540	<i>fpvE</i>	ABC transporter permease	4.29	8.7E-18	-6.20	1.8E-02
PA2408	PA14_33550	<i>fpvD</i>	ABC transporter ATP-binding protein	5.11	8.0E-31		
PA2407	PA14_33560	<i>fpvC</i>	FpvC	4.85	1.1E-19	-6.32	2.0E-02
PA2406	PA14_33570	<i>fpvK</i>	hypothetical protein	6.00	8.9E-28		
PA2405	PA14_33580	<i>fpvJ</i>	hypothetical protein	5.33	3.6E-15		
PA2404	PA14_33590	<i>fpvH</i>	hypothetical protein	6.68	4.1E-30		
PA2403	PA14_33600	<i>fpvG</i>	FpvG	4.72	2.4E-23	-5.89	9.6E-03
PA2402	PA14_33610		probable non-ribosomal peptide synthetase	13.25	6.1E-32	-8.95	2.0E-02
PA2400	PA14_33630	<i>pvdJ</i>	PvdJ	17.29	4.0E-50	-8.89	9.6E-03
PA2399	PA14_33650	<i>pvdD</i>	pyoverdine synthetase D	16.10	2.1E-35	-7.77	8.5E-03
PA2398	PA14_33680	<i>fpvA</i>	ferripyoverdine receptor	6.55	7.7E-15	-7.29	1.9E-03
PA2397	PA14_33690	<i>pvdE</i>	pyoverdine biosynthesis protein PvdE	10.94	3.2E-19	-9.69	8.5E-03
PA2396	PA14_33700	<i>pvdF</i>	pyoverdine synthetase F	9.65	1.4E-24	-5.65	3.0E-02
PA2395	PA14_33710	<i>pvdO</i>	protein PvdO	12.72	4.6E-11	-10.49	2.5E-02
PA2394	PA14_33720	<i>pvdN</i>	protein PvdN	12.07	3.5E-13	-9.75	1.9E-02
PA2393	PA14_33730		putative dipeptidase	12.25	1.3E-12	-8.28	3.5E-02
PA2392	PA14_33740	<i>pvdP</i>	PvdP	10.99	8.5E-21	-10.46	2.1E-02
PA2391	PA14_33750	<i>opmQ</i>	probable outer membrane protein precursor	3.59	1.7E-22	-3.18	2.5E-02
PA2390	PA14_33760	<i>pvdT</i>	PvdT	3.28	2.4E-21		

PA2389	PA14_33770	<i>pvdR</i>	PvdR	3.49	7.8E-20		
PA2387	PA14_33800	<i>fvpI</i>	FvpI	2.16	1.8E-33		
PA2386	PA14_33810	<i>pvdA</i>	L-ornithine N5-oxygenase	11.76	1.3E-19	-8.77	1.0E-02
PA2385	PA14_33820	<i>pvdQ</i>	3-oxo-C12-homoserine lactone acylase PvdQ	10.86	2.7E-18	-8.43	3.6E-02
PA2384	PA14_33830		hypothetical protein	15.30	1.5E-20	-9.14	1.3E-02
PA2383	PA14_33840		probable transcriptional regulator	2.86	4.3E-17		
PA2381	PA14_33870		hypothetical protein	-2.29	1.5E-11		
PA2380	PA14_33880		hypothetical protein			-1.67	7.9E-03
PA2378	PA14_33900		probable aldehyde dehydrogenase			1.51	4.8E-03
PA2377	PA14_33910		hypothetical protein	7.94	1.3E-10		
PA2374	PA14_33940	<i>tseF</i>	TseF	2.45	7.4E-10		
PA2373	PA14_33960	<i>vgrG3</i>	VgrG3	2.87	1.6E-08		
	PA14_33970		hypothetical protein	2.18	1.1E-12	-2.02	9.6E-03
	PA14_33980		hypothetical protein	4.74	1.2E-20		
PA2371	PA14_33990	<i>clpV3</i>	ClpV3	5.36	7.2E-47		
PA2370	PA14_34000	<i>hsiH3</i>	HsiH3	4.38	6.6E-16		
PA2369	PA14_34010	<i>hsiG3</i>	HsiG3	3.95	3.5E-22		
PA2368	PA14_34020	<i>hsiF3</i>	HsiF3	4.63	1.1E-08		
PA2367	PA14_34030	<i>hcp3</i>	Hcp3	3.05	1.2E-12		
PA2366	PA14_34050	<i>hsiC3</i>	HsiC3	3.09	1.9E-21		
PA2365	PA14_34070	<i>hsiB3</i>	HsiB3	2.26	5.1E-14		
PA2364	PA14_34080	<i>lip3</i>	Lip3	2.32	1.0E-11		
PA2363	PA14_34100	<i>hsiJ3</i>	HsiJ3	2.30	2.5E-18		
PA2362	PA14_34110	<i>dotU3</i>	DotU3	1.93	9.0E-07		
PA2361	PA14_34130	<i>icmF3</i>	IcmF3	2.27	1.1E-19		
PA2360	PA14_34140	<i>hsiA3</i>	hypothetical protein	2.79	4.1E-19		
PA2359	PA14_34150	<i>sfa3</i>	probable transcriptional regulator	-1.97	1.5E-07		
PA2356	PA14_34190	<i>msuD</i>	methanesulfonate sulfonatase MsuD	-1.58	2.2E-02		
PA2348	PA14_34290		DszA family monooxygenase	-2.21	8.3E-03		
PA2346	PA14_34320		DszC family monooxygenase	-1.66	3.4E-02		
PA2342	PA14_34360	<i>mtlD</i>	mannitol dehydrogenase	1.74	2.1E-02		
PA2338	PA14_34420		probable binding protein component of ABC maltose/mannitol transporter	1.51	4.6E-03		
PA2337	PA14_34440	<i>mtlR</i>	transcriptional regulator MtlR	1.53	1.7E-04		
PA2331	PA14_34460		hypothetical protein	-1.89	2.9E-11	-2.21	1.3E-02
PA2330	PA14_34490		hypothetical protein	-1.72	3.2E-08		
PA2329	PA14_34500		probable ATP-binding component of ABC transporter	-1.70	6.4E-06	-3.14	2.7E-03
PA2328	PA14_34510		hypothetical protein	-1.74	2.9E-12		
PA2324	PA14_34580		hypothetical protein	-1.61	6.0E-06		

PA2320	PA14_34660	<i>gntR</i>	transcriptional regulator GntR	1.59	1.3E-19		
PA2313	PA14_34720		hypothetical protein	-2.52	4.5E-08		
PA2312	PA14_34730		XRE family transcriptional regulator	-3.04	3.5E-15		
PA2311	PA14_34740		hypothetical protein	-3.01	2.5E-09		
PA2310	PA14_34750		taurine catabolism dioxygenase	-2.95	9.0E-16		
PA2309	PA14_34770		ABC transporter substrate-binding protein	-1.89	3.0E-04		
PA2305	PA14_34810	<i>ambB</i>	AmbB	2.66	3.6E-41		
PA2304	PA14_34820	<i>ambC</i>	AmbC	3.48	2.7E-20		
PA2303	PA14_34830	<i>ambD</i>	AmbD	3.59	1.2E-30		
PA2302	PA14_34840	<i>ambE</i>	AmbE	4.17	1.5E-86		
PA2301	PA14_34850		hypothetical protein	2.44	1.9E-37		
PA2300	PA14_34870	<i>chiC</i>	chitinase	1.96	2.1E-16		
PA2299	PA14_34880		probable transcriptional regulator	1.99	7.2E-14		
PA2298	PA14_34900		probable oxidoreductase	1.61	3.6E-11		
PA2288	PA14_35000		hypothetical protein	-1.58	5.5E-07		
PA2283	PA14_35050		hypothetical protein	-1.94	4.1E-03		
PA2275	PA14_35150		probable alcohol dehydrogenase (Zn-dependent)	-2.01	4.7E-06		
PA2272	PA14_35190	<i>pbpC</i>	penicillin-binding protein 3A	1.90	2.8E-20		
PA2268	PA14_35240		hypothetical protein	-8.85	9.2E-43		
PA2267	PA14_35250		probable transcriptional regulator	1.63	1.5E-06		
PA2266	PA14_35270		probable cytochrome c precursor	-2.40	1.2E-12	1.52	2.3E-02
PA2265	PA14_35290		gluconate dehydrogenase	-2.74	1.4E-16		
PA2264	PA14_35300		conserved hypothetical protein	-2.66	1.3E-13		
PA2263	PA14_35320		probable 2-hydroxyacid dehydrogenase	-2.64	5.4E-11		
PA2262	PA14_35330		probable 2-ketogluconate transporter	-3.07	7.9E-15		
PA2261	PA14_35340		probable 2-ketogluconate kinase	-3.29	3.5E-15		
PA2260	PA14_35360		hypothetical protein	-3.50	2.8E-13	1.68	1.8E-02
PA2259	PA14_35370	<i>ptxS</i>	transcriptional regulator PtxS	-2.14	1.3E-08		
PA2258	PA14_35380	<i>ptxR</i>	transcriptional regulator PtxR	2.38	1.7E-13		
PA2245	PA14_35550	<i>pslO</i>	hypothetical protein	4.24	5.3E-07		
PA2244	PA14_35570	<i>pslN</i>	hypothetical protein	3.85	2.5E-26		
PA2235	PA14_35690	<i>pslE</i>	PsIE	-1.53	3.1E-04		
	PA14_35740		transposase	1.72	2.9E-20		
	PA14_35750		tpnA repressor protein	2.16	2.8E-09		
	PA14_35760		hypothetical protein	1.78	4.5E-17	-2.45	3.7E-03
	PA14_35780		hypothetical protein			-1.62	1.2E-02
	PA14_35800		hypothetical protein	1.60	2.7E-15		
	PA14_35830	<i>tnpT</i>	cointegrate resolution protein			-1.84	1.7E-02

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	PA14_35940		acyl-CoA synthetase	1.64	2.5E-02		
	PA14_35950		dehydrogenase	1.76	3.3E-02		
	PA14_36010		hypothetical protein	1.64	3.9E-06		
PA2204	PA14_36200		probable binding protein component of ABC transporter	-2.10	4.2E-11	-1.57	3.2E-02
PA2203	PA14_36220		probable amino acid permease	-2.95	5.3E-18		
PA2202	PA14_36230		amino acid ABC transporter permease	-2.66	1.2E-16		
PA2196	PA14_36300		TetR family transcriptional regulator	1.56	5.0E-10		
PA2195	PA14_36310	<i>hcnC</i>	hydrogen cyanide synthase HcnC	2.10	2.8E-16		
PA2194	PA14_36320	<i>hcnB</i>	hydrogen cyanide synthase HcnB	1.87	2.1E-13		
PA2193	PA14_36330	<i>hcnA</i>	hydrogen cyanide synthase HcnA	1.72	1.5E-08		
PA2191	PA14_36345	<i>exoY</i>	adenylate cyclase ExoY	1.70	2.2E-06	-1.73	2.7E-02
PA2189	PA14_36350		hypothetical protein	2.88	8.4E-07		
PA2187	PA14_36360		hypothetical protein	3.74	1.9E-07		
PA2181	PA14_36370		hypothetical protein	4.84	2.1E-15		
PA2180	PA14_36375		hypothetical protein	4.06	1.9E-39		
PA2179	PA14_36390		hypothetical protein	4.27	6.5E-23		
	PA14_36400		hypothetical protein	1.79	1.9E-02		
PA2178	PA14_36410		hypothetical protein	3.68	5.5E-09		
PA2177	PA14_36420		probable sensor/response regulator hybrid	2.34	3.7E-18		
PA2176	PA14_36450		hypothetical protein	3.87	1.0E-27		
PA2175	PA14_36460		hypothetical protein	4.34	1.0E-28		
PA2174	PA14_36470		hypothetical protein	1.85	2.9E-06		
	PA14_36480		hypothetical protein	3.73	8.5E-17		
PA2173	PA14_36490		hypothetical protein	4.27	6.6E-21		
PA2172	PA14_36500		hypothetical protein	3.50	1.2E-33		
PA2171	PA14_36520		hypothetical protein	2.74	4.4E-21		
PA2169	PA14_36530		hypothetical protein	2.34	2.0E-09		
PA2168	PA14_36540		hypothetical protein	4.63	3.4E-19		
PA2167	PA14_36550		hypothetical protein	4.03	1.3E-35		
PA2166	PA14_36560		hypothetical protein	5.06	7.3E-36		
PA2165	PA14_36570		probable glycogen synthase	4.33	1.0E-55		
PA2164	PA14_36580		probable glycosyl hydrolase	4.00	5.2E-53		
PA2163	PA14_36590		hypothetical protein	4.06	2.0E-43		
PA2162	PA14_36605		probable glycosyl hydrolase	3.17	1.7E-22		
PA2161	PA14_36620		hypothetical protein	2.44	4.0E-07		
PA2160	PA14_36630		probable glycosyl hydrolase	1.96	1.2E-04		
PA2159	PA14_36650		conserved hypothetical protein	2.53	1.4E-13		

PA2158	PA14_36660		probable alcohol dehydrogenase (Zn-dependent)	2.75	2.1E-14		
PA2157	PA14_36670		hypothetical protein	2.94	5.3E-11		
PA2156	PA14_36680		conserved hypothetical protein	2.50	1.1E-05		
PA2155	PA14_36690		probable phospholipase	2.51	2.0E-08		
PA2154	PA14_36700		conserved hypothetical protein	1.97	1.0E-02		
PA2153	PA14_36710	<i>glgB</i>	1,4-alpha-glucan branching enzyme	2.98	7.6E-20		
PA2152	PA14_36730		probable trehalose synthase	3.75	3.9E-72		
PA2151	PA14_36740		conserved hypothetical protein	4.52	3.1E-50		
PA2150	PA14_36760		conserved hypothetical protein	3.94	1.1E-26		
PA2149	PA14_36770		hypothetical protein	4.84	6.1E-10		
PA2148	PA14_36780		conserved hypothetical protein	3.83	3.1E-16		
	PA14_36790		hypothetical protein	3.50	7.4E-08		
PA2147	PA14_36810	<i>katE</i>	catalase HP11	2.91	4.0E-24		
PA2146	PA14_36820		conserved hypothetical protein	2.61	1.3E-12	-1.80	1.9E-02
PA2145	PA14_36830		hypothetical protein	2.26	8.5E-07		
PA2144	PA14_36840	<i>glgP</i>	glycogen phosphorylase	3.89	3.7E-51		
PA2143	PA14_36850		hypothetical protein	3.58	3.4E-32		
PA2142	PA14_36870		probable short-chain dehydrogenase	3.86	6.3E-18		
PA2141	PA14_36880		hypothetical protein	4.95	2.1E-07		
PA2140	PA14_36890		probable metallothionein	8.66	3.5E-04		
PA2170	PA14_36900		hypothetical protein	5.62	2.7E-06		
PA2138	PA14_36910	<i>ligD</i>	Multifunctional non-homologous end joining protein LigD	3.43	7.4E-17		
PA2137	PA14_36920		hypothetical protein	3.25	5.6E-18		
PA2136	PA14_36930		hypothetical protein	3.91	6.5E-05		
PA2135	PA14_36960		probable transporter	2.75	1.3E-14		
PA2134	PA14_36980		hypothetical protein	2.66	5.0E-17		
PA2133	PA14_36990		Cyclic-guanylate-specific phosphodiesterase	-1.95	4.7E-03		
PA2132	PA14_37000	<i>cupA5</i>	chaperone CupA5	-4.71	1.4E-05		
PA2131	PA14_37010	<i>cupA4</i>	fimbrial subunit CupA4	-5.04	9.0E-10		
PA2130	PA14_37030	<i>cupA3</i>	usher	-3.54	3.7E-17		
PA2129	PA14_37040	<i>cupA2</i>	chaperone CupA2	-4.66	2.1E-23		
PA2128	PA14_37060	<i>cupA1</i>	fimbrial subunit CupA1	-4.55	7.1E-80		
PA2121	PA14_37140		probable transcriptional regulator	1.60	4.0E-03		
PA2118	PA14_37190	<i>ada</i>	O6-methylguanine-DNA methyltransferase	1.72	4.9E-10		
PA2108	PA14_37340		probable decarboxylase	2.97	1.2E-16		
PA2107	PA14_37350		hypothetical protein	5.03	1.6E-14		
PA2099	PA14_37360		probable short-chain dehydrogenase	1.57	3.8E-02		

PA2094	PA14_37420		transmembrane sensor protein	3.73	7.9E-13		
PA2093	PA14_37430		probable sigma-70 factor, ECF subfamily	2.53	2.4E-07		
PA2092	PA14_37440		MFS transporter	3.49	6.1E-13		
PA2091	PA14_37460		permease	2.94	3.3E-09		
PA2090	PA14_37470		flavin-dependent oxidoreductase	3.33	3.0E-12		
PA2089	PA14_37490		hypothetical protein	2.59	1.4E-18		
PA2088	PA14_37510		hypothetical protein	3.55	1.9E-13		
PA2087	PA14_37520		hypothetical protein	3.24	4.1E-07		
PA2086	PA14_37530		hydrolase	3.08	1.4E-08		
PA2085	PA14_37550		ring-hydroxylating dioxygenase small subunit	2.74	9.5E-05		
PA2084	PA14_37560		probable asparagine synthetase	2.32	2.2E-07		
PA2082	PA14_37580	<i>kynR</i>	KynR	1.52	1.6E-04		
PA2081	PA14_37590	<i>kynB</i>	kynurenine formamidase, KynB	1.51	4.1E-06		
PA2080	PA14_37610	<i>kynU</i>	kynureninase KynU	1.53	5.9E-06		
PA2079	PA14_37630		probable amino acid permease	1.81	1.1E-07		
	PA14_37670		hypothetical protein	1.86	2.4E-04		
PA2072	PA14_37690		conserved hypothetical protein	1.68	8.2E-17		
PA2071	PA14_37710	<i>fusA2</i>	elongation factor G	1.78	4.4E-26		
PA2067	PA14_37770		probable hydrolase	1.57	2.8E-18		
PA2063	PA14_37820		hypothetical protein	-1.54	9.2E-12		
PA2061	PA14_37840	<i>sppD</i>	ABC transporter ATP-binding protein, SppD	1.59	4.2E-03		
PA2051	PA14_37980		Fe ²⁺ -dicitrate sensor, membrane protein	-3.32	5.8E-08		
PA2050	PA14_37990		RNA polymerase sigma factor	-4.51	1.5E-13		
PA2046	PA14_38050		hypothetical protein	3.02	9.0E-14		
PA2042	PA14_38110		probable transporter (membrane subunit)	-1.78	9.3E-27		
PA2041	PA14_38130		Amino acid permease	-2.04	1.0E-12		
PA2040	PA14_38140	<i>pauA4</i>	Glutamylpolyamine synthetase	-1.53	8.6E-08		
PA2039	PA14_38160		hypothetical protein	-2.18	6.0E-17		
PA2038	PA14_38170		hypothetical protein	-2.06	8.4E-11		
PA2034	PA14_38210		hypothetical protein	1.59	1.4E-02		
PA2033	PA14_38220		hypothetical protein	1.70	6.5E-04		
PA2032	PA14_38250		probable transcriptional regulator	1.60	8.7E-18		
PA2031	PA14_38260		hypothetical protein	1.77	2.3E-08		
PA2030	PA14_38270		hypothetical protein	1.66	7.1E-09		
PA2027	PA14_38310		hypothetical protein	1.88	4.3E-03		
PA2021	PA14_38370		hypothetical protein	3.71	1.9E-13		

PA2020	PA14_38380	<i>mexZ</i>	MexZ			1.63	2.8E-02
PA2019	PA14_38395	<i>mexX</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux membrane fusion protein MexX precursor	-1.78	3.4E-07	8.54	3.5E-22
PA2018	PA14_38410	<i>mexY</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux transporter MexY	-1.59	2.1E-06	8.04	1.3E-36
PA2016	PA14_38430	<i>liuR</i>	regulator of liu genes			-2.29	7.8E-03
PA1990	PA14_38770	<i>pqqH</i>	PqqH	2.17	4.3E-17		
PA1989	PA14_38780	<i>pqqE</i>	pyrroloquinoline quinone biosynthesis protein E	1.56	3.3E-07		
PA1988	PA14_38790	<i>pqqD</i>	pyrroloquinoline quinone biosynthesis protein D	1.95	1.2E-06		
PA1987	PA14_38800	<i>pqqC</i>	pyrroloquinoline quinone biosynthesis protein C	1.79	2.2E-09		
PA1986	PA14_38820	<i>pqqB</i>	pyrroloquinoline quinone biosynthesis protein B	1.74	7.9E-09		
PA1982	PA14_38860	<i>exaA</i>	quinoprotein ethanol dehydrogenase	1.71	1.6E-02		
PA1973	PA14_39010	<i>pqqF</i>	pyrroloquinoline quinone biosynthesis protein F	1.56	1.7E-05		
PA1964	PA14_39130		probable ATP-binding component of ABC transporter	-1.71	6.2E-10		
PA1960	PA14_39180		hypothetical protein	-1.63	1.3E-09		
PA1959	PA14_39190	<i>bacA</i>	bacitracin resistance protein	-2.03	3.3E-41		
PA1951	PA14_39270	<i>fapF</i>	FapF	1.98	1.8E-16		
PA1942	PA14_39420		hypothetical protein	-1.52	3.2E-02		
	PA14_39470		hypothetical protein			-1.63	1.9E-02
PA1934	PA14_39500		hypothetical protein	4.65	5.6E-18		
PA1933	PA14_39520		probable hydroxylase large subunit	3.24	2.0E-45		
PA1932	PA14_39530		probable hydroxylase molybdopterin-containing subunit	3.38	6.6E-31		
PA1931	PA14_39540		probable ferredoxin	3.15	1.3E-24		
PA1930	PA14_39560		probable chemotaxis transducer	1.52	2.8E-05		
PA1927	PA14_39590	<i>metE</i>	5-methyltetrahydropteroyltriglutamate-homocysteine S-methyltransferase	-1.73	2.8E-12		
PA1921	PA14_39660		hypothetical protein	2.23	1.0E-08		
PA1920	PA14_39690	<i>nrdD</i>	class III (anaerobic) ribonucleoside-triphosphate reductase subunit, NrdD	2.75	3.2E-23		
	PA14_39700		hypothetical protein	3.17	3.7E-10		
PA1919	PA14_39710	<i>nrdG</i>	class III (anaerobic) ribonucleoside-triphosphate reductase activating protein, 'activase', NrdG	4.24	8.1E-07		

PA1918	PA14_39720		amino acid oxidase	1.99	4.3E-03		
PA1914	PA14_39780		conserved hypothetical protein	2.83	1.4E-12		
PA1913	PA14_39790		hypothetical protein	-3.09	4.5E-25		
PA1912	PA14_39800	<i>femI</i>	ECF sigma factor, FemI	-1.59	2.6E-03		
PA1910	PA14_39820	<i>femA</i>	ferric-mycobactin receptor, FemA	-1.53	2.7E-03		
PA1907	PA14_39860		hypothetical protein	1.77	7.2E-06		
	PA14_39880	<i>phzG2</i>	pyridoxamine 5'-phosphate oxidase	3.26	7.2E-24		
PA1901	PA14_39945	<i>phzC2</i>	phenazine biosynthesis protein PhzC	2.38	2.0E-17		
PA4212	PA14_39945	<i>phzC1</i>	phenazine biosynthesis protein PhzC	2.38	2.0E-17		
PA1900	PA14_39960	<i>phzB2</i>	probable phenazine biosynthesis protein	2.43	4.0E-16		
PA1899	PA14_39970	<i>phzA2</i>	probable phenazine biosynthesis protein	2.62	9.3E-20	-1.67	9.8E-06
PA1898	PA14_39980	<i>qscR</i>	quorum-sensing control repressor	1.73	2.7E-07		
PA1897	PA14_39990		hypothetical protein	1.50	3.3E-04		
PA1896	PA14_40010		hypothetical protein	1.79	2.4E-07		
PA1895	PA14_40020		hypothetical protein	1.79	4.0E-08	-2.12	2.0E-02
PA1894	PA14_40030		hypothetical protein	1.89	1.7E-12	-1.54	2.1E-02
PA1893	PA14_40040		hypothetical protein	1.88	1.2E-10		
PA1892	PA14_40050		hypothetical protein	1.68	7.5E-08		
PA1891	PA14_40060		hypothetical protein	1.94	1.9E-08		
PA1889	PA14_40080		hypothetical protein	1.52	9.5E-08		
PA1882	PA14_40170		probable transporter	-1.99	5.9E-06		
PA1879	PA14_40210		hypothetical protein	-1.51	1.6E-03		
PA1878	PA14_40220		hypothetical protein	-2.25	3.1E-19		
PA1877	PA14_40230		probable secretion protein	2.10	2.2E-14		
PA1876	PA14_40240		probable ATP-binding/permease fusion ABC transporter	2.03	2.8E-16		
PA1875	PA14_40250		probable outer membrane protein precursor	2.29	5.4E-24		
PA1874	PA14_40260		hypothetical protein	2.17	5.0E-18		
PA1871	PA14_40290	<i>lasA</i>	LasA protease precursor	5.84	1.2E-82		
PA1860	PA14_40430		hypothetical protein	1.54	4.0E-07		
PA1852	PA14_40560		hypothetical protein	1.75	4.7E-13		
PA1847	PA14_40630	<i>nfuA</i>	NfuA	-1.70	1.3E-33		
PA1845	PA14_40650	<i>tsiI</i>	TsiI	-1.51	3.5E-05		
	PA14_40750	<i>pvdD</i>	pyoverdine synthetase D	2.02	5.5E-15		
PA1838	PA14_40770	<i>cysI</i>	sulfite reductase	-1.93	9.3E-22		
PA1837	PA14_40780		hypothetical protein	-1.75	2.8E-13		
PA1824	PA14_40940		conserved hypothetical protein	-2.07	2.9E-15		
PA1805	PA14_41190	<i>ppiD</i>	peptidyl-prolyl cis-trans isomerase D	-1.69	4.6E-24		

PA1803	PA14_41220	<i>lon</i>	Lon protease	-1.63	1.1E-25		
PA1801	PA14_41240	<i>clpP</i>	ClpP	-1.51	3.7E-18		
PA1797	PA14_41280		hypothetical protein	1.98	2.8E-11		
	PA14_41290		hypothetical protein	2.31	2.5E-03		
	PA14_41300		hypothetical protein	-1.69	3.7E-09		
PA1786	PA14_41480	<i>nasS</i>	NasS	-1.75	7.6E-10	1.78	2.8E-04
PA1776	PA14_41575	<i>sigX</i>	ECF sigma factor SigX			-1.59	1.4E-02
PA1768	PA14_41690		hypothetical protein			-1.85	1.6E-02
PA1757	PA14_41830	<i>thrH</i>	homoserine kinase	-1.67	1.0E-17		
PA1755	PA14_41860		hypothetical protein	-1.60	1.7E-06		
PA1751	PA14_41910		hypothetical protein	1.52	3.6E-07		
PA1748	PA14_41950		probable enoyl-CoA hydratase/isomerase	-1.84	3.2E-27		
PA1747	PA14_41960		hypothetical protein	-2.33	5.4E-05		
PA1745	PA14_41980		hypothetical protein	1.92	1.2E-11		
PA1733	PA14_42130		conserved hypothetical protein	1.87	1.8E-14		
PA1732	PA14_42140		conserved hypothetical protein	1.72	7.1E-09	1.52	2.4E-02
PA1731	PA14_42150		conserved hypothetical protein	1.92	2.1E-15		
PA1730	PA14_42160		conserved hypothetical protein	1.98	1.5E-28		
PA1725	PA14_42250	<i>pscL</i>	type III export protein PscL	2.14	1.4E-14	-1.93	2.5E-02
PA1724	PA14_42260	<i>pscK</i>	type III export protein PscK	1.74	9.9E-06		
PA1723	PA14_42270	<i>pscJ</i>	type III export protein PscJ	1.62	8.1E-08		
PA1722	PA14_42280	<i>pscI</i>	type III export protein PscI	1.60	1.3E-05		
PA1721	PA14_42290	<i>pscH</i>	type III export protein PscH	1.61	2.3E-05		
PA1720	PA14_42300	<i>pscG</i>	type III export protein PscG	1.62	2.3E-08		
PA1719	PA14_42310	<i>pscF</i>	type III export protein PscF	1.54	1.0E-05		
PA1717	PA14_42340	<i>pscD</i>	type III export protein PscD	1.78	2.6E-07		
PA1716	PA14_42350	<i>pscC</i>	Type III secretion outer membrane protein PscC precursor	1.70	2.0E-07	-1.62	2.6E-02
PA1715	PA14_42360	<i>pscB</i>	type III export apparatus protein	1.76	9.4E-07		
PA1714	PA14_42380	<i>exsD</i>	ExsD	2.01	1.3E-15	-1.61	1.3E-02
PA1713	PA14_42390	<i>exsA</i>	transcriptional regulator ExsA	2.73	1.3E-24	-2.43	1.5E-07
PA1712	PA14_42400	<i>exsB</i>	exoenzyme S synthesis protein B	1.88	8.8E-10		
PA1711	PA14_42410	<i>exsE</i>	ExsE	1.84	1.1E-13		
PA1710	PA14_42430	<i>exsC</i>	ExsC, exoenzyme S synthesis protein C precursor.	1.84	3.1E-12		
PA1709	PA14_42440	<i>popD</i>	Translocator outer membrane protein PopD precursor			-1.72	1.0E-02
PA1708	PA14_42450	<i>popB</i>	translocator protein PopB			-2.32	8.7E-06
PA1707	PA14_42460	<i>pcrH</i>	regulatory protein PcrH			-1.84	2.7E-02
PA1706	PA14_42470	<i>pcrV</i>	type III secretion protein PcrV			-2.27	2.7E-04

PA1703	PA14_42500	<i>pcrD</i>	type III secretory apparatus protein PcrD			-2.24	2.7E-04
PA1698	PA14_42550	<i>popN</i>	Type III secretion outer membrane protein PopN precursor			-2.24	5.6E-03
PA1696	PA14_42580	<i>pscO</i>	translocation protein in type III secretion	1.58	3.5E-03		
PA1690	PA14_42660	<i>pscU</i>	translocation protein in type III secretion	1.53	5.6E-04		
PA1673	PA14_42860		hypothetical protein	1.84	6.9E-08		
PA1672	PA14_42870		hypothetical protein	1.51	1.3E-10		
PA5266	PA14_43080	<i>vgrG14</i>	VgrG14	-1.61	1.0E-02		
	PA14_43090	<i>tap</i>	Tap	-1.62	2.3E-03		
PA1649	PA14_43180		probable short-chain dehydrogenase	-1.99	1.2E-04		
PA1624	PA14_43520		hypothetical protein			1.88	1.8E-02
PA1608	PA14_43710		probable chemotaxis transducer	-1.93	1.6E-18		
PA1606	PA14_43730		hypothetical protein	2.98	1.4E-12		
PA1605	PA14_43740		hypothetical protein	2.47	4.1E-12		
PA1598	PA14_43830		conserved hypothetical protein	-1.55	1.1E-03		
PA1596	PA14_43850	<i>htpG</i>	heat shock protein HtpG	-2.67	2.6E-10		
PA1580	PA14_44070	<i>gltA</i>	citrate synthase			-1.63	3.7E-02
	PA14_44090		Fe-S-cluster oxidoreductase	-1.51	4.7E-05		
PA1577	PA14_44110		hypothetical protein	-1.96	8.4E-08		
PA1574	PA14_44140		conserved hypothetical protein	-1.65	2.6E-15		
PA1571	PA14_44170		hypothetical protein	1.87	7.2E-15	1.53	3.4E-02
	PA14_44230		hypothetical protein	-1.80	3.3E-02		
PA1566	PA14_44240	<i>pauA3</i>	Glutamylpolyamine synthetase	-1.82	5.3E-03		
PA1565	PA14_44260	<i>pauB2</i>	FAD-dependent oxidoreductase	-1.55	1.9E-03		
PA1562	PA14_44290	<i>acnA</i>	aconitate hydratase 1	1.72	3.4E-11		
PA1556	PA14_44350	<i>ccoO2</i>	Cytochrome c oxidase, cbb3-type, CcoO subunit	1.72	1.1E-05		
PA1555	PA14_44360	<i>ccoP2</i>	Cytochrome c oxidase, cbb3-type, CcoP subunit	1.73	1.8E-06		
PA1554	PA14_44370	<i>ccoN1</i>	Cytochrome c oxidase, cbb3-type, CcoN subunit	-1.85	3.8E-26		
PA1553	PA14_44380	<i>ccoO1</i>	Cytochrome c oxidase, cbb3-type, CcoO subunit	-1.75	4.7E-25		
PA1552.1	PA14_44390	<i>ccoQ1</i>	Cytochrome c oxidase, cbb3-type, CcoQ subunit	-1.64	1.3E-16		
PA1552	PA14_44400	<i>ccoP1</i>	Cytochrome c oxidase, cbb3-type, CcoP subunit	-1.65	4.1E-21		
PA1551	PA14_44420		probable ferredoxin	-1.58	1.7E-11		

PA1549	PA14_44440		probable cation-transporting P-type ATPase	-1.54	6.9E-12		
PA1547	PA14_44460		hypothetical protein	-1.53	9.2E-06		
PA1545	PA14_44480		hypothetical protein			-1.78	3.0E-02
PA1543	PA14_44500	<i>apt</i>	adenine phosphoribosyltransferase	-1.52	2.1E-17		
PA1542	PA14_44510		hypothetical protein	-2.57	2.9E-19		
PA1541	PA14_44520		drug efflux transporter	-5.57	1.5E-10		
PA1540	PA14_44530		multidrug efflux system protein MdtI	-2.40	6.7E-05		
PA1538	PA14_44560		probable flavin-containing monooxygenase	-1.91	7.7E-07		
PA1537	PA14_44570		probable short-chain dehydrogenase	-1.74	6.7E-04		
PA1525	PA14_44700	<i>alkB2</i>	alkane-1-monooxygenase 2	1.83	1.7E-04		
PA1524	PA14_44710	<i>xdhA</i>	xanthine dehydrogenase	1.82	8.4E-05		
PA1523	PA14_44740	<i>xdhB</i>	xanthine dehydrogenase	1.83	9.0E-07		
PA1515	PA14_44850	<i>alc</i>	allantoicase	1.54	7.9E-06		
PA0263	PA14_44890	<i>hcpC</i>	secreted protein Hcp	-1.65	1.6E-02		
PA1512	PA14_44890	<i>hcpA</i>	secreted protein Hcp	-1.65	1.6E-02		
PA1511	PA14_44900	<i>vgrG2a</i>	VgrG2a			-1.74	1.4E-02
PA1510	PA14_44910	<i>tplE</i>	type 6 PGAP1-like effector, TplE			-1.58	3.7E-02
PA1502	PA14_45000	<i>gcl</i>	glyoxylate carbonylase	-1.79	3.9E-03		
PA1494	PA14_45100	<i>muiA</i>	mucoidy inhibitor gene A	-1.76	3.1E-12		
PA1493	PA14_45110	<i>cysP</i>	sulfate-binding protein of ABC transporter	-1.68	9.4E-26	-1.55	1.3E-02
PA1484	PA14_45250		probable transcriptional regulator	1.54	5.6E-05		
PA1439	PA14_45850		conserved hypothetical protein	-1.69	2.5E-15		
PA1435	PA14_45910		probable Resistance-Nodulation-Cell Division (RND) efflux membrane fusion protein precursor	-1.57	1.1E-02		
PA1431	PA14_45950	<i>rsaL</i>	regulatory protein RsaL	3.01	2.1E-74	-1.77	1.7E-02
PA1429	PA14_45970		probable cation-transporting P-type ATPase	1.82	7.6E-16		
PA1428	PA14_45980		conserved hypothetical protein	-2.40	1.5E-12		
PA1425	PA14_46010		probable ATP-binding component of ABC transporter	-1.71	8.2E-10		
PA1423	PA14_46030	<i>bdlA</i>	BdlA	-1.62	8.6E-06		
PA1408	PA14_46240		hypothetical protein	2.28	4.3E-16	1.57	2.8E-02
PA1404	PA14_46280		hypothetical protein	3.39	4.7E-27		
PA1403	PA14_46290		probable transcriptional regulator	2.02	4.2E-07		
	PA14_46460		hypothetical protein			-1.79	9.5E-03
	PA14_46510		hypothetical protein	1.83	2.2E-19		

	PA14_46520		hypothetical protein	1.79	4.0E-08		
	PA14_46530		hypothetical protein	1.85	1.2E-12		
	PA14_46540		hypothetical protein	2.21	1.8E-28		
	PA14_46550		ribonuclease	1.82	3.5E-18		
PA1356	PA14_46750		hypothetical protein	2.68	2.5E-19		
PA1355	PA14_46760		hypothetical protein	1.97	5.1E-04		
PA1351	PA14_46810		probable sigma-70 factor, ECF subfamily	1.90	1.7E-10		
PA1350	PA14_46820		hypothetical protein	1.86	8.1E-11		
PA1349	PA14_46830		conserved hypothetical protein	1.63	3.2E-05		
PA1348	PA14_46840		hypothetical protein	2.40	6.4E-16		
PA1346	PA14_46860		hypothetical protein	1.85	2.7E-04		
PA1343	PA14_46900		hypothetical protein	-1.64	2.7E-06		
PA1330	PA14_47060		probable short-chain dehydrogenase	1.75	3.0E-04		
PA1324	PA14_47120		hypothetical protein	2.26	1.1E-19		
PA1323	PA14_47130		hypothetical protein	2.35	3.2E-20		
PA1321	PA14_47150	<i>cyoE</i>	cytochrome o ubiquinol oxidase protein CyoE	1.88	6.0E-09		
PA1320	PA14_47160	<i>cyoD</i>	cytochrome o ubiquinol oxidase subunit IV	1.88	4.4E-05		
PA1317	PA14_47210	<i>cyoA</i>	cytochrome o ubiquinol oxidase subunit II			-1.69	6.0E-04
PA1316	PA14_47230		probable major facilitator superfamily (MFS) transporter	-1.56	5.9E-03		
PA1314	PA14_47250		hypothetical protein	1.55	1.9E-02		
PA1311	PA14_47280	<i>phnX</i>	2-phosphonoacetaldehyde hydrolase	1.61	8.8E-04		
PA1302	PA14_47380		probable heme utilization protein precursor	-1.54	1.7E-04		
PA1301	PA14_47390		probable transmembrane sensor	1.55	2.4E-03		
PA1299	PA14_47410		conserved hypothetical protein	-1.74	5.1E-13		
PA1296	PA14_47440		probable 2-hydroxyacid dehydrogenase	-1.51	2.8E-03		
PA1291	PA14_47510		hypothetical protein	2.20	1.1E-08		
PA1288	PA14_47540		probable outer membrane protein precursor	-1.68	2.7E-38		
PA1286	PA14_47560		probable major facilitator superfamily (MFS) transporter	-1.79	7.3E-05		
PA1281	PA14_47650	<i>cobV</i>	cobalamin (5'-phosphate) synthase	1.53	1.2E-10		
PA1262	PA14_47900		MFS transporter	-2.14	2.5E-04		
PA1260	PA14_47920	<i>lhpP</i>	ABC transporter periplasmic-binding protein, LhpP	-3.12	2.1E-05		
PA1256	PA14_47960	<i>lhpO</i>	ABC transporter ATP-binding	-2.09	7.5E-03		

			protein, LhpO				
PA1255	PA14_47970	<i>lhpK</i>	D-hydroxyproline epimerase, LhpK	-2.11	2.9E-04		
PA1254	PA14_48000	<i>lhpC</i>	delta1-pyrroline-4-hydroxy-2-carboxylate deaminase, LphC	-6.19	1.7E-13		
PA1253	PA14_48010	<i>lhpG</i>	semialdehyde dehydrogenase	-2.04	4.5E-04		
PA1252	PA14_48020	<i>dprA</i>	DprA	1.91	1.5E-10		
PA1250	PA14_48040	<i>aprI</i>	alkaline proteinase inhibitor AprI	2.39	9.1E-55		
PA1249	PA14_48060	<i>aprA</i>	alkaline metalloproteinase precursor	8.45	1.9E-102	-1.54	1.8E-05
PA1248	PA14_48090	<i>aprF</i>	Alkaline protease secretion outer membrane protein AprF precursor	3.70	1.1E-64		
PA1247	PA14_48100	<i>aprE</i>	alkaline protease secretion protein AprE	3.60	2.4E-88		
PA1246	PA14_48115	<i>aprD</i>	alkaline protease secretion protein AprD	3.12	8.0E-65		
PA1245	PA14_48140	<i>aprX</i>	AprX	3.39	6.1E-98		
PA1243	PA14_48160		probable sensor/response regulator hybrid	3.15	1.4E-40		
PA1242	PA14_48170	<i>sprP</i>	SprP	2.30	3.9E-26		
PA1240	PA14_48200		probable enoyl-CoA hydratase/isomerase	3.08	2.1E-13		
PA1239	PA14_48210		hypothetical protein	1.91	1.3E-03		
PA1238	PA14_48240		outer membrane component of multidrug efflux pump	1.69	4.3E-02		
PA1221	PA14_48530		hypothetical protein	2.24	3.0E-14		
PA1220	PA14_48540		hypothetical protein	2.72	1.1E-18		
PA1219	PA14_48550		hypothetical protein	2.28	2.1E-08		
PA1218	PA14_48560		hypothetical protein	2.90	5.3E-17		
PA1217	PA14_48570		probable 2-isopropylmalate synthase	2.91	1.0E-11		
PA1216	PA14_48590		hypothetical protein	3.29	6.3E-22		
PA1215	PA14_48600		hypothetical protein	2.75	1.1E-19		
PA1214	PA14_48610		hypothetical protein	3.55	3.5E-26		
PA1213	PA14_48620		hypothetical protein	3.36	2.1E-22		
PA1212	PA14_48630		probable major facilitator superfamily (MFS) transporter	3.14	8.2E-15		
PA1211	PA14_48640		hypothetical protein	3.41	1.9E-19		
PA1200	PA14_48780		conserved hypothetical protein	1.82	1.8E-25	1.58	3.0E-02
PA1198	PA14_48800		conserved hypothetical protein			-1.63	1.3E-02
PA1196	PA14_48830	<i>ddaR</i>	transcriptional regulator DdaR	1.59	2.7E-07		
PA0727	PA14_48890		hypothetical protein from bacteriophage Pf1	1.61	4.5E-03		
	PA14_49020	<i>pf5r</i>	Pf5 repressor C			-1.70	1.3E-02

	PA14_49030		hypothetical protein			-1.50	1.9E-02
PA1190	PA14_49050		conserved hypothetical protein	2.07	1.2E-07	1.70	4.3E-03
PA1183	PA14_49130	<i>dctA</i>	C4-dicarboxylate transport protein	-4.42	1.1E-05		
PA1180	PA14_49170	<i>phoQ</i>	two-component sensor PhoQ	-2.02	4.7E-16		
PA1179	PA14_49180	<i>phoP</i>	two-component response regulator PhoP	-1.80	5.5E-14		
PA1178	PA14_49200	<i>oprH</i>	PhoP/Q and low Mg ²⁺ inducible outer membrane protein H1 precursor	-1.84	5.8E-30		
PA1177	PA14_49210	<i>napE</i>	periplasmic nitrate reductase protein NapE	1.74	6.5E-06		
PA1176	PA14_49220	<i>napF</i>	ferredoxin protein NapF	1.70	1.1E-09		
PA1175	PA14_49230	<i>napD</i>	NapD protein of periplasmic nitrate reductase	1.66	2.4E-06		
PA1174	PA14_49250	<i>napA</i>	periplasmic nitrate reductase protein NapA	1.67	1.6E-10		
PA1173	PA14_49260	<i>napB</i>	cytochrome c-type protein NapB precursor	1.52	5.0E-03		
PA1172	PA14_49270	<i>napC</i>	cytochrome c-type protein NapC	1.75	1.1E-06		
PA1169	PA14_49300		probable lipoygenase	-1.56	3.8E-05		
PA1168	PA14_49310		hypothetical protein	-1.93	5.2E-09	-1.77	9.6E-03
PA1164	PA14_49350		conserved hypothetical protein			-1.52	2.4E-02
PA1159	PA14_49410		probable cold-shock protein	2.14	5.5E-44		
	PA14_49480		hypothetical protein			-2.26	4.3E-03
	PA14_49510	<i>pyoS3 I</i>	immunity protein S3I structural gene			-1.82	1.9E-04
	PA14_49520	<i>pyoS3 A</i>	pyocin killing protein	1.66	2.0E-07	-3.07	2.6E-11
PA1148	PA14_49560	<i>toxA</i>	exotoxin A precursor	2.71	7.5E-03		
PA1137	PA14_49690		probable oxidoreductase	-11.61	2.0E- 105		
PA1134	PA14_49720		hypothetical protein	4.00	1.3E-17		
PA1132	PA14_49740		hypothetical protein	-1.56	6.7E-18		
PA1130	PA14_49760	<i>rhlC</i>	rhamnosyltransferase 2	1.85	2.6E-16		
PA1129	PA14_49780	<i>fosA</i>	foscimycin resistance protein, FosA	1.87	9.8E-04		
PA1128	PA14_49790		probable transcriptional regulator	1.66	1.9E-05		
PA1127	PA14_49800		probable oxidoreductase	1.80	4.2E-21		
PA1123	PA14_49850		hypothetical protein	-1.55	1.5E-05		
PA1116	PA14_49930		hypothetical protein	-2.09	1.1E-20		
PA1114	PA14_49960		hypothetical protein	1.55	6.0E-05		
	PA14_50000		hypothetical protein	-1.61	2.1E-04		
PA1112	PA14_50010		conserved hypothetical protein	1.59	2.5E-09		
PA1111	PA14_50020		hypothetical protein	2.85	5.1E-18		

PA1096	PA14_50240		hypothetical protein	-1.55	1.8E-12		
PA1095	PA14_50250		hypothetical protein	-1.52	8.9E-19		
PA1094	PA14_50270	<i>fliD</i>	flagellar capping protein FliD	-1.65	2.7E-25		
PA1093	PA14_50280		hypothetical protein	-2.32	2.7E-26		
PA1092	PA14_50290	<i>fliC</i>	flagellin type B	-2.22	3.5E-30		
PA1066	PA14_50610		probable short-chain dehydrogenase	1.79	9.1E-05		
PA1055	PA14_50720	<i>shaB</i>	ShaB	-1.64	8.3E-09		
PA1041	PA14_50880		probable outer membrane protein precursor	1.73	2.6E-07		
PA1034	PA14_50950		hypothetical protein			-1.53	2.1E-02
PA1028	PA14_51040	<i>amaA</i>	L-Pipecolate oxidase	1.87	1.7E-06		
PA1027	PA14_51050	<i>amaB</i>	delta1-Piperidine-6-carboxylate dehydrogenase	1.72	3.3E-07		
PA1024	PA14_51080		NADH:quinone reductase	1.61	5.1E-04		
PA1020	PA14_51120		probable acyl-CoA dehydrogenase	1.72	1.7E-04		
PA0990	PA14_51490		conserved hypothetical protein	2.68	9.5E-14		
	PA14_51520	<i>spcU</i>	SpcU	2.03	2.0E-18		
	PA14_51530	<i>exoU</i>	ExoU	1.91	4.8E-15		
	PA14_51590		hypothetical protein	1.57	3.1E-04		
PA0978	PA14_51630		conserved hypothetical protein	1.78	4.9E-02		
PA0976	PA14_51670		conserved hypothetical protein	-2.36	9.8E-25		
PA0975	PA14_51680		probable radical activating enzyme	-2.19	2.5E-27		
PA0971	PA14_51730	<i>tolA</i>	TolA protein			-1.62	2.4E-03
PA0970	PA14_51740	<i>tolR</i>	TolR protein			-1.53	1.8E-02
PA0968	PA14_51770		conserved hypothetical protein			-1.70	1.1E-02
PA0945	PA14_52040	<i>purM</i>	phosphoribosylaminoimidazole synthetase	-1.57	4.3E-24		
PA0937	PA14_52140		conserved hypothetical protein			-1.93	1.7E-02
PA0922	PA14_52330		hypothetical protein	-1.93	3.8E-20		
PA0921	PA14_52340		hypothetical protein	-1.67	2.0E-07		
PA0916	PA14_52420		conserved hypothetical protein	-1.83	2.7E-14		
PA0915	PA14_52430		conserved hypothetical protein	-2.18	2.2E-20		
PA0914	PA14_52440		hypothetical protein	-2.45	1.9E-18		
PA0913	PA14_52460	<i>mgtE</i>	MgtE	-1.86	1.1E-57		
PA0911	PA14_52480	<i>alpE</i>	AlpE	-4.05	3.1E-34		
PA0910	PA14_52490	<i>alpD</i>	AlpD	-4.47	2.0E-37		
PA0909	PA14_52500	<i>alpC</i>	AlpC	-4.18	2.7E-12		
PA0908	PA14_52510	<i>alpB</i>	AlpB	-2.72	5.0E-06		
PA0907	PA14_52520	<i>alpA</i>	lysis phenotype activator, AlpA	-1.74	5.1E-06		
PA0905	PA14_52570	<i>rsmA</i>	RsmA			-1.88	8.8E-03
PA0887	PA14_52800	<i>acsA</i>	acetyl-coenzyme A synthetase	2.29	3.9E-04		

PA0884	PA14_52840		probable C4-dicarboxylate-binding periplasmic protein	1.89	6.6E-03		
PA0866	PA14_53050	<i>aroP2</i>	aromatic amino acid transport protein AroP2	-1.79	1.3E-27		
PA0861	PA14_53140	<i>rbdA</i>	RbDA	1.61	5.3E-18		
PA0853	PA14_53230		probable oxidoreductase	1.61	3.2E-10		
PA0852	PA14_53250	<i>cbpD</i>	chitin-binding protein CbpD precursor	1.53	5.0E-11		
PA0843	PA14_53370	<i>plcR</i>	phospholipase accessory protein PlcR precursor	1.71	8.8E-05		
PA0840	PA14_53400		probable oxidoreductase	-2.10	3.2E-05		
PA0839	PA14_53410		probable transcriptional regulator	-1.53	2.7E-04		
PA0837	PA14_53430	<i>slyD</i>	peptidyl-prolyl cis-trans isomerase SlyD	-1.77	5.8E-19		
	PA14_53590					-2.18	7.2E-03
	PA14_53600					-1.91	1.8E-02
PA0826	PA14_53620		hypothetical protein	-1.62	2.9E-02		
PA0820	PA14_53670		hypothetical protein			-1.97	1.5E-02
	PA14_53680			-1.95	1.8E-02		
PA0816	PA14_53720		probable transcriptional regulator	1.82	2.1E-10		
PA0814	PA14_53740		conserved hypothetical protein	1.67	7.2E-03		
PA0807	PA14_53820	<i>ampD_{h3}</i>	AmpDh3	-2.02	5.0E-48		
PA0802	PA14_53870		hypothetical protein	1.92	8.8E-08		
PA0801	PA14_53880		hypothetical protein	1.52	6.6E-06		
PA0800	PA14_53890		hypothetical protein	1.55	9.5E-03		
PA0798	PA14_53910	<i>pmtA</i>	phospholipid methyltransferase	1.81	3.0E-12		
PA0792	PA14_54000	<i>prpD</i>	propionate catabolic protein PrpD	2.01	1.4E-17		
PA0781	PA14_54180		hypothetical protein	1.63	1.6E-02		
PA0779	PA14_54210	<i>asrA</i>	AsrA	-4.20	8.4E-36		
PA0778	PA14_54220	<i>icp</i>	inhibitor of cysteine peptidase	-2.36	4.1E-25		
PA0777	PA14_54230		hypothetical protein	-1.60	3.7E-07		
PA0755	PA14_54520	<i>opdH</i>	cis-aconitate porin OpdH	3.23	1.2E-25		
PA0754	PA14_54540		hypothetical protein	3.09	4.4E-23		
PA0753	PA14_54550		hypothetical protein	4.58	7.9E-11		
PA0752	PA14_54570		conserved hypothetical protein	3.09	4.3E-19		
PA0751	PA14_54580		conserved hypothetical protein	2.77	1.4E-12		
PA0747	PA14_54620		probable aldehyde dehydrogenase	1.61	2.2E-06		
PA0746	PA14_54630		probable acyl-CoA dehydrogenase	1.58	2.5E-05		
PA0745	PA14_54640	<i>dspI</i>	DspI	1.75	2.7E-08		
PA0744	PA14_54660		probable enoyl-CoA	1.87	2.8E-10		

			hydratase/isomerase				
PA0743	PA14_54670		probable 3-hydroxyisobutyrate dehydrogenase	1.99	1.2E-17		
PA0740	PA14_54700	<i>sdsA1</i>	SDS hydrolase SdsA1	-1.54	1.5E-03		
	PA14_54750		hypothetical protein	1.79	1.5E-05		
PA0732	PA14_54810		hypothetical protein	1.84	2.9E-12		
	PA14_54850		hypothetical protein			-1.53	2.2E-03
	PA14_55000		ABC transporter periplasmic protein	-1.52	1.1E-02		
	PA14_55040		ferric enterobactin transporter ATP-binding protein	-1.55	3.2E-02		
	PA14_55060		hypothetical protein			-1.79	3.2E-02
PA0709	PA14_55140		hypothetical protein	1.88	2.5E-02		
PA0707	PA14_55160	<i>toxR</i>	transcriptional regulator ToxR	5.47	2.4E-17	-4.44	5.8E-05
PA0699	PA14_55280		peptidyl-prolyl cis-trans isomerase, PpiC-type	1.56	2.6E-02		
PA0698	PA14_55290		hypothetical protein	2.10	1.6E-02		
PA0675	PA14_55550	<i>vreI</i>	ECF subfamily RNA polymerase sigma-70 factor	-2.57	8.4E-10		
PA0674	PA14_55560	<i>vreA</i>	VreA	-1.74	2.0E-06		
PA0672	PA14_55580	<i>hemO</i>	heme oxygenase			-2.82	9.8E-05
PA0671	PA14_55590		hypothetical protein	-2.74	8.4E-06		
PA0670	PA14_55600		hypothetical protein	-1.78	2.3E-05		
PA4290	PA14_55710		probable chemotaxis transducer	1.98	1.0E-04		
PA4292	PA14_55760		probable phosphate transporter	-1.57	2.6E-07		
PA4293	PA14_55770	<i>pprA</i>	two-component sensor PprA	2.54	8.6E-18		
PA4294	PA14_55780		hypothetical protein	2.21	2.5E-17		
PA4299	PA14_55820	<i>tadD</i>	TadD	2.58	1.3E-19		
PA4298	PA14_55840		hypothetical protein	2.43	2.9E-06		
PA4300	PA14_55850	<i>tadC</i>	TadC	2.67	2.7E-11	1.77	2.1E-02
PA4301	PA14_55860	<i>tadB</i>	TadB	2.41	5.1E-17		
PA4302	PA14_55880	<i>tadA</i>	TadA ATPase	2.27	5.3E-14		
PA4303	PA14_55890	<i>tadZ</i>	TadZ	2.23	3.3E-13		
PA4304	PA14_55900	<i>rcpA</i>	RcpA	2.20	2.3E-13		
PA4305	PA14_55920	<i>rcpC</i>	RcpC	2.16	1.7E-14		
PA4306	PA14_55930	<i>flp</i>	Type IVb pilin, Flp	1.84	4.1E-25		
PA4309	PA14_55980	<i>pctA</i>	chemotactic transducer PctA	-1.50	3.7E-16		
PA4310	PA14_56000	<i>pctB</i>	chemotactic transducer PctB	-1.86	5.1E-25		
PA4311	PA14_56010		conserved hypothetical protein	2.17	2.1E-21		
PA4312	PA14_56030		conserved hypothetical protein	1.71	6.0E-22		
PA4313	PA14_56040		hypothetical protein	1.70	3.1E-16		
PA4316	PA14_56070	<i>sbcB</i>	exodeoxyribonuclease I			-1.51	2.6E-02

PA4328	PA14_56210		hypothetical protein	1.61	2.9E-06		
PA4333	PA14_56280		probable fumarase	-1.63	1.5E-25		
PA4335	PA14_56340		hypothetical protein	2.18	1.3E-20		
PA4336	PA14_56360		conserved hypothetical protein	1.93	3.5E-12		
PA4338	PA14_56370		hypothetical protein	2.22	7.3E-20		
PA4337	PA14_56380		hypothetical protein	2.04	2.4E-11		
PA4344	PA14_56420		probable hydrolase	2.98	7.4E-41		
PA4345	PA14_56480		hypothetical protein	3.30	3.0E-30		
PA4346	PA14_56520		hypothetical protein	2.68	1.7E-12		
PA4349	PA14_56540		hypothetical protein	1.89	3.1E-18		
PA4352	PA14_56550		conserved hypothetical protein	2.05	6.1E-11		
PA4355	PA14_56640	<i>pyeM</i>	PyeM	-1.55	1.6E-04		
PA4357	PA14_56660		conserved hypothetical protein	1.68	1.1E-08		
PA4360	PA14_56690		hypothetical protein			-2.76	6.0E-04
PA4362	PA14_56720		hypothetical protein	1.50	3.0E-07		
PA4366	PA14_56730	<i>sodB</i>	superoxide dismutase			1.62	3.5E-02
PA4364	PA14_56750		hypothetical protein	-4.36	1.1E-35		
PA4365	PA14_56770	<i>lysE</i>	Lysine efflux permease	-4.66	1.9E-35		
PA4370	PA14_56810	<i>icmP</i>	Insulin-cleaving metalloproteinase outer membrane protein precursor	1.74	1.9E-10		
PA4371	PA14_56830		hypothetical protein			-1.75	1.2E-02
PA4385	PA14_56990	<i>groEL</i>	GroEL protein	-1.76	7.6E-04		
PA4386	PA14_57010	<i>groES</i>	GroES protein	-2.19	2.5E-04		
PA4388	PA14_57020		hypothetical protein			1.52	3.0E-02
PA4387	PA14_57030		conserved hypothetical protein	-3.22	1.8E-51		
PA4390	PA14_57050		hypothetical protein	1.86	1.3E-17		
PA4396	PA14_57130		two-component response regulator	1.60	1.5E-17		
PA4397	PA14_57140	<i>panE</i>	ketopantoate reductase	-1.52	9.8E-15		
PA4398	PA14_57160		two-component sensor	-1.78	1.2E-28		
PA4409	PA14_57290	<i>ftsQ</i>	cell division protein FtsQ			-1.96	7.8E-03
PA4417	PA14_57390	<i>murE</i>	UDP-N-acetylmuramoylalanyl-D-glutamate-2, 6-diaminopimelate ligase			-1.54	4.5E-02
PA4430	PA14_57540		probable cytochrome b	-1.55	1.3E-22		
PA4431	PA14_57560		probable iron-sulfur protein	-1.52	8.8E-23		
PA4433	PA14_57580	<i>rplM</i>	50S ribosomal protein L13	-1.55	2.7E-18		
PA4434	PA14_57590		probable oxidoreductase	1.61	2.2E-20		
PA4442	PA14_57690	<i>cysN</i>	ATP sulfurylase GTP-binding subunit/APS kinase	-1.95	1.1E-16		
PA4443	PA14_57710	<i>cysD</i>	ATP sulfurylase small subunit	-2.04	4.2E-23		
PA4448	PA14_57770	<i>hisD</i>	histidinol dehydrogenase	-1.51	9.6E-13		

PA4452	PA14_57820		conserved hypothetical protein			-1.55	1.3E-02
PA4467	PA14_57980		hypothetical protein	1.72	1.6E-03		
PA4468	PA14_57990	<i>sodM</i>	superoxide dismutase	1.78	1.6E-02	-2.12	3.4E-02
PA4470	PA14_58000	<i>fumC1</i>	fumarate hydratase	1.66	1.8E-02	-2.48	3.4E-02
PA4469	PA14_58010		hypothetical protein	1.54	1.8E-02		
PA4475	PA14_58070		conserved hypothetical protein	-1.60	1.4E-18		
PA4498	PA14_58360	<i>mdpA</i>	metallo-dipeptidase aeruginosa, MdpA	-1.92	9.8E-17		
PA4499	PA14_58375	<i>psdR</i>	Pseudomonas dipeptide regulator, PdsR	-1.60	7.2E-10		
PA4500	PA14_58380	<i>dppA3</i>	probable binding protein component of ABC transporter	-1.50	1.7E-17		
PA4501	PA14_58390	<i>opdD</i>	Glycine-glutamate dipeptide porin OpdP	-1.79	4.5E-25		
PA4502	PA14_58410	<i>dppA4</i>	probable binding protein component of ABC transporter	-1.73	9.6E-25		
PA4503	PA14_58420	<i>dppB</i>	dipeptide ABC transporter permease DppB	-1.59	1.4E-23		
PA4504	PA14_58440	<i>dppC</i>	dipeptide ABC transporter permease DppC	-1.67	2.1E-17		
PA4505	PA14_58450	<i>dppD</i>	dipeptide ABC transporter ATP- binding protein DppD	-1.67	3.7E-12		
PA4507	PA14_58490		hypothetical protein	-2.07	3.2E-21		
PA4511	PA14_58500		conserved hypothetical protein			2.11	1.4E-03
PA4508	PA14_58510		probable transcriptional regulator	-1.57	7.7E-06		
PA4519	PA14_58610	<i>speC</i>	ornithine decarboxylase	-2.16	3.2E-84		
PA4518	PA14_58620		hypothetical protein	-2.03	1.0E-19		
PA4523	PA14_58670		hypothetical protein	1.56	2.2E-42		
PA4542	PA14_58900	<i>clpB</i>	ClpB protein	-2.80	1.1E-22		
	PA14_59120		hypothetical protein	1.78	1.4E-03		
	PA14_59160	<i>crpP</i>	CrpP	1.56	2.0E-02		
	PA14_59190		hypothetical protein	1.68	2.4E-09		
PA0985	PA14_59220	<i>pyoS5</i>	pyocin S5			-2.88	2.6E-09
PA0984	PA14_59230		colicin immunity protein	2.48	2.7E-16		
	PA14_59240	<i>pilL2</i>	type IV B pilus protein	-2.15	1.3E-05		
	PA14_59380		hypothetical protein			-1.61	2.7E-02
	PA14_59410		hypothetical protein	2.08	1.4E-03		
	PA14_59440		hypothetical protein	-1.57	3.9E-02		
	PA14_59480		hypothetical protein	-1.67	6.9E-04		
	PA14_59490		hypothetical protein	-2.03	7.3E-03		
	PA14_59510		hypothetical protein	-2.09	2.4E-02		
	PA14_59520		hypothetical protein	-3.12	4.4E-04		

	PA14_59550		hypothetical protein	-1.73	7.5E-09	-1.65	2.6E-02
	PA14_59560		transposase	-2.40	1.2E-09		
	PA14_59570		transposase	-5.75	4.5E-12		
	PA14_59770	<i>rcsB</i>	two component response regulator	1.67	7.1E-09		
	PA14_59840		hypothetical protein			-2.50	4.1E-02
	PA14_59845		hypothetical protein			-3.33	4.7E-02
	PA14_60040		hypothetical protein			-1.75	3.9E-02
PA1935	PA14_60080		hypothetical protein	1.52	2.1E-18		
	PA14_60090		hypothetical protein			-1.52	2.1E-02
	PA14_60140		xerD-like integrase	-1.60	5.5E-07		
PA4552	PA14_60280	<i>pilW</i>	type 4 fimbrial biogenesis protein PilW	1.59	8.9E-17		
PA4556	PA14_60310	<i>pilE</i>	type 4 fimbrial biogenesis protein PilE			-1.89	1.7E-02
PA4557	PA14_60320	<i>lytB</i>	LytB protein			-1.98	1.4E-02
PA4563	PA14_60390	<i>rpsT</i>	30S ribosomal protein S20	-1.65	9.8E-17		
PA4566	PA14_60420	<i>obg</i>	GTP-binding protein Obg	-1.69	5.1E-11		
PA4569	PA14_60460	<i>ispB</i>	octaprenyl-diphosphate synthase			-1.56	4.0E-02
PA4572	PA14_60490	<i>fklB</i>	peptidyl-prolyl cis-trans isomerase FklB	-2.33	1.1E-47		
PA4577	PA14_60560		hypothetical protein	1.58	4.0E-04		
PA4582	PA14_60630		conserved hypothetical protein	-1.79	1.2E-07		
PA4602	PA14_60870	<i>glyA3</i>	serine hydroxymethyltransferase	-2.04	3.1E-33		
PA4607	PA14_60950		hypothetical protein	1.90	3.4E-06		
PA4610	PA14_61000		hypothetical protein	-1.59	2.9E-03		
PA4612	PA14_61020		conserved hypothetical protein	-3.58	1.4E-14		
PA4613	PA14_61040	<i>katB</i>	catalase	-6.37	2.2E-29		
PA4624	PA14_61150	<i>cdrB</i>	cyclic diguanylate-regulated TPS partner B, CdrB	-1.98	1.9E-24		
PA4623	PA14_61180			-1.71	3.8E-03		
PA4625	PA14_61190	<i>cdrA</i>	cyclic diguanylate-regulated TPS partner A, CdrA	-2.22	4.9E-24		
PA4628	PA14_61220	<i>lysP</i>	lysine-specific permease	-1.71	1.5E-16		
PA4629	PA14_61250		hypothetical protein	-1.79	3.3E-09		
PA4630	PA14_61270		hypothetical protein	-1.72	3.5E-06		
PA4633	PA14_61290		probable chemotaxis transducer	-1.65	1.3E-22		
PA4635	PA14_61330		conserved hypothetical protein	-4.66	1.6E-22		
	PA14_61340		hypothetical protein	1.63	1.2E-04		
	PA14_61380		hypothetical protein			-1.97	1.3E-02
PA4644	PA14_61440		hypothetical protein	-1.86	1.1E-16		
PA4645	PA14_61450		probable purine/pyrimidine	-1.77	1.8E-25		

			phosphoribosyl transferase				
PA4646	PA14_61460	<i>upp</i>	uracil phosphoribosyltransferase	-1.52	2.4E-12		
PA4654	PA14_61560		probable major facilitator superfamily (MFS) transporter	-2.11	4.0E-10		
PA4658	PA14_61600		hypothetical protein	-1.69	2.4E-08		
PA4660	PA14_61610	<i>phr</i>	deoxyribodipyrimidine photolyase	-2.00	1.0E-11		
PA4659	PA14_61620		probable transcriptional regulator	-1.91	2.0E-11		
PA4661	PA14_61640	<i>pagL</i>	Lipid A 3-O-deacylase	2.26	3.7E-22		
PA4670	PA14_61750	<i>prs</i>	ribose-phosphate pyrophosphokinase			-1.72	2.1E-05
PA4671	PA14_61770		probable ribosomal protein L25	-1.64	3.0E-31		
PA4672	PA14_61780		peptidyl-tRNA hydrolase	-1.51	3.3E-10		
PA4673	PA14_61790		conserved hypothetical protein	-1.52	3.4E-16		
	PA14_61845	<i>higB</i>	HigB			-2.32	1.5E-02
PA4680	PA14_61910		hypothetical protein	1.65	1.7E-02		
PA4688	PA14_62000	<i>hitB</i>	iron (III)-transport system permease HitB	1.56	4.0E-12		
PA4689	PA14_62010		hypothetical protein	-1.51	4.7E-17		
PA4692	PA14_62020		conserved hypothetical protein	-1.93	4.8E-18		
	PA14_62030		paraquat-inducible protein A-like protein	-1.52	3.5E-12		
PA4691	PA14_62100		hypothetical protein	-1.86	1.1E-10		
PA4714	PA14_62350		conserved hypothetical protein	-2.08	6.3E-30		
PA4719	PA14_62420		probable transporter	-1.67	3.2E-16		
PA4720	PA14_62440	<i>trmA</i>	tRNA (uracil-5-)-methyltransferase	-1.54	8.0E-11		
PA4731	PA14_62590	<i>panD</i>	aspartate 1-decarboxylase precursor	-2.08	2.3E-46		
PA4738	PA14_62670		conserved hypothetical protein	2.46	1.4E-16		
PA4739	PA14_62680		conserved hypothetical protein	2.34	1.0E-12		
PA4740	PA14_62690	<i>pnp</i>	polyribonucleotide nucleotidyltransferase	-1.91	2.0E-17		
PA4743	PA14_62730	<i>rbfA</i>	ribosome-binding factor A	-1.93	3.2E-17		
PA4744	PA14_62740	<i>infB</i>	translation initiation factor IF-2	-1.79	1.1E-18		
PA4745	PA14_62760	<i>nusA</i>	N utilization substance protein A	-1.85	5.2E-18		
PA4746	PA14_62770		conserved hypothetical protein	-1.61	1.0E-08		
PA4752	PA14_62860	<i>ftsJ</i>	cell division protein FtsJ	-1.56	7.4E-12		
PA4753	PA14_62870		conserved hypothetical protein	-1.56	1.1E-10		
PA4757	PA14_62910		conserved hypothetical protein	-1.55	1.3E-08		
PA4758	PA14_62920	<i>carA</i>	carbamoyl-phosphate synthase small chain	-1.58	1.4E-15		
PA4759	PA14_62930	<i>dapB</i>	dihydrodipicolinate reductase	-2.68	2.1E-12		
PA4760	PA14_62940	<i>dnaJ</i>	DnaJ protein	-3.53	5.0E-20		
PA4761	PA14_62960	<i>dnaK</i>	DnaK protein	-5.83	5.7E-34		

PA4762	PA14_62970	<i>grpE</i>	heat shock protein GrpE	-5.86	3.4E-36		
PA4763	PA14_62990	<i>recN</i>	DNA repair protein RecN	-1.85	5.0E-29		
PA4785	PA14_63220		probable acyl-CoA thiolase	1.71	4.4E-09		
PA4783	PA14_63230		conserved hypothetical protein	-1.76	2.2E-10		
PA4786	PA14_63250		probable short-chain dehydrogenase	2.03	8.4E-21		
PA4787	PA14_63270		probable transcriptional regulator	1.64	1.6E-13	1.59	4.6E-02
PA4788	PA14_63290		hypothetical protein	1.54	2.4E-05		
PA4792	PA14_63330		conserved hypothetical protein	2.63	1.2E-14		
PA4808	PA14_63530	<i>sela</i>	L-seryl-tRNA(ser) selenium transferase			1.71	3.3E-04
PA4810	PA14_63550	<i>fdnI</i>	nitrate-inducible formate dehydrogenase, gamma subunit			1.62	7.4E-04
PA4811	PA14_63570	<i>fdnH</i>	nitrate-inducible formate dehydrogenase, beta subunit			1.69	4.1E-04
PA4813	PA14_63620	<i>lipC</i>	lipase LipC	1.84	1.4E-04		
PA4826	PA14_63660		hypothetical protein	-3.70	1.5E-97		
PA4817	PA14_63680		hypothetical protein	-2.02	6.5E-07		
PA4822	PA14_63750		hypothetical protein	-3.41	5.2E-23		
PA4823	PA14_63770		hypothetical protein	-4.27	2.2E-04		
PA4824	PA14_63780		hypothetical protein	-6.15	7.6E-25		
PA4825	PA14_63800	<i>mgtA</i>	Mg(2+) transport ATPase, P-type 2	-8.53	4.6E-92		
PA4839	PA14_63850	<i>speA</i>	arginine decarboxylase (ADC)	-2.23	5.5E-70		
PA4832	PA14_63890		probable short-chain dehydrogenase	1.69	8.2E-04		
PA4833	PA14_63900		conserved hypothetical protein	1.51	6.9E-08		
PA4835	PA14_63920	<i>cntM</i>	CntM	1.61	2.9E-04		
PA4836	PA14_63940	<i>cntL</i>	CntL	2.33	5.6E-07		
PA4837	PA14_63960	<i>cntO</i>	CntO	1.73	1.1E-04		
PA4840	PA14_63990		conserved hypothetical protein	-1.73	1.2E-27		
PA4843	PA14_64030	<i>gcbA</i>	GcbA	-1.93	2.1E-48		
PA4844	PA14_64060	<i>ctpL</i>	CtpL	-2.06	1.8E-06		
PA4850	PA14_64120	<i>prmA</i>	ribosomal protein L11 methyltransferase	-1.59	6.7E-20		
PA4870	PA14_64410		conserved hypothetical protein	-1.84	4.7E-08		
PA4873	PA14_64440		probable heat-shock protein	-2.65	2.9E-26		
PA4876	PA14_64470	<i>osmE</i>	osmotically inducible lipoprotein OsmE	2.88	8.9E-30		
PA4877	PA14_64480		hypothetical protein	2.95	1.2E-29		
PA4878	PA14_64490	<i>brlR</i>	BrlR	-1.83	1.6E-13		
PA4879	PA14_64500		conserved hypothetical protein	1.63	1.0E-09		
PA4880	PA14_64510		probable bacterioferritin	1.74	7.2E-06		
PA4881	PA14_64530		hypothetical protein	-1.51	1.5E-02		

PA4888	PA14_64590	<i>desB</i>	acyl-CoA delta-9-desaturase, DesB	1.56	1.3E-03		
PA4889	PA14_64610		probable oxidoreductase	1.69	1.5E-05	-1.71	2.9E-02
PA4892	PA14_64660	<i>ureF</i>	urease accessory protein UreF	-1.70	2.9E-03		
PA4899	PA14_64670		probable aldehyde dehydrogenase	1.52	2.5E-09		
PA4894	PA14_64680		hypothetical protein	-1.55	1.1E-03		
PA4895	PA14_64690		transmembrane sensor	-1.82	3.3E-06		
PA4896	PA14_64700		probable sigma-70 factor, ECF subfamily	-1.93	1.3E-05		
PA4897	PA14_64710		TonB-dependent receptor	-2.83	7.8E-11		
PA4900	PA14_64750		probable major facilitator superfamily (MFS) transporter	1.77	6.3E-10		
PA4905	PA14_64810	<i>vanB</i>	vanillate O-demethylase	1.87	1.1E-02		
PA4908	PA14_64840		hypothetical protein	1.73	6.6E-05		
PA4909	PA14_64850		probable ATP-binding component of ABC transporter	1.73	1.7E-06		
PA4910	PA14_64860		branched chain amino acid ABC transporter ATP binding protein	1.59	2.5E-05		
PA4913	PA14_64890		probable binding protein component of ABC transporter	1.82	2.0E-18		
PA4915	PA14_64900		probable chemotaxis transducer	2.30	9.6E-40		
PA4925	PA14_65030		conserved hypothetical protein	2.42	7.0E-27		
PA4928	PA14_65060		conserved hypothetical protein			1.63	1.4E-02
PA4931	PA14_65110	<i>dnaB</i>	replicative DNA helicase	-1.97	4.3E-22		
PA4932	PA14_65130	<i>rplI</i>	50S ribosomal protein L9	-1.74	1.1E-19		
PA4933	PA14_65150		hypothetical protein	-1.78	8.7E-18		
PA4934	PA14_65160	<i>rpsR</i>	30S ribosomal protein S18	-1.79	1.1E-16		
PA4935	PA14_65170	<i>rpsF</i>	30S ribosomal protein S6	-1.79	4.8E-20		
PA4978	PA14_65810		hypothetical protein	1.54	9.3E-04		
PA5020	PA14_66350		probable acyl-CoA dehydrogenase	-1.96	2.3E-07		
PA5024	PA14_66410		conserved hypothetical protein	-3.11	2.1E-28		
PA5025	PA14_66420	<i>metY</i>	homocysteine synthase	-1.58	3.0E-04		
PA5027	PA14_66440		hypothetical protein	1.50	8.8E-04	-1.86	1.9E-02
PA5034	PA14_66540	<i>hemE</i>	uroporphyrinogen decarboxylase	-1.97	1.2E-29		
PA5042	PA14_66630	<i>pilO</i>	type 4 fimbrial biogenesis protein PilO			-1.90	9.6E-03
PA5043	PA14_66640	<i>pilN</i>	type 4 fimbrial biogenesis protein PilN			-1.50	3.0E-02
PA5046	PA14_66670		malic enzyme	-1.52	2.7E-17		
PA5049	PA14_66700	<i>rpmE</i>	50S ribosomal protein L31	-1.60	2.0E-11		
PA5053	PA14_66760	<i>hslV</i>	heat shock protein HslV	-4.88	2.8E-59		
PA5054	PA14_66770	<i>hslU</i>	heat shock protein HslU	-5.13	2.5E-32		

PA5055	PA14_66790		hypothetical protein	-3.73	1.8E-33		
PA5058	PA14_66830	<i>phaC2</i>	poly(3-hydroxyalkanoic acid) synthase 2	1.54	4.6E-07		
PA5059	PA14_66840		probable transcriptional regulator	1.72	1.1E-09		
PA5062	PA14_66880		conserved hypothetical protein			-2.07	8.1E-03
PA5068	PA14_66950	<i>tatA</i>	translocation protein TatA			-1.80	3.7E-02
PA5069	PA14_66960	<i>tatB</i>	translocation protein TatB			-1.53	4.9E-02
PA5072	PA14_66990		probable chemotaxis transducer	-2.02	2.8E-40		
PA5074	PA14_67010		probable ATP-binding component of ABC transporter	-1.59	1.1E-19		
PA5075	PA14_67030		probable permease of ABC transporter	-1.77	7.5E-30		
PA5076	PA14_67040		probable binding protein component of ABC transporter	-1.97	2.4E-69		
	PA14_67180	<i>tli5b4</i>	type VI secretion lipase immunity protein, Tli5b4			-1.83	2.0E-02
	PA14_67210	<i>tli5b4</i>	type VI secretion lipase immunity protein, Tli5b4			-2.74	1.8E-04
PA5091	PA14_67230	<i>hutG</i>	N-formylglutamate amidohydrolase	-1.51	5.0E-09		
PA5093	PA14_67250		probable histidine/phenylalanine ammonia-lyase	-1.51	6.8E-10		
PA5094	PA14_67260		probable ATP-binding component of ABC transporter	-1.57	5.1E-10		
PA5095	PA14_67270		probable permease of ABC transporter	-1.56	2.6E-07		
PA5096	PA14_67280		probable binding protein component of ABC transporter	-1.87	1.5E-17		
PA5098	PA14_67300	<i>hutH</i>	histidine ammonia-lyase	-2.29	2.6E-25		
PA5097	PA14_67310		probable amino acid permease	-2.04	1.3E-23		
PA5099	PA14_67320		probable transporter	-2.23	7.9E-31		
PA5100	PA14_67340	<i>hutU</i>	urocanase	-2.17	1.1E-41		
PA5103	PA14_67350	<i>puuR</i>	PuuR	-2.08	4.4E-16		
PA5102	PA14_67380		hypothetical protein	-2.92	2.9E-14		
PA5104	PA14_67400		conserved hypothetical protein	-1.78	8.4E-21		
PA5105	PA14_67410	<i>hutC</i>	histidine utilization repressor HutC	-1.98	2.7E-27		
PA5106	PA14_67420		conserved hypothetical protein	-1.61	3.0E-22		
PA5107	PA14_67440	<i>blc</i>	outer membrane lipoprotein Blc			-1.71	7.3E-06
PA5111	PA14_67490	<i>gloA3</i>	lactoylglutathione lyase	1.52	4.1E-12		
PA5117	PA14_67530	<i>typA</i>	regulatory protein TypA	-1.84	6.7E-13		
PA5120	PA14_67620		hypothetical protein	-1.94	9.7E-12		
PA5150	PA14_68000		probable short-chain dehydrogenase	1.56	4.6E-09		
PA5159	PA14_68120		multidrug resistance protein	1.56	5.1E-08		

PA5170	PA14_68260	<i>arcD</i>	arginine/ornithine antiporter	2.38	3.4E-12		
PA5171	PA14_68300	<i>arcA</i>	arginine deiminase	1.78	2.2E-05		
PA5172	PA14_68330	<i>arcB</i>	ornithine carbamoyltransferase, catabolic	2.32	1.6E-08		
PA5173	PA14_68340	<i>arcC</i>	carbamate kinase	2.76	4.3E-16		
PA5181	PA14_68400		probable oxidoreductase	-4.22	3.3E-161		
PA5180	PA14_68430		conserved hypothetical protein	-3.48	2.4E-48		
PA5194	PA14_68610		hypothetical protein	-1.93	2.6E-35		
PA5196	PA14_68630		hypothetical protein			-2.27	4.1E-02
PA5203	PA14_68720	<i>gshA</i>	glutamate--cysteine ligase	-1.60	2.4E-40		
PA5208	PA14_68770		conserved hypothetical protein	1.82	7.0E-13		
PA5207	PA14_68780		probable phosphate transporter	1.50	1.5E-05		
PA5212	PA14_68820		hypothetical protein	1.87	2.5E-11		
PA5213	PA14_68840	<i>gcvPI</i>	glycine cleavage system protein P1	1.57	1.8E-15		
PA5220	PA14_68930		hypothetical protein	1.82	2.2E-17		
PA5244	PA14_69240		conserved hypothetical protein	-1.56	1.7E-10		
	PA14_69350		hypothetical protein			-1.65	4.2E-02
PA5261	PA14_69450	<i>algR</i>	alginate biosynthesis regulatory protein AlgR	1.58	2.3E-12		
PA5262	PA14_69470	<i>fimS</i>	FimS	1.92	5.2E-19		
PA5266	PA14_69550	<i>vgrG6</i>	VgrG6	-1.54	4.1E-02		
PA0263	PA14_69560	<i>hcpC</i>	secreted protein Hcp	-1.61	4.3E-04		
PA5267	PA14_69560	<i>hcpB</i>	secreted protein Hcp	-1.61	4.3E-04		
PA5284	PA14_69760		hypothetical protein	-1.53	1.1E-04		
PA5288	PA14_69795	<i>glnK</i>	nitrogen regulatory protein P-II 2			1.52	2.0E-02
PA5311	PA14_70120		probable major facilitator superfamily (MFS) transporter	-2.56	4.3E-23		
PA5313	PA14_70140	<i>gabT2</i>	Transaminase	-1.74	8.2E-21		
PA5314	PA14_70170		hypothetical protein	-1.56	4.6E-07		
PA5317	PA14_70190	<i>dppA5</i>	probable binding protein component of ABC dipeptide transporter			-1.60	1.6E-02
PA5319	PA14_70200	<i>radC</i>	DNA repair protein RadC	1.67	6.0E-16		
PA5325	PA14_70300	<i>sphA</i>	SphA	-1.61	1.3E-02		
PA5328	PA14_70340	<i>sphB</i>	SphB	-2.33	9.1E-04		
PA5334	PA14_70400	<i>rph</i>	ribonuclease PH	-1.55	1.8E-23		
PA5352	PA14_70650		conserved hypothetical protein	2.46	9.4E-03		
PA5353	PA14_70670	<i>glcF</i>	glycolate oxidase subunit GlcF	2.18	1.2E-03		
PA5357	PA14_70720		hypothetical protein	-1.96	2.6E-16		
PA5359	PA14_70730		hypothetical protein	1.67	3.0E-07		
PA5368	PA14_70830	<i>pstC</i>	membrane protein component of	-1.81	4.8E-23	1.63	3.4E-02

			ABC phosphate transporter				
PA5369	PA14_70850	<i>pstS</i>	phosphate ABC transporter, periplasmic phosphate-binding protein, PstS	-1.72	2.3E-22		
PA5381	PA14_71080		hypothetical protein	1.65	8.5E-04		
PA5383	PA14_71100		hypothetical protein	-2.49	2.5E-10		
PA5389	PA14_71170	<i>cdhR</i>	CdhR, transcriptional regulator	1.59	1.1E-03		
PA5406	PA14_71360		hypothetical protein	-2.80	9.5E-16		
PA5407	PA14_71370		hypothetical protein	-3.33	8.4E-24		
PA5411	PA14_71420	<i>gbcB</i>	GbcB	1.58	2.6E-02		
PA5421	PA14_71560	<i>fdhA</i>	glutathione-independent formaldehyde dehydrogenase	2.01	1.2E-08		
PA5425	PA14_71590	<i>purK</i>	phosphoribosylaminoimidazole carboxylase	-1.53	1.3E-10		
PA5426	PA14_71600	<i>purE</i>	phosphoribosylaminoimidazole carboxylase, catalytic subunit	-1.55	9.0E-10		
PA5427	PA14_71620	<i>adhA</i>	alcohol dehydrogenase	1.53	3.9E-04		
PA5432	PA14_71690		probable acetyltransferase	1.53	4.1E-03		
PA5433	PA14_71700		conserved hypothetical protein	1.65	1.1E-04		
PA5437	PA14_71740		probable transcriptional regulator	-3.30	2.5E-79		
PA5447	PA14_71900	<i>wbpZ</i>	glycosyltransferase WbpZ			-1.60	9.0E-03
PA5471	PA14_72110	<i>armZ</i>	ArmZ	-3.42	5.8E-24		
PA5470	PA14_72200		probable peptide chain release factor	-3.97	4.2E-26		
PA5472	PA14_72210		hypothetical protein			3.40	2.3E-19
PA5473	PA14_72220		conserved hypothetical protein	1.79	3.7E-14		
PA5474	PA14_72230		probable metalloprotease	1.54	5.1E-23		
PA5475	PA14_72250		hypothetical protein	1.52	3.3E-04		
PA5478	PA14_72300		conserved hypothetical protein	-1.56	1.1E-13	-1.75	2.0E-02
PA5479	PA14_72320	<i>gltP</i>	proton-glutamate symporter	-1.63	2.3E-15		
PA5481	PA14_72340		hypothetical protein	3.32	1.9E-21		
PA5483	PA14_72360	<i>algB</i>	two-component response regulator AlgB	1.91	2.3E-11		
PA5482	PA14_72370		hypothetical protein	2.87	6.3E-17		
PA5484	PA14_72380	<i>kinB</i>	KinB	1.89	1.4E-16		
PA5493	PA14_72480	<i>polA</i>	DNA polymerase I			-1.55	3.9E-02
PA5496	PA14_72510	<i>nrdJb</i>	class II (cobalamin-dependent) ribonucleotide-diphosphate reductase subunit, NrdJb	1.52	2.9E-06		
PA5503	PA14_72600		probable ATP-binding component of ABC transporter	-1.66	5.1E-16		
PA5504	PA14_72620		D-methionine ABC transporter membrane protein	-1.63	7.1E-18		

PA5505	PA14_72630		probable TonB-dependent receptor	-1.50	2.2E-24		
PA5520	PA14_72820		hypothetical protein	1.59	1.8E-09		
	PA14_72830		hypothetical protein	1.59	1.0E-03		
PA5528	PA14_72920		hypothetical protein	-1.62	4.1E-24		
PA5530	PA14_72940		C5-dicarboxylate transporter	-11.70	1.4E-56		
PA5532	PA14_72970		hypothetical protein			-1.88	1.7E-02
PA5533	PA14_72990		hypothetical protein	-1.61	9.9E-08		
PA5534	PA14_73000		hypothetical protein	1.61	2.2E-03		
PA5535	PA14_73010		conserved hypothetical protein	1.54	2.3E-04		
PA5538	PA14_73040	<i>amiA</i>	N-acetylmuramoyl-L-alanine amidase	2.05	7.5E-05		
PA5540	PA14_73060		hypothetical protein	2.39	5.6E-04		
PA5541	PA14_73070	<i>pyrQ</i>	dihydroorotase	1.81	3.0E-03		
PA5543	PA14_73100		hypothetical protein	1.71	6.5E-04		
PA5546	PA14_73120		conserved hypothetical protein	1.64	5.8E-16		
PA5548	PA14_73160		probable major facilitator superfamily (MFS) transporter	-2.01	4.1E-08		
PA5556	PA14_73250	<i>atpA</i>	ATP synthase alpha chain	-1.52	1.1E-16		
PA5558	PA14_73280	<i>atpF</i>	ATP synthase B chain			-1.62	2.0E-02
PA5566	PA14_73390		hypothetical protein	-2.20	5.5E-05		

B.2 PAO1 RNA-Seq and proteomic data

Table A2. Compilation of all PAO1 RNA-Seq and proteomic data reported in this thesis.

PAO1	Name	Product Name	PA0805.1 vs. EV RNA-Seq		PA0805.1 Proteomics		PA2952.1 vs. EV RNA-Seq		PA2952.1 Proteomics	
			FC	padj	FC	p	FC	padj	FC	p
PA0001	<i>dnaA</i>	chromosomal replication initiator protein DnaA			1.1	1.1E-02				
PA0005	<i>lptA</i>	lysophosphatidic acid acyltransferase, LptA			1.17	2.0E-03				
PA0006		conserved hypothetical protein					-1.6	6.5E-09		
PA0007		hypothetical protein	1.9	1.5E-14	1.18	7.3E-03				
PA0010	<i>tag</i>	DNA-3-methyladenine glycosidase I					-1.7	1.1E-06		
PA0011	<i>htrB1</i>	acyltransferase HtrB1			1.08	4.3E-03				
PA0019	<i>def</i>	polypeptide deformylase			-1.12	2.0E-04			-1.05	4.8E-03
PA0020	<i>tsaP</i>	T4P secretin-associated protein TsaP	-2.0	6.8E-11	-1.35	1.0E-03			-1.22	2.9E-03
PA0022		conserved hypothetical protein					-1.8	2.9E-08		
PA0024	<i>hemF</i>	coproporphyrinogen III oxidase, aerobic			-1.1	2.3E-03			-1.1	2.6E-03
PA0025	<i>aroE</i>	shikimate dehydrogenase			-1.07	1.5E-02				
PA0033	<i>hptC</i>	Histidine phosphotransfer protein HptC					1.7	2.7E-03		
PA0035	<i>trpA</i>	tryptophan synthase alpha chain							1.1	2.0E-02
PA0038		hypothetical protein	1.6	1.1E-03			-1.7	5.1E-05		
PA0044	<i>exoT</i>	exoenzyme T	-4.1	1.2E-26						
PA0045		hypothetical protein	-1.6	1.3E-02						
PA0046		hypothetical protein	-1.6	1.9E-02			-2.0	1.8E-04		
PA0047		hypothetical protein	-2.0	5.3E-03			-2.0	2.7E-03		
PA0048		probable transcriptional regulator					-1.6	2.0E-02		
PA0050		hypothetical protein	2.7	7.1E-14			-2.2	4.4E-11		
PA0051	<i>phzH</i>	potential phenazine-modifying enzyme	2.5	9.4E-13						
PA0052		hypothetical protein	2.0	2.2E-06						

PA0054		conserved hypothetical protein					14.0	7.0E-14		
PA0057		hypothetical protein			1.2	6.5E-03				
PA0059	<i>osmC</i>	osmotically inducible protein OsmC	1.6	3.4E-03			2.2	9.3E-12		
PA0062		hypothetical protein					2.2	7.1E-10		
PA0064		hypothetical protein			1.19	8.6E-03				
PA0066		conserved hypothetical protein					-1.6	6.1E-05		
PA0070	<i>tagQ1</i>	TagQ1			1.22	2.2E-02				
PA0071	<i>tagR1</i>	TagR1			1.37	1.8E-03			1.13	4.6E-02
PA0075	<i>pppA</i>	PppA			1.45	1.1E-02			1.17	1.8E-02
PA0076	<i>tagF1</i>	TagF1	1.6	1.5E-02						
PA0077	<i>icmF1</i>	IcmF1			1.37	4.7E-04			1.15	2.2E-02
PA0078	<i>tssL1</i>	TssL1	1.6	1.3E-03	1.31	5.6E-03			1.19	1.6E-02
PA0079	<i>tssK1</i>	TssK1	1.6	1.4E-04	1.4	3.1E-03			1.18	2.4E-02
PA0080	<i>tssJ1</i>	TssJ1	1.5	1.7E-07						
PA0081	<i>fha1</i>	Fha1					1.5	9.1E-11		
PA0082	<i>tssA1</i>	TssA1	1.5	4.1E-05	1.48	2.7E-03			1.39	6.8E-03
PA0083	<i>tssB1</i>	TssB1	1.7	2.8E-06			-1.8	2.7E-09		
PA0084	<i>tssC1</i>	TssC1	1.6	5.7E-04	1.52	4.7E-03			1.25	2.8E-02
PA0085	<i>hcp1</i>	Hcp1	1.7	3.9E-05	2.14	4.5E-04	-2.3	1.3E-14	1.38	1.1E-02
PA0086	<i>tagJ1</i>	TagJ1	1.7	1.6E-04			-1.8	6.7E-07		
PA0087	<i>tssE1</i>	TssE1	1.9	1.7E-04						
PA0088	<i>tssF1</i>	TssF1	1.6	3.7E-03						
PA0090	<i>clpV1</i>	ClpV1	1.6	1.5E-03	1.54	3.4E-03	-1.5	7.3E-04	1.21	4.1E-02
PA0091	<i>vgrG1</i>	VgrG1	1.5	6.0E-03	1.23	2.4E-04			1.16	1.1E-03
PA0094	<i>eagT6</i>	EagT6			1.38	4.7E-04				
PA0095		vgrG1b	1.6	4.4E-09						
PA0096		hypothetical protein	2.1	1.4E-06			-1.7	5.8E-04		
PA0097		hypothetical protein	1.6	2.0E-07			-1.6	5.3E-08		
PA0098		hypothetical protein	1.7	6.2E-04						
PA0099		type VI effector protein	1.6	6.4E-06						
PA0100		hypothetical protein	1.5	2.0E-06	1.29	4.4E-04	-1.6	1.0E-09	1.14	2.3E-03
PA0102		probable carbonic anhydrase	1.9	1.4E-09	1.18	2.0E-03			1.24	2.3E-03
PA0103		probable sulfate transporter	2.5	9.0E-07						

PA0104		hypothetical protein	2.0	1.9E-05						
PA0105	<i>coxB</i>	cytochrome c oxidase, subunit II	1.9	1.1E-09	1.16	5.8E-05			1.14	1.9E-02
PA0106	<i>coxA</i>	cytochrome c oxidase, subunit I	1.8	4.2E-11	1.29	6.5E-03				
PA0107		conserved hypothetical protein	1.8	3.1E-12						
PA0108	<i>coIII</i>	cytochrome c oxidase, subunit III	1.7	1.4E-12						
PA0109		hypothetical protein	2.0	1.7E-05						
PA0110		hypothetical protein	1.6	2.6E-06	1.27	6.9E-04	2.0	9.6E-17	1.13	1.3E-02
PA0111		hypothetical protein					1.8	1.5E-09		
PA0112		hypothetical protein	1.5	8.0E-04						
PA0113		probable cytochrome c oxidase assembly factor	1.7	6.1E-07			1.6	5.5E-08		
PA0114	<i>senC</i>	SenC			1.16	1.2E-02	1.5	7.9E-08		
PA0118		hypothetical protein			1.2	4.2E-02	2.1	9.4E-18		
PA0122	<i>rahU</i>	rahU	2.3	3.0E-07	2.04	1.4E-02				
PA0125		hypothetical protein					-3.0	9.6E-10		
PA0127		hypothetical protein	1.6	2.9E-05	1.37	1.5E-02				
PA0128		conserved hypothetical protein					-1.9	1.8E-13		
PA0132	<i>bauA</i>	Beta-alanine:pyruvate transaminase	1.6	3.3E-03						
PA0134		probable guanine deaminase	1.6	3.1E-04						
PA0136		probable ATP-binding component of ABC transporter	2.3	7.4E-03						
PA0137		probable permease of ABC transporter	2.0	3.0E-02			2.6	1.6E-04		
PA0138		probable permease of ABC transporter	2.0	4.8E-03						
PA0143	<i>nuh</i>	purine nucleosidase Nuh			-1.2	9.8E-04			-1.09	5.9E-03
PA0144		hypothetical protein			-1.52	2.6E-02			-1.36	2.5E-02
PA0145		hypothetical protein	1.9	7.2E-05						
PA0147		probable oxidoreductase	1.7	3.6E-02			1.6	3.3E-02		
PA0150		anti-sigma factor	-1.7	2.9E-02						
PA0153	<i>pcaH</i>	protocatechuate 3,4-dioxygenase, beta subunit	2.4	3.3E-09						

PA0154	<i>pcaG</i>	protocatechuate 3,4-dioxygenase, alpha subunit	2.4	8.4E-06	2.04	8.1E-06			1.57	1.5E-04
PA0155	<i>pcaR</i>	transcriptional regulator PcaR					1.8	5.5E-14		
PA0156	<i>triA</i>	Resistance-Nodulation-Cell Division (RND) triclosan efflux membrane fusion protein, TriA			1.49	2.7E-02				
PA0158	<i>triC</i>	Resistance-Nodulation-Cell Division (RND) triclosan efflux transporter, TriC			1.16	2.4E-04				
PA0161		hypothetical protein					-1.7	4.9E-05		
PA0165		hypothetical protein					1.6	9.0E-07		
PA0166		probable transporter	2.4	1.6E-02						
PA0171		hypothetical protein	1.8	1.5E-03						
PA0173		probable methylesterase	1.7	8.3E-04						
PA0174		conserved hypothetical protein	1.6	4.5E-04	1.24	1.6E-02				
PA0175		probable chemotaxis protein methyltransferase	1.9	2.3E-05			1.6	5.8E-04		
PA0176	<i>aer2</i>	aerotaxis transducer Aer2	1.9	4.0E-05						
PA0177		probable purine-binding chemotaxis protein	1.8	3.1E-04	1.24	1.4E-02	1.5	1.7E-03		
PA0178		probable two-component sensor	1.8	8.5E-06						
PA0179		probable two-component response regulator	2.0	2.0E-06						
PA0180	<i>cttP</i>	chemotactic transducer for trichloroethylene [positive chemotaxis], CttP	2.3	3.2E-11	1.27	1.5E-02				
PA0182		probable short-chain dehydrogenase					-1.7	1.2E-03	1.12	9.8E-03
PA0187		hypothetical protein	5.1	5.2E-06						
PA0188		hypothetical protein	4.4	1.0E-06						
PA0190		probable acid phosphatase					4.4	2.9E-16		
PA0196	<i>pntB</i>	pyridine nucleotide transhydrogenase, beta subunit			1.08	2.6E-02			1.1	4.8E-02
PA0200		hypothetical protein	2.2	4.2E-04			1.9	2.4E-04		
PA0201		hypothetical protein					-1.7	2.8E-02		

PA0211	<i>mdcD</i>	malonate decarboxylase beta subunit					-1.5	2.0E-02		
PA0216		malonate transporter MadM					-1.6	6.0E-03		
PA0217		probable transcriptional regulator					1.6	1.8E-03		
PA0219		probable aldehyde dehydrogenase					1.9	1.1E-04		
PA0222		hypothetical protein	-1.7	8.5E-03						
PA0223		probable dihydrodipicolinate synthetase	1.9	1.9E-04						
PA0224		probable aldolase	2.7	8.3E-07						
PA0226		probable CoA transferase, subunit A	3.3	3.0E-13	1.43	5.7E-04			1.4	5.1E-03
PA0227		probable CoA transferase, subunit B	3.7	2.2E-20						
PA0228	<i>pcaF</i>	beta-ketoadipyl CoA thiolase PcaF	3.2	3.0E-17	1.26	8.5E-03			1.3	4.1E-03
PA0229	<i>pcaT</i>	dicarboxylic acid transporter PcaT	2.2	9.1E-06						
PA0230	<i>pcaB</i>	3-carboxy-cis,cis- muconate cycloisomerase	1.7	7.5E-06						
PA0231	<i>pcaD</i>	beta-ketoadipate enol- lactone hydrolase					1.6	2.2E-05		
PA0232	<i>pcaC</i>	gamma- carboxymuconolactone decarboxylase	1.5	8.2E-03						
PA0237		probable oxidoreductase	2.3	1.1E-03						
PA0238		hypothetical protein	2.2	7.4E-03						
PA0240		probable porin	1.9	2.7E-02			2.9	2.6E-06		
PA0241		probable major facilitator superfamily (MFS) transporter	4.5	3.5E-22						
PA0242		hypothetical protein	4.9	3.0E-17	1.22	4.6E-03			1.22	4.2E-03
PA0243		probable transcriptional regulator							1.1	1.1E-02
PA0244		hypothetical protein	6.4	2.5E-21						
PA0245	<i>aroQ2</i>	3-dehydroquinate dehydratase	3.4	3.2E-11			1.6	2.8E-03		
PA0246		probable major facilitator superfamily (MFS) transporter					-1.5	6.8E-03		

PA0247	<i>pobA</i>	p-hydroxybenzoate hydroxylase	1.6	2.6E-02						
PA0254	<i>hudA</i>	HudA	1.5	1.0E-03						
PA0258		hypothetical protein					-1.6	2.3E-05		
PA0259	<i>tla3</i>	type 6 lipase adaptor, Tla3			1.57	4.8E-04			1.55	1.2E-04
PA0265	<i>davD</i>	glutaric semialdehyde dehydrogenase			-1.13	4.9E-02				
PA0268		probable transcriptional regulator	1.5	3.0E-03						
PA0274		hypothetical protein	-1.5	2.8E-02						
PA0277		conserved hypothetical protein			1.22	8.5E-03				
PA0278		hypothetical protein					-2.2	1.1E-02		
PA0281	<i>cysW</i>	sulfate transport protein CysW	-1.7	2.2E-03						
PA0282	<i>cysT</i>	sulfate transport protein CysT	-1.6	2.6E-03						
PA0283	<i>sbp</i>	sulfate-binding protein precursor	-1.6	1.3E-05						
PA0290		hypothetical protein					1.5	3.7E-05		
PA0292	<i>aguA</i>	agmatine deiminase			1.18	6.5E-03			1.12	3.4E-02
PA0293	<i>aguB</i>	N-carbamoylputrescine amidohydrolase	3.9	4.1E-30	1.83	8.0E-06			1.56	8.7E-05
PA0295		probable periplasmic polyamine binding protein	-2.1	4.8E-14						
PA0299	<i>spuC</i>	Polyamine:pyruvate transaminase			-1.26	8.2E-03	-1.5	2.5E-27	-1.18	2.2E-02
PA0300	<i>spuD</i>	polyamine transport protein			-1.25	2.3E-02			-1.16	4.1E-02
PA0301	<i>spuE</i>	polyamine transport protein			-1.26	7.6E-04			-1.11	1.4E-02
PA0302	<i>spuF</i>	polyamine transport protein PotG			-1.28	3.3E-04			-1.17	9.1E-03
PA0307		hypothetical protein					-1.6	1.8E-02		
PA0317		D-2-hydroxyglutarate dehydrogenase					-1.5	7.6E-14		
PA0322		probable transporter					1.6	6.7E-03		
PA0328	<i>aaaA</i>	arginine-specific autotransporter of Pseudomonas aeruginosa, AaaA			-1.33	2.5E-04			-1.23	4.0E-03

PA0329		conserved hypothetical protein			1.38	2.1E-02				
PA0330	<i>rpiA</i>	ribose 5-phosphate isomerase			-1.39	3.6E-03				
PA0331	<i>ilvA1</i>	threonine dehydratase, biosynthetic			-1.19	2.8E-04			-1.15	3.2E-04
PA0334		probable major facilitator superfamily (MFS) transporter	-1.7	2.9E-02						
PA0336	<i>rppH</i>	RNA pyrophosphohydrolase, RppH			-1.07	4.9E-02				
PA0337	<i>ptsP</i>	phosphoenolpyruvate-protein phosphotransferase PtsP			-1.14	3.6E-03				
PA0340		conserved hypothetical protein	-1.8	4.0E-04						
PA0341	<i>lgt</i>	prolipoprotein diacylglycerol transferase	-1.7	9.1E-06						
PA0342	<i>thyA</i>	thymidylate synthase							-1.05	3.5E-02
PA0345		hypothetical protein					1.5	3.7E-06		
PA0346		hypothetical protein	-1.8	1.6E-03						
PA0350	<i>folA</i>	dihydrofolate reductase	-1.5	4.9E-04						
PA0352		probable transporter	-1.7	5.9E-05						
PA0353	<i>ilvD</i>	dihydroxy-acid dehydratase			-1.07	3.4E-03				
PA0356		hypothetical protein	-1.6	3.7E-06			-1.6	3.6E-08		
PA0357	<i>mutM</i>	formamidopyrimidine-DNA glycosylase			-1.14	2.1E-02			-1.11	1.5E-02
PA0358		hypothetical protein	-1.5	6.0E-04						
PA0359		hypothetical protein	-2.1	1.3E-21	-1.59	1.3E-03			-1.33	1.8E-02
PA0364	<i>laoA</i>	LaoA			-1.09	4.4E-02				
PA0371		hypothetical protein			-1.2	1.7E-03				
PA0373	<i>ftsY</i>	signal recognition particle receptor FtsY			-1.14	3.5E-03			-1.07	2.0E-02
PA0381	<i>thiG</i>	thiamine biosynthesis protein, thiazole moiety			-1.09	2.1E-02				
PA0382	<i>micA</i>	DNA mismatch repair protein MicA	-1.9	4.1E-06						
PA0383		conserved hypothetical protein	-1.8	6.5E-06						
PA0385		hypothetical protein	-1.5	3.3E-03						

PA0386		probable oxidase	-1.9	6.5E-06						
PA0387		conserved hypothetical protein			-1.48	2.0E-02				
PA0388		hypothetical protein					1.7	8.6E-20	-1.15	2.9E-02
PA0389		hypothetical protein	-1.7	6.4E-06						
PA0390	<i>metX</i>	homoserine O-acetyltransferase	-1.6	2.3E-04						
PA0391		hypothetical protein	-2.2	5.7E-09						
PA0393	<i>proC</i>	pyrroline-5-carboxylate reductase			-1.15	1.1E-02			-1.09	4.1E-02
PA0395	<i>pilT</i>	twitching motility protein PilT			-1.13	1.4E-03				
PA0396	<i>pilU</i>	twitching motility protein PilU			-1.15	3.9E-04			-1.12	3.6E-03
PA0398		hypothetical protein					-1.6	5.2E-07		
PA0399		cystathionine beta-synthase					-1.6	3.0E-15		
PA0400		probable cystathionine gamma-lyase			-1.23	4.8E-04				
PA0403	<i>pyrR</i>	transcriptional regulator PyrR					1.6	1.8E-04		
PA0406	<i>tonB3</i>	TonB3	-1.9	2.3E-07						
PA0408	<i>pilG</i>	twitching motility protein PilG	-2.1	2.8E-17	-1.52	2.5E-03			-1.33	4.9E-02
PA0409	<i>pilH</i>	twitching motility protein PilH	-2.4	2.2E-29	-1.64	1.2E-02				
PA0410	<i>pilI</i>	twitching motility protein PilI	-2.4	1.1E-16	-1.48	6.8E-04				
PA0411	<i>pilJ</i>	twitching motility protein PilJ	-2.8	4.3E-24	-1.49	4.8E-05			-1.32	1.6E-04
PA0412	<i>pilK</i>	methyltransferase PilK	-2.4	2.3E-19						
PA0413	<i>chpA</i>	component of chemotactic signal transduction system	-2.4	1.9E-33	-1.24	3.8E-06			-1.17	2.3E-05
PA0414	<i>chpB</i>	probable methylesterase	-2.3	3.1E-24						
PA0415	<i>chpC</i>	probable chemotaxis protein	-2.2	2.0E-13			-1.6	3.3E-06		
PA0416	<i>chpD</i>	probable transcriptional regulator	-2.0	9.0E-07						
PA0417	<i>chpE</i>	probable chemotaxis protein	-2.8	7.8E-04						
PA0419		conserved hypothetical protein	-1.5	2.2E-03						

PA0420	<i>bioA</i>	adenosylmethionine-8-amino-7-oxononanoate aminotransferase							-1.1	1.4E-02
PA0421		hypothetical protein			-1.16	1.3E-04			-1.1	1.3E-03
PA0422		conserved hypothetical protein			1.22	7.9E-04			1.18	1.9E-02
PA0426	<i>mexB</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux transporter MexB			1.15	1.4E-02				
PA0429		hypothetical protein			1.21	9.7E-03				
PA0432	<i>sahH</i>	S-adenosyl-L-homocysteine hydrolase			-1.12	8.4E-03				
PA0437	<i>codA</i>	cytosine deaminase	-1.6	3.6E-06						
PA0439		probable oxidoreductase	5.0	9.4E-07						
PA0440		probable oxidoreductase	3.7	1.1E-05						
PA0441	<i>dht</i>	dihydropyrimidinase	5.0	1.2E-05			2.1	1.9E-02		
PA0443		probable transporter	3.3	3.6E-05			1.7	4.5E-02		
PA0444		N-carbamoyl-beta-alanine amidohydrolase	2.5	6.2E-05						
PA0447	<i>gcdH</i>	glutaryl-CoA dehydrogenase			-1.07	3.9E-02			-1.06	3.1E-02
PA0451		conserved hypothetical protein	1.7	1.9E-05			1.6	3.1E-06		
PA0452		probable stomatin-like protein	1.6	4.1E-02						
PA0453		hypothetical protein					1.6	4.2E-03		
PA0454		conserved hypothetical protein			-1.15	1.8E-02				
PA0455	<i>dbpA</i>	RNA helicase DbpA			1.13	3.1E-02			1.18	1.7E-02
PA0457.1		hypothetical membrane protein					2.0	1.6E-04		
PA0459		probable ClpA/B protease ATP binding subunit	1.7	3.3E-04	1.89	9.0E-04			1.51	1.7E-03
PA0460		hypothetical protein	1.6	1.2E-04						
PA0463	<i>creB</i>	two-component response regulator CreB					1.8	2.4E-13		
PA0470	<i>fiuA</i>	Ferrichrome receptor FiuA					4.3	2.3E-23		
PA0471	<i>fiuR</i>	FiuR	-1.8	4.6E-04						
PA0472	<i>fiuI</i>	FiuI	-2.0	4.2E-04			1.9	5.0E-05		
PA0473		probable glutathione S-transferase							1.06	3.4E-02

PA0476		probable permease	2.4	1.4E-03			2.0	2.0E-03		
PA0479		probable transcriptional regulator	1.6	2.5E-04						
PA0482	<i>glcB</i>	malate synthase G			1.15	1.6E-02			1.14	2.9E-02
PA0483		probable acetyltransferase	1.9	2.1E-08	1.25	1.1E-02	1.6	2.6E-06		
PA0484		conserved hypothetical protein	2.1	1.7E-07						
PA0493		probable biotin-requiring enzyme					-2.2	1.0E-02		
PA0496		conserved hypothetical protein					-1.7	1.9E-03		
PA0497		hypothetical protein	1.5	7.4E-04						
PA0498		hypothetical protein	1.9	1.5E-05						
PA0499		probable pili assembly chaperone	1.9	3.1E-03						
PA0502		probable biotin biosynthesis protein bioH			-1.14	3.9E-02				
PA0505		hypothetical protein					2.2	1.0E-13		
PA0506		probable acyl-CoA dehydrogenase	1.8	2.7E-08					1.09	2.7E-03
PA0508		probable acyl-CoA dehydrogenase			1.09	1.3E-02				
PA0510	<i>nirE</i>	NirE					2.3	3.4E-03		
PA0514	<i>nirL</i>	heme d1 biosynthesis protein NirL					2.0	4.3E-02		
PA0523	<i>norC</i>	nitric-oxide reductase subunit C	2.2	2.9E-02						
PA0524	<i>norB</i>	nitric-oxide reductase subunit B	1.9	1.5E-02						
PA0528		probable transcriptional regulator					1.8	1.9E-08		
PA0529		conserved hypothetical protein					-1.5	5.8E-03		
PA0530		probable class III pyridoxal phosphate-dependent aminotransferase	1.6	3.6E-02						
PA0532		hypothetical protein					10.7	1.1E-27		
PA0535		probable transcriptional regulator	-1.7	1.2E-03						
PA0540		hypothetical protein					-1.7	1.4E-04		

PA0542		conserved hypothetical protein			-1.11	2.8E-03	-1.8	6.5E-13	-1.1	3.3E-02
PA0543		hypothetical protein	1.5	2.7E-02						
PA0545		hypothetical protein					-1.8	1.6E-05		
PA0546	<i>metK</i>	methionine adenosyltransferase			1.24	1.4E-02			1.16	2.6E-02
PA0548	<i>tktA</i>	transketolase			-1.04	3.7E-02				
PA0552	<i>pgk</i>	phosphoglycerate kinase					-1.6	3.2E-10		
PA0555	<i>fda</i>	fructose-1,6-bisphosphate aldolase			-1.16	4.1E-02				
PA0556		hypothetical protein	-1.6	4.5E-03						
PA0557		hypothetical protein					2.7	5.2E-20		
PA0559		conserved hypothetical protein	-1.5	3.6E-05						
PA0563		conserved hypothetical protein					-1.6	7.7E-08		
PA0568		hypothetical protein					-1.6	6.2E-05		
PA0575		conserved hypothetical protein					2.3	2.3E-14		
PA0578		conserved hypothetical protein	-1.5	3.6E-04						
PA0579	<i>rpsU</i>	30S ribosomal protein S21	-1.5	3.6E-04			-2.2	3.2E-17		
PA0582	<i>folB</i>	dihydroneopterin aldolase					-2.3	5.3E-13		
PA0586		conserved hypothetical protein	1.7	2.2E-05	1.15	4.4E-02				
PA0587		conserved hypothetical protein	1.7	2.7E-06	1.17	2.7E-02				
PA0588		conserved hypothetical protein	1.8	2.3E-06	1.25	3.1E-02				
PA0589		conserved hypothetical protein					1.7	4.0E-14		
PA0590	<i>apaH</i>	bis(5'-nucleosyl)-tetrphosphatase			-1.07	3.1E-02				
PA0591		conserved hypothetical protein			1.13	2.0E-02	-1.9	3.9E-15	1.11	9.6E-03
PA0594	<i>surA</i>	peptidyl-prolyl cis-trans isomerase SurA			-1.14	7.6E-03				
PA0595	<i>lptD</i>	LPS-assembly protein LptD			-1.06	3.1E-02				
PA0599		hypothetical protein			1.35	1.7E-02				

PA0602		probable binding protein component of ABC transporter	-2.5	1.0E-11	-1.32	3.1E-04	-1.9	8.4E-09	-1.18	6.7E-03
PA0604	<i>agtB</i>	AgtB			-1.18	4.5E-03	-1.7	3.2E-17		
PA0607	<i>rpe</i>	ribulose-phosphate 3-epimerase	-1.5	3.3E-04						
PA0608		probable phosphoglycolate phosphatase	-1.7	1.9E-06						
PA0609	<i>trpE</i>	anthranilate synthetase component I							1.04	3.0E-02
PA0612	<i>ptrB</i>	repressor, PtrB	2.5	6.3E-04						
PA0613		hypothetical protein	1.8	8.6E-05						
PA0614		hypothetical protein	3.8	1.2E-11			2.1	4.1E-06		
PA0615		hypothetical protein	2.3	2.4E-08			-1.6	9.5E-04		
PA0616		hypothetical protein	3.6	2.0E-24						
PA0617		probable bacteriophage protein	3.4	1.0E-16						
PA0618		probable bacteriophage protein	3.7	7.0E-18						
PA0619		probable bacteriophage protein	4.2	3.5E-24						
PA0620		probable bacteriophage protein	2.3	2.1E-17						
PA0621		conserved hypothetical protein	2.0	5.2E-08						
PA0622		probable bacteriophage protein	3.3	2.2E-21						
PA0623		probable bacteriophage protein	3.1	1.7E-15			-1.6	6.9E-04		
PA0624		hypothetical protein	3.2	8.7E-12						
PA0625		hypothetical protein	3.0	1.4E-28						
PA0626		hypothetical protein	2.0	1.8E-07						
PA0627		conserved hypothetical protein	2.3	5.7E-04						
PA0628		conserved hypothetical protein	3.2	2.5E-11						
PA0629		conserved hypothetical protein	3.3	1.3E-09						
PA0630		hypothetical protein	3.1	1.1E-04			2.0	2.7E-03		
PA0632		hypothetical protein	5.6	1.9E-05			-3.0	5.3E-03		
PA0633		hypothetical protein	2.9	6.2E-21						
PA0634		hypothetical protein	3.1	3.8E-19						

PA0635		hypothetical protein	3.2	1.9E-14						
PA0636		hypothetical protein	3.5	9.1E-39						
PA0637		conserved hypothetical protein	3.8	2.4E-08						
PA0638		probable bacteriophage protein	3.9	1.5E-17						
PA0639		conserved hypothetical protein	3.0	8.4E-10						
PA0640		probable bacteriophage protein	3.4	4.5E-24						
PA0641		probable bacteriophage protein	3.0	3.6E-36						
PA0642		hypothetical protein	1.9	4.8E-05						
PA0643		hypothetical protein	1.9	1.8E-09						
PA0644		hypothetical protein	1.6	1.2E-03			-1.6	7.9E-04		
PA0648		hypothetical protein					-1.5	5.4E-06		
PA0649	<i>trpG</i>	anthranilate synthase component II			-1.08	3.6E-02				
PA0651	<i>trpC</i>	indole-3-glycerol-phosphate synthase							1.08	1.2E-02
PA0652	<i>vfr</i>	transcriptional regulator Vfr			-1.17	3.9E-04			-1.11	2.2E-03
PA0654	<i>speD</i>	S-adenosylmethionine decarboxylase proenzyme	-1.7	1.0E-04						
PA0658		probable short-chain dehydrogenase					1.6	2.7E-10		
PA0660		hypothetical protein			1.11	3.7E-02				
PA0662	<i>argC</i>	N-acetyl-gamma-glutamyl-phosphate reductase					-1.7	9.5E-17		
PA0663		hypothetical protein			-1.08	1.1E-02				
PA0664		hypothetical protein	-1.6	8.8E-06			-1.5	3.8E-07		
PA0665		conserved hypothetical protein					-1.6	9.7E-18		
PA0669		probable DNA polymerase alpha chain	1.6	3.5E-05						
PA0670		hypothetical protein	1.9	8.3E-03						
PA0671		hypothetical protein	1.9	2.6E-02						
PA0672	<i>hemO</i>	heme oxygenase	-1.6	3.0E-02						
PA0688	<i>lapA</i>	low-molecular-weight alkaline phosphatase A, LapA					2.2	2.6E-05		
PA0704		probable amidase			-1.18	3.3E-03				

PA0705	<i>migA</i>	alpha-1,6-rhamnosyltransferase MigA							-1.12	4.6E-02
PA0709		hypothetical protein	1.6	4.1E-02						
PA0718		hypothetical protein of bacteriophage Pf1	1.7	2.4E-02						
PA0719		hypothetical protein of bacteriophage Pf1	1.6	1.9E-02						
PA0722		hypothetical protein of bacteriophage Pf1					1.8	1.3E-05		
PA0723	<i>coaB</i>	coat protein B of bacteriophage Pf1					1.5	2.0E-06		
PA0729		hypothetical protein			1.11	5.9E-03				
PA0730		probable transferase	2.2	4.9E-04			2.0	2.0E-04		
PA0732		hypothetical protein	1.6	4.5E-04						
PA0733		probable pseudouridylate synthase					3.7	5.8E-21		
PA0735		hypothetical protein			1.41	1.1E-03			1.2	1.0E-03
PA0737		hypothetical protein	2.0	1.4E-03			2.0	1.1E-04		
PA0738		conserved hypothetical protein	2.0	1.0E-02			2.5	4.6E-06		
PA0741		conserved hypothetical protein	1.8	2.7E-07						
PA0743		probable 3-hydroxyisobutyrate dehydrogenase	2.6	1.5E-60						
PA0744		probable enoyl-CoA hydratase/isomerase	3.2	7.6E-174	2.05	1.8E-05			1.93	6.7E-05
PA0745	<i>dspI</i>	DspI	3.3	3.9E-54	2.33	8.4E-06			2.19	2.2E-05
PA0746		probable acyl-CoA dehydrogenase	3.4	3.4E-88	1.8	3.0E-05			1.63	9.8E-05
PA0747		probable aldehyde dehydrogenase	4.1	3.4E-80	1.56	2.2E-06			1.36	9.6E-05
PA0751		conserved hypothetical protein	-1.7	2.8E-03						
PA0752		conserved hypothetical protein	-1.6	4.5E-04						
PA0754		hypothetical protein					5.4	2.0E-21		
PA0755	<i>opdH</i>	cis-aconitate porin OpdH	-1.6	1.8E-03						
PA0757		probable two-component sensor	-1.5	9.9E-04						

PA0760		conserved hypothetical protein					-2.1	1.4E-12		
PA0762	<i>algU</i>	sigma factor AlgU			1.23	9.5E-03				
PA0763	<i>mucA</i>	anti-sigma factor MucA	1.7	5.7E-05						
PA0767	<i>lepA</i>	GTP-binding protein LepA							-1.04	3.3E-02
PA0768	<i>lepB</i>	signal peptidase I			1.06	2.6E-02				
PA0769		hypothetical protein			-1.16	6.5E-03			-1.08	4.1E-02
PA0774		conserved hypothetical protein	-1.9	9.6E-06						
PA0775		conserved hypothetical protein	-1.7	5.2E-08	-1.14	2.1E-02				
PA0776		hypothetical protein					1.5	2.7E-03		
PA0777		hypothetical protein	-1.6	1.2E-02						
PA0778	<i>icp</i>	inhibitor of cysteine peptidase			-1.09	1.1E-02				
PA0781		hypothetical protein					14.6	3.2E-08		
PA0782	<i>putA</i>	proline dehydrogenase PutA	-1.9	1.7E-06	-1.17	2.1E-02				
PA0783	<i>putP</i>	sodium/proline symporter PutP	-2.5	6.7E-09	-1.19	3.0E-02			-1.18	2.0E-02
PA0788		hypothetical protein					1.6	4.8E-03		
PA0789		probable amino acid permease	-2.0	5.7E-07	-1.23	3.9E-03	-1.6	1.2E-04	-1.19	6.2E-03
PA0799		probable helicase	-1.6	5.1E-08						
PA0801		hypothetical protein	-1.9	4.3E-06						
PA0805		hypothetical protein					-1.6	4.0E-04		
PA0806		hypothetical protein	1.7	1.7E-02						
PA0807	<i>ampD_{h3}</i>	AmpDh3	2.2	8.3E-07			2.3	1.5E-11		
PA0808		hypothetical protein	1.9	4.0E-03						
PA0812		hypothetical protein					1.6	1.2E-02		
PA0813		hypothetical protein	1.5	2.4E-02						
PA0819		hypothetical protein	1.9	2.3E-02						
PA0820		hypothetical protein	3.4	5.4E-50						
PA0826		hypothetical protein	2.1	3.2E-09						
PA0826	.1	translated portion of tmRNA gene ssrA					3654 99.3	1.1E- 175		
PA0828		probable transcriptional regulator					-2.0	2.0E-02		
PA0830		hypothetical protein	2.6	1.2E-14						

PA0834		conserved hypothetical protein	-1.6	3.8E-05						
PA0836	<i>ackA</i>	acetate kinase							-1.05	4.8E-02
PA0837	<i>slyD</i>	peptidyl-prolyl cis-trans isomerase SlyD			-1.45	1.4E-02	-1.5	5.3E-09		
PA0840		probable oxidoreductase	-1.6	3.7E-03	-1.13	2.4E-02	-1.9	8.8E-06		
PA0843	<i>plcR</i>	phospholipase accessory protein PlcR precursor					1.6	3.5E-03		
PA0846		probable sulfate uptake protein					-1.5	3.4E-08		
PA0850		hypothetical protein					2.0	3.1E-05		
PA0856		hypothetical protein					1.7	7.0E-11		
PA0861	<i>rbdA</i>	RbDA			1.13	5.0E-02				
PA0863		probable oxidoreductase			1.1	1.5E-03			1.11	6.2E-03
PA0865	<i>hpd</i>	4-hydroxyphenylpyruvate dioxygenase			-1.25	5.6E-03				
PA0866	<i>aroP2</i>	aromatic amino acid transport protein AroP2	-1.9	1.5E-08			-1.9	7.6E-12		
PA0868		conserved hypothetical protein					-2.0	1.3E-07		
PA0869	<i>pbpG</i>	D-alanyl-D-alanine-endopeptidase			-1.14	4.6E-02				
PA0877		probable transcriptional regulator					-1.5	2.6E-02		
PA0888	<i>aotJ</i>	arginine/ornithine binding protein AotJ			-1.22	2.4E-04				
PA0889	<i>aotQ</i>	arginine/ornithine transport protein AotQ			-1.13	2.0E-03			-1.1	8.2E-03
PA0892	<i>aotP</i>	arginine/ornithine transport protein AotP			-1.13	2.3E-03	-1.5	1.4E-07	-1.12	1.8E-02
PA0893	<i>argR</i>	transcriptional regulator ArgR			1.17	3.8E-03				
PA0894		hypothetical protein					-1.8	2.1E-02		
PA0895	<i>aruC</i>	N2-Succinylornithine 5-aminotransferase (SOAT) = N2-acetylornithine 5-aminotransferase (ACOAT)			-1.15	3.2E-02				
PA0897	<i>aruG</i>	subunit II of arginine N2-succinyltransferase = ornithine N2-succinyltransferase			-1.14	3.5E-02				

PA0898	<i>aruD</i>	N-Succinylglutamate 5-semialdehyde dehydrogenase	-1.5	5.4E-04						
PA0900		hypothetical protein			-1.38	9.9E-03	1.6	1.9E-08	-1.32	1.8E-02
PA0902		hypothetical protein			-1.12	3.9E-02				
PA0907	<i>alpA</i>	lysis phenotype activator, AlpA	1.6	1.4E-02						
PA0908	<i>alpB</i>	AlpB	2.2	2.1E-02			1.7	4.9E-02		
PA0909	<i>alpC</i>	AlpC	2.2	1.9E-02						
PA0910	<i>alpD</i>	AlpD	2.7	7.3E-05						
PA0911	<i>alpE</i>	AlpE	2.0	4.0E-03						
PA0913	<i>mgtE</i>	MgtE			-1.1	2.1E-02				
PA0914		hypothetical protein	-1.6	2.7E-02						
PA0916		conserved hypothetical protein			-1.12	1.9E-02				
PA0918		cytochrome b561			1.3	1.1E-03				
PA0919		alanyl-phosphatidylglycerol hydrolase			1.18	2.0E-02				
PA0920		alanyl-phosphatidylglycerol synthase			1.2	5.4E-03			1.12	3.4E-02
PA0921		hypothetical protein					-2.0	1.0E-08		
PA0927	<i>ldhA</i>	D-lactate dehydrogenase (fermentative)			1.19	1.2E-03			1.1	4.5E-02
PA0929		two-component response regulator	-1.7	1.9E-03						
PA0930		two-component sensor	-1.6	1.5E-02						
PA0932	<i>cysM</i>	cysteine synthase B			1.13	2.2E-03			1.04	4.0E-02
PA0936	<i>lpxO2</i>	lipopolysaccharide biosynthetic protein LpxO2			1.13	9.8E-03				
PA0938	<i>wzz2</i>	Wzz2			1.25	5.1E-03				
PA0939		hypothetical protein	1.9	1.8E-02						
PA0940		hypothetical protein	1.6	6.6E-03						
PA0941		hypothetical protein	1.6	1.2E-02	-1.3	6.6E-04			-1.13	4.2E-03
PA0942		probable transcriptional regulator	1.5	1.2E-03						
PA0945	<i>purM</i>	phosphoribosylaminoimidazole synthetase			-1.08	2.6E-02				
PA0946		hypothetical protein			-1.14	1.7E-02				

PA0947		conserved hypothetical protein					-1.6	4.8E-06		
PA0950		probable arsenate reductase			-1.27	4.7E-02	-2.4	2.1E-20		
PA0952		hypothetical protein	-2.5	4.7E-08			-2.5	3.4E-10		
PA0953		probable thioredoxin			1.07	6.2E-03				
PA0956	<i>proS</i>	prolyl-tRNA synthetase							1.06	2.5E-02
PA0958	<i>oprD</i>	Basic amino acid, basic peptide and imipenem outer membrane porin OprD precursor			-1.41	1.5E-03			-1.2	1.2E-02
PA0959		hypothetical protein	1.8	1.3E-06	1.1	5.7E-03			1.09	1.9E-02
PA0962	<i>dps</i>	DNA-binding protein from starved cells, Dps			1.18	2.4E-02				
PA0963	<i>aspS</i>	aspartyl-tRNA synthetase	-1.6	2.8E-09	-1.21	2.2E-03			-1.19	3.6E-03
PA0964	<i>pmpR</i>	pqsR-mediated PQS regulator, PmpR	-1.6	8.6E-08	-1.18	3.2E-04			-1.08	2.7E-02
PA0972	<i>tolB</i>	TolB protein			1.11	3.8E-03			1.08	3.5E-02
PA0973	<i>oprL</i>	Peptidoglycan associated lipoprotein OprL precursor					-1.5	1.5E-07		
PA0979		conserved hypothetical protein					-1.6	4.3E-02		
PA0980		hypothetical protein					-2.3	2.2E-03		
PA0981		hypothetical protein					-1.6	1.7E-04		
PA0982		hypothetical protein	1.6	7.5E-05						
PA0983		conserved hypothetical protein	1.6	1.3E-03						
PA0985	<i>pyoS5</i>	pyocin S5	2.8	1.1E-23						
PA0986		conserved hypothetical protein	1.9	8.3E-03						
PA0988		hypothetical protein					1.7	2.9E-15		
PA0990		conserved hypothetical protein	1.6	2.0E-04			1.8	1.2E-08		
PA0999	<i>pqsD</i>	3-oxoacyl-[acyl-carrier-protein] synthase III			1.08	3.6E-02				
PA1005		conserved hypothetical protein			-1.12	3.9E-04				
PA1006		Protein PA1006					-1.7	6.8E-04		
PA1007		conserved hypothetical protein	-1.9	9.3E-06			-1.6	1.3E-04		
PA1008	<i>bcp</i>	bacterioferritin comigratory protein			-1.08	5.0E-02				

PA1009		hypothetical protein					1.6	1.2E-06		
PA1010	<i>dapA</i>	dihydrodipicolinate synthase			-1.28	3.9E-02				
PA1011		hypothetical protein			-1.1	8.1E-03				
PA1012		conserved hypothetical protein	-1.6	6.4E-07						
PA1013	<i>purC</i>	phosphoribosylaminoimidazole-succinocarboxamide synthase			-1.09	4.7E-02				
PA1023		probable short-chain dehydrogenase			-1.09	1.0E-02				
PA1026		hypothetical protein	-1.6	3.3E-05			-1.8	3.6E-07	-1.17	1.4E-02
PA1032	<i>quiP</i>	QuiP			-1.13	1.5E-02				
PA1033		probable glutathione S-transferase			-1.22	6.7E-04			-1.18	1.6E-04
PA1036		hypothetical protein			-1.22	2.9E-03				
PA1038		hypothetical protein					1.8	8.0E-05		
PA1041		probable outer membrane protein precursor	1.5	5.7E-03						
PA1042		conserved hypothetical protein					-1.7	2.8E-05		
PA1043		hypothetical protein			-1.46	4.1E-03			-1.24	3.8E-02
PA1044		hypothetical protein					-2.0	4.2E-03		
PA1048		probable outer membrane protein precursor	1.9	1.5E-06	1.44	2.4E-02	1.6	1.2E-04	1.35	2.8E-02
PA1049	<i>pdxH</i>	pyridoxine 5'-phosphate oxidase	1.5	8.9E-05						
PA1052		conserved hypothetical protein			-1.1	1.3E-02				
PA1058	<i>shaE</i>	ShaE	1.7	2.9E-02						
PA1063		hypothetical protein					-1.9	2.7E-07		
PA1069		hypothetical protein			1.1	4.5E-02				
PA1070	<i>braG</i>	branched-chain amino acid transport protein BraG			1.21	1.6E-03				
PA1071	<i>braF</i>	branched-chain amino acid transport protein BraF			1.27	2.7E-02				
PA1074	<i>braC</i>	branched-chain amino acid transport protein BraC			-1.16	6.4E-03				
PA1077	<i>flgB</i>	flagellar basal-body rod protein FlgB	1.7	5.3E-11						
PA1078	<i>flgC</i>	flagellar basal-body rod protein FlgC	1.7	5.1E-10						

PA1079	<i>flgD</i>	flagellar basal-body rod modification protein FlgD	1.6	8.1E-09						
PA1080	<i>flgE</i>	flagellar hook protein FlgE	1.6	9.5E-11						
PA1081	<i>flgF</i>	flagellar basal-body rod protein FlgF	1.7	5.1E-11						
PA1082	<i>flgG</i>	flagellar basal-body rod protein FlgG	1.6	4.5E-07						
PA1083	<i>flgH</i>	flagellar L-ring protein precursor FlgH			1.15	2.5E-02			1.12	4.9E-02
PA1084	<i>flgI</i>	flagellar P-ring protein precursor FlgI	1.5	1.6E-08						
PA1085	<i>flgJ</i>	flagellar protein FlgJ	1.5	2.4E-06						
PA1088		hypothetical protein							1.09	1.9E-02
PA1092	<i>fliC</i>	flagellin type B	1.6	4.7E-06						
PA1094	<i>fliD</i>	flagellar capping protein FliD	1.5	4.9E-06						
PA1097	<i>fleQ</i>	transcriptional regulator FleQ			1.18	5.0E-03				
PA1099	<i>fleR</i>	two-component response regulator	1.5	3.9E-08						
PA1100	<i>fliE</i>	flagellar hook-basal body complex protein FliE	1.8	6.3E-08			-1.6	1.6E-06		
PA1101	<i>fliF</i>	Flagella M-ring outer membrane protein precursor	1.5	3.5E-11						
PA1103		probable flagellar assembly protein			1.22	2.8E-02				
PA1106		hypothetical protein					1.7	8.0E-11		
PA1111		hypothetical protein	1.9	1.0E-03			1.7	6.9E-04		
PA1116		hypothetical protein	-1.7	3.4E-06					-1.15	6.4E-03
PA1117		hypothetical protein					-1.5	1.4E-04		
PA1118		hypothetical protein	1.8	3.1E-04						
PA1119	<i>yfiB</i>	YfiB			1.24	1.5E-02	1.6	2.4E-16		
PA1126		hypothetical protein			1.27	1.6E-02			1.18	9.1E-03
PA1127		probable oxidoreductase	1.6	1.9E-28	1.23	1.5E-02			1.31	4.2E-03
PA1130	<i>rhlC</i>	rhamnosyltransferase 2	1.6	5.8E-04						
PA1136		probable transcriptional regulator	1.8	1.4E-04						
PA1144		probable major facilitator superfamily (MFS) transporter	2.0	1.2E-02						

PA1150	<i>pys2</i>	pyocin S2	1.6	2.5E-05						
PA1152		hypothetical protein					-1.6	2.5E-05		
PA1157		probable two-component response regulator			1.17	5.5E-04			1.1	6.5E-03
PA1159		probable cold-shock protein			-1.44	2.4E-02				
PA1161	<i>rrmA</i>	rRNA methyltransferase			-1.11	9.6E-03				
PA1162	<i>dapE</i>	succinyl-diaminopimelate desuccinylase			-1.33	3.5E-04			-1.19	5.5E-03
PA1166		hypothetical protein	1.8	2.2E-06						
PA1167		hypothetical protein					1.5	1.2E-04		
PA1168		hypothetical protein	2.2	5.7E-06						
PA1169		probable lipoxygenase					-2.8	3.6E-10		
PA1171	<i>sltB2</i>	SlbB2			1.07	1.6E-02				
PA1172	<i>napC</i>	cytochrome c-type protein NapC	1.9	1.2E-06	1.32	2.2E-03				
PA1173	<i>napB</i>	cytochrome c-type protein NapB precursor	1.8	2.5E-05			1.8	1.5E-06		
PA1174	<i>napA</i>	periplasmic nitrate reductase protein NapA	1.9	2.7E-08						
PA1175	<i>napD</i>	NapD protein of periplasmic nitrate reductase	1.9	9.7E-05						
PA1176	<i>napF</i>	ferredoxin protein NapF	2.1	3.1E-06			1.8	4.2E-06		
PA1177	<i>napE</i>	periplasmic nitrate reductase protein NapE	2.3	3.2E-05			-2.2	1.0E-06		
PA1178	<i>oprH</i>	PhoP/Q and low Mg ²⁺ inducible outer membrane protein H1 precursor					1.5	5.2E-09		
PA1179	<i>phoP</i>	two-component response regulator PhoP					-1.5	6.1E-21		
PA1185		probable glutathione S-transferase					1.7	3.2E-02		
PA1190		conserved hypothetical protein	1.9	1.9E-03						
PA1192		conserved hypothetical protein			-1.34	1.1E-02				
PA1203		hypothetical protein					1.5	1.5E-05		
PA1204		NAD(P)H quinone oxidoreductase			-1.25	5.3E-04				
PA1205		conserved hypothetical protein			-1.11	1.4E-02				

PA1206		hypothetical protein							-1.09	2.2E-02
PA1213		hypothetical protein					1.7	4.9E-09		
PA1214		hypothetical protein	1.6	5.2E-05					1.08	3.9E-02
PA1215		hypothetical protein							1.07	4.1E-02
PA1216		hypothetical protein			-1.09	1.2E-02				
PA1217		probable 2-isopropylmalate synthase	1.5	2.4E-05					1.08	8.3E-03
PA1218		hypothetical protein	1.5	1.9E-04	-1.19	1.4E-02				
PA1219		hypothetical protein	1.6	1.1E-05						
PA1220		hypothetical protein	1.6	4.6E-06	1.14	1.4E-02	1.6	6.2E-09		
PA1221		hypothetical protein	1.7	4.1E-07						
PA1222		probable membrane-bound lytic murein transglycolase A	-1.6	4.1E-08						
PA1223		probable transcriptional regulator					-1.6	3.7E-03		
PA1227		hypothetical protein					-1.5	3.5E-02		
PA1228		hypothetical protein	-3.4	1.7E-12						
PA1234		hypothetical protein	-1.5	7.5E-03						
PA1239		hypothetical protein	2.8	1.5E-04						
PA1240		probable enoyl-CoA hydratase/isomerase	2.0	6.1E-05						
PA1244		hypothetical protein			-1.34	1.9E-02	1.8	2.3E-16		
PA1246	<i>aprD</i>	alkaline protease secretion protein AprD					1.6	1.8E-10		
PA1247	<i>aprE</i>	alkaline protease secretion protein AprE			-1.12	5.4E-03			-1.06	4.4E-02
PA1248	<i>aprF</i>	Alkaline protease secretion outer membrane protein AprF precursor			-1.18	4.6E-03				
PA1250	<i>aprI</i>	alkaline proteinase inhibitor AprI			-1.25	1.0E-02			-1.15	2.5E-02
PA1254	<i>lhpC</i>	delta1-pyrroline-4-hydroxy-2-carboxylate deaminase, LphC	2.3	2.3E-03						
PA1255	<i>lhpK</i>	D-hydroxyproline epimerase, LhpK	2.0	9.7E-04						
PA1256	<i>lhpO</i>	ABC transporter ATP-binding protein, LhpO	1.8	2.4E-02			12.8	2.5E-39		
PA1259	<i>lhpH</i>	LhpH	2.1	4.9E-03						

PA1260	<i>lhpP</i>	ABC transporter periplasmic-binding protein, LhpP	2.1	1.8E-04	1.09	3.5E-02				
PA1261	<i>lhpR</i>	Transcriptional regulator, LhpR					2.0	2.3E-03		
PA1263		hypothetical protein					1.5	7.0E-07		
PA1271		probable tonB-dependent receptor	-1.6	1.3E-04	-1.27	2.0E-02				
PA1272	<i>cobO</i>	cob(I)alamin adenosyltransferase	-1.6	4.5E-05	-1.16	8.6E-03			-1.16	1.3E-02
PA1273	<i>cobB</i>	cobyric acid a,c-diamide synthase	-1.8	1.3E-05						
PA1274		conserved hypothetical protein	-1.8	1.0E-02			-1.9	2.2E-03		
PA1275	<i>cobD</i>	cobalamin biosynthetic protein CobD	-1.6	1.2E-02						
PA1276	<i>cobC</i>	cobalamin biosynthetic protein CobC	-1.7	1.0E-02						
PA1277	<i>cobQ</i>	cobyric acid synthase	-1.9	1.0E-05						
PA1278	<i>cobP</i>	cobinamide kinase	-2.0	1.4E-05						
PA1279	<i>cobU</i>	nicotinate-nucleotide--dimethylbenzimidazole phosphoribosyltransferase	-1.7	4.9E-04			-1.5	3.0E-03		
PA1280		hypothetical protein	-2.4	7.7E-04						
PA1281	<i>cobV</i>	cobalamin (5'-phosphate) synthase	-1.7	4.3E-03						
PA1285		probable transcriptional regulator					1.7	5.1E-07		
PA1287		probable glutathione peroxidase			-1.28	2.1E-02				
PA1289		hypothetical protein	2.4	1.0E-06			1.6	1.5E-03		
PA1290		probable transcriptional regulator							1.3	1.1E-02
PA1292		probable 3-mercaptopyruvate sulfurtransferase			-1.12	1.8E-03				
PA1307		conserved hypothetical protein	-1.5	3.8E-08						
PA1308		hypothetical protein	-1.7	6.4E-06						
PA1315		probable transcriptional regulator			1.08	2.5E-02			1.09	3.3E-02
PA1320	<i>cyoD</i>	cytochrome o ubiquinol oxidase subunit IV					-2.8	8.4E-04		

PA1322		probable TonB-dependent receptor	2.0	1.3E-04						
PA1324		hypothetical protein			1.3	1.5E-02	2.7	2.6E-13		
PA1325		conserved hypothetical protein	-1.8	2.1E-08	-1.54	1.5E-02				
PA1326	<i>ilvA2</i>	threonine dehydratase, biosynthetic	-2.0	6.1E-06	-1.44	9.3E-03				
PA1328		probable transcriptional regulator					1.7	5.1E-06		
PA1337	<i>ansB</i>	glutaminase-asparaginase							-1.08	3.9E-02
PA1338	<i>ggt</i>	gamma-glutamyltranspeptidase precursor			-1.39	8.0E-03				
PA1341	<i>aatQ</i>	AatQ							-1.05	4.9E-02
PA1342	<i>aatJ</i>	AatJ			-1.1	3.8E-02				
PA1348		hypothetical protein	1.9	6.4E-05						
PA1349		conserved hypothetical protein	1.7	1.4E-02						
PA1350		hypothetical protein	1.7	5.4E-03						
PA1356		hypothetical protein	1.7	7.1E-03			1.6	2.4E-03		
PA1357		conserved hypothetical protein			-1.26	2.6E-04			-1.18	2.4E-03
PA1358		hypothetical protein					1.7	3.7E-10		
PA1360		conserved hypothetical protein					-1.7	4.7E-02		
PA1363		ECF sigma factor	-1.7	2.4E-03						
PA1364		probable transmembrane sensor	-1.9	1.3E-02						
PA1365		probable siderophore receptor	-1.5	1.6E-03						
PA1371		hypothetical protein			1.43	3.3E-03				
PA1372		hypothetical protein	1.5	9.0E-06	1.2	5.2E-04			1.19	6.0E-04
PA1375	<i>pdxB</i>	erythronate-4-phosphate dehydrogenase			-1.08	1.5E-02			-1.11	4.2E-03
PA1376	<i>aceK</i>	isocitrate dehydrogenase kinase/phosphatase			-1.14	2.5E-02			-1.13	3.6E-02
PA1383		hypothetical protein	1.6	1.3E-08	1.6	1.9E-07			1.27	8.4E-05
PA1384	<i>galE</i>	UDP-glucose 4-epimerase	1.7	1.5E-03						
PA1385		probable glycosyl transferase	2.0	1.2E-06						

PA1386		probable ATP-binding component of ABC transporter	1.8	1.2E-09						
PA1387		hypothetical protein	1.7	1.3E-07						
PA1388		hypothetical protein	1.5	8.6E-03						
PA1397		probable two-component response regulator	-1.7	5.3E-05						
PA1398		hypothetical protein			-1.12	7.2E-03				
PA1399		probable transcriptional regulator					1.6	7.5E-03		
PA1405		probable helicase	-1.7	4.9E-04						
PA1408		hypothetical protein					14.8	3.0E-30		
PA1411		hypothetical protein	-1.5	2.1E-02						
PA1414		hypothetical protein	2.2	8.3E-04			-2.2	4.4E-05		
PA1415		hypothetical protein					1.6	1.0E-08		
PA1423	<i>bdlA</i>	BdlA	1.9	1.4E-06						
PA1429		probable cation-transporting P-type ATPase	1.6	8.2E-03						
PA1430	<i>lasR</i>	transcriptional regulator LasR			-1.28	4.9E-02				
PA1431	<i>rsaL</i>	regulatory protein RsaL	1.7	6.8E-04	1.25	8.3E-03	2.0	8.0E-08		
PA1442		conserved hypothetical protein					-1.5	1.0E-09		
PA1445	<i>fliO</i>	flagellar protein FliO							-1.05	3.6E-02
PA1450		conserved hypothetical protein					-2.1	1.6E-06		
PA1451		conserved hypothetical protein					-1.9	6.4E-07		
PA1452	<i>flhA</i>	flagellar biosynthesis protein FlhA			1.28	1.3E-02				
PA1461	<i>motD</i>	MotD			1.12	6.9E-03			1.11	1.3E-02
PA1462		probable plasmid partitioning protein			1.1	4.4E-03			1.05	3.3E-03
PA1471		hypothetical protein	1.6	6.8E-03			2.3	5.1E-10		
PA1474		hypothetical protein	1.5	5.7E-06						
PA1478		hypothetical protein	-2.3	1.3E-03			-1.7	3.3E-02		
PA1483	<i>cycH</i>	cytochrome c-type biogenesis protein							-1.07	3.3E-02
PA1487		probable carbohydrate kinase	1.6	2.5E-03						

PA1488		hypothetical protein	1.6	6.4E-03						
PA1489		hypothetical protein	1.6	7.9E-04						
PA1490		probable transcriptional regulator			1.16	2.3E-02				
PA1491		probable transporter	1.5	2.9E-02						
PA1492		hypothetical protein	1.7	3.9E-02						
PA1493	<i>cysP</i>	sulfate-binding protein of ABC transporter			1.22	2.4E-02			1.33	3.7E-03
PA1502	<i>gcl</i>	glyoxylate carboligase	2.8	3.1E-06						
PA1503		hypothetical protein					1.6	4.8E-02		
PA1504		probable transcriptional regulator			-1.15	1.7E-03				
PA1507		probable transporter	1.7	1.5E-04						
PA1509	<i>tplEi</i>	immunity protein, TplEi	1.5	1.6E-06						
PA1510	<i>tplE</i>	type 6 PGAP1-like effector, TplE	1.5	1.1E-09						
PA1512	<i>hcpA</i>	secreted protein Hcp					1.6	1.4E-02		
PA1513		hypothetical protein	1.5	2.9E-04	1.3	8.8E-03				
PA1514		ureidoglycolate hydrolase YbbT	1.6	2.5E-02						
PA1515	<i>alc</i>	allantoicase	1.9	1.3E-05						
PA1516		hypothetical protein	1.7	2.4E-03	-1.2	3.1E-02	1.5	3.8E-03		
PA1517		conserved hypothetical protein	2.1	4.9E-07	1.1	2.8E-02	1.7	8.9E-06		
PA1518		conserved hypothetical protein	1.5	5.6E-05						
PA1519		probable transporter	1.6	1.9E-02			2.5	5.0E-09		
PA1523	<i>xdhB</i>	xanthine dehydrogenase			1.16	2.4E-02				
PA1524	<i>xdhA</i>	xanthine dehydrogenase	1.6	9.2E-04			1.6	2.0E-05		
PA1527		conserved hypothetical protein			-1.12	8.0E-04			-1.09	3.2E-03
PA1528	<i>zipA</i>	cell division protein ZipA			1.08	2.8E-02			1.07	3.3E-02
PA1530		hypothetical protein			1.44	1.7E-02			1.37	5.0E-03
PA1531		hypothetical protein					1.6	1.0E-06		
PA1532	<i>dnaX</i>	DNA polymerase subunits gamma and tau			-1.2	1.6E-02				
PA1538		probable flavin-containing monooxygenase	1.7	7.7E-04						
PA1545		hypothetical protein	1.6	1.2E-04						

PA1546	<i>hemN</i>	oxygen-independent coproporphyrinogen III oxidase	2.3	6.0E-06	1.41	4.4E-02				
PA1552	<i>ccoP1</i>	Cytochrome c oxidase, cbb3-type, CcoP subunit	-1.6	5.2E-08	-1.31	4.2E-05			-1.36	6.1E-07
PA1552 .1	<i>ccoQ1</i>	Cytochrome c oxidase, cbb3-type, CcoQ subunit	-1.8	2.8E-10						
PA1553	<i>ccoO1</i>	Cytochrome c oxidase, cbb3-type, CcoO subunit	-1.7	3.0E-10	-1.55	8.3E-04	-1.8	1.5E-17	-1.41	1.4E-02
PA1554	<i>ccoN1</i>	Cytochrome c oxidase, cbb3-type, CcoN subunit	-1.6	7.3E-10					-1.12	4.9E-02
PA1555	<i>ccoP2</i>	Cytochrome c oxidase, cbb3-type, CcoP subunit	1.9	3.8E-02	1.45	4.1E-02				
PA1555 .1	<i>ccoQ2</i>	Cytochrome c oxidase, cbb3-type, CcoQ subunit			-1.55	3.7E-03			-1.49	5.3E-03
PA1556	<i>ccoO2</i>	Cytochrome c oxidase, cbb3-type, CcoO subunit	2.1	2.6E-02						
PA1557	<i>ccoN2</i>	Cytochrome c oxidase, cbb3-type, CcoN subunit	2.1	3.5E-02						
PA1559		hypothetical protein					1.9	3.9E-02		
PA1561	<i>aer</i>	aerotaxis receptor Aer			1.25	1.4E-02				
PA1571		hypothetical protein					1.5	1.1E-02		
PA1574		conserved hypothetical protein	-1.6	4.4E-05	-1.15	3.6E-03			-1.1	3.3E-02
PA1577		hypothetical protein	-1.6	3.4E-02						
PA1581	<i>sdhC</i>	succinate dehydrogenase (C subunit)	-1.6	5.6E-07	-1.1	3.3E-02	-2.0	2.5E-18		
PA1582	<i>sdhD</i>	succinate dehydrogenase (D subunit)	-1.6	2.0E-04	-1.18	3.9E-02	1.7	1.0E-06	-1.24	2.2E-02
PA1583	<i>sdhA</i>	succinate dehydrogenase (A subunit)	-1.6	1.4E-06	-1.25	3.9E-06			-1.17	1.4E-04
PA1584	<i>sdhB</i>	succinate dehydrogenase (B subunit)			-1.2	3.0E-03			-1.16	9.0E-03
PA1585	<i>sucA</i>	2-oxoglutarate dehydrogenase (E1 subunit)							-1.1	4.1E-02
PA1586	<i>sucB</i>	dihydrolipoamide succinyltransferase (E2 subunit)			-1.24	7.3E-04	-1.5	1.4E-12	-1.14	3.1E-03
PA1587	<i>lpd</i>	dihydrolipoamide dehydrogenase Lpd			-1.19	7.8E-04				
PA1588	<i>sucC</i>	succinyl-CoA synthetase beta chain	-1.5	5.3E-06	-1.14	2.3E-02				

PA1589	<i>sucD</i>	succinyl-CoA synthetase alpha chain			-1.39	5.5E-04			-1.15	2.0E-02
PA1591		hypothetical protein	-1.7	9.3E-04						
PA1592		hypothetical protein	1.9	2.5E-04			2.2	6.6E-08		
PA1594		hypothetical protein							1.29	1.2E-02
PA1602		probable oxidoreductase	1.5	4.5E-02						
PA1606		hypothetical protein	1.8	8.2E-03			1.6	1.0E-02		
PA1608		probable chemotaxis transducer			1.1	2.8E-02				
PA1614	<i>gpsA</i>	glycerol-3-phosphate dehydrogenase, biosynthetic			-1.11	1.3E-02			-1.11	2.4E-03
PA1616		conserved hypothetical protein					1.7	2.2E-10		
PA1618		conserved hypothetical protein			-1.1	1.8E-02			-1.08	2.1E-02
PA1619		probable transcriptional regulator	-1.5	1.8E-03						
PA1621		probable hydrolase	3.3	7.0E-50	1.54	5.1E-04			1.23	6.4E-03
PA1622		probable hydrolase	3.3	3.4E-32						
PA1624		hypothetical protein			-1.15	5.9E-03			-1.11	2.3E-02
PA1627		probable transcriptional regulator					2.2	1.4E-08		
PA1638		conserved hypothetical protein	-1.5	1.2E-02						
PA1642	<i>selD</i>	selenophosphate synthetase			-1.15	8.9E-03				
PA1643		conserved hypothetical protein			1.07	3.8E-02				
PA1652		hypothetical protein					-1.8	4.5E-02		
PA1659	<i>hsiF2</i>	HsiF2	1.6	1.3E-04						
PA1661	<i>hsiH2</i>	HsiH2	1.5	8.1E-03			-1.8	6.7E-05		
PA1664	<i>orfX</i>	OrfX					-2.3	6.1E-03		
PA1666	<i>lip2</i>	Lip2			1.33	1.8E-04	-1.8	2.5E-05	1.09	1.5E-02
PA1669	<i>icmF2</i>	IcmF2					-1.8	1.4E-07		
PA1670	<i>stp1</i>	Stp1					-1.6	5.0E-03		
PA1673		hypothetical protein	2.2	4.3E-03	1.34	3.4E-02				
PA1676		hypothetical protein					-2.0	3.1E-05		
PA1678		probable DNA methylase					-1.6	7.1E-06		
PA1681	<i>aroC</i>	chorismate synthase			-1.18	4.5E-05			-1.08	2.4E-03

PA1682		probable MFS metabolite transporter	-1.7	3.7E-03						
PA1683		probable sugar aldolase			-1.1	4.7E-02				
PA1685	<i>masA</i>	enolase-phosphatase E-1	-1.5	7.1E-05						
PA1687	<i>speE</i>	spermidine synthase	-1.9	2.0E-06	-1.1	1.3E-02				
PA1688		hypothetical protein	-1.5	1.5E-06						
PA1689		conserved hypothetical protein	-1.7	1.5E-07	-1.31	5.1E-06			-1.16	8.4E-05
PA1690	<i>pscU</i>	translocation protein in type III secretion	-4.7	7.7E-09						
PA1691	<i>pscT</i>	translocation protein in type III secretion	-3.5	2.0E-04						
PA1692		probable translocation protein in type III secretion	-4.5	3.5E-05						
PA1693	<i>pscR</i>	translocation protein in type III secretion	-2.3	4.9E-09						
PA1694	<i>pscQ</i>	translocation protein in type III secretion	-8.6	5.6E-12			-2.3	1.2E-03		
PA1695	<i>pscP</i>	translocation protein in type III secretion	-7.8	6.7E-18						
PA1696	<i>pscO</i>	translocation protein in type III secretion	-12.2	2.4E-11						
PA1697		ATP synthase in type III secretion system	-9.1	2.3E-42						
PA1698	<i>popN</i>	Type III secretion outer membrane protein PopN precursor	-8.7	1.0E-32						
PA1699	<i>pcr1</i>	Pcr1	-5.4	7.3E-09						
PA1700	<i>pcr2</i>	Pcr2	-4.2	1.1E-03			-3.3	9.0E-03		
PA1701	<i>pcr3</i>	Pcr3	-7.7	1.9E-06						
PA1703	<i>pcrD</i>	type III secretory apparatus protein PcrD	-4.2	3.8E-40			-1.6	2.0E-06		
PA1705	<i>pcrG</i>	regulator in type III secretion	-9.3	5.4E-12						
PA1706	<i>pcrV</i>	type III secretion protein PcrV	-7.0	1.2E-32			-1.6	9.4E-04		
PA1707	<i>pcrH</i>	regulatory protein PcrH	-8.6	4.9E-26			-1.9	1.7E-04		
PA1708	<i>popB</i>	translocator protein PopB	-7.2	1.7E-48			-2.2	8.9E-11		
PA1709	<i>popD</i>	Translocator outer membrane protein PopD precursor	-6.1	9.0E-41			-1.8	1.5E-06		

PA1710	<i>exsC</i>	ExsC, exoenzyme S synthesis protein C precursor.	-3.9	1.8E-37			-1.7	2.4E-08		
PA1711	<i>exsE</i>	ExsE	-4.0	2.3E-16						
PA1712	<i>exsB</i>	exoenzyme S synthesis protein B	-4.3	1.3E-48			-1.8	3.1E-10		
PA1713	<i>exsA</i>	transcriptional regulator ExsA	-4.8	6.3E-62						
PA1714	<i>exsD</i>	ExsD	-3.8	8.1E-34	-1.87	8.1E-04			-1.29	3.2E-02
PA1715	<i>pscB</i>	type III export apparatus protein	-6.3	3.4E-11			-2.4	3.2E-04		
PA1716	<i>pscC</i>	Type III secretion outer membrane protein PscC precursor	-5.3	7.5E-47						
PA1717	<i>pscD</i>	type III export protein PscD	-5.7	1.3E-14			-2.2	9.0E-05		
PA1718	<i>pscE</i>	type III export protein PscE	-6.5	2.9E-08						
PA1719	<i>pscF</i>	type III export protein PscF	-5.2	1.9E-20			-1.6	3.0E-03		
PA1720	<i>pscG</i>	type III export protein PscG	-5.3	8.6E-14			-1.7	6.4E-03		
PA1721	<i>pscH</i>	type III export protein PscH	-7.2	2.5E-09						
PA1722	<i>pscI</i>	type III export protein PscI	-3.9	2.7E-09			-2.2	3.5E-04		
PA1723	<i>pscJ</i>	type III export protein PscJ	-5.4	3.4E-34	-1.41	4.2E-03	-1.7	4.1E-06		
PA1724	<i>pscK</i>	type III export protein PscK	-2.6	2.4E-03						
PA1725	<i>pscL</i>	type III export protein PscL	-4.0	4.6E-20						
PA1726	<i>bglX</i>	periplasmic beta-glucosidase			-1.16	3.7E-02				
PA1728		hypothetical protein	2.3	4.5E-05						
PA1729		conserved hypothetical protein	1.9	2.5E-05						
PA1730		conserved hypothetical protein	1.9	2.8E-03			1.5	1.9E-02		
PA1731		conserved hypothetical protein	1.8	9.0E-03			1.7	2.3E-03		
PA1732		conserved hypothetical protein	1.6	2.8E-02			2.0	2.0E-04		
PA1733		conserved hypothetical protein	1.7	9.2E-03	-1.22	3.8E-02	1.8	4.8E-04		

PA1740		hypothetical protein	1.9	2.6E-02						
PA1745		hypothetical protein	1.7	4.3E-06	1.29	3.3E-03	1.7	2.9E-08		
PA1746		hypothetical protein	2.3	2.5E-03						
PA1751		hypothetical protein					-1.6	1.4E-04		
PA1752		hypothetical protein			-1.15	1.2E-02				
PA1753		conserved hypothetical protein	1.6	7.2E-10						
PA1754	<i>cysB</i>	transcriptional regulator CysB			1.21	3.2E-02				
PA1755		hypothetical protein			-1.28	1.3E-03				
PA1757	<i>thrH</i>	homoserine kinase			-1.23	4.6E-03			-1.17	2.8E-02
PA1768		hypothetical protein			1.91	3.6E-04	1.6	1.1E-05	1.41	6.3E-04
PA1769		conserved hypothetical protein			-1.06	3.5E-02				
PA1770	<i>ppsA</i>	phosphoenolpyruvate synthase			-1.09	6.1E-04			-1.05	1.3E-02
PA1771	<i>estX</i>	EstX	-1.7	1.4E-05						
PA1773	<i>cmaX</i>	CmaX protein			1.28	5.2E-03			1.21	2.2E-02
PA1775	<i>cmpX</i>	conserved cytoplasmic membrane protein, CmpX protein			1.2	3.8E-04				
PA1777	<i>oprF</i>	Major porin and structural outer membrane porin OprF precursor			1.34	1.1E-02				
PA1781	<i>nirB</i>	assimilatory nitrite reductase large subunit	1.5	3.9E-03	-1.06	1.7E-02			-1.09	2.7E-03
PA1782		probable serine/threonine-protein kinase					1.8	4.4E-04		
PA1784		hypothetical protein	2.4	1.5E-04			2.2	4.7E-05		
PA1785	<i>nasT</i>	NasT	1.8	3.3E-02	-1.26	1.3E-04			-1.11	7.0E-03
PA1786	<i>nasS</i>	NasS	1.8	1.9E-02	-1.22	3.4E-02	1.7	1.2E-02		
PA1787	<i>acnB</i>	aconitate hydratase 2			-1.13	8.9E-04			-1.06	5.9E-03
PA1792		conserved hypothetical protein	-1.7	1.5E-06						
PA1793	<i>ppiB</i>	peptidyl-prolyl cis-trans isomerase B	-1.5	3.2E-05	-1.31	3.8E-03				
PA1797		hypothetical protein	2.9	2.6E-02			2.8	1.0E-02		
PA1798	<i>parS</i>	two-component sensor, ParS			1.17	2.3E-02				
PA1800	<i>tig</i>	trigger factor					-1.5	6.3E-07		
PA1802	<i>clpX</i>	ClpX			-1.12	1.1E-02				

PA1807	<i>nppD</i>	NppD			-1.08	4.6E-02				
PA1810	<i>nppA2</i>	NppA2			-1.07	2.0E-02				
PA1813		probable hydroxyacylglutathione hydrolase			-1.09	1.6E-02			-1.06	8.0E-03
PA1821		probable enoyl-CoA hydratase/isomerase			-1.09	3.7E-02				
PA1822	<i>fimL</i>	hypothetical protein			-1.13	1.1E-02				
PA1823	<i>nudC</i>	NudC					-1.6	1.9E-08		
PA1824		conserved hypothetical protein					-1.8	8.0E-03		
PA1827		probable short-chain dehydrogenase					-1.9	1.1E-02		
PA1831		hypothetical protein			1.1	3.8E-02				
PA1832		probable protease			1.11	1.1E-02				
PA1835		hypothetical protein	1.7	5.1E-05						
PA1836		probable transcriptional regulator					-1.5	2.5E-03		
PA1837		hypothetical protein			-1.21	1.1E-03				
PA1840		hypothetical protein					-2.3	5.8E-14		
PA1844	<i>tseI</i>	TseI			1.63	1.2E-02				
PA1845	<i>tsiI</i>	TsiI	1.5	1.4E-02						
PA1847	<i>nfuA</i>	NfuA					1.6	2.8E-18		
PA1852		hypothetical protein					1.7	3.2E-06		
PA1858	<i>str</i>	streptomycin 3"- phosphotransferase					1.6	5.1E-04		
PA1859		probable transcriptional regulator	1.6	5.8E-04						
PA1868	<i>xqhA</i>	secretion protein XqhA	-2.1	4.8E-05						
PA1870		hypothetical protein	1.7	3.2E-04						
PA1871	<i>lasA</i>	LasA protease precursor	1.7	2.0E-04						
PA1873		hypothetical protein	1.5	2.2E-02						
PA1874		hypothetical protein	2.3	4.2E-52						
PA1875		probable outer membrane protein precursor	2.3	3.5E-45						
PA1876		probable ATP- binding/permease fusion ABC transporter	2.2	4.2E-42	1.11	1.4E-02				
PA1877		probable secretion protein	2.1	6.1E-35	1.53	2.2E-05			1.28	3.5E-03
PA1878		hypothetical protein	3.8	1.3E-51	2.37	3.7E-05			2.02	3.7E-06

PA1879		hypothetical protein	2.5	3.4E-10						
PA1880		probable oxidoreductase	3.3	9.3E-38	1.56	1.6E-04			1.33	5.4E-04
PA1881		probable oxidoreductase	3.1	2.0E-27	1.28	1.1E-02			1.18	4.5E-02
PA1882		probable transporter	1.6	2.4E-02						
PA1885		conserved hypothetical protein	1.6	1.2E-02			2.3	5.1E-09		
PA1887		hypothetical protein	1.7	2.9E-02						
PA1888		hypothetical protein	2.2	1.1E-03			1.8	5.5E-03		
PA1889		hypothetical protein	1.6	2.2E-03						
PA1892		hypothetical protein			-1.29	1.7E-02				
PA1893		hypothetical protein			-1.11	4.6E-02				
PA1896		hypothetical protein			-1.2	7.9E-04			-1.07	2.6E-02
PA1897		hypothetical protein			-1.9	4.0E-02				
PA1899	<i>phzA2</i>	probable phenazine biosynthesis protein	1.7	2.6E-08					1.1	4.7E-02
PA1900	<i>phzB2</i>	probable phenazine biosynthesis protein	2.0	3.0E-10	1.25	4.3E-02				
PA1901	<i>phzC2</i>	phenazine biosynthesis protein PhzC	1.9	2.2E-06	1.44	4.5E-03			1.31	2.4E-03
PA1903	<i>phzE2</i>	phenazine biosynthesis protein PhzE			1.24	7.2E-04			1.17	2.9E-04
PA1905	<i>phzG2</i>	probable pyridoxamine 5'-phosphate oxidase	1.5	2.7E-05	1.16	9.7E-03				
PA1911	<i>femR</i>	sigma factor regulator, FemR					1.9	1.5E-02		
PA1912	<i>femI</i>	ECF sigma factor, FemI					1.9	1.5E-03		
PA1914		conserved hypothetical protein	1.8	2.9E-08						
PA1920	<i>nrdD</i>	class III (anaerobic) ribonucleoside-triphosphate reductase subunit, NrdD					1.7	1.0E-02		
PA1921		hypothetical protein					2.2	9.0E-06		
PA1922		probable TonB-dependent receptor					8.4	2.6E-04		
PA1923		hypothetical protein					5.7	4.3E-07		
PA1926		Uncharacterized protein	-1.7	2.8E-08						
PA1927	<i>metE</i>	5-methyltetrahydropteroyltri glutamate-homocysteine S-methyltransferase	2.5	1.6E-09	1.46	3.9E-03				

PA1929		hypothetical protein					1.6	8.8E-03		
PA1930		probable chemotaxis transducer	1.6	6.8E-03			1.7	3.9E-04		
PA1931		probable ferredoxin					1.7	1.7E-03		
PA1932		probable hydroxylase molybdopterin-containing subunit	1.8	2.2E-03			2.5	8.1E-10		
PA1933		probable hydroxylase large subunit	1.5	5.6E-03			1.7	9.2E-06		
PA1937		conserved hypothetical protein					-1.8	3.4E-02		
PA1938		conserved hypothetical protein	1.7	3.4E-02						
PA1943		hypothetical protein					1.6	2.9E-06		
PA1944		hypothetical protein	1.6	4.5E-07	1.15	1.4E-03				
PA1945		probable transcriptional regulator	1.5	3.6E-03						
PA1946	<i>rbsB</i>	binding protein component precursor of ABC ribose transporter	1.6	9.6E-08	1.17	9.6E-04			1.11	5.4E-03
PA1949	<i>rbsR</i>	ribose operon repressor RbsR							1.07	1.6E-02
PA1957		hypothetical protein					1.6	7.1E-04		
PA1960		hypothetical protein					-1.6	1.1E-03		
PA1964		probable ATP-binding component of ABC transporter	-1.9	3.6E-06	-1.28	9.6E-03			-1.17	4.3E-02
PA1965		hypothetical protein					-1.7	3.5E-04		
PA1967		hypothetical protein	1.8	2.6E-05						
PA1969		hypothetical protein			-1.2	1.8E-02				
PA1980	<i>eraR</i>	response regulator EraR					-1.8	1.1E-02		
PA1982	<i>exaA</i>	quinoprotein ethanol dehydrogenase							-1.31	3.8E-02
PA1986	<i>pqqB</i>	pyrroloquinoline quinone biosynthesis protein B					1.5	3.2E-05		
PA1987	<i>pqqC</i>	pyrroloquinoline quinone biosynthesis protein C					-1.6	7.4E-06	-1.21	1.8E-04
PA1994		hypothetical protein					1.7	2.9E-08		
PA1995		hypothetical protein					1.5	4.7E-06		
PA1996	<i>ppiC1</i>	peptidyl-prolyl cis-trans isomerase C1					2.5	1.2E-17		

PA2000	<i>dchB</i>	dehydrocarnitine CoA transferase, DchB	-1.6	1.8E-03						
PA2001	<i>atoB</i>	acetyl-CoA acetyltransferase			-1.17	9.9E-03				
PA2002		conserved hypothetical protein	-1.6	2.6E-04			-1.6	6.4E-06		
PA2003	<i>bdhA</i>	3-hydroxybutyrate dehydrogenase			1.19	3.4E-03				
PA2011	<i>liuE</i>	3-hydroxy-3-methylglutaryl-CoA lyase			-1.12	2.4E-02				
PA2018	<i>mexY</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux transporter MexY	1.8	6.5E-04						
PA2019	<i>mexX</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux membrane fusion protein MexX precursor	1.9	4.9E-07	1.53	5.4E-04				
PA2020	<i>mexZ</i>	MexZ			1.13	4.3E-02				
PA2021		hypothetical protein	2.3	2.1E-03						
PA2022		probable nucleotide sugar dehydrogenase	1.8	4.0E-03						
PA2023	<i>galU</i>	UTP--glucose-1-phosphate uridylyltransferase			-1.13	2.4E-02			-1.12	7.2E-03
PA2024		probable ring-cleaving dioxygenase	1.7	9.7E-03			1.5	1.3E-02		
PA2031		hypothetical protein					-2.4	3.9E-20		
PA2035		probable decarboxylase	1.8	5.0E-06						
PA2036		hypothetical protein	1.9	1.5E-04			-2.1	1.2E-05		
PA2038		hypothetical protein	-2.8	4.7E-03						
PA2039		hypothetical protein	-2.9	5.2E-08						
PA2044		hypothetical protein			-1.22	2.4E-04			-1.11	3.0E-04
PA2046		hypothetical protein					2.0	5.8E-04		
PA2047	<i>cmrA</i>	chloramphenicol resistance activator CmrA	1.9	5.5E-11	1.25	1.9E-03				
PA2048		hypothetical protein	2.6	2.3E-20			2.4	6.9E-26		
PA2052	<i>cynS</i>	cyanate lyase					2.0	1.1E-05		
PA2064	<i>pcoB</i>	copper resistance protein B precursor	1.8	5.7E-03						
PA2065	<i>pcoA</i>	copper resistance protein A precursor	1.8	5.7E-05						

PA2066		hypothetical protein	1.7	7.4E-07						
PA2067		probable hydrolase	1.7	7.2E-08						
PA2068		probable major facilitator superfamily (MFS) transporter	1.8	2.7E-09						
PA2069		probable carbamoyl transferase	1.8	7.6E-09	1.17	2.2E-03			1.15	1.1E-02
PA2071	<i>fusA2</i>	elongation factor G	1.6	1.4E-03						
PA2072		conserved hypothetical protein	1.7	1.1E-04	1.16	1.4E-02			1.13	3.3E-02
PA2081	<i>kynB</i>	kynurenine formamidase, KynB					1.6	1.1E-09		
PA2082	<i>kynR</i>	KynR			1.18	5.2E-03			1.12	8.0E-03
PA2087		hypothetical protein					9.9	2.7E-09		
PA2097		probable flavin-binding monooxygenase	3.5	7.8E-27	1.31	8.2E-03			1.18	3.9E-02
PA2098		probable esterase/deacetylase	3.5	1.2E-05						
PA2099		probable short-chain dehydrogenase	4.4	4.2E-09						
PA2101		conserved hypothetical protein	2.2	4.6E-05						
PA2102		hypothetical protein	1.6	8.8E-05						
PA2103		probable molybdopterin biosynthesis protein MoeB	1.8	3.5E-11						
PA2104		probable cysteine synthase	1.5	4.8E-05						
PA2107		hypothetical protein					1.9	1.6E-02		
PA2108		probable decarboxylase	2.0	4.3E-04						
PA2110		hypothetical protein	-1.6	4.5E-02						
PA2112		conserved hypothetical protein	-1.9	3.0E-03						
PA2113	<i>opdO</i>	pyroglutamate porin OpdO	-2.2	7.0E-05						
PA2114		probable major facilitator superfamily (MFS) transporter	-1.9	8.0E-08						
PA2119		alcohol dehydrogenase (Zn-dependent)	1.9	1.3E-02	1.2	2.9E-02				
PA2122		hypothetical protein					1.9	1.7E-06		
PA2126	<i>cgrC</i>	cupA gene regulator C, CgrC	2.2	1.2E-05			1.7	8.5E-05		
PA2126.1	<i>cgrB</i>	cupA gene regulator B, CgrB	1.8	7.6E-03			2.3	2.4E-07		

PA2127	<i>cgrA</i>	cupA gene regulator A, CgrA	1.8	4.3E-06						
PA2134		hypothetical protein	2.8	2.2E-05			2.6	2.1E-06		
PA2135		probable transporter	1.8	4.2E-02			2.1	8.0E-04		
PA2136		hypothetical protein	2.5	1.6E-02						
PA2137		hypothetical protein	1.9	9.4E-03						
PA2138	<i>ligD</i>	Multifunctional non-homologous end joining protein LigD	1.6	4.7E-02						
PA2139		hypothetical protein	3.8	3.6E-03			3.3	2.3E-04		
PA2140		probable metallothionein	4.2	5.1E-04			2.8	1.2E-03		
PA2141		hypothetical protein	2.3	1.5E-02			2.5	5.0E-04		
PA2142		probable short-chain dehydrogenase	2.3	9.1E-04	1.17	4.0E-02				
PA2143		hypothetical protein	2.5	1.0E-04			5.6	1.8E-20		
PA2144	<i>glgP</i>	glycogen phosphorylase	2.1	3.0E-04	1.21	4.0E-02	2.4	1.4E-07		
PA2145		hypothetical protein	2.7	1.2E-06						
PA2146		conserved hypothetical protein	4.0	6.3E-05						
PA2147	<i>katE</i>	catalase HPII	2.8	6.8E-09			2.0	3.0E-06	1.33	7.7E-03
PA2148		conserved hypothetical protein	2.9	6.5E-07			1.6	7.3E-03		
PA2149		hypothetical protein	2.4	1.1E-03			2.7	3.5E-06		
PA2150		conserved hypothetical protein	2.2	6.3E-04			1.9	8.1E-04		
PA2151		conserved hypothetical protein	1.8	7.7E-03			2.3	1.8E-06		
PA2152		probable trehalose synthase	2.2	3.0E-04	1.19	1.9E-02	2.4	1.2E-06		
PA2153	<i>glgB</i>	1,4-alpha-glucan branching enzyme	2.1	2.1E-03			2.4	8.8E-06		
PA2154		conserved hypothetical protein	2.6	8.9E-04			2.0	2.4E-03		
PA2155		probable phospholipase	3.4	1.5E-06			2.5	9.6E-06		
PA2156		conserved hypothetical protein	3.4	5.0E-04			2.8	2.4E-04		
PA2157		hypothetical protein	3.1	1.0E-06			2.5	5.9E-07		
PA2158		probable alcohol dehydrogenase (Zn-dependent)	3.1	2.1E-06			2.0	4.7E-04		

PA2159		conserved hypothetical protein	2.9	5.7E-06			2.6	8.4E-07		
PA2160		probable glycosyl hydrolase	2.8	1.0E-05			1.9	1.3E-03		
PA2161		hypothetical protein	2.4	1.7E-03			2.4	1.1E-04		
PA2162		probable glycosyl hydrolase	2.5	8.7E-05			2.1	1.1E-04		
PA2163		hypothetical protein	2.6	1.0E-05			2.1	5.5E-05		
PA2164		probable glycosyl hydrolase	2.2	4.8E-05	1.27	2.4E-02	2.0	1.7E-05		
PA2165		probable glycogen synthase	2.4	3.7E-06			2.0	1.5E-05		
PA2167		hypothetical protein	2.0	9.5E-04			1.9	2.0E-04		
PA2168		hypothetical protein	2.2	8.3E-03			2.4	2.4E-04		
PA2169		hypothetical protein	3.7	6.4E-05						
PA2170		hypothetical protein	3.2	7.4E-06			2.7	6.3E-07		
PA2171		hypothetical protein	3.4	6.2E-05	1.46	3.7E-02	2.0	1.1E-02		
PA2172		hypothetical protein	3.2	1.4E-07			2.9	3.2E-09		
PA2173		hypothetical protein	2.8	2.8E-05			3.1	1.4E-08		
PA2174		hypothetical protein	1.7	1.6E-02			1.6	1.8E-02		
PA2175		hypothetical protein					1.8	1.9E-02		
PA2176		hypothetical protein	1.8	8.8E-03			2.2	1.9E-05		
PA2177		probable sensor/response regulator hybrid	1.8	2.5E-04						
PA2178		hypothetical protein					2.5	8.3E-03		
PA2179		hypothetical protein	3.2	4.1E-05			1.9	6.1E-03		
PA2180		hypothetical protein	2.0	1.2E-03			2.3	5.4E-07		
PA2181		hypothetical protein	2.4	4.2E-03						
PA2182		hypothetical protein	1.8	2.2E-03						
PA2183		hypothetical protein	2.3	1.0E-02						
PA2184		conserved hypothetical protein	2.4	1.6E-04			2.4	4.6E-06		
PA2185	<i>katN</i>	non-heme catalase KatN	1.9	6.0E-03			1.8	2.0E-03		
PA2186		hypothetical protein					3.7	4.8E-07		
PA2187		hypothetical protein	2.7	3.5E-04			3.0	1.1E-06		
PA2188		probable alcohol dehydrogenase (Zn-dependent)					1.7	3.2E-02		
PA2189		hypothetical protein	2.9	7.6E-04						

PA2190		conserved hypothetical protein	2.4	4.2E-04			2.4	1.1E-05		
PA2191	<i>exoY</i>	adenylate cyclase ExoY	-3.8	1.2E-17			-2.0	6.6E-07		
PA2192		conserved hypothetical protein	1.9	3.4E-03			1.6	1.1E-02		
PA2194	<i>hcnB</i>	hydrogen cyanide synthase HcnB			1.26	2.7E-02				
PA2198		hypothetical protein					2.0	4.7E-15		
PA2199		probable dehydrogenase			1.11	2.0E-02				
PA2205		hypothetical protein	1.5	2.5E-02						
PA2221		conserved hypothetical protein	1.6	3.3E-02						
PA2222		hypothetical protein	3.8	9.6E-27	1.6	1.7E-04			1.23	1.5E-02
PA2223		hypothetical protein	2.1	1.2E-17	1.52	1.9E-02				
PA2224		hypothetical protein	2.2	1.4E-09						
PA2225		hypothetical protein	2.1	9.7E-06						
PA2226	<i>qsrO</i>	QsrO	2.1	8.1E-10						
PA2227	<i>vqsM</i>	AraC-type transcriptional regulator VqsM	1.8	3.3E-06						
PA2228		hypothetical protein	1.7	9.9E-09						
PA2229		conserved hypothetical protein	1.6	1.3E-03						
PA2231	<i>pslA</i>	PslA	1.9	1.3E-09	1.29	2.2E-03			1.21	3.2E-02
PA2232	<i>pslB</i>	PslB	1.8	8.7E-12	1.34	6.5E-03			1.19	3.2E-02
PA2233	<i>pslC</i>	PslC	1.6	5.4E-09	1.14	4.5E-02				
PA2234	<i>pslD</i>	PslD	1.7	4.9E-18	1.29	5.6E-03				
PA2235	<i>pslE</i>	PslE	1.7	2.6E-09	1.19	4.8E-03				
PA2236	<i>pslF</i>	PslF	1.6	1.4E-07						
PA2237	<i>pslG</i>	PslG	1.5	1.4E-14	1.19	4.1E-03				
PA2238	<i>pslH</i>	PslH	1.7	1.1E-06	1.28	1.8E-03			1.12	4.0E-02
PA2239	<i>pslI</i>	PslI	1.6	7.4E-05	1.13	4.6E-02				
PA2243	<i>pslM</i>	hypothetical protein	1.7	5.1E-03						
PA2244	<i>pslN</i>	hypothetical protein	1.9	8.2E-03			1.7	8.8E-03		
PA2246	<i>bkdR</i>	transcriptional regulator BkdR			1.06	2.1E-02				
PA2253	<i>ansA</i>	L-asparaginase I					1.7	3.6E-06		
PA2258	<i>ptxR</i>	transcriptional regulator PtxR	2.2	1.2E-05						
PA2259	<i>ptxS</i>	transcriptional regulator PtxS	1.8	1.6E-04						

PA2260		hypothetical protein	5.0	8.7E-04			2.4	2.6E-02		
PA2261		probable 2-ketogluconate kinase	1.8	4.7E-02			2.0	6.6E-03		
PA2262		probable 2-ketogluconate transporter	2.0	2.0E-02						
PA2263		probable 2-hydroxyacid dehydrogenase	1.8	1.9E-02			1.6	2.0E-02		
PA2265		gluconate dehydrogenase			1.09	6.6E-03				
PA2269		conserved hypothetical protein	1.6	2.2E-02						
PA2273	<i>soxR</i>	SoxR	2.4	1.5E-09						
PA2275		probable alcohol dehydrogenase (Zn-dependent)	7.0	5.8E-79	2.12	9.8E-07			1.75	9.1E-06
PA2276		probable transcriptional regulator	3.4	2.8E-38	1.27	9.3E-04			1.13	4.3E-03
PA2277	<i>arsR</i>	ArsR protein	2.3	1.9E-06						
PA2295		probable permease of ABC transporter	1.6	2.7E-02			-5.2	1.6E-20		
PA2300	<i>chiC</i>	chitinase	1.7	9.2E-07	1.28	3.0E-02				
PA2302	<i>ambE</i>	AmbE	1.6	4.8E-10	1.13	1.1E-02				
PA2303	<i>ambD</i>	AmbD	1.7	1.2E-07						
PA2304	<i>ambC</i>	AmbC	1.8	3.1E-12	1.12	1.0E-04			1.08	8.6E-04
PA2305	<i>ambB</i>	AmbB	1.6	3.8E-12						
PA2325		hypothetical protein					2.5	2.9E-03		
PA2328		hypothetical protein					6.1	2.7E-31		
PA2337	<i>mtlR</i>	transcriptional regulator MtlR					1.6	9.3E-04		
PA2338		probable binding protein component of ABC maltose/mannitol transporter	-1.8	1.1E-05						
PA2339		probable binding-protein-dependent maltose/mannitol transport protein	-2.1	1.9E-02						
PA2344	<i>mtlZ</i>	fructokinase	-1.8	4.3E-02						
PA2352		probable glycerophosphoryl diester phosphodiesterase	-2.4	5.4E-10			-1.5	8.0E-04		
PA2356	<i>msuD</i>	methanesulfonate sulfonatase MsuD	2.3	6.8E-03			1.8	1.4E-02		

PA2357	<i>msuE</i>	NADH-dependent FMN reductase MsuE	2.3	2.2E-03			2.9	1.9E-07		
PA2358		hypothetical protein	2.9	8.0E-03			2.2	1.8E-02		
PA2361	<i>icmF3</i>	IcmF3	1.5	1.6E-05						
PA2362	<i>dotU3</i>	DotU3	1.9	1.1E-05			-2.0	1.4E-06		
PA2363	<i>hsiJ3</i>	HsiJ3	1.7	1.8E-09						
PA2364	<i>lip3</i>	Lip3	1.6	7.4E-05						
PA2365	<i>hsiB3</i>	HsiB3	1.9	7.4E-09						
PA2366	<i>hsiC3</i>	HsiC3	1.9	1.8E-07						
PA2367	<i>hcp3</i>	Hcp3	1.8	2.2E-06						
PA2368	<i>hsiF3</i>	HsiF3	1.7	3.1E-03			-1.6	2.3E-03		
PA2369	<i>hsiG3</i>	HsiG3	1.9	3.2E-11						
PA2370	<i>hsiH3</i>	HsiH3	2.2	1.9E-06						
PA2371	<i>clpV3</i>	ClpV3	1.7	9.5E-07						
PA2372		hypothetical protein	1.7	1.4E-05						
PA2373	<i>vgrG3</i>	VgrG3	1.7	4.7E-07			1.5	4.9E-07		
PA2374	<i>tseF</i>	TseF	1.7	5.2E-06						
PA2376		probable transcriptional regulator	1.6	1.4E-03						
PA2377		hypothetical protein	1.7	3.1E-02						
PA2378		probable aldehyde dehydrogenase	1.8	2.5E-16	1.2	3.9E-03			1.2	1.0E-02
PA2379		probable oxidoreductase	1.8	1.5E-11	1.17	1.3E-02			1.27	1.5E-02
PA2381		hypothetical protein	2.0	9.8E-05						
PA2382	<i>lldA</i>	L-lactate dehydrogenase			-1.2	3.4E-02			-1.22	3.2E-02
PA2384		hypothetical protein	3.3	3.6E-04						
PA2388	<i>fpvR</i>	FpvR			-1.3	1.2E-02				
PA2390	<i>pvdT</i>	PvdT	-1.6	5.0E-03						
PA2391	<i>opmQ</i>	probable outer membrane protein precursor	-1.7	1.1E-02						
PA2393		putative dipeptidase					1.7	2.9E-02		
PA2397	<i>pvdE</i>	pyoverdine biosynthesis protein PvdE					2.6	6.6E-04		
PA2398	<i>fpvA</i>	ferripyoverdine receptor	1.7	4.8E-04						
PA2411		probable thioesterase	1.8	4.1E-03			1.6	1.3E-02		
PA2412		conserved hypothetical protein	1.7	4.9E-02						

PA2413	<i>pvdH</i>	L-2,4-diaminobutyrate:2-ketoglutarate 4-aminotransferase, PvdH	1.6	3.1E-02			1.6	1.4E-02		
PA2414		L-sorbose dehydrogenase	2.1	5.4E-05			1.5	7.6E-03		
PA2415		hypothetical protein	2.2	6.7E-04						
PA2416	<i>treA</i>	periplasmic trehalase precursor	2.1	5.9E-04			2.2	5.1E-06		
PA2423		hypothetical protein					2.0	6.3E-12		
PA2426	<i>pvdS</i>	sigma factor PvdS					2.1	2.0E-02		
PA2433		hypothetical protein	2.0	9.5E-04			3.7	2.3E-16		
PA2435		probable cation-transporting P-type ATPase					1.7	3.9E-05		
PA2436		hypothetical protein	-2.2	8.6E-10	-1.32	1.1E-02			-1.34	4.5E-03
PA2437		hypothetical protein					2.7	2.9E-07		
PA2439		hypothetical protein					1.9	1.1E-02		
PA2442	<i>gcvT2</i>	glycine cleavage system protein T2			-1.16	9.9E-03				
PA2444	<i>glyA2</i>	serine hydroxymethyltransferase	-1.7	6.4E-03	-1.27	2.6E-03	-1.9	2.3E-04		
PA2445	<i>gcvP2</i>	glycine cleavage system protein P2	-1.6	6.3E-05						
PA2446	<i>gcvH2</i>	glycine cleavage system protein H2			-1.26	4.5E-02	-1.9	4.7E-06		
PA2452		hypothetical protein	2.4	1.4E-03						
PA2453		hypothetical protein	-2.0	4.1E-06			-1.5	2.5E-03		
PA2455		hypothetical protein					-1.6	3.9E-03		
PA2459		hypothetical protein					-1.9	6.2E-04		
PA2464		hypothetical protein					-1.7	2.3E-06		
PA2467	<i>foxR</i>	Anti-sigma factor FoxR	-1.6	1.3E-02			2.1	6.2E-07		
PA2476	<i>dsbG</i>	thiol:disulfide interchange protein DsbG							-1.1	1.1E-02
PA2483		conserved hypothetical protein	1.7	6.2E-12	1.29	4.3E-05			1.24	1.8E-04
PA2485		hypothetical protein	1.7	1.4E-03						
PA2486	<i>ptrC</i>	Pseudomonas type III repressor gene C, PtrC	2.2	1.2E-05			2.9	2.6E-13		
PA2491	<i>mexS</i>	MexS			-1.25	2.0E-03			-1.18	5.9E-03
PA2493	<i>mexE</i>	Resistance-Nodulation-Cell Division (RND)			1.11	1.2E-02				

		multidrug efflux membrane fusion protein MexE precursor								
PA2494	<i>mexF</i>	Resistance-Nodulation- Cell Division (RND) multidrug efflux transporter MexF					1.7	2.7E-02		
PA2504		hypothetical protein	1.8	2.2E-03			1.7	2.9E-04		
PA2507	<i>cata</i>	catechol 1,2-dioxygenase			-1.45	2.0E-03				
PA2508	<i>catC</i>	muconolactone delta- isomerase					1.8	1.5E-05		
PA2511	<i>antR</i>	AntR					1.7	2.7E-03		
PA2512	<i>antA</i>	anthranilate dioxygenase large subunit			-1.21	5.2E-03				
PA2513	<i>antB</i>	anthranilate dioxygenase small subunit			-1.63	4.7E-03				
PA2514	<i>antC</i>	anthranilate dioxygenase reductase			-1.35	3.8E-03				
PA2523	<i>czcR</i>	CzcR	2.3	4.9E-08						
PA2524	<i>czcS</i>	CzcS	2.2	1.2E-04						
PA2525	<i>opmB</i>	OpmB							1.67	3.0E-02
PA2528	<i>muxA</i>	MuxA			-1.11	2.3E-03			-1.1	6.5E-03
PA2529		hypothetical protein							-1.15	4.6E-02
PA2532	<i>tpx</i>	thiol peroxidase			-1.16	2.4E-03				
PA2535		probable oxidoreductase			-1.07	3.6E-02			-1.09	3.4E-02
PA2544		hypothetical protein			1.14	2.0E-02				
PA2545	<i>xthA</i>	exodeoxyribonuclease III			-1.15	8.2E-03			-1.13	1.3E-02
PA2546		probable ring-cleaving dioxygenase	1.6	2.5E-02	1.49	5.2E-03				
PA2552		probable acyl-CoA dehydrogenase			-1.08	3.1E-03				
PA2553		probable acyl-CoA thiolase			-1.31	1.3E-02	-1.5	6.2E-07		
PA2554		probable short-chain dehydrogenase	-1.7	2.5E-05					-1.05	4.1E-02
PA2555		probable AMP-binding enzyme			-1.14	3.8E-02				
PA2560		hypothetical protein	1.9	1.0E-21			1.7	5.5E-20		
PA2562		hypothetical protein	2.1	3.8E-06	1.36	4.8E-02				
PA2564		hypothetical protein	3.0	4.3E-08						
PA2565		hypothetical protein	2.7	9.5E-06						

PA2566		conserved hypothetical protein	3.2	4.1E-09						
PA2569		hypothetical protein	2.2	2.2E-07						
PA2570	<i>lecA</i>	LecA	7.3	2.4E-08	2.41	3.4E-03				
PA2571		probable two-component sensor	2.0	3.1E-06						
PA2572		probable two-component response regulator	1.9	8.1E-06	1.29	1.4E-02				
PA2573		probable chemotaxis transducer	2.0	3.0E-06	1.25	1.1E-03				
PA2574	<i>alkB1</i>	alkane-1-monooxygenase	1.6	1.5E-03						
PA2575		hypothetical protein					1.5	1.1E-13		
PA2576		hypothetical protein					-1.5	3.6E-02		
PA2577		probable transcriptional regulator	1.7	3.4E-05						
PA2581		hypothetical protein			1.28	1.1E-03				
PA2584	<i>pgsA</i>	CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyltransferase			1.23	1.2E-02				
PA2592		probable periplasmic spermidine/putrescine-binding protein			1.08	1.3E-02				
PA2594		conserved hypothetical protein			-1.06	6.7E-03				
PA2596		conserved hypothetical protein					-2.3	6.5E-03		
PA2612	<i>serS</i>	seryl-tRNA synthetase			-1.11	1.0E-02				
PA2615	<i>ftsK</i>	cell division protein FtsK			-1.05	2.5E-02				
PA2617	<i>aat</i>	leucyl/phenylalanyl-tRNA-protein transferase			1.09	4.4E-02				
PA2618		hypothetical protein	1.6	1.5E-04						
PA2620	<i>clpA</i>	ATP-binding protease component ClpA	1.6	4.8E-06	1.16	1.1E-02				
PA2622	<i>cspD</i>	cold-shock protein CspD	1.8	1.5E-05	1.25	6.0E-03				
PA2623	<i>icd</i>	isocitrate dehydrogenase			1.12	3.6E-02				
PA2626	<i>trmU</i>	tRNA methyltransferase							-1.05	2.4E-02
PA2629	<i>purB</i>	adenylosuccinate lyase	-1.7	4.8E-07	-1.18	2.2E-03			-1.1	1.7E-02
PA2630		conserved hypothetical protein	-2.1	1.1E-06			-1.5	1.4E-03		
PA2634	<i>aceA</i>	isocitrate lyase AceA			-1.14	3.1E-03				

PA2639	<i>nuoD</i>	NADH dehydrogenase I chain C,D			1.15	9.0E-05			1.08	1.7E-03
PA2642	<i>nuoG</i>	NADH dehydrogenase I chain G			1.16	3.3E-03				
PA2647	<i>nuoL</i>	NADH dehydrogenase I chain L			1.22	2.2E-04			1.13	6.4E-03
PA2653		probable transporter	-1.8	7.6E-04						
PA2660		hypothetical protein			-1.1	1.3E-03			-1.06	7.6E-03
PA2663	<i>ppyR</i>	psl and pyoverdine operon regulator, PpyR					2.1	1.5E-04		
PA2664	<i>fhp</i>	flavoheomoprotein	1.7	1.1E-02					-1.11	4.9E-02
PA2665	<i>fhpR</i>	Transcriptional activator of P. aeruginosa flavohemoglobin, FhpR							1.07	1.7E-02
PA2682		conserved hypothetical protein	-1.8	3.8E-04	-1.79	3.9E-04			-1.28	2.8E-02
PA2696		probable transcriptional regulator	1.5	4.5E-03						
PA2697		hypothetical protein	1.9	5.2E-03						
PA2698		probable hydrolase			1.23	2.6E-04			1.19	3.2E-03
PA2699		hypothetical protein	1.7	2.5E-05						
PA2700	<i>opdB</i>	proline porin OpdB					1.7	2.1E-05		
PA2706		hypothetical protein					1.5	1.0E-07		
PA2708		hypothetical protein					1.6	3.1E-03		
PA2709	<i>cysK</i>	cysteine synthase A			-1.2	3.9E-03			-1.13	3.6E-02
PA2712		hypothetical protein					-1.7	3.1E-02		
PA2713		conserved hypothetical protein					2.1	1.4E-16		
PA2715		probable ferredoxin					2.1	1.9E-03		
PA2719		hypothetical protein					1.7	6.3E-10		
PA2721		hypothetical protein			-1.13	4.7E-02				
PA2725		probable chaperone			1.19	1.1E-02				
PA2730		hypothetical protein			1.04	4.2E-02			1.05	1.9E-02
PA2734		hypothetical protein			1.11	5.0E-02				
PA2737		conserved hypothetical protein					1.5	4.3E-30		
PA2743	<i>infC</i>	translation initiation factor IF-3			1.09	3.3E-02				
PA2744	<i>thrS</i>	threonyl-tRNA synthetase			-1.06	4.6E-02				
PA2746		hypothetical protein	2.9	3.6E-09			2.0	5.6E-06		

PA2747		hypothetical protein					1.6	2.2E-03		
PA2753		hypothetical protein	2.4	4.4E-03						
PA2754		conserved hypothetical protein	1.9	1.3E-04						
PA2755	<i>eco</i>	ecotin precursor			1.26	9.7E-05			1.17	1.7E-03
PA2756		hypothetical protein					-1.8	3.9E-12		
PA2757		hypothetical protein					-1.8	3.2E-02		
PA2759		hypothetical protein	3.3	1.4E-19						
PA2760	<i>oprQ</i>	OprQ	-1.6	3.0E-03						
PA2761		hypothetical protein	-3.0	6.1E-11	-1.4	1.8E-03			-1.31	7.1E-04
PA2763		hypothetical protein					-2.3	1.7E-05		
PA2770		hypothetical protein			1.13	4.1E-04			1.1	1.4E-03
PA2771		diguanylate cyclase with a self-blocked I-site, Dcsbis	1.8	3.8E-09						
PA2776	<i>pauB3</i>	FAD-dependent oxidoreductase			1.42	6.9E-03				
PA2777		conserved hypothetical protein	1.6	4.6E-03						
PA2778		hypothetical protein			1.18	4.0E-02				
PA2779		hypothetical protein	1.5	3.3E-03						
PA2781		hypothetical protein	1.6	4.0E-04						
PA2782	<i>bamI</i>	biofilm-associated metzincin Inhibitor, BamI	-1.8	2.8E-04						
PA2783	<i>mep72</i>	Mep72	-2.5	9.2E-05			-1.8	5.2E-03		
PA2788		probable chemotaxis transducer	1.7	6.3E-03						
PA2790		hypothetical protein	1.6	4.9E-04						
PA2793		hypothetical protein			1.25	6.4E-03				
PA2797		hypothetical protein			1.1	4.3E-03			1.08	2.9E-03
PA2799		hypothetical protein	1.7	1.2E-04						
PA2800	<i>vacJ</i>	VacJ			-1.41	1.1E-02				
PA2816		hypothetical protein					2.4	1.4E-12		
PA2819		hypothetical protein	2.1	1.8E-02						
PA2823		conserved hypothetical protein			-1.34	6.3E-04				
PA2826		probable glutathione peroxidase			1.06	9.1E-03			1.05	3.7E-03
PA2828		probable aminotransferase			-1.24	1.8E-03			-1.11	2.0E-02
PA2829		hypothetical protein	-2.2	2.8E-04						

PA2830	<i>htpX</i>	heat shock protein HtpX			1.18	1.3E-02				
PA2840		probable ATP-dependent RNA helicase	-2.0	1.7E-08						
PA2843		probable aldolase			-1.08	1.3E-02			-1.08	2.1E-02
PA2846		probable transcriptional regulator	1.6	7.3E-03						
PA2848		probable transcriptional regulator					1.6	1.3E-02		
PA2849	<i>ohrR</i>	OhrR	1.6	2.2E-05	1.11	2.8E-02				
PA2850	<i>ohr</i>	organic hydroperoxide resistance protein			1.36	2.0E-03				
PA2851	<i>efp</i>	translation elongation factor P	-1.6	2.4E-05	-1.16	3.2E-03			-1.11	2.2E-02
PA2853	<i>oprI</i>	Outer membrane lipoprotein OprI precursor			1.34	2.8E-02				
PA2857		probable ATP-binding component of ABC transporter			1.15	5.8E-04			1.12	7.9E-03
PA2859	<i>greB</i>	transcription elongation factor GreB					-1.6	7.0E-06		
PA2864		conserved hypothetical protein	1.5	1.1E-03						
PA2869		hypothetical protein			2.04	9.7E-03	2.3	2.6E-15		
PA2870		diguanylate cyclase					1.7	1.5E-06		
PA2873	<i>tgpA</i>	transglutaminase protein A, TgpA	-1.9	2.8E-07						
PA2874		hypothetical protein	-2.2	1.5E-05						
PA2876	<i>pyrF</i>	orotidine 5'-phosphate decarboxylase			-1.19	2.3E-02				
PA2878		hypothetical protein	2.7	6.6E-03						
PA2882		probable two-component sensor					2.3	5.0E-03		
PA2885	<i>atuR</i>	putative repressor of atu genes			-1.17	2.7E-02				
PA2886	<i>atuA</i>	expressed protein with apparent function in citronellol catabolism	1.8	6.7E-09						
PA2887	<i>atuB</i>	putative dehydrogenase involved in catabolism of citronellol	1.7	7.3E-04						
PA2888	<i>atuC</i>	geranyl-CoA carboxylase, beta-subunit	1.6	3.0E-04						

PA2889	<i>atvR</i>	atypical virulence-related response regulator AtvR	1.6	7.7E-04						
PA2895	<i>sbrR</i>	SbrR					1.5	2.2E-05		
PA2896	<i>sbrI</i>	SbrI					1.5	1.6E-06		
PA2900		probable outer membrane protein precursor			-1.1	1.1E-02				
PA2901		hypothetical protein	-1.6	1.1E-04						
PA2902		hypothetical protein			-1.19	8.7E-04			-1.16	2.9E-03
PA2903	<i>cobJ</i>	precorrin-3 methylase CobJ	-1.5	8.2E-03	-1.17	4.8E-02				
PA2904	<i>cobI</i>	precorrin-2 methyltransferase CobI	-1.8	3.9E-08			-1.6	3.3E-06		
PA2905	<i>cobH</i>	precorrin isomerase CobH	-1.6	2.1E-03						
PA2907	<i>cobL</i>	precorrin-6y-dependent methyltransferase CobL	-1.5	3.2E-03						
PA2908	<i>cbiD</i>	cobalamin biosynthetic protein CbiD	-1.5	8.1E-03						
PA2911		probable TonB-dependent receptor	-2.4	2.8E-19						
PA2912		probable ATP-binding component of ABC transporter	-2.2	1.9E-05						
PA2913		hypothetical protein	-2.1	6.8E-04						
PA2914		probable permease of ABC transporter	-2.3	3.5E-03						
PA2917		probable transcriptional regulator					1.7	1.0E-06		
PA2918		probable short-chain dehydrogenase			-1.24	7.5E-04	1.5	8.4E-04	-1.14	1.9E-03
PA2920		probable chemotaxis transducer	1.5	9.4E-03						
PA2928		hypothetical protein	2.9	7.9E-19						
PA2929		hypothetical protein	4.5	6.2E-45						
PA2931	<i>cifR</i>	CifR					-1.6	1.9E-03		
PA2932	<i>morB</i>	morphinone reductase	2.0	2.8E-02						
PA2937		hypothetical protein	2.2	5.2E-04			2.1	4.7E-05		
PA2938		probable transporter	1.8	1.3E-04						
PA2939		probable aminopeptidase	2.3	3.7E-24	1.59	1.5E-03			1.44	1.2E-02
PA2944	<i>cobN</i>	cobalamin biosynthetic protein CobN			-1.15	2.9E-02			-1.13	2.4E-02
PA2948	<i>cobM</i>	precorrin-3 methylase	-1.6	1.5E-05						

PA2949		esterase			-1.1	4.9E-02				
PA2950	<i>pfm</i>	Pfm			-1.1	1.4E-02				
PA2952	<i>etfB</i>	electron transfer flavoprotein beta-subunit			1.07	5.2E-03			1.09	1.0E-03
PA2953		electron transfer flavoprotein-ubiquinone oxidoreductase							1.07	4.4E-03
PA2958		hypothetical protein	1.5	6.1E-05			1.5	6.0E-07		
PA2962	<i>tmk</i>	thymidylate kinase			-1.11	9.8E-03				
PA2965	<i>fabF1</i>	beta-ketoacyl-acyl carrier protein synthase II			-1.16	1.9E-02				
PA2967	<i>fabG</i>	3-oxoacyl-[acyl-carrier- protein] reductase							1.07	1.0E-02
PA2968	<i>fabD</i>	malonyl-CoA-[acyl- carrier-protein] transacylase			-1.17	1.7E-02				
PA2973		probable peptidase	-1.6	9.1E-11	-1.18	9.7E-03			-1.17	9.9E-03
PA2974		probable hydrolase	-1.6	2.0E-06						
PA2975	<i>rluC</i>	ribosomal large subunit pseudouridine synthase C			-1.17	4.4E-03			-1.13	1.3E-02
PA2977	<i>murB</i>	UDP-N- acetylpyruvoylglucosamin e reductase	-1.6	9.3E-05						
PA2978	<i>ptpA</i>	phosphotyrosine protein phosphatase	-1.6	2.4E-04			-1.6	1.0E-05		
PA2981	<i>lpxK</i>	tetraacyldisaccharide 4*- kinase	-1.7	1.6E-04						
PA2982		conserved hypothetical protein	-2.0	1.3E-09						
PA2983		probable tolQ-type transport protein	-2.2	6.1E-10	-1.27	5.9E-04	-1.6	4.8E-06	-1.2	6.7E-03
PA2985		hypothetical protein					1.8	7.9E-15		
PA2986	<i>lolC</i>	lipoprotein localization protein LolC					-2.5	7.4E-17		
PA2988	<i>lolE</i>	lipoprotein localization protein LolE	-1.6	2.4E-06						
PA2989		hypothetical protein			-1.13	2.6E-02				
PA2994	<i>nqrF</i>	Na ⁺ -translocating NADH:quinone oxidoreductase, subunit Nqr6			-1.14	1.5E-02	-1.5	1.2E-07		
PA2996	<i>nqrD</i>	Na ⁺ -translocating NADH:uniquinone					-1.8	4.3E-13		

		oxidoreductase subunit Nqr4								
PA2997	<i>nqrC</i>	Na+-translocating NADH:ubiquinone oxidoreductase subunit Nrq3			-1.27	4.5E-03				
PA2998	<i>nqrB</i>	Na+-translocating NADH:ubiquinone oxidoreductase subunit Nrq2	-1.5	9.1E-08	-1.2	4.3E-03				
PA2999	<i>nqrA</i>	Na+-translocating NADH:ubiquinone oxidoreductase subunit Nrq1			-1.18	1.3E-02				
PA3000	<i>aroP1</i>	aromatic amino acid transport protein AroP1	-1.8	2.2E-05						
PA3001		probable glyceraldehyde- 3-phosphate dehydrogenase			-1.09	2.6E-02				
PA3003		hypothetical protein			-1.21	1.1E-02				
PA3004		5-methylthioadenosine phosphorylase MtnP			-1.16	4.2E-02				
PA3005	<i>nagZ</i>	beta-N-acetyl-D- glucosaminidase			-1.14	3.6E-02				
PA3006	<i>psrA</i>	transcriptional regulator PsrA			1.09	3.4E-02			1.14	1.6E-02
PA3007	<i>lexA</i>	repressor protein LexA	1.8	5.6E-23	1.1	6.1E-03				
PA3008		hypothetical protein	1.5	3.7E-07						
PA3013	<i>faoB</i>	fatty-acid oxidation complex beta-subunit			-1.06	2.1E-02				
PA3018		hypothetical protein					-1.6	1.8E-03		
PA3019		probable ATP-binding component of ABC transporter			-1.11	4.2E-02				
PA3022		hypothetical protein			-1.21	7.9E-03			-1.17	3.0E-02
PA3028	<i>moeA</i> 2	molybdenum cofactor biosynthesis protein A2			1.17	1.2E-02				
PA3032	<i>snr1</i>	cytochrome c Snr1	2.3	4.3E-08	1.41	1.9E-02	2.0	2.3E-08		
PA3033		hypothetical protein					-1.9	2.0E-04		
PA3034		probable transcriptional regulator			-1.1	1.8E-02				
PA3038	<i>opdQ</i>	OpdQ							-1.05	4.0E-02
PA3039		probable transporter	1.6	1.5E-03						

PA3040		conserved hypothetical protein	1.5	3.3E-03	1.37	2.3E-02				
PA3041		hypothetical protein	1.6	5.3E-04			1.8	1.0E-07	1.49	1.6E-02
PA3042		hypothetical protein					2.0	1.5E-11		
PA3063	<i>pelB</i>	PelB	1.7	2.3E-02						
PA3066		hypothetical protein					-1.6	6.7E-03		
PA3069		hypothetical protein					1.6	1.5E-07		
PA3071		hypothetical protein	-1.9	5.2E-07						
PA3073		hypothetical protein	-1.6	9.5E-03						
PA3076		hypothetical protein			-1.3	1.2E-02			-1.21	9.0E-03
PA3078	<i>cprS</i>	CprS	-1.5	1.3E-03						
PA3079		hypothetical protein	-1.7	4.2E-07	1.2	1.4E-02				
PA3080		hypothetical protein	-1.9	1.5E-07	-1.19	1.6E-02				
PA3081		conserved hypothetical protein	-2.0	3.8E-08	-1.11	3.0E-02				
PA3082	<i>gbt</i>	glycine betaine transmethylase	-2.4	6.2E-11	-1.29	4.1E-03				
PA3083	<i>pepN</i>	aminopeptidase N			-1.14	2.1E-04			-1.1	5.2E-03
PA3091		hypothetical protein	-1.6	1.1E-12	-1.2	4.8E-03			-1.16	1.3E-02
PA3093		hypothetical protein			1.31	5.6E-05			1.17	1.0E-03
PA3095	<i>xcpZ</i>	general secretion pathway protein M			1.16	8.8E-03				
PA3097	<i>xcpX</i>	general secretion pathway protein K			1.07	3.0E-02				
PA3102	<i>xcpS</i>	general secretion pathway protein F			1.1	1.1E-02			1.09	1.8E-02
PA3103	<i>xcpR</i>	general secretion pathway protein E			1.13	5.7E-03				
PA3104	<i>xcpP</i>	secretion protein XcpP					2.0	7.0E-18		
PA3112	<i>accD</i>	acetyl-CoA carboxylase beta subunit			-1.09	3.0E-02	-1.6	2.5E-10		
PA3114	<i>truA</i>	tRNA-pseudouridine synthase I			-1.18	5.1E-03				
PA3116		probable aspartate-semialdehyde dehydrogenase					2.7	1.4E-12		
PA3120	<i>leuD</i>	3-isopropylmalate dehydratase small subunit			-1.19	2.1E-02				
PA3122		probable transcriptional regulator			1.17	3.0E-03			1.11	7.9E-03

PA3123		conserved hypothetical protein					1.6	1.8E-07		
PA3138	<i>uvrB</i>	excinuclease ABC subunit B			-1.21	1.3E-03			-1.09	2.8E-02
PA3139		probable amino acid aminotransferase			-1.19	1.1E-02				
PA3141	<i>wbpM</i>	nucleotide sugar epimerase/dehydratase WbpM			1.25	8.3E-03			1.16	1.5E-02
PA3142		integrase	1.8	1.3E-14						
PA3143		transposase	1.6	8.8E-13						
PA3144		transposase with Helix-turn-helix Hin domain	1.7	2.7E-11						
PA3145	<i>wbpL</i>	glycosyltransferase WbpL			1.17	5.7E-03				
PA3146	<i>wbpK</i>	probable NAD-dependent epimerase/dehydratase WbpK							1.08	4.6E-02
PA3147	<i>wbpJ</i>	probable glycosyl transferase WbpJ			1.14	1.8E-03	-1.5	1.0E-04	1.14	3.4E-02
PA3148	<i>wbpI</i>	UDP-N-acetylglucosamine 2-epimerase WbpI			1.23	7.0E-04			1.2	6.3E-05
PA3150	<i>wbpG</i>	LPS biosynthesis protein WbpG			1.13	2.0E-02			1.15	5.8E-03
PA3151	<i>hisF2</i>	imidazoleglycerol-phosphate synthase, cyclase subunit			1.13	1.1E-02	-1.6	6.9E-05		
PA3152	<i>hisH2</i>	glutamine amidotransferase			1.08	1.8E-02				
PA3155	<i>wbpE</i>	UDP-2-acetamido-2-dideoxy-d-ribo-hex-3-uluronic acid transaminase, wbpE	1.5	4.8E-11						
PA3156	<i>wbpD</i>	UDP-2-acetamido-3-amino-2,3-dideoxy-d-glucuronic acid N-acetyltransferase, WbpD			1.18	4.3E-04				
PA3158	<i>wbpB</i>	UDP-2-acetamido-2-deoxy-d-glucuronic acid 3-dehydrogenase, WbpB			1.14	5.7E-04			1.1	1.6E-02
PA3159	<i>wbpA</i>	UDP-N-acetyl-d-glucosamine 6-Dehydrogenase			1.21	6.2E-05			1.13	4.8E-03
PA3160	<i>wzz</i>	O-antigen chain length regulator			1.27	2.3E-02				

PA3161	<i>himD</i>	integration host factor beta subunit					-2.2	2.0E-19	1.59	4.6E-02
PA3162	<i>rpsA</i>	30S ribosomal protein S1					-1.5	3.1E-06		
PA3167	<i>serC</i>	3-phosphoserine aminotransferase			-1.09	2.5E-02				
PA3169		5-methylthioribose-1-phosphate isomerase MtnA			-1.07	1.5E-03			-1.06	9.3E-03
PA3174	<i>hutR</i>	HutR	-1.7	1.8E-02						
PA3177		hypothetical protein	1.7	6.2E-05						
PA3178		hypothetical protein					-1.8	5.6E-08		
PA3179		conserved hypothetical protein			1.2	3.2E-05			1.08	1.0E-02
PA3181		2-keto-3-deoxy-6-phosphogluconate aldolase			-1.22	1.4E-02				
PA3182	<i>pgl</i>	6-phosphogluconolactonase			-1.17	1.7E-02				
PA3187		probable ATP-binding component of ABC transporter	-1.6	1.2E-02						
PA3188		probable permease of ABC sugar transporter	-1.7	7.4E-04			-1.7	3.8E-04		
PA3189		probable permease of ABC sugar transporter	-1.6	1.9E-02			-2.2	5.3E-07		
PA3190		probable binding protein component of ABC sugar transporter					-1.8	1.0E-07		
PA3202		conserved hypothetical protein			-1.36	1.4E-02				
PA3205		hypothetical protein	1.6	4.2E-07	1.17	3.9E-02				
PA3209		conserved hypothetical protein	-1.8	3.9E-02			-2.0	1.4E-02		
PA3210	<i>trkH</i>	potassium uptake protein TrkH	-1.7	8.3E-05						
PA3213		hypothetical protein			-1.14	7.4E-04			-1.1	7.8E-03
PA3214		hypothetical protein							-1.07	4.4E-02
PA3216		hypothetical protein					1.9	8.8E-14		
PA3220		probable transcriptional regulator					1.5	2.2E-04		
PA3221	<i>csaA</i>	CsaA protein	-2.0	6.9E-08	-1.21	1.3E-02	-1.7	3.7E-06	-1.14	2.9E-02
PA3222		hypothetical protein	-1.6	1.7E-02			-1.9	1.8E-04		
PA3224		hypothetical protein			-1.32	1.3E-04			-1.13	6.1E-03
PA3225		transcriptional regulator			1.14	1.6E-02				

PA3227	<i>ppiA</i>	peptidyl-prolyl cis-trans isomerase A			1.07	5.2E-03	1.6	3.7E-13	1.06	9.8E-04
PA3228		probable ATP-binding/permease fusion ABC transporter			1.15	3.7E-04			1.08	3.6E-02
PA3235		conserved hypothetical protein			1.1	4.8E-02	-2.1	8.1E-18		
PA3240		conserved hypothetical protein	1.5	5.1E-05	1.14	1.4E-03				
PA3243	<i>minC</i>	cell division inhibitor MinC							-1.05	1.9E-02
PA3245	<i>minE</i>	cell division topological specificity factor MinE					-1.7	3.9E-20		
PA3252		probable permease of ABC transporter					1.8	1.7E-05		
PA3256		probable oxidoreductase					-1.7	6.0E-13		
PA3261		hypothetical protein	1.6	2.8E-13			1.8	6.4E-33		
PA3262		probable peptidyl-prolyl cis-trans isomerase, FkbP-type							1.15	1.9E-02
PA3263		conserved hypothetical protein					-1.8	3.2E-10		
PA3265		probable transporter					-2.2	1.6E-05		
PA3266	<i>capB</i>	cold acclimation protein B	-1.5	1.1E-04	-1.67	3.2E-02				
PA3268		probable TonB-dependent receptor	-2.6	5.1E-08						
PA3270		hypothetical protein			1.2	4.3E-03			1.12	3.3E-02
PA3271		probable two-component sensor			1.09	1.9E-02				
PA3276		hypothetical protein	-1.7	3.4E-04			-1.5	9.3E-04		
PA3277		probable short-chain dehydrogenase					8.5	1.0E-45		
PA3278		hypothetical protein	-2.9	1.5E-08			-2.4	2.2E-06		
PA3283		conserved hypothetical protein	1.6	4.4E-03			-1.6	2.4E-03		
PA3286		hypothetical protein			-1.15	1.4E-03			-1.06	1.7E-02
PA3291	<i>tliI</i>	TliI					-1.7	7.0E-04		
PA3293		hypothetical protein	1.6	3.8E-02						
PA3295		probable HIT family protein			-1.35	1.3E-02				
PA3300	<i>fadD2</i>	long-chain-fatty-acid--CoA ligase			1.09	1.9E-02				

PA3307		hypothetical protein	1.6	8.7E-04						
PA3308	<i>hepA</i>	RNA helicase HepA	-1.7	1.5E-09	-1.22	2.9E-03			-1.16	8.8E-03
PA3310		conserved hypothetical protein	-1.5	2.3E-03						
PA3312		probable 3-hydroxyisobutyrate dehydrogenase					-1.7	8.6E-04		
PA3313		hypothetical protein			-1.15	3.0E-03				
PA3314		probable ATP-binding component of ABC transporter			1.31	2.6E-03			1.18	1.8E-02
PA3315		probable permease of ABC transporter					-1.8	7.1E-04		
PA3317		hypothetical protein			1.1	4.0E-02				
PA3319	<i>plcN</i>	non-hemolytic phospholipase C precursor	1.6	1.6E-03						
PA3324		probable short-chain dehydrogenase	1.5	4.0E-02						
PA3325		conserved hypothetical protein	1.6	2.9E-02						
PA3326	<i>clpP2</i>	ClpP2			1.38	1.3E-04			1.24	2.2E-03
PA3327		probable non-ribosomal peptide synthetase	1.6	9.1E-06						
PA3328		probable FAD-dependent monooxygenase	1.5	6.3E-05	1.15	2.6E-03			1.06	9.3E-04
PA3329		hypothetical protein			1.23	3.6E-02				
PA3330		probable short chain dehydrogenase			1.37	1.6E-02			1.23	1.9E-02
PA3332		conserved hypothetical protein			1.42	5.7E-03	-1.7	4.5E-09	1.28	3.7E-03
PA3333	<i>fabH2</i>	3-oxoacyl-[acyl-carrier-protein] synthase III			1.1	5.7E-03				
PA3334	<i>acp3</i>	Acp3					-3.3	6.5E-51		
PA3335		hypothetical protein			1.29	4.4E-02	-2.0	8.5E-18		
PA3336		probable major facilitator superfamily (MFS) transporter			1.37	3.2E-03	-1.8	6.9E-12		
PA3340		hypothetical protein	1.8	9.7E-08						
PA3341		probable transcriptional regulator			1.23	4.2E-03			1.13	2.0E-03

PA3346	<i>hsbR</i>	HptB-dependent secretion and biofilm regulator HsbR	1.8	3.6E-09	1.22	1.2E-02				
PA3347	<i>hsbA</i>	HptB-dependent secretion and biofilm anti anti-sigma factor HsbA	1.7	4.9E-05						
PA3348		probable chemotaxis protein methyltransferase	1.5	5.3E-07						
PA3349		probable chemotaxis protein	1.6	3.3E-06	1.24	1.4E-02				
PA3350		hypothetical protein	1.6	3.1E-15	1.17	4.2E-03				
PA3351	<i>flgM</i>	FlgM	1.5	1.2E-07						
PA3352		hypothetical protein	1.5	2.7E-14						
PA3353		hypothetical protein			1.06	2.5E-02				
PA3354		hypothetical protein	1.6	2.5E-04						
PA3360		probable secretion protein	1.8	1.6E-02						
PA3361	<i>lecB</i>	fucose-binding lectin PA-IIL	2.9	1.2E-07						
PA3366	<i>amiE</i>	aliphatic amidase			-1.19	2.8E-02				
PA3367		hypothetical protein					-1.7	1.2E-02		
PA3369		hypothetical protein					1.7	2.9E-03		
PA3371		hypothetical protein					1.9	2.1E-04		
PA3372		conserved hypothetical protein					2.1	3.1E-08		
PA3374		conserved hypothetical protein					3.1	2.9E-08		
PA3384	<i>phnC</i>	ATP-binding component of ABC phosphonate transporter	2.0	6.5E-03						
PA3386		conserved hypothetical protein					-1.8	2.6E-04		
PA3392	<i>nosZ</i>	nitrous-oxide reductase precursor	1.7	3.5E-02						
PA3397	<i>fprA</i>	FprA			-1.13	7.8E-03			-1.09	3.2E-02
PA3415		probable dihydrolipoamide acetyltransferase	2.0	1.6E-03						
PA3416		probable pyruvate dehydrogenase E1 component, beta chain	2.0	1.7E-03						
PA3417		probable pyruvate dehydrogenase E1 component, alpha subunit	2.1	1.2E-03						

PA3418	<i>ldh</i>	leucine dehydrogenase	1.9	1.7E-04			1.6	2.9E-03		
PA3430		probable aldolase					1.6	3.2E-06		
PA3436		hypothetical protein	1.7	1.0E-02			2.1	2.0E-05		
PA3438	<i>folE1</i>	GTP cyclohydrolase I precursor			-1.31	2.9E-04			-1.2	4.3E-03
PA3440		conserved hypothetical protein			-1.29	5.0E-02	1.9	8.0E-15		
PA3441		probable molybdopterin-binding protein					-2.0	2.6E-02		
PA3451		hypothetical protein	2.2	1.8E-06						
PA3452	<i>mqaA</i>	malate:quinone oxidoreductase			1.11	9.6E-03				
PA3453		conserved hypothetical protein			-1.09	3.8E-02				
PA3454		probable acyl-CoA thiolase			-1.15	2.4E-02			-1.1	4.2E-02
PA3456		hypothetical protein							-1.15	1.4E-02
PA3458		probable transcriptional regulator					-1.5	6.2E-03		
PA3459		probable glutamine amidotransferase	1.6	3.2E-03			2.1	2.2E-08		
PA3460		probable acetyltransferase	1.6	7.4E-04			1.6	3.7E-05		
PA3461		conserved hypothetical protein					2.0	1.6E-08		
PA3466		probable ATP-dependent RNA helicase			-1.17	4.2E-03			-1.14	2.2E-04
PA3468		conserved hypothetical protein	-1.6	5.2E-06						
PA3471		probable malic enzyme							1.04	1.9E-02
PA3477	<i>rhlR</i>	transcriptional regulator RhlR	1.8	1.9E-05	1.17	1.9E-02				
PA3478	<i>rhlB</i>	rhamnosyltransferase chain B	2.4	3.0E-04						
PA3479	<i>rhlA</i>	rhamnosyltransferase chain A	2.6	1.1E-04						
PA3480		probable deoxycytidine triphosphate deaminase							1.05	3.2E-02
PA3482	<i>metG</i>	methionyl-tRNA synthetase			-1.1	1.6E-02			-1.08	3.3E-02
PA3486	<i>vgrG4b</i>	VgrG4b	1.7	6.9E-04						
PA3496		hypothetical protein	1.5	7.9E-03			1.9	3.2E-07		

PA3498		probable oxidoreductase	3.3	1.9E-25						
PA3499		hypothetical protein	1.8	2.4E-02						
PA3512		probable permease of ABC transporter					1.6	2.7E-02		
PA3519		hypothetical protein	1.8	1.2E-04						
PA3520		hypothetical protein	2.6	6.8E-11						
PA3522	<i>mexQ</i>	MexQ					-1.6	1.8E-02		
PA3525	<i>argG</i>	argininosuccinate synthase			-1.11	3.9E-02				
PA3526	<i>motY</i>	MotY	1.6	2.3E-07						
PA3529		alkylhydroperoxide reductase C			-1.2	4.3E-02				
PA3538		probable ATP-binding component of ABC transporter			-1.22	5.4E-03				
PA3540	<i>algD</i>	GDP-mannose 6-dehydrogenase AlgD	7.1	2.9E-09						
PA3541	<i>alg8</i>	alginate biosynthesis protein Alg8	2.8	4.7E-05			1.6	3.8E-02		
PA3542	<i>alg44</i>	alginate biosynthesis protein Alg44	2.1	2.7E-02						
PA3543	<i>algK</i>	alginate biosynthetic protein AlgK precursor					-3.2	6.6E-10		
PA3544	<i>algE</i>	Alginate production outer membrane protein AlgE precursor	2.7	1.8E-04			1.9	2.3E-03		
PA3545	<i>algG</i>	alginate-c5-mannuronan-epimerase AlgG	2.4	9.7E-05						
PA3547	<i>algL</i>	poly(beta-d-mannuronate) lyase precursor AlgL	2.0	3.5E-02						
PA3548	<i>algI</i>	alginate o-acetyltransferase AlgI	1.8	3.9E-02						
PA3550	<i>algF</i>	alginate o-acetyltransferase AlgF	1.7	4.7E-02						
PA3551	<i>algA</i>	phosphomannose isomerase / guanosine 5'-diphospho-D-mannose pyrophosphorylase	1.8	1.3E-03						
PA3552	<i>arnB</i>	ArnB					2.1	1.8E-04		
PA3553	<i>arnC</i>	ArnC					2.5	3.1E-08		
PA3554	<i>arnA</i>	ArnA					1.6	9.4E-03		
PA3556	<i>arnT</i>	inner membrane L-Ara4N transferase ArnT					1.7	1.5E-03		

PA3558	<i>arnF</i>	ArnF					2.5	1.0E-05		
PA3559		probable nucleotide sugar dehydrogenase					2.0	3.8E-04		
PA3567		probable oxidoreductase			-1.13	1.0E-02				
PA3568		probable acetyl-coa synthetase			1.16	2.5E-02			1.14	2.7E-02
PA3570	<i>mmsA</i>	methylmalonate-semialdehyde dehydrogenase			1.16	1.1E-02			1.15	7.0E-03
PA3572		hypothetical protein	1.5	7.0E-03						
PA3573		probable major facilitator superfamily (MFS) transporter	-1.7	2.0E-04						
PA3574	<i>nalD</i>	NalD			1.12	5.6E-03				
PA3579		probable carbohydrate kinase			-1.11	1.3E-02				
PA3580		conserved hypothetical protein					1.7	1.5E-16		
PA3582	<i>glpK</i>	glycerol kinase			1.13	2.6E-02			1.12	2.2E-02
PA3583	<i>glpR</i>	glycerol-3-phosphate regulon repressor			1.06	2.0E-03			1.06	1.3E-03
PA3584	<i>glpD</i>	glycerol-3-phosphate dehydrogenase			1.12	7.7E-03			1.11	9.2E-03
PA3588		probable porin					1.9	5.2E-03		
PA3598		conserved hypothetical protein					1.9	1.5E-06		
PA3600		conserved hypothetical protein					5.1	6.6E-03		
PA3601		conserved hypothetical protein	3.3	8.8E-03			3.1	2.7E-03		
PA3602		conserved hypothetical protein					1.5	1.2E-07		
PA3603	<i>dgkA</i>	diacylglycerol kinase	-1.6	2.2E-05						
PA3607	<i>potA</i>	polyamine transport protein PotA	-2.4	1.7E-04						
PA3608	<i>potB</i>	polyamine transport protein PotB	-2.3	9.1E-03						
PA3609	<i>potC</i>	polyamine transport protein PotC	-2.7	4.3E-03						
PA3610	<i>potD</i>	polyamine transport protein PotD	-2.5	1.9E-08						
PA3611		hypothetical protein			-1.36	1.9E-04			-1.19	1.8E-02

PA3612		conserved hypothetical protein	-1.5	2.8E-04			1.8	5.2E-12		
PA3613		hypothetical protein	1.5	2.7E-03						
PA3614		hypothetical protein			1.13	2.8E-02				
PA3617	<i>recA</i>	RecA protein			1.09	3.4E-02				
PA3621	<i>fdxA</i>	ferredoxin I	-1.6	4.0E-03			-2.1	3.1E-09		
PA3622	<i>rpoS</i>	sigma factor RpoS	1.8	1.4E-09	1.17	5.1E-03			1.13	1.1E-02
PA3623		conserved hypothetical protein	1.7	2.2E-10	-1.2	1.0E-02				
PA3626		conserved hypothetical protein			-1.11	4.4E-02				
PA3629	<i>adhC</i>	alcohol dehydrogenase class III					-1.5	1.9E-18	1.12	2.4E-03
PA3632		conserved hypothetical protein					-1.7	4.9E-05		
PA3633	<i>ygbP</i>	4-diphosphocytidyl-2-C-methylerythritol synthase	-1.5	1.0E-05						
PA3636	<i>kdsA</i>	2-dehydro-3-deoxyphosphooctonate aldolase			-1.13	1.6E-03				
PA3637	<i>pyrG</i>	CTP synthase			-1.08	1.2E-02				
PA3638		conserved hypothetical protein					-1.6	7.0E-05		
PA3639	<i>accA</i>	acetyl-coenzyme A carboxylase carboxyl transferase (alpha subunit)			-1.05	4.4E-02				
PA3640	<i>dnaE</i>	DNA polymerase III, alpha chain							-1.08	3.0E-02
PA3641		probable amino acid permease	-1.9	3.7E-06	-1.2	8.1E-03	-1.6	5.5E-05	-1.11	4.4E-02
PA3646	<i>lpxD</i>	UDP-3-O-[3-hydroxylauroyl] glucosamine N-acyltransferase			1.09	1.7E-02				
PA3647		probable outer membrane protein precursor					-1.8	7.4E-17		
PA3648	<i>opr86</i>	outer membrane protein Opr86							-1.04	2.7E-02
PA3649	<i>mucP</i>	MucP			-1.15	7.2E-03	-2.0	2.8E-21	-1.08	2.8E-02
PA3651	<i>cdsA</i>	phosphatidate cytidyltransferase					-1.6	7.8E-07		
PA3652	<i>uppS</i>	undecaprenyl pyrophosphate synthetase			-1.1	3.3E-02			-1.09	4.5E-02

PA3657	<i>map</i>	methionine aminopeptidase			1.12	6.1E-04			1.12	3.6E-03
PA3661		hypothetical protein	2.6	7.0E-05						
PA3663		hypothetical protein					-1.7	2.9E-06		
PA3666	<i>dapD</i>	tetrahydrodipicolinate succinylase			-1.13	9.1E-03				
PA3675		hypothetical protein	-1.6	2.0E-04						
PA3676	<i>mexK</i>	MexK							1.12	4.6E-02
PA3677	<i>mexJ</i>	MexJ			1.15	3.7E-02				
PA3682		hypothetical protein			-1.06	3.9E-02				
PA3683		conserved hypothetical protein	-1.5	1.3E-04						
PA3684		hypothetical protein					3.2	7.1E-24		
PA3685	<i>yeaZ</i>	YeaZ	-1.6	6.0E-03						
PA3686	<i>adk</i>	adenylate kinase			-1.21	6.4E-04				
PA3687	<i>ppc</i>	phosphoenolpyruvate carboxylase			1.11	3.6E-02				
PA3689		probable transcriptional regulator			1.06	2.4E-02			1.1	3.0E-04
PA3691		hypothetical protein	1.7	2.5E-03	1.12	3.3E-02				
PA3692	<i>lptF</i>	Lipotoxon F, LptF	1.7	8.2E-04			2.1	7.2E-09		
PA3693		conserved hypothetical protein	-1.5	8.1E-05						
PA3694		hypothetical protein	-1.5	3.9E-02	-1.08	3.1E-03	-2.0	2.9E-04	-1.09	3.3E-04
PA3695		hypothetical protein	-1.5	2.2E-05						
PA3700	<i>lysS</i>	lysyl-tRNA synthetase	-1.6	3.7E-04						
PA3702	<i>wspR</i>	WspR			-1.08	1.4E-02				
PA3707	<i>wspB</i>	hypothetical protein			1.11	3.9E-02				
PA3708	<i>wspA</i>	probable chemotaxis transducer			1.11	1.5E-02				
PA3710		probable GMC-type oxidoreductase			-1.2	2.9E-02				
PA3713	<i>spdH</i>	spermidine dehydrogenase, SpdH	-1.8	4.6E-06	-1.42	8.0E-04			-1.18	2.1E-02
PA3718		probable major facilitator superfamily (MFS) transporter	1.7	1.5E-02						
PA3720		hypothetical protein					-1.5	3.5E-02		
PA3723		probable FMN oxidoreductase	1.6	4.0E-05						

PA3724	<i>lasB</i>	elastase LasB	1.6	1.7E-07						
PA3725	<i>recJ</i>	single-stranded-DNA-specific exonuclease RecJ	-1.7	1.0E-06						
PA3726		conserved hypothetical protein	-1.5	7.6E-04						
PA3727		hypothetical protein			1.19	4.9E-02				
PA3728		hypothetical protein			1.37	2.1E-02				
PA3730		hypothetical protein					-1.7	2.6E-06		
PA3734		hypothetical protein	2.9	2.1E-06			1.6	2.2E-02		
PA3736	<i>hom</i>	homoserine dehydrogenase			-1.09	1.8E-03			-1.05	2.2E-03
PA3737	<i>dsbC</i>	thiol:disulfide interchange protein DsbC	-1.6	4.9E-08						
PA3738	<i>xerD</i>	integrase/recombinase XerD	-1.5	4.5E-05						
PA3741		hypothetical protein	-1.7	3.3E-03						
PA3742	<i>rplS</i>	50S ribosomal protein L19					-1.9	6.9E-18		
PA3744	<i>rimM</i>	16S rRNA processing protein					-1.6	3.7E-08		
PA3745	<i>rpsP</i>	30S ribosomal protein S16					-2.5	1.9E-33		
PA3746	<i>ffh</i>	signal recognition particle protein Ffh			-1.11	6.6E-03			-1.11	1.4E-02
PA3754		hypothetical protein			-1.15	1.2E-02				
PA3757	<i>nagR</i>	Transcriptional regulator of N-Acetylglucosamine catabolism operon					1.5	2.6E-03		
PA3758		probable N-acetylglucosamine-6-phosphate deacetylase					1.6	1.2E-04		
PA3759		probable aminotransferase					1.9	6.5E-07		
PA3760		N-Acetyl-D-Glucosamine phosphotransferase system transporter			-1.11	1.2E-02				
PA3763	<i>purL</i>	phosphoribosylformylglycinamide synthase			-1.16	7.0E-04			-1.1	5.1E-03
PA3768		probable metallo-oxidoreductase			-1.19	2.6E-02			-1.15	3.6E-02
PA3769	<i>guaA</i>	GMP synthase	-1.6	3.1E-05						
PA3770	<i>guaB</i>	inosine-5'-monophosphate dehydrogenase	-1.5	3.2E-05	-1.2	7.7E-03				
PA3779		hypothetical protein			-1.27	4.6E-02				
PA3784		hypothetical protein	1.8	1.4E-02			-1.7	7.3E-03		

PA3785		conserved hypothetical protein	1.9	5.1E-03			-1.7	6.3E-03		
PA3786		hypothetical protein	1.6	1.1E-03			1.7	3.9E-07		
PA3787		conserved hypothetical protein					1.6	6.2E-09		
PA3788		hypothetical protein					1.7	8.2E-06		
PA3789		hypothetical protein					-1.8	6.6E-06		
PA3790	<i>oprC</i>	Putative copper transport outer membrane porin OprC precursor			1.19	8.7E-03			1.17	7.2E-04
PA3794		hypothetical protein					-1.6	2.3E-05		
PA3795		probable oxidoreductase					1.7	9.3E-11		
PA3807	<i>ndk</i>	nucleoside diphosphate kinase					-1.6	6.3E-09		
PA3808		conserved hypothetical protein					-1.6	4.0E-14		
PA3812	<i>iscA</i>	probable iron-binding protein IscA					-1.6	1.0E-08		
PA3816	<i>cysE</i>	O-acetylserine synthase							1.19	1.8E-02
PA3817		probable methyltransferase			1.39	2.1E-02				
PA3819		conserved hypothetical protein	1.9	7.8E-05	1.16	3.2E-02	2.2	1.6E-09	1.21	2.3E-02
PA3820	<i>secF</i>	secretion protein SecF	-1.7	4.8E-06			-1.5	4.4E-05		
PA3821	<i>secD</i>	secretion protein SecD	-1.7	8.6E-05						
PA3822		conserved hypothetical protein					-1.7	3.6E-09		
PA3823	<i>tgt</i>	queuine tRNA-ribosyltransferase	-2.0	2.0E-06					-1.1	2.0E-02
PA3824	<i>queA</i>	S-adenosylmethionine:trna ribosyltransferase-isomerase	-1.7	3.6E-04						
PA3827	<i>lptG</i>	Lipopolysaccharide export system permease protein LptG	-1.6	2.0E-04	-1.09	3.2E-02				
PA3835		hypothetical protein	1.9	5.7E-05						
PA3836		hypothetical protein			-1.42	5.2E-03				
PA3838		probable ATP-binding component of ABC transporter			-1.14	1.0E-02				
PA3840		conserved hypothetical protein	-1.9	2.6E-07						
PA3841	<i>exoS</i>	exoenzyme S	-4.1	1.2E-41			-1.5	5.3E-06		

PA3842	<i>spcS</i>	specific Pseudomonas chaperone for ExoS, SpcS	-3.0	8.3E-16						
PA3843		hypothetical protein	-5.5	1.4E-19						
PA3846		hypothetical protein			-1.16	1.0E-02				
PA3847		conserved hypothetical protein					1.8	1.4E-09		
PA3849		conserved hypothetical protein			1.12	3.0E-02				
PA3850		hypothetical protein					1.8	2.9E-09		
PA3857	<i>pcs</i>	phosphatidylcholine synthase					1.6	2.8E-09		
PA3858		probable amino acid-binding protein			-1.21	1.2E-02				
PA3861	<i>rhl</i>	ATP-dependent RNA helicase RhlB	-1.6	8.9E-10						
PA3862	<i>dauB</i>	NAD(P)H-dependent anabolic L-arginine dehydrogenase, DauB			1.14	1.5E-02				
PA3865		probable amino acid binding protein	1.5	2.1E-12						
PA3865.1		pyocin S4 immunity protein					-1.6	3.7E-06		
PA3866		Pyocin S4	1.7	1.9E-09						
PA3869		hypothetical protein					-1.7	7.0E-03		
PA3878	<i>narX</i>	two-component sensor NarX					1.6	1.1E-07		
PA3887	<i>nhaP</i>	Na ⁺ /H ⁺ antiporter NhaP					-1.8	1.8E-14		
PA3888	<i>opuC D</i>	OpuC ABC transporter, permease protein, OpuCD					1.8	4.5E-06		
PA3890	<i>opuC B</i>	OpuC ABC transporter, permease protein, OpuCB					2.6	2.3E-10		
PA3891	<i>opuC A</i>	OpuC ABC transporter, ATP-binding protein, OpuCA					1.8	7.0E-08		
PA3896		probable 2-hydroxyacid dehydrogenase			-1.13	3.3E-03				
PA3897		hypothetical protein	-2.3	6.8E-03						
PA3899	<i>fecI</i>	FecI	-1.7	1.3E-02			1.6	7.4E-03		
PA3902		hypothetical protein					1.7	6.0E-08		
PA3903	<i>prfC</i>	peptide chain release factor 3	-1.6	6.2E-07	-1.15	1.5E-03			-1.12	6.4E-03
PA3904		hypothetical protein					-1.5	7.4E-07		

PA3908		hypothetical protein			1.34	1.8E-02	-1.6	1.9E-05		
PA3918	<i>moaC</i>	molybdopterin biosynthetic protein C			-1.08	9.7E-03			-1.06	3.5E-02
PA3919		conserved hypothetical protein	1.8	3.9E-04	1.1	3.6E-02				
PA3920		probable metal transporting P-type ATPase			1.13	4.5E-02				
PA3923		hypothetical protein			-1.14	2.1E-02				
PA3925		probable acyl-CoA thiolase			-1.21	2.4E-02				
PA3926		probable major facilitator superfamily (MFS) transporter					-2.0	3.1E-02		
PA3928		hypothetical protein					1.5	6.3E-07		
PA3946	<i>rocS1</i>	two-component sensor RocS1	1.7	4.3E-07						
PA3947	<i>rocR</i>	RocR	1.6	7.5E-06						
PA3950		probable ATP-dependent RNA helicase			-1.17	2.1E-03			-1.17	1.9E-03
PA3953		conserved hypothetical protein					2.0	3.0E-05		
PA3959		hypothetical protein	-1.9	1.2E-03						
PA3963		probable transporter					1.9	3.3E-09		
PA3967		hypothetical protein	-1.6	2.4E-03	-1.24	1.8E-02			-1.14	2.5E-02
PA3968		probable pseudouridine synthase					-1.5	1.7E-03		
PA3970	<i>amn</i>	AMP nucleosidase			-1.12	2.3E-04				
PA3975	<i>thiD</i>	phosphomethylpyrimidine kinase			-1.13	2.2E-03				
PA3977	<i>hemL</i>	glutamate-1-semialdehyde 2,1-aminomutase			-1.25	8.9E-03				
PA3979		hypothetical protein	-1.5	1.1E-04						
PA3982		conserved hypothetical protein					1.5	3.9E-11		
PA3983		conserved hypothetical protein			1.53	2.4E-05			1.21	9.2E-04
PA3984	<i>lnt</i>	apolipoprotein N-acyltransferase			-1.03	3.2E-02				
PA3986		hypothetical protein	2.0	4.4E-04						
PA3989	<i>hola</i>	DNA polymerase III, delta subunit			-1.21	2.0E-02				

PA3996	<i>lis</i>	lipoate synthase			-1.1	4.3E-02				
PA4000	<i>rlpA</i>	RlpA			-1.17	3.1E-03				
PA4003	<i>pbpA</i>	penicillin-binding protein 2	-1.7	3.6E-08					-1.04	5.0E-02
PA4004		conserved hypothetical protein	-1.6	5.0E-05						
PA4005		conserved hypothetical protein	-1.5	3.7E-07	-1.15	4.9E-03	-1.7	2.8E-14		
PA4006	<i>nadD 1</i>	nicotinate mononucleotide adenylyltransferase NadD1	-1.6	2.9E-06			1.6	2.3E-08		
PA4013		conserved hypothetical protein					-1.7	3.8E-04		
PA4014		hypothetical protein					-3.2	7.9E-06		
PA4017		conserved hypothetical protein							-1.1	2.2E-02
PA4019	<i>ubiX</i>	UbiX					-1.5	2.3E-03		
PA4020	<i>mpl</i>	UDP-N- acetylmuramate:L-alanyl- gamma-D-glutamyl-meso- diaminopimelate ligase			-1.2	1.9E-03			-1.11	3.2E-03
PA4024	<i>eutB</i>	ethanolamine ammonia- lyase large subunit			-1.22	2.3E-04	1.6	3.3E-09	-1.18	5.9E-04
PA4027		hypothetical protein					1.8	3.5E-05		
PA4030		conserved hypothetical protein	-1.6	1.2E-04						
PA4031	<i>ppa</i>	inorganic pyrophosphatase	-1.5	9.2E-07						
PA4035		hypothetical protein			-1.16	1.8E-04			-1.1	8.0E-03
PA4042	<i>xseB</i>	exodeoxyribonuclease VII small subunit					-2.1	2.7E-08		
PA4044	<i>dxs</i>	1-deoxyxylulose-5- phosphate synthase			-1.13	9.5E-04			-1.1	9.4E-03
PA4045		conserved hypothetical protein					-1.6	2.8E-04		
PA4046		hypothetical protein			-1.15	1.1E-02			-1.1	4.8E-02
PA4048		hypothetical protein	-1.5	4.2E-04			-1.6	6.1E-06		
PA4050	<i>pgpA</i>	phosphatidylglycerophosp hatase A					-2.4	7.9E-10		
PA4051	<i>thiL</i>	thiamine monophosphate kinase	-1.6	3.0E-04						
PA4052	<i>nusB</i>	NusB protein			-1.1	2.2E-02			-1.08	2.7E-02

PA4054	<i>ribB</i>	GTP cyclohydrolase II / 3,4-dihydroxy-2-butanone 4-phosphate synthase	-1.8	3.1E-08	-1.15	4.9E-03			-1.09	3.6E-02
PA4055	<i>ribC</i>	riboflavin synthase alpha chain	-1.7	6.1E-06	-1.31	4.3E-03			-1.18	4.1E-02
PA4056	<i>ribD</i>	riboflavin-specific deaminase/reductase							-1.15	4.8E-02
PA4057	<i>nrdR</i>	NrdR					-1.5	2.6E-06		
PA4058		hypothetical protein					2.8	4.8E-25		
PA4063		hypothetical protein					18.6	2.1E-07		
PA4064		probable ATP-binding component of ABC transporter					7.3	5.2E-07		
PA4065		hypothetical protein					4.3	1.4E-03		
PA4066		hypothetical protein					2.9	9.4E-03		
PA4067	<i>oprG</i>	Outer membrane protein OprG precursor	1.7	2.6E-06	1.63	3.5E-02				
PA4068		probable epimerase			-1.13	1.2E-02			-1.08	2.9E-02
PA4070		probable transcriptional regulator	1.5	3.3E-02			2.0	1.1E-05		
PA4074		probable transcriptional regulator	2.2	2.7E-03						
PA4078		probable nonribosomal peptide synthetase	1.6	3.4E-03						
PA4080		probable response regulator	1.5	5.3E-04						
PA4081	<i>cupB6</i>	fimbrial subunit CupB6					-1.7	3.4E-02		
PA4085	<i>cupB2</i>	chaperone CupB2	1.5	3.7E-02						
PA4090		hypothetical protein			-1.25	2.4E-03	1.7	3.9E-09	-1.2	4.0E-03
PA4092	<i>hpaC</i>	4-hydroxyphenylacetate 3- monooxygenase small chain	2.3	4.7E-02						
PA4093		hypothetical protein					-3.3	1.1E-04		
PA4101	<i>bfmR</i>	BfmR			-1.16	5.8E-03				
PA4104		conserved hypothetical protein					3.9	1.3E-11		
PA4108		cyclic di-GMP phosphodiesterase					1.6	1.8E-06		
PA4119	<i>aph</i>	aminoglycoside 3'- phosphotransferase type IIb	-1.7	9.2E-04						

PA4121		conserved hypothetical protein	2.9	1.8E-03						
PA4122		conserved hypothetical protein	2.1	4.5E-02						
PA4123	<i>hpcC</i>	5-carboxy-2-hydroxymuconate semialdehyde dehydrogenase	1.5	4.4E-02						
PA4128		conserved hypothetical protein					3.3	3.6E-07		
PA4139		hypothetical protein	2.6	7.3E-17						
PA4140		hypothetical protein	2.2	3.8E-05						
PA4154		conserved hypothetical protein			1.41	3.5E-02				
PA4157		probable transcriptional regulator			1.06	4.5E-02				
PA4163		hypothetical protein			-1.2	1.2E-03			-1.09	1.7E-02
PA4164		hypothetical protein					-1.6	5.2E-07		
PA4170		hypothetical protein	1.6	8.5E-04						
PA4171		probable protease	1.6	1.2E-02	1.14	1.4E-02	1.9	1.1E-05		
PA4172		probable nuclease	1.8	1.4E-03			2.4	3.7E-10		
PA4175	<i>piv</i>	protease IV	1.9	1.7E-05						
PA4176	<i>ppiC2</i>	peptidyl-prolyl cis-trans isomerase C2			-1.13	1.2E-02	-1.7	1.9E-17		
PA4178	<i>eftM</i>	SAM-dependent methyltransferase , EftM	-1.6	2.5E-02						
PA4179		probable porin	-2.3	4.4E-03						
PA4181		hypothetical protein	-1.8	2.4E-03						
PA4203	<i>nmoR</i>	NmoR	1.5	4.6E-02						
PA4204	<i>ppgL</i>	periplasmic gluconolactonase, PpgL					1.7	3.7E-08		
PA4205	<i>mexG</i>	hypothetical protein	1.8	2.0E-14	1.59	9.1E-05			1.24	1.2E-03
PA4206	<i>mexH</i>	probable Resistance-Nodulation-Cell Division (RND) efflux membrane fusion protein precursor	1.7	7.2E-13	1.11	2.8E-02			1.07	3.4E-02
PA4207	<i>mexI</i>	probable Resistance-Nodulation-Cell Division (RND) efflux transporter			1.16	1.3E-03				
PA4208	<i>opmD</i>	probable outer membrane protein precursor			1.14	4.4E-02				

PA4212	<i>phzC1</i>	phenazine biosynthesis protein PhzC			1.44	4.5E-03			1.31	2.4E-03
PA4213	<i>phzD1</i>	phenazine biosynthesis protein PhzD			1.2	1.4E-03			1.14	6.5E-04
PA4214	<i>phzE1</i>	phenazine biosynthesis protein PhzE			1.24	7.2E-04			1.17	2.9E-04
PA4216	<i>phzG1</i>	probable pyridoxamine 5'-phosphate oxidase					-2.0	1.5E-03		
PA4218	<i>ampP</i>	AmpP	-1.8	1.5E-05	-1.18	1.8E-02				
PA4219	<i>ampO</i>	AmpO	-1.8	4.3E-04						
PA4220		hypothetical protein	-1.6	8.3E-03			-1.5	4.2E-03		
PA4221	<i>fptA</i>	Fe(III)-pyochelin outer membrane receptor precursor	-1.6	1.4E-08	-1.37	1.1E-02				
PA4222		probable ATP-binding component of ABC transporter			1.39	3.1E-03			1.25	1.7E-02
PA4223		probable ATP-binding component of ABC transporter	-1.6	4.3E-05						
PA4225	<i>pchF</i>	pyochelin synthetase			-1.19	4.7E-02				
PA4228	<i>pchD</i>	pyochelin biosynthesis protein PchD			-1.31	1.7E-02				
PA4229	<i>pchC</i>	pyochelin biosynthetic protein PchC			-1.22	3.3E-02	1.7	8.9E-07		
PA4230	<i>pchB</i>	salicylate biosynthesis protein PchB			-1.48	4.7E-02				
PA4235	<i>ftnA</i>	bacterial ferritin			1.29	3.2E-04			1.11	7.1E-03
PA4236	<i>kata</i>	catalase	1.8	1.7E-08	1.33	4.6E-03			1.18	2.1E-03
PA4237	<i>rplQ</i>	50S ribosomal protein L17					-1.7	1.0E-08		
PA4238	<i>rpoA</i>	DNA-directed RNA polymerase alpha chain			1.1	3.2E-02	-1.7	1.1E-09		
PA4239	<i>rpsD</i>	30S ribosomal protein S4					-1.7	6.2E-11		
PA4241	<i>rpsM</i>	30S ribosomal protein S13					-1.7	4.1E-10		
PA4242	<i>rpmJ</i>	50S ribosomal protein L36					-1.9	1.3E-12		
PA4243	<i>secY</i>	secretion protein SecY					-1.6	9.0E-07		
PA4244	<i>rplO</i>	50S ribosomal protein L15					-1.6	2.4E-09		
PA4245	<i>rpmD</i>	50S ribosomal protein L30					-1.9	5.7E-14		
PA4246	<i>rpsE</i>	30S ribosomal protein S5					-1.5	1.3E-06		
PA4247	<i>rplR</i>	50S ribosomal protein L18					-1.5	2.0E-05		
PA4249	<i>rpsH</i>	30S ribosomal protein S8			-1.15	2.7E-02	-2.9	3.2E-42		

PA4250	<i>rpsN</i>	30S ribosomal protein S14					-1.6	3.3E-07		
PA4252	<i>rplX</i>	50S ribosomal protein L24			-1.18	1.3E-02	-1.9	6.0E-15	-1.12	3.2E-02
PA4253	<i>rplN</i>	50S ribosomal protein L14					-2.1	1.9E-18		
PA4254	<i>rpsQ</i>	30S ribosomal protein S17					-2.0	3.8E-14		
PA4255	<i>rpmC</i>	50S ribosomal protein L29					-2.9	4.5E-24		
PA4256	<i>rplP</i>	50S ribosomal protein L16					-1.9	1.4E-13		
PA4258	<i>rplV</i>	50S ribosomal protein L22					-1.8	5.1E-13		
PA4260	<i>rplB</i>	50S ribosomal protein L2					-1.6	4.3E-08		
PA4261	<i>rplW</i>	50S ribosomal protein L23					-2.7	2.3E-30		
PA4262	<i>rplD</i>	50S ribosomal protein L4					-2.2	5.1E-22		
PA4263	<i>rplC</i>	50S ribosomal protein L3					-1.7	3.9E-09		
PA4264	<i>rpsJ</i>	30S ribosomal protein S10					-2.0	1.5E-19		
PA4265	<i>tufA</i>	elongation factor Tu					-1.8	1.9E-13		
PA4266	<i>fusA1</i>	elongation factor G					-1.9	1.1E-13		
PA4269	<i>rpoC</i>	DNA-directed RNA polymerase beta* chain					-1.6	6.0E-11		
PA4270	<i>rpoB</i>	DNA-directed RNA polymerase beta chain					-1.6	1.5E-10		
PA4271	<i>rplL</i>	50S ribosomal protein L7 / L12	-1.6	1.9E-04						
PA4272	<i>rplJ</i>	50S ribosomal protein L10	-1.7	4.2E-05			-1.5	7.2E-05		
PA4273	<i>rplA</i>	50S ribosomal protein L1					-1.7	6.3E-09		
PA4275	<i>nusG</i>	transcription antitermination protein NusG					-2.1	4.0E-19		
PA4278		hypothetical protein	1.9	5.6E-17			-1.6	2.3E-12		
PA4279		hypothetical protein	1.9	1.0E-09	1.46	4.8E-06			1.28	4.8E-06
PA4280	<i>birA</i>	BirA bifunctional protein	1.9	1.2E-07	1.3	1.4E-02	-1.5	2.1E-05		
PA4281	<i>sbcD</i>	exonuclease SbcD							1.11	3.8E-02
PA4288		probable transcriptional regulator	2.2	1.9E-07						
PA4290		probable chemotaxis transducer							1.06	4.8E-02
PA4292		probable phosphate transporter	-1.8	1.0E-07						
PA4293	<i>pprA</i>	two-component sensor PprA	2.2	5.0E-16	1.31	3.8E-03			1.18	2.5E-02
PA4294		hypothetical protein	2.3	1.4E-20						
PA4295	<i>fppA</i>	Flp prepilin peptidase A, FppA	1.7	9.8E-05						

PA4296	<i>pprB</i>	two-component response regulator, PprB	1.8	6.4E-07	1.12	1.1E-03			1.08	2.0E-02
PA4297	<i>tadG</i>	TadG	1.5	1.1E-02			2.4	7.6E-11		
PA4298		hypothetical protein	2.3	1.9E-07						
PA4299	<i>tadD</i>	TadD	1.9	1.4E-06	1.23	3.0E-03			1.14	1.2E-02
PA4300	<i>tadC</i>	TadC	1.8	1.2E-05	1.29	8.1E-03				
PA4301	<i>tadB</i>	TadB	2.0	1.5E-06						
PA4302	<i>tadA</i>	TadA ATPase	1.9	2.8E-08	1.2	5.0E-02				
PA4303	<i>tadZ</i>	TadZ	2.1	5.3E-11	1.22	1.4E-02				
PA4304	<i>rcpA</i>	RcpA	2.0	1.3E-10						
PA4305	<i>rcpC</i>	RcpC	2.1	8.4E-10						
PA4306	<i>flp</i>	Type IVb pilin, Flp	1.8	1.4E-03						
PA4308		conserved hypothetical protein			-1.08	3.4E-02				
PA4311		conserved hypothetical protein					4.7	2.5E-23		
PA4312		conserved hypothetical protein					1.9	4.3E-11		
PA4314	<i>purU1</i>	formyltetrahydrofolate deformylase			1.08	1.8E-02				
PA4315	<i>mvaT</i>	transcriptional regulator MvaT, P16 subunit			1.26	2.6E-02				
PA4319		conserved hypothetical protein					1.9	6.5E-06		
PA4320		hypothetical protein			1.18	2.2E-02				
PA4326		hypothetical protein	1.6	5.1E-05	1.43	1.3E-03	1.9	4.8E-12	1.2	2.0E-02
PA4328		hypothetical protein	1.7	7.6E-04						
PA4329	<i>pykA</i>	pyruvate kinase II			-1.11	2.2E-03			-1.08	8.3E-03
PA4333		probable fumarase			-1.14	1.1E-02				
PA4336		conserved hypothetical protein			-1.27	4.3E-02	1.7	1.5E-07		
PA4348		conserved hypothetical protein	1.6	4.8E-02						
PA4354		conserved hypothetical protein					1.6	7.4E-05		
PA4357		conserved hypothetical protein					1.9	2.5E-03		
PA4358	<i>feoB</i>	FeoB					1.6	1.8E-02		
PA4359		conserved hypothetical protein					2.6	2.7E-06		
PA4360		hypothetical protein			-1.06	2.8E-02				

PA4366	<i>sodB</i>	superoxide dismutase			-1.23	2.1E-04				
PA4367	<i>bifA</i>	BifA			-1.1	2.6E-02				
PA4370	<i>icmP</i>	Insulin-cleaving metalloproteinase outer membrane protein precursor	-1.7	6.1E-07	-1.26	2.5E-02			-1.23	2.1E-02
PA4371		hypothetical protein	-1.8	6.6E-04						
PA4372		hypothetical protein	-1.7	1.1E-05	-1.21	1.8E-02			-1.21	1.4E-02
PA4373		hypothetical protein	-1.7	3.7E-07						
PA4374	<i>mexV</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux membrane fusion protein MexV			1.16	1.1E-02	2.9	2.2E-18	1.11	2.8E-02
PA4377		hypothetical protein	1.9	5.4E-04						
PA4378	<i>warB</i>	WarB			-1.29	4.0E-02				
PA4385	<i>groEL</i>	GroEL protein							1.04	3.2E-02
PA4386	<i>groES</i>	GroES protein					-2.1	3.0E-23		
PA4388		hypothetical protein			-1.06	3.3E-02				
PA4395		conserved hypothetical protein			-1.12	3.6E-02				
PA4396		two-component response regulator	-2.2	4.8E-11						
PA4401		probable glutathione S-transferase			1.23	4.2E-03			1.13	4.5E-02
PA4402	<i>argJ</i>	glutamate N-acetyltransferase			-1.14	1.1E-03				
PA4404		hypothetical protein	-1.6	5.2E-06			-1.5	1.8E-06		
PA4407	<i>ftsZ</i>	cell division protein FtsZ			1.13	4.2E-02			1.14	2.0E-02
PA4408	<i>ftsA</i>	cell division protein FtsA			1.06	2.6E-02			1.1	7.4E-03
PA4411	<i>murC</i>	UDP-N-acetylmuramate--alanine ligase			1.2	9.1E-04			1.12	9.2E-04
PA4414	<i>murD</i>	UDP-N-acetylmuramoylalanine--D-glutamate ligase			1.11	9.5E-03			1.08	1.4E-02
PA4416	<i>murF</i>	UDP-N-acetylmuramoylalanyl-D-glutamyl-2, 6-diaminopimelate--D-alanyl-D-alanyl ligase			1.15	7.0E-04			1.11	2.8E-02
PA4417	<i>murE</i>	UDP-N-acetylmuramoylalanyl-D-			1.12	2.6E-03			1.09	1.1E-02

		glutamate-2, 6-diaminopimelate ligase								
PA4418	<i>ftsI</i>	penicillin-binding protein 3			1.13	2.9E-02			1.12	4.3E-02
PA4421		conserved hypothetical protein			1.2	1.7E-02				
PA4425		sedoheptulose 7-phosphate isomerase GmhA							1.07	4.7E-03
PA4428	<i>sspA</i>	stringent starvation protein A					-1.6	3.3E-06		
PA4429		probable cytochrome c1 precursor					-1.8	2.2E-12		
PA4430		probable cytochrome b					-1.7	8.4E-13		
PA4432	<i>rpsI</i>	30S ribosomal protein S9	-1.5	1.0E-03					-1.16	9.2E-03
PA4433	<i>rplM</i>	50S ribosomal protein L13	-1.6	3.5E-05						
PA4434		probable oxidoreductase			1.12	5.9E-03				
PA4435		probable acyl-CoA dehydrogenase	6.9	1.2E-65	2.15	2.9E-05			1.69	2.1E-05
PA4438		conserved hypothetical protein	-1.8	3.3E-08	-1.12	1.0E-02				
PA4440		hypothetical protein			-1.25	1.7E-02	-1.6	7.7E-09		
PA4441		hypothetical protein			-1.14	1.7E-02				
PA4443	<i>cysD</i>	ATP sulfurylase small subunit			-1.12	3.9E-02				
PA4448	<i>hisD</i>	histidinol dehydrogenase			1.09	3.3E-02				
PA4452		conserved hypothetical protein			1.3	8.2E-04	4.8	9.6E-87		
PA4454		conserved hypothetical protein					-1.6	1.5E-12		
PA4456		probable ATP-binding component of ABC transporter			1.12	2.4E-03				
PA4460	<i>lptH</i>	LptH			1.07	3.7E-03	1.5	7.3E-10	1.02	1.2E-02
PA4462	<i>rpoN</i>	RNA polymerase sigma-54 factor			1.16	3.2E-02				
PA4463		conserved hypothetical protein	1.7	4.3E-05	1.27	4.8E-03			1.24	4.8E-02
PA4464	<i>ptsN</i>	nitrogen regulatory IIA protein	1.7	1.6E-10						
PA4465		conserved hypothetical protein			1.12	2.6E-03			1.08	2.0E-02
PA4466		probable phosphoryl carrier protein			1.22	2.7E-03			1.14	1.8E-02

PA4467		hypothetical protein					2.0	3.0E-03		
PA4472	<i>pmbA</i>	PmbA protein			-1.44	3.1E-02				
PA4473		hypothetical protein					1.5	1.8E-06		
PA4474		conserved hypothetical protein			-1.08	2.2E-02				
PA4477	<i>cafA</i>	cytoplasmic axial filament protein			1.06	1.7E-02				
PA4491	<i>magB</i>	MagB			1.22	1.1E-02				
PA4493	<i>roxR</i>	RoxR			1.26	2.5E-02			1.17	2.8E-02
PA4496	<i>dppA1</i>	probable binding protein component of ABC transporter			-1.27	1.2E-03			-1.15	1.7E-02
PA4497	<i>dppA2</i>	probable binding protein component of ABC transporter			-1.21	1.1E-02	6.4	1.7E-16		
PA4500	<i>dppA3</i>	probable binding protein component of ABC transporter			-1.25	3.0E-03			-1.11	3.9E-02
PA4501	<i>opdD</i>	Glycine-glutamate dipeptide porin OpdP			-1.43	4.7E-06			-1.19	1.2E-04
PA4502	<i>dppA4</i>	probable binding protein component of ABC transporter			-1.52	9.6E-05			-1.18	2.1E-02
PA4503	<i>dppB</i>	dipeptide ABC transporter permease DppB			-1.35	4.8E-02				
PA4504	<i>dppC</i>	dipeptide ABC transporter permease DppC			-1.21	5.3E-03				
PA4505	<i>dppD</i>	dipeptide ABC transporter ATP-binding protein DppD			-1.13	3.9E-02			-1.12	3.8E-02
PA4506	<i>dppF</i>	dipeptide ABC transporter ATP-binding protein DppF			-1.11	9.9E-03				
PA4513		probable oxidoreductase	-1.8	3.0E-05						
PA4514		probable outer membrane receptor for iron transport	-1.6	5.9E-03	-1.35	5.8E-03				
PA4515		conserved hypothetical protein	-1.8	8.6E-07			1.8	3.1E-10		
PA4516		hypothetical protein	-1.7	6.0E-05			2.2	8.4E-15		
PA4518		hypothetical protein					-2.2	7.8E-06		
PA4519	<i>speC</i>	ornithine decarboxylase			1.4	5.5E-04			1.17	1.0E-02
PA4523		hypothetical protein			1.19	8.0E-03				

PA4524	<i>nadC</i>	nicotinate-nucleotide pyrophosphorylase			1.06	2.4E-02				
PA4525	<i>pilA</i>	type 4 fimbrial precursor PilA	-1.6	2.0E-04	-1.3	3.4E-03	-2.9	7.2E-24		
PA4527	<i>pilC</i>	still frameshift type 4 fimbrial biogenesis protein PilC (putative pseudogene)			-1.21	7.2E-04			-1.09	6.1E-03
PA4528	<i>pilD</i>	type 4 prepilin peptidase PilD	-1.8	1.1E-08						
PA4540		hypothetical protein					2.5	4.9E-03		
PA4542	<i>clpB</i>	ClpB protein			1.08	1.5E-03				
PA4545	<i>comL</i>	competence protein ComL	-1.5	1.5E-04						
PA4546	<i>pilS</i>	two-component sensor PilS			1.28	3.1E-03			1.09	3.5E-02
PA4548		probable D-amino acid oxidase	-1.7	2.0E-06	-1.22	2.4E-02	-1.6	6.6E-08		
PA4550	<i>fimU</i>	type 4 fimbrial biogenesis protein FimU	-1.7	2.0E-06	-1.11	4.9E-02				
PA4551	<i>pilV</i>	type 4 fimbrial biogenesis protein PilV	-2.0	9.3E-07	-1.1	1.7E-02				
PA4552	<i>pilW</i>	type 4 fimbrial biogenesis protein PilW	-1.7	9.2E-08	-1.22	2.4E-03			-1.09	4.8E-02
PA4553	<i>pilX</i>	type 4 fimbrial biogenesis protein PilX	-1.6	1.4E-04						
PA4554	<i>pilY1</i>	type 4 fimbrial biogenesis protein PilY1	-1.6	9.6E-08					-1.15	4.9E-02
PA4555	<i>pilY2</i>	type 4 fimbrial biogenesis protein PilY2	-1.5	6.9E-05	-1.34	7.3E-03				
PA4556	<i>pilE</i>	type 4 fimbrial biogenesis protein PilE			-1.64	9.4E-03				
PA4559	<i>lspA</i>	prolipoprotein signal peptidase					-1.5	1.3E-07		
PA4560	<i>ileS</i>	isoleucyl-tRNA synthetase			-1.15	1.3E-02				
PA4567	<i>rpmA</i>	50S ribosomal protein L27	-1.6	1.5E-06	-1.29	2.7E-02				
PA4568	<i>rplU</i>	50S ribosomal protein L21					-1.5	3.2E-05		
PA4570		hypothetical protein					-1.7	2.3E-02		
PA4571		probable cytochrome c	1.9	3.2E-05						
PA4572	<i>fklB</i>	peptidyl-prolyl cis-trans isomerase FklB			-1.54	2.4E-02				
PA4573		hypothetical protein	2.0	8.3E-04			1.6	1.3E-02		
PA4574		conserved hypothetical protein					-1.6	1.7E-04		

PA4576		probable ATP-dependent protease			-1.08	2.7E-03			-1.07	1.8E-02
PA4577		hypothetical protein	1.5	4.6E-02						
PA4579		hypothetical protein			-1.1	2.7E-03				
PA4583		conserved hypothetical protein	1.5	3.9E-05						
PA4585	<i>rtcA</i>	RNA 3'-terminal phosphate cyclase	1.7	1.1E-02						
PA4588	<i>gdhA</i>	glutamate dehydrogenase	1.5	1.8E-03	1.3	1.7E-02	-1.7	2.3E-07	1.19	3.2E-02
PA4590	<i>pra</i>	protein activator	1.6	1.4E-06						
PA4596	<i>esrC</i>	EsrC					1.7	8.3E-04		
PA4600	<i>nfxB</i>	transcriptional regulator NfxB			1.25	4.7E-02				
PA4601	<i>morA</i>	motility regulator	-1.5	1.2E-12						
PA4602	<i>glyA3</i>	serine hydroxymethyltransferase	-1.7	1.5E-08	-1.37	4.1E-04				
PA4604		conserved hypothetical protein							1.16	4.2E-02
PA4606		conserved hypothetical protein			1.19	7.6E-03				
PA4607		hypothetical protein	2.0	7.8E-08						
PA4608		hypothetical protein	2.1	1.4E-07	1.29	4.9E-02				
PA4609	<i>radA</i>	DNA repair protein RadA			1.06	4.4E-02				
PA4611		hypothetical protein	1.7	2.9E-03			1.6	9.9E-04		
PA4613	<i>katB</i>	catalase							1.16	1.7E-02
PA4616		probable c4-dicarboxylate-binding protein	-3.3	1.9E-10	-1.48	9.0E-04	-1.5	1.7E-02	-1.21	2.1E-02
PA4622		probable major facilitator superfamily (MFS) transporter	-1.9	1.9E-04						
PA4624	<i>cdrB</i>	cyclic diguanylate-regulated TPS partner B, CdrB	2.3	1.4E-31	1.25	1.7E-02				
PA4625	<i>cdrA</i>	cyclic diguanylate-regulated TPS partner A, CdrA	4.2	7.6E-58						
PA4627		conserved hypothetical protein			-1.16	2.4E-02				
PA4628	<i>lysP</i>	lysine-specific permease	-1.9	1.2E-05						
PA4632		hypothetical protein			-1.13	4.3E-02				
PA4633		probable chemotaxis transducer	1.6	1.7E-06	1.13	7.2E-03			1.09	2.7E-02

PA4636		hypothetical protein			-1.13	1.1E-04			-1.11	1.8E-04
PA4638		hypothetical protein					-2.9	7.5E-12		
PA4639		hypothetical protein					1.5	1.2E-12		
PA4640	<i>mgoB</i>	malate:quinone oxidoreductase			-1.07	2.8E-02				
PA4642		hypothetical protein			-1.26	1.7E-02	-1.8	5.9E-09		
PA4644		hypothetical protein			-1.19	3.2E-02				
PA4645		probable purine/pyrimidine phosphoribosyl transferase			-1.14	4.8E-05			-1.11	6.1E-04
PA4646	<i>upp</i>	uracil phosphoribosyltransferase			-1.05	5.5E-03				
PA4647	<i>uraA</i>	uracil permease			1.31	8.9E-03			1.22	2.3E-02
PA4648	<i>cupE1</i>	Pilin subunit CupE1	2.6	2.7E-16			1.8	8.2E-10		
PA4649	<i>cupE2</i>	Pilin subunit CupE2	2.1	1.8E-12			1.9	4.2E-14		
PA4650	<i>cupE3</i>	Pilin subunit CupE3	1.9	1.9E-06			1.7	3.5E-06		
PA4651	<i>cupE4</i>	Pilin assembly chaperone CupE4	2.0	5.2E-20	1.28	1.3E-03			1.17	2.3E-02
PA4652	<i>cupE5</i>	Fimbrial usher protein CupE5	1.7	1.7E-07						
PA4653	<i>cupE6</i>	Adhesin-like protein CupE6	1.7	1.1E-06			1.6	1.2E-07		
PA4655	<i>hemH</i>	ferrochelatase					1.6	8.1E-12		
PA4656		conserved hypothetical protein			1.09	1.9E-02				
PA4657		hypothetical protein					1.7	6.7E-07		
PA4658		hypothetical protein					1.6	2.2E-10		
PA4659		probable transcriptional regulator			1.13	1.8E-02				
PA4660	<i>phr</i>	deoxyribodipyrimidine photolyase			1.14	4.5E-02				
PA4661	<i>pagL</i>	Lipid A 3-O-deacylase			1.34	1.7E-02				
PA4668	<i>lolB</i>	lipoprotein localization protein LolB			-1.1	3.2E-02				
PA4669	<i>ipk</i>	isopentenyl monophosphate kinase					2.1	1.1E-15		
PA4671		probable ribosomal protein L25	-1.5	4.5E-04	-1.25	2.6E-02				
PA4672		peptidyl-tRNA hydrolase					-2.2	7.4E-14		
PA4675	<i>chtA</i>	ChtA	-1.7	7.8E-05						
PA4680		hypothetical protein					1.6	6.0E-03		
PA4683		hypothetical protein	-2.6	2.5E-18						

PA4686		hypothetical protein			-1.24	3.0E-02	12.3	9.0E-46		
PA4687	<i>hitA</i>	ferric iron-binding periplasmic protein HitA			-1.24	3.9E-03				
PA4688	<i>hitB</i>	iron (III)-transport system permease HitB	-1.7	7.3E-06					-1.07	2.7E-02
PA4689		hypothetical protein			1.08	1.5E-02				
PA4694	<i>ilvC</i>	ketol-acid reductoisomerase			1.07	4.0E-02			1.09	1.2E-02
PA4695	<i>ilvH</i>	acetolactate synthase isozyme III small subunit			1.07	1.0E-02			1.06	2.1E-02
PA4696	<i>ilvI</i>	acetolactate synthase large subunit			1.13	1.1E-02			1.1	3.4E-02
PA4698		hypothetical protein					-1.8	1.4E-08		
PA4702		hypothetical protein					2.3	7.1E-10		
PA4703		hypothetical protein	1.9	2.7E-07			1.7	3.4E-07		
PA4704	<i>cbpA</i>	cAMP-binding protein A			-1.13	3.1E-02			-1.11	6.3E-03
PA4708	<i>phuT</i>	Heme-transport protein, PhuT			-1.13	3.4E-02				
PA4715		probable aminotransferase			1.19	1.9E-03			1.2	2.0E-03
PA4719		probable transporter	-1.8	3.6E-09						
PA4720	<i>trmA</i>	tRNA (uracil-5-)-methyltransferase	-1.6	6.9E-08						
PA4722		probable aminotransferase			-1.15	1.4E-02			-1.07	1.3E-02
PA4724		probable aminoacyl-transfer RNA synthetase (class I)	-1.6	7.9E-06						
PA4726	<i>cbrB</i>	two-component response regulator CbrB			-1.24	2.5E-04	1.5	4.4E-25	-1.13	8.9E-04
PA4735		hypothetical protein			1.07	3.0E-02				
PA4741	<i>rpsO</i>	30S ribosomal protein S15			-1.12	3.4E-02	-1.7	1.5E-15		
PA4748	<i>tpiA</i>	triosephosphate isomerase			-1.08	4.5E-02	-1.7	8.2E-07		
PA4749	<i>glmM</i>	phosphoglucosamine mutase							1.09	2.3E-02
PA4751	<i>ftsH</i>	cell division protein FtsH			1.08	9.0E-03				
PA4755	<i>greA</i>	transcription elongation factor GreA					-1.8	8.5E-13		
PA4758	<i>carA</i>	carbamoyl-phosphate synthase small chain			-1.1	1.9E-02				
PA4763	<i>recN</i>	DNA repair protein RecN			1.12	1.5E-03				
PA4764	<i>fur</i>	ferric uptake regulation protein							1.08	3.1E-02

PA4768	<i>smpB</i>	SmpB protein			1.17	6.2E-03			1.15	1.4E-02
PA4769		probable transcriptional regulator			1.35	2.8E-02				
PA4771	<i>lldD</i>	L-lactate dehydrogenase			1.14	7.8E-04			1.04	1.2E-02
PA4774	<i>speE2</i>	SpeE2					1.8	1.0E-05		
PA4775		hypothetical protein					7.7	3.5E-49		
PA4777	<i>pmrB</i>	PmrB: two-component regulator system signal sensor kinase PmrB					1.5	5.4E-03		
PA4778	<i>cueR</i>	CueR			-1.17	6.5E-03			-1.14	3.1E-02
PA4780		conserved hypothetical protein							-1.16	3.6E-02
PA4781		cyclic di-GMP phosphodiesterase	1.6	2.0E-04			1.6	5.4E-06		
PA4782		hypothetical protein					-1.7	9.1E-04		
PA4784		probable transcriptional regulator					1.5	2.0E-05		
PA4787		probable transcriptional regulator			-1.11	8.5E-03				
PA4788		hypothetical protein					2.1	3.3E-13		
PA4793		hypothetical protein					1.7	6.9E-15		
PA4798		hypothetical protein			-1.2	2.0E-02	1.5	1.3E-03	-1.2	6.8E-03
PA4808	<i>sela</i>	L-seryl-tRNA(ser) selenium transferase			1.42	8.9E-04			1.18	4.2E-02
PA4809	<i>fdhE</i>	FdhE protein			-1.2	2.5E-02				
PA4810	<i>fdnI</i>	nitrate-inducible formate dehydrogenase, gamma subunit					-1.6	5.5E-08		
PA4817		hypothetical protein	-2.5	1.5E-04						
PA4822		hypothetical protein					17.1	2.3E-21		
PA4827		arylamine N-acetyltransferase			-1.09	9.1E-03	1.5	1.3E-04		
PA4828		conserved hypothetical protein			-1.22	1.1E-03				
PA4829	<i>lpd3</i>	dihydrolipoamide dehydrogenase 3			1.16	1.7E-03				
PA4830		hypothetical protein	1.8	1.4E-02						
PA4834	<i>cntI</i>	CntI					6.6	3.8E-03		
PA4835	<i>cntM</i>	CntM					9.4	1.9E-04		
PA4836	<i>cntL</i>	CntL					11.4	4.6E-05		
PA4837	<i>cntO</i>	CntO					21.0	1.6E-07		

PA4838		hypothetical protein					3.0	6.4E-06		
PA4843	<i>gcbA</i>	GcbA	-2.0	4.4E-18						
PA4844	<i>ctpL</i>	CtpL	-1.7	4.8E-02			4.0	1.8E-11		
PA4845	<i>dipZ</i>	thiol:disulfide interchange protein DipZ			1.05	2.4E-02				
PA4851		hypothetical protein			-1.12	2.9E-05			-1.11	7.2E-04
PA4855	<i>purD</i>	phosphoribosylamine--glycine ligase	-1.5	2.0E-04	-1.09	1.6E-02				
PA4857	<i>tspR</i>	TspR					1.9	7.0E-05		
PA4858		conserved hypothetical protein			-1.36	8.7E-03			-1.14	3.7E-02
PA4861		probable ATP-binding component of ABC transporter			-1.16	4.2E-03	1.5	1.5E-02	-1.1	2.0E-02
PA4864	<i>ureD</i>	urease accessory protein					2.0	1.8E-14		
PA4865	<i>ureA</i>	urease gamma subunit					1.8	7.5E-08		
PA4868	<i>ureC</i>	urease alpha subunit			-1.21	1.1E-03			-1.12	4.2E-02
PA4869		hypothetical protein	-1.9	5.5E-08						
PA4872		hypothetical protein			-1.12	1.2E-02			-1.08	1.1E-02
PA4873		probable heat-shock protein	-2.0	1.3E-05						
PA4874		conserved hypothetical protein							-1.23	1.7E-02
PA4875		hypothetical protein					2.3	8.8E-18		
PA4876	<i>osmE</i>	osmotically inducible lipoprotein OsmE	1.8	6.5E-04						
PA4877		hypothetical protein	1.8	1.7E-03						
PA4879		conserved hypothetical protein					1.7	7.0E-08		
PA4880		probable bacterioferritin					2.7	1.1E-10		
PA4886		probable two-component sensor	-1.7	2.3E-02						
PA4887		probable major facilitator superfamily (MFS) transporter	-1.6	1.5E-03						
PA4888	<i>desB</i>	acyl-CoA delta-9-desaturase, DesB	-2.0	4.2E-05						
PA4891	<i>ureE</i>	urease accessory protein UreE					1.6	6.2E-03		
PA4892	<i>ureF</i>	urease accessory protein UreF					2.3	1.5E-10		

PA4893	<i>ureG</i>	urease accessory protein UreG			-1.52	7.0E-04			-1.3	7.5E-03
PA4894		hypothetical protein					1.6	1.4E-05		
PA4897		TonB-dependent receptor					1.7	2.6E-04		
PA4900		probable major facilitator superfamily (MFS) transporter	1.8	4.3E-03						
PA4904	<i>vanA</i>	vanillate O-demethylase oxygenase subunit	1.9	1.5E-02						
PA4907		probable short-chain dehydrogenase					1.5	1.2E-17		
PA4909		probable ATP-binding component of ABC transporter			-1.16	1.8E-02				
PA4910		branched chain amino acid ABC transporter ATP binding protein			-1.28	1.5E-02			-1.15	2.6E-02
PA4911		probable permease of ABC branched-chain amino acid transporter			-1.37	3.1E-02				
PA4914	<i>amaR</i>	transcriptional regulator, AmaR					1.6	1.5E-05		
PA4915		probable chemotaxis transducer	1.7	8.1E-05						
PA4916	<i>nrtR</i>	Nudix-related transcriptional regulator NrtR	1.6	1.8E-08	1.18	4.6E-03				
PA4917	<i>nadD</i> 2	nicotinate mononucleotide adenylyltransferase NadD2	1.6	1.1E-05			2.0	2.6E-15		
PA4922	<i>azu</i>	azurin precursor					1.8	6.1E-17		
PA4925		conserved hypothetical protein	2.1	4.1E-06	1.29	2.4E-02	1.6	2.8E-04		
PA4928		conserved hypothetical protein							-1.12	2.3E-02
PA4930	<i>alr</i>	biosynthetic alanine racemase			-1.22	2.0E-02			-1.1	4.8E-02
PA4931	<i>dnaB</i>	replicative DNA helicase			1.05	4.0E-02				
PA4932	<i>rplI</i>	50S ribosomal protein L9			-1.16	1.5E-02	-2.4	7.8E-18	-1.12	2.8E-02
PA4933		hypothetical protein	-1.6	2.3E-03			-1.8	4.2E-06		
PA4934	<i>rpsR</i>	30S ribosomal protein S18	-1.6	2.8E-05						
PA4935	<i>rpsF</i>	30S ribosomal protein S6	-1.6	6.4E-05						
PA4937	<i>rnr</i>	exoribonuclease RNase R			1.13	1.4E-03				

PA4938	<i>purA</i>	adenylosuccinate synthetase			-1.09	1.9E-02				
PA4939		conserved hypothetical protein			-1.11	1.4E-03	1.6	7.5E-08	-1.07	7.0E-03
PA4940		conserved hypothetical protein					-1.9	1.7E-08		
PA4941	<i>hflC</i>	protease subunit HflC			1.11	9.5E-03				
PA4942	<i>hflK</i>	protease subunit HflK			1.34	4.8E-04			1.2	1.5E-03
PA4946	<i>mutL</i>	DNA mismatch repair protein MutL			-1.09	5.8E-03			-1.07	2.9E-02
PA4947	<i>amiB</i>	N-acetylmuramoyl-L-alanine amidase			-1.16	1.7E-03				
PA4952		conserved hypothetical protein			1.08	2.4E-02				
PA4953	<i>motB</i>	chemotaxis protein MotB			-1.2	3.2E-03				
PA4957	<i>psd</i>	phosphatidylserine decarboxylase	-1.5	1.1E-06						
PA4959	<i>fimX</i>	FimX	-1.5	2.7E-07						
PA4961		hypothetical protein			-1.15	3.1E-02				
PA4964	<i>parC</i>	topoisomerase IV subunit A			-1.12	4.2E-03			-1.12	2.8E-03
PA4965		hypothetical protein	-1.7	1.1E-04						
PA4966		hypothetical protein	-1.5	2.5E-05						
PA4967	<i>parE</i>	topoisomerase IV subunit B	-1.6	3.5E-07	-1.09	4.8E-03			-1.1	7.9E-04
PA4968		conserved hypothetical protein	-1.7	9.1E-09						
PA4969	<i>cpdA</i>	Cyclic AMP (cAMP) Phosphodiesterase, CpdA	-1.8	1.6E-08						
PA4972		hypothetical protein			-1.11	3.0E-02				
PA4974		probable outer membrane protein precursor			-1.22	2.5E-02				
PA4975		NAD(P)H quinone oxidoreductase					-1.6	2.9E-03		
PA4985		Uncharacterized protein	2.0	8.3E-11						
PA4986		probable oxidoreductase	1.9	9.1E-05						
PA4995		probable acyl-CoA dehydrogenase					-1.7	1.6E-05		
PA4999	<i>waaL</i>	O-antigen ligase, WaaL	-1.9	3.9E-08						
PA5002	<i>dnpA</i>	de-N-acetylase involved in persistence, DnpA	-1.6	2.5E-04						
PA5004	<i>wapH</i>	WapH			1.12	2.1E-03				

PA5007	<i>wapG</i>	WapG			1.07	4.9E-02				
PA5009	<i>waaP</i>	lipopolysaccharide kinase WaaP			1.1	3.9E-02				
PA5011	<i>waaC</i>	heptosyltransferase I							-1.07	3.0E-02
PA5012	<i>waaF</i>	heptosyltransferase II			-1.19	6.1E-05				
PA5014	<i>glnE</i>	glutamate-ammonia-ligase adenylyltransferase			1.11	1.1E-02				
PA5015	<i>aceE</i>	pyruvate dehydrogenase			1.08	4.0E-03			1.09	1.5E-03
PA5018	<i>msrA</i>	peptide methionine sulfoxide reductase			-1.13	4.2E-03				
PA5023		conserved hypothetical protein			1.17	1.6E-02				
PA5024		conserved hypothetical protein	-1.7	4.0E-03						
PA5027		hypothetical protein	2.3	2.4E-03			1.8	1.1E-02		
PA5029		probable transcriptional regulator					1.5	2.5E-05		
PA5030		probable major facilitator superfamily (MFS) transporter	1.5	1.3E-03						
PA5033		hypothetical protein	-1.7	3.5E-03						
PA5035	<i>gltD</i>	glutamate synthase small chain			1.04	3.4E-02				
PA5037		hypothetical protein			1.17	8.0E-03				
PA5040	<i>pilQ</i>	Type 4 fimbrial biogenesis outer membrane protein PilQ precursor	-1.6	8.0E-11	-1.38	4.7E-03				
PA5041	<i>pilP</i>	type 4 fimbrial biogenesis protein PilP	-1.7	1.2E-08						
PA5042	<i>pilO</i>	type 4 fimbrial biogenesis protein PilO	-1.7	2.6E-12	-1.26	9.0E-04				
PA5043	<i>pilN</i>	type 4 fimbrial biogenesis protein PilN	-1.7	2.1E-10	1.77	6.6E-04			1.38	9.1E-03
PA5044	<i>pilM</i>	type 4 fimbrial biogenesis protein PilM	-1.5	1.5E-10	-1.27	5.6E-03				
PA5049	<i>rpmE</i>	50S ribosomal protein L31					-1.6	7.7E-09		
PA5054	<i>hslU</i>	heat shock protein HslU			1.07	4.4E-02				
PA5057	<i>phaD</i>	poly(3-hydroxyalkanoic acid) depolymerase					1.5	5.8E-04		
PA5058	<i>phaC2</i>	poly(3-hydroxyalkanoic acid) synthase 2	1.8	7.2E-05			1.7	1.1E-05		

PA5060	<i>phaF</i>	polyhydroxyalkanoate synthesis protein PhaF	3.1	3.7E-37	2.69	2.9E-04			1.82	2.6E-03
PA5061		conserved hypothetical protein	1.6	6.9E-03					-1.49	3.8E-02
PA5063	<i>ubiE</i>	ubiquinone biosynthesis methyltransferase UbiE			1.08	1.1E-02				
PA5064		hypothetical protein			-1.18	3.7E-02				
PA5065	<i>ubiB</i>	ubiquinone biosynthetic protein UbiB			1.06	1.1E-03				
PA5071		conserved hypothetical protein	-1.8	2.4E-03						
PA5075		probable permease of ABC transporter			-1.19	4.1E-02	-1.5	1.5E-07		
PA5076		probable binding protein component of ABC transporter			-1.23	5.2E-04			-1.17	1.3E-03
PA5078	<i>opgG</i>	OpgG			-1.08	2.3E-03			-1.06	1.0E-02
PA5082	<i>dguC</i>	DguC			-1.08	2.4E-02				
PA5091	<i>hutG</i>	N-formylglutamate amidohydrolase			-1.2	4.4E-02				
PA5092	<i>hutI</i>	imidazolone-5-propionate hydrolase HutI			-1.1	2.6E-02				
PA5094		probable ATP-binding component of ABC transporter			-1.14	1.1E-02			-1.15	3.6E-03
PA5096		probable binding protein component of ABC transporter			-1.54	2.2E-04			-1.4	2.9E-05
PA5097		probable amino acid permease					-1.6	2.1E-04		
PA5098	<i>hutH</i>	histidine ammonia-lyase			-1.15	1.1E-02				
PA5100	<i>hutU</i>	urocanase			-1.12	1.5E-02			-1.07	4.7E-02
PA5101		hypothetical protein					1.5	3.6E-05		
PA5102		hypothetical protein	1.8	3.0E-02						
PA5106		conserved hypothetical protein	-1.5	1.2E-03						
PA5108		hypothetical protein					-2.5	1.4E-21		
PA5109		hypothetical protein			-1.21	3.2E-03				
PA5117	<i>typA</i>	regulatory protein TypA	-1.6	2.3E-05						
PA5118	<i>thiI</i>	thiazole biosynthesis protein ThiI	-1.6	7.4E-06						

PA5124	<i>ntrB</i>	two-component sensor NtrB					1.7	6.6E-06		
PA5128	<i>secB</i>	secretion protein SecB	-1.6	8.7E-05						
PA5129	<i>grxC</i>	GrxC					1.6	5.4E-05		
PA5130		conserved hypothetical protein			-1.13	1.5E-02				
PA5131	<i>pgm</i>	phosphoglycerate mutase			-1.08	4.0E-02				
PA5134	<i>ctpA</i>	carboxyl-terminal processing protease, CtpA			-1.13	2.1E-04			-1.11	5.3E-03
PA5135		conserved hypothetical protein	-1.6	4.9E-03						
PA5137		hypothetical protein	-2.2	4.8E-33	-1.26	3.2E-03			-1.25	2.4E-02
PA5138		hypothetical protein	-2.2	1.1E-17	-1.34	5.0E-04			-1.21	6.9E-03
PA5139		hypothetical protein	-3.5	2.6E-14	-1.53	2.5E-04			-1.36	2.6E-04
PA5140	<i>hisF1</i>	imidazoleglycerol- phosphate synthase, cyclase subunit	-1.5	9.7E-06	-1.17	1.9E-03				
PA5141	<i>hisA</i>	phosphoribosylformimino- 5-aminoimidazole carboxamide			-1.23	1.0E-02	-1.8	5.3E-09		
PA5146		hypothetical protein			-1.07	8.3E-04				
PA5148		conserved hypothetical protein					2.1	6.4E-14		
PA5152		probable ATP-binding component of ABC transporter			-1.13	4.6E-02				
PA5154		probable permease of ABC transporter	-1.6	5.6E-03			-1.6	6.8E-04		
PA5156		hypothetical protein					3.7	9.9E-05		
PA5164	<i>rmlC</i>	dTDP-4-dehydrorhamnose 3,5-epimerase			1.1	4.0E-02				
PA5165	<i>dctB</i>	DctB							1.07	4.6E-02
PA5166	<i>dctD</i>	DctD			1.13	1.1E-04				
PA5170	<i>arcD</i>	arginine/ornithine antiporter	2.5	1.1E-11	1.43	3.2E-03			1.18	3.9E-02
PA5171	<i>arcA</i>	arginine deiminase	2.4	7.3E-12	1.78	3.8E-03			1.35	2.0E-02
PA5172	<i>arcB</i>	ornithine carbamoyltransferase, catabolic	2.4	5.2E-12	1.62	4.3E-03			1.39	1.1E-02
PA5173	<i>arcC</i>	carbamate kinase	2.3	2.6E-11	1.65	6.1E-03			1.3	3.0E-02
PA5174		probable beta-ketoacyl synthase			-1.1	3.1E-04			-1.04	8.3E-04

PA5178		conserved hypothetical protein	1.6	1.0E-05	1.26	2.7E-02				
PA5180		conserved hypothetical protein					1.5	2.0E-04		
PA5182		hypothetical protein	1.8	1.1E-07			1.6	1.3E-07		
PA5187		probable acyl-CoA dehydrogenase			1.11	3.5E-03			1.1	1.5E-02
PA5189		probable transcriptional regulator					1.6	3.6E-05		
PA5192	<i>pckA</i>	phosphoenolpyruvate carboxykinase			-1.14	1.1E-02				
PA5193	<i>yrjI</i>	heat shock protein HSP33	-1.7	2.3E-12	-1.37	1.3E-03			-1.21	2.1E-02
PA5197	<i>rimK</i>	ribosomal protein S6 modification protein							-1.11	4.0E-02
PA5198		LD-carboxypeptidase			-1.07	3.8E-02				
PA5199	<i>amgS</i>	AmgS			-1.08	9.3E-03				
PA5200	<i>amgR</i>	AmgR			-1.22	1.8E-02				
PA5201		conserved hypothetical protein			-1.16	1.6E-02				
PA5202		hypothetical protein			-1.15	4.1E-02				
PA5204	<i>argA</i>	N-acetylglutamate synthase			-1.14	3.0E-02				
PA5210		probable secretion pathway ATPase			-1.15	6.6E-03			-1.15	6.8E-03
PA5212		hypothetical protein	1.6	1.3E-02			1.5	5.4E-03		
PA5213	<i>gcvP1</i>	glycine cleavage system protein P1	1.9	1.8E-06						
PA5214	<i>gcvH1</i>	glycine cleavage system protein H1			-1.32	4.1E-02				
PA5215	<i>gcvT1</i>	glycine-cleavage system protein T1			-1.08	1.6E-02				
PA5216		probable permease of ABC iron transporter	-1.5	9.6E-04						
PA5227		conserved hypothetical protein					2.0	8.1E-18		
PA5228		conserved hypothetical protein			1.09	3.2E-03	4.7	5.7E-234		
PA5229		conserved hypothetical protein					2.1	4.0E-16		
PA5232		conserved hypothetical protein			1.15	8.6E-03	-1.6	2.0E-25		
PA5239	<i>rho</i>	transcription termination factor Rho			-1.2	9.1E-03				

PA5241	<i>ppx</i>	exopolyphosphatase			1.1	1.8E-02			1.08	1.2E-03
PA5245		conserved hypothetical protein			-1.24	5.5E-03				
PA5248		hypothetical protein	-1.7	6.6E-08						
PA5252		probable ATP-binding component of ABC transporter							1.05	2.2E-02
PA5254		probable peptidyl-prolyl cis-trans isomerase, FkbP-type			-1.19	1.5E-02				
PA5257		hypothetical protein			1.08	2.5E-02				
PA5260	<i>hemC</i>	porphobilinogen deaminase							-1.06	1.6E-02
PA5261	<i>algR</i>	alginate biosynthesis regulatory protein AlgR	1.6	1.4E-05			1.6	5.2E-08		
PA5266	<i>vgrG6</i>	VgrG6	1.9	7.3E-04						
PA5269		hypothetical protein					-1.6	2.3E-07		
PA5271		hypothetical protein			-1.29	2.0E-02	-1.6	4.3E-13		
PA5274	<i>rnk</i>	nucleoside diphosphate kinase regulator	-1.5	1.5E-05	-1.26	3.5E-02				
PA5276	<i>lppL</i>	Lipopeptide LppL precursor					-3.4	3.9E-20		
PA5277	<i>lysA</i>	diaminopimelate decarboxylase			-1.11	4.9E-04				
PA5280	<i>sss</i>	site-specific recombinase Sss	-1.6	1.4E-03						
PA5288	<i>glnK</i>	nitrogen regulatory protein P-II 2					1.6	4.5E-04		
PA5291	<i>betT2</i>	BetT2			1.18	7.6E-04	1.5	1.3E-08	1.11	2.1E-02
PA5293		probable transcriptional regulator			1.05	3.7E-02			1.07	4.5E-02
PA5296	<i>rep</i>	ATP-dependent DNA helicase Rep	-1.6	3.8E-05						
PA5298		xanthine phosphoribosyltransferase	-1.6	1.4E-06	-1.35	3.5E-03				
PA5301	<i>pauR</i>	PauR			-1.22	1.7E-02				
PA5306		conserved hypothetical protein			1.12	1.1E-02	2.3	2.5E-29	1.09	5.7E-03
PA5309	<i>pauB4</i>	FAD-dependent oxidoreductase			1.2	2.1E-02				
PA5315	<i>rpmG</i>	50S ribosomal protein L33					-1.6	3.4E-07		

PA5320	<i>coaC</i>	Phosphopantothenoylcysteine synthase/(R)-4'-phospho-N-pantothenoylcysteine decarboxylase			-1.21	4.0E-03				
PA5333		conserved hypothetical protein			1.14	2.4E-02	-1.6	1.7E-04		
PA5344	<i>oxyR</i>	OxyR			-1.04	4.5E-02				
PA5345	<i>recG</i>	ATP-dependent DNA helicase RecG			-1.21	4.6E-04			-1.14	2.4E-03
PA5349	<i>rubB</i>	rubredoxin reductase			-1.1	6.5E-03				
PA5351	<i>rubA1</i>	Rubredoxin 1			-1.34	2.9E-02	-4.2	3.2E-63		
PA5354	<i>glcE</i>	glycolate oxidase subunit GlcE			1.05	1.3E-02				
PA5355	<i>glcD</i>	glycolate oxidase subunit GlcD					-1.6	7.9E-13		
PA5356	<i>glcC</i>	transcriptional regulator GlcC	1.7	7.2E-07			2.2	1.1E-18		
PA5359		hypothetical protein	1.8	2.2E-07						
PA5366	<i>pstB</i>	ATP-binding component of ABC phosphate transporter			1.13	5.0E-04			1.07	5.1E-03
PA5376	<i>cbcV</i>	CbcV			-1.16	4.5E-02				
PA5378	<i>cbcX</i>	CbcX			-1.2	1.8E-02				
PA5380	<i>gbdR</i>	GbdR	1.6	2.5E-02						
PA5399	<i>dgcB</i>	DgcB, Dimethylglycine catabolism					1.9	2.6E-06		
PA5403		probable transcriptional regulator					1.7	1.1E-03		
PA5406		hypothetical protein	-2.3	2.4E-03			-3.4	3.7E-05		
PA5407		hypothetical protein	-2.9	3.5E-06			1.6	1.9E-02		
PA5413	<i>ltaA</i>	low specificity l-threonine aldolase			-1.1	2.5E-02				
PA5414		hypothetical protein			-1.19	1.8E-02	1.7	6.6E-08		
PA5424		conserved hypothetical protein					-2.0	1.8E-12		
PA5425	<i>purK</i>	phosphoribosylaminoimidazole carboxylase	-1.7	4.4E-08						
PA5426	<i>purE</i>	phosphoribosylaminoimidazole carboxylase, catalytic subunit	-1.7	6.9E-08	-1.17	1.3E-02				
PA5427	<i>adhA</i>	alcohol dehydrogenase	2.0	4.6E-03	1.5	3.4E-02				

PA5429	<i>aspA</i>	aspartate ammonia-lyase					1.5	2.5E-03		
PA5434	<i>mtr</i>	tryptophan permease	-1.6	3.6E-04						
PA5435		probable transcarboxylase subunit							1.06	1.1E-03
PA5443	<i>uvrD</i>	DNA helicase II			-1.1	2.3E-02			-1.11	2.3E-02
PA5446		hypothetical protein	1.7	2.1E-05			-1.6	6.3E-06		
PA5448	<i>wbpY</i>	glycosyltransferase WbpY	-1.6	1.2E-03						
PA5449	<i>wbpX</i>	glycosyltransferase WbpX	-1.6	3.8E-09						
PA5452	<i>wbpW</i>	phosphomannose isomerase/GDP-mannose WbpW			-1.13	3.0E-02				
PA5453	<i>gmd</i>	GDP-mannose 4,6-dehydratase			-1.12	3.1E-02			-1.12	1.0E-02
PA5454	<i>rmd</i>	oxidoreductase Rmd			-1.25	4.1E-03				
PA5456		putative glycosyltransferase	-1.6	1.5E-05						
PA5457		methyltransferase	-1.5	6.5E-04						
PA5459		putative methyltransferase	-1.6	1.9E-06						
PA5460		hypothetical protein	2.2	6.6E-04						
PA5469		conserved hypothetical protein	-2.2	3.7E-03			-1.7	4.0E-02		
PA5471	.1	PA5471 leader peptide					-2.0	3.8E-05		
PA5472		hypothetical protein	-1.8	6.1E-07	-1.85	9.5E-03	-1.7	1.6E-07		
PA5473		conserved hypothetical protein					1.6	4.5E-06		
PA5474		probable metalloprotease			1.12	1.2E-02				
PA5475		hypothetical protein	2.8	1.8E-03						
PA5477		hypothetical protein					1.6	3.0E-10		
PA5479	<i>gltP</i>	proton-glutamate symporter	-1.6	7.1E-05						
PA5482		hypothetical protein					-2.5	5.5E-07		
PA5483	<i>algB</i>	two-component response regulator AlgB			1.17	1.4E-02				
PA5484	<i>kinB</i>	KinB			1.23	2.6E-03			1.1	6.5E-03
PA5485	<i>ampD_{h2}</i>	AmpDh2			1.08	2.0E-02				
PA5487		hypothetical protein			1.17	5.6E-03			1.13	2.2E-02
PA5492		conserved hypothetical protein			1.21	2.6E-03			1.13	4.8E-03

PA5493	<i>polA</i>	DNA polymerase I			-1.08	1.6E-04			-1.08	1.5E-03
PA5495	<i>thrB</i>	homoserine kinase			-1.06	3.4E-03				
PA5496	<i>nrdJb</i>	class II (cobalamin-dependent) ribonucleotide-diphosphate reductase subunit, NrdJb	1.7	1.8E-03						
PA5497	<i>nrdJa</i>	class II (cobalamin-dependent) ribonucleotide-diphosphate reductase subunit, NrdJa	1.6	4.0E-03						
PA5499	<i>zur</i>	zinc uptake regulator, Zur					2.3	6.3E-06		
PA5500	<i>znuC</i>	zinc transport protein ZnuC					2.3	9.5E-08		
PA5502		hypothetical protein			-1.12	3.4E-02				
PA5503		probable ATP-binding component of ABC transporter	-1.7	1.8E-05	-1.11	3.3E-02				
PA5504		D-methionine ABC transporter membrane protein	-1.7	2.8E-07						
PA5519		conserved hypothetical protein			1.13	4.4E-02				
PA5520		hypothetical protein	1.6	7.7E-10						
PA5521		probable short-chain dehydrogenase	1.5	3.5E-09	1.19	1.1E-02			1.11	4.4E-02
PA5523		probable aminotransferase	1.6	7.8E-06	1.08	4.0E-02				
PA5526		hypothetical protein	1.8	6.3E-04						
PA5527		hypothetical protein	1.8	1.5E-04						
PA5528		hypothetical protein			1.2	8.1E-03			1.15	9.5E-03
PA5532		hypothetical protein					2.0	6.1E-16		
PA5534		hypothetical protein					4.1	2.3E-04		
PA5535		conserved hypothetical protein					4.0	3.3E-04		
PA5536	<i>dksA2</i>	DksA2					27.7	4.2E-06		
PA5538	<i>amiA</i>	N-acetylmuramoyl-L-alanine amidase					4.6	4.7E-04		
PA5539		hypothetical protein					15.7	3.6E-07		
PA5540		hypothetical protein					3.9	6.3E-03		
PA5541	<i>pyrQ</i>	dihydroorotase					6.7	7.7E-04		
PA5542		Pseudomonas imipenem beta-lactamase PIB-1			1.15	2.8E-03			1.13	3.8E-03

PA5546		conserved hypothetical protein	1.5	2.0E-04						
PA5547		conserved hypothetical protein	3.3	2.9E-32						
PA5551		hypothetical protein			1.29	3.3E-02				
PA5552	<i>glmU</i>	glucosamine-1-phosphate acetyltransferase/N-acetylglucosamine-1-phosphate uridyltransferase			1.12	2.2E-02				
PA5553	<i>atpC</i>	ATP synthase epsilon chain			1.14	2.2E-02	-1.9	3.4E-12		
PA5554	<i>atpD</i>	ATP synthase beta chain					-1.8	3.0E-12		
PA5555	<i>atpG</i>	ATP synthase gamma chain			1.06	2.6E-02	-1.7	3.7E-09		
PA5556	<i>atpA</i>	ATP synthase alpha chain			1.1	1.9E-02	-1.6	2.3E-07		
PA5558	<i>atpF</i>	ATP synthase B chain			1.16	1.3E-02				
PA5559	<i>atpE</i>	atp synthase C chain					-1.9	1.2E-10		
PA5560	<i>atpB</i>	ATP synthase A chain			1.24	1.4E-03			1.24	1.4E-02
PA5562	<i>spoOJ</i>	chromosome partitioning protein Spo0J			1.12	5.7E-04			1.08	6.2E-03
PA5563	<i>soj</i>	chromosome partitioning protein Soj			1.13	1.8E-03			1.08	3.9E-02
PA5569	<i>rnpA</i>	ribonuclease P protein component			1.17	7.5E-05			1.08	8.2E-03
PA5570	<i>rpmH</i>	50S ribosomal protein L34			-1.38	9.9E-03	-4.2	1.6E-77		

B.3 Other Supplementary Tables

Table A3. 17 additional resistome genes with corresponding mutants showing tobramycin resistance under swarming conditions. Evidence of dysregulation comes from swarm vs. swim RNA-Seq. PA14 transposon mutants in selected genes were tested for altered tobramycin susceptibility under swarming conditions using the agar dilution method (inhibitory concentrations shown in $\mu\text{g/ml}$ of tobramycin, along with images of swarming colonies at 1 $\mu\text{g/ml}$).



















PA14	PAO1	Name	Product Name	Fold change	Swarming inhibitory concentration	
PA14 WT					1	
PA14_07980	PA0613		hypothetical protein	-4.3	2	
PA14_08000	PA0615		hypothetical protein	-2.6	2	
PA14_08010	PA0616	<i>gpV</i>	R2 pyocin membrane-piercing spike	-3.6	2	
PA14_08020	PA0617	<i>gpW</i>	bacteriophage protein	-4.8	2	
PA14_08030	PA0618		phage baseplate assembly protein	-5.3	2	
PA14_08050	PA0620		tail fiber protein	-4.1	2	
PA14_08060	PA0621		tail fiber assembly protein	-3.9	2	
PA14_08090	PA0623	<i>gpFII</i>	phage tail tube protein	-7.4	2	
PA14_08100	PA0624		hypothetical protein	-6.4	2	
PA14_08120	PA0625		tail length determinator protein	-5.4	2	
PA14_08130	PA0626	<i>gpU</i>	phage P2-like protein	-4.6	2	
PA14_08180	PA0630		hypothetical protein	-6.3	2	
PA14_08230	PA0635		hypothetical protein	-6.8	2	
PA14_08240	PA0636		Lambda phage tail tape-measure protein-like	-5.6	2	
PA14_08260	PA0638		minor tail protein L	-5.4	2	
PA14_08270	PA0639		hypothetical protein	-6.1	2	
PA14_08280	PA0640		bacteriophage protein	-5.1	2	

Table A4. Swarming inhibitory concentrations ($\mu\text{g/ml}$) of PA14 mutants on BM2 swarm plates at 0.5% agar. $n \geq 3$.

Strain	Swarming inhibitory concentration ($\mu\text{g/ml}$)				
	Amikacin	Ceftazidime	Erythromycin	Tobramycin	Trimethoprim
PA14 WT	1-2	0.8	75	1	10

<i>priN</i>	1-2	0.8	75-150	2	20
<i>wbpW</i>	1-2	0.8	75	2	10

Table A5. Standard MIC ($\mu\text{g/ml}$) of PA14 mutants in liquid media. $n = 3$.

Media	LB		BM2	
Strain	Tobramycin	Trimethoprim	Tobramycin	Trimethoprim
PA14 WT	4-8	64-128	1-2	32-64
<i>priN</i>	4	128-256	1-2	32-64
<i>wbpW</i>	4-8	64	2	32-64

Table A6. Tobramycin MIC ($\mu\text{g/ml}$) in LB for additional selected PA14 mutants. $n = 3$.

Strain	MIC ($\mu\text{g/ml}$)
PA14 WT	4-8
PA0613	4
PA0617	4
PA0624	4
PA0634	4-8
PA2128	4-8
PA3670	4
PA3836	4
PA5542	4-8

Table A7. Tobramycin MIC ($\mu\text{g/ml}$) in BM2 glucose with 0.1% CAA and no $(\text{NH}_4)_2\text{SO}_4$. $n = 3$.

Strain	Plasmid	MIC
PAO1	pHERD20T (EV)	1-2
PAO1	PA0805.1	2
PAO1 WT	-	1-2
$\Delta\text{PA0805.1}$	-	1-2
$\Delta\text{PA0805.1}^+$	Chromosomal insertion of PA0805.1	1-2

Table A8. sRNA targets predicted *in silico* for PA0805.1.

Locus	Name	Description	Predicted by
PA0142		hypothetical protein	TargetRNA2, IntaRNA2
PA0564		probable transcriptional regulator	TargetRNA2, IntaRNA2
PA1248	<i>aprF</i>	alkaline protease secretion outer membrane protein AprF precursor	RNAPredator, IntaRNA2
PA1644		conserved hypothetical protein	RNAPredator, IntaRNA2
PA1912	<i>femI</i>	ECF sigma factor, FemI	TargetRNA2, RNAPredator
PA2619	<i>infA</i>	initiation factor	RNAPredator, IntaRNA2
PA2677	<i>hplR</i>	probable type II secretion protein	RNAPredator, IntaRNA2
PA2783	<i>mep72</i>	Mep72	RNAPredator, IntaRNA2

Locus	Name	Description	Predicted by
PA3105	<i>xcpQ</i>	general secretion pathway protein D	RNAPredator, IntaRNA2
PA3339	<i>plpD</i>	patatin-like protein, PlpD	TargetRNA2, IntaRNA2
PA3840	<i>ybiN</i>	conserved hypothetical protein	RNAPredator, IntaRNA2
PA4539		hypothetical protein	RNAPredator, IntaRNA2
PA5157	<i>marR</i>	probable transcriptional regulator	TargetRNA2, RNAPredator
PA5187		probable acyl-CoA dehydrogenase	TargetRNA2, IntaRNA2

Table A9. MIC ($\mu\text{g/ml}$) assessed by the standard broth microdilution assay in BM2 glycerol 0.1% CAA with no $(\text{NH}_4)_2\text{SO}_4$. $n \geq 3$.

	MIC (μg/ml)				
Strain	Tobramycin		Trimethoprim		
% arabinose	0	0.3	0	0.3	1.0
WT EV	1	1-2	32-64	32-64	32-64
PA2952.1	2	2	32-64	32	16-32

Table A10. sRNA targets predicted *in silico* for PA2952.1.

Locus	Name	Description	Predicted by
PA0625		hypothetical protein	RNAPredator, TargetRNA2
PA0828		probable transcriptional regulator	RNAPredator, TargetRNA2
PA1711	<i>exsE</i>	negative regulator of type III secretion	IntaRNA2, TargetRNA2
PA1886	<i>polB</i>	DNA polymerase II	IntaRNA2, RNAPredator
PA2459		hypothetical protein	RNAPredator, TargetRNA2
PA2626	<i>trmU</i>	tRNA methyltransferase	IntaRNA2, RNAPredator
PA2942		probable magnesium chelatase	IntaRNA2, RNAPredator
PA3657	<i>map</i>	methionine aminopeptidase	IntaRNA2, RNAPredator