

Supplemental Table 1: Analysis of Aztreonam Resistance Genes Identified from <i>in vitro</i> Selection in Clinical <i>P. aeruginosa</i> Isolate Pairs								
Locus Name	Common Gene name	No Exposure Group % (n=12)	Low Resistance Group % (n=12)	Medium Resistance Group % (n=25)	High Resistance Group % (n=11)	AZLI Isolates with Nonsyn Mutations % (n=48)	AZLI dN/dS	Significance of dN/dS Relative to No Exposure Group (<i>p</i> value)
PA4110	<i>ampC</i>	0.00	0.00	28.00	63.64	29.17	UND*	6.20E-05
PA4418	<i>ftsI</i>	8.33	16.67	48.00	72.73	45.83	11.67	9.68E-03
PA3831	<i>pepA</i>	0.00	8.33	16.00	18.18	14.58	9.00	5.05E-02
PA5038	<i>aroB</i>	0.00	16.67	0.00	0.00	4.17	0.33	1.59E-01
PA4020	<i>mpl</i>	16.67	25.00	40.00	36.36	35.42	UND	1.71E-01
PA2620	<i>clpA</i>	8.33	25.00	16.00	18.18	18.75	UND	3.13E-01
PA14_23460	<i>orfN</i>	8.33	0.00	0.00	0.00	0.00	UND	3.39E-01
PA3047	<i>dacB</i>	8.33	0.00	4.00	9.09	4.17	2.00	5.02E-01
PA3721	<i>nalC</i>	0.00	8.33	0.00	0.00	2.08	0.50	5.69E-01
PA5556	<i>atpA</i>	8.33	0.00	8.00	0.00	4.17	1.50	5.84E-01
PA3574	<i>nalD</i>	8.33	8.33	8.00	0.00	6.25	3.00	6.44E-01
PA3206	-	8.33	0.00	12.00	0.00	6.25	3.00	6.60E-01
PA2492	<i>mexT</i>	8.33	8.33	12.00	18.18	12.50	UND	6.70E-01
PA0424	<i>mexR</i>	8.33	16.67	12.00	0.00	10.42	UND	8.28E-01
PA4732	<i>pgi</i>	8.33	0.00	20.00	27.27	16.67	3.00	8.35E-01
PA2494	<i>mexF</i>	25.00	0.00	28.00	18.18	18.75	12.00	1.00E+00
PA1180	<i>phoQ</i>	0.00	0.00	4.00	0.00	2.08	1.00	1.00E+00
PA5554	<i>atpD</i>	0.00	0.00	4.00	0.00	2.08	1.00	1.00E+00
PA2621	<i>clpS</i>	0.00	0.00	0.00	0.00	0.00	UND	UND

*UND= Undefined, due to an absence of synonymous mutations

Supplemental Table 2: Genes enriched by Aztreonam Tn-Seq

Locus Name	Common Gene Name	Product	TnSeq Read Count (log2 scale)				Fold increase in Reads Relative to Control		
			Control (Azt 0 µg/mL)	Azt 1.0 µg/mL	Azt 2.0 µg/mL	Azt 4.0 µg/mL	Azt 1.0 µg/mL	Azt 2.0 µg/mL	Azt 4.0 µg/mL
PA0424	<i>mexR</i>	Multidrug resistance operon repressor MexR	12.87	20.93	21.60	22.26	1.63	1.68	1.73
PA3574	<i>nalD</i>	NalD	13.48	22.16	22.47	21.87	1.64	1.67	1.62
PA4522	<i>ampD</i>	Beta-lactamase expression regulator AmpD	10.45	16.00	13.20	10.67	1.53	1.26	1.02
PA5203	<i>gshA</i>	Glutamate-cysteine ligase	6.82	10.45	5.54	6.59	1.53	0.81	0.97
PA2493	<i>mexE</i>	RND multidrug efflux membrane fusion protein MexE precursor	6.72	15.43	6.95	5.76	2.29	1.03	0.86
PA3047	<i>dacB</i>	Probable D-alanyl-D-alanine carboxypeptidase	12.04	19.17	12.07	9.94	1.59	1.00	0.82
PA2494	<i>mexF</i>	RND multidrug efflux transporter MexF	8.14	16.69	10.84	6.59	2.05	1.33	0.81
PA3831	<i>pepA</i>	Leucine aminopeptidase	11.74	17.99	9.27	9.09	1.53	0.79	0.77
PA3166	<i>pheA</i>	Chorismate mutase	5.40	10.20	3.37	0.00	1.89	0.62	0.00
PA2492	<i>mexT</i>	Transcriptional regulator MexT	5.40	9.65	2.37	0.00	1.79	0.44	0.00
PA4525	<i>pilA</i>	Type 4 fimbrial precursor PilA	7.21	12.23	5.69	0.00	1.70	0.79	0.00
PA4556	<i>pilE</i>	Type 4 fimbrial biogenesis protein PilE	7.68	12.09	3.37	0.00	1.58	0.44	0.00