

Table S1: *P. aeruginosa* intergenic regions under positive selection. Mutations in intergenic regions were identified as positively selected by Khademi *et al.* (81) and sorted in this table according to the index of interest (Column D). For each intergenic region, the index was calculated by multiplying the number of intergenic mutations (Column A) by the number of impacted lineages (Column B) and the number of independent studies identifying the region as mutated (Column C).

Name of up-stream gene	Name of down-stream gene	PAO1 locus	Product	A	B	C	D	References
				No. of intergenic mutation	No. of lineages with mutated isolate	No. of independent studies identifying the region as mutated	Index of interest (Column A x Column B x Column C)	
<i>phuS</i>	<i>phuR</i>	PA4709 - PA4710	PhuS//Heme/Hemoglobin uptake outer membrane receptor PhuR precursor	40	4	4	640	7,9,18,81
		PA0428 - PA0429	probable ATP-dependent RNA helicase//hypothetical protein	34	10	1	340	81
		PA4786 - PA4787	probable short-chain dehydrogenase//probable transcriptional regulator	28	12	1	336	81
		PA4690.5 - PA4691	16S ribosomal RNA//hypothetical protein	54	6	1	324	81
		PA2535 - PA2536	probable oxidoreductase//probable phosphatidate cytidyltransferase	18	6	2	216	7,81
<i>motY</i>	<i>pyrC</i>	PA3526 - PA3527	probable outer membrane protein precursor//dihydroorotase	32	6	1	192	81
		PA3230 - PA3231	conserved hypothetical protein//downstream hypothetical protein	24	7	1	168	81
<i>algL</i>	<i>algI</i>	PA3547 - PA3548	poly(beta-d-mannuronate) lyase precursor AlgL//alginate o-acetyltransferase AlgI	14	6	2	168	7,81
		PA0976.1 - PA0977	tRNA-Lys//hypothetical protein	26	6	1	156	81
<i>rplU</i>	<i>ispB</i>	PA4568 - PA4569	50S ribosomal protein L21//octaprenyl-diphosphate synthase	22	7	1	154	81
<i>phzM</i>	<i>phzA1</i>	PA4209 - PA4210	probable phenazine-specific methyltransferase//probable phenazine biosynthesis protein	12	6	2	144	7,81
<i>oprO</i>		PA3280 - PA3281	Pyrophosphate-specific outer membrane porin OprO precursor//hypothetical protein	10	5	2	100	7,81
<i>ldh</i>		PA3418 - PA3419	leucine dehydrogenase//hypothetical protein	10	5	2	100	7,81
<i>ampR</i>	<i>ampC</i>	PA4109 - PA4110	transcriptional regulator AmpR//beta-lactamase precursor	12	4	2	96	9,81
	<i>rmlB</i>	PA5160.1 - PA5161	tRNA-Thr//dTDP-D-glucose 4,6-dehydratase	16	6	1	96	81
		PA1334 - PA1335	probable oxidoreductase//probable two-component response regulator	28	3	1	84	81
		PA0979 - PA0980	conserved hypothetical protein//hypothetical protein	16	5	1	80	81
<i>ndvB</i>		PA1163 - PA1164	NdvB//conserved hypothetical protein	10	4	2	80	7,81
<i>norM</i>		PA1361 - PA1362	NorM//hypothetical protein	10	4	2	80	7,81
		PA3965 - PA3966	probable transcriptional regulator//hypothetical protein	16	5	1	80	81
		PA1941 - PA1942	hypothetical protein//hypothetical protein	12	6	1	72	81
<i>etfB</i>		PA2952 - PA2953	electron transfer flavoprotein beta-subunit//electron transfer flavoprotein-ubiquinone oxidoreductase	14	5	1	70	81
	<i>aph</i>	PA4118 - PA4119	hypothetical protein//aminoglycoside 3'-phosphotransferase type IIb	14	5	1	70	81
<i>lptD</i>		PA0595 - PA0596	LPS-assembly protein LptD//hypothetical protein	16	4	1	64	81
<i>pdxB</i>	<i>aceK</i>	PA1375 - PA1376	erythronate-4-phosphate dehydrogenase//isocitrate dehydrogenase kinase/phosphatase	12	5	1	60	81
		PA1841 - PA1842	hypothetical protein//hypothetical protein	12	5	1	60	81
<i>xthA</i>		PA2545 - PA2546	exodeoxyribonuclease III//probable ring-cleaving dioxygenase	20	3	1	60	81
<i>moaC</i>		PA3918 - PA3919	molybdopterin biosynthetic protein C//conserved hypothetical protein	12	5	1	60	81
		PA4960 - PA4961	probable phosphoserine phosphatase//hypothetical protein	12	5	1	60	81
<i>poxB</i>		PA5297 - PA5298	pyruvate dehydrogenase (cytochrome)//xanthine phosphoribosyltransferase	12	5	1	60	81
		PA0588 - PA0589	conserved hypothetical protein//conserved hypothetical protein	14	4	1	56	81
		PA0977 - PA0978	hypothetical protein//conserved hypothetical protein	14	4	1	56	81
		PA1191 - PA1192	hypothetical protein//conserved hypothetical protein	14	4	1	56	81
		PA3687 - PA3688	phosphoenolpyruvate carboxylase//hypothetical protein	14	4	1	56	81
<i>ppc</i>		PA1348 - PA1349	hypothetical protein//conserved hypothetical protein	10	5	1	50	81
	<i>bacA</i>	PA1958 - PA1959	probable transporter//bacitracin resistance protein	16	3	1	48	81
		PA3779 - PA3780	hypothetical protein//putative TRAP-type C4-dicarboxylate transport	12	4	1	48	81
		PA3785 - PA3786	conserved hypothetical protein//hypothetical protein	8	3	2	48	7,81
		PA4792 - PA4793	conserved hypothetical protein//hypothetical protein	16	3	1	48	81
		PA5491 - PA5492	probable cytochrome//conserved hypothetical protein	8	3	2	48	7,81
		PA0980 - PA0981	hypothetical protein//hypothetical protein	14	3	1	42	81
		PA3341 - PA3342	probable transcriptional regulator//hypothetical protein	14	3	1	42	81
	<i>phrD</i>		PA0714 - PA0714.1	hypothetical protein//PhrD	10	4	1	40

	PA1243 - PA1244	probable sensor/response regulator hybrid//hypothetical protein	10	4	1	40	81
<i>opdT</i>	PA2505 - PA2506	tyrosine porin OpdT//hypothetical protein	10	4	1	40	81
	PA4089 - PA4090	probable short-chain dehydrogenase//hypothetical protein	10	4	1	40	81
	PA0574.1 - PA0575	tRNA-Met//conserved hypothetical protein	12	3	1	36	81
<i>tyrZ</i>	PA0668 - PA0668.1	tyrosyl-tRNA synthetase 2//16S ribosomal RNA	18	2	1	36	81
	<i>ccoP1</i> PA1551 - PA1552	probable ferredoxin/Cytochrome c oxidase, ccb3-type, CcoQ subunit	12	3	1	36	81
	<i>hisF1</i> PA5139 - PA5140	hypothetical protein//imidazoleglycerol-phosphate synthase, cyclase subunit	12	3	1	36	81
<i>plsB</i>	PA3673 - PA3674	glycerol-3-phosphate acyltransferase//hypothetical protein	6	3	2	36	7,81
<i>cerN</i>	PA0845 - PA0846	CerN//probable sulfate uptake protein	10	3	1	30	81
<i>ctpH</i>	PA2561 - PA2562	probable chemotaxis transducer//hypothetical protein	10	3	1	30	81
	<i>guaA</i> PA3768 - PA3769	probable metallo-oxidoreductase//GMP synthase	10	3	1	30	81
	PA1142 - PA1143	probable transcriptional regulator//hypothetical protein	8	3	1	24	81
<i>nagZ</i>	<i>psrA</i> PA3005 - PA3006	beta-N-acetyl-D-glucosaminidase//transcriptional regulator PsrA	8	3	1	24	81
<i>gshB</i>	<i>pilG</i> PA0407 - PA0408	glutathione synthetase//twitching motility protein PilG	6	3	1	18	81
	<i>plcR</i> PA0842 - PA0843	glycosyl transferase//phospholipase accessory protein PlcR precursor	6	3	1	18	81
<i>popD</i>	<i>exsC</i> PA1709 - PA1710	Translocator outer membrane protein PopD precursor//ExsC, exoenzyme S synthesis protein C pr	6	3	1	18	81
<i>hmgA</i>	PA2009 - PA2010	homogentisate 1,2-dioxygenase//probable transcriptional regulator	6	3	1	18	81
	PA2069 - PA2070	probable carbamoyl transferase//hypothetical protein	6	3	1	18	81
	PA2418 - PA2419	hypothetical protein//probable hydrolase	6	3	1	18	81
<i>phzG1</i>	<i>phzS</i> PA4216 - PA4217	probable pyridoxamine 5'-phosphate oxidase//flavin-containing monooxygenase	6	3	1	18	81
	PA4873 - PA4874	probable heat-shock protein//conserved hypothetical protein	6	3	1	18	81
<i>nasS</i>	<i>acnB</i> PA1786 - PA1787	NasS//aconitate hydratase 2	10	1	1	10	81
	<i>treA</i> PA2415 - PA2416	hypothetical protein//periplasmic trehalase precursor	8	1	1	8	81
<i>rluC</i>	<i>rne</i> PA2975 - PA2976	ribosomal large subunit pseudouridine synthase C//ribonuclease E	8	1	1	8	81
	PA0014 - PA0015	hypothetical protein//hypothetical protein	6	1	1	6	81
	PA1013.1 - PA1014	tRNA-Ser//probable glycosyl transferase	6	1	1	6	81
<i>hcnC</i>	PA2195 - PA2196	hydrogen cyanide synthase HcnC//probable transcriptional regulator	6	1	1	6	81
	PA2480 - PA2481	probable two-component sensor//hypothetical protein	6	1	1	6	81
	<i>apeA</i> PA2855 - PA2856	hypothetical protein//lysophospholipase A	6	1	1	6	81
	<i>pyrF</i> PA2875 - PA2876	conserved hypothetical protein//orotidine 5'-phosphate decarboxylase	6	1	1	6	81
<i>rsmZ</i>	<i>rpoS</i> PA3621.1 - PA3622	regulatory RNA RsmZ//sigma factor RpoS	6	1	1	6	81
	PA4040 - PA4041	hypothetical protein//hypothetical protein	6	1	1	6	81
	PA4837 - PA4838	probable outer membrane protein precursor//hypothetical protein	6	1	1	6	81
	<i>polA</i> PA5492 - PA5493	conserved hypothetical protein//DNA polymerase I	6	1	1	6	81