

**Table S3.** List and characteristics of the 48 genes involved in mutational resistance studied

<b>Gene</b>	<b>Product</b>	<b>Description</b>	<b>Antibiotics affected</b>
PA0004 <i>gyrB</i>	DNA gyrase subunit B	DNA replication, recombination, modification and repair	Fluoroquinolones
PA0424 <i>mexR</i>	Multidrug resistance operon repressor MexR	Repressor of the MexRAB-OprM operon	Fluoroquinolones, $\beta$ -lactams
PA0425 <i>mexA</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux membrane fusion protein MexA	Membrane fusion protein of the MexAB-OprM multidrug efflux complex	Fluoroquinolones, $\beta$ -lactams
PA0426 <i>mexB</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux transporter MexB	Inner membrane multidrug exporter of the efflux complex MexAB-OprM	Fluoroquinolones, $\beta$ -lactams
PA0427 <i>oprM</i>	Outer membrane protein OprM	Outer membrane factor protein. It is part of the MexAB-OprM, MexVW-OprM, MexXY-OprM and the AmrAB-OprM complex	$\beta$ -lactams
PA0807 <i>ampDh3</i>	AmpDh3 amidase	AmpC transcriptional regulator	$\beta$ -lactams
PA0869 ( <i>pbp6/7</i> , <i>pbpG</i> )	D-alanyl-D-alanine endopeptidase	Peptidoglycan biosynthesis	$\beta$ -lactams
PA0958 <i>oprD</i>	Outer membrane protein OprD	Transport of small molecules	Carbapenems
PA1179 <i>phoP</i>	Two-component response regulator PhoP	Contributes to bacterial tolerance to polymyxin B by directly regulating genes involved in LPS modification and membrane integrity maintenance	Polymyxins
PA1180 <i>phoQ</i>	Two-component sensor PhoQ	Contributes to bacterial tolerance to polymyxin B by directly regulating genes involved in LPS modification and membrane integrity maintenance	Polymyxins
PA1777 <i>oprF</i>	Outer membrane protein F	Transport of small molecules	$\beta$ -lactams
PA1798 <i>parS</i>	Two-component sensor ParS	ParS is involved in resistance to multiple antibiotics through regulation of LPS modification, efflux pumps and porins	Polymyxins, fluoroquinolones, aminoglycosides, carbapenems, cefepime
PA1799 <i>parR</i>	Two-component response regulator ParR	ParR is involved in resistance to multiple antibiotics through regulation of LPS modification, efflux pumps and porins	Polymyxins, fluoroquinolones, aminoglycosides, carbapenems, cefepime
PA2018 <i>mexY</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux transporter MexY	RND-type membrane protein of the efflux complex MexXY-OprM	$\beta$ -lactams
PA2019 <i>mexX</i>	Resistance-Nodulation-Cell Division (RND) multidrug efflux membrane fusion protein MexX	Multidrug efflux lipoprotein	$\beta$ -lactams
PA2020 <i>mexZ</i>	Transcriptional regulator MexZ	Downregulates the MexXY multidrug transporter operon	Fluoroquinolones, aminoglycosides, cefepime
PA2023 <i>galU</i>	UTP-glucose-1-phosphate uridylyltransferase	Central intermediary metabolism. Synthesis of the LPS core	$\beta$ -lactams
PA2272 <i>pbpC</i>	Penicillin-binding protein 3A	Peptidoglycan biosynthesis	$\beta$ -lactams
PA2491 <i>mexS</i>	Oxidoreductase	Suppressor of MexT	Fluoroquinolones, carbapenems
PA2492 <i>mexT</i>	Transcriptional regulator MexT	Activator of the multidrug pump MexEF-OprN and OprD regulator	Fluoroquinolones, carbapenems

PA2493 <i>mexE</i>	Resistance-nodulation-cell division (RND) multidrug efflux membrane fusion protein MexE	Membrane fusion protein of the MexEF-OprN multidrug efflux complex	Fluoroquinolones
PA2494 <i>mexF</i>	Resistance-nodulation-cell division (RND) multidrug efflux transporter MexF	Multidrug inner membrane transporter of the MexEF-OprN complex	Fluoroquinolones
PA2495 <i>oprN</i>	Multidrug efflux outer membrane protein OprN	Outer membrane channel component of the MexEF-OprN multidrug efflux complex	Fluoroquinolones
PA3047 <i>dacB</i> (PBP4)	D-alanyl-D-alanine carboxypeptidase	AmpC transcriptional regulator. Peptidoglycan biosynthesis	$\beta$ -lactams
PA3168 <i>gyrA</i>	DNA gyrase subunit A	DNA replication, recombination, modification and repair	Fluoroquinolones
PA3574 <i>nalD</i>	Transcriptional regulator NalD	Repressor of MexAB-OprM	Fluoroquinolones, $\beta$ -lactams
PA3721 <i>nalC</i>	Transcriptional regulator NalC	Repressor of PA3720-PA3719, which are positive regulators of MexAB-OprM	Fluoroquinolones, $\beta$ -lactams
PA3999 <i>dacC</i> (PBP5)	D-ala-D-ala-carboxypeptidase	AmpC transcriptional regulator. Peptidoglycan biosynthesis	$\beta$ -lactams
PA4003 <i>pbpA</i> (PBP2)	Penicillin-binding protein 2	Peptidoglycan biosynthesis	$\beta$ -lactams
PA4020 <i>mpl</i>	UDP-N-acetylmuramate:L-alanyl-gamma-D-glutamyl-meso-diaminopimelate ligase	AmpC transcriptional regulator. Peptidoglycan biosynthesis	$\beta$ -lactams
PA4109 <i>ampR</i>	Transcriptional regulator AmpR	AmpC transcriptional regulator	$\beta$ -lactams
PA4110 <i>ampC</i>	$\beta$ -lactamase AmpC	Intrinsic AmpC $\beta$ -lactamase	$\beta$ -lactams
PA4266 <i>fusA1</i>	Elongation factor G	Translation, post-translational modification, degradation.	Aminoglycosides
PA4418 <i>ftsI</i> (PBP3)	Penicillin-binding protein 3	Cell division protein FtsI. Peptidoglycan biosynthesis	$\beta$ -lactams
PA4522 <i>ampD</i>	N-acetyl-anhydromuranmyl-L-alanine amidase	AmpC regulator. Peptidoglycan biosynthesis.	$\beta$ -lactams
PA4597 <i>oprJ</i>	Multidrug efflux outer membrane protein OprJ	Outer membrane channel component of the MexCD-OprJ multidrug efflux complex.	Fluoroquinolones
PA4598 <i>mexD</i>	Resistance-nodulation-cell division (RND) multidrug efflux transporter MexD	Multidrug inner membrane transporter of the MexCD-OprJ complex.	Fluoroquinolones
PA4599 <i>mexC</i>	Resistance-nodulation-cell division (RND) multidrug efflux membrane fusion protein MexC	Membrane fusion protein of the MexCD-OprJ multidrug efflux complex.	Fluoroquinolones
PA4600 <i>nfxB</i>	Transcriptional regulator NfxB	Transcriptional regulator of MexCD-OprJ	Fluoroquinolones, cefepime
PA4700 <i>pbp1b</i>	Penicillin-binding protein 1B	Peptidoglycan biosynthesis.	$\beta$ -lactams
PA4776 <i>pmrA</i>	Two-component regulator system response regulator PmrA	Regulates the PA3552-PA3559 LPS modification operon Involved in polymyxin resistance	Polymyxins
PA4777 <i>pmrB</i>	Two-component regulator system signal sensor kinase PmrB	Regulates the PA3552-PA3559 LPS modification operon Involved in polymyxin resistance	Polymyxins

PA4964 <i>parC</i>	DNA topoisomerase IV subunit A	DNA replication, recombination, modification and repair.	Fluoroquinolones
PA4967 <i>parE</i>	DNA topoisomerase IV subunit B	DNA replication, recombination, modification and repair.	Fluoroquinolones
PA5045 <i>pbp1a</i>	Penicillin-binding protein 1A	Peptidoglycan biosynthesis.	$\beta$ -lactams
PA5235 <i>glpT</i>	Glycerol-3-phosphate transporter	Transport of small molecules.	Fosfomicin
PA5471 <i>armZ</i>	Transcriptional regulator ArmZ	Regulator of MexXY efflux pump	Aminoglycosides, cefepime
PA5485 <i>ampDh2</i>	Protein AmpDh2	AmpC transcriptional regulator. Peptidoglycan biosynthesis.	$\beta$ -lactams

Source: <https://www.ncbi.nlm.nih.gov/gene/>; <https://www.pseudomonas.com/>. López-Causapé C, Cabot G, Del Barrio-Tofiño E, Oliver A. The Versatile Mutational Resistome of *Pseudomonas aeruginosa*. *Front Microbiol.* 2018; 9: 685.