Table S3: AMR-Associated Gene Candidates:

		NSM Count				
Functional Role:	**Gene:**	**1982-M6152**	**2019-043682**	**Description:**	**Associated AMR:**	**Reference:**
Topoisomerases	gyrA	0	8	DNA gyrase subunit A	fluoroquinolones	Sulyok, K.M.; Kreizinger, Z.; Wehmann, E.; Lysnyansky, I.; Bányai, K.; Marton, S.; Jerzsele, Á.; Rónai, Z.; Turcsányi, I.; Makrai, L.; et al. Mutations Associated with Decreased Susceptibility to Seven Antimicrobial Families in Field and Laboratory-Derived Mycoplasma bovis Strains. Antimicrobial Agents and Chemotherapy 2017, 61, doi:10.1128/AAC.01983-16.
	gyrB	0	6	type IIA DNA topoisomerase subunit B	fluoroquinolones	Sulyok, K.M.; Kreizinger, Z.; Wehmann, E.; Lysnyansky, I.; Bányai, K.; Marton, S.; Jerzsele, Á.; Rónai, Z.; Turcsányi, I.; Makrai, L.; et al. Mutations Associated with Decreased Susceptibility to Seven Antimicrobial Families in Field and Laboratory-Derived Mycoplasma bovis Strains. Antimicrobial Agents and Chemotherapy 2017, 61, doi:10.1128/AAC.01983-16.
	parC	1*	19*	DNA topoisomerase IV subunit A	fluoroquinolones	Sulyok, K.M.; Kreizinger, Z.; Wehmann, E.; Lysnyansky, I.; Bányai, K.; Marton, S.; Jerzsele, Á.; Rónai, Z.; Turcsányi, I.; Makrai, L.; et al. Mutations Associated with Decreased Susceptibility to Seven Antimicrobial Families in Field and Laboratory-Derived Mycoplasma bovis Strains. Antimicrobial Agents and Chemotherapy 2017, 61, doi:10.1128/AAC.01983-16.
	parE	0	4	DNA topoisomerase IV subunit B	fluoroquinolones	Perichon, B.; Tankovic, J.; Courvalin, P. Characterization of a mutation in the parE gene that confers fluoroquinolone resistance in Streptococcus pneumoniae. Antimicrob. Agents Chemother. 1997, 41, 1166–1167, doi:10.1128/AAC.41.5.1166.
	topA	0	1^	type I DNA topoisomerase		
Protein Synthesis:						
Methyltransferases:	MBOVPG45_RS00465	0	2	tRNA (cytidine(34)-2'-O)-methyltransferase		
	MBOVPG45_RS00470	0	7	RNA methyltransferase		
	MBOVPG45_RS02280	0	4	16S rRNA (uracil(1498)-N(3))-methyltransferase		
	rlmB	0	5	23S rRNA (guanosine(2251)-2'-O)-methyltransferase RlmB	Predicted AMR	Michel, G.; Sauvé, V.; Larocque, R.; Li, Y.; Matte, A.; Cygler, M. The Structure of the RlmB 23S rRNA Methyltransferase Reveals a New Methyltransferase Fold with a Unique Knot. Structure 2002, 10, 1303–1315, doi:10.1016/S0969-2126(02)00852-3.
	rlmD	0	11	23S rRNA (uracil(1939)-C(5))-methyltransferase RlmD		
	rlmH	0	1	23S rRNA (pseudouridine(1915)-N(3))-methyltransferase RlmH		
	rsmA	0	6	16S rRNA (adenine(1518)-N(6)/adenine(1519)-N(6))-dimethyltransferase RsmA	aminoglycosides	Fyfe, C.; Grossman, T.H.; Kerstein, K.; Sutcliffe, J. Resistance to Macrolide Antibiotics in Public Health Pathogens. Cold Spring Harb Perspect Med 2016, 6, a025395, doi:10.1101/cshperspect.a025395.

	rsmD	0	1	16S rRNA (guanine(966)-N(2))-methyltransferase RsmD	aminoglycosides	Fyfe, C.; Grossman, T.H.; Kerstein, K.; Sutcliffe, J. Resistance to Macrolide Antibiotics in Public Health Pathogens. Cold Spring Harb Perspect Med 2016, 6, a025395, doi:10.1101/cshperspect.a025395.
	rsmH	0	5	16S rRNA (cytosine(1402)-N(4))-methyltransferase RsmH	aminoglycosides	Fyfe, C.; Grossman, T.H.; Kerstein, K.; Sutcliffe, J. Resistance to Macrolide Antibiotics in Public Health Pathogens. Cold Spring Harb Perspect Med 2016, 6, a025395, doi:10.1101/cshperspect.a025395.
	rsmI	0	5	16S rRNA (cytidine(1402)-2'-O)-methyltransferase	aminoglycosides	Fyfe, C.; Grossman, T.H.; Kerstein, K.; Sutcliffe, J. Resistance to Macrolide Antibiotics in Public Health Pathogens. Cold Spring Harb Perspect Med 2016, 6, a025395, doi:10.1101/cshperspect.a025395.
	trmB	0	4^	tRNA (guanosine(46)-N7)-methyltransferase TrmB		
30S Ribosomal Proteins	rpsB	0	3	30S ribosomal protein S2	aminoglycosides	Feng, Y.; Jonker, M.J.; Moustakas, I.; Brul, S.; ter Kuile, B.H. Dynamics of Mutations during Development of Resistance by Pseudomonas aeruginosa against Five Antibiotics. Antimicrob. Agents Chemother. 2016, 60, 4229–4236, doi:10.1128/AAC.00434-16.
	rpsC	2	1	30S ribosomal protein S3	tetracyclines	Grossman, T.H. Tetracycline Antibiotics and Resistance. Cold Spring Harb Perspect Med 2016, 6, a025387, doi:10.1101/cshperspect.a025387.
	rpsD	0	2	30S ribosomal protein S4		
	rpsE	1	2	30S ribosomal protein S5	aminoglycosides	Wang, Z; Kong, LC; Jia, BY; Liu, SM; Jiang, XY; Ma, HX. Aminoglycoside susceptibility of Pasteurella multocida isolates from bovine respiratory infections in China and mutations in ribosomal protein S5 associated with high-level induced spectinomycin resistance. J Vet Med Sci 2017, 79, 1678–1681, doi:10.1292/jvms.17-0219.
	rpsH	0	1	30S ribosomal protein S8		
	rpsJ	1	0	30S ribosomal protein S10	tetracyclines	Hu, M.; Nandi, S.; Davies, C.; Nicholas, R.A. High-Level Chromosomally Mediated Tetracycline Resistance in Neisseria gonorrhoeae Results from a Point Mutation in the rpsJ Gene Encoding Ribosomal Protein S10 in Combination with the mtrR and penB Resistance Determinants. Antimicrobial Agents and Chemotherapy 2005, 49, 4327–4334, doi:10.1128/AAC.49.10.4327-4334.2005.
	rpsP	0	2	30S ribosomal protein S16		
	rpsS	0	1	30S ribosomal protein S19		
	rbfA	0	1	30S ribosome-binding factor RbfA		
50S Ribosomal Proteins	MBOVPG45_RS00445	0	1	50S ribosomal protein L1		
	rplB	0	1	50S ribosomal protein L2		
	rplC	0	1	50S ribosomal protein L3	pleuromutilins	Long, K.S.; Hansen, L.H.; Jakobsen, L.; Vester, B. Interaction of Pleuromutilin Derivatives with the Ribosomal Peptidyl Transferase Center. AAC 2006, 50, 1458–1462, doi:10.1128/AAC.50.4.1458-1462.2006.

	rplD	0	10	50S ribosomal protein L4	linezolid	Hölzel, C.S.; Harms, K.S.; Schwaiger, K.; Bauer, J. Resistance to Linezolid in a Porcine Clostridium perfringens Strain Carrying a Mutation in the rplD Gene Encoding the Ribosomal Protein L4. Antimicrobial Agents and Chemotherapy 2010, 54, 1351–1353, doi:10.1128/AAC.01208-09.
	MBOVPG45_RS03525	0	2	50S ribosomal protein L10		
	rplV	0	1	50S ribosomal protein L22	macrolides	Cagliero, C.; Mouline, C.; Cloeckaert, A.; Payot, S. Synergy between Efflux Pump CmeABC and Modifications in Ribosomal Proteins L4 and L22 in Conferring Macrolide Resistance in Campylobacter jejuni and Campylobacter coli. Antimicrobial Agents and Chemotherapy 2006, 50, 3893–3896, doi:10.1128/AAC.00616-06.
	MBOVPG45_RS01360	0	1	50S ribosomal protein L24		
	rpmE	0	1	50S ribosomal protein L31	multi-drug resistance	Liu, A.; Tran, L.; Becket, E.; Lee, K.; Chinn, L.; Park, E.; Tran, K.; Miller, J.H. Antibiotic Sensitivity Profiles Determined with an Escherichia coli Gene Knockout Collection: Generating an Antibiotic Bar Code. AAC 2010, 54, 1393–1403, doi:10.1128/AAC.00906-09.
tRNA ligases	alaS	1	8^	alanine--tRNA ligase	novobiocin	Milija, J.; Lilic, M.; Janjusevic, R.; Jovanovic, G.; Savic, D.J. tRNA Synthetase Mutants of Escherichia coli K-12 Are Resistant to the Gyrase Inhibitor Novobiocin. Journal of Bacteriology 1999, 181, 2979–2983, doi:10.1128/JB.181.9.2979-2983.1999.
	MBOVPG45_RS01640	0	5	arginine--tRNA ligase		
	asnS	0	1	asparagine--tRNA ligase	multi-drug resistance	Magalhães, S.; Aroso, M.; Roxo, I.; Ferreira, S.; Cerveira, F.; Ramalheira, E.; Ferreira, R.; Vitorino, R. Proteomic profile of susceptible and multidrug-resistant clinical isolates of Escherichia coli and Klebsiella pneumoniae using label-free and immunoproteomic strategies. Research in Microbiology 2017, 168, 222–233, doi:10.1016/j.resmic.2016.12.002.
	MBOVPG45_RS00205	0	9	class I tRNA ligase family protein		
	MBOVPG45_RS01150	0	6^	glutamate--tRNA ligase		
	MBOVPG45_RS02730	0	2	glycine--tRNA ligase		
	MBOVPG45_RS02640	0	1	histidine--tRNA ligase		
	ileS	1	5^	isoleucine--tRNA ligase	pseudomonic acid	Yanagisawa, T.; Lee, J.T.; Wu, H.C.; Kawakami, M. Relationship of protein structure of isoleucyl-tRNA synthetase with pseudomonic acid resistance of Escherichia coli. A proposed mode of action of pseudomonic acid as an inhibitor of isoleucyl-tRNA synthetase. J. Biol. Chem. 1994, 269, 24304–24309.
	MBOVPG45_RS03145	0	1	isoleucine--tRNA ligase		
	MBOVPG45_RS02255	0	16	leucine--tRNA ligase		
	lysS	0	3	lysine--tRNA ligase	methicillin (B-lactam)	Dordel, J.; Kim, C.; Chung, M.; Pardos de la Gándara, M.; Holden, M.T.J.; Parkhill, J.; de Lencastre, H.; Bentley, S.D.; Tomasz, A. Novel Determinants of Antibiotic Resistance: Identification of Mutated Loci in Highly Methicillin-Resistant Subpopulations of Methicillin-Resistant Staphylococcus aureus. mBio 2014, 5, e01000-13, doi:10.1128/mBio.01000-13.

	MBOVPG45_RS03150	0	10	methionine--tRNA ligase		
	pheS	0	2	phenylalanine--tRNA ligase subunit alpha	multi-drug resistance	Magalhães, S.; Aroso, M.; Roxo, I.; Ferreira, S.; Cerveira, F.; Ramalheira, E.; Ferreira, R.; Vitorino, R. Proteomic profile of susceptible and multidrug-resistant clinical isolates of Escherichia coli and Klebsiella pneumoniae using label-free and immunoproteomic strategies. Research in Microbiology 2017, 168, 222–233, doi:10.1016/j.resmic.2016.12.002.
	MBOVPG45_RS00380	0	18	phenylalanine--tRNA ligase subunit beta		
	serS	0	1	serine--tRNA ligase		
	MBOVPG45_RS02170	1	8^	threonine--tRNA ligase		
	trpS	0	1	tryptophan--tRNA ligase		
	MBOVPG45_RS04210	0	9^	tyrosine--tRNA ligase		
	MBOVPG45_RS00740	0	7^	valine--tRNA ligase		
	tilS	0	8	tRNA lysidine(34) synthetase TilS		
	thiI	0	4	tRNA 4-thiouridine(8) synthase ThiI		
	mnmA	0	5	tRNA 2-thiouridine(34) synthase MnmA		
ABC Transporters:						
	MBOVPG45_RS00090	0	1	ABC transporter ATP-binding protein		
	MBOVPG45_RS00180	0	2	ABC transporter permease		
	MBOVPG45_RS00555	0	2	ABC transporter permease		
	MBOVPG45_RS00570	0	4	ATP-binding cassette domain-containing protein		
	MBOVPG45_RS00600	0	1	ATP-binding cassette domain-containing protein		
	MBOVPG45_RS01485	0	2	energy-coupling factor transporter transmembrane protein EcfT		
	MBOVPG45_RS01540	0	1	sugar ABC transporter permease		
	MBOVPG45_RS01545	0	4	ATP-binding cassette domain-containing protein		
	MBOVPG45_RS01720	0	1	ABC transporter permease subunit		
	MBOVPG45_RS01770	0	1	ABC transporter ATP-binding protein		
	MBOVPG45_RS01775	1	7	ABC transporter permease		
	MBOVPG45_RS02005	0	5	ABC transporter ATP-binding protein		
	MBOVPG45_RS02710	0	1	ABC transporter permease subunit		
	MBOVPG45_RS02715	0	2	ATP-binding cassette domain-containing protein		
	MBOVPG45_RS02905	1	1	ABC transporter permease subunit		
	MBOVPG45_RS03425	0	1	ATP-binding cassette domain-containing protein		
	MBOVPG45_RS03465	0	4	ABC transporter ATP-binding protein		
	MBOVPG45_RS03705	0	6^	carbohydrate ABC transporter permease		
	MBOVPG45_RS03710	0	1	sugar ABC transporter permease		
	MBOVPG45_RS04310	0	5	ABC transporter ATP-binding protein		
	MBOVPG45_RS04315	1	89	ABC transporter permease		

^Contains a gene-disrupting NSM.

*Identical NSM