

Table S3

Locus	Gene	Product	<i>S. agalactiae</i> A909	<i>S. pneumoniae</i>	<i>S. pyogenes</i> MGAS5448	<i>S. sanguinis</i>	Essential in other bacteria <sup>a</sup>	Core Genome <sup>b</sup>
SMU_01	<i>dnaA</i>	chromosomal replication initiator protein DnaA	essential	non	essential	essential	-	yes
SMU_02	<i>dnaN</i>	DNA polymerase III, beta subunit	essential	non	essential	essential	-	yes
SMU_07	<i>pth</i>	peptidyl-tRNA hydrolase	essential	essential	non	essential	-	yes
SMU_1045c	<i>ppnK</i>	NAD(+) kinase (ATP-NAD kinase)	essential	essential	essential	essential	-	no
SMU_1051	<i>nifS</i>	aminotransferase (class V); possible iron-sulfur cofactor synthesis protein; pyridoxal-phosphate dependent aminotransferase	non	essential	essential	essential	-	no
SMU_1075	<i>dfp</i>	DNA/pantothenate metabolism flavoprotein	non	essential	essential	non	-	no
SMU_1085	<i>rf1</i>	peptide chain release factor 1	essential	essential	essential	essential	-	yes
SMU_1114	<i>gyrA</i>	DNA gyrase A subunit	essential	non	essential	essential	-	yes
SMU_1115	<i>ldh</i>	L-lactate dehydrogenase	non	non	non	non	essential	yes
SMU_1126	<i>coaA</i>	pantothenate kinase	non	essential	essential	non	-	yes
SMU_1136	<i>pstC</i>	phosphate ABC transporter, permease	essential	non	non	essential	-	yes
SMU_1137	<i>pstC1</i>	phosphate ABC transporter, permease	essential	non	non	non	-	yes
SMU_1138	<i>pstS</i>	phosphate ABC transporter, periplasmic phosphate-binding protein	essential	non	non	essential	-	yes
SMU_1143c	<i>mreA</i>	bifunctional protein: riboflavin kinase/flavin adenine dinucleotide (FAD) synthase	essential	non	essential	essential	-	yes

<b>SMU_1187</b>	<i>glmS</i>	L-glutamine-D-fructose-6-phosphate amidotransferase	essential	essential	essential	essential	-	yes
<b>SMU_1190</b>	<i>pykF</i>	pyruvate kinase	essential	essential	essential	essential	-	yes
<b>SMU_1191</b>	<i>pfk</i>	6-phosphofructokinase	essential	essential	essential	essential	-	yes
<b>SMU_1192</b>	<i>dnaE</i>	DNA-polymerase III subunit alpha	essential	essential	essential	essential	-	yes
<b>SMU_1201c</b>	-	conserved hypothetical protein	non	non	non	non	non	yes
<b>SMU_1204</b>	<i>parC</i>	DNA topoisomerase IV subunit A	essential	essential	essential	essential	-	no
<b>SMU_1210</b>	<i>parE</i>	DNA topoisomerase IV subunit B	essential	essential	essential	essential	-	no
<b>SMU_1211</b>	-	conserved hypothetical protein	essential	essential	essential	essential	-	no
<b>SMU_123</b>	<i>polC</i>	DNA polymerase III, alpha subunit	essential	non	essential	essential	-	yes
<b>SMU_1247</b>	<i>eno</i>	enolase	essential	essential	essential	essential	-	no
<b>SMU_1277</b>	<i>gyrB</i>	DNA gyrase subunit B	essential	essential	essential	essential	-	no
<b>SMU_1294</b>	<i>flaW</i>	flavodoxin	essential	non	non	non	-	yes
<b>SMU_13</b>	-	cell-cycle protein, PP-loop superfamily	essential	non	essential	essential	-	yes
<b>SMU_1326</b>	<i>prfB</i>	peptide chain release factor	essential	essential	essential	essential	-	no
<b>SMU_1426c</b>	<i>femD</i>	phosphoglucosamine mutase (phosphoacetylglucosamine mutase)	essential	essential	essential	essential	-	yes
<b>SMU_1429</b>	<i>murC2</i>	UDP-N-acetylmuramyl tripeptide synthetase	essential	essential	essential	essential	-	yes
<b>SMU_1457</b>	<i>rmlB</i>	dTDP-glucose-4,6-dehydratase	essential	essential	essential	non	-	yes
<b>SMU_1460</b>	<i>rmlC</i>	dTDP-4-dehydrorhamnose 3,5-epimerase	essential	non	non	non	-	yes
<b>SMU_1461</b>	<i>rmlA</i>	glucose-1-phosphate thymidyltransferase	essential	non	essential	essential	-	yes

<b>SMU_1465c</b>	<i>dnaD</i>	DNA replication protein DnaD	essential	essential	non	essential	-	yes
<b>SMU_1474c</b>	<i>rnz</i>	ribonuclease Z	essential	essential	essential	essential	-	yes
<b>SMU_15</b>	<i>ftsH</i>	cell division protein FtsH	essential	non	essential	non	-	yes
<b>SMU_1510</b>	<i>syfB</i>	phenylalanyl-tRNA synthetase, beta subunit	essential	essential	essential	essential	-	yes
<b>SMU_1512</b>	<i>syfA</i>	phenylalanyl-tRNA synthetase, alpha subunit	essential	non	essential	essential	-	yes
<b>SMU_1528</b>	<i>atpB</i>	ATPase beta subunit	essential	essential	essential	essential	-	yes
<b>SMU_1529</b>	<i>atpC</i>	ATPase, gamma subunit	essential	essential	essential	essential	-	yes
<b>SMU_1530</b>	<i>atpD</i>	ATP synthase alpha subunit	essential	essential	essential	essential	-	yes
<b>SMU_1534</b>	<i>atpH</i>	ATPase, c subunit	essential	non	non	essential	-	yes
<b>SMU_1543</b>	<i>dnlJ</i>	DNA ligase	essential	essential	essential	essential	-	yes
<b>SMU_1573</b>	<i>metK</i>	S-adenosylmethionine synthetase	essential	essential	essential	essential	-	yes
<b>SMU_158</b>	<i>cysS</i>	cysteinyl-tRNA synthetase	essential	non	essential	essential	-	yes
<b>SMU_1581</b>	<i>dnaX</i>	DNA polymerase III subunits gamma and tau	essential	essential	essential	essential	-	yes
<b>SMU_1609c</b>	<i>secG</i>	preprotein translocase, SecG subunit	essential	essential	essential	essential	-	yes
<b>SMU_1613c</b>	-	dephospho-CoA kinase	essential	essential	essential	essential	-	yes
<b>SMU_1618</b>	<i>dagK</i>	diacylglycerol kinase	non	non	essential	non	-	yes
<b>SMU_1625</b>	<i>pyrH</i>	uridylyate kinase (UMP-kinase)	essential	essential	essential	essential	-	yes
<b>SMU_1626</b>	<i>rl1</i>	50S ribosomal protein L1	essential	non	essential	essential	-	yes
<b>SMU_1627</b>	<i>rl11</i>	50S ribosomal protein L11	essential	non	non	essential	-	yes
<b>SMU_1663</b>	<i>kthY</i>	thymidylate kinase manganese-dependent	essential	non	essential	essential	-	yes
<b>SMU_1687</b>	<i>ppaC</i>	inorganic pyrophosphatase (type II PPase)	essential	essential	non	essential	-	yes
<b>SMU_169</b>	<i>rplM</i>	50S ribosomal protein L13	essential	non	non	essential	-	yes
<b>SMU_1734</b>	<i>accA</i>	acetyl-CoA carboxylase alpha subunit	essential	essential	essential	essential	-	yes

<b>SMU_1735</b>	<i>accD</i>	acetyl-CoA carboxylase beta subunit	essential	essential	essential	essential	-	yes
<b>SMU_1736</b>	<i>accC</i>	acetyl-CoA carboxylase biotin carboxylase subunit	essential	essential	essential	essential	-	yes
<b>SMU_1737</b>	<i>fabZ</i>	(3R)-hydroxymyristoyl-(acyl carrier protein) dehydratase	essential	essential	non	essential	-	yes
<b>SMU_1738</b>	<i>bccP</i>	biotin carboxyl carrier protein of acetyl-CoA carboxylase	essential	essential	essential	essential	-	yes
<b>SMU_1740</b>	<i>fabG</i>	3-oxoacyl-acyl-carrier-protein reductase / 3-ketoacyl-acyl carrier protein reductase	essential	essential	essential	essential	-	yes
<b>SMU_1742c</b>	<i>fabK</i>	trans-2-enoyl-ACP reductase II	essential	essential	non	essential	-	yes
<b>SMU_1743</b>	<i>acp</i>	acyl carrier protein	essential	non	essential	essential	-	yes
<b>SMU_1748</b>	<i>akh</i>	aspartate kinase / homoserine dehydrogenase	non	non	non	non	essential	yes
<b>SMU_1783</b>	<i>proS</i>	prolyl-tRNA synthetase phosphatidate	essential	essential	essential	essential	-	yes
<b>SMU_1785</b>	<i>cdsA</i>	cytidyltransferase (CDP-diglyceride synthase)	essential	non	essential	essential	-	yes
<b>SMU_1799</b>	<i>nadD</i>	nicotinate mononucleotide adenylyltransferase (nicotinate-nucleotide adenylyltransferase)	essential	essential	essential	non	-	yes
<b>SMU_18</b>	-	hypothetical protein	non	non	non	non	non	no
<b>SMU_1801c</b>	-	conserved hypothetical protein, GTP-binding	non	essential	non	non	-	yes
<b>SMU_1802c</b>	-	conserved hypothetical protein	essential	essential	essential	essential	-	yes
<b>SMU_1819</b>	<i>gatB</i>	glutamyl-tRNA (Gln) amidotransferase subunit B	essential	essential	essential	essential	-	yes
<b>SMU_1820c</b>	<i>gatA</i>	glutamyl-tRNA(Gln) amidotransferase subunit A	essential	non	essential	essential	-	yes

<b>SMU_1821c</b>	<i>gatC</i>	glutamyl-tRNA (Gln) amidotransferase subunit C	essential	essential	essential	essential	-	yes
<b>SMU_1834</b>	<i>alr</i>	alanine racemase	essential	essential	non	essential	-	yes
<b>SMU_1836</b>	<i>aroG</i>	phospho-2-dehydro-3-deoxyheptonate aldolase (DAHP synthase)	non	non	non	non	essential	yes
<b>SMU_1837</b>	<i>aroH</i>	3-deoxy-7-phosphoheptulonate synthase	non	non	non	non	essential	no
<b>SMU_1852</b>	-	cation transporter, CorA family	essential	non	essential	non	-	yes
<b>SMU_1859</b>	<i>ssb</i>	single-stranded DNA-binding protein	essential	essential	non	essential	-	yes
<b>SMU_1860</b>	<i>rs6</i>	30S ribosomal protein S6	non	non	non	essential	-	yes
<b>SMU_1886</b>	<i>sys</i>	seryl-tRNA synthetase	non	essential	essential	essential	-	yes
<b>SMU_1920</b>	<i>pgdA</i>	phosphoglycerate dehydrogenase	essential	essential	essential	essential	-	yes
<b>SMU_1921</b>	<i>dnaI</i>	DNA replication protein; primosome component	essential	essential	essential	essential	-	yes
<b>SMU_1922</b>	<i>dnaB</i>	chromosome replication initiation and membrane attachment protein	essential	non	essential	essential	-	yes
<b>SMU_1943</b>	<i>syl</i>	leucyl-tRNA synthetase	essential	non	essential	essential	-	yes
<b>SMU_1948</b>	<i>secE</i>	preprotein translocase, SecE subunit	essential	non	non	essential	-	yes
<b>SMU_1954</b>	<i>groEL</i>	chaperonin GroEL	non	essential	essential	essential	-	yes
<b>SMU_2000</b>	<i>rl17</i>	50S ribosomal protein L17	essential	non	essential	essential	-	yes
<b>SMU_2001</b>	<i>rpoA</i>	DNA-directed RNA polymerase, alpha subunit	essential	non	essential	essential	-	yes
<b>SMU_2004</b>	<i>if1</i>	translation initiation factor IF-1	essential	non	essential	essential	-	yes

<b>SMU_2005</b>	<i>adk</i>	adenylate kinase (ATP-AMP transphosphorylase) (superoxide-inducible protein 16)	essential	essential	non	essential	-	yes
<b>SMU_2006</b>	<i>secY</i>	preprotein translocase	essential	non	essential	essential	-	yes
<b>SMU_2007</b>	<i>rl15</i>	50S ribosomal protein L15, N-terminal fragment	essential	non	non	non	-	yes
<b>SMU_2008</b>	<i>rl30</i>	50S ribosomal protein L30	essential	non	essential	non	-	yes
<b>SMU_2010</b>	<i>rl18</i>	50S ribosomal protein L18	non	non	non	essential	-	yes
<b>SMU_2012</b>	<i>rs8</i>	30S ribosomal protein S8	essential	non	non	essential	-	yes
<b>SMU_2014</b>	<i>rs14</i>	30S ribosomal protein S14	essential	non	non	essential	-	yes
<b>SMU_2015</b>	<i>rl5</i>	50S ribosomal protein L5	essential	non	non	non	-	yes
<b>SMU_2016</b>	<i>rl24</i>	50S ribosomal protein L24	essential	non	non	essential	-	yes
<b>SMU_2017</b>	<i>rl14</i>	50S ribosomal protein L14	essential	non	non	essential	-	yes
<b>SMU_2018</b>	<i>rs17</i>	30S ribosomal protein S17	essential	non	non	essential	-	yes
<b>SMU_2019</b>	<i>rl29</i>	50s ribosomal protein L29	essential	non	non	non	-	yes
<b>SMU_2020</b>	<i>rl16</i>	50S ribosomal protein L16	essential	non	essential	essential	-	yes
<b>SMU_2021</b>	<i>rs3</i>	30S ribosomal protein S3	essential	non	essential	essential	-	yes
<b>SMU_2022</b>	<i>rl22</i>	50S ribosomal protein L22	essential	non	essential	essential	-	yes
<b>SMU_2023c</b>	<i>rps19</i>	30S ribosomal protein S19, C-terminal fragment	essential	non	non	essential	-	yes
<b>SMU_2024c</b>	<i>rl4</i>	50S ribosomal protein L4, N-terminal fragment	essential	non	essential	essential	-	yes
<b>SMU_2025</b>	<i>rl3</i>	50S ribosomal protein L3	essential	non	essential	essential	-	yes
<b>SMU_2031</b>	<i>eftS</i>	translation elongation factor Ts	essential	non	essential	essential	-	yes
<b>SMU_2032</b>	<i>rs2</i>	30S ribosomal protein S2	non	non	essential	essential	-	yes
<b>SMU_2093</b>	<i>argR</i>	arginine repressor	non	non	non	non	essential	yes
<b>SMU_2102</b>	<i>hisS</i>	histidine-tRNA synthetase	essential	non	essential	essential	-	yes
<b>SMU_2135c</b>	<i>rpsD</i>	30S Ribosomal protein S4	essential	non	essential	essential	-	yes



<b>SMU_415</b>	-	conserved hypothetical protein, phosphotransferase enzyme family	essential	non	essential	essential	-	yes
<b>SMU_418</b>	<i>nusA</i>	transcription termination-antitermination factor NusA; elongation factor	non	essential	essential	non	-	yes
<b>SMU_419</b>	-	conserved hypothetical protein	essential	essential	non	non	-	yes
<b>SMU_421</b>	<i>infB</i>	translation initiation factor IF-2	essential	non	essential	non	-	yes
<b>SMU_445</b>	<i>sygA</i>	glycyl-tRNA synthetase alpha subunit	essential	essential	essential	essential	-	yes
<b>SMU_446</b>	<i>sygB</i>	glycyl tRNA synthetase beta subunit	essential	non	essential	essential	-	yes
<b>SMU_455</b>	<i>pbp2x</i>	penicillin-binding protein 2X	essential	essential	essential	essential	-	yes
<b>SMU_456</b>	<i>mraY</i>	phospho-N-acetylmuramoyl-pentapeptide-transferase	essential	essential	essential	essential	-	yes
<b>SMU_465</b>	<i>nadE</i>	NAD(+) synthetase (nitrogen-regulatory protein)	essential	non	essential	essential	-	yes
<b>SMU_471</b>	-	conserved hypothetical protein	non	non	non	non	essential	yes
<b>SMU_478</b>	<i>kguA</i>	guanylate kinase	essential	non	essential	essential	-	yes
<b>SMU_481</b>	<i>fmt</i>	methionyl-tRNA formyltransferase	essential	essential	essential	essential	-	yes
<b>SMU_517</b>	<i>coaD</i>	phosphopantetheine adenylyltransferase; lipopolysaccharide core biosynthesis protein	essential	essential	essential	essential	-	yes
<b>SMU_548</b>	<i>murD</i>	D-glutamic acid adding enzyme MurD; UDP-N-acetylmuramoylalanine--D-glutamate ligase	essential	essential	essential	essential	-	yes
<b>SMU_551</b>	<i>ftsA</i>	cell division protein FtsA	essential	essential	essential	non	-	yes

<b>SMU_558</b>	<i>ileS</i>	isoleucine-tRNA synthetase	essential	essential	essential	essential	-	yes
<b>SMU_589</b>	<i>hlpA</i>	histone-like DNA-binding protein	essential	essential	non	essential	-	yes
<b>SMU_596</b>	<i>pmgY</i>	phosphoglycerate mutase D-Ala-D-Ala adding enzyme; UDP-N-acetylmuramoylalanyl-D-	essential	non	non	essential	-	yes
<b>SMU_603</b>	<i>murF</i>	glutamyl-2,6-diaminopimelate-D-alanyl-D-alanyl ligase (UDP-N-acetylmuramyl pentapeptide synthase)	essential	essential	essential	essential	-	yes
<b>SMU_628</b>	<i>holA</i>	DNA polymerase III, delta subunit	essential	non	essential	essential	-	yes
<b>SMU_629</b>	<i>sod</i>	superoxide dismutase	non	non	non	non	essential	yes
<b>SMU_650</b>	<i>alaS</i>	alanyl-tRNA synthetase (alanine--tRNA ligase)	essential	non	essential	essential	-	yes
<b>SMU_667</b>	<i>nrdB</i>	ribonucleotide reductase, small subunit	essential	non	non	essential	-	yes
<b>SMU_668c</b>	<i>nrdA</i>	ribonucleotide reductase, large subunit	essential	essential	non	essential	-	yes
<b>SMU_675</b>	<i>ptsl</i>	phosphoenolpyruvate-protein phosphotransferase (enzyme I)	essential	non	non	non	-	yes
<b>SMU_697</b>	<i>infC</i>	translation initiation factor IF-3	essential	essential	non	essential	-	yes
<b>SMU_699</b>	<i>rplT</i>	50S ribosomal protein L20	essential	non	non	essential	-	yes
<b>SMU_70</b>	<i>thrC</i>	threonine synthase	non	non	non	non	essential	yes
<b>SMU_712</b>	<i>capP</i>	phosphoenolpyruvate carboxylase	non	non	non	non	essential	yes
<b>SMU_713</b>	<i>ftsW</i>	cell division protein	essential	essential	essential	essential	-	yes
<b>SMU_714</b>	<i>tuf</i>	translation elongation factor Tu	essential	non	essential	essential	-	yes
<b>SMU_715</b>	<i>tpiA</i>	triosephosphate isomerase	essential	essential	non	essential	-	yes

<b>SMU_716</b>	murN	peptidoglycan branched peptide synthesis protein, alanine adding enzyme; methicillin resistance factor	non	non	essential	non	-	yes
<b>SMU_738</b>	-	hypothetical protein	non	non	non	non	non	no
<b>SMU_754</b>	-	HPr (serine) kinase/phosphatase	essential	non	essential	non	-	yes
<b>SMU_766</b>	-	transposase	non	non	non	non	non	no
<b>SMU_773c</b>	lysS	lysyl-tRNA synthetase	essential	essential	essential	essential	-	yes
<b>SMU_777</b>	aroD	3-dehydroquinate dehydratase	non	non	non	non	essential	yes
<b>SMU_778</b>	aroE	shikimate 5-dehydrogenase	non	non	non	non	essential	yes
<b>SMU_779</b>	aroB	3-dehydroquinate synthase	non	non	non	non	essential	yes
<b>SMU_780</b>	aroC	chorismate synthase	non	non	non	non	essential	yes
<b>SMU_784</b>	aroA	3-phosphoshikimate 1-carboxyvinyltransferase (5-enolpyruvylshikimate-3-phosphate synthase)	non	non	non	non	essential	yes
<b>SMU_785</b>	aroK	shikimate kinase	non	non	non	non	essential	yes
<b>SMU_801</b>	obg	GTP-binding protein, GTP1/Obg family	essential	essential	essential	essential	-	yes
<b>SMU_81</b>	grpE	co-chaperone protein GrpE	essential	non	essential	non	-	yes
<b>SMU_821</b>	dnaG	DNA primase	essential	essential	essential	essential	-	yes
<b>SMU_822</b>	rpoD	RNA polymerase sigma-70 factor	essential	essential	essential	essential	-	yes
<b>SMU_824</b>	rmID	dTDP-4-keto-L-rhamnose reductase	essential	non	essential	non	-	yes
<b>SMU_827</b>	rgpC	polysaccharide ABC transporter membrane-spanning protein	non	non	essential	non	-	yes
<b>SMU_830</b>	rgpF	polysaccharide biosynthesis protein	non	non	essential	non	-	yes

<b>SMU_846</b>	rplU	Ribosomal protein L21-within SMU_847c on opposite strand	essential	non	non	non	-	yes
<b>SMU_849</b>	rpmA	50S ribosomal protein L27	essential	non	non	essential	-	yes
<b>SMU_868</b>	trmD	tRNA (guanine-N1)-methyltransferase	non	essential	essential	essential	-	no
<b>SMU_939</b>	fni	isopentenyl-diphosphate delta-isomerase	non	non	essential	essential	-	yes
<b>SMU_942</b>	mvaA	3-hydroxy-3-methylglutaryl-CoA reductase	essential	essential	non	essential	-	no
<b>SMU_943c</b>	hmcM	hydroxymethylglutaryl-CoA synthase	essential	essential	essential	essential	-	no
<b>SMU_947</b>	dfrA	dihydrofolate reductase	essential	essential	essential	essential	-	no
<b>SMU_950</b>	era	GTP-binding protein	essential	essential	essential	essential	-	no
<b>SMU_957</b>	rplJ	50S ribosomal protein L10	essential	non	essential	non	-	no
<b>SMU_959c</b>	-	hypothetical protein	non	non	non	non	non	no
<b>SMU_960</b>	rpl	50S ribosomal protein L7/L12	essential	non	non	essential	-	no
<b>SMU_965</b>	hom	homoserine dehydrogenase	non	non	non	non	essential	no
<b>SMU_966</b>	thrB	homoserine kinase	non	non	non	non	essential	no
<b>SMU_97</b>	pyrG	CTP synthetase	essential	non	non	non	-	yes
<b>SMU_989</b>	asd	aspartate-semialdehyde dehydrogenase	non	non	non	non	essential	no
<b>SMU_99</b>	fbaA	fructose-bisphosphate aldolase	essential	essential	essential	essential	-	yes
<b>SMU_993</b>	ylqL	GTP-binding protein	non	non	non	non	essential	no

<sup>a</sup>Essential genes not conserved among the streptococci strains were compared against the rest of the essential genomes stored in the DEG

<sup>b</sup>A gene is defined as being in the accessory genome if only 1 of the 67 sequenced strains lacks the gene