

# Supplementary Materials: A Functional ClpXP Protease is Required for Induction of the Accessory Toxin Genes, *tst*, *sed*, and *sec*

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**Table S1.** Significantly differentially expressed\* genes between RN4282 wild-type and RN4282 expressing the *ClpX*<sup>1265E</sup> variant.

Pan Gene id <sup>A</sup>	Pan Gene Symbol <sup>B</sup>	Fold Change <sup>C</sup>	<i>p</i> <sub>adj</sub>	Product
SAUPAN006313000	betA	32.5	6.70 × 10 <sup>-55</sup>	oxygen-dependent choline dehydrogenase
SAUPAN006314000	betB	31.8	1.79 × 10 <sup>-73</sup>	betaine-aldehyde dehydrogenase
SAUPAN001141000	lrgA	11.9	2.27 × 10 <sup>-12</sup>	antiholin-like protein LrgA
SAUPAN006063000	SAUSA300_2423	10.9	3.49 × 10 <sup>-2</sup>	hypothetical protein
SAUPAN005063000	SAUSA300_1937	8.5	1.34 × 10 <sup>-3</sup>	Sa3int prophage protein
SAUPAN001142000	lrgB	8.3	1.75 × 10 <sup>-16</sup>	antiholin-like protein LrgB
SAUPAN005056000	NWMN_1891	7.1	9.11 × 10 <sup>-6</sup>	Sa3int prophage protein
SAUPAN005055000	SAUSA300_1934	6.4	1.17 × 10 <sup>-8</sup>	Sa3int prophage encoded protein( tail protein)
SAUPAN000943000	sasD	5.8	3.49 × 10 <sup>-6</sup>	LPXTG cell wall anchor domain
SAUPAN006110000	sarU	5.8	5.91 × 10 <sup>-14</sup>	Transcriptional regulator
SAUPAN005244000	ear	5.7	1.94 × 10 <sup>-7</sup>	<b>SaPI1 encoded protin Ear,</b>
SAUPAN005623000	SAUSA300_2164	5.4	2.86 × 10 <sup>-7</sup>	Conserved protein. Signal peptide.
SAUPAN005361000	SAUSA300_2041	5.0	2.72 × 10 <sup>-10</sup>	hypothetical protein
NWMN_RS10890	NWMN_RS10890	5.0	3.30 × 10 <sup>-5</sup>	Hypothetical Sa3int prophage protein
SAUPAN005899000	SAUSA300_2325	5.0	6.27 × 10 <sup>-14</sup>	putative type II DNA modification enzyme
JKDJBECI_01742	-	5.0	2.77 × 10 <sup>-9</sup>	tRNA-Arg(ccg)
SAUPAN005138000	SAUSA300_1938	4.9	4.82 × 10 <sup>-6</sup>	Sa3int prophage protein. putative capsid protein
SAUPAN001245000	gehB	4.8	6.17 × 10 <sup>-18</sup>	lipase
SAUPAN006318000	cusT	4.6	3.10 × 10 <sup>-11</sup>	choline transporter BetT
SAUPAN002480000	SAUSA300_0602	4.5	7.57 × 10 <sup>-12</sup>	hypothetical protein
SAUPAN005928000	narG	4.4	4.32 × 10 <sup>-3</sup>	nitrate reductase subunit alpha
SAUPAN005933000	nirR	4.4	1.45 × 10 <sup>-2</sup>	nitrite reductase transcriptional regulator NirR
SAUPAN002548000	sarX (SAUSA300_0654)	4.1	4.06 × 10 <sup>-13</sup>	MarR family transcriptional regulator
SAUPAN005061000	SAUSA300_1936	4.1	4.15 × 10 <sup>-2</sup>	conserved hypothetical phage protein
SAUSA300_RS10655	-	4.0	3.45 × 10 <sup>-2</sup>	hypothetical protein
SAUSA300_RS05270	-	3.9	1.06 × 10 <sup>-5</sup>	hypothetical protein
SAUPAN005046000	SAUSA300_1929	3.9	1.59 × 10 <sup>-3</sup>	Sa3int prophage encoded protein (tail component)
JKDJBECI_02004	-	3.9	8.40 × 10 <sup>-3</sup>	tRNA-Ile(gat)
SAUPAN001175000	esxA	3.7	1.21 × 10 <sup>-8</sup>	T7SS EsxA

SAUPAN002816000	ohr (SAUSA300_0786)	3.7	$1.94 \times 10^{-3}$	Putative organic hydroperoxide reductase
SAUPAN005052000	SAUSA300_1932	3.7	$2.21 \times 10^{-2}$	Sa3int prophage encoded protein
SAUSA300_RS10625	-	3.7	$1.99 \times 10^{-2}$	Sa3int prophage encoded protein
SAUPAN001863000	ulaA	3.7	$4.55 \times 10^{-8}$	PTS ascorbate transporter subunit IIC.
SAUPAN006030000	cntK	3.6	$4.87 \times 10^{-5}$	Histidine isomerase
SAUSA300_RS10500	-	3.5	$3.17 \times 10^{-4}$	MAP domain-containing protein
SAUPAN003448000	mraZ	3.5	$7.81 \times 10^{-9}$	division/cell wall cluster transcriptional repressor
SAUPAN003164000	spxA	3.5	$9.11 \times 10^{-14}$	regulatory protein Spx
SAUPAN002481000	SAUSA300_0603	3.5	$5.24 \times 10^{-6}$	hypothetical membrane protein
SAUPAN000662000	SAUSA300_1941	3.4	$5.56 \times 10^{-3}$	Sa3int prophage encoded protein (terminase)
SAUPAN003449000	mraW	3.3	$1.46 \times 10^{-5}$	Putative S-adenosyl-methyltransferase
SAUPAN005389000	SAUSA300_2056	3.3	$2.53 \times 10^{-4}$	conserved membrane protein
SAUPAN005245000	tst	3.2	$1.13 \times 10^{-3}$	<b>toxic shock syndrome toxin-1 TSST-1</b>
SAUPAN002802000	cspC	3.2	$3.82 \times 10^{-3}$	cold-shock protein
SAUPAN003211000	comK1	3.2	$1.27 \times 10^{-6}$	ComK competence transcription factor
SAUPAN005139000	SAUSA300_1939	3.2	$9.72 \times 10^{-5}$	Sa3int prophage encoded protein
SAUPAN000910000	sarS	3.1	$2.14 \times 10^{-7}$	Virulence regulator
SAUPAN004572000	epiG	3.1	$9.94 \times 10^{-8}$	antibiotic epidermin immunity protein F,
SAUPAN004573000	epiE	3.0	$9.35 \times 10^{-7}$	lantibiotic epidermin immunity protein F.
SAUPAN004574000	epiF	3.0	$1.41 \times 10^{-4}$	bacitracin ABC transporter ATP-binding protein
SAUPAN004575000	epiP	3.0	$3.24 \times 10^{-5}$	lantibiotic epidermin. protease EpiP
SAUPAN004939000	SAUSA300_1890	3.0	$1.31 \times 10^{-4}$	Cysteine protease. staphopain
SAUPAN004396000	fhs	3.0	$1.27 \times 10^{-6}$	formate—tetrahydrofolate ligase
SAUPAN004585000	epiA	3.0	$5.98 \times 10^{-5}$	lantibiotic epidermin
SAUPAN003450000	ftsL	3.0	$1.42 \times 10^{-4}$	cell division protein FtsL
SAUPAN001228000	SAUSA300_0307	3.0	$8.15 \times 10^{-6}$	5'-nucleotidase. lipoprotein e(P4) family
SAUSA300_RS10495	-	2.9	$3.04 \times 10^{-3}$	MAP domain-containing protein
SAUPAN004024000	srrB	2.9	$2.67 \times 10^{-5}$	two-component sensor histidine kinase
JKDJBECI_00383	-	2.9	$1.94 \times 10^{-7}$	hypothetical protein
SAUPAN003637000	SAUSA300_1205	2.9	$3.77 \times 10^{-2}$	hypothetical protein
SAUPAN002374000	SAUSA300_0575	2.9	$2.07 \times 10^{-7}$	hypothetical protein
SAUPAN005018000	scn	2.8	$6.20 \times 10^{-4}$	staphylococcal complement inhibitor SCIN
SAUPAN002347000	hxlA	2.8	$1.15 \times 10^{-4}$	putative hexulose-6-phosphate synthase.

SAUSA300_RS13715	-	2.8	$1.10 \times 10^{-5}$	hypothetical membrane protein
SAUPAN006035000	SAUSA300_2416	2.8	$3.08 \times 10^{-6}$	glucose 1-dehydrogenase-like protein
SAUPAN002348000	hxlB	2.8	$3.51 \times 10^{-5}$	6-phospho-3-hexuloisomerase.
SAUPAN002823000	SAUSA300_0793	2.8	$1.10 \times 10^{-4}$	conserved protein.
SAUPAN001865000	SAUSA300_0332	2.8	$3.31 \times 10^{-3}$	Putative PTS transporter.
SAUPAN004576000	epiD	2.6	$3.48 \times 10^{-2}$	lantibiotic epidermin biosynthesis protein EpiD
SAUPAN005023000	sak	2.6	$1.17 \times 10^{-3}$	Sa3int prophage encoded staphylokinase
SAUPAN001971000	SAUSA300_0372	2.6	$1.36 \times 10^{-2}$	conserved protein
SAUPAN004358000	SAUSA300_1653	2.6	$2.58 \times 10^{-3}$	metal-dependent hydrolase
SAUSA300_RS10645	-	2.5	$3.77 \times 10^{-3}$	Sa3int prophage encoded protein
SAUPAN003698000	thrD	2.5	$8.22 \times 10^{-5}$	aspartate kinase
SAUPAN006490000	rnpA	2.5	$3.67 \times 10^{-4}$	ribonuclease P protein component
SAUPAN006028000	SAUSA300_2412	2.5	$5.06 \times 10^{-3}$	conserved protein.
SAUSA300_RS14095	-	2.5	$3.55 \times 10^{-5}$	hypothetical protein
SAUPAN005951000	SAUSA300_2361	2.5	$1.08 \times 10^{-5}$	hypothetical protein
SAUPAN001864000	SAUSA300_0331	2.5	$5.06 \times 10^{-3}$	Putative PTS transporter.
SAUPAN004025000	srrA	2.5	$1.28 \times 10^{-4}$	DNA-binding response regulator
SAUPAN006464000	SAUSA300_2632	2.5	$1.31 \times 10^{-3}$	Conserved membrane protein
SAUPAN003129000	-	2.5	$3.78 \times 10^{-4}$	Membrane protein
SAUPAN005949000	mdeA/SAUSA300_2360	2.4	$3.08 \times 10^{-6}$	Putative efflux pump
SAUPAN000942000	sodM	2.4	$1.32 \times 10^{-3}$	Superoxide dismutase [Mn/Fe] 2
SAUPAN001005000	SAUSA300_0171	2.4	$1.93 \times 10^{-3}$	putative cation transporter
SAUPAN006029000	cntL	2.4	$3.09 \times 10^{-2}$	Staphylopin biosynthesis
SAUPAN002813000	SAUSA300_0785	2.4	$1.54 \times 10^{-2}$	N-acetyltransferase
SAUPAN006197000	cidB	2.4	$4.94 \times 10^{-4}$	holin-like protein CidB
SAUSA300_RS10345	-	2.4	$1.63 \times 10^{-2}$	staphostatin A
SAUPAN003631000	SAUSA300_1203	2.4	$1.93 \times 10^{-2}$	hypothetical protein
SAUPAN005239000	SAUSA300_1980	2.4	$1.89 \times 10^{-3}$	N-acetyltransferase
JKDJBECI_00385	-	2.4	$2.62 \times 10^{-5}$	hypothetical protein
SAUPAN003126000	SAUSA300_0884	2.4	$6.42 \times 10^{-3}$	hypothetical protein
SAUPAN005281000	agrA	2.3	$3.71 \times 10^{-6}$	DNA-binding response regulator
SAUPAN002892000	SAUSA300_0816	2.3	$1.34 \times 10^{-3}$	Conserved protein of unknown function
SAUPAN005048000	-	2.3	$2.36 \times 10^{-3}$	Sa3int prophage protein
SAUPAN006033000	SAUSA300_2415	2.3	$1.26 \times 10^{-3}$	hypothetical protein
SAUPAN002822000	SAUSA300_0792	2.3	$1.36 \times 10^{-2}$	hypothetical protein
JKDJBECI_00384	-	2.3	$1.14 \times 10^{-4}$	hypothetical protein
SAUPAN005192000	lukH	2.3	$4.28 \times 10^{-2}$	succinyl-diaminopimelate desuccinylase
SAUPAN000037000	adsA	2.3	$1.30 \times 10^{-5}$	AdsA nucleotidase
SAUPAN005279000	agrC	2.3	$8.37 \times 10^{-6}$	Quorum sensing
SAUPAN003133000	opp-3B	2.3	$3.67 \times 10^{-4}$	ABC transporter permease
SAUPAN005496000	mtlR/SAUSA300_2106	2.3	$9.14 \times 10^{-3}$	conseved protein
SAUPAN002835000	SAUSA300_0794	2.3	$1.09 \times 10^{-2}$	topiosmerase.
SAUPAN005897000	scrA	2.3	$3.54 \times 10^{-3}$	PTS sucrose transporter subunit IIBC

SAUPAN005275000	<b>agrB</b>	<b>2.3</b>	$1.56 \times 10^{-5}$	accessory gene regulator AgrB
SAUPAN005498000	mtlA	<b>2.3</b>	$5.88 \times 10^{-4}$	mannitol-specific phosphotransferase
SAUSA300_RS10880	-	<b>2.2</b>	$9.14 \times 10^{-3}$	hypothetical protein
SAUPAN001008000	SAUSA300_0172	<b>2.2</b>	$3.51 \times 10^{-2}$	conserved hypothetical protein
SAUPAN003654000	SAUSA300_1210	<b>2.2</b>	$3.97 \times 10^{-3}$	hypothetical protein
SAUPAN005883000	SAUSA300_2315	<b>2.2</b>	$1.35 \times 10^{-2}$	Conserved secreted protein
SAUPAN001034000	murQ	<b>2.2</b>	$3.31 \times 10^{-3}$	N-acetylmuramic acid 6-phosphate etherase
SAUPAN005388000	murA	<b>2.2</b>	$1.49 \times 10^{-3}$	peptidoglycan biosynthesis
SAUPAN002836000	SAUSA300_0795	<b>2.2</b>	$3.35 \times 10^{-2}$	Putative thiol reductase thioredoxin.
SAUPAN002669000	SAUSA300_0739	<b>2.2</b>	$1.89 \times 10^{-3}$	Putative autolysin (CHAP and LysM domain)
SAUSA300_RS03975	prf2	<b>2.2</b>	$1.28 \times 10^{-4}$	peptide chain release factor 2
SAUPAN005915000	narK	<b>2.2</b>	$1.43 \times 10^{-2}$	nitrite extrusion protein
SAUPAN005580000	amaP/SAUSA300_2144	<b>2.2</b>	$4.70 \times 10^{-3}$	hypothetical protein
SAUPAN000894000	norC	<b>2.2</b>	$8.58 \times 10^{-3}$	Efflux pump NorC
SAUPAN006196000	cidC	<b>2.1</b>	$3.25 \times 10^{-4}$	pyruvate oxidase
SAUPAN006107000	sasG	<b>2.1</b>	$1.56 \times 10^{-4}$	LPXTG-motif cell wall anchor
SAUSA300_RS09325	-	<b>2.1</b>	$3.10 \times 10^{-4}$	MarR family transcriptional regulator
SAUPAN003251000	sspA	<b>2.1</b>	$2.73 \times 10^{-4}$	V8 serine protease.
SAUPAN004030000	xerD	<b>2.1</b>	$6.65 \times 10^{-4}$	tyrosine recombinase XerD
SAUPAN001012000	ssuC/SAUSA300_0176	<b>2.1</b>	$1.08 \times 10^{-1}$	ABC transporter permease.
SAUPAN005440000	manA	<b>2.1</b>	$1.28 \times 10^{-4}$	mannose-6-phosphate isomerase.
SAUPAN003692000	SAUSA300_1221	<b>2.1</b>	$1.19 \times 10^{-2}$	conserved protein
SAUPAN004317000	phoP	<b>2.1</b>	$1.58 \times 10^{-3}$	DNA-binding response regulator
SAUPAN001862000	SAUSA300_0329	<b>2.1</b>	$1.67 \times 10^{-2}$	putative oxidoreductase
SAUPAN004046000	SAUSA300_1458	<b>2.1</b>	$1.93 \times 10^{-3}$	conserved protein
SAUPAN002570000	<b>mgrA</b>	<b>2.1</b>	$3.17 \times 10^{-4}$	MarR family transcriptional regulator
SAUPAN003936000	engA	<b>2.1</b>	$2.70 \times 10^{-4}$	ribosome-associated GTPase EngA
SAUPAN003057000	SAUSA300_0858	<b>2.1</b>	$1.34 \times 10^{-4}$	conserved protein
SAUPAN003134000	oppC	<b>2.1</b>	$8.97 \times 10^{-3}$	oligopeptide ABC transporter permease
SAUPAN001123000	tarI/SAUSA300_0245	<b>2.1</b>	$5.71 \times 10^{-4}$	TarI
SAUPAN003451000	pbpA	<b>2.1</b>	$2.29 \times 10^{-2}$	penicillin-binding protein 1
SAUPAN003135000	oppD	<b>2.1</b>	$1.31 \times 10^{-2}$	ABC transporter ATP-binding protein.
SAUPAN005276000	<b>agrD</b>	<b>2.1</b>	$1.36 \times 10^{-2}$	cyclic lactone autoinducer peptide
SAUPAN005500000	mtlD	<b>2.0</b>	$3.00 \times 10^{-3}$	mannitol-1-phosphate 5-dehydrogenase
SAUPAN005274000	<b>Hld/RNAlII</b>	<b>2.0</b>	$8.80 \times 10^{-3}$	delta-hemolysin/RNAlII
SAUPAN005578000	asp23	<b>2.0</b>	$4.94 \times 10^{-3}$	Asp23 envelope stress response protein
SAUPAN005387000	fabZ	<b>2.0</b>	$7.46 \times 10^{-3}$	fatty acid biosynthesis
SAUPAN006489000	trmE	<b>2.0</b>	$1.13 \times 10^{-3}$	tRNA modification GTPase TrmE
SAUPAN002232000	SAUSA300_0471/veg	<b>2.0</b>	$9.89 \times 10^{-3}$	hypothetical protein

SAUPAN003935000	gpsA	2.0	$5.22 \times 10^{-4}$	glycerol-3-phosphate dehydrogenase (NAD(P)(+))
SAUPAN003803000	SAUSA300_1284/cvfB	2.0	$3.15 \times 10^{-3}$	S1 RNA binding domain-containing protein
SAUPAN005439000	SAUSA300_2095	2.0	$9.03 \times 10^{-4}$	conserved protein
SAUPAN001900000	metE	2.0	$1.89 \times 10^{-3}$	homocysteine methyltransferase
SAUPAN002714000	rnr	2.0	$3.76 \times 10^{-3}$	ribonuclease R
SAUPAN001013000	SAUSA300_0177	2.0	$4.00 \times 10^{-2}$	conserved protein.
SAUPAN003808000	dapA	2.0	$3.62 \times 10^{-2}$	4-hydroxy-tetrahydrodipicolinate synthase
SAUPAN004316000	phoR	2.0	$4.41 \times 10^{-3}$	sensor histidine kinase
JKDJBECI_00373	-	2.0	$6.47 \times 10^{-3}$	hypothetical protein
SAUPAN003249000	sspC	2.0	$1.70 \times 10^{-3}$	staphostatin B
SAUPAN006210000	clpL	2.0	$1.88 \times 10^{-2}$	ATP-dependent chaperone ClpL
SAUPAN005803000	glvC	2.0	$1.32 \times 10^{-3}$	PTS alpha-glucoside transporter subunit IIBC
SAUPAN003746000	glcT	0.5	$3.77 \times 10^{-3}$	protein GlcT
SAUPAN002314000	rpoB	0.5	$3.77 \times 10^{-3}$	DNA-directed RNA polymerase subunit beta
SAUPAN006189000	-	0.5	$2.97 \times 10^{-2}$	alpha/beta hydrolase
SAUPAN006326000	cysJ	0.5	$1.56 \times 10^{-2}$	(NADPH) flavoprotein subunit
SAUPAN001981000	ahpF	0.5	$1.51 \times 10^{-2}$	alkyl hydroperoxide reductase subunit F
SAUPAN002328000	-	0.5	$1.93 \times 10^{-2}$	HAD family hydrolase
SAUPAN003440000	psm $\beta$ 1	0.5	$3.96 \times 10^{-2}$	PSM $\beta$ 1
SAUPAN000975000	capB	0.5	$3.35 \times 10^{-2}$	capsular polysaccharide biosynthesis protein Cap5B
SAUPAN003392000	-	0.5	$2.60 \times 10^{-2}$	metal-dependent phosphodiesterase
SAUPAN005723000	-	0.5	$2.63 \times 10^{-2}$	MFS transporter
SAUPAN004195000	-	0.5	$1.15 \times 10^{-2}$	hypothetical protein
SAUPAN006293000	panB	0.5	$1.24 \times 10^{-2}$	hydroxymethyltransferase
SAUPAN005704000	-	0.5	$5.46 \times 10^{-3}$	hypothetical protein
SAUPAN000035000	wall	0.5	$8.12 \times 10^{-3}$	hypothetical protein
SAUPAN006202000	-	0.5	$1.41 \times 10^{-2}$	CHAP domain-containing protein
SAUPAN005444000	cziB	0.5	$3.45 \times 10^{-2}$	cation transporter
SAUPAN002315000	rpoC	0.5	$1.32 \times 10^{-3}$	DNA-directed RNA polymerase subunit beta'
SAUPAN005301000	tseE	0.5	$7.48 \times 10^{-3}$	tRNA (adenosine(37)-N6)-TseE
SAUPAN000935000	galE	0.5	$3.75 \times 10^{-2}$	NAD-dependent dehydratase
SAUPAN002502000	-	0.5	$8.94 \times 10^{-3}$	sodium:proton antiporter
SAUPAN002164000	mpsB	0.5	$3.87 \times 10^{-3}$	hypothetical protein
SAUPAN003241000	-	0.5	$1.44 \times 10^{-2}$	acetyltransferase
SAUPAN006136000	-	0.5	$1.41 \times 10^{-2}$	hypothetical protein
SAUPAN006109000	sarT	0.5	$1.57 \times 10^{-2}$	transcriptional regulator
SAUPAN005268000	sdrH	0.5	$7.94 \times 10^{-3}$	hypothetical protein
SAUPAN005300000	tseB	0.5	$1.37 \times 10^{-2}$	tRNA threonylcarbamoyltransferase c
SAUPAN006292000	panC	0.5	$4.94 \times 10^{-3}$	pantoate—beta-alanine ligase

SAUPAN001869000	mepA	0.5	$4.55 \times 10^{-2}$	multidrug efflux MATE transporter MepA
SAUPAN002252000	ftsH	0.5	$3.86 \times 10^{-4}$	zinc metalloprotease
SAUPAN004943000	-	0.5	$3.58 \times 10^{-2}$	NETI motif-containing protein
SAUPAN001098000	prsS	0.5	$8.31 \times 10^{-3}$	PrsW family intramembrane metalloprotease
SAUPAN006448000	-	0.5	$1.93 \times 10^{-2}$	hypothetical protein
SAUPAN006325000	-	0.5	$2.02 \times 10^{-2}$	precorrin-2 dehydrogenase
SAUPAN001173000	-	0.5	$2.60 \times 10^{-2}$	DUF5080 domain-containing protein
SAUPAN002321000	-	0.5	$2.66 \times 10^{-2}$	N-acetyl-L,L-diaminopimelate deacetylase
SAUPAN005993000	-	0.5	$2.63 \times 10^{-3}$	NAD(P)-dependent oxidoreductase
SAUPAN003787000	opp-2B	0.5	$1.94 \times 10^{-3}$	peptide ABC transporter permease
SAUPAN001984000	nfrA	0.5	$8.31 \times 10^{-3}$	NADPH-dependent oxidoreductase
SAUPAN003331000	mntH	0.5	$7.37 \times 10^{-3}$	divalent metal cation transporter
SAUPAN002533000	-	0.5	$1.41 \times 10^{-2}$	alpha/beta hydrolase
SAUPAN000387000	-	0.5	$1.70 \times 10^{-3}$	LysR family transcriptional regulator
SAUPAN002101000	-	0.5	$2.24 \times 10^{-3}$	membrane protein
SAUPAN002183000	-	0.5	$3.23 \times 10^{-2}$	hypothetical protein
SAUPAN006233000	-	0.5	$3.79 \times 10^{-2}$	N-acetyltransferase
SAUPAN004501000	metK	0.5	$3.00 \times 10^{-3}$	S-adenosylmethionine synthase
SAUPAN006457000	rarD	0.5	$7.64 \times 10^{-4}$	protein RarD
SAUPAN005501000	fmtB	0.5	$7.48 \times 10^{-3}$	hypothetical protein
SAUPAN003171000	pepF	0.5	$2.37 \times 10^{-3}$	oligoendopeptidase F
SAUPAN004277000	tag	0.5	$1.13 \times 10^{-3}$	DNA-3-methyladenine glycosylase I
SAUPAN003441000	psm $\beta$ 2	0.5	$1.31 \times 10^{-3}$	hemolytic protein
SAUPAN005722000	-	0.5	$3.43 \times 10^{-2}$	MarR family transcriptional regulator
SAUPAN002102000	-	0.5	$4.61 \times 10^{-3}$	NAD(P)-dependent oxidoreductase
SAUPAN001102000	opp-5A	0.5	$5.22 \times 10^{-4}$	nickel ABC transporter substrate-binding protein
SAUPAN006159000	fbp	0.5	$8.53 \times 10^{-3}$	fructose 1,6-bisphosphatase
SAUPAN000148000	-	0.4	$3.18 \times 10^{-3}$	hypothetical protein
SAUPAN003257000	-	0.4	$4.62 \times 10^{-4}$	acyltransferase
SAUPAN005997000	opuCD	0.4	$6.78 \times 10^{-4}$	amino acid ABC transporter permease
SAUPAN000938000	-	0.4	$3.31 \times 10^{-3}$	transferase
SAUPAN005998000	opuCC	0.4	$4.44 \times 10^{-4}$	amino acid transporter
SAUPAN005608000	-	0.4	$7.79 \times 10^{-3}$	MerR family transcriptional regulator
SAUPAN006191000	-	0.4	$1.93 \times 10^{-3}$	acyl-CoA thioester hydrolase
SAUPAN005606000	-	0.4	$1.56 \times 10^{-3}$	aldo/keto reductase
SAUPAN001171000	-	0.4	$3.43 \times 10^{-2}$	DUF5079 domain-containing protein
SAUPAN003058000	-	0.4	$1.32 \times 10^{-3}$	NADH-dependent flavin oxidoreductase

SAUPAN000902000	-	0.4	$1.93 \times 10^{-2}$	oleate hydratase
SAUPAN002142000	lpl3	0.4	$4.70 \times 10^{-2}$	tandem-type lipoprotein
SAUPAN005375000	thiD	0.4	$3.77 \times 10^{-3}$	kinase/phosphomethylpyrimidine kinase
SAUPAN002631000	nrdF	0.4	$3.58 \times 10^{-3}$	ribonucleotide-diphosphate reductase subunit beta
SAUPAN006437000	-	0.4	$3.95 \times 10^{-6}$	polysaccharide deacetylase
SAUPAN000902000	-	0.4	$7.88 \times 10^{-3}$	oleate hydratase
SAUPAN003593000	-	0.4	$1.26 \times 10^{-3}$	2-oxoacid ferredoxin oxidoreductase subunit beta
SAUPAN002282000	-	0.4	$8.80 \times 10^{-4}$	PLP-dependent aminotransferase family protein
SAUPAN006177000	-	0.4	$3.24 \times 10^{-5}$	peptide ABC transporter permease
SAUPAN005741000	fdhD	0.4	$1.80 \times 10^{-4}$	sulfurtransferase FdhD
SAUPAN003757000	-	0.4	$3.21 \times 10^{-5}$	DNA repair protein MucB
SAUPAN006190000	-	0.4	$9.72 \times 10^{-5}$	thiol reductase thioredoxin
SAUPAN006420000	gehA	0.4	$2.75 \times 10^{-3}$	Lipase 1
SAUPAN005767000	ssaA	0.4	$4.51 \times 10^{-6}$	CHAP domain-containing protein
SAUPAN005934000	-	0.4	$1.25 \times 10^{-4}$	N-acetyltransferase
SAUPAN001163000	lytM	0.4	$7.59 \times 10^{-4}$	glycyl-glycine endopeptidase LytM
SAUPAN003592000	-	0.4	$7.10 \times 10^{-4}$	2-oxoglutarate ferredoxin oxidoreductase
SAUPAN003680000	-	0.4	$2.69 \times 10^{-5}$	low specificity L-threonine aldolase
SAUPAN003201000	-	0.3	$4.55 \times 10^{-9}$	membrane protein
SAUPAN006322000	nrdD	0.3	$1.98 \times 10^{-2}$	anaerobic ribonucleoside-triphosphate reductase
SAUPAN005999000	opuCB	0.3	$2.71 \times 10^{-3}$	choline ABC transporter permease
SAUPAN006408000	cap1B	0.3	$2.87 \times 10^{-3}$	capsular polysaccharide biosynthesis protein Cap5B
SAUPAN003815000	msa	0.3	$5.43 \times 10^{-6}$	protein msa
SAUPAN006409000	cap1A	0.3	$3.70 \times 10^{-2}$	capsular polysaccharide biosynthesis protein CapA
SAUPAN006176000	-	0.3	$8.40 \times 10^{-4}$	peptide ABC transporter ATP-binding protein
SAUPAN006459000	nixA	0.3	$1.27 \times 10^{-6}$	nickel transporter NixA
SAUPAN005381000	sceD	0.3	$8.80 \times 10^{-4}$	transglycosylase SceD
SAUPAN006218000	-	0.3	$2.16 \times 10^{-5}$	maltose O-acetyltransferase
SAUPAN006000000	opuCA	0.3	$1.21 \times 10^{-8}$	glycine/betaine ABC transporter ATP-binding protein
SAUPAN006366000	argR	0.3	$1.55 \times 10^{-5}$	ArgR family transcriptional regulator
SAUSA300_RS06715	-	0.2	$1.10 \times 10^{-5}$	hypothetical protein
SAUPAN006321000	nrdG	0.2	$1.62 \times 10^{-5}$	anaerobic ribonucleoside-triphosphate reductase activating
NWMN_RS11100	-	0.2	$1.04 \times 10^{-16}$	hypothetical protein
SAUPAN005772000	-	0.2	$1.18 \times 10^{-6}$	CHAP domain-containing protein

SAUPAN005759000	ureD	<b>0.2</b>	$9.35 \times 10^{-26}$	urease accessory protein
SAUPAN005756000	ureE	<b>0.2</b>	$8.85 \times 10^{-23}$	urease accessory protein UreE
SAUPAN005758000	ureG	<b>0.2</b>	$2.88 \times 10^{-23}$	urease accessory protein UreG
SAUPAN005757000	ureF	<b>0.2</b>	$2.23 \times 10^{-26}$	urease accessory protein UreF
SAUPAN005755000	ureC	<b>0.2</b>	$1.72 \times 10^{-21}$	urease subunit alpha
SAUPAN005753000	ureA	<b>0.2</b>	$3.77 \times 10^{-16}$	urease subunit gamma
SAUPAN005754000	ureB	<b>0.2</b>	$3.52 \times 10^{-21}$	urease subunit beta
SAUPAN005752000	-	<b>0.1</b>	$3.08 \times 10^{-18}$	urea transporter
NWMN_RS10980	-	<b>0.0</b>	$6.24 \times 10^{-27}$	hypothetical protein
SAUPAN005109000	-	<b>0.0</b>	$4.93 \times 10^{-26}$	hypothetical protein

\* Genes were considered differentially expressed if they showed a  $\geq 2$ -fold change in expression with  $p_{\text{adj}} < 0.05$ . <sup>A</sup>: RN8242 genes were annotated using the AureoWiki database (<http://aureowiki.med.uni-greifswald.de>) using preferentially the pan-genome gene id and otherwise with identifiers corresponding to the strain-specific gene to which they map. Open reading frames in the RN4282 genome that could not be assigned to any of the five strains in Aureowiki (NCTC 8325, COL. Newman, USA300\_FPR3757, and N315) were annotated using a prokka-generated identifier and reported as hypothetical proteins. <sup>B</sup>: Genes encoding known transcriptional regulators of virulence genes are shown in bold. In case no pan genome symbol was provided in AureoWiki, the gene annotations for the *S. aureus* model strain USA300\_FPR3757 were used. <sup>C</sup>: Fold changes in RN4282 wild type/RN4282clpXI265E are shown (genes expressed  $>2$  fold more in wild-type cells are listed in the top of the table (shaded pink). Genes expressed  $>2$  fold more in RN4282clpXI265E cells are listed in the bottom of the table shaded green).