

**Additional file 1.** Genes found differentially expressed in the *femAB+* backcross BB1305 compared to the wild type BB903. The selection of regulated genes is based on statistical significance of moderated *t*-scores and thus also includes genes with a log<sub>2</sub>(fold change) < |1|. The genes are clustered according to their cellular main role as in the *S. aureus* N315 genome annotation on the DOGAN website ([http://www.bio.nite.go.jp/dogan/MicroTop?GENOME\\_ID=n315](http://www.bio.nite.go.jp/dogan/MicroTop?GENOME_ID=n315), as of September 24, 2006).

CATEGORY		Process	ORF ID	Gene	Product	log <sub>2</sub> (fold change)	p-value				
<b>CELL ENVELOPE AND CELLULAR PROCESSES</b>											
<b>Cell wall</b>											
<u>down</u>											
SA0793	<i>dltA</i>	D-alanine-D-alanyl carrier protein ligase				-1.03	0.02				
SA1283	<i>pbpB</i>	PBP2				-0.47	0.04				
<b>Membrane bioenergetics (electron transport chain and ATP synthase)</b>											
<u>down</u>											
SA0937		cytochrome D ubiquinol oxidase subunit 1 homologue				-0.70	<0.005				
<u>up</u>											
SA0210		hypothetical protein, similar to NADH-dependent dehydrogenase				1.84	<0.005				
SA0211		hypothetical protein, similar to NADH-dependent dehydrogenase				1.65	<0.005				
<b>Transport / binding proteins and lipoproteins</b>											
<u>down</u>											
SA0617	<i>vraG</i>	ABC transporter permease				-0.80	0.04				
SA0640		hypothetical protein, similar to ABC transporter required for expression of cytochrome bd				-0.57	0.04				
SA0655	<i>fruA</i>	fructose specific permease				-1.28	0.01				
SA0691		lipoprotein, similar to ferrichrome ABC transporter				-0.77	0.02				
SA0794	<i>dltB</i>	DltB membrane protein				-1.30	0.01				
SA0796	<i>dltD</i>	poly(glycerophosphate chain) D-alanine transfer protein				-1.38	<0.005				
SA0950	<i>potA</i>	spermidine/putrescine ABC transporter, ATP-binding protein homologue				-0.43	0.03				
SA1042	<i>pyrP</i>	uracil permease				-2.37	<0.005				
SA1183	<i>opuD</i>	glycine betaine transporter				-0.83	0.03				
SA1269		Blt-like protein				-1.47	<0.005				
SA1270		hypothetical protein, similar to amino acid permease				-1.10	0.01				
SA1505	<i>lysP</i>	lysine-specific permease				-0.92	0.01				
SA1893		lipoprotein precursor				-0.75	0.02				
SA1987		glycine betaine transporter <i>opuD</i> homologue				-1.07	0.02				
SA2303		hypothetical protein, similar to membrane spanning protein				-1.50	0.01				
SA2339		hypothetical protein, similar to antibiotic transport-associated protein				-1.68	<0.005				
<u>up</u>											
SA0186		hypothetical protein, similar to sucrose phosphotransferase enzyme II				1.40	0.02				
SA0208		maltose/maltodextrin transport permease homologue				1.49	<0.005				
SA0209		maltose/maltodextrin transport permease homologue				2.02	<0.005				
SA0260		hypothetical protein, similar to ribose transporter RbsU				0.66	0.01				
SA0318		hypothetical protein, similar to transport protein SgaT				1.53	<0.005				

CATEGORY			
Process			
ORF ID	Gene	Product	
SA0320		hypothetical protein, similar to PTS fructose-specific enzyme IIBC component	2.26 <0.005
SA0599		ATP-binding cassette transporter A	0.45 0.04
SA1140	<i>glpF</i>	glycerol uptake facilitator	1.39 <0.005
SA2167	<i>scrA</i>	PTS system, sucrose-specific IIBC component	0.70 0.02
SA2235	<i>opuCC</i>	glycine betaine/carnitine/choline ABC transporter (osmoprotec) <i>opuCC</i>	0.90 0.01
SA2426	<i>arcD</i>	arginine/ornithine antiporter	1.37 <0.005
<b>INFORMATION PATHWAYS</b>			
<b>DNA modification and repair</b>			
<u>up</u>			
SA1512		hypothetical protein, similar to formamidopyrimidine-DNA glycosylase	0.51 0.04
<b>DNA recombination</b>			
<u>up</u>			
SA1313		probable ATP-dependent DNA helicase RecQ	0.61 0.02
<b>DNA replication</b>			
<u>up</u>			
SA1525	<i>dnaE</i>	DNA polymerase III, alpha chain	0.66 <0.005
<b>Protein folding</b>			
<u>down</u>			
SA1409	<i>dnaK</i>	DnaK protein (HSP70)	-0.71 <0.005
<u>up</u>			
SA1659	<i>prsA</i>	peptidyl-prolyl cis/trans isomerase homologue	1.03 0.01
<b>Protein synthesis</b>			
<u>down</u>			
SA0009	<i>serS</i>	seryl-tRNA synthetase	-0.75 0.02
SA0475	<i>lysS</i>	lysyl-tRNA synthetase	-0.56 <0.005
SA0496	<i>rplA</i>	50S ribosomal protein L1 (BL1)	-0.62 0.04
SA0959		GTP-binding elongation factor homologue	-0.76 0.03
SA1456	<i>aspS</i>	aspartyl-tRNA synthetase	-0.86 0.03
SA2041	<i>rpsC</i>	30S ribosomal protein S3	-0.73 0.01
<b>RNA synthesis</b>			
<u>down</u>			
SA0501	<i>rpoC</i>	RNA polymerase beta-prime chain	-0.55 0.01
SA1041	<i>pyrR</i>	pyrimidine operon repressor chain A	-1.80 <0.005
SA1956		lytic regulatory protein truncated with Tn554	-0.82 0.03
<u>up</u>			
SA0187		hypothetical protein, similar to transcription regulator	1.90 <0.005
SA0321		hypothetical protein, similar to transcription antiterminator BglG family	2.52 <0.005
SA1339	<i>malR</i>	maltose operon transcriptional repressor	2.07 <0.005
SA1700	<i>vraR</i>	two-component response regulator	0.38 0.05
SA1847	<i>scrR</i>	sucrose operon repressor	0.63 0.01
SA2295	<i>gntR</i>	gluconate operon transcriptional repressor	1.49 0.02
SA2320		hypothetical protein, similar to regulatory protein PfoR	1.08 0.03
SA2424		hypothetical protein, similar to transcription regulator Crp/Fnr family protein	1.28 <0.005

CATEGORY					
Process					
ORF ID	Gene	Product		log <sub>2</sub> (fold change)	p-value
<b>INTERMEDIARY METABOLISM</b>					
<b>Metabolism of lipids</b>					
<u>down</u>					
SA0548	<i>mvaD</i>	mevalonate diphosphate decarboxylase		-0.62	0.02
SA0843	<i>fab</i>	3-oxoacyl-[acyl-carrier-protein] synthase		-0.81	0.03
SA1073	<i>fabD</i>	malonyl CoA-acyl carrier protein transacylase		-0.60	0.01
SA1074	<i>fabG</i>	3-oxoacyl-(acyl-carrier protein) reductase		-0.65	<0.005
<u>up</u>					
SA0220		hypothetical protein, similar to glycerophosphodiester phosphodiesterase		0.84	<0.005
SA0820	<i>glpQ</i>	glycerophosphoryl diester phosphodiesterase		0.59	0.03
SA2349	<i>crtM</i>	squalene synthase		0.79	0.01
<b>Metabolism of amino acids and related molecules</b>					
<u>down</u>					
SA1150	<i>glnA</i>	glutamine-ammonia ligase		-1.03	<0.005
SA1271		threonine deaminase IlvA homologue		-0.99	<0.005
SA1272		alanine dehydrogenase		-1.14	<0.005
SA1608	<i>metK</i>	S-adenosylmethionine synthetase		-0.49	0.04
SA1858	<i>ilvD</i>	dihydroxy-acid dehydratase		-0.80	0.03
SA1859	<i>ilvB</i>	acetolactate synthase large subunit		-1.18	0.05
SA2125		hypothetical protein, similar to formiminoglutamate		-0.79	0.04
<u>up</u>					
SA1012	<i>argF</i>	ornithine carbamoyltransferase		1.57	<0.005
SA2082	<i>ureA</i>	urease gamma subunit		1.73	<0.005
SA2086	<i>ureF</i>	urease accessory protein UreF		0.88	0.01
SA2121	<i>hutL</i>	imidazolonepropionate		1.39	0.04
SA2122	<i>hutU</i>	urocanate hydratase		2.00	<0.005
SA2318		hypothetical protein, similar to L-serine dehydratase		0.85	<0.005
SA2319		hypothetical protein, similar to beta-subunit of L-serine dehydratase		0.69	0.01
SA2425	<i>arcC</i>	carbamoyl kinase		1.49	<0.005
SA2427	<i>arcB</i>	ornithine transcarbamoylase		1.65	<0.005
SA2428	<i>arcA</i>	arginine-deiminase		2.04	<0.005
<b>Metabolism of carbohydrates and related molecules</b>					
<u>down</u>					
SA1088	<i>sucC</i>	succinyl-CoA synthetase (beta subunit)		-0.99	<0.005
SA1089	<i>sucD</i>	succinyl-CoA synthetase (alpha subunit)		-0.91	<0.005
<u>up</u>					
SA0143	<i>adhE</i>	alcohol-acetaldehyde dehydrogenase		0.85	0.01
SA0258	<i>rbsK</i>	probable ribokinase		0.71	<0.005
SA0304	<i>nanA</i>	N-acetylneuraminate lyase subunit		1.73	<0.005
SA0305		hypothetical protein, similar to glucokinase		1.50	<0.005
SA0433		alpha-glucosidase		1.53	0.01
SA1142	<i>glpD</i>	aerobic glycerol-3-phosphate dehydrogenase		1.10	0.04
SA1338	<i>malA</i>	alpha-D-1,4-glucosidase		1.17	<0.005
SA1556	<i>acuC</i>	acetoin utilization protein		1.71	0.04
SA2294	<i>gntK</i>	gluconokinase		1.66	<0.005
SA2304	<i>fbp</i>	fructose-bisphosphatase		0.90	0.01

CATEGORY	Process	ORF ID	Gene	Product	$\log_2(\text{fold change})$	p-value
<b>Metabolism of coenzymes and prosthetic groups</b>						
	<u>up</u>	SA1259	<i>dfrA</i>	dihydrofolate reductase	0.62	<0.005
<b>Metabolism of nucleotides and nucleic acids</b>						
	<u>down</u>	SA0016	<i>purA</i>	adenylosuccinate synthase	-1.13	0.03
		SA1043	<i>pyrB</i>	aspartate transcarbamoylase chain A	-2.02	<0.005
		SA1044	<i>pyrC</i>	dihydroorotate	-2.67	<0.005
		SA1046	<i>pyrAB</i>	carbamoyl-phosphate synthase large chain	-1.85	0.01
		SA1048	<i>pyrE</i>	orotate phosphoribosyltransferase	-1.78	0.01
	<u>up</u>	SA0131	<i>pnp</i>	purine nucleoside phosphorylase	0.83	<0.005
		SA1013		hypothetical protein, similar to carbamate kinase	2.18	0.01
		SA2410	<i>nrdD</i>	anaerobic ribonucleoside-triphosphate reductase	0.96	<0.005
<b>NO SIMILARITY</b>						
	<u>up</u>	SA0663		hypothetical protein	1.13	<0.005
		SA1210		hypothetical protein	0.58	0.02
		SA1476		hypothetical protein	1.95	<0.005
<b>OTHER FUNCTIONS</b>						
<b>Adaption to atypical conditions</b>						
	<u>up</u>	SA0147	<i>capD</i>	capsular polysaccharide synthesis enzyme Cap5D	0.81	<0.005
<b>Detoxification</b>						
	<u>up</u>	SA1238		hypothetical protein, similar to tellurite resistance protein	0.54	0.04
<b>Miscellaneous</b>						
	<u>down</u>	SA1193	<i>fmtC</i>	oxacillin resistance-related FmtC protein	-1.12	<0.005
<b>Pathogenic factors (toxins and colonization factors)</b>						
	<u>down</u>	SA0587		lipoprotein, streptococcal adhesin PsaA homologue	-0.55	0.01
	<u>up</u>	SA0091	<i>plc</i>	1-phosphatidylinositol phosphodiesterase precursor	1.69	0.02
		SA0900	<i>sspB</i>	cysteine protease precursor	1.07	0.02
		SA1007		alpha-hemolysin precursor	1.64	0.02
		SA1630	<i>splB</i>	serine protease SplB [Pathogenicity island SaPIn3]	2.48	<0.005
		SA1752	<i>(hlb)</i>	truncated beta-hemolysin	1.96	0.01
		SA1811	<i>(hlb)</i>	truncated beta-hemolysin	2.06	<0.005
		SA1813		hypothetical protein, similar to leukocidin chain LukM precursor	1.64	0.04
		SA2430	<i>aur</i>	zinc metalloproteinase aureolysin	2.05	0.01
		SA2463	<i>lip</i>	triacylglycerol lipase precursor	1.68	<0.005

CATEGORY		Process	ORF ID	Gene	Product			
				$\log_2(\text{fold change})$		<i>p</i> -value		
<b>Phage-related functions</b>								
<u>up</u>								
SA0252	<i>lrgA</i>	holin-like protein LrgA				1.24	0.03	
SA0754		hypothetical protein, similar to lactococcal prophage ps3 protein 05				1.26	0.01	
SA1782		hypothetical protein [Bacteriophage phiN315]				1.92	<0.005	
SA1785		hypothetical protein [Bacteriophage phiN315]				2.27	<0.005	
SA1786		hypothetical protein [Bacteriophage phiN315]				2.29	<0.005	
SA1797		hypothetical protein [Bacteriophage phiN315]				2.56	<0.005	
SAS063		hypothetical protein [Bacteriophage phiN315]				2.08	<0.005	
<b>Transposon and IS</b>								
<u>up</u>								
SA2387	<i>tnpB</i>	transposition regulatory protein TnpB - <i>S. aureus</i> transposon Tn554				1.21	0.04	
<b>SIMILAR TO UNKNOWN PROTEINS</b>								
<u>down</u>								
SA0100		conserved hypothetical protein				-0.66	<0.005	
SA0477		conserved hypothetical protein				-1.47	<0.005	
SA0701		conserved hypothetical protein				-0.51	0.03	
SA1536		conserved hypothetical protein				-0.72	0.01	
SA2143		conserved hypothetical protein				-0.82	0.02	
SA2305		conserved hypothetical protein				-0.67	0.03	
SA2328		conserved hypothetical protein				-0.42	0.02	
<u>up</u>								
SA0184		conserved hypothetical protein				2.35	<0.005	
SA0185		conserved hypothetical protein				2.43	<0.005	
SA0789		conserved hypothetical protein				0.54	0.04	
SA1014		conserved hypothetical protein				1.54	<0.005	
SA1258		conserved hypothetical protein				0.43	0.04	
SA1661		conserved hypothetical protein				0.45	0.05	
SA1690		conserved hypothetical protein				0.60	0.01	