

Supplemental Information for:

Critical Roles of Arginine in Growth and Biofilm Development by *Streptococcus gordonii*

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Jakubovics *et al.*, Supplemental figure S1

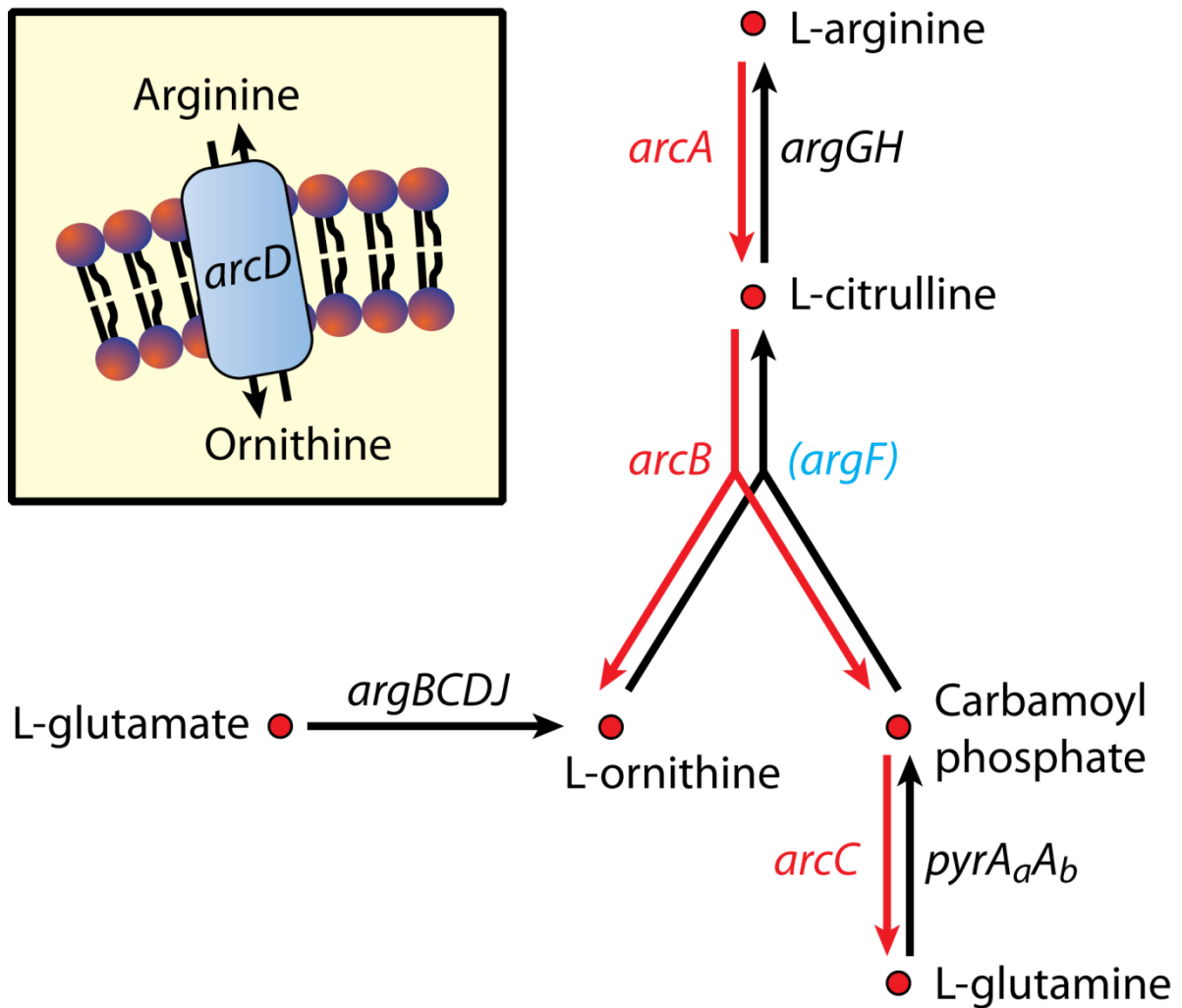


Figure S1. Genes involved in arginine metabolism and transport in *S. gordonii*. The pathways for arginine biosynthesis and catabolism are indicated by black and red arrows, respectively. Genes encoding enzymes in the pathway are shown in black (biosynthetic genes) or red (catabolism genes), and the *argF* gene which is not present in *S. gordonii*, is in parantheses and coloured blue. Inset shows the predicted function of the *arcD* gene product as an arginine-ornithine antiporter.

Jakubovics *et al.*, Supplemental figure S3

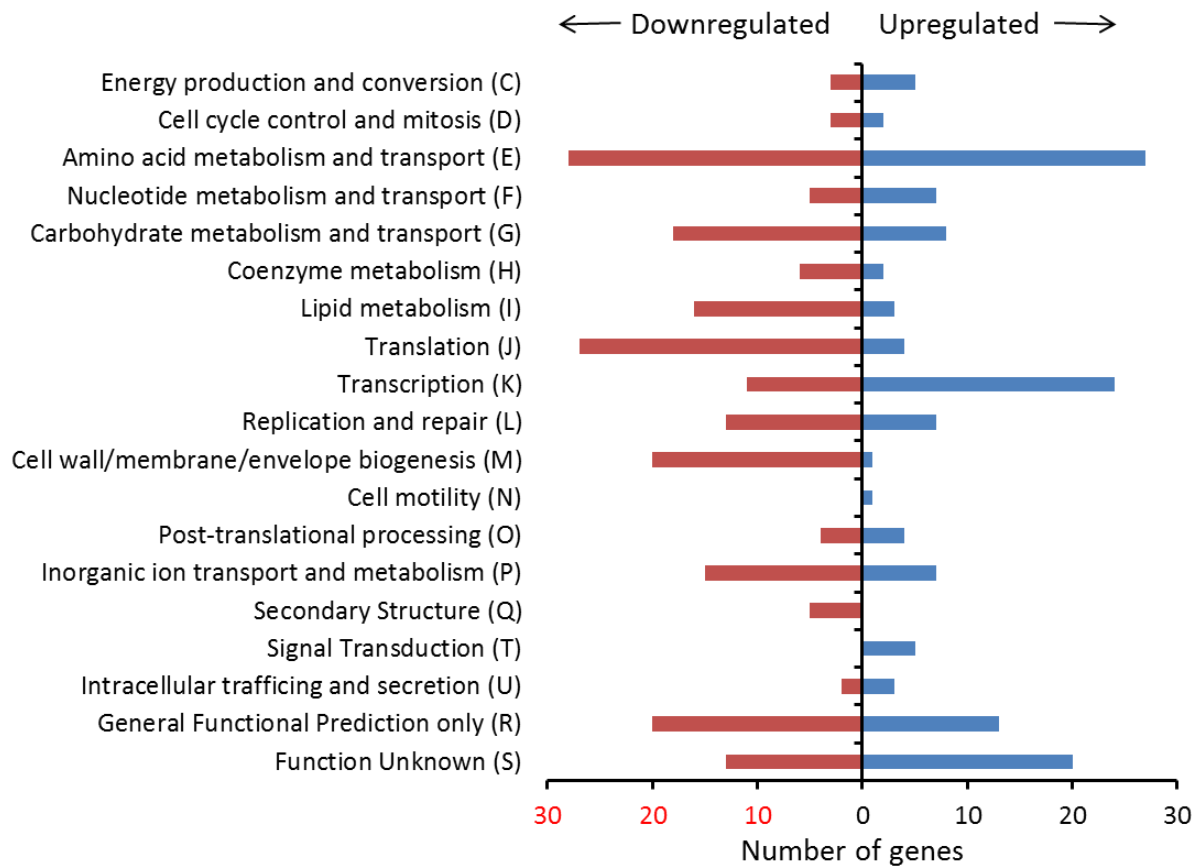


Figure S3. Total number of genes in COGFun categories that were regulated in response to arginine depletion by microarray analysis. Groups of genes that were up- or down-regulated in no arginine compared with high arginine are shown.

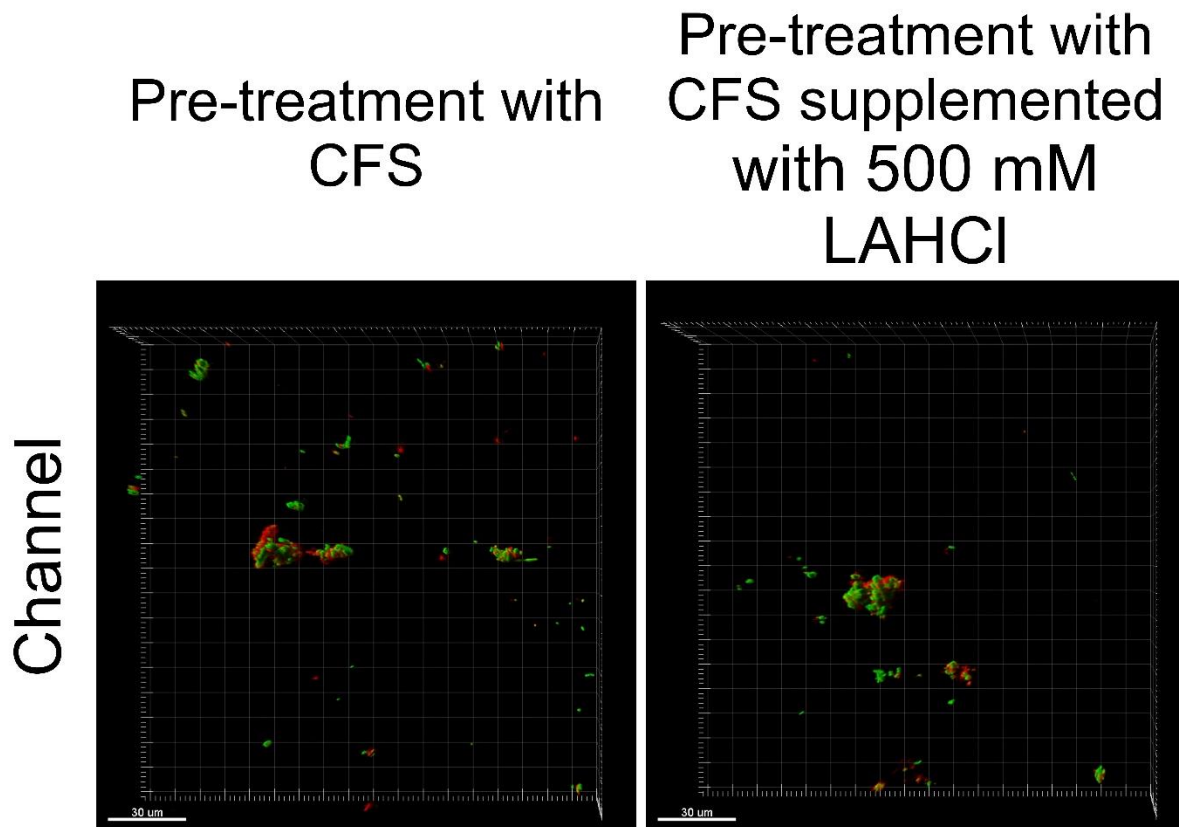


Figure S4. Effects of L-arginine on initial colonisation of *S. gordonii* in the microfluidics biofilm model. Images show two representative Bioflux channels: one that was pre-treated with cell free saliva (CFS) before inoculation with *S. gordonii* (left panel), and one that was pre-treated with CFS supplemented with 500 mM L-arginine monohydrochloride before inoculation with *S. gordonii* (right panel). After inoculation, the cells within the channels were immediately treated with LIVE/DEAD stain, and visualized by confocal laser scanning microscopy.

Jakubovics *et al.*, Supplemental figure S5

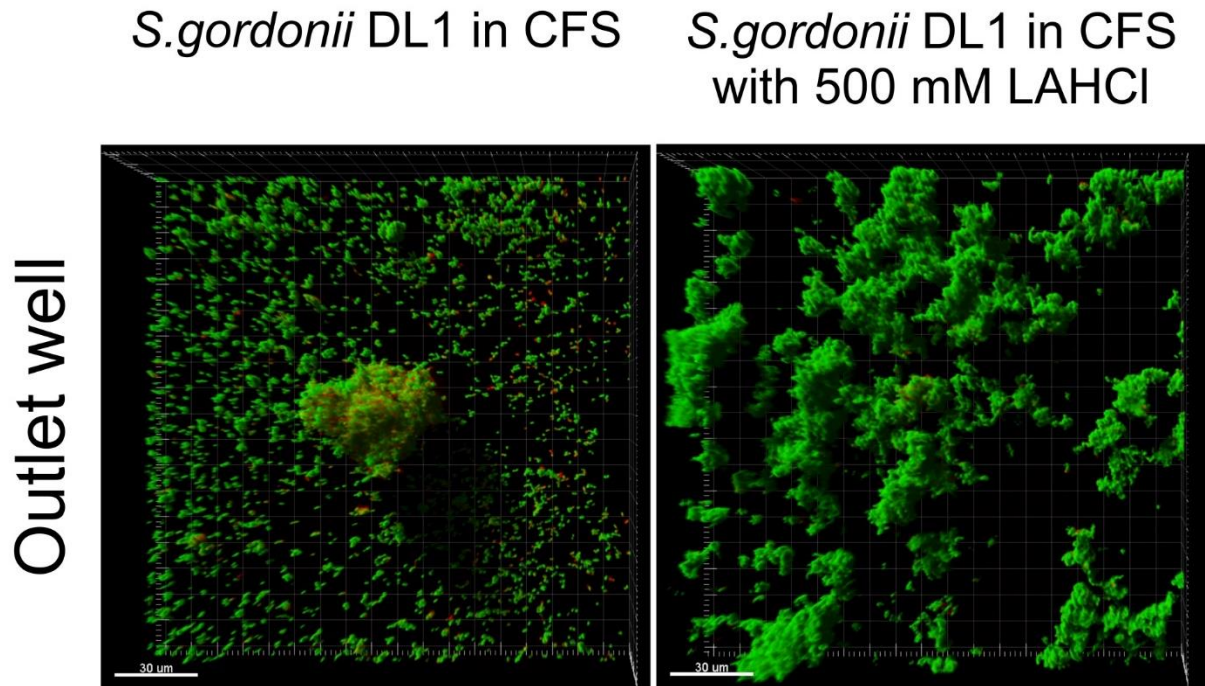


Figure S5. Accumulation of *S. gordonii* cells in the effluent from the microfluidics model system. Images show two representative Bioflux outlet wells: one containing effluent *S. gordonii* DL1 cells after 20 hour growth in cell free saliva (CFS, left panel), and one containing effluent *S.gordonii* DL1 cells after 20 hour growth in cell free saliva supplemented with 500 mM L-arginine monohydrochloride (LAHCL, right panel). Following growth, cells were treated with LIVE/DEAD stain, and visualised by confocal laser scanning microscopy.

Jakubovics *et al.*, Supplemental figure S6

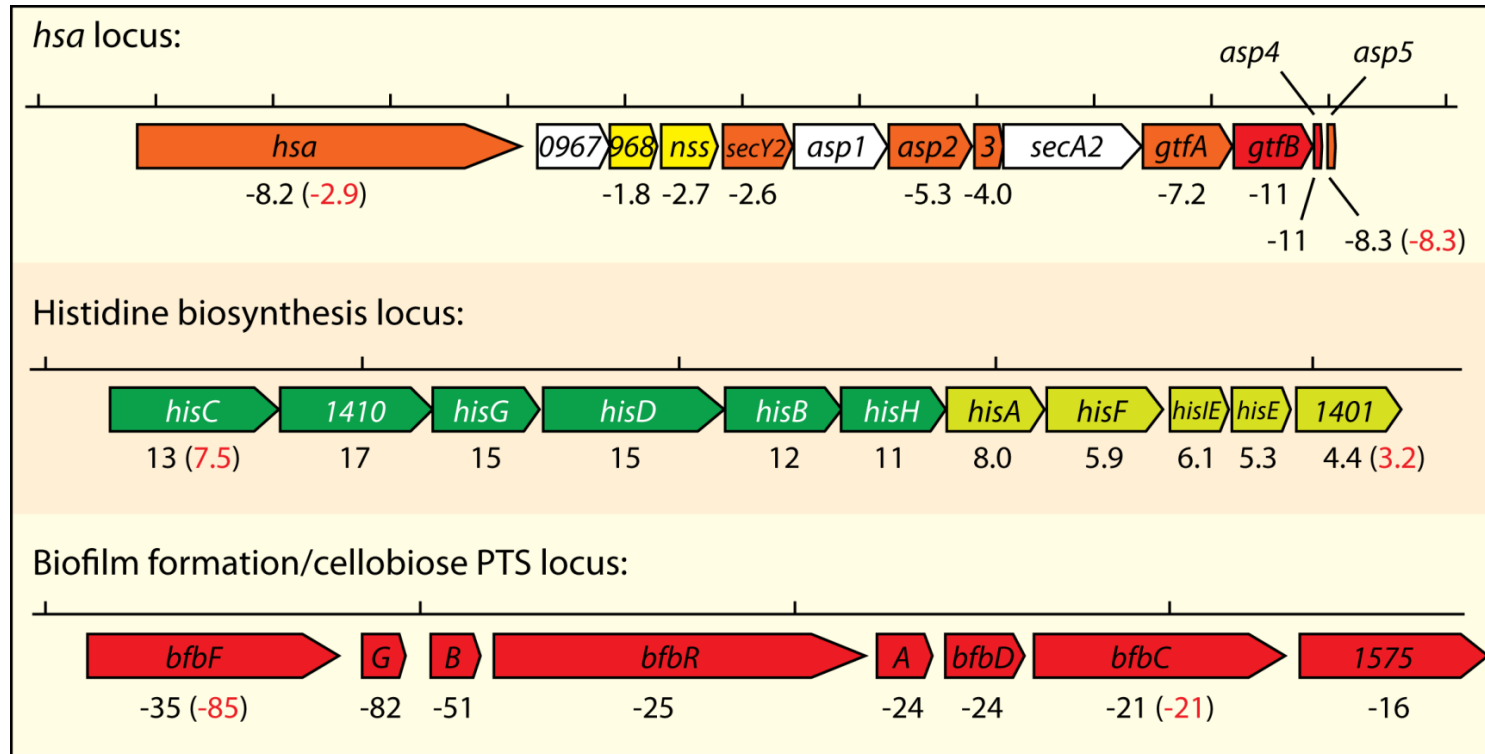


Figure S6. Gene expression across selected multi-gene loci. The genes within the *hsa* locus (SGO_0966-SGO_0978), the histidine biosynthesis locus (SGO_1401-SGO_1411) and the biofilm formation/cellobiose PTS locus (SGO_1575-SGO_1582) are shown. The colour coding of genes is based on data from microarray analysis and indicates the following responses to a shift from 0.5 mM arginine to no arginine: >10-fold down-regulation, red; between 2- and 10-fold down-regulation, orange; not significantly regulated, yellow; >10-fold up-regulation, dark green; between 2- and 10-fold up-regulation, light green; not analysed by microarray, white. Relative gene expression levels are given below each gene, and negative values indicate down-regulation in response to arginine depletion. The expression of selected genes was also measured by qRT-PCR and values are shown in red in parentheses. The scale bars indicate 2 kbp between each marker.

Jakubovics *et al.*, Supplemental table S1

Table S1. Complete list of genes that were significantly regulated in response to arginine depletion. Operon structures were predicted on the basis of gene orientation and expression data. Consecutive genes predicted to be within operons are presented in the same colour (white or yellow). Clusters of orthologous groups based on predicted function (COGFun) categories are defined in the legend to Fig. S3.

Locus_tag	Gene Name	Fold Change	Strand	COGFun	Description
SGO_0014	pgsA	-2.92	+	I	CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyltransferase
SGO_0015	cbiO	-3.78	+	P	ABC transporter (ATP-binding protein)
SGO_0016	cbiO	-5.69	+	P	ABC transporter ATP-binding protein
SGO_0017	SGO_0017	-6.10	+	P	ABC-type putative cobalt transport system, permease
SGO_0021	SGO_0021	26.67	+		hypothetical protein
SGO_0042	SGO_0042	2.65	-	K	transcription regulator, GntR family
SGO_0053	SGO_0053	2.87	+		hypothetical protein
SGO_0079	SGO_0079	2.41	+		hypothetical protein
SGO_0089	SGO_0089	5.49	+	P	cation efflux system protein
SGO_0090	SGO_0090	9.79	-	K	transcriptional regulator, TetR family
SGO_0091	SGO_0091	36.62	+	S	integral membrane protein
SGO_0092	SGO_0092	12.28	+		hypothetical protein
SGO_0093	SGO_0093	10.64	+		hypothetical protein
SGO_0094	SGO_0094	4.48	+		lipoprotein, putative
SGO_0095	mccF	3.17	-	V	microcin immunity protein MccF, putative
SGO_0117	SGO_0117	2.37	+		hypothetical protein
SGO_0133	SGO_0133	-2.42	+	C	ATP synthase (F/14-kDa) subunit
SGO_0136	SGO_0136	-3.62	+	C	v-type sodium ATP synthase, chain B
SGO_0138	SGO_0138	3.57	+		LysM domain protein
SGO_0141	SGO_0141	-3.44	+	R	hydrolase, haloacid dehalogenase-like family

SGO_0157	SGO_0157	4.04	+		hypothetical protein
SGO_0171	radA	-2.21	+	O	DNA repair protein RadA
SGO_0172	SGO_0172	-2.65	+	S	conserved hypothetical protein TIGR00266
SGO_0173	SGO_0173	-2.44	+	P	Carbonic anhydrase
SGO_0175	argG	269.33	+	E	argininosuccinate synthase
SGO_0176	argH	207.89	+	E	argininosuccinate lyase
SGO_0177	SGO_0177	342.42	+		hypothetical protein
SGO_0178	rnpA	4.22	+	J	ribonuclease P protein component
SGO_0179	SGO_0179	4.08	+	U	Membrane protein oxaA 1 precursor
SGO_0180	jag	3.03	+	R	hypothetical protein
SGO_0181	SGO_0181	2.87	+		lipoprotein, putative
SGO_0182	sapR	2.59	+		sakacin A production response regulator
SGO_0185	SGO_0185	3.33	-	K	transcription regulator-like protein yozG
SGO_0186	SGO_0186	2.32	-		hypothetical protein
SGO_0204	rpsL	-3.74	+	J	ribosomal protein S12
SGO_0205	rpsG	-3.40	+	J	ribosomal protein S7
SGO_0228	SGO_0228	2.37	+	K	transcription regulator, MerR family
SGO_0235	SGO_0235	-2.72	+	G	glycerol uptake facilitator protein-like protein
SGO_0236	SGO_0236	-2.33	+	S	hypothetical protein
SGO_0238	SGO_0238	-2.77	+	V	beta-lactamase-like or putative esterase
SGO_0242	SGO_0242	-3.43	+	C	FMN-dependent dehydrogenase family protein
SGO_0243	SGO_0243	-3.58	-	I	hydroxymethylglutaryl-CoA reductase, degradative
SGO_0253	SGO_0253	-4.05	-		hypothetical protein
SGO_0254	SGO_0254	-2.84	-	L	helicase, RecD/TraA family
SGO_0280	trzA	2.99	+	FR	ethylmeline chlorohydrolase
SGO_0288	SGO_0288	-2.01	+	E	GDSL-like lipase/acylhydrolase
SGO_0297	arb	2.62	+	G	6-phospho-beta-glucosidase
SGO_0300		4.77	-		hypothetical protein

SGO_0301	SGO_0301	9.60	-	V	ABC transporter ATP-binding protein-like protein
SGO_0303	SGO_0303	2.88	-	V	ABC transporter ATP-binding protein-like protein
SGO_0322	SGO_0322	-3.69	+		hypothetical protein
SGO_0323	SGO_0323	-6.93	+	J	pseudouridine synthase rRNA-specific
SGO_0334	SGO_0334	4.91	-	I	cinnamoyl ester hydrolase, putative
SGO_0337	trx	5.27	+		thioredoxin
SGO_0339	SGO_0339	3.45	-		hypothetical protein
SGO_0340	SGO_0340	2.06	+	R	hypothetical protein
SGO_0354	SGO_0354	2.09	-	S	membrane spanning protein
SGO_0360	SGO_0360	3.82	-	L	site-specific recombinase, phage integrase family
SGO_0368	merA	3.32	+	C	mercury(II) reductase
SGO_0391	SGO_0391	-2.13	+	G	phosphoglycerate mutase
SGO_0395	SGO_0395	2.10	+	K	transcriptional regulator, Cro/C1 family
SGO_0396	SGO_0396	3.67	+	K	Transcriptional regulator, PadR family
SGO_0397	SGO_0397	3.98	+		hypothetical protein
SGO_0398	SGO_0398	2.55	+	V	ABC transporter ATP-binding protein
SGO_0405	SGO_0405	2.74	+	G	Beta-N-acetylhexosaminidase precursor
SGO_0408	zmpB	-4.72	+		zinc metalloproteinase B
SGO_0410	SGO_0410	3.32	+	S	integral membrane protein
SGO_0414	SGO_0414	2.77	+	S	hypothetical protein
SGO_0415	secA	2.51	+	U	preprotein translocase, SecA subunit
SGO_0417	acpS	3.18	+	I	holo-(acyl-carrier-protein) synthase
SGO_0418	alr	2.26	+	M	alanine racemase
SGO_0427	SGO_0427	6.77	-	T	universal stress protein family
SGO_0428	SGO_0428	2.53	+		hypothetical protein
SGO_0430	SGO_0430	3.21	+		LPXTG cell wall surface protein
SGO_0431	SGO_0431	-4.79	+	K	GTP-sensing transcriptional pleiotropic repressor codY
SGO_0432	entB	-4.52	+	Q	isochorismatase family protein

SGO_0434	aspS	-3.13	+	J	aspartyl-tRNA synthetase
SGO_0437	gatB	-3.74	+	J	glutamyl-tRNA(Gln) amidotransferase, B subunit
SGO_0438	SGO_0438	-2.43	+		hypothetical protein
SGO_0447	nadD	-2.03	+	H	nicotinate (nicotinamide) nucleotide adenylyltransferase
SGO_0449	SGO_0449	-2.19	+	Q	isochorismatase family protein
SGO_0450	SGO_0450	-2.81	+	S	iojap-related protein
SGO_0451	SGO_0451	-4.39	+		methyltransferase
SGO_0452	SGO_0452	-3.86	+	R	hypothetical protein
SGO_0453	SGO_0453	-2.91	+		lipoprotein, putative
SGO_0465	SGO_0465	-2.32	+		hypothetical protein
SGO_0467	SGO_0467	-3.53	+	P	ATP binding protein of ABC transporter
SGO_0477	SGO_0477	2.01	-	R	cell wall binding protein
SGO_0489	SGO_0489	-2.60	+	P	cobalt transport family protein
SGO_0490	SGO_0490	-2.31	+		CAAX amino terminal protease family
SGO_0493	SGO_0493	2.12	-	K	transcriptional regulator, TetR family, putative
SGO_0496	rgg	5.55	+		transcriptional regulator Rgg
SGO_0500	rggD	2.14	-		putative transcriptional regulator RggD
SGO_0506	rgfB	-9.08	+	R	RgfB
SGO_0508	nrdR	3.59	+	K	transcriptional regulator, NrdR family
SGO_0509	SGO_0509	2.52	+	L	Replication initiation and membrane attachment protein (DnaB) superfamily
SGO_0515	murC	-2.47	+	M	UDP-N-acetylmuramate--alanine ligase
SGO_0523	SGO_0523	3.31	+	J	spoU rRNA Methylase family protein
SGO_0524	SGO_0524	3.11	+	R	HD domain protein
SGO_0526	ilvB	-3.37	+	EH	acetolactate synthase, large subunit, biosynthetic type
SGO_0527	ilvH	-2.99	+	E	acetolactate synthase, small subunit
SGO_0528	ilvC	-2.79	+	EH	ketol-acid reductoisomerase
SGO_0529	ilvA	-3.77	+	E	threonine dehydratase
SGO_0553	SGO_0553	2.15	+		acetyltransferase

SGO_0558	SGO_0558	-2.07	+		hypothetical protein
SGO_0560	hsdM	-2.32	+	V	type I restriction-modification system, M subunit
SGO_0561	SGO_0561	3.71	+		hypothetical protein
SGO_0562	SGO_0562	3.98	+	R	Helix-turn-helix domain protein
SGO_0563	SGO_0563	3.70	+		hypothetical protein
SGO_0564	SGO_0564	3.41	+		hypothetical protein
SGO_0567	SGO_0567	-5.64	+		hypothetical protein
SGO_0568	glyQ	-4.79	+	J	glycyl-tRNA synthetase, alpha subunit
SGO_0569	glyS	-5.94	+	J	glycyl-tRNA synthetase, beta subunit
SGO_0570	SGO_0570	-3.15	+	S	hypothetical protein
SGO_0571	SGO_0571	4.12	-		hypothetical protein
SGO_0572	SGO_0572	4.99	-	K	transcription regulator
SGO_0575	pbp2X	-3.74	+	M	penicillin-binding protein 2X
SGO_0576	mraY	-4.41	+	M	phospho-N-acetylmuramoyl-pentapeptide-transferase
SGO_0580	SGO_0580	-4.92	+		hypothetical protein
SGO_0589	SGO_0589	3.90	+		methylase
SGO_0596	priA	2.46	+	L	primosomal protein N''
SGO_0597	fmt	2.01	+	J	methionyl-tRNA formyltransferase
SGO_0601	SGO_0601	3.90	+	S	hypothetical protein
SGO_0602	SGO_0602	4.88	+	T	histidine kinase
SGO_0624	SGO_0624	8.86	-		hypothetical protein
SGO_0637	SGO_0637	-2.67	+	J	acetyltransferase, GNAT family
SGO_0639	valS	-3.10	+	J	valyl-tRNA synthetase
SGO_0643	SGO_0643	-2.90	+	L	cytosine-specific methyltransferase
SGO_0645	SGO_0645	32.39	-		hypothetical protein
SGO_0646	SGO_0646	36.26	-		hypothetical protein
SGO_0647	SGO_0647	42.30	-	L	ImpB/MucB/SamB family protein
SGO_0648	SGO_0648	54.12	-	K	putative transcriptional repressor

SGO_0665	SGO_0665	3.92	+	P	non-heme iron-containing ferritin
SGO_0666	SGO_0666	3.11	+	S	Bacterial protein of unknown function (DUF910) family
SGO_0667	SGO_0667	2.76	+	P	rhodanese family protein
SGO_0681	ileS	-11.12	+	J	isoleucyl-tRNA synthetase
SGO_0682	SGO_0682	4.91	-	K	transcription regulator
SGO_0684	SGO_0684	2.91	-		hypothetical protein
SGO_0685	SGO_0685	2.49	-	LR	MutT/nudix family protein
SGO_0687	SGO_0687	4.20	+	S	hypothetical protein
SGO_0688	SGO_0688	3.77	-	O	ATP dependent Clp protease, ATP-binding subunit, ClpE
SGO_0697	SGO_0697	-2.11	+	K	transcription regulator
SGO_0698	recN	-3.01	+	L	DNA repair protein RecN
SGO_0699	SGO_0699	-3.26	+		Serine/threonine protein phosphatase
SGO_0709	SGO_0709	4.37	+	J	acetyltransferase, GNAT family
SGO_0713	era	-4.41	+	R	GTP-binding protein Era
SGO_0714	SGO_0714	-4.58	+	R	hypothetical protein
SGO_0715	mutM	-5.20	+	L	formamidopyrimidine-DNA glycosylase
SGO_0716	coaE	-8.18	+	H	dephospho-CoA kinase
SGO_0717	SGO_0717	-7.52	+	G	Multi-drug resistance efflux pump
SGO_0726	SGO_0726	2.78	-		putative transcriptional regulator TetR/AcrR family
SGO_0734	SGO_0734	3.38	+	KT	PspC domain protein
SGO_0758	SGO_0758	3.25	-	O	glutathione peroxidase
SGO_0763	murA	-2.66	+	M	UDP-N-acetylglucosamine 1-carboxyvinyltransferase
SGO_0764	SGO_0764	-4.51	+		hypothetical protein
SGO_0765	endA	-2.68	+		DNA-entry nuclease
SGO_0777	SGO_0777	-6.84	+		hypothetical protein
SGO_0778	thrS	-6.84	+	J	threonyl-tRNA synthetase
SGO_0784	smc	-5.23	+	D	chromosome segregation protein SMC
SGO_0785	SGO_0785	-7.51	+	R	Cof family protein

SGO_0786	SGO_0786	-6.49	+	R	Cof family protein
SGO_0787	ftsY	-6.21	+	U	cell division protein FtsY
SGO_0792	SGO_0792	-3.90	+	K	hypothetical protein
SGO_0793	SGO_0793	-4.99	+	S	hypothetical protein
SGO_0804	murB	-3.16	+	M	UDP-N-acetylenolpyruvoylglucosamine reductase
SGO_0805	potA	-5.41	+	E	spermidine/putrescine import ATP-binding protein PotA
SGO_0806	potB	-6.59	+	E	spermidine/putrescine import ATP-binding protein PotB
SGO_0807	potC	-8.99	+	E	spermidine/putrescine import ATP-binding protein PotC
SGO_0808	potD	-9.92	+	E	spermidine/putrescine ABC transporter
SGO_0814	SGO_0814	-2.44	+	E	aminotransferase, class-V
SGO_0816	SGO_0816	-2.75	+	O	hypothetical protein
SGO_0817	SGO_0817	-2.68	+		hypothetical protein
SGO_0831	SGO_0831	-13.73	-		hypothetical protein
SGO_0832	SGO_0832	-13.26	+		hypothetical protein
SGO_0839	SGO_0839	2.08	+	K	TfoX N-terminal domain superfamily
SGO_0840	SGO_0840	2.76	+	K	Transcriptional regulator, MarR family
SGO_0841	SGO_0841	2.46	+	CR	oxidoreductase
SGO_0842	SGO_0842	2.69	+	P	rhodanese family protein
SGO_0845	SGO_0845	6.11	-		cell wall binding protein
SGO_0846	SGO_0846	9.35	+		possible cell wall protein
SGO_0858	SGO_0858	-2.28	+	R	ABC transporter ATP-binding protein
SGO_0859	pheS	-6.31	+	J	phenylalanyl-tRNA synthetase, alpha subunit
SGO_0860	SGO_0860	-5.90	+	R	acetyltransferase, GNAT family
SGO_0861	pheT	-8.91	+	J	phenylalanyl-tRNA synthetase, beta subunit
SGO_0865	SGO_0865	2.82	+		hypothetical protein
SGO_0870	SGO_0870	2.38	-	S	hypothetical protein
SGO_0872	SGO_0872	2.79	+		Hypothetical cytosolic protein
SGO_0873	SGO_0873	2.63	+		Hypothetical cytosolic protein

SGO_0874	SGO_0874	10.11	+		lipoprotein, putative
SGO_0883	SGO_0883	4.01	+		transporter, probable SP1116
SGO_0912	SGO_0912	3.24	+	K	SlyA-like protein
SGO_0935	SGO_0935	2.35	+		CDP-diglyceride synthetase
SGO_0943	SGO_0943	2.15	+		hypothetical protein
SGO_0948	pgdA	2.31	+	G	peptidoglycan N-acetylglucosamine deacetylase A
SGO_0957	SGO_0957	3.85	+		hypothetical protein
SGO_0958	SGO_0958	2.14	+		hypothetical protein
SGO_0964	pdxK	3.32	+	H	pyridoxal kinase-like protein
SGO_0965	SGO_0965	2.72	+	S	integral membrane protein
SGO_0966	hsa	-8.22	+		streptococcal hemagglutinin
SGO_0970	secY	-2.56	+	U	preprotein translocase, SecY subunit
SGO_0971	asp1	-2.89	+		accessory secretory protein
SGO_0972	asp2	-5.26	+		accessory secretory protein
SGO_0973	asp3	-4.03	+		accessory secretory protein
SGO_0975	gtfA	-7.16	+	M	glycosyl transferase, group 1 SP1758
SGO_0976	gtfB	-10.81	+		hypothetical protein
SGO_0977	asp4	-10.50	+		hypothetical protein
SGO_0978	asp5	-8.31	+		hypothetical protein
SGO_0985	SGO_0985	-2.21	-	E	amino acid permease protein SP0711
SGO_0990	SGO_0990	2.24	+	G	transporter, major facilitator family
SGO_0995	SGO_0995	-2.05	+	R	metallo-beta-lactamase superfamily protein
SGO_1007	SGO_1007	-2.87	+	E	oxidoreductase, DadA family protein SP1608
SGO_1008	SGO_1008	-4.23	+	F	Phosphohydrolase (MutT/nudix family protein)
SGO_1015	SGO_1015	-4.53	+		hypothetical protein
SGO_1016	SGO_1016	-6.10	+		putative glycosyltransferase
SGO_1017	SGO_1017	-8.06	+	S	hypothetical protein
SGO_1024	SGO_1024	-2.34	+	GM	putative polysaccharide ABC transporter

SGO_1025	rgp	-2.76	+		glycosyltransferase
SGO_1026	SGO_1026	-3.95	+	M	rhamnosyltransferase
SGO_1027	SGO_1027	-7.58	+	M	hypothetical protein
SGO_1035	gloA	2.49	+	E	lactoylglutathione lyase
SGO_1053	app	-2.46	+	G	inositol monophosphatase family protein
SGO_1056	pstC	-2.28	+	P	phosphate transport protein PstC
SGO_1057	pstA	-2.47	+	P	phosphate permease protein PstA
SGO_1058	pstB2	-2.56	+	P	phosphate-transporter 2
SGO_1059	pstB1	-3.43	+	P	phosphate transporter 1
SGO_1060	SGO_1060	-3.34	+	P	phosphate transport system regulatory protein
SGO_1065	SGO_1065	2.84	+		hypothetical protein
SGO_1074	SGO_1074	-3.01	+	H	hypothetical protein
SGO_1075	SGO_1075	2.19	-	G	alpha-amylase precursor
SGO_1082	SGO_1082	-4.25	+	R	lipoprotein
SGO_1102	SGO_1102	18.72	+		PyrR bifunctional protein
SGO_1103	carA	23.70	+	EF	carbamoyl-phosphate synthase, small subunit
SGO_1104	carB	21.43	+	EF	carbamoyl-phosphate synthase, large subunit
SGO_1105	SGO_1105	28.94	+		Leucine-rich repeat containing protein
SGO_1106	SGO_1106	28.46	+		hypothetical protein
SGO_1107	SGO_1107	4.91	+	F	PyrR bifunctional protein
SGO_1108	SGO_1108	3.39	+	F	uracil permease
SGO_1109	pyrB	3.03	+	F	aspartate carbamoyltransferase
SGO_1110	SGO_1110	4.52	+		surface antigen SCP-like domain
SGO_1118	SGO_1118	-5.12	+	R	ABC transporter ATP-binding protein SP1553
SGO_1122	SGO_1122	2.43	+	S	hypothetical protein
SGO_1126	xerS	5.30	+	L	Tyrosine recombinase xerC
SGO_1134	SGO_1134	4.08	-	I	hypothetical protein
SGO_1135	SGO_1135	3.58	-	S	Putative esterase superfamily

SGO_1136	SGO_1136	2.87	-	R	Putative esterase superfamily
SGO_1137	SGO_1137	9.13	-	P	formate-nitrate transporter
SGO_1138	SGO_1138	3.96	-	NU	autolysin, N-acetylmuramidase-like protein
SGO_1183	brnQ	-2.06	-	E	branched-chain amino acid transport system II carrier protein
SGO_1186	SGO_1186	-2.90	-	V	permease ATP-binding protein
SGO_1187	SGO_1187	-3.23	-	V	permease ATP-binding protein
SGO_1194	SGO_1194	4.81	-		phosphoribosylanthranilate isomerase, putative
SGO_1195	SGO_1195	4.20	-		hypothetical protein
SGO_1196	satD	4.53	-		SatD-like protein
SGO_1206	asd	-4.01	-	E	aspartate-semialdehyde dehydrogenase
SGO_1210	fhs	3.64	-	F	formate--tetrahydrofolate ligase
SGO_1215	manB	2.16	+	G	phosphomannomutase
SGO_1230	srtA	-2.35	-	M	sortase A
SGO_1234	rpsA	-2.55	-	J	30S ribosomal protein S1
SGO_1239	parC	-6.02	-	L	DNA topoisomerase IV, A subunit
SGO_1240	SGO_1240	-8.98	-		CAAX amino terminal protease family
SGO_1241	SGO_1241	-9.11	-		aminoglycoside adenylyltransferase
SGO_1242	SGO_1242	-6.79	-		lipoprotein, putative
SGO_1243	SGO_1243	-6.31	-		hypothetical protein
SGO_1244	SGO_1244	-5.79	-		hypothetical protein
SGO_1245	parE	-7.42	-	L	DNA topoisomerase IV, B subunit
SGO_1256	SGO_1256	3.26	-	HC	Dihydroorotate dehydrogenase electron transfer subunit
SGO_1258	SGO_1258	-5.99	-	K	NAD-dependent deacetylase (Regulatory protein SIR2-like protein)
SGO_1278	SGO_1278	14.26	-		hypothetical protein
SGO_1279	SGO_1279	17.98	-		hypothetical protein
SGO_1280	SGO_1280	3.89	-	KT	putative membrane-associated Zn-dependent protease
SGO_1281	SGO_1281	3.83	-	K	penicillinase repressor, putative
SGO_1282	SGO_1282	8.14	-	S	integral membrane protein

SGO_1314	SGO_1314	-4.22	-	P	metal binding lipoprotein
SGO_1317	SGO_1317	6.90	+		hypothetical protein
SGO_1337	SGO_1337	3.49	+	P	cation efflux family protein
SGO_1361	SGO_1361	-2.18	-	O	ADP-ribosylhydrolase
SGO_1371	SGO_1371	-3.59	-	E	prephenate dehydrogenase
SGO_1372	aroC	-3.89	-	E	chorismate synthase
SGO_1373	aroB	-3.65	-	E	3-dehydroquinate synthase
SGO_1374	aroE	-5.59	-	E	shikimate 5-dehydrogenase
SGO_1375	aroD	-2.20	-	E	3-dehydroquinate dehydratase, type I
SGO_1377	SGO_1377	-2.39	+	M	sulfatase
SGO_1383	rplS	-2.83	-	J	ribosomal protein L19
SGO_1384	SGO_1384	2.60	-	D	CrcB-like integral membrane protein
SGO_1385	SGO_1385	2.56	-	D	CrcB-like integral membrane protein
SGO_1386	SGO_1386	3.09	-	E	chorismate mutase
SGO_1388	pulA	-4.61	-	G	pullulanase, type I
SGO_1389	SGO_1389	-2.63	-	IR	conserved hypothetical protein TIGR00147
SGO_1390	ligA	-2.64	-	L	DNA ligase, NAD-dependent
SGO_1391	SGO_1391	-6.04	-	S	hypothetical protein
SGO_1396	SGO_1396	-4.62	-	S	ribonuclease BN-family, putative
SGO_1397	map	-4.27	-	J	methionine aminopeptidase, type I
SGO_1401	SGO_1401	4.36	-	ER	Histidinol-phosphatase
SGO_1402	hisE	5.35	-	E	phosphoribosyl-ATP pyrophosphohydrolase
SGO_1403	hisIE	6.14	-	E	Phosphoribosyl-AMP cyclohydrolase
SGO_1404	hisF	5.87	-	E	imidazoglycerol phosphate synthase, cyclase subunit
SGO_1405	hisA	7.95	-	E	phosphoribosylformimino-5-aminoimidazole carboxamide ribotide isomerase
SGO_1406	hisH	11.15	-	E	imidazole glycerol phosphate synthase, glutamine amidotransferase subunit
SGO_1407	hisB	12.45	-	E	Imidazoglycerol-phosphate dehydratase (IGPD)
SGO_1408	hisD	15.18	-	E	histidinol dehydrogenase

SGO_1409	hisG	15.14	-	E	ATP phosphoribosyltransferase
SGO_1410	SGO_1410	17.01	-	E	tRNA synthetase class II core domain (G, H, P, S and T)
SGO_1411	hisC	13.42	-	E	histidinol-phosphate aminotransferase
SGO_1413	SGO_1413	-3.38	-	L	first chain of major exonuclease RexA
SGO_1434	thiJ	-2.01	-	R	4-methyl-5(beta-hydroxyethyl)-thiazole monophosphate synthesis protein
SGO_1435	mreB	-2.67	-	D	cell shape determining protein
SGO_1443	SGO_1443	-3.52	-		hypothetical protein
SGO_1444	SGO_1444	-3.39	-		hypothetical protein
SGO_1446	murF	-2.95	-	M	UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D- alanine ligase
SGO_1455	rplA	-3.40	-	J	ribosomal protein L1
SGO_1456	rplK	-4.10	-	J	ribosomal protein L11
SGO_1465	SGO_1465	-3.69	-	R	uncharacterized ABC transporter ATP-binding protein SP0770
SGO_1472	SGO_1472	-2.13	-		acetyltransferase, GNAT family
SGO_1482	SGO_1482	-3.02	-	E	amino acid permease family protein SP1001
SGO_1483	SGO_1483	2.30	-		putative permease protein
SGO_1485	SGO_1485	5.81	-		hypothetical protein
SGO_1498	SGO_1498	2.76	-		putative permease protein
SGO_1500	SGO_1500	2.78	-		hypothetical protein
SGO_1501	SGO_1501	2.45	-		hypothetical protein
SGO_1506	SGO_1506	-3.93	+	P	hypothetical protein
SGO_1527	SGO_1527	2.36	-	KG	Lactose phosphotransferase system repressor
SGO_1528	SGO_1528	4.78	-		hypothetical protein
SGO_1529	SGO_1529	3.85	-		hypothetical protein
SGO_1534	SGO_1534	-3.90	-	P	ArsC family
SGO_1535	ogt	-4.27	-	L	methylated-DNA-[protein]-cysteine S-methyltransferase
SGO_1536	SGO_1536	-3.34	-	R	conserved hypothetical protein TIGR00096
SGO_1558	nrdE	-3.90	+	F	ribonucleoside-diphosphate reductase large chain
SGO_1559	nrdF	-2.26	+	F	ribonucleoside-diphosphate reductase, beta subunit

SGO_1563	SGO_1563	4.19	-		hypothetical protein
SGO_1564	SGO_1564	4.51	-	K	transcription regulator, probable -related protein
SGO_1566	argD	260.85	-	E	Acetylornithine aminotransferase (ACOAT)
SGO_1567	argB	306.44	-	E	acetylglutamate kinase
SGO_1568	argJ	319.95	-	E	arginine biosynthesis bifunctional protein ArgJ
SGO_1569	argC	520.12	-	E	N-acetyl-gamma-glutamyl-phosphate reductase
SGO_1575	SGO_1575 bfbC	-15.59	-	R	competence protein CoiA
SGO_1576	(celD)	-21.10	-	G	PTS system, IIC component
SGO_1577	bfbD bfbA	-23.63	-		hypothetical protein
SGO_1578	(celC)	-24.43	-	G	PTS system, Lactose/Cellobiose specific IIA subunit
SGO_1579	bfbR bfbB	-24.98	-	K	transcription antiterminator BglG family
SGO_1580	(celB)	-51.14	-	G	PTS system, Lactose/Cellobiose specific IIB subunit
SGO_1581	bfbG bfbF	-81.92	-	S	MtN3/saliva family protein
SGO_1582	(celA)	-35.01	-	G	6-phospho-beta-glucosidase
SGO_1584	SGO_1584	-2.59	-		anion symport for sucrose, putative
SGO_1589	arcT	6.10	-	E	putative transaminase/peptidase
SGO_1590	arcD	4.13	-	S	arginine-ornithine antiporter
SGO_1591	arcC	-3.84	-	E	carbamate kinase
SGO_1593	arcA	-3.21	-	E	arginine deiminase
SGO_1594	SGO_1594	2.21	-	T	Crp/Fnr family protein
SGO_1595	SGO_1595	2.32	-		integral membrane protein
SGO_1597	SGO_1597	2.72	-	S	hypothetical protein
SGO_1609	SGO_1609	-6.48	-	LKJ	ATP-dependent RNA helicase, DEAD/DEAH box family
SGO_1611	icd	2.45	-	C	Isocitrate dehydrogenase
SGO_1620	SGO_1620	2.98	-	S	hypothetical protein

SGO_1625	SGO_1625	2.92	-		acetoin utilization putative/CBS domain protein
SGO_1626	SGO_1626	-3.43	-	E	branched-chain amino acid transport protein
SGO_1627	SGO_1627	-3.67	-	E	branched-chain amino acid transport protein
SGO_1628	braE	-3.75	-	E	branched-chain amino acid permease protein
SGO_1629	livH	-3.68	-	E	branched-chain amino acid permease protein
SGO_1630	SGO_1630	-2.77	-	E	branched-chain amino acid transport protein
SGO_1641	SGO_1641	-2.27	-	S	Bacterial protein of unknown function (DUF871)
SGO_1642	SGO_1642	-2.20	-		hypothetical protein
SGO_1643	SGO_1643	-2.43	-	G	PTS system, cellobiose-specific IIC component, putative
SGO_1655	SGO_1655	3.73	-	R	CBS domain protein/possible hemolysin
SGO_1656	SGO_1656	44.43	-	C	phosphoenolpyruvate carboxykinase
SGO_1659	SGO_1659	-2.13	+		hypothetical protein
SGO_1668	SGO_1668	-7.85	-	S	conserved hypothetical protein TIGR00278
SGO_1669	SGO_1669	-4.57	-	J	ribosomal large subunit pseudouridine synthase B
SGO_1670	scpB	-4.42	-	K	segregation and condensation protein B
SGO_1671	scpA	-4.15	-	S	Uncharacterised ACR, COG1354
SGO_1672	xerD	-3.02	-	L	recombinase, site specific
SGO_1683	serS	-2.07	+	J	seryl-tRNA synthetase
SGO_1684	SGO_1684	-4.18	-	I	acyl-CoA dehydrogenase family
SGO_1685	SGO_1685	-3.08	-	S	putative peroxidase / antioxidant
SGO_1686	SGO_1686	-17.15	-		hypothetical protein
SGO_1687	accA	-12.33	-	I	acetyl-CoA carboxylase, carboxyl transferase, alpha subunit
SGO_1688	accD	-12.75	-	I	acetyl-CoA carboxylase, carboxyl transferase, beta subunit
SGO_1689	accC	-15.18	-	I	acetyl-CoA carboxylase, biotin carboxylase
SGO_1690	fabZ	-10.47	-	I	beta-hydroxyacyl-(acyl-carrier-protein) dehydratase FabZ
SGO_1691	accB	-10.16	-	I	acetyl-CoA carboxylase, biotin carboxyl carrier protein
SGO_1692	SGO_1692	-11.32	-	IQ	3-oxoacyl-[acyl-carrier-protein] synthase
SGO_1693	fabG	-9.30	-	IQR	3-oxoacyl-(acyl-carrier-protein) reductase

SGO_1694	fabD	-8.80	-	I	malonyl CoA-acyl carrier protein transacylase
SGO_1695	SGO_1695	-8.07	-	R	enoyl-acyl carrier protein(ACP) reductase
SGO_1696	SGO_1696	-6.41	+		hypothetical protein
SGO_1697	acpP	-7.69	-	IQ	Acyl carrier protein
SGO_1698	SGO_1698	-11.93	-	I	3-oxoacyl-[acyl-carrier-protein] synthase III
SGO_1699	SGO_1699	-12.55	-	K	transcriptional regulator, MarR family
SGO_1700	SGO_1700	-30.82	-	I	enoyl-CoA hydratase/isomerase family protein
SGO_1715	hppH	3.62	-	E	oligopeptide-binding lipoprotein
SGO_1716	SGO_1716	6.21	-	E	oligopeptide binding protein
SGO_1727	SGO_1727	2.25	+	E	amino acid-binding permease protein
SGO_1728	glnQ	2.73	+	E	glutamine ABC transporter ATP-binding protein
SGO_1729	SGO_1729	4.62	-		hypothetical protein
SGO_1734	SGO_1734	2.55	-	V	ABC transporter ATP-binding protein SP2003
SGO_1736	SGO_1736	2.26	-	S	alkaline shock protein
SGO_1737	rpmB	-2.40	-	J	ribosomal protein L28
SGO_1738	SGO_1738	2.08	-		hypothetical protein
SGO_1745	fba	-2.58	-	G	fructose-1,6-bisphosphate aldolase, class II
SGO_1748	pyrG	-4.18	-	F	CTP synthase
SGO_1750	SGO_1750	3.11	-	V	ABC-type multidrug/protein/lipid transport system, ATPase component
SGO_1751	SGO_1751	4.02	-	V	ABC-type multidrug/protein/lipid transport system, ATPase component
SGO_1752	SGO_1752	5.83	-	K	transcription regulator, MarR family
SGO_1753	SGO_1753	-2.25	-		hypothetical protein
SGO_1754	SGO_1754	-2.59	-	J	formylmethionine deformylase
SGO_1785	SGO_1785	-6.05	+	O	nickel-cobalt-cadmium resistance protein; NccN
SGO_1791	SGO_1791	2.61	-	G	PTS system, Lactose/Cellobiose specific IIA subunit
SGO_1806	ftcD	3.30	+	E	glutamate formiminotransferase
SGO_1815	SGO_1815	2.34	-		hypothetical protein
SGO_1820	SGO_1820	2.38	+		hypothetical protein

SGO_1824	prmA	-2.36	-	J	ribosomal protein L11 methyltransferase
SGO_1830	mga	5.31	-	K	Mga-like regulatory protein
SGO_1831	SGO_1831	9.20	+		integral membrane protein
SGO_1832	SGO_1832	9.83	+		hypothetical protein
SGO_1833	SGO_1833	9.40	+	S	lipoprotein, putative
SGO_1835	SGO_1835	10.55	+		hypothetical protein
SGO_1838	SGO_1838	2.33	+	V	ABC transporter domain protein
SGO_1839	SGO_1839	2.36	-		hypothetical protein
SGO_1840	SGO_1840	2.53	-		hypothetical protein
SGO_1846	SGO_1846	-4.37	-		hypothetical protein
SGO_1847	polC	-5.28	-	L	DNA polymerase III, alpha subunit, Gram-positive type
SGO_1856	SGO_1856	2.82	-	O	ATP-dependent proteinase ATP-binding chain
SGO_1857	SGO_1857	-3.73	-	G	PTS system, IIABC components
SGO_1858	SGO_1858	-2.46	+	G	beta-fructofuranosidase/sucrose 6 phosphate hydrolase
SGO_1876	SGO_1876	-2.72	-		uncharacterized membrane protein, putative
SGO_1878	SGO_1878	-2.54	-	K	transcriptional regulator, TetR family domain protein
SGO_1880	ssb	-2.53	-	L	single-strand binding protein
SGO_1912	SGO_1912	-2.44	-	H	Bifunctional folate synthesis protein
SGO_1936	adcA	-3.34	-	R	metal-binding (Mn) permease precursor, lipoprotein
SGO_1937	adcB	-4.06	-	P	ABC transporter permease, Mn
SGO_1940	SGO_1940	2.37	+		transport protein
SGO_1959	rpoA	-2.53	-	K	DNA-directed RNA polymerase, alpha subunit
SGO_1979	rpsC	-2.49	-	J	ribosomal protein S3
SGO_1984	rplD	-3.26	-	J	ribosomal protein L4/L1 family
SGO_1998	clpB	2.23	-	O	ATP-dependent Clp proteinase, ATP-binding chain
SGO_1999	ctsR	2.59	-	K	transcription regulator ctsR
SGO_2012	SGO_2012	2.98	-		transmembrane protein
SGO_2015	wefE	-12.31	-		possible polysaccharide transport protein

SGO_2016	glf	-10.69	-	MG	nucleotide sugar dehydratase, putative
SGO_2017	wzx	-12.93	-	I	nucleotidyl transferase, putative
SGO_2018	wzy	-9.75	-		extracellular polysaccharide polymerase putative
SGO_2019	wefD (licD)	-8.42	-	M	licD3 protein
SGO_2020	wefC	-8.99	-	M	glycosyltransferase
SGO_2021	wefB	-8.65	-		Extracellular polysaccharide glycosyltransferase
SGO_2022	wefA	-10.44	-	MG	UDP-glucose 4-epimerase BH3715
SGO_2023	wchF	-9.59	-	M	galactosyltransferase
SGO_2024	wchA	-8.48	-	MG	Extracellular polysaccharide biosynthesis
SGO_2025	wze	-7.63	-	D	putative autophosphorylating protein tyrosine kinase
SGO_2026	wzd	-8.39	-	M	polysaccharide export protein, MPA1 family
SGO_2027	wzh	-4.87	-	GM	wzh/Putative phosphotyrosine-protein phosphatase
SGO_2028	wzg	-4.03	-	K	transcriptional regulator
SGO_2036	SGO_2036	-2.65	-		hypothetical protein
SGO_2040	SGO_2040	2.96	-	S	hypothetical protein
SGO_2041	SGO_2041	2.85	-	L	conserved hypothetical protein TIGR00250
SGO_2042	SGO_2042	2.91	-	S	Bacterial protein of unknown function (DUF965) superfamily
SGO_2043	SGO_2043	3.45	-		lipoprotein, putative
SGO_2044	spxA	2.17	-	P	spxA-like transcriptional regulator
SGO_2051	SGO_2051	2.16	+	K	transcriptional regulator, Cro/Ci family
SGO_2061	SGO_2061	2.10	-		hypothetical protein
SGO_2083	SGO_2083	3.43	+	K	putative transcriptional regulator
SGO_2084	SGO_2084	3.73	+	R	NAD(P)H dehydrogenase, quinone family
SGO_2098	rpsD	-12.54	-	J	ribosomal protein S4
SGO_2102	SGO_2102	3.10	-	S	hypothetical protein
SGO_2103	SGO_2103	2.73	-	R	hydrolase, haloacid dehalogenase-like family
SGO_2106	SGO_2106	-2.29	-	FE	ribose-phosphate diphosphokinase

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Table S2. Primers used in this study.

Target gene	Primer	Primer sequence (5'-3') ^a
<i>Mutagenesis and complementation</i>		
<i>arcB</i>	arcBF1	ATCTTCGCGTCTTCTCTGTA ACTT
	arcBR1	ACTGTTCCCTTGAATTCCTAAGGTATTCTAACTCTGCACGGGTAA
	arcBF2	AAGCTTATCGAATTCGTCGATAGCTTTAGTCCGCCCTCATT
	arcBR2	AGTTGCTCCGCTCTTCTCA
	arcBF3	TCGCTTTTGTGAATTCGGAATAGCTTTAGTCCGCCCTCATT
	arcBR3	ATTTAACTTGAATTCCTAAGGTATTCTAACTCTGCACGGGTAA
	arcBF4	TCGTGGTGGACCTCGTTGTAT
	arcBR4	TAAAATGAGGGCGGACTAAA
	arcBF5	GAAAGTAGATGACAAATTCAGTATTCCAAGGACGTAG
	arcBR5	ATTACCCCAGGCGTTTTATACTTTTGGAAATGTAAAGATTACCT AAAGTTGCAGC
	ParcAF1	GCGAAAATGAGACGTAACCAGGTTCTCAAAGGTTGAGAGAA G
ParcAR1	TTGTCATCTACTTTCCTCCTTGTCTTTGCG	
<i>pyrB</i>	pyrBF1	CCAGTGACTAGCTACGGAGAG
	pyrBR1	ACTGTTCCCTTGAATTCCTAAAAGAGCGATTTGATTAGATGA
	pyrBF2	AAGCTTATCGAATTCGTCGACGGCGTTTTTGTGAGAA
	pyrBR2	CTACTTGTGCTTTTGCCAGAT
	pyrBF3	TCGCTTTTGTGAATTCGGAACGGCGTTTTTGTGAGAA
	pyrBR3	ATTTAACTTGAATTCCTAAGAAGAGCGATTTGATTAGATGA
<i>arcR</i>	arcRF1	GATTATCGCTTGGTTTATGAGGAG
	arcRR1	CTGCCATTGAATGTTTTGATAAGC
	arcRF2	CAAAACATTCAATGGCAGAATTCAGGGAACGAATTAACGAT GTC
	arcRR2	CGACCCGTTTCTGTTGACAATCTA
	arcRF3	CGAGCGCTACCAAACGTCTACG
	arcRR3	CAAATATATCCTCCTCACTCAGGGAACGAATTAACGATGTCT
	arcRF4	GAAAAAATGGTGGAAACACCGGCCTAGCCCAGTCTTTTG

	arcRR4	TTGACCGACAAGGGCATCTGATTAT
<i>argR</i>	argRF1	ATTTTCGCCCTTGCCTTCA
	argRR1	TTTCATTTTCCCCTCGATAGTTGT
	argRF2	<i>CTATCGAGGGGAAAATGAAAGAATTCTGCAGTGCTGGCTAAC</i> ATCAT
	argRR2	ATAGAAATCACCCATACGAAACAG
<i>ahrC</i>	ahrCF1	GATTTTTATGCAAGGTCAGAA
	ahrCR1	GGTAGGAAAGCCATGTTATTAGA
	ahrCF2	<i>AATAACATGGCTTTCCTACCCTGTGTTGCCTGAATTCCTGACT</i> G
	ahrCR2	GTTTAATTTTCGATATGCCAAGAG
<i>argD</i>	argDF1	CCTGCAGGGGCTCTATTA
	argDR1	<i>CGAGGTCCACCACGATCCTTTTCCTTTATTTATCTAC</i>
	argDF2	<i>CCGCCCTCATTTTTATGTCTATGATAATGGTGTTTTTGA</i>
	argDR2	GTCTGTCTTGATACTTCTGCTCTC
<i>ermAM</i>	ermF1	CTTAGGAATTC AAGTTAAATTAATGCTA
	ermR1	TTCCGAATTCACAAAAGCGACTCATAG
<i>aphA3</i>	aphA3F1	GACGGCCAGTGAATTCGAGC
	aphA3R1	GACCTTTACAGAATTCCTCTATG
	aphA3F2	TTAGAATTC AAGGAACAGTGAATTGGAG
	aphA3R2	CGACGAATTCGATAAGCTTTTTAGACATCTAAATC
<i>aad9</i>	aad9F1	AGTGAGGAGGATATATTTGAATAC
	aad9R1	GTGTTTCCACCATTTTTTCAAT
pPE1010	pPE_F1	ACGTCTCATTTTCGCCAAAAGTTGG
	pPE_R1	AACGCCTGGGGTAATGACTCTCT
<i>RT-PCR</i>		
<i>arcA</i>	1446F	GAAATTCGCGACCAATTCAT
	1446R	GCTGCTTCTGGAATTTCTGG
<i>arcB</i>	1447F	AGTTTTGGGCCGTATGTTTG
	1447R	TCGTCAGTCAAACCATTCCA
<i>qRT-PCR</i>		
SGO_0846	0846F	TGACAGATCCAAACGATCCA
	0846R	TCTTGAATGGCAATGGTTGA
<i>arcB</i>	1592F	GACCCTTCAGGAAATGCAAC

	1592R	TCGGCAGGGTCATACTTTTC
<i>asp5</i>	0978F	CATTTTTTCAGCGACTCG
	0978R	TCTTTTTCCCAAAGTTTCTTTCC
<i>hisC</i>	1411F	GCAGTTGGAGGAAATTCTGG
	1411R	CAGCATCCTTGAAAAGGTC
<i>bfbC</i>	1576F	ATTTTGGCGCCTATGACATC
	1576R	CCCAAGAAGGCTCCTATTCC
<i>bfbF</i>	1582F	TATCCGGCTACTTGCAATCC
	1582R	GCTCGCTAAAGTCCACCTTG
SGO_1686	1686F	AAGATCGCACTCAGCCTTTG
	1686R	TATCGCCTAAGCGAAACAGG
<i>wefE</i>	2015F	TCCTTGACCCTGAGCATTTTC
	2015R	CCATAAGGACATTCCGCAAC
<i>wzg</i>	2028F	GACCCATGCGGGTATTTATG
	2028R	CACCACCCAAAAGGTCAATC
SGO_1401	1401F	ATTACGAGGGCGAGATTGTC
	1401R	GGTTGCCATATTGCTGGTTC
<i>queA</i>	1587F	GCGACGCCCTTGTCATGAAT
	1587R	CGTGACCACCAGTTCCAGGT
<i>hsa</i>	0966F	GACCCTTCAGGAAATGCAAC
	0966R	TCGGCAGGGTCATACTTTTC
SGO_1699	1699F	GAAACTCCCAATGCAACTCC
	1699R	CCACACGACGATCAATATCAG
<i>asp5</i>	0978F	CAATTTTTTCAGCGACTCG
	0978R	TCTTTTTCCCAAAGTTTCTTTCC
<i>recN</i>	0698F	ATGAGGATTTTCGTTGCCTTG
	0698R	CGAGCCTTATGCTCCTCTTTG
<i>mutS</i>	2056F	CTCAACTCGGCAATGTCCCT
	2056R	CCTCTTCACGAATGCGCATG

^a*EcoRI* sites introduced into primers to facilitate cloning are underlined; 5' extension regions for PCR ligation mutagenesis are shown in italics.

Jakubovics *et al.*, Supplemental reference

Garnett, J.A., Marincs, F., Baumberg, S., Stockley, P.G. & Phillips, S.E. (2008) Structure and function of the arginine repressor-operator complex from *Bacillus subtilis*. *J Mol Biol* **379**: 284-298.