

Table S1. Upregulated gene in acid-stressed *L. rhamnosus* GG.

General functional category and gene ID†	Gene	Predicted function	Fold change vs control*	
			pH 4.5, 1 h	pH 4.5, 24 h
Hypothetical protein				
LGG_01121		hypothetical protein	4.00	7.14
LGG_01155		hypothetical protein	3.34	5.97
LGG_01096		hypothetical protein	3.34	6.83
LGG_01676		hypothetical protein	3.03	4.31
LGG_01128		hypothetical protein	2.76	7.05
LGG_01105		hypothetical protein	2.68	7.33
LGG_01098		hypothetical protein	3.12	7.09
LGG_01120		hypothetical protein	2.61	6.75
LGG_01136		hypothetical protein	4.17	8.77
LGG_01137		hypothetical protein	2.33	6.76
LGG_02887		hypothetical protein	2.37	7.58
LGG_01102		hypothetical protein	3.46	7.08
LGG_01118		hypothetical protein	2.47	6.31
LGG_01131		hypothetical protein	3.06	7.41
LGG_01103		hypothetical protein	3.25	7.43
LGG_01141		hypothetical protein	2.70	6.45
LGG_01140		hypothetical protein	2.32	5.80
LGG_01135		hypothetical protein	2.20	6.71
LGG_00181		hypothetical protein	1.58	3.64
LGG_01151		hypothetical protein	1.81	3.74
LGG_02594		hypothetical protein	1.49	2.06
LGG_00523		hypothetical protein	1.22	2.33
LGG_01592		hypothetical protein	1.06	2.93
LGG_01150		hypothetical protein	2.36	3.96
LGG_01073		hypothetical protein	1.95	3.78
LGG_02611		hypothetical protein	2.00	3.32
LGG_01372		hypothetical protein	1.51	0.95
LGG_00708		hypothetical protein	1.48	1.02
LGG_02128		hypothetical protein	1.39	0.58
LGG_02633		hypothetical protein	1.15	0.67
LGG_01900		hypothetical protein	3.34	3.35
LGG_00047		hypothetical protein	1.49	2.30
LGG_01250		hypothetical protein	1.41	1.85
LGG_02855		hypothetical protein	1.61	1.49
LGG_00390	<i>aroE</i>	hypothetical protein	1.72	1.14
LGG_01275		hypothetical protein	1.80	1.16
LGG_01042		hypothetical protein	1.83	2.20
LGG_01462		hypothetical protein	2.48	1.82
LGG_01967		hypothetical protein	2.20	2.43

LGG_00660		hypothetical protein	1.38	1.38
LGG_00877		hypothetical protein	1.58	1.53
LGG_02700		hypothetical protein	1.36	1.83
LGG_01517		hypothetical protein	1.49	0.79
LGG_00097		hypothetical protein	3.06	3.91
LGG_00081		hypothetical protein	2.92	2.50
LGG_01110		hypothetical protein	3.15	7.68
LGG_01119		hypothetical protein	3.15	6.85
LGG_01130		hypothetical protein	2.91	7.55
LGG_01115		hypothetical protein	2.52	7.43
LGG_01111		hypothetical protein	2.61	7.29
LGG_02888		hypothetical protein	2.46	7.19
LGG_01113		hypothetical protein	2.18	7.23
LGG_01117		hypothetical protein	1.85	6.45
LGG_02895		hypothetical protein	1.84	7.47
LGG_02891		hypothetical protein	2.17	7.32
LGG_01116		hypothetical protein	1.96	6.86
LGG_01100		hypothetical protein	3.17	8.01
LGG_01099		hypothetical protein	3.37	8.17
LGG_01091		hypothetical protein	1.37	2.31
LGG_01114		hypothetical protein	2.17	6.51
LGG_02890		hypothetical protein	3.17	8.54
Adhesion protein				
LGG_02372	<i>spaF</i>	pilus specific adhesion protein	1.34	3.34
Phage-related protein				
LGG_02893		phage-related DNA replication protein	2.07	7.51
LGG_01109		phage-related DNA-binding protein	1.86	5.34
LGG_01122		phage-related HNH endonuclease	3.54	6.98
LGG_01142		phage-related holin	2.46	6.39
LGG_01086	<i>int</i>	phage-related integrase	1.32	3.70
LGG_01143	<i>lys</i>	phage-related lysin	1.99	5.71
LGG_01133		phage-related major structural protein	2.28	6.78
LGG_01134		phage-related major tail protein	3.71	7.71
LGG_01129	<i>gpG</i>	phage-related minor capsid protein	2.84	7.20
LGG_01126		phage-related portal protein	2.95	6.93
LGG_01123		phage-related ribonucleoside-diphosphate	3.46	6.67
LGG_01138		phage-related tail component	1.74	5.98
LGG_01139		phage-related tail-host interaction protein	1.75	5.78
LGG_01523		phage-related tail-host specificity protein	1.25	3.48
LGG_01125	<i>Rorf447</i>	phage-related terminase large subunit	2.67	6.45
LGG_01535		phage-related terminase large subunit	2.32	4.52
LGG_01124	<i>Rorf172</i>	phage-related terminase small subunit	2.88	6.39
LGG_01521		phage-related holin	2.70	3.25
LGG_01537	<i>tnp R</i>	phage-related resolvase	3.09	3.39

LGG_01095	<i>Cpg</i>	phage-related transcriptional regulator Cro/CI family	1.41	1.38
LGG_00021		abortive infection protein	2.29	2.93
LGG_01132		phage-related head tail joining protein	3.21	7.19
LGG_02896	<i>sb56</i>	phage-related HNH endonuclease	1.47	7.28
LGG_01112		phage-related holliday junction resolvase	1.96	7.00
LGG_01909		phage-related infection protein	2.03	3.80
LGG_01525		phage-related minor tail protein	2.00	3.88
LGG_01127		phage-related Mu protein F like protein	3.27	7.39
LGG_02900		phage-related portal protein	1.04	7.09
LGG_01524		phage-related tail component	1.58	4.05
LGG_02898	<i>terL</i>	phage-related terminase large subunit	1.43	7.15
LGG_02894		phage-related virulence-associated protein E	1.85	7.58
Transporter related protein				
LGG_00104		transporter major facilitator superfamily MFS_1	2.42	4.38
LGG_02662	<i>yniG</i>	transporter major facilitator superfamily MFS_1, EmrB/QacA family protein	1.63	2.44
LGG_02691	<i>iolF</i>	transporter major facilitator superfamily MFS_1, sugar transporter/ L-rhamnose-proton symport	1.58	3.29
LGG_01153	<i>is38</i>	transposase Is4 family protein	1.25	3.58
LGG_01948		ABC transporter ATP-binding protein	1.52	3.58
LGG_01065	<i>bglH</i>	PTS system beta-glucoside-specific transporter subunit IIABC	2.04	5.60
LGG_00015	<i>pfpI</i>	PgpI family intracellular protease	1.31	2.95
LGG_02417		cation efflux protein	1.25	2.31
LGG_02421	<i>mtsB</i>	ABC transporter ATP-binding protein	2.32	3.58
LGG_02798		di- and tricarboxylate transporter	1.87	1.27
LGG_00461	<i>is23</i>	transposase	1.72	1.44
Membrane protein				
LGG_00710	<i>ygbF</i>	membrane protein	1.97	1.34
LGG_00023		metal-dependent membrane protease	2.06	2.50
LGG_00068		membrane protein	1.02	3.88
Transcriptional regulator				
LGG_02679	<i>gntR</i>	GntR family transcriptional regulator	1.25	3.58
LGG_02246	<i>ytrA</i>	GntR family transcriptional regulator	1.52	3.58
LGG_00069		TetR family transcriptional regulator	2.04	5.60
LGG_00191	<i>glpR</i>	DeoR family transcriptional regulator	1.31	2.95
LGG_02129		MarR family transcriptional regulator	1.25	2.31
LGG_00709	<i>ydaE</i>	PadR family transcriptional regulator	2.32	3.58
LGG_01866		transcriptional antiterminator	1.87	1.27
LGG_00117		transcriptional regulator	1.72	1.44
LGG_01954	<i>lciC</i>	XRE family transcriptional regulator	1.25	3.58
LGG_02739		GntR family transcriptional regulator	1.52	3.58
Stress response				
LGG_02240	<i>groES</i>	co-chaperonin GroES	1.39	2.53
LGG_01072	<i>cspC</i>	CspA family cold shock protein	1.75	1.26

DNA related protein				
LGG_01106		replication protein	2.14	6.75
LGG_01107	<i>ssb3</i>	single-stranded DNA-binding protein	1.74	5.97
LGG_01010	<i>umuC</i>	ImpB/MucB/SamB family protein	2.01	3.84
LGG_01104		RecT family protein	3.02	7.33
LGG_00436	<i>tnp R</i>	resolvase	1.57	2.20
LGG_01361	<i>fruR</i>	fructose repressor	2.00	2.47
Enzyme				
LGG_00433	<i>menC</i>	N-acylamino acid recemase	1.58	2.54
LGG_01064	<i>bglA</i>	6-phospho-beta-glucosidase	1.30	4.61
LGG_00093		alpha-mannosidase (GH38)	1.22	3.15

* Fold change in normalized gene expression represents the average value calculated from three independent replicates and expressed as $\log_2(\text{fold change of treatment}/\text{fold change of control})$; $p < 0.05$. Control, LGG treated in pH 7.0 for 24h; pH 4.5 1h, LGG cells stressed in pH 4.5 for 1h; pH 4.5 24h, LGG cells stressed in pH 4.5 for 24h.

† Gene ID represent the locus tag used in Genebank for chromosomal or plasmid-carried genes in *L. rhamnosus* GG.

Table S2. Downregulated gene in acid-stressed *L. rhamnosus* GG.

General functional category and gene ID†	Gene	Predicted function	Fold change vs control*	
			pH 4.5, 1 h	pH 4.5, 24 h
Carbohydrate transport, metabolism				
LGG_02192	<i>bglE</i>	PTS system beta-glucoside-specific transporter subunit IIABC	-2.83	-0.89
LGG_00409	<i>frwA2</i>	PTS system fructose-specific transporter subunit IIA	-2.81	-1.64
LGG_02647	<i>tagT</i>	PTS system fructose-specific transporter subunit IIABC	-3.81	-2.04
LGG_00345	<i>gatA</i>	PTS system galactitol-specific transporter subunit IIA	-3.01	-2.53
LGG_00346	<i>gatB</i>	PTS system galactitol-specific transporter subunit IIB	-3.35	-2.46
LGG_00343	<i>gatC</i>	PTS system galactitol-specific transporter subunit IIC	-3.84	-2.80
LGG_02910	<i>mtl F</i>	PTS system mannitol-specific transporter subunit IIA	-3.71	-1.49
LGG_02912	<i>mtl A</i>	PTS system mannitol-specific transporter subunit IIBC	-4.71	-2.17
LGG_02779	<i>leoF</i>	PTS system mannose/fructose/N-acetylglactosamine-specific transporter subunit IIC	-3.59	-1.33
LGG_00416	<i>pts</i>	PTS system mannose-specific transporter subunit IIA	-2.87	-1.09
LGG_00415	<i>pts</i>	PTS system mannose-specific transporter subunit IIB	-2.86	-1.00
LGG_02837	<i>manC</i>	PTS system mannose-specific transporter subunit IIC	-2.58	-1.44
LGG_02837	<i>manC</i>	PTS system mannose-specific transporter subunit IIC	-2.58	-1.44
LGG_00417	<i>manZ</i>	PTS system mannose-specific transporter subunit IICD	-3.39	-1.58
Amino acid transport, metabolism				
LGG_01271	<i>glnQ</i>	amino acid ABC transporter ATP-binding protein	-2.83	-2.11
LGG_02849	<i>glnQ</i>	amino acid ABC transporter ATP-binding protein	-2.82	-2.06
LGG_02009	<i>glnQ</i>	amino acid ABC transporter ATP-binding protein	-2.36	-1.49
LGG_00478	<i>yecC</i>	amino acid ABC transporter ATP-binding protein	-3.10	-1.05
LGG_00573	<i>yecS</i>	amino acid ABC transporter permease	-3.00	-1.20
LGG_01270	<i>glnP</i>	amino acid ABC transporter permease	-2.72	-1.56
LGG_02816	<i>glnP</i>	amino acid ABC transporter permease	-3.37	-1.47
LGG_02007	<i>glnP</i>	amino acid ABC transporter permease	-2.41	-1.31
LGG_00481		amino acid ABC transporter permease	-2.38	-1.05
LGG_00479		amino acid ABC transporter substrate binding protein	-3.67	-1.99
LGG_02008	<i>glnH</i>	amino acid ABC transporter substrate-binding protein	-3.15	-1.61
LGG_01272	<i>glnH</i>	amino acid ABC transporter substrate-binding protein	-3.10	-2.05
LGG_00572	<i>fliY</i>	amino acid ABC transporter substrate-binding protein	-2.49	-1.08
LGG_01197	<i>metN</i>	ABC transporter ATP-binding protein	-2.78	-1.05
LGG_00359	<i>oppA</i>	ABC transporter oligopeptide-binding protein	-2.67	-0.85
LGG_00201	<i>oppA</i>	ABC transporter oligopeptide-binding protein	-2.55	-0.65
LGG_01196	<i>metQ</i>	ABC transporter substrate-binding protein, NLPA lipoprotein	-2.36	-1.23
LGG_01195	<i>metQ</i>	ABC transporter substrate-binding protein, NLPA lipoprotein	-3.54	-0.36
LGG_00907	<i>pstC</i>	phosphate ABC transporter permease	-2.60	-1.49
LGG_01293	<i>pstS</i>	phosphate ABC transporter substrate-binding protein	-2.29	-0.98
LGG_02581		multidrug ABC transporter ATPase/permease	-2.96	-1.53
LGG_00168	<i>pbuO</i>	xanthine/uracil permease family protein	-3.85	-3.53
LGG_00600	<i>oxlT</i>	transporter major facilitator superfamily MFS_1, oxalate:formate antiporter	-3.03	-2.18
Nucleotide transport and metabolism				
LGG_01941	<i>oppD</i>	oligopeptide ABC transporter ATP-binding protein	-2.77	-1.32

LGG_01945	<i>oppA</i>	oligopeptide ABC transporter periplasmic protein	-2.40	-1.31
LGG_01943	<i>oppC</i>	oligopeptide ABC transporter permease	-2.95	-1.43
LGG_01944	<i>oppB</i>	oligopeptide ABC transporter permease	-2.78	-1.14
LGG_01813	<i>purK</i>	phosphoribosylaminoimidazole carboxylase ATPase subunit	-3.96	-3.04
LGG_01814	<i>purE</i>	phosphoribosylaminoimidazole carboxylase, catalytic subunit	-4.05	-3.78
LGG_01812	<i>purC</i>	phosphoribosylaminoimidazolesuccinocarboxamide	-4.38	-2.75
LGG_01810	<i>purQ</i>	phosphoribosylformylglycinamide synthase I	-3.64	-2.27
LGG_01809	<i>purL</i>	phosphoribosylformylglycinamide synthase II	-2.94	-1.28
LGG_01811	<i>purS</i>	phosphoribosylformylglycinamide synthase subunit purS	-4.64	-2.06
LGG_01322	<i>pdhC</i>	pyruvate dehydrogenase complex E2 component, dihydrolipoyllysine-residue acetyltransferase	-3.39	-0.40
LGG_01321	<i>pdhB</i>	pyruvate dehydrogenase E1 component subunit beta	-3.54	-0.58
Transcriptional regulator				
LGG_00372	<i>rbsR</i>	LacI family transcriptional regulator	-3.61	-0.67
LGG_00419		LacI family transcriptional regulator	-3.13	-1.68
LGG_02911		transcriptional regulator	-4.44	-1.66
LGG_00418	<i>tal</i>	transaldolase	-3.45	-1.95
LGG_00896	<i>yfiA</i>	ribosomal subunit interface protein	-2.70	-0.97
Hypothetical protein				
LGG_02805		hypothetical protein	-2.89	-0.29
LGG_00073		hypothetical protein	-3.93	-2.94
LGG_00072		hypothetical protein	-3.94	-2.70
LGG_00008		hypothetical protein	-2.77	-2.71
LGG_02089		hypothetical protein	-3.40	-1.27
LGG_00749		hypothetical protein	-2.69	-1.60
LGG_02179		hypothetical protein	-2.78	-1.31
LGG_01942		hypothetical protein	-2.81	-1.21
LGG_01548		hypothetical protein	-2.83	-1.96
LGG_00422		hypothetical protein	-2.98	-1.11
Membrane protein				
LGG_01383		membrane protein	-3.23	-2.75
LGG_00127	<i>yleB</i>	outer surface protein	-3.23	-1.41
LGG_00633	<i>amtB</i>	ammonium transporter	-1.91	-0.91
LGG_00780	<i>dltD</i>	extramembranal protein DltD	-2.65	-1.96
Phosphate synthase subunit				
LGG_01456	<i>carB</i>	carbamoyl-phosphate synthase large subunit	-3.17	-0.91
LGG_01457	<i>carA</i>	carbamoyl-phosphate synthase small subunit	-2.26	-0.78
Synthase, catalyze, transfer, proteolysis enzyme				
LGG_00643	<i>glpD</i>	alpha-glycerophosphate oxidase	-4.50	-1.61
LGG_00071		amidohydrolase	-2.60	-1.95
LGG_01808	<i>purF</i>	amidophosphoribosyltransferase	-2.77	-1.10
LGG_02639	<i>avtA</i>	aminotransferase	-4.40	-4.08
LGG_02034	<i>spxA</i>	arsenate reductase family protein	-2.74	-0.53
LGG_00113	<i>lysC</i>	aspartate kinase	-2.72	-2.06
LGG_00115	<i>asd</i>	aspartate semialdehyde dehydrogenase	-2.66	-1.54

LGG_02090		cytosine permease	-3.98	-1.36
LGG_00112	<i>lysA</i>	diaminopimelate decarboxylase	-3.47	-2.53
LGG_00114	<i>dapF</i>	diaminopimelate epimerase	-3.25	-2.10
LGG_00108	<i>dapB</i>	dihydrodipicolinate reductase	-3.31	-1.38
LGG_00109	<i>dapA</i>	dihydrodipicolinate synthase	-3.76	-2.01
LGG_01458	<i>pyrC</i>	dihydroorotase	-2.19	-0.02
LGG_01455	<i>purD</i>	dihydroorotate dehydrogenase 1B	-3.33	-1.34
LGG_00644	<i>glpK</i>	glycerol kinase	-5.60	-3.03
LGG_02088	<i>hyuA</i>	hydantoinase/oxoprolinase	-3.01	-0.83
LGG_02909	<i>mtlD</i>	mannitol-1-phosphate 5-dehydrogenase	-3.70	-1.41
LGG_00596	<i>metF</i>	methylenetetrahydrofolate reductase	-3.46	-2.05
LGG_00477		opine/octopine dehydrogenase	-2.38	-1.21
LGG_01453	<i>pyrE</i>	orotate phosphoribosyltransferase	-2.70	-1.63
LGG_01454	<i>pyrF</i>	orotidine 5-phosphate decarboxylase	-3.17	-1.70
LGG_00342	<i>srlD</i>	sorbitol-6-phosphate 2-dehydrogenase	-3.35	-1.74
LGG_02032	<i>fbp</i>	fructose-1,6-bisphosphatase	-2.84	-1.58
LGG_00653	<i>galK</i>	galactokinase	-3.21	-1.37
LGG_02913	<i>nagB</i>	glucosamine-6-phosphate deaminase	-3.66	-1.05
LGG_00110	<i>hipO</i>	M20/M25/M40 family peptidase	-3.86	-2.62
LGG_00358	<i>pepT</i>	peptidase T	-2.48	-0.74
LGG_02027	<i>glgB</i>	glycogen branching protein	-2.85	-0.98
LGG_00428	<i>ilvH</i>	DNA-directed RNA polymerase subunit delta	-2.29	-1.21
Lipoprotein				
LGG_02926	<i>metQ</i>	NLPA lipoprotein	-2.82	-0.77

* Fold change in normalized gene expression represents the average value calculated from three independent replicates and expressed as $\log_2(\text{fold change of treatment} / \text{fold change of control})$; $p < 0.05$. Control, LGG treated in pH 7.0 for 24h; pH 4.5 1h, LGG cells stressed in pH 4.5 for 1h; pH 4.5 24h, LGG cells stressed in pH 4.5 for 24 h.

† Gene ID represent the locus tag used in Genbank for chromosomal or plasmid-carried genes in *L. rhamnosus* CG.