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A Specific Mutation in the Promoter Region of the Silent *cel* Cluster Accounts for the Appearance of Lactose-Utilizing *Lactococcus lactis* MG1363

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SUPPLEMENTAL MATERIAL

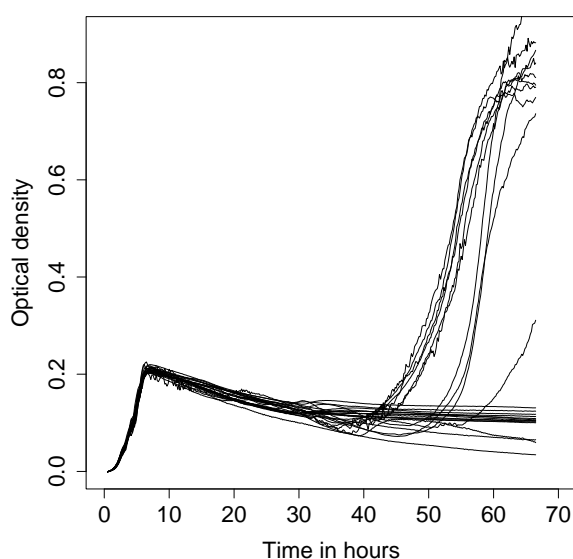
Strain or plasmid	Description	Source reference	or
<i>E. coli</i> DH5 α	F- ϕ 80/ <i>lacZ</i> Δ M15 Δ (<i>lacZYA-argF</i>) U169 <i>rec1A end1A hsdR17 gyrA96 supE4 4thi-1 relA1</i>	Invitrogen (Carlsbad, CA)	
<i>L. lactis</i> strains			
MG1363 (=MGwt)	<i>L. lactis</i> subsp. <i>cremoris</i> plasmid-free derivative of NCDO712 (Prt ⁻ , Lac ⁻).	2	
NZ9000	Derivative of MG1363 carrying <i>pepN::nisRK</i>	3	
HB21 (=MGLac ⁺)	Lac ⁺ derivative of MG1363, carrying an A to G transition at nt 174861 in the genome sequence at NCBI (Acc. Nr.: NC_009004)	This work	
MGLac ⁺ <i>nisRK</i>	MGLac ⁺ carrying <i>pseudo10::nisRK</i>	This work	
MGLac ⁺ <i>nisRK</i> Δ <i>celB</i>	MGLac ⁺ <i>nisRK</i> carrying a chromosomal deletion of <i>celB</i>	This work	
MGLac ⁺ Δ <i>ptcBA</i>	MGLac ⁺ carrying a chromosomal deletion of <i>ptcBA</i>	This work	
MGLac ⁺ Δ <i>bgIS</i>	MGLac ⁺ carrying a chromosomal deletion of <i>bgIS</i>	This work	
MGLac ⁺ <i>Pcel-gfp</i>	MGLac ⁺ carrying a single chromosomal copy of pSEUDO:: <i>Pcel-gfp</i>	This work	
MGLac ⁺ <i>Pcel*-gfp</i>	MGLac ⁺ carrying a single chromosomal copy of pSEUDO:: <i>Pcel*-gfp</i>	This work	
MGLac ⁺ Δ <i>ccpA</i> <i>Pcel*-gfp</i>	MGLac ⁺ carrying a chromosomal deletion of <i>ccpA</i> .		
MGLac ⁺ <i>nisRK</i> Δ <i>celB</i> pNZ <i>celB</i>	Derivative of MGLac ⁺ <i>nisRK</i> with deletion of <i>celB</i> carrying pNZ <i>celB</i>	This work	
Plasmids			

pSEUDO-GFP	Em ^r , with GFP-SF, for integration in <i>L. lactis</i> pseudogene 10	5	
pJWV102_gfp	Amp ^r , Tet ^r , with <i>gfp</i> * behind <i>PczcD</i>		Veening, manuscript in preparation
pSEUDO-gfp*	Em ^r , derivative of pSEUDO-GFP carrying <i>gfp</i> * for integration in <i>L. lactis</i> pseudogene 10	This work	
pCS1966:: <i>pseudo10</i> :: <i>nisRK</i>	Em ^r , with <i>nisRK</i> genes, for integration in <i>L. lactis</i> pseudogene 10	5	
pNZ8048	Cm ^r , gene expression vector carrying a nisin-inducible <i>PnisA</i>	1	
pNZ <i>celB</i>	pNZ8048 <i>celB</i> behind <i>PnisA</i>		This work
pILORI4	Em ^r ; pIL252 carrying the multiple cloning site and promoterless <i>lacZ</i> of pORI13	4	
pILORI4:: <i>Pcel</i>	pILORI4, <i>lacZ</i> behind <i>Pcel</i>		This work
pILORI4:: <i>Pcel</i> *	pILORI4, <i>lacZ</i> behind <i>Pcel</i> *		This work
pCS1966	Em ^r , <i>L. lactis</i> integration vector, OroP-based selection	6	
pCS1966- <i>celB</i> '	pCS1966 containing <i>celB</i> deletion construct		This work
pCS1966- <i>ptcBA</i> '	pCS1966 containing <i>ptcBA</i> deletion construct		This work
pCS1966- <i>bgIS</i> '	pCS1966 containing <i>bgIS</i> deletion construct		This work
pCS1966- <i>ccpA</i> '	pCS1966 containing <i>ccpA</i> deletion construct		This work
pSEUDO:: <i>Pcel</i> -gfp	pSEUDO-gfp* with <i>Pcel</i>		This work
pSEUDO:: <i>Pcel</i> *-gfp	pSEUDO-gfp* with <i>Pcel</i> *		This work

S1. Strains and plasmids used in this study.

Primer	Sequence (5'to 3')	Enzyme
KocelB1F	GCATTCTAGACAGACGGTGTTCGACTTGAC	<i>XbaI</i>
KocelB2R	GCATGGATCCCGCAGTAATCCGTTTCATGG	<i>BamHI</i>
KocelB3F	GCATGGATCCCGCAGCTAACAAGTTGGAAG	<i>BamHI</i>
KocelB4R	CGTACTCGAGGATTCCCAGCCGCCATACAG	<i>XhoI</i>
KoPtcBA1F	GCATTCTAGATCGGGATTTGGCAAGTCAGG	<i>XbaI</i>
KoPtcBA2R	GCATGGATCCGCACATGCAAGTGCAATAAC	<i>BamHI</i>
KoPtcBA3F	GCATGGATCCCAAGAACGACGCCTTCAAGC	<i>BamHI</i>
KoPtcBA4R	CGTACTCGAGGGTAATTGCCTCGTTAAGTC	<i>XhoI</i>
Pllmg_0186ZR	GCATTCTAGATCCGCCTCAAAGTTTGAACG	<i>XbaI</i>
Pllmg_0186F	CCGCTAGCATGCAAGCCATACTTCGTGAATAC	<i>SphI</i>
CelB_F	AGATCCATGGATGAACGGAATTACTGCGTGGATGGAG	<i>NcoI</i>
CelB_Rev	GATCTCTAGATAAATCTTACCAGATTTAAC	<i>XbaI</i>
KobglS1F	GCATTCTAGATCGTTATCTGGGTACCATTC	<i>XbaI</i>
KobglS2Rev	GCATGGATCCTTCCATATTATCCCCACTGG	<i>BamHI</i>
KobglS3F	GCATGGATCCAAACAAAGAGCACTCAAGTG	<i>BamHI</i>
KobglS4Rev	CGTACTCGAGCTTTGAAAGCCTCCGTTTAC	<i>XhoI</i>
CelB_F	AGATCCATGGATGAACGGAATTACTGCGTGGATGGAG	<i>NcoI</i>
CelB_R	GATCTCTAGATAAATCTTACCAGATTTAAC	<i>XbaI</i>
0186_1Rev	TCCACCATCACTTCCATTCC	-
0186_2Rev	TGATTGGCATAATTTACAAC	-
0186_3Rev	AAAGCTGCAAGTACTCCTTC	-
0186_4Rev	GCAAGTACTCCTTCTTTATC	-
gfp_sf_F	GCATCTCGAGTACTGATTAATAAAGGAGGACAAAC	<i>XhoI</i>
gfp_sf_R	CGATGGATCCGAAATACGGGCAGACATGGC	<i>BamHI</i>

S2. Primers used in this study.



S3. Growth of 24 individual cultures of MG1363(Lac⁻) in M17 medium supplemented with lactose. All the cultures eventually started to grow on lactose.

Gene name	Locus	Bayesian p	Fold	Function
<i>llmg_0186</i>	<i>llmg_0186</i>	2.68E-10	85.6	outer surface protein, β -glucosidase motif
<i>galP</i>	<i>llmg_2237</i>	2.61E-10	40.9	galactose permease, the Leloir pathway
<i>llmg_0188</i>	<i>llmg_0188</i>	6.96E-06	38.5	protein of unknown function
<i>celB</i>	<i>llmg_0187</i>	6.53E-06	37.1	PTS system, cellobiose-specific IIC component
<i>hadL</i>	<i>llmg_0254</i>	4.88E-09	26.5	cryptic haloacid dehalogenase
<i>galM</i>	<i>llmg_2236</i>	2.94E-10	24.7	galactose mutarotase, the Leloir pathway
<i>metC</i>	<i>llmg_1776</i>	1.34E-09	24.6	cystathionine gamma-synthase
<i>galK</i>	<i>llmg_2235</i>	5.69E-10	22.0	galactokinase, the Leloir pathway
<i>tnp905</i>	<i>llmg_2493</i>	7.17E-10	17.4	transposase for insertion sequence element IS905N
<i>oppF</i>	<i>llmg_0698</i>	5.03E-09	16.0	oligopeptide transport ATP-ase
<i>cysK</i>	<i>llmg_1775</i>	1.28E-08	14.3	O-acetylserine sulfhydrylase
<i>llmg_2164</i>	<i>llmg_2164</i>	1.44E-09	14.0	protein of unknown function, CesSR regulon
<i>cspA</i>	<i>llmg_1847</i>	4.97E-09	11.9	cold shock-like protein CspA
<i>tnp905</i>	<i>llmg_2493</i>	1.35E-08	10.7	transposase for insertion sequence element IS905N
<i>llmg_1330</i>	<i>llmg_1330</i>	4.87E-09	9.7	putative membrane protein
<i>llmg_0334</i>	<i>llmg_0334</i>	2.89E-07	8.8	putative thiamine transporter
<i>oppA</i>	<i>llmg_0701</i>	2.71E-08	8.7	oligopeptide transport ATP-ase
<i>oppB</i>	<i>llmg_0699</i>	4.62E-06	8.3	oligopeptide transport ATP-ase
<i>adhE</i>	<i>llmg_2432</i>	6.94E-08	8.3	bifunctional acetaldehyde-CoA/alcohol dehydrogenase
<i>plpB</i>	<i>llmg_0336</i>	2.48E-08	8.2	D-methionine-binding lipoprotein precursor
<i>thiE</i>	<i>llmg_1218</i>	1.08E-07	7.9	thiamine-phosphate pyrophosphorylase
<i>galT</i>	<i>llmg_2234</i>	1.09E-08	7.9	galactose 1-P uridylyltransferase, the Leloir pathway
<i>oppC</i>	<i>llmg_0700</i>	3.72E-07	7.7	oligopeptide transport ATP-ase
<i>oppD</i>	<i>llmg_0697</i>	1.12E-07	7.5	oligopeptide transport ATP-ase

<i>pfl</i>	<i>llmg_0629</i>	1.57E-08	7.4	pyruvate formate lyase
<i>llmg_0301</i>	<i>llmg_0301</i>	3.52E-08	7.2	MerR family transcriptional regulator
<i>ps431</i>	<i>llmg_2111</i>	8.05E-07	7.1	pseudogene (prophage gene)
<i>galE</i>	<i>llmg_2233</i>	2.27E-07	7.1	UDP-galactose-4-epimerase, the Leloir pathway
<i>argG</i>	<i>llmg_0138</i>	8.52E-08	7.1	arginine metabolism
<i>llmg_2163</i>	<i>llmg_2163</i>	1.01E-07	7.0	protein of unknown function, CesSR regulon
<i>argH</i>	<i>llmg_0139</i>	3.01E-08	7.0	arginine metabolism
<i>llmg_pseudo02</i>	<i>llmg_pseudo02</i>	7.05E-08	6.9	pseudogene 02 (MFS transporter)
<i>llmg_0281</i>	<i>llmg_0281</i>	2.09E-08	6.3	anaerobic ribonucleoside triphosphate reductase
<i>murB</i>	<i>llmg_1329</i>	7.19E-08	6.2	UDP-N-acetylenolpyruvoylglucosamine reductase
<i>busAB</i>	<i>llmg_1049</i>	5.31E-08	6.1	glycine betaine/proline ABC transporter
<i>noxE</i>	<i>llmg_0408</i>	1.38E-08	6.0	NADH oxidase
<i>vacB1</i>	<i>llmg_1586</i>	1.94E-08	6.0	exoribonuclease
<i>pyrB</i>	<i>llmg_0893</i>	2.87E-08	5.5	pyrimidine metabolism
<i>vacB1</i>	<i>llmg_1586</i>	5.99E-08	5.3	exoribonuclease
<i>llmg_0099</i>	<i>llmg_0099</i>	3.85E-08	5.1	50S ribosomal protein L32
<i>cspD2</i>	<i>llmg_1238</i>	4.11E-05	5.0	cold shock-like protein
<i>llmg_2194</i>	<i>llmg_2194</i>	9.30E-08	4.9	protein of unknown function
<i>llmg_0070</i>	<i>llmg_0070</i>	8.25E-08	4.8	putative permease
<i>pyrC</i>	<i>llmg_1508</i>	1.95E-06	4.6	pyrimidine metabolism
<i>llmg_2322</i>	<i>llmg_2322</i>	1.86E-07	4.6	protein of unknown function
<i>nusG</i>	<i>llmg_2388</i>	2.69E-06	4.6	transcription antitermination protein
<i>carA</i>	<i>llmg_0894</i>	5.15E-07	4.5	carbamoyl phosphate synthase
<i>ahpC</i>	<i>llmg_0356</i>	2.91E-07	4.5	alkyl hydroperoxide reductase subunit C
<i>cspD</i>	<i>llmg_1256</i>	1.86E-06	4.5	cold shock-like protein
<i>llmg_0333</i>	<i>llmg_0333</i>	2.39E-06	4.4	tRNA synthetase
<i>pyrP</i>	<i>llmg_0891</i>	3.33E-07	4.3	pyrimidine metabolism
<i>bglS</i>	<i>llmg_0190</i>	1.23E-07	4.1	phospho-β-glucosidase
<i>mvaA</i>	<i>llmg_0931</i>	6.90E-07	4.0	hydroxymethylglutaryl-CoA reductase
<i>plpD</i>	<i>llmg_0340</i>	3.98E-07	4.0	D-methionine-binding lipoprotein precursor
<i>glnA</i>	<i>llmg_2484</i>	2.11E-06	3.9	glutamine synthetase
<i>llmg_1920</i>	<i>llmg_1920</i>	1.99E-05	3.8	HD superfamily hydrolase
<i>busAA</i>	<i>llmg_1048</i>	3.76E-07	3.8	glycine betaine/proline ABC transporter
<i>hrcA</i>	<i>llmg_1576</i>	2.40E-07	3.7	heat-inducible transcription repressor
<i>llmg_0300</i>	<i>llmg_0300</i>	4.39E-07	3.7	protein of unknown function
<i>metE2</i>	<i>llmg_1849</i>	1.38E-06	3.7	cysteine and methionine metabolism
<i>llmg_1103</i>	<i>llmg_1103</i>	3.59E-07	3.7	protein of unknown function
<i>argE</i>	<i>llmg_0536</i>	3.59E-05	3.7	arginine metabolism
<i>pmi</i>	<i>llmg_1789</i>	1.33E-06	3.7	mannose-6-phosphate isomerase
<i>llmg_0877</i>	<i>llmg_0877</i>	5.94E-05	3.6	proten of unknown function
<i>llmg_1806</i>	<i>llmg_1806</i>	5.20E-07	3.6	protein of unknown function
<i>llmg_0872</i>	<i>llmg_0872</i>	2.54E-07	3.6	protein of unknown function
<i>rplM</i>	<i>llmg_2546</i>	3.53E-06	3.6	ribosomal protein
<i>rpsA</i>	<i>llmg_1724</i>	2.45E-05	3.6	ribosomal protein
<i>llmg_1811</i>	<i>llmg_1811</i>	2.35E-07	3.5	tRNA (guanine-N(7))-methyltransferase
<i>gnd</i>	<i>llmg_0586</i>	1.18E-06	3.5	6-phosphogluconate dehydrogenase

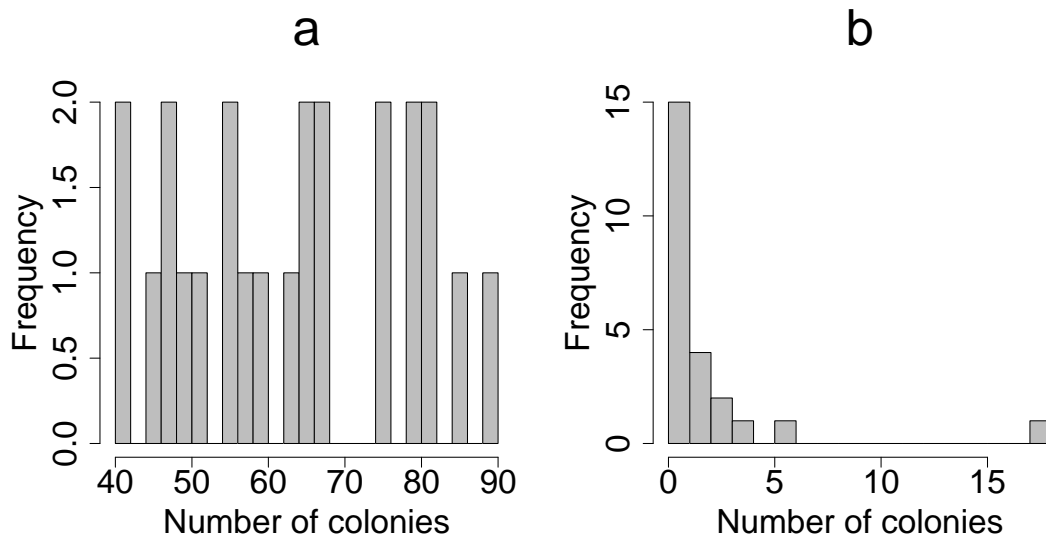
<i>dnal</i>	<i>llmg_1808</i>	7.12E-07	3.5	primosomal protein Dnal
<i>llmg_0508</i>	<i>llmg_0508</i>	9.98E-07	3.5	cysteine synthase
<i>rplS</i>	<i>llmg_1671</i>	0.000160381	3.4	ribosomal protein
<i>llmg_1762</i>	<i>llmg_1762</i>	5.19E-06	3.4	protein of unknown function
<i>pepT</i>	<i>llmg_1994</i>	3.21E-06	3.3	tripeptide aminopeptidase
<i>llmg_0417</i>	<i>llmg_0417</i>	1.81E-06	3.3	protein of unknown function
<i>llmg_0097</i>	<i>llmg_0097</i>	1.91E-06	3.3	putative flavoprotein oxygenase
<i>noxB</i>	<i>llmg_1734</i>	2.07E-06	3.3	NADH dehydrogenase
<i>llmg_1584</i>	<i>llmg_1584</i>	8.51E-07	3.3	phosphatase
<i>enoB</i>	<i>llmg_pseudo08</i>	1.72E-06	3.3	pseudogene 08 (enolase)
<i>llmg_1807</i>	<i>llmg_1807</i>	1.26E-06	3.3	nitroreductase family protein
<i>rplM</i>	<i>llmg_2546</i>	9.53E-06	3.2	ribonuclease HIII
<i>guaB</i>	<i>llmg_0230</i>	2.68E-06	3.2	inositol-5-monophosphate dehydrogenase
<i>llmg_0095</i>	<i>llmg_0095</i>	2.20E-06	3.1	putative esterase
<i>dnaB</i>	<i>llmg_1809</i>	3.42E-06	3.1	chromosome replication initiation/membrane attachment protein
<i>llmg_1089</i>	<i>llmg_1089</i>	9.11E-06	3.1	protein of unknown function
<i>fruC</i>	<i>llmg_1569</i>	5.51E-05	3.0	1-phosphofructokinase
<i>pepC</i>	<i>llmg_2069</i>	1.02E-06	3.0	hydrolase
<i>pyrF</i>	<i>llmg_1107</i>	1.31E-06	3.0	pyrimidine metabolism
<i>pepN</i>	<i>llmg_0319</i>	2.87E-06	3.0	pepidase N
<i>llmg_0873</i>	<i>llmg_0873</i>	1.78E-06	3.0	protein of unknown function
<i>thiD1</i>	<i>llmg_1217</i>	2.53E-05	2.9	phosphomethylpyrimidine kinase
<i>llmg_1127</i>	<i>llmg_1127</i>	5.63E-06	2.9	protein of unknown function
<i>glnR</i>	<i>llmg_2485</i>	0.00016258	2.9	glutamine synthetase repressor
<i>busAB</i>	<i>llmg_1049</i>	1.53E-05	2.9	glycine betaine/proline ABC transporter
<i>llmg_1550</i>	<i>llmg_1550</i>	3.96E-06	2.9	GroEI-homologous protein
<i>llmg_0506</i>	<i>llmg_0506</i>	2.64E-06	2.8	cell wall-associated protein
<i>gerCA</i>	<i>llmg_1111</i>	4.18E-06	2.8	heptaprenyl diphosphate synthase component I
<i>cmhR</i>	<i>llmg_0947</i>	3.82E-06	2.8	transcriptional regulator
<i>noxA</i>	<i>llmg_1735</i>	1.26E-06	2.8	NADH dehydrogenase
<i>fruA</i>	<i>llmg_1568</i>	3.34E-06	2.8	PTS system, fructose specific IIBC components
<i>fruR</i>	<i>llmg_1570</i>	1.68E-05	2.8	lactose transport regulator, fructose operon transcriptional repressor
<i>nadR</i>	<i>llmg_2241</i>	5.76E-06	2.8	putative nicotinamide-nucleotide adenylyltransferase
<i>llmg_0781</i>	<i>llmg_0781</i>	0.000189108	2.7	protein of unknown function
<i>vicX</i>	<i>llmg_0412</i>	2.02E-06	2.7	ribonuclease Z
<i>llmg_0704</i>	<i>llmg_0704</i>	5.69E-06	2.7	protein of unknown function
<i>thrC</i>	<i>llmg_2387</i>	4.19E-06	2.7	threonine synthase
<i>menE</i>	<i>llmg_1832</i>	3.38E-06	2.7	O-succinylbenzoic acid-CoA ligase
<i>aldC</i>	<i>llmg_1464</i>	3.02E-06	2.7	acetolactate decarboxylase, butanoate metabolism
<i>rpsF</i>	<i>llmg_2475</i>	0.000128226	2.6	ribosomal protein
<i>oppB2</i>	<i>llmg_2026</i>	7.03E-05	2.6	peptide ABC transporter
<i>menA</i>	<i>llmg_0197</i>	2.56E-05	2.6	1,4-dihydroxy-2-naphthoate octaprenyltransferase
<i>llmg_0685</i>	<i>llmg_0685</i>	8.28E-05	2.6	protein of unknown function
<i>llmg_2386</i>	<i>llmg_2386</i>	6.76E-06	2.6	putative MATE family transporter
<i>llmg_2423</i>	<i>llmg_2423</i>	8.10E-06	2.6	protein of unknown function

<i>pyrR</i>	<i>llmg_0890</i>	1.92E-05	2.6	pyrimidine metabolism
<i>dar</i>	<i>llmg_0339</i>	6.55E-06	2.6	acetoin(diacetyl)reductase
<i>rpmE</i>	<i>llmg_0906</i>	5.08E-06	2.6	ribosomal protein
<i>rpsD</i>	<i>llmg_0296</i>	0.000121058	2.6	ribosomal protein
<i>rpsL</i>	<i>llmg_2558</i>	6.96E-06	2.6	ribosomal protein
<i>llmg_0007</i>	<i>llmg_0007</i>	2.24E-05	2.6	protein of unknown function
<i>thiL</i>	<i>llmg_0930</i>	5.36E-06	2.6	acetyl-CoA C-acetyltransferase
<i>rex</i>	<i>llmg_1514</i>	6.13E-06	2.5	redox-sensing transcriptional repressor Rex
<i>llmg_0241</i>	<i>llmg_0241</i>	2.68E-05	2.5	protein of unknown function
<i>llmg_0538</i>	<i>llmg_0538</i>	0.000248717	2.5	protein of unknown function
<i>pgk</i>	<i>llmg_0253</i>	5.51E-05	2.5	phosphoglycerate kinase
<i>mntH</i>	<i>llmg_1490</i>	3.62E-06	2.5	putative proton-dependent manganese transporter
<i>ispB</i>	<i>llmg_1110</i>	4.46E-06	2.5	heptaprenyl diphosphate synthase component II
<i>kinD</i>	<i>llmg_1649</i>	1.20E-05	2.5	CesS sensor kinase
<i>frdC</i>	<i>llmg_1441</i>	6.78E-06	2.5	fumarate reductase flavoprotein subunit
<i>arcB</i>	<i>llmg_2312</i>	9.00E-10	-92.9	ornithine carbamoyltransferase
<i>arcD1</i>	<i>llmg_2311</i>	1.33E-06	-48.7	arginine/ornithine antiporter
<i>arcA</i>	<i>llmg_2313</i>	6.53E-09	-48.7	arginine deiminase
<i>arcC1</i>	<i>llmg_2310</i>	2.53E-06	-44.9	carbamate kinase
<i>arcC2</i>	<i>llmg_2309</i>	4.85E-06	-39.5	carbamate kinase
<i>llmg_0959</i>	<i>llmg_0959</i>	1.06E-07	-31.8	β -glucosidase
<i>pgmB</i>	<i>llmg_0456</i>	9.94E-07	-26.9	β -phosphoglucomutase
<i>llmg_0960</i>	<i>llmg_0960</i>	9.22E-07	-23.4	β -glucosidase
<i>yfiA</i>	<i>llmg_0616</i>	7.14E-08	-18.6	putative sigma 54 modulation protein
<i>trePP</i>	<i>llmg_0455</i>	2.53E-05	-16.9	putative trehalose/maltose hydrolase
<i>rpe2</i>	<i>llmg_0957</i>	1.67E-07	-16.1	ribulose phosphate 3-epimerase
<i>mtlR</i>	<i>llmg_0023</i>	5.64E-09	-12.8	transcriptional regulator mtl mannitol operon MtlR
<i>llmg_0454</i>	<i>llmg_0454</i>	8.45E-06	-8.3	β -glucoside-specific PTS system IIABC component
<i>als</i>	<i>llmg_1309</i>	2.37E-08	-7.8	acetolactate synthase
<i>TrePP</i>	<i>llmg_0455</i>	0.000260121	-7.5	putative trehalose/maltose hydrolase
<i>glpD</i>	<i>llmg_1098</i>	1.28E-08	-7.3	glycerol 3-phosphate dehydrogenase
<i>llmg_1990</i>	<i>llmg_1990</i>	9.09E-05	-6.9	protein of unknown function
<i>glpD</i>	<i>llmg_1098</i>	1.15E-07	-6.8	glycerol 3-phosphate dehydrogenase
<i>rpiB</i>	<i>llmg_0958</i>	0.000159752	-6.1	ribose 5-phosphate isomerase B
<i>arcT</i>	<i>llmg_2308</i>	1.69E-08	-6.0	arginine deiminase pathway
<i>llmg_2431</i>	<i>llmg_2431</i>	2.16E-08	-5.8	protein of unknown function
<i>llmg_1299</i>	<i>llmg_1299</i>	5.47E-08	-5.3	protein of unknown function
<i>llmg_1302</i>	<i>llmg_1302</i>	9.10E-07	-5.3	putative membrane protein
<i>adhA</i>	<i>llmg_1991</i>	5.62E-07	-5.1	alcohol dehydrogenase
<i>glpF2</i>	<i>llmg_1097</i>	3.81E-07	-4.8	glycerol uptake facilitator
<i>mtlF</i>	<i>llmg_0024</i>	0.001312068	-4.8	PTS system, mannitol-specific IIA component
<i>llmg_1300</i>	<i>llmg_1300</i>	9.13E-06	-4.6	protein of unknown function
<i>llmg_1385</i>	<i>llmg_1385</i>	1.52E-07	-4.4	protein of unknown function
<i>llmg_1301</i>	<i>llmg_1301</i>	9.02E-07	-4.3	protein of unknown function
<i>gntP</i>	<i>llmg_2467</i>	3.69E-06	-4.1	gluconate:H ⁺ symporter
<i>mtlA</i>	<i>llmg_0022</i>	2.07E-07	-4.1	PTS system, mannitol-specific IIBC component

<i>rpsN</i>	<i>llmg_2370</i>	7.06E-06	-4.1	ribosomal protein
<i>orf24</i>	<i>llmg_1384</i>	3.18E-07	-3.9	protein of unknown function
<i>rbsD</i>	<i>llmg_0786</i>	4.09E-06	-3.9	ribosomal protein
<i>rgpE</i>	<i>llmg_0216</i>	2.76E-07	-3.8	glycosyltransferase
<i>rgpF</i>	<i>llmg_0217</i>	5.88E-07	-3.8	rhamnosyltransferase
<i>rbsC</i>	<i>llmg_0788</i>	5.33E-05	-3.8	ribosomal protein
<i>llmg_1303</i>	<i>llmg_1303</i>	1.10E-06	-3.8	tryptophan-rich sensory protein
<i>llmg_1396</i>	<i>llmg_1396</i>	1.20E-06	-3.8	protein of unknown function
<i>ltrD</i>	<i>llmg_1375</i>	2.28E-06	-3.8	LtrD protein
<i>ltrC</i>	<i>llmg_1376</i>	1.96E-06	-3.8	putative DNA primase
<i>glgD</i>	<i>llmg_1873</i>	6.08E-07	-3.7	protein of unknown function
<i>llmg_1468</i>	<i>llmg_1468</i>	1.22E-06	-3.6	protein of unknown function
<i>llmg_1497</i>	<i>llmg_1497</i>	1.25E-06	-3.5	putative hydrolase
<i>orf30</i>	<i>llmg_1377</i>	1.48E-05	-3.5	protein of unknown function
<i>matR</i>	<i>llmg_1371</i>	5.34E-07	-3.5	maturase
<i>clpB</i>	<i>llmg_0986</i>	5.50E-07	-3.5	ATP-dependent Clp protease
<i>ascB</i>	<i>llmg_0751</i>	5.62E-05	-3.4	6-phospho- β -glucosidase
<i>rplE</i>	<i>llmg_2371</i>	1.74E-06	-3.4	ribosomal protein
<i>llmg_0286</i>	<i>llmg_0286</i>	5.86E-07	-3.4	protein of unknown function
<i>phoU</i>	<i>llmg_1895</i>	2.31E-06	-3.3	phosphate transport system regulator
<i>orf28</i>	<i>llmg_1379</i>	1.44E-06	-3.3	protein of unknown function
<i>orf26</i>	<i>llmg_1382</i>	3.47E-05	-3.2	protein of unknown function
<i>chb</i>	<i>llmg_2200</i>	5.51E-05	-3.2	putative chitin binding protein
<i>rplX</i>	<i>llmg_2372</i>	5.54E-06	-3.2	ribosomal protein
<i>cstA</i>	<i>llmg_0430</i>	7.43E-07	-3.2	carbon starvation protein A
<i>llmg_0453</i>	<i>llmg_0453</i>	4.53E-05	-3.1	PTS system, β -glucosides-specific IIA component
<i>llmg_0963</i>	<i>llmg_0963</i>	0.000315217	-3.1	PTS system, IIC component
<i>llmg_2465</i>	<i>llmg_2465</i>	1.45E-06	-3.1	protein of unknown function
<i>llrA</i>	<i>llmg_0908</i>	5.81E-06	-3.0	two-component system regulator llrA
<i>llmg_0047</i>	<i>llmg_0047</i>	2.71E-06	-3.0	protein of unknown function
<i>llmg_1496</i>	<i>llmg_1496</i>	2.12E-06	-3.0	protein of unknown function
<i>mtIA</i>	<i>llmg_0022</i>	1.58E-06	-3.0	PTS system, mannitol-specific IIBC component
<i>llmg_0228</i>	<i>llmg_0228</i>	1.83E-06	-3.0	protein of unknown function
<i>llmg_0053</i>	<i>llmg_0053</i>	1.70E-05	-2.9	protein of unknown function
<i>rpsN</i>	<i>llmg_2370</i>	0.000431286	-2.9	ribosomal protein
<i>ptcA</i>	<i>llmg_0438</i>	2.63E-06	-2.9	cellobiose-specific PTS IIA component
<i>orf18</i>	<i>llmg_1390</i>	2.26E-05	-2.9	protein of unknown function
<i>orf22</i>	<i>llmg_1386</i>	3.43E-05	-2.9	protein of unknown function
<i>llmg_1993</i>	<i>llmg_1993</i>	5.54E-05	-2.8	protein of unknown function
<i>malG</i>	<i>llmg_0737</i>	4.36E-05	-2.8	maltose ABC transporter permease
<i>matR</i>	<i>llmg_1371</i>	6.58E-06	-2.8	maturase
<i>llmg_1517</i>	<i>llmg_1517</i>	8.35E-06	-2.7	putative acidic phosphatase
<i>recN</i>	<i>llmg_1685</i>	1.07E-05	-2.7	DNA repair protein
<i>cluA</i>	<i>llmg_1398</i>	2.31E-05	-2.7	protein of unknown function
<i>llmg_1093</i>	<i>llmg_1093</i>	2.56E-05	-2.7	protein of unknown function
<i>llmg_1467</i>	<i>llmg_1467</i>	3.54E-05	-2.7	protein of unknown function

<i>llmg_0510</i>	<i>llmg_0510</i>	5.13E-06	-2.7	protein of unknown function
<i>ponA</i>	<i>llmg_0511</i>	1.06E-05	-2.7	penicillin-binding protein 1A
<i>llmg_0005</i>	<i>llmg_0005</i>	0.000645883	-2.7	protein of unknown function
<i>rplN</i>	<i>llmg_2373</i>	0.000259466	-2.7	ribosomal protein
<i>chiC</i>	<i>llmg_2199</i>	3.08E-06	-2.7	acidic endochitinase
<i>llmg_pseudo77</i>	<i>llmg_pseudo77</i>	5.57E-06	-2.7	pseudogene 77(hypothetical protein)
<i>arcD2</i>	<i>llmg_2307</i>	6.72E-05	-2.7	arginine deiminase pathway
<i>cstA</i>	<i>llmg_0430</i>	3.83E-05	-2.7	carbon starvation protein A
<i>glnQ</i>	<i>llmg_1943</i>	2.42E-05	-2.7	glutamine ABC transporter
<i>llmg_2483</i>	<i>llmg_2483</i>	7.11E-06	-2.7	protein of unknown function
<i>gntK</i>	<i>llmg_2468</i>	1.39E-05	-2.7	gluconate kinase, pentose phosphate pathway
<i>llmg_1391</i>	<i>llmg_1391</i>	9.30E-06	-2.6	protein of unknown function
<i>orf18</i>	<i>llmg_1390</i>	2.17E-05	-2.6	protein of unknown function
<i>mapA</i>	<i>llmg_0745</i>	4.65E-06	-2.6	maltose phosphorylase
<i>ocd</i>	<i>llmg_1149</i>	3.95E-05	-2.6	ornithine cyclodeaminase
<i>rlx</i>	<i>llmg_1372</i>	1.08E-05	-2.6	relaxase LtrB
<i>rplB</i>	<i>llmg_2380</i>	0.000163961	-2.5	ribosomal protein
<i>llmg_1093</i>	<i>llmg_1093</i>	1.81E-05	-2.5	protein of unknown function
<i>snf</i>	<i>llmg_2319</i>	5.47E-06	-2.5	helicase

S4. Significant expression changes of the genes during growth of MG1363 Lac⁺ on lactose as compared to growth on undefined carbon sources of the rich M17 medium.



S5. Distribution of colonies on selective plates in a fluctuation assay. a. The number of MGLac⁺ colonies on CDM supplemented with lactose after plating 24 individual cultures. b. The number of colonies on CDM supplemented with rifampicin after plating 24 individual cultures. The number of cells plated per culture in panel a was 1.6×10^8 , while twice as many cells were plated for the cultures shown in panel b.

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