# Supplementary Information

Roles of adenine methylation in the physiology of *Lacticaseibacillus paracasei*
Zhao and Zhang et al.

# Markov Chain Model − Cluster of Orthologous Groups of Proteins

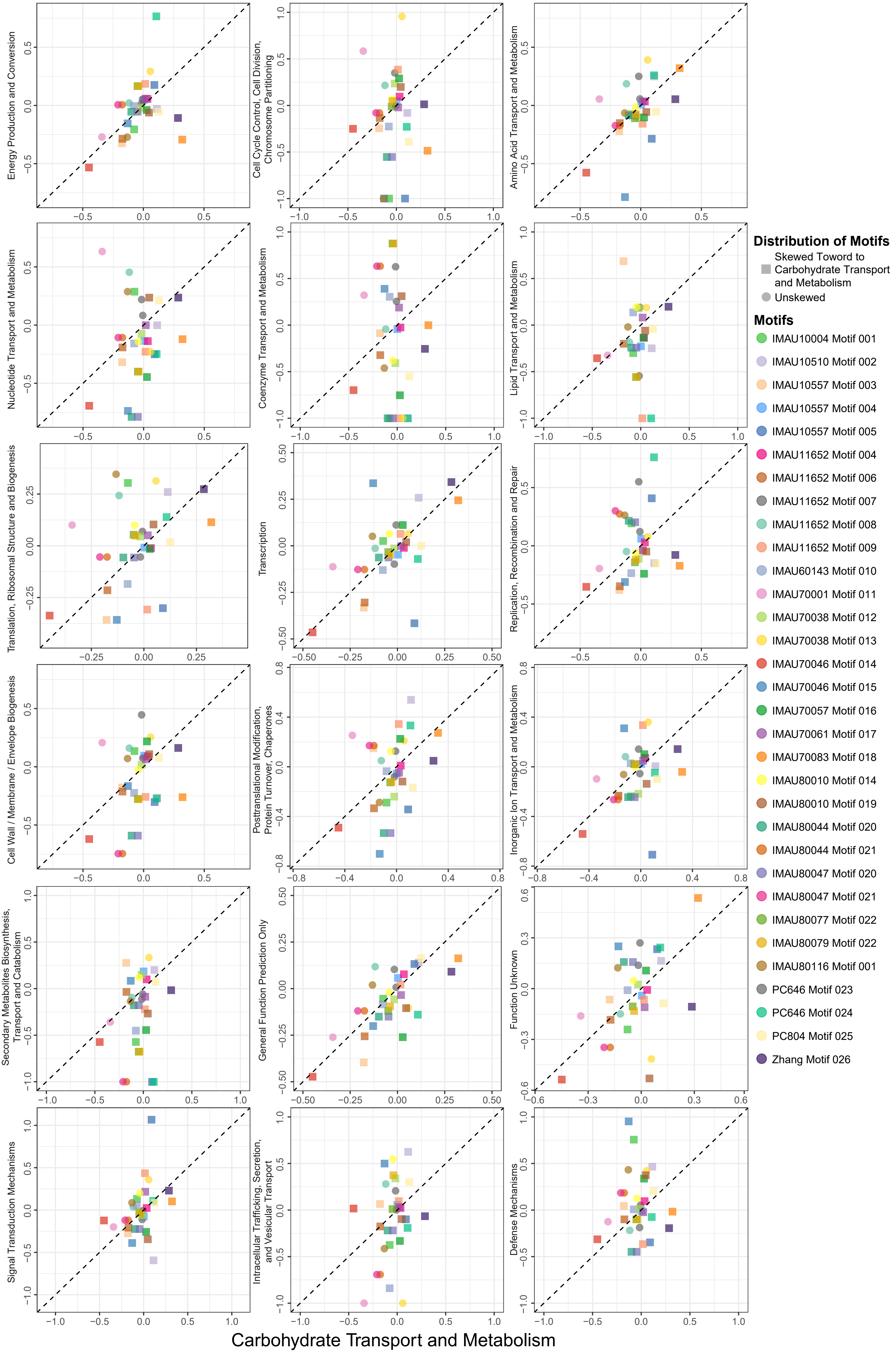

**Figure S1 Skewed distribution of methylation sites towards the coding sequences (CDS) of genes in the Clusters of Orthologous Groups of proteins (COG) functional category of carbohydrate transport and metabolism [G].** The results are generated by the Markov chain approach that considers composition. The distance between a symbol and its projection on the diagonal line measures the extent of usage biases between the COG functional category [G] and each of the other 18 COG functional categories shown. Symbols below and above the diagonal line represent skewing towards the COG functional category [G] and the COG functional category specified in each plot, respectively. Strains with more than nine (among the 18) COG functional categories located below the diagonal line are considered to have an overall skewed distribution (towards the COG functional category [G]). Each symbol represents the data of a specific motif, and each motif is represented by a different color, assigned to a specific number. Motifs of skewed and unskewed distribution are represented by a square or a circle, respectively.


40
30
20
10
0
map00010 Glycolysis / Gluconeogenesis
−−−− K00016 L−lactate dehydrogenase [EC:1.1.1.27]
−−−− K00134 glyceraldehyde 3−phosphate dehydrogenase (phosphorylating) [EC:1.2.1.12]
−−−− K00382 dihydrolipoamide dehydrogenase [EC:1.8.1.4]
−−−− K00627 pyruvate dehydrogenase E2 component (dihydrolipoamide acetyltransferase) [EC:2.3.1.12]
−−−− K00845 glucokinase [EC:2.7.1.2]
−−−− K00850 6−phosphofructokinase 1 [EC:2.7.1.11]
−−−− K00873 pyruvate kinase [EC:2.7.1.40]
−−−− K00927 phosphoglycerate kinase [EC:2.7.2.3]
−−−− K01006 pyruvate, orthophosphate dikinase [EC:2.7.9.1]
−−−− K01223 6−phospho−beta−glucosidase [EC:3.2.1.86]
−−−− K01610 phosphoenolpyruvate carboxykinase (ATP) [EC:4.1.1.49]
−−−− K01624 fructose−bisphosphate aldolase, class II [EC:4.1.2.13]
−−−− K01689 enolase [EC:4.2.1.11]
−−−− K01785 aldose 1−epimerase [EC:5.1.3.3]
−−−− K01803 triosephosphate isomerase (TIM) [EC:5.3.1.1]
−−−− K01810 glucose−6−phosphate isomerase [EC:5.3.1.9]
−−−− K01834 2,3−bisphosphoglycerate−dependent phosphoglycerate mutase [EC:5.4.2.11]
−−−− K01835 phosphoglucomutase [EC:5.4.2.2]
−−−− K04041 fructose−1,6−bisphosphatase III [EC:3.1.3.11]
−−−− K04072 acetaldehyde dehydrogenase / alcohol dehydrogenase [EC:1.2.1.10 1.1.1.1]
−−−− K06859 glucose−6−phosphate isomerase, archaeal [EC:5.3.1.9]
−−−− K20118 glucose PTS system EIICBA or EIICB component [EC:2.7.1.199]
map00020 Citrate cycle (TCA cycle)
−−−− K00244 fumarate reductase flavoprotein subunit [EC:1.3.5.4]
−−−− K00382 dihydrolipoamide dehydrogenase [EC:1.8.1.4]
−−−− K00627 pyruvate dehydrogenase E2 component (dihydrolipoamide acetyltransferase) [EC:2.3.1.12]
−−−− K01610 phosphoenolpyruvate carboxykinase (ATP) [EC:4.1.1.49]
−−−− K01679 fumarate hydratase, class II [EC:4.2.1.2]
−−−− K01958 pyruvate carboxylase [EC:6.4.1.1]
map00030 Pentose phosphate pathway
−−−− K00033 6−phosphogluconate dehydrogenase [EC:1.1.1.44 1.1.1.343]
−−−− K00034 glucose 1−dehydrogenase [EC:1.1.1.47]
−−−− K00036 glucose−6−phosphate 1−dehydrogenase [EC:1.1.1.49 1.1.1.363]
−−−− K00615 transketolase [EC:2.2.1.1]
−−−− K00850 6−phosphofructokinase 1 [EC:2.7.1.11]
−−−− K00852 ribokinase [EC:2.7.1.15]
−−−− K00874 2−dehydro−3−deoxygluconokinase [EC:2.7.1.45]
−−−− K00948 ribose−phosphate pyrophosphokinase [EC:2.7.6.1]
−−−− K01619 deoxyribose−phosphate aldolase [EC:4.1.2.4]
−−−− K01621 xylulose−5−phosphate/fructose−6−phosphate phosphoketolase [EC:4.1.2.9 4.1.2.22]
−−−− K01624 fructose−bisphosphate aldolase, class II [EC:4.1.2.13]
−−−− K01625 2−dehydro−3−deoxyphosphogluconate aldolase / (4S)−4−hydroxy−2−oxoglutarate aldolase [EC:4.1.2.14 4.1.3.42]
−−−− K01783 ribulose−phosphate 3−epimerase [EC:5.1.3.1]
−−−− K01807 ribose 5−phosphate isomerase A [EC:5.3.1.6]
−−−− K01810 glucose−6−phosphate isomerase [EC:5.3.1.9]
−−−− K01835 phosphoglucomutase [EC:5.4.2.2]
−−−− K01839 phosphopentomutase [EC:5.4.2.7]
−−−− K04041 fructose−1,6−bisphosphatase III [EC:3.1.3.11]
−−−− K06859 glucose−6−phosphate isomerase, archaeal [EC:5.3.1.9]
−−−− K07404 6−phosphogluconolactonase [EC:3.1.1.31]
−−−− K08093 3−hexulose−6−phosphate synthase [EC:4.1.2.43]
−−−− K08094 6−phospho−3−hexuloisomerase [EC:5.3.1.27]
−−−− K17463 2−dehydro−3−deoxy−phosphogluconate aldolase [EC:4.1.2.14]
−−−− K17464 D−glucosaminate PTS system EIIA component [EC:2.7.1.203]
−−−− K17465 D−glucosaminate PTS system EIIB component [EC:2.7.1.203]
−−−− K17466 D−glucosaminate PTS system EIIC component
−−−− K17467 D−glucosaminate PTS system EIID component
map00040 Pentose and glucuronate interconversions
−−−− K00065 2−dehydro−3−deoxy−D−gluconate 5−dehydrogenase [EC:1.1.1.127]
−−−− K00848 rhamnulokinase [EC:2.7.1.5]
−−−− K00854 xylulokinase [EC:2.7.1.17]
−−−− K00963 UTP−−glucose−1−phosphate uridylyltransferase [EC:2.7.7.9]
−−−− K01628 L−fuculose−phosphate aldolase [EC:4.1.2.17]
−−−− K01783 ribulose−phosphate 3−epimerase [EC:5.1.3.1]
−−−− K01805 xylose isomerase [EC:5.3.1.5]
−−−− K01815 4−deoxy−L−threo−5−hexosulose−uronate ketol−isomerase [EC:5.3.1.17]
−−−− K03077 L−ribulose−5−phosphate 4−epimerase [EC:5.1.3.4]
−−−− K03078 3−dehydro−L−gulonate−6−phosphate decarboxylase [EC:4.1.1.85]
−−−− K03079 L−ribulose−5−phosphate 3−epimerase [EC:5.1.3.22]
−−−− K05352 ribitol−5−phosphate 2−dehydrogenase (NADP+) [EC:1.1.1.405]
−−−− K09988 D−lyxose ketol−isomerase [EC:5.3.1.15]
map00051 Fructose and mannose metabolism
−−−− K00009 mannitol−1−phosphate 5−dehydrogenase [EC:1.1.1.17]
−−−− K00068 sorbitol−6−phosphate 2−dehydrogenase [EC:1.1.1.140]
−−−− K00848 rhamnulokinase [EC:2.7.1.5]
−−−− K00850 6−phosphofructokinase 1 [EC:2.7.1.11]
−−−− K00882 1−phosphofructokinase [EC:2.7.1.56]
−−−− K01624 fructose−bisphosphate aldolase, class II [EC:4.1.2.13]
−−−− K01628 L−fuculose−phosphate aldolase [EC:4.1.2.17]
−−−− K01803 triosephosphate isomerase (TIM) [EC:5.3.1.1]
−−−− K01805 xylose isomerase [EC:5.3.1.5]
−−−− K01809 mannose−6−phosphate isomerase [EC:5.3.1.8]
−−−− K01813 L−rhamnose isomerase [EC:5.3.1.14]
−−−− K02768 fructose PTS system EIIA component [EC:2.7.1.202]
−−−− K02769 fructose PTS system EIIB component [EC:2.7.1.202]
−−−− K02770 fructose PTS system EIIBC or EIIC component [EC:2.7.1.202]
−−−− K02781 glucitol/sorbitol PTS system EIIA component [EC:2.7.1.198]
−−−− K02782 glucitol/sorbitol PTS system EIIB component [EC:2.7.1.198]
−−−− K02783 glucitol/sorbitol PTS system EIIC component
−−−− K02793 mannose PTS system EIIA component [EC:2.7.1.191]
−−−− K02794 mannose PTS system EIIAB component [EC:2.7.1.191]
−−−− K02795 mannose PTS system EIIC component
−−−− K02796 mannose PTS system EIID component
−−−− K02798 mannitol PTS system EIIA component [EC:2.7.1.197]
−−−− K02800 mannitol PTS system EIICBA or EIICB component [EC:2.7.1.197]
−−−− K02812 sorbose PTS system EIIA component [EC:2.7.1.206]
−−−− K02813 sorbose PTS system EIIB component [EC:2.7.1.206]
−−−− K02814 sorbose PTS system EIIC component
−−−− K02815 sorbose PTS system EIID component
−−−− K03332 fructan beta−fructosidase [EC:3.2.1.80]
−−−− K04041 fructose−1,6−bisphosphatase III [EC:3.1.3.11]
−−−− K19956 L−sorbose 1−phosphate reductase [EC:1.1.1.−]
map00052 Galactose metabolism
−−−− K00845 glucokinase [EC:2.7.1.2]
−−−− K00849 galactokinase [EC:2.7.1.6]
−−−− K00850 6−phosphofructokinase 1 [EC:2.7.1.11]
−−−− K00917 tagatose 6−phosphate kinase [EC:2.7.1.144]
−−−− K00963 UTP−−glucose−1−phosphate uridylyltransferase [EC:2.7.7.9]
−−−− K01182 oligo−1,6−glucosidase [EC:3.2.1.10]
−−−− K01190 beta−galactosidase [EC:3.2.1.23]
−−−− K01220 6−phospho−beta−galactosidase [EC:3.2.1.85]
−−−− K01635 tagatose 1,6−diphosphate aldolase [EC:4.1.2.40]
−−−− K01684 galactonate dehydratase [EC:4.2.1.6]
−−−− K01784 UDP−glucose 4−epimerase [EC:5.1.3.2]
−−−− K01785 aldose 1−epimerase [EC:5.1.3.3]
−−−− K01819 galactose−6−phosphate isomerase [EC:5.3.1.26]
−−−− K01835 phosphoglucomutase [EC:5.4.2.2]
−−−− K01854 UDP−galactopyranose mutase [EC:5.4.99.9]
−−−− K02082 D−galactosamine 6−phosphate deaminase/isomerase [EC:3.5.99.−]
−−−− K02745 N−acetylgalactosamine PTS system EIIB component [EC:2.7.1.−]
−−−− K02746 N−acetylgalactosamine PTS system EIIC component
−−−− K02747 N−acetylgalactosamine PTS system EIID component
−−−− K02773 galactitol PTS system EIIA component [EC:2.7.1.200]
−−−− K02774 galactitol PTS system EIIB component [EC:2.7.1.200]
−−−− K02775 galactitol PTS system EIIC component
−−−− K02786 lactose PTS system EIIA component [EC:2.7.1.207]
−−−− K02788 lactose PTS system EIICB component [EC:2.7.1.207]
−−−− K07407 alpha−galactosidase [EC:3.2.1.22]
−−−− K10984 galactosamine PTS system EIIB component [EC:2.7.1.−]
−−−− K10986 galactosamine PTS system EIID component
−−−− K12111 evolved beta−galactosidase subunit alpha [EC:3.2.1.23]
−−−− K12308 beta−galactosidase [EC:3.2.1.23]
map00053 Ascorbate and aldarate metabolism
−−−− K02821 ascorbate PTS system EIIA or EIIAB component [EC:2.7.1.194]
−−−− K02822 ascorbate PTS system EIIB component [EC:2.7.1.194]
−−−− K03077 L−ribulose−5−phosphate 4−epimerase [EC:5.1.3.4]
−−−− K03078 3−dehydro−L−gulonate−6−phosphate decarboxylase [EC:4.1.1.85]
−−−− K03079 L−ribulose−5−phosphate 3−epimerase [EC:5.1.3.22]
−−−− K03475 ascorbate PTS system EIIC component
−−−− K03476 L−ascorbate 6−phosphate lactonase [EC:3.1.1.−]
map00500 Starch and sucrose metabolism
−−−− K00688 glycogen phosphorylase [EC:2.4.1.1]
−−−− K00691 maltose phosphorylase [EC:2.4.1.8]
−−−− K00700 1,4−alpha−glucan branching enzyme [EC:2.4.1.18]
−−−− K00703 starch synthase [EC:2.4.1.21]
−−−− K00845 glucokinase [EC:2.7.1.2]
−−−− K00963 UTP−−glucose−1−phosphate uridylyltransferase [EC:2.7.7.9]
−−−− K00975 glucose−1−phosphate adenylyltransferase [EC:2.7.7.27]
−−−− K01182 oligo−1,6−glucosidase [EC:3.2.1.10]
−−−− K01208 cyclomaltodextrinase / maltogenic alpha−amylase / neopullulanase [EC:3.2.1.54 3.2.1.133 3.2.1.135]
−−−− K01223 6−phospho−beta−glucosidase [EC:3.2.1.86]
−−−− K01226 trehalose−6−phosphate hydrolase [EC:3.2.1.93]
−−−− K01232 maltose−6'−phosphate glucosidase [EC:3.2.1.122]
−−−− K01810 glucose−6−phosphate isomerase [EC:5.3.1.9]
−−−− K01835 phosphoglucomutase [EC:5.4.2.2]
−−−− K01838 beta−phosphoglucomutase [EC:5.4.2.6]
−−−− K02750 alpha−glucoside PTS system EIICB component [EC:2.7.1.208 2.7.1.−]
−−−− K02759 cellobiose PTS system EIIA component [EC:2.7.1.196 2.7.1.205]
−−−− K02760 cellobiose PTS system EIIB component [EC:2.7.1.196 2.7.1.205]
−−−− K02761 cellobiose PTS system EIIC component
−−−− K02810 sucrose PTS system EIIBCA or EIIBC component [EC:2.7.1.211]
−−−− K05349 beta−glucosidase [EC:3.2.1.21]
−−−− K06859 glucose−6−phosphate isomerase, archaeal [EC:5.3.1.9]
map00520 Amino sugar and nucleotide sugar metabolism
−−−− K00075 UDP−N−acetylmuramate dehydrogenase [EC:1.3.1.98]
−−−− K00790 UDP−N−acetylglucosamine 1−carboxyvinyltransferase [EC:2.5.1.7]
−−−− K00820 glutamine−−−fructose−6−phosphate transaminase (isomerizing) [EC:2.6.1.16]
−−−− K00845 glucokinase [EC:2.7.1.2]
−−−− K00849 galactokinase [EC:2.7.1.6]
−−−− K00963 UTP−−glucose−1−phosphate uridylyltransferase [EC:2.7.7.9]
−−−− K00975 glucose−1−phosphate adenylyltransferase [EC:2.7.7.27]
−−−− K01207 beta−N−acetylhexosaminidase [EC:3.2.1.52]
−−−− K01443 N−acetylglucosamine−6−phosphate deacetylase [EC:3.5.1.25]
−−−− K01784 UDP−glucose 4−epimerase [EC:5.1.3.2]
−−−− K01791 UDP−N−acetylglucosamine 2−epimerase (non−hydrolysing) [EC:5.1.3.14]
−−−− K01809 mannose−6−phosphate isomerase [EC:5.3.1.8]
−−−− K01810 glucose−6−phosphate isomerase [EC:5.3.1.9]
−−−− K01835 phosphoglucomutase [EC:5.4.2.2]
−−−− K01854 UDP−galactopyranose mutase [EC:5.4.99.9]
−−−− K02564 glucosamine−6−phosphate deaminase [EC:3.5.99.6]
−−−− K02793 mannose PTS system EIIA component [EC:2.7.1.191]
−−−− K02794 mannose PTS system EIIAB component [EC:2.7.1.191]
−−−− K02795 mannose PTS system EIIC component
−−−− K02796 mannose PTS system EIID component
−−−− K03431 phosphoglucosamine mutase [EC:5.4.2.10]
−−−− K04042 bifunctional UDP−N−acetylglucosamine pyrophosphorylase / glucosamine−1−phosphate N−acetyltransferase [EC:2.7.7.23 2.3.1.157]
−−−− K06859 glucose−6−phosphate isomerase, archaeal [EC:5.3.1.9]
−−−− K07106 N−acetylmuramic acid 6−phosphate etherase [EC:4.2.1.126]
−−−− K12373 hexosaminidase [EC:3.2.1.52]
−−−− K20118 glucose PTS system EIICBA or EIICB component [EC:2.7.1.199]
map00620 Pyruvate metabolism
−−−− K00016 L−lactate dehydrogenase [EC:1.1.1.27]
−−−− K00027 malate dehydrogenase (oxaloacetate−decarboxylating) [EC:1.1.1.38]
−−−− K00029 malate dehydrogenase (oxaloacetate−decarboxylating)(NADP+) [EC:1.1.1.40]
−−−− K00158 pyruvate oxidase [EC:1.2.3.3]
−−−− K00244 fumarate reductase flavoprotein subunit [EC:1.3.5.4]
−−−− K00382 dihydrolipoamide dehydrogenase [EC:1.8.1.4]
−−−− K00625 phosphate acetyltransferase [EC:2.3.1.8]
−−−− K00626 acetyl−CoA C−acetyltransferase [EC:2.3.1.9]
−−−− K00627 pyruvate dehydrogenase E2 component (dihydrolipoamide acetyltransferase) [EC:2.3.1.12]
−−−− K00656 formate C−acetyltransferase [EC:2.3.1.54]
−−−− K00873 pyruvate kinase [EC:2.7.1.40]
−−−− K00925 acetate kinase [EC:2.7.2.1]
−−−− K01006 pyruvate, orthophosphate dikinase [EC:2.7.9.1]
−−−− K01610 phosphoenolpyruvate carboxykinase (ATP) [EC:4.1.1.49]
−−−− K01679 fumarate hydratase, class II [EC:4.2.1.2]
−−−− K01958 pyruvate carboxylase [EC:6.4.1.1]
−−−− K01962 acetyl−CoA carboxylase carboxyl transferase subunit alpha [EC:6.4.1.2 2.1.3.15]
−−−− K01963 acetyl−CoA carboxylase carboxyl transferase subunit beta [EC:6.4.1.2 2.1.3.15]
−−−− K02160 acetyl−CoA carboxylase biotin carboxyl carrier protein
−−−− K03777 D−lactate dehydrogenase (quinone) [EC:1.1.5.12]
−−−− K03778 D−lactate dehydrogenase [EC:1.1.1.28]
−−−− K04072 acetaldehyde dehydrogenase / alcohol dehydrogenase [EC:1.2.1.10 1.1.1.1]
−−−− K07248 lactaldehyde dehydrogenase / glycolaldehyde dehydrogenase [EC:1.2.1.22 1.2.1.21]
−−−− K20509 carboxybiotin decarboxylase [EC:7.2.4.1]
−−−− K22212 malolactic enzyme [EC:4.1.1.101]
map00630 Glyoxylate and dicarboxylate metabolism
−−−− K00382 dihydrolipoamide dehydrogenase [EC:1.8.1.4]
−−−− K00600 glycine hydroxymethyltransferase [EC:2.1.2.1]
−−−− K00626 acetyl−CoA C−acetyltransferase [EC:2.3.1.9]
−−−− K00865 glycerate 2−kinase [EC:2.7.1.165]
−−−− K01091 phosphoglycolate phosphatase [EC:3.1.3.18]
−−−− K01458 N−formylglutamate deformylase [EC:3.5.1.68]
−−−− K01625 2−dehydro−3−deoxyphosphogluconate aldolase / (4S)−4−hydroxy−2−oxoglutarate aldolase [EC:4.1.2.14 4.1.3.42]
−−−− K01915 glutamine synthetase [EC:6.3.1.2]
−−−− K02437 glycine cleavage system H protein
−−−− K07248 lactaldehyde dehydrogenase / glycolaldehyde dehydrogenase [EC:1.2.1.22 1.2.1.21]
map00640 Propanoate metabolism
−−−− K00016 L−lactate dehydrogenase [EC:1.1.1.27]
−−−− K00140 malonate−semialdehyde dehydrogenase (acetylating) / methylmalonate−semialdehyde dehydrogenase [EC:1.2.1.18 1.2.1.27]
−−−− K00382 dihydrolipoamide dehydrogenase [EC:1.8.1.4]
−−−− K00625 phosphate acetyltransferase [EC:2.3.1.8]
−−−− K00656 formate C−acetyltransferase [EC:2.3.1.54]
−−−− K00925 acetate kinase [EC:2.7.2.1]
−−−− K01962 acetyl−CoA carboxylase carboxyl transferase subunit alpha [EC:6.4.1.2 2.1.3.15]
−−−− K01963 acetyl−CoA carboxylase carboxyl transferase subunit beta [EC:6.4.1.2 2.1.3.15]
−−−− K02160 acetyl−CoA carboxylase biotin carboxyl carrier protein
−−−− K19745 acrylyl−CoA reductase (NADPH) [EC:1.3.1.−]
map00650 Butanoate metabolism
−−−− K00244 fumarate reductase flavoprotein subunit [EC:1.3.5.4]
−−−− K00626 acetyl−CoA C−acetyltransferase [EC:2.3.1.9]
−−−− K00656 formate C−acetyltransferase [EC:2.3.1.54]
−−−− K00929 butyrate kinase [EC:2.7.2.7]
−−−− K01574 acetoacetate decarboxylase [EC:4.1.1.4]
−−−− K01575 acetolactate decarboxylase [EC:4.1.1.5]
−−−− K01641 hydroxymethylglutaryl−CoA synthase [EC:2.3.3.10]
−−−− K01652 acetolactate synthase I/II/III large subunit [EC:2.2.1.6]
−−−− K04072 acetaldehyde dehydrogenase / alcohol dehydrogenase [EC:1.2.1.10 1.1.1.1]
−−−− K20509 carboxybiotin decarboxylase [EC:7.2.4.1]
−−−− K23351 glutaconyl−CoA/methylmalonyl−CoA decarboxylase subunit gamma
map00660 C5−Branched dibasic acid metabolism
−−−− K01575 acetolactate decarboxylase [EC:4.1.1.5]
−−−− K01652 acetolactate synthase I/II/III large subunit [EC:2.2.1.6]
−−−− K10218 4−hydroxy−4−methyl−2−oxoglutarate aldolase [EC:4.1.3.17]
map00562 Inositol phosphate metabolism
−−−− K00010 myo−inositol 2−dehydrogenase / D−chiro−inositol 1−dehydrogenase [EC:1.1.1.18 1.1.1.369]
−−−− K00140 malonate−semialdehyde dehydrogenase (acetylating) / methylmalonate−semialdehyde dehydrogenase [EC:1.2.1.18 1.2.1.27]
−−−− K01803 triosephosphate isomerase (TIM) [EC:5.3.1.1]
−−−− K03335 inosose dehydratase [EC:4.2.1.44]
−−−− K03336 3D−(3,5/4)−trihydroxycyclohexane−1,2−dione acylhydrolase (decyclizing) [EC:3.7.1.22]
−−−− K03337 5−deoxy−glucuronate isomerase [EC:5.3.1.30]
−−−− K03338 5−dehydro−2−deoxygluconokinase [EC:2.7.1.92]
−−−− K22230 scyllo−inositol 2−dehydrogenase (NADP+) [EC:1.1.1.−]
IMAU10004
IMAU10510
IMAU10557
PC646
IMAU11652
IMAU60143
IMAU70001
IMAU70038
IMAU70046
IMAU70057
IMAU70061
IMAU70083
IMAU80010
PC804
IMAU80044
IMAU80047
IMAU80077
IMAU80079
IMAU80116
Zhang

**Figure S2 Heatmap showing the distribution of methylation sites across coding sequences of 20 *Lacticaseibacillus paracasei* isolates, annotated based on the Kyoto Encyclopedia of Genes and Genomes (KEGG) database.** X-axis shows the isolate number; y-axis indicates the specific KEGG category. The color scale represents the percentage of methylation sites in a specific KEGG Orthology (KO), calculated as: the number of methylation sites within the coding sequences of a specific KO divided by the total number of methylation sites across all KOs. The quotient was converted to permillage. The color bar represents the relative distribution of m6A methylation in various KOs.

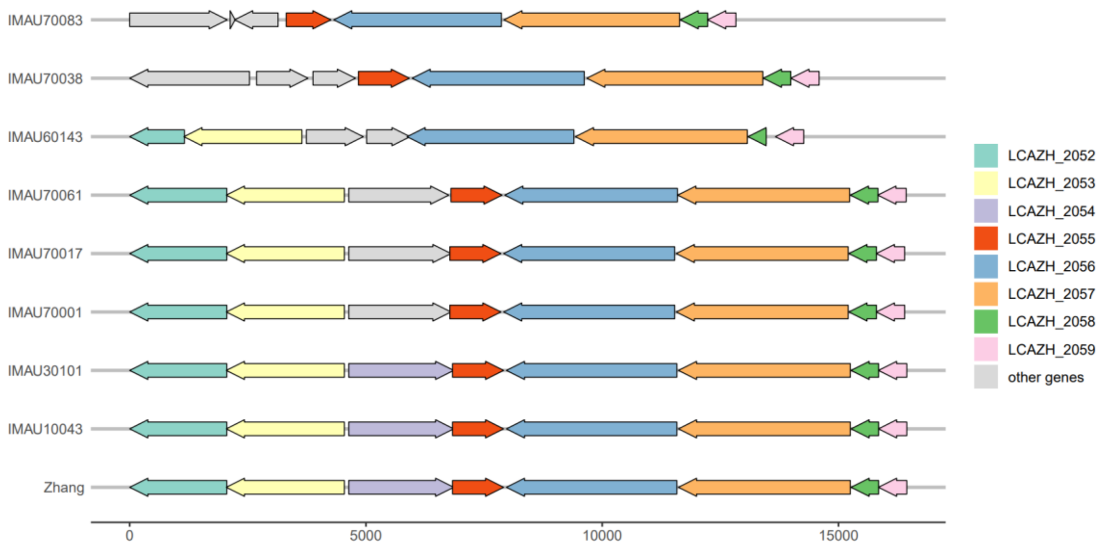

**Figure S3 Comparative analysis of the gene organization of the bacteriophage exclusion (BREX) system in various *Lacticaseibacillus paracasei* strains.** A complete or partial BREX gene cluster was detected in nine of the 28 investigated strains. A complete BREX system cassette in this species (previously identified in *Lacticaseibacillus paracasei* Zhang) includes eight genes, namely LCAZH_2052 (protease Lon-related BREX system protein *BrxL*, *brxL*), LCAZH_2053 (phosphatase PglZ type A, *pglZ*), LCAZH_2054 (a putative DNA MTase), LCAZH_2055 (site-specific integrase, *int*), LCAZH_2056 (adenine-specific DNA-methyltransferase, *pglX*), LCAZH_2057 (P-loop protein *BrxC*, *brxC*), LCAZH_2058 (DUF1788 domain-containing protein, *brxB*), and LCAZH_2059 (DUF1819 family protein, *brxA*). Colored arrows represent different genes, and the arrow head represents gene orientation. The scale at the bottom indicates gene length (bp).

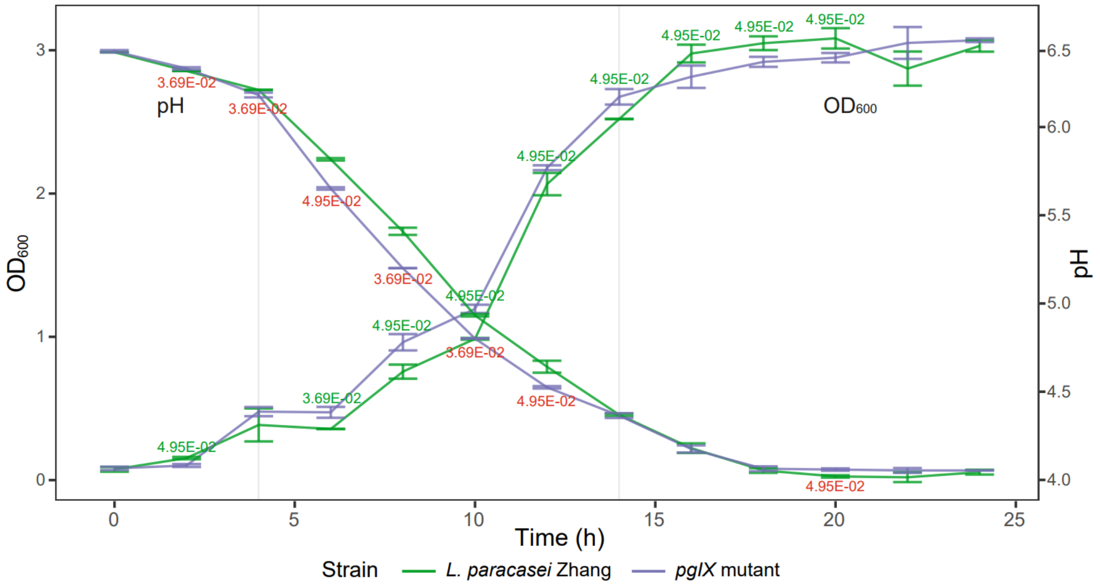

**Figure S4 Growth curves of *Lacticaseibacillus* (*L.*) *paracasei* Zhang wild type (n = 3) and *pglX* mutant (n = 3), determined by changes in optical density at 600 nm ($OD_{600}$) and pH of the bacterial cultures over time.** X-axis indicates different time points; y-axis indicates $OD_{600}$ and pH. The logarithmic growth phase (from 4 h to 14 h) is framed by two vertical lines. Error bars represent SD; and the measure of centre for the error bars represents the mean. Statistical difference was tested by the Wilcoxon rank-sum test (two-sided). The *P* values less than 0.05 are labeled. All exact *P* values are provided in the data source file.

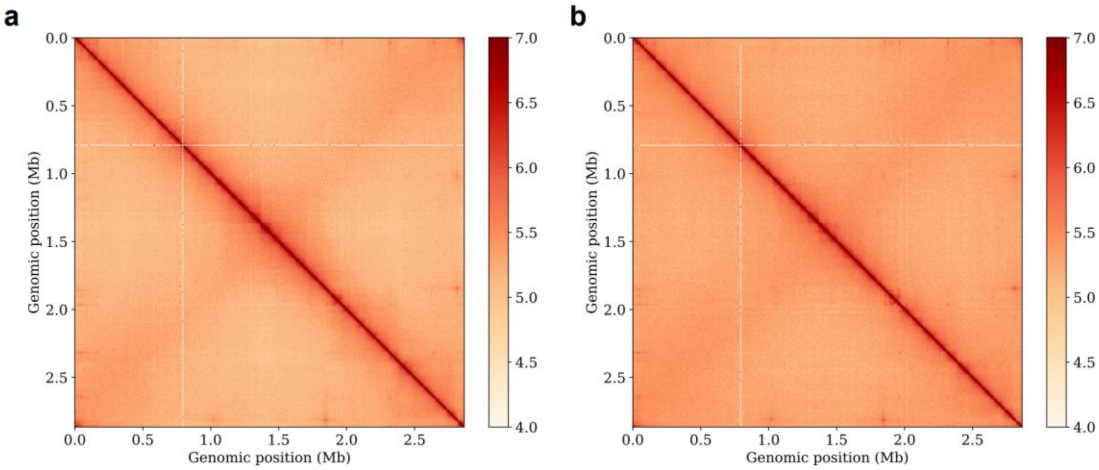

**Figure S5 High-throughput chromosome conformation capture (Hi-C) contact maps of *Lacticaseibacillus paracasei* Zhang *pglX* mutant (a) and wild type (b).** Both x- and y-axes show the position in the reference genome (Mb). The color bar indicates the interaction intensity; and the greater the numerical value, the stronger the interaction.

**Table S1 General information of methyltransferases in 28 *Lacticaseibacillus paracasei* isolates.**

| Isolate | Query ID | Global identity | E-value | Bit score | REBASE:EnzType |
|---|---|---|---|---|---|
| IMAU10004 | IMAU10004_01400 | 97.70 | 0 | 611 | EnzType:putative Type II methyltransferase |
| IMAU10004 | IMAU10004_01689 | 100.00 | 0 | 3207 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU10004 | IMAU10004_02169 | 98.17 | 0 | 1429 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU10004 | IMAU10004_02170 | 97.66 | 0 | 775 | EnzType:putative Type I specificity subunit |
| IMAU10004 | IMAU10004_02172 | 74.74 | 5.41E-180 | 509 | EnzType:putative Type I specificity subunit |
| IMAU10004 | IMAU10004_02173 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| IMAU10004 | IMAU10004_02174 | 100.00 | 0 | 2109 | EnzType:putative Type I restriction enzyme |
| IMAU10043 | IMAU10043_01924 | 99.86 | 0 | 1519 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU10043 | IMAU10043_01926 | 100.00 | 0 | 2487 | EnzType:Type II methyltransferase |
| IMAU10510 | IMAU10510_02100 | 92.69 | 0 | 1346 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU10510 | IMAU10510_02102 | 96.94 | 2.44E-136 | 382 | EnzType:putative Type I specificity subunit |
| IMAU10510 | IMAU10510_02104 | 100.00 | 0 | 813 | EnzType:putative Type I specificity subunit |
| IMAU10510 | IMAU10510_02105 | 100.00 | 0 | 1101 | EnzType:putative Type I methyltransferase |
| IMAU10510 | IMAU10510_02106 | 100.00 | 0 | 2112 | EnzType:putative Type I restriction enzyme |
| IMAU10557 | IMAU10557_00932 | 100.00 | 0 | 801 | EnzType:putative Type II restriction enzyme |
| IMAU10557 | IMAU10557_00934 | 86.73 | 0 | 790 | EnzType:putative Type II methyltransferase |
| IMAU10557 | IMAU10557_01985 | 93.27 | 0 | 634 | EnzType:putative Type II methyltransferase |
| IMAU10557 | IMAU10557_02103 | 51.63 | 1.19E-128 | 367 | EnzType:putative Type II methyltransferase |
| IMAU10557 | IMAU10557_02239 | 100.00 | 0 | 1452 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU10557 | IMAU10557_02240 | 93.78 | 0 | 762 | EnzType:putative Type I specificity subunit |
| IMAU10557 | IMAU10557_02242 | 73.49 | 1.78E-113 | 323 | EnzType:putative Type I specificity subunit |
| IMAU10557 | IMAU10557_02243 | 100.00 | 0 | 1101 | EnzType:putative Type I methyltransferase |
| IMAU10557 | IMAU10557_02244 | 100.00 | 0 | 2112 | EnzType:putative Type I restriction enzyme |

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|---|---|---|---|---|---|
| IMAU10557 | IMAU10557_03106 | 99.03 | 0 | 640 | EnzType:putative Type II restriction enzyme |
| IMAU10557 | IMAU10557_03107 | 98.42 | 0 | 1026 | EnzType:putative Type II methyltransferase |
| IMAU10557 | IMAU10557_03183 | 99.03 | 0 | 640 | EnzType:putative Type II restriction enzyme |
| IMAU10557 | IMAU10557_03184 | 95.86 | 0 | 1001 | EnzType:putative Type II methyltransferase |
| IMAU10685 | IMAU10685_02033 | 77.95 | 0 | 610 | EnzType:putative Type I specificity subunit |
| IMAU10685 | IMAU10685_02035 | 54.43 | 1.51E-157 | 445 | EnzType:putative Type I specificity subunit |
| IMAU10685 | IMAU10685_02037 | 83.25 | 4.42E-125 | 353 | EnzType:putative Type I specificity subunit |
| IMAU10685 | IMAU10685_02038 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| IMAU10685 | IMAU10685_02039 | 99.70 | 0 | 2104 | EnzType:putative Type I restriction enzyme |
| IMAU10685 | IMAU10685_02919 | 51.09 | 0 | 1106 | EnzType:putative Type I restriction enzyme |
| IMAU10685 | IMAU10685_02920 | 97.96 | 0 | 1095 | EnzType:putative Type I methyltransferase |
| IMAU10685 | IMAU10685_02921 | 72.44 | 0 | 536 | EnzType:putative Type I specificity subunit |
| PC646 | IMAU11646_02220 | 99.58 | 0 | 1446 | EnzType:putative Type IV methyl-directed restriction enzyme |
| PC646 | IMAU11646_02221 | 67.82 | 4.53E-170 | 483 | EnzType:putative Type I specificity subunit |
| PC646 | IMAU11646_02223 | 75.06 | 3.09E-175 | 496 | EnzType:putative Type I specificity subunit |
| PC646 | IMAU11646_02224 | 100.00 | 0 | 1099 | EnzType:putative Type I methyltransferase |
| PC646 | IMAU11646_02225 | 100.00 | 0 | 2112 | EnzType:putative Type I restriction enzyme |
| PC646 | IMAU11646_03112 | 52.89 | 7.06E-147 | 417 | EnzType:putative Type II methyltransferase |
| PC646 | IMAU11646_03125 | 72.96 | 2.71E-180 | 509 | EnzType:Type I specificity subunit |
| PC646 | IMAU11646_03126 | 99.07 | 0 | 1108 | EnzType:putative Type I methyltransferase |
| PC646 | IMAU11646_03127 | 98.96 | 0 | 2160 | EnzType:putative Type I restriction enzyme |
| IMAU11652 | IMAU11652_00589 | 98.70 | 0 | 1104 | EnzType:putative Type I methyltransferase |
| IMAU11652 | IMAU11652_00590 | 99.34 | 0 | 2163 | EnzType:putative Type I restriction enzyme |
| IMAU11652 | IMAU11652_00914 | 99.74 | 0 | 800 | EnzType:putative Type II restriction enzyme |
| IMAU11652 | IMAU11652_00915 | 102.06 | 0 | 899 | EnzType:putative Type II methyltransferase |
| IMAU11652 | IMAU11652_01218 | 52.32 | 1.85E-53 | 166 | EnzType:putative Type II methyltransferase |

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|---|---|---|---|---|---|
| IMAU11652 | IMAU11652_02049 | 100.00 | 4.99E-176 | 486 | EnzType:putative Type II methyltransferase |
| IMAU11652 | IMAU11652_02050 | 100.00 | 0 | 3046 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU11652 | IMAU11652_02168 | 99.58 | 0 | 1447 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU11652 | IMAU11652_02169 | 75.69 | 0 | 550 | EnzType:putative Type I specificity subunit |
| IMAU11652 | IMAU11652_02171 | 79.74 | 3.63E-174 | 494 | EnzType:putative Type I specificity subunit |
| IMAU11652 | IMAU11652_02172 | 99.25 | 0 | 1093 | EnzType:putative Type I methyltransferase |
| IMAU11652 | IMAU11652_02173 | 99.80 | 0 | 2105 | EnzType:putative Type I restriction enzyme |
| IMAU11652 | IMAU11652_02997 | 67.92 | 0 | 1209 | EnzType:putative Type III restriction enzyme |
| IMAU11652 | IMAU11652_02998 | 72.02 | 0 | 945 | EnzType:putative Type III methyltransferase |
| IMAU30101 | IMAU30101_01926 | 99.86 | 0 | 1519 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU30101 | IMAU30101_01928 | 100.00 | 0 | 2487 | EnzType:Type II methyltransferase |
| IMAU60143 | IMAU60143_00356 | 100.00 | 0 | 513 | EnzType:putative Type II methyltransferase |
| IMAU60143 | IMAU60143_01813 | 91.74 | 0 | 709 | EnzType:putative Type II restriction enzyme |
| IMAU60143 | IMAU60143_01814 | 87.42 | 0 | 601 | EnzType:putative Type II methyltransferase |
| IMAU60143 | IMAU60143_01852 | 98.68 | 1.32E-109 | 311 | EnzType:putative Type II methyltransferase |
| IMAU60143 | IMAU60143_02004 | 73.33 | 4.66E-172 | 482 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU60143 | IMAU60143_02010 | 79.28 | 0 | 1922 | EnzType:putative Type II methyltransferase |
| IMAU60143 | IMAU60143_02228 | 98.68 | 1.32E-109 | 311 | EnzType:putative Type II methyltransferase |
| IMAU70001 | IMAU70001_01390 | 97.70 | 0 | 611 | EnzType:putative Type II methyltransferase |
| IMAU70001 | IMAU70001_01684 | 84.02 | 0 | 2704 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70001 | IMAU70001_01694 | 84.02 | 0 | 2697 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70001 | IMAU70001_02182 | 89.68 | 0 | 2141 | EnzType:putative Type II methyltransferase |
| IMAU70001 | IMAU70001_02631 | 99.56 | 4.49E-170 | 469 | EnzType:putative Type II methyltransferase |
| IMAU70001 | IMAU70001_02675 | 90.23 | 0 | 1769 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70017 | IMAU70017_01372 | 97.70 | 0 | 611 | EnzType:putative Type II methyltransferase |
| IMAU70017 | IMAU70017_01665 | 84.02 | 0 | 2701 | EnzType:putative Type IIG restriction enzyme/methyltransferase |

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|---|---|---|---|---|---|
| IMAU70017 | IMAU70017_02154 | 89.68 | 0 | 2141 | EnzType:putative Type II methyltransferase |
| IMAU70018 | IMAU70018_01630 | 98.55 | 0 | 560 | EnzType:putative Type II methyltransferase |
| PC724 | IMAU70024_02098 | 98.92 | 0 | 565 | EnzType:putative Type I specificity subunit |
| PC724 | IMAU70024_02102 | 99.44 | 0 | 1093 | EnzType:putative Type I methyltransferase |
| PC724 | IMAU70024_02103 | 99.41 | 0 | 2099 | EnzType:putative Type I restriction enzyme |
| IMAU70027 | IMAU70027_01671 | 66.54 | 0 | 2165 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70027 | IMAU70027_02208 | 98.17 | 0 | 1429 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU70027 | IMAU70027_02209 | 96.10 | 0 | 866 | EnzType:putative Type I specificity subunit |
| IMAU70027 | IMAU70027_02211 | 79.12 | 0 | 637 | EnzType:putative Type I specificity subunit |
| IMAU70027 | IMAU70027_02214 | 85.53 | 0 | 944 | EnzType:putative Type I methyltransferase |
| IMAU70027 | IMAU70027_02216 | 100.00 | 0 | 2109 | EnzType:putative Type I restriction enzyme |
| IMAU70038 | IMAU70038_00491 | 87.82 | 0 | 723 | EnzType:putative Type II methyltransferase |
| IMAU70038 | IMAU70038_00492 | 81.64 | 0 | 696 | EnzType:putative Type II restriction enzyme |
| IMAU70038 | IMAU70038_01968 | 79.92 | 4.08E-147 | 411 | EnzType:putative Type II methyltransferase |
| IMAU70038 | IMAU70038_02006 | 93.08 | 0 | 2353 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70038 | IMAU70038_02146 | 98.31 | 0 | 1432 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU70038 | IMAU70038_02147 | 95.08 | 0 | 754 | EnzType:putative Type I specificity subunit |
| IMAU70038 | IMAU70038_02149 | 71.57 | 5.72E-172 | 489 | EnzType:putative Type I specificity subunit |
| IMAU70038 | IMAU70038_02150 | 99.81 | 0 | 1098 | EnzType:putative Type I methyltransferase |
| IMAU70038 | IMAU70038_02151 | 100.00 | 0 | 2109 | EnzType:putative Type I restriction enzyme |
| IMAU70046 | IMAU70046_01967 | 96.06 | 0 | 1400 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU70046 | IMAU70046_01968 | 56.09 | 2.95E-156 | 447 | EnzType:putative Type I specificity subunit |
| IMAU70046 | IMAU70046_01970 | 75.06 | 2.53E-160 | 459 | EnzType:putative Type I specificity subunit |
| IMAU70046 | IMAU70046_01971 | 100.00 | 0 | 1126 | EnzType:putative Type I methyltransferase |
| IMAU70046 | IMAU70046_01972 | 98.16 | 0 | 2105 | EnzType:putative Type I restriction enzyme |
| IMAU70046 | IMAU70046_02430 | 100.00 | 0 | 513 | EnzType:putative Type II methyltransferase |

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|---|---|---|---|---|---|
| IMAU70046 | IMAU70046_02782 | 98.67 | 0 | 2154 | EnzType:putative Type I restriction enzyme |
| IMAU70046 | IMAU70046_02783 | 98.70 | 0 | 1106 | EnzType:putative Type I methyltransferase |
| IMAU70046 | IMAU70046_02784 | 82.35 | 5.01E-174 | 495 | EnzType:putative Type I specificity subunit |
| IMAU70057 | IMAU70057_01997 | 100.00 | 4.99E-176 | 486 | EnzType:putative Type II methyltransferase |
| IMAU70057 | IMAU70057_01999 | 91.33 | 0 | 2786 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70057 | IMAU70057_02126 | 99.86 | 0 | 1450 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU70057 | IMAU70057_02127 | 60.71 | 1.43E-83 | 245 | EnzType:putative Type I specificity subunit |
| IMAU70057 | IMAU70057_02128 | 59.12 | 1.09E-175 | 492 | EnzType:putative Type I specificity subunit |
| IMAU70057 | IMAU70057_02130 | 73.13 | 0 | 515 | EnzType:putative Type I specificity subunit |
| IMAU70057 | IMAU70057_02131 | 100.00 | 0 | 1101 | EnzType:putative Type I methyltransferase |
| IMAU70057 | IMAU70057_02132 | 100.00 | 0 | 2112 | EnzType:putative Type I restriction enzyme |
| IMAU70057 | IMAU70057_03015 | 57.10 | 0 | 1114 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70061 | IMAU70061_02182 | 85.69 | 0 | 2065 | EnzType:putative Type II methyltransferase |
| IMAU70061 | IMAU70061_02400 | 90.12 | 1.14E-108 | 309 | EnzType:putative Type II methyltransferase |
| IMAU70061 | IMAU70061_02401 | 70.00 | 2.65E-130 | 372 | EnzType:putative Type II methyltransferase |
| IMAU70061 | IMAU70061_02606 | 93.03 | 3.36E-178 | 492 | EnzType:putative Type II methyltransferase |
| IMAU70061 | IMAU70061_02618 | 99.70 | 0 | 2036 | EnzType:putative Type III restriction enzyme |
| IMAU70061 | IMAU70061_02619 | 99.52 | 0 | 1281 | EnzType:putative Type III methyltransferase |
| IMAU70061 | IMAU70061_02622 | 59.70 | 7.54E-24 | 88.2 | EnzType:putative control protein |
| IMAU70083 | IMAU70083_02830 | 100.00 | 0 | 699 | EnzType:putative Type II methyltransferase |
| IMAU70083 | IMAU70083_02860 | 93.44 | 5.85E-173 | 479 | EnzType:putative Type II methyltransferase |
| IMAU70083 | IMAU70083_02888 | 73.80 | 0 | 1039 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70083 | IMAU70083_02892 | 86.70 | 0 | 2065 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU70083 | IMAU70083_03037 | 100.00 | 0 | 1452 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU70083 | IMAU70083_03038 | 100.00 | 0 | 784 | EnzType:putative Type I specificity subunit |
| IMAU70083 | IMAU70083_03040 | 69.55 | 0 | 543 | EnzType:putative Type I specificity subunit |

|  |  |  |  |  |  |
|---|---|---|---|---|---|
| IMAU70083 | IMAU70083_03041 | 100.00 | 0 | 1101 | EnzType:putative Type I methyltransferase |
| IMAU70083 | IMAU70083_03042 | 100.00 | 0 | 2112 | EnzType:putative Type I restriction enzyme |
| IMAU80010 | IMAU80010_00598 | 61.54 | 6.76E-164 | 469 | EnzType:putative Type I specificity subunit |
| IMAU80010 | IMAU80010_00599 | 99.63 | 0 | 1112 | EnzType:putative Type I methyltransferase |
| IMAU80010 | IMAU80010_00600 | 98.67 | 0 | 2154 | EnzType:putative Type I restriction enzyme |
| IMAU80010 | IMAU80010_01951 | 99.60 | 0 | 530 | EnzType:putative Type II methyltransferase |
| IMAU80010 | IMAU80010_02191 | 98.03 | 0 | 1427 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU80010 | IMAU80010_02192 | 72.85 | 0 | 568 | EnzType:putative Type I specificity subunit |
| IMAU80010 | IMAU80010_02194 | 95.59 | 0 | 800 | EnzType:putative Type I specificity subunit |
| IMAU80010 | IMAU80010_02195 | 100.00 | 0 | 1127 | EnzType:putative Type I methyltransferase |
| IMAU80010 | IMAU80010_02196 | 98.83 | 0 | 2116 | EnzType:putative Type I restriction enzyme |
| PC804 | IMAU80040_00345 | 75.59 | 0 | 1590 | EnzType:putative Type I restriction enzyme |
| PC804 | IMAU80040_00346 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| PC804 | IMAU80040_00347 | 50.94 | 4.85E-96 | 280 | EnzType:putative Type I specificity subunit |
| PC804 | IMAU80040_00352 | 95.83 | 0 | 805 | EnzType:putative Type I specificity subunit |
| PC804 | IMAU80040_00353 | 98.31 | 0 | 1432 | EnzType:putative Type IV methyl-directed restriction enzyme |
| PC804 | IMAU80040_00475 | 91.33 | 0 | 2788 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| PC804 | IMAU80040_00477 | 100.00 | 4.99E-176 | 486 | EnzType:putative Type II methyltransferase |
| PC804 | IMAU80040_02981 | 99.66 | 0 | 2436 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU80044 | IMAU80044_01670 | 94.88 | 0 | 1923 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU80044 | IMAU80044_02167 | 75.25 | 1.58E-178 | 506 | EnzType:putative Type I specificity subunit |
| IMAU80044 | IMAU80044_02169 | 95.14 | 0 | 759 | EnzType:putative Type I specificity subunit |
| IMAU80044 | IMAU80044_02170 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| IMAU80044 | IMAU80044_02171 | 100.00 | 0 | 2108 | EnzType:putative Type I restriction enzyme |
| IMAU80047 | IMAU80047_01669 | 94.88 | 0 | 1923 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU80047 | IMAU80047_02165 | 75.25 | 1.58E-178 | 506 | EnzType:putative Type I specificity subunit |

| | | | | | |
|---|---|---|---|---|---|
| IMAU80047 | IMAU80047_02167 | 95.14 | 0 | 759 | EnzType:putative Type I specificity subunit |
| IMAU80047 | IMAU80047_02168 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| IMAU80047 | IMAU80047_02169 | 100.00 | 0 | 2108 | EnzType:putative Type I restriction enzyme |
| IMAU80048 | IMAU80048_01446 | 75.59 | 0 | 1590 | EnzType:putative Type I restriction enzyme |
| IMAU80048 | IMAU80048_01447 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| IMAU80048 | IMAU80048_01451 | 68.06 | 7.82E-162 | 461 | EnzType:putative Type I specificity subunit |
| IMAU80048 | IMAU80048_01453 | 98.31 | 0 | 1432 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU80048 | IMAU80048_01561 | 91.33 | 0 | 2788 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU80048 | IMAU80048_01563 | 100.00 | 4.99E-176 | 486 | EnzType:putative Type II methyltransferase |
| IMAU80077 | IMAU80077_02185 | 59.41 | 5.62E-81 | 239 | EnzType:putative Type I specificity subunit |
| IMAU80077 | IMAU80077_02187 | 97.02 | 0 | 797 | EnzType:putative Type I specificity subunit |
| IMAU80077 | IMAU80077_02188 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| IMAU80077 | IMAU80077_02189 | 99.80 | 0 | 2104 | EnzType:putative Type I restriction enzyme |
| IMAU80077 | IMAU80077_02667 | 99.59 | 0 | 513 | EnzType:putative Type II methyltransferase |
| IMAU80077 | IMAU80077_02701 | 66.12 | 0 | 1299 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU80079 | IMAU80079_02188 | 59.41 | 5.62E-81 | 239 | EnzType:putative Type I specificity subunit |
| IMAU80079 | IMAU80079_02190 | 97.02 | 0 | 797 | EnzType:putative Type I specificity subunit |
| IMAU80079 | IMAU80079_02191 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| IMAU80079 | IMAU80079_02192 | 99.80 | 0 | 2104 | EnzType:putative Type I restriction enzyme |
| IMAU80079 | IMAU80079_02672 | 99.59 | 0 | 513 | EnzType:putative Type II methyltransferase |
| IMAU80079 | IMAU80079_02704 | 66.12 | 0 | 1299 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU80116 | IMAU80116_00959 | 89.45 | 0 | 511 | EnzType:putative Type II methyltransferase |
| IMAU80116 | IMAU80116_01342 | 97.70 | 0 | 611 | EnzType:putative Type II methyltransferase |
| IMAU80116 | IMAU80116_01634 | 99.94 | 0 | 3207 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| IMAU80116 | IMAU80116_02175 | 58.93 | 0 | 848 | EnzType:putative Type IV methyl-directed restriction enzyme |
| IMAU80116 | IMAU80116_02176 | 97.66 | 0 | 775 | EnzType:putative Type I specificity subunit |

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|---|---|---|---|---|---|
| IMAU80116 | IMAU80116_02178 | 74.74 | 5.41E-180 | 509 | EnzType:putative Type I specificity subunit |
| IMAU80116 | IMAU80116_02179 | 100.00 | 0 | 1100 | EnzType:putative Type I methyltransferase |
| IMAU80116 | IMAU80116_02180 | 99.90 | 0 | 2107 | EnzType:putative Type I restriction enzyme |
| IMAU80116 | IMAU80116_02703 | 52.05 | 3.33E-91 | 266 | EnzType:putative Type II methyltransferase |
| Zhang | LCAZH_2054 | 99.86 | 0 | 1519 | EnzType:putative Type IIG restriction enzyme/methyltransferase |
| Zhang | LCAZH_2056 | 100.00 | 0 | 2487 | EnzType:Type II methyltransferase |

**Table S2 Differentially expressed genes in *pglX* mutant in comparison with its wild type.**

| Gene locus | Gene description | Fold change | Gene name |
|---|---|---|---|
| LCAZH_0009 | deoxyribose-phosphate aldolase | 1.57 | deoC |
| LCAZH_0020 | metal-dependent membrane protease | 1.63 | - |
| LCAZH_0022 | hypothetical protein | 2.10 | - |
| LCAZH_0057 | metal-dependent membrane protease | 1.80 | - |
| LCAZH_0058 | 2-keto-3-deoxy-6-phosphogluconate aldolase | 3.51 | eda |
| LCAZH_0060 | hypothetical protein | 2.26 | - |
| LCAZH_0061 | hypothetical protein | 2.25 | - |
| LCAZH_0063 | multidrug ABC transporter ATPase/permease | 1.03 | - |
| LCAZH_0095 | hypothetical protein | 1.18 | - |
| LCAZH_0096 | hypothetical protein | 1.05 |  |
| LCAZH_0097 | ABC transporter ATP-binding protein | 1.18 | ABC-2.A |
| LCAZH_0117 | phospholipase A2 family enzyme | 1.57 | - |
| LCAZH_0118 | hypothetical protein | 1.56 | - |
| LCAZH_0187 | helicase subunit of the Holliday junction resolvase-like ATPase | 1.47 | ycaJ |
| LCAZH_0188 | acetate kinase | 1.32 | ackA |
| LCAZH_0190 | hypothetical protein | 2.02 | - |
| LCAZH_0191 | hypothetical protein | 2.14 | fbaA |
| LCAZH_0192 | PTS system ascorbate-specific transporter subunit IIC | 1.86 | ulaA |
| LCAZH_0218 | flavodoxin | 1.25 | - |
| LCAZH_0257 | inositol dehydrogenase | 1.11 | iolG |
| LCAZH_0264 | H+/gluconate symporter-like permease | 1.72 | TC.GNTP |
| LCAZH_0311 | lacto-N-biosidase | 2.89 | HEXA_B |
| LCAZH_0330 | hypothetical protein | 1.33 | patB |
| LCAZH_0331 | peptidase | 1.63 | pepP |
| LCAZH_0332 | PTS system transporter subunit IIc | 1.72 | celB |
| LCAZH_0335 | endoglucanase | 2.11 | - |
| LCAZH_0336 | transcription antiterminator | 2.49 | licR |
| LCAZH_0341 | hypothetical protein | 1.85 | - |
| LCAZH_0353 | hypothetical protein | 1.03 | - |
| LCAZH_0357 | ribose/xylose/arabinose/galactoside ABC transporter permease | 1.85 | rbsC |
| LCAZH_0358 | sugar ABC transporter periplasmic protein | 1.63 | rbsB |
| LCAZH_0371 | hypothetical protein | 1.03 | - |
| LCAZH_0377 | transcriptional antiterminator and PTS system component IIA | 2.14 | - |
| LCAZH_0378 | PTS system galactitol-specific transporter subunit IIB | 2.20 | ulaB |
| LCAZH_0379 | hypothetical protein | 2.08 | ulaA |

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|---|---|---|---|
| LCAZH_0380 | hypothetical protein | 2.93 | - |
| LCAZH_0381 | fructose/tagatose bisphosphate aldolase | 1.94 | fbaA |
| LCAZH_0402 | levA protein | 4.11 | agaF |
| LCAZH_0403 | PTS system mannose/fructose/N-acetylgalactosamine-specific transporter subunit IIB | 3.92 | manX |
| LCAZH_0404 | levC protein | 3.89 | manY |
| LCAZH_0405 | PTS system mannose/fructose/N-acetylgalactosamine-specific transporter subunit IID | 4.02 | - |
| LCAZH_0406 | hypothetical protein | 4.05 | - |
| LCAZH_0407 | fructan hydrolase | 5.16 | fruA |
| LCAZH_0413 | 6-phospho 3-hexuloisomerase | 1.27 | hxlB |
| LCAZH_0449 | oxidoreductase | 1.14 | ohyA |
| LCAZH_0456 | redox protein%2C regulator of disulfide bond formation | 1.41 | osmC |
| LCAZH_0540 | hypothetical protein | 1.28 | - |
| LCAZH_0542 | hypothetical protein | 1.08 | - |
| LCAZH_0554 | l-lactate dehydrogenase | 2.10 | ldh |
| LCAZH_0559 | redox protein%2C regulator of disulfide bond formation | 1.68 | osmC |
| LCAZH_0603 | PTS system galacitol-specific transporter subunit IIA | 1.92 | gatA |
| LCAZH_0604 | PTS system galactitol-specific transporter subunit IIB | 1.73 | gatB |
| LCAZH_0605 | PTS system galacitol transporter subunit EIIC | 1.32 | gatC |
| LCAZH_0606 | hypothetical protein | 1.18 | - |
| LCAZH_0728 | hypothetical protein | 1.21 | - |
| LCAZH_0802 | comX | 1.59 | - |
| LCAZH_0870 | ribosome-associated protein Y (PSrp-1) | 1.03 | - |
| LCAZH_0927 | alpha-glucosidase | 1.10 | dexB |
| LCAZH_0928 | sugar ABC transporter periplasmic protein | 1.56 | cycB,<br>ganO |
| LCAZH_0931 | maltose ABC transporter permease | 1.40 | ganQ |
| LCAZH_1074 | Zn-dependent protease | 1.04 | |
| LCAZH_1299 | PDH (acetyl-transferring) E1 component subunit alpha | 1.35 | pdhA |
| LCAZH_1300 | PDH E1 component beta subunit | 1.34 | pdhB |
| LCAZH_1301 | dihydrolipoamide acetyltransferase | 1.41 | pdhC |
| LCAZH_1302 | dihydrolipoyl dehydrogenase | 1.42 | pdhD |
| LCAZH_1372 | hypothetical protein | 1.47 | - |
| LCAZH_1396 | pyruvate-formate lyase | 2.13 | pflD |
| LCAZH_1398 | pyruvate-formate lyase-activating enzyme | 1.43 | pflA |
| LCAZH_1431 | dihydrolipoamide acetyltransferase family | 1.56 | bkdB |

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|---|---|---|---|
| LCAZH_1432 | alpha-ketoacid dehydrogenase subunit beta | 1.14 | bkdA2 |
| LCAZH_1433 | thiamine pyrophosphate-dependent dehydrogenase E1 component subunit alpha | 1.24 | bkdA1 |
| LCAZH_1435 | acetate kinase | 1.04 | buk |
| LCAZH_1463 | lipoate-protein ligase A | 1.50 | lplA |
| LCAZH_1464 | hypothetical protein | 1.39 | - |
| LCAZH_1509 | hypothetical protein | 1.21 | ppsR |
| LCAZH_1774 | pyruvate oxidase or other thiamine pyrophosphate-requiring enzyme | 1.42 | poxL |
| LCAZH_1782 | aldose 1-epimerase | 1.15 | - |
| LCAZH_1883 | hypothetical protein | 1.09 | - |
| LCAZH_2129 | hypothetical protein | 2.03 | - |
| LCAZH_2142 | alanine dehydrogenase | 1.36 | ald |
| LCAZH_2143 | threonine dehydratase | 1.23 | ilvA |
| LCAZH_2144 | hypothetical protein | 1.19 | - |
| LCAZH_2145 | hypothetical protein | 1.28 | - |
| LCAZH_2146 | dipeptidase | 1.03 | pepDA |
| LCAZH_2151 | beta-glucosidase/6-phospho-beta-glucosidase/beta-galactosidase | 1.96 | bglA |
| LCAZH_2152 | PTS system trehalose transporter subunitt IIBC | 2.59 | bglF |
| LCAZH_2336 | hypothetical protein | 1.85 | - |
| LCAZH_2346 | hypothetical protein | 1.07 | - |
| LCAZH_2347 | lactococcin A ABC transporter permease | 1.12 | blpB |
| LCAZH_2348 | ABC transporter | 1.16 | blpA |
| LCAZH_2349 | hypothetical protein | 1.61 | |
| LCAZH_2350 | sensor histidine kinase PrcK | 1.22 | agrC, |
| LCAZH_2351 | response regulator of the LytR/AlgR family | 1.40 | agrA |
| LCAZH_2361 | hypothetical protein | 1.81 | - |
| LCAZH_2362 | immunity protein PlnI%2C membrane-bound protease CAAX family | 1.10 | - |
| LCAZH_2563 | galactose mutarotase-like protein | 1.49 | - |
| LCAZH_2632 | PTS system galactitol-specific transporter subunit IIC | 1.20 | gatC |
| LCAZH_2635 | 2-dehydro-3-deoxyphosphogluconate aldolase/4-hydroxy-2-oxoglutarate aldolase | 1.82 | eda |
| LCAZH_2636 | transcriptional antiterminator | 1.72 | - |
| LCAZH_2637 | PTS system cellobiose-specific transporter subunit IIA | 2.78 | celC |
| LCAZH_2638 | PTS system cellobiose-specific transporter subunit IIB | 2.80 | celA |
| LCAZH_2639 | beta-glucosidase | 2.16 | bglA |
| LCAZH_2640 | transcriptional regulator/sugar kinase | 1.91 | |
| LCAZH_2641 | hypothetical protein | 2.12 | |
| LCAZH_2642 | alpha-mannosidase | 2.05 | mngB |

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|---|---|---|---|
| LCAZH_2643 | PTS system cellobiose-specific transporter subunit IIC | 2.25 | - |
| LCAZH_2645 | hypothetical protein | 4.49 | fucA |
| LCAZH_2646 | hypothetical protein | 4.39 | |
| LCAZH_2647 | PTS system galacitol transporter subunit EIIC | 3.85 | gatC |
| LCAZH_2648 | PTS system galacitol transporter subunit EIIB | 2.93 | gatB |
| LCAZH_2649 | PTS system galacitol transporter subunit EIIA | 2.87 | gatA |
| LCAZH_2658 | subtilisin-like serine protease | 1.89 | - |
| LCAZH_2659 | hypothetical protein | 2.53 | - |
| LCAZH_2660 | hypothetical protein | 2.53 | - |
| LCAZH_2661 | preprotein translocase subunit YajC | 2.82 | yajC |
| LCAZH_2662 | PTS system mannose/fructose-specific transporter subunit IIA | 2.48 | agaF |
| LCAZH_2663 | PTS system mannose-specific transporter subunit IID | 3.22 | agaE |
| LCAZH_2664 | PTS system N-acetylgalactosamine transporter subunit EIIC | 3.26 | agaW |
| LCAZH_2665 | PTS system mannose/fructose/N-acetylgalactosamine-specific transporter subunit IIB | 3.11 | agaV |
| LCAZH_2666 | glucuronyl hydrolase | 2.64 | ugl |
| LCAZH_2667 | hypothetical protein | 2.07 | - |
| LCAZH_2669 | 5-keto 4-deoxyuronate isomerase | 2.33 | kduI |
| LCAZH_2670 | short-chain alcohol dehydrogenase | 2.31 | kduD |
| LCAZH_2682 | mannose-6-phosphate isomerase | 1.32 | glvA |
| LCAZH_2692 | RpiR family transcriptional regulator | 1.86 | - |
| LCAZH_2693 | PTS system transporter subunit IIA | 2.33 | crr |
| LCAZH_2696 | hypothetical protein | 1.98 | - |
| LCAZH_2697 | triosephosphate isomerase | 1.67 | tpiA |
| LCAZH_2698 | fructose/tagatose bisphosphate aldolase | 1.82 | fbaA |
| LCAZH_2699 | PTS system galactitol-specific transporter subunit IIB | 3.35 | gatB |
| LCAZH_2700 | PTS system galacitol transporter subunit EIIC | 1.64 | gatC |
| LCAZH_2701 | PTS system galacitol-specific transporter subunit IIA | 2.71 | gatA |
| LCAZH_2702 | hypothetical protein | 3.46 | - |
| LCAZH_2703 | transcriptional antiterminator | 2.76 | manR |
| LCAZH_2704 | hypothetical protein | 2.51 | - |
| LCAZH_2720 | hypothetical protein | 1.06 | - |
| LCAZH_2722 | hypothetical protein | 1.27 | - |
| LCAZH_2727 | PTS system sorbitol transporter subunit EIIA | 1.08 | srlB |
| LCAZH_2728 | PTS system sorbitol transporter subunit EIIBC | 1.30 | srlE |
| LCAZH_2729 | PTS system sorbitol transporter subunit EIIC | 1.42 | srlA |
| LCAZH_2731 | sorbitol operon transcription regulator | 1.56 | - |

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|---|---|---|---|
| LCAZH_2732 | sorbitol-6-phosphate dehydrogenase | 1.77 | srlD |
| LCAZH_2733 | ribulose-5-phosphate 4-epimerase-like epimerase/aldolase | 2.02 | araD |
| LCAZH_2734 | HAD superfamily hydrolase | 1.02 | - |
| LCAZH_2735 | L-xylulose-5-phosphate 3-epimerase | 3.12 | ulaE |
| LCAZH_2736 | lactose transport regulator | 1.23 | - |
| LCAZH_2737 | 3-hexulose-6-phosphate synthase | 1.03 | ulaD |
| LCAZH_2738 | PTS system galactitol-specific transporter subunit IIB | 1.07 | ulaB |
| LCAZH_2739 | hypothetical protein | 1.63 | ulaA |
| LCAZH_2740 | PTS system mannitol/fructose-specific transporter subunit IIA | 1.70 | ulaC |
| LCAZH_2741 | Zn-dependent hydrolase of the beta-lactamase fold | 1.84 | ulaG |
| LCAZH_2744 | PTS system mannitol/fructose-specific transporter subunit IIA | 2.39 | fruB |
| LCAZH_2747 | sorbitol operon transcription regulator | 1.54 | manR |
| LCAZH_2753 | major facilitator superfamily permease | 1.29 |  |
| LCAZH_2755 | alpha-L-fucosidase | 1.27 | FUCA |
| LCAZH_2767 | alcohol dehydrogenase | 1.01 | - |
| LCAZH_2839 | aryl-alcohol dehydrogenase-like protein | 1.40 | - |
| LCAZH_2841 | PTS system mannose-specific transporter subunit IID | 1.22 | manZ |
| LCAZH_2842 | PTS system mannose-specific transporter subunit IIC | 1.29 | manY |
| LCAZH_2843 | PTS system mannose/fructose-specific transporter subunit IIA | 1.29 | manXa |
| LCAZH_2897 | HAD superfamily hydrolase | 1.03 | - |
| LCAZH_2936 | sugar ABC transporter permease | 1.42 | ganP |
| LCAZH_2967 | ketohydroxyglutarate aldolase | 2.20 | eda |
| LCAZH_2968 | 2-dehydro-3-deoxygluconokinase | 2.30 | kdgK |
| LCAZH_0201 | oligopeptide ABC transporter periplasmic protein | -1.05 | oppA |
| LCAZH_0280 | ABC transporter ATPase | -1.36 | - |
| LCAZH_0484 | hypothetical protein | -1.23 | - |
| LCAZH_0485 | hypothetical protein | -1.24 | - |
| LCAZH_0486 | surface protein | -1.29 | - |
| LCAZH_0487 | sortase | -1.20 | srtA |
| LCAZH_0754 | catabolite control protein A | -1.33 | lacI |
| LCAZH_0987 | gamma-aminobutyrate permease-like permease | -1.32 | TC.AAT |
| LCAZH_0988 | 1-acyl-sn-glycerol-3-phosphate acyltransferase | -1.16 | - |
| LCAZH_0989 | lipopolysaccharide biosynthesis glycosyltransferase | -1.11 | - |
| LCAZH_0991 | 1-acyl-sn-glycerol-3-phosphate acyltransferase | -1.04 | - |

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|---|---|---|---|
| LCAZH_1116 | DNA-entry nuclease | -1.48 | endA |
| LCAZH_1117 | hypothetical protein | -1.57 | - |
| LCAZH_1275 | major facilitator superfamily permease | -1.32 | - |
| LCAZH_1335 | PTS system mannitol/fructose-specific transporter subunit IIABC | -5.47 | fruB |
| LCAZH_1336 | tagatose-6-phosphate kinase | -5.26 | fruK |
| LCAZH_1337 | lactose transport regulator | -5.37 | fruR |
| LCAZH_1351 | 6-phosphofructokinase | -1.23 | pfkA |
| LCAZH_1352 | pyruvate kinase | -1.06 | pyk |
| LCAZH_1360 | hypothetical protein | -1.56 | - |
| LCAZH_1749 | sugar permease | -1.53 | iolT |
| LCAZH_1838 | hypothetical protein | -2.15 | - |
| LCAZH_1872 | major facilitator superfamily permease | -1.23 | - |
| LCAZH_1929 | amino acid transporter | -1.30 | - |
| LCAZH_1988 | Clp protease/DnaK/DnaJ chaperone ATP-binding subunit | -1.07 | clpL |
| LCAZH_2066 | nucleoside-diphosphate-sugar epimerase | -1.15 | - |
| LCAZH_2071 | 3-hydroxymyristoyl-ACP dehydratase | -1.01 | fabZ |
| LCAZH_2072 | biotin carboxyl carrier protein | -1.12 | accB |
| LCAZH_2150 | transcriptional regulator | -1.24 | lmrA |
| LCAZH_2192 | cell wall-associated hydrolase | -1.31 | - |
| LCAZH_2308 | phosphoenolpyruvate synthase/pyruvate phosphate dikinase | -1.14 | ppdK |
| LCAZH_RS00165 | putative holin-like toxin | -1.02 | - |

**Table S3 Composition of the chemical defined medium.**

| Component | Content (g/L) | Component | Content (g/L) | Component | Content (g/L) |
|---|---|---|---|---|---|
| Glucose | 10 | Alanine | 0.1 | Niacin | 0.001 |
| Sodium acetate | 5 | Arginine | 0.1 | Pantothenic acid | 0.001 |
| $KH_2PO_4$ | 3 | Aspartic acid | 0.2 | Pyridoxine | 0.002 |
| $K_2HPO_4$ | 3 | Cysteinic acid | 0.2 | Riboflavin | 0.001 |
| $MgSO_4\cdot 7H_2O$ | 0.2 | Glutamine | 0.2 | Parahydrobenzoic acid | 0.01 |
| $MnSO_4\cdot 4H_2O$ | 0.05 | Glutamic acid | 0.2 | Folic acid | 0.001 |
| $FeSO_4\cdot 7H_2O$ | 0.02 | Glycine | 0.1 | Cyanoglycosamine | 0.001 |
| Tween 80 | 1 | Histidonic acid | 0.1 | D-biotin | 0.01 |
| | | Isoleucine | 0.1 | Thiamine-sol | 0.01 |
| | | Leucine | 0.1 | Inosine | 0.01 |
| | | Lysergic acid | 0.1 | Adenosine | 0.01 |
| | | Phenylalanine | 0.1 | Xanthan Ridge | 0.01 |
| | | Methionine | 0.1 | Uracadine | 0.01 |
| | | Proline | 0.1 | Thymidine | 0.01 |
| | | Serine | 0.1 | | |
| | | Threonine | 0.1 | | |
| | | Tryptophan | 0.1 | | |
| | | Tyrosine | 0.1 | | |
| | | Valine | 0.1 | | |