

**Table S1.** Presence of catabolic genes in the genome (chromosome or plasmids) of *Lactiplantibacillus plantarum* LL441 involved in growth in milk and formation of flavour (taste and aroma) compounds.

Protein/Description	Gene/Operon	Function	Chromosome	Plasmid
<b>Proteases</b>				
ATP-dependent zinc metalloprotease	<i>ftsH</i>	Cleavage of transmembrane sequences, cell division	1	
Clp protease	<i>clpCEPX</i>	Turnover of cellular proteins	1	
ClpCP protease substrate adapter protein	<i>mecA</i>	Activates protein degradation by ClpCP complex	1	
DegP/HtrA serine protease	<i>htrA</i>	Clearance of denatured or aggregated proteins from the inner-membrane and periplasmic space	1	
Hsl protease	<i>hslUV</i>	ATP-binding and protease subunits	1	
Intracellular protease	-	-	1	
Late competence processing protease	<i>comC</i>	Processing of DNA during uptake		
Lon-like protease with PDZ domain	-	Quality-control of proteins	1	
Membrane-associated zinc metalloprotease	<i>yugP</i>	Hydrolyses Met if followed by Ala, Pro, or Ser	1	
Membrane protease family protein	-	-	1	
Periplasmic protease	-	-	1	
Phage proteases	-	-	1	
SOS-response repressor and protease	<i>lexA</i>	Autoproteolysis in SOS response	1	
YmfH protease	<i>ymfH</i>		1	
Zinc protease	-	-	1	
<b>Peptidases</b>				
D-alanyl-D-alanine dipeptidase	-	-	1	
Aminopeptidase C	<i>pepC</i>	General cysteine aminopeptidase	2	
Aminopeptidase YpdF	<i>ypdF</i>	Hydrolyses Xaa-Pro bonds when Xaa is Ala, Asn or Met	1	
D-alanyl-D-alanine carboxypeptidase	<i>dacA</i>	Cross-linking of peptidoglycan chains; PBP	2	
Dipeptidase	-	-	4	
ImmA/IrrE family metallo-endopeptidase	-	-	-	1 pLL441-1
Lysyl aminopeptidase	-	-	1	
M15 family metallopeptidase	-	Cell wall biosynthesis	1	
Methionine aminopeptidase	<i>pepM</i>	Release of Met from proteins and peptides	1	
Multimodular transpeptidase-transglycosylase	-	Peptidoglycan biosynthesis, probably PBPs	2	
Muramoyl tetrapeptide carboxypeptidase	-	-	1	

Neutral endopeptidase	<i>pepO</i>	Degradation of casein-derived peptides	1
Oligoendopeptidase F	<i>pepF</i>	Hydrolyses 7-17 amino acids long peptides	2
Proline iminopeptidase	<i>pepI</i>	Releases proline from peptides	3
SprT-family zinc metallopeptidase	<i>sprT</i>	-	1
Tripeptide aminopeptidase	<i>pepT</i>	Amino degradation of tripeptides	1
Xaa-His dipeptidase	<i>pepV</i>	Hydrolysis of Xaa-His dipeptides	1
Xaa-Pro dipeptidase	<i>pepX</i>	Release dipeptides when Pro is at the second position	2

### Lactose, citrate, amino acid, and peptide transporters

Amino acid permease, GabP family	-	Transport of amino acids	5
Amino acid permease, YdaO	<i>ydaO</i>	Transport of amino acids	1
Cysteine ABC transporter	<i>cydCD</i>	Transport of cysteine	1
Di-tripeptide/cation symporter DtpT	<i>dtpT</i>	Transport of di- and tripeptides	1
D-serine/D-alanine/glycine transporter	-	Transporter of serine, alanine, glycine	3
Glutamine ABC transporter	<i>glnHPQ</i>	Transport of basic amino acids	1
Lactose permease	<i>lacP</i>	Transport of lactose	2
$\beta$ -galactosidase	<i>lacZ</i>	Lactose degradation	1
$\beta$ -galactosidase LacLM	<i>lacLM</i>	Lactose degradation	1
Methionine ABC transporter	-	Transport of Met	3
Na(+)-dependent branched-chain amino acid transporter	<i>brnQ</i>	Transport of branched chain amino acids	2
Oligopeptide ABC transporter	<i>oppABCD</i>	Transport of oligopeptides	1
Oligopeptide ABC transporter	<i>oppA</i>	Substrate binding protein	5
Proton/glutamate symporter	-	Transport of glutamate	1
Serine transporter	-	Transport of serine	1
Tyrosine transporter	<i>nhaC</i>	Transport of tyrosine	2

### Aminotransferases and transaminases

Aspartate aminotransferase	<i>aspAT</i>	Reversible transfer of a $\alpha$ -amino group between Asp and Glu	6
Branched-chain amino acid aminotransferase	<i>bcaT</i>	Cys, Val, Leu, Iso and Met, synthesis and metabolism, synthesis of secondary metabolites	1
Glutamine amidotransferase, class 1	<i>pfpI</i>	Removal of the ammonia group from glutamine	2
Glutamine-dependent methylthiobutyrate transaminase	-	Cys and Met metabolism, metabolic pathways	1
Glutamine-fructose-6-P aminotransferase	<i>glmS</i>	Ala and Glu, metabolism, metabolic pathways	1
Histidinol-phosphate aminotransferase	-	Glu and His metabolic pathways	1

L,D-transpeptidase	-	Cross-linking of peptide stems in peptidoglycans	1	
Multimodular transpeptidase-transglycosidase	-	-	2	
N-acetylornithine aminotransferase	<i>rocD</i>	Arg biosynthesis, metabolic pathways, synthesis of secondary metabolites	1	
Phosphoserine aminotransferase	-	Gly, Ser, Thr, Cys and Met metabolism, synthesis of secondary metabolites	1	
Pyruvate transaminase	-	Ala metabolism	1	
<b>Dehydrogenases</b>				
1,3-propanediol dehydrogenase	-	Glycerolipid, propanoate metabolism	1	
Aldehyde dehydrogenase	<i>adhE</i>	Fatty acids degradation, amino acids synthesis and degradation, synthesis of secondary metabolites	1	
Alanine dehydrogenase	<i>ala-dh</i>	Ala, Asp and Glu metabolism, metabolic pathways	1	
Alcohol dehydrogenase class III	<i>adh</i>	Glycolysis, fatty acid degradation, Tyr metabolism, pyruvate metabolism	3	1, pLL441-2
D-lactate dehydrogenase	<i>ldhD</i>	Synthesis of secondary metabolites	2	
L-lactate dehydrogenase	<i>ldhL</i>	Glycolysis, Cys and Met metabolism, synthesis of secondary metabolites	5	
Homoserine dehydrogenase	-	Gly, Ser, Thr and Cys, Met metabolism, Lys synthesis, metabolic pathways	2	
NADP-specific glutamate dehydrogenase	<i>gdhA</i>	Arg synthesis, Ala and Asp metabolism, metabolic pathways	1	
Histidinol dehydrogenase	-	His biosynthesis and biosynthesis of secondary metabolites	1	
<b>Lyases</b>				
Argininosuccinate lyase	-	Arg biosynthesis, Ala, Asp and Glu metabolism, metabolic pathways, biosynthesis of secondary metabolites	1	
Argininosuccinate synthase	-	Arg biosynthesis, Ala, Asp and Glu metabolism, metabolic pathways, biosynthesis of secondary metabolites	1	
Citrate lyase complex	<i>citCDEFG</i>	Formation of pyruvate from citrate	1	
Cystathionine beta-lyase	<i>cglB</i>	Production of sulphur compounds	1	
Cystathionine beta-synthase	<i>cbs</i>	Transulfuration from homocysteine to cystathionine	1	
Cystathionine gamma-lyase	<i>cglA</i>	Gly, Ser, Met, Cys and Thr metabolism, metabolic pathways	1	
Cystathionine gamma-synthase	<i>cgs</i>	Formation of cystathionine from cysteine	1	
D-serine ammonia-lyase	-	Gly, Ser and Thr metabolism, D-amino acid metabolism, metabolic pathways	1	
S-ribosylhomocysteine lyase	<i>luxS</i>	Cys and Met metabolism, metabolic pathways	1	

Aspartate ammonia-lyase	<i>aspA</i>	Ala, Asp and Glu metabolism	1
Aspartate ammonia-ligase	<i>asnA</i>	Ala, Gsp and Glu metabolism	1
<b>Esterases/lipases</b>			
Alpha/beta hydrolase	-	Lipid transport and metabolism	3
Hydrolase HAD	-	-	7
Esterase/lipase	<i>estA</i>	Lipid transport and metabolism	1
Glycerophosphoryl diester phosphodiesterase	<i>glpQ</i>	Glycerophospholipid metabolism	2
Lipase/Acylhydrolase	-	-	1
Phosphoesterase	-	Release of membrane-linked proteins with glycosylphosphatidylinositol anchors	1

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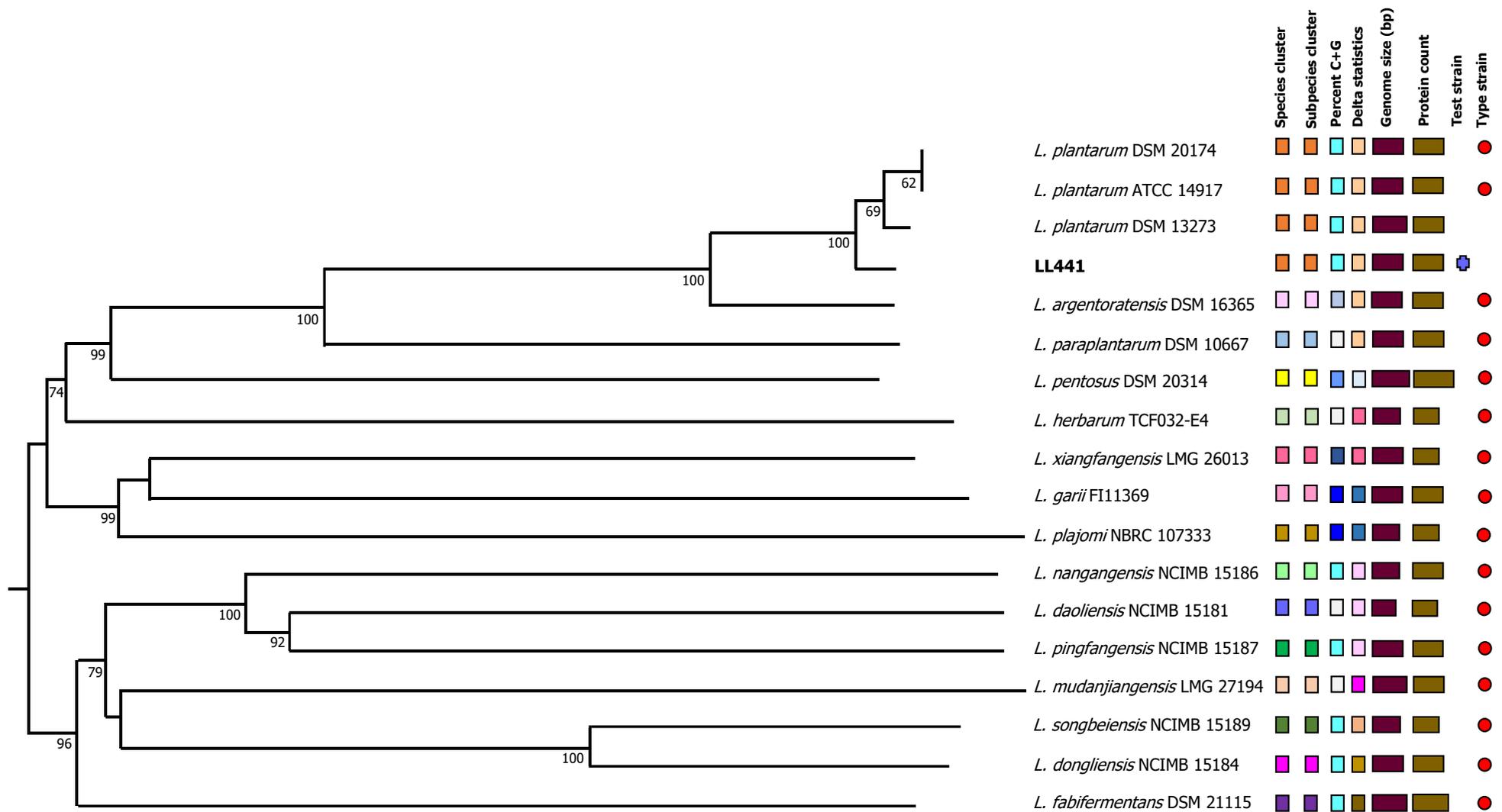
Colours denote different functional categories.

**Table S2.** Presence of “probiotic marker genes” (PMGs<sup>a</sup>) involved in stress resistance (acid, osmotic, oxidative, temperature), bile salt hydrolase activity, adhesion ability or gut persistence in the *Lactiplantibacillus plantarum* LL441 genome (chromosome or plasmids).

Protein/description	Gene/operon	Function	Chromosome	Plasmid
1-acylglycerol-3-phosphate <i>O</i> -acyltransferase	<i>plsC</i>	Acid stress	1	
60 kDa chaperonin	<i>groL / groEL</i>	Acid stress	1	
ATP synthase	<i>atpABCDEFGH</i>	Acid stress	1	
ATP-dependent Clp protease	<i>clpCEPX</i>	Acid stress	1	
Chaperone protein ClpB	<i>clpB</i>	Acid stress	1	
D-alanine-D-alanyl carrier protein ligase	<i>dltA</i>	Acid stress	1	
Glucose-6-phosphate isomerase	<i>gpi</i>	Acid stress	1	
Glutamate decarboxylase	<i>gadB</i>	Acid stress	1	
Glyceraldehyde-3-phosphate dehydrogenase	<i>gap</i>	Acid stress	1	
GMP synthase [glutamine-hydrolyzing]	<i>guaA</i>	Acid stress	1	
GTP pyrophosphokinase	<i>relA</i>	Acid stress	2	
L-lactate dehydrogenase	<i>ldh</i>	Acid stress	5	
D-alanine transfer protein	<i>dltD</i>	Acid stress	1	
Protein RecA	<i>recA</i>	Acid stress	1	
Pyruvate kinase	<i>pyk</i>	Acid stress	1	
Triosephosphate isomerase	<i>tpiA</i>	Acid stress	1	
Chaperone protein DnaK / HSP-70	<i>dnaK</i>	Acid stress / bile resistance	1	
Copper transporting ATPase	<i>copA</i>	Acid stress / bile resistance	1	-
Enolase	<i>eno</i>	Acid stress / bile resistance	2	
Ornithine carbamoyltransferase	<i>arcB</i>	Acid stress / bile resistance	1	
Phosphoglycerate kinase	<i>pgk</i>	Acid stress / bile resistance	1	
10 kDa chaperonin	<i>groS / groES</i>	Acid stress / bile resistance / temperature	1	
Chaperone protein DnaJ	<i>dnaJ</i>	Acid stress / bile resistance / temperature	1	
Heat shock protein GrpE / HSP-70 cofactor	<i>grpE</i>	Acid stress / bile resistance / temperature	1	
Serine protease HtrA	<i>htrA / degP</i>	Acid stress / bile resistance / temperature	1	
S-ribosylhomocysteine lyase	<i>luxS</i>	Acid stress / bile resistance / temperature / production of antimicrobial compounds	1	
30S ribosomal protein S3	<i>rpsC</i>	Bile resistance	1	
30S ribosomal protein S5	<i>rpsE</i>	Bile resistance	1	

50S ribosomal protein L4	<i>rplD</i>	Bile resistance	1	
50S ribosomal protein L5	<i>rplE</i>	Bile resistance	1	
50S ribosomal protein L6	<i>rplF</i>	Bile resistance	1	
Arginine-tRNA synthetase (ligase)	<i>argS</i>	Bile resistance	1	-
Choloylglycine hydrolase	<i>cbh / bsh</i>	Bile resistance	3	
CTP synthase	<i>pyrG</i>	Bile resistance	1	
DD-transpeptidase / penicillin-sensitive transpeptidase / penicillin-binding protein 1A	<i>ponA / pbp1A</i>	Bile resistance	1	
Dihydrolipoyl dehydrogenase	<i>pdhD / lpdA</i>	Bile resistance	1	
DNA protection during starvation protein	<i>dps</i>	Bile resistance	1	pLL441-7
Endopeptidase PepO	<i>pepO</i>	Bile resistance	1	
Glucosamine-6-phosphate deaminase	<i>nagB / gnp</i>	Bile resistance	1	
Glutamine synthetase		Bile resistance	1	
Oligopeptide-binding protein OppA	<i>oppA</i>	Bile resistance	6	
Sortase A	<i>srtA</i>	Bile resistance / adhesion	1	
Glycerol facilitator-aquaporin Z	<i>gla</i>	Osmotic stress	1	
Glycerol uptake facilitator	<i>glpF</i>	Osmotic stress	5	
Glycine betaine transport system	<i>opuAA, opuAB</i>	Osmotic stress	1	
Choline transport system	<i>opuBA, opuBB, opuBC, opuBD</i>	Osmotic stress	1	
Glycine betaine/carnitine transport permease protein GbuB	<i>gbuB</i>	Osmotic stress	1	
Peptide methionine sulfoxide reductase MsrB	<i>msrB</i>	Oxidative stress	1	
Exodeoxyribonuclease III	<i>exoA</i>	Adhesion	1	
Lipoprotein signal peptidase	<i>lspA</i>	Adhesion	1	
PTS system, cellobiose-specific EIIC component	<i>celB</i>	Gut persistence	7	
Pyruvate carboxylase	<i>pycA</i>	Adhesion	1	
Trehalose-6-phosphate hydrolase	<i>treA</i>	Gut persistence	2	

<sup>a</sup>PMGs as defined by Carpi et al. (2022). Only complete genes are being reported; Colours denote different functional categories.



**Figure S1.-** Phylogenomic analysis of LL441 and strains of species and subspecies of the *Lactiplantibacillus plantarum* group. The tree was inferred from Genome BLAST Distance Phylogeny (GBDP) with FastME 2.1.6.1 at the DSMZ Type Strain Genome Server (<http://ggdc.dsmz.de/>; Accessed on November 2022). Branch lengths were scaled in terms of the approach distance of formula d5. The numbers above branches are GBDP pseudo-bootstrap support values >60% from 100 replications (average branch support of 85.2%). The tree was rooted at the midpoint. The colour scheme on the right denotes with the same tone strains considered as belonging to the same taxon.