

Table S1. Main classes of common metabolites to *L.fermentum* U-21 and *L.fermentum* 279 detected in the aqueous phase of culture supernatant.

Metabolite	Class
Glycine (Gly)	Amino acids and derivatives
Alanine (Ala)	
Valine (Val)	
Leucine (Leu)	
Isoleucine (Ile)	
Aspartic acid (Asp)	
Asparagine (Asn)	
Glutamic acid (Glu)	
Glutamine (Gln)	
Serine (Ser)	
Threonine (Thr)	
Methionine (Met)	
Lysine (Lys)	
Histidine (His)	
Proline (Pro)	
Phenylalanine (Phe)	
Tyrosine (Tyr)	
Tryptophan (Trp)	
2-Aminocaprylic acid	
Norleucine	
Homocysteine	
Homoserine	
Norvaline	
Ornithine	
N-Methyl- α -aminoisobutyric acid	
β -Alanine	
5-Hydroxytryptophan	
Pyroglutamic acid	
Aceturic acid	
α -Methyl-L-tyrosine	
N,N-Dimethylglycine	
N-Acetyl-L-glutamic acid	
Carnitine	
Propanoic acid	Organic acid
Cinnamic acid	
Succinic acid	
Fumaric acid	
Formic acid	
Maleic acid	
Malonic acid	
Phthalic acid	
Propanedioic acid	
Oxalic acid	
2-Aminobutanoic acid	
2-Hydroxybutyric acid	
3-Hydroxybutyric acid	
Glycolic acid	
Lactic Acid	
Tartaric acid	

Methylcitric acid	
Maltose	
Melibiose	
Mannobiose	
Cellobiose	
Lactose	
Turanose	
Erythrose	
Xylose	
Galactose	
Glucose	
Mannose	
Tagatose	
Fructose	
2-Keto-gluconic acid	
Gluconic acid	
Mannonic acid	Saccharides
Ribonic acid	
Xylonic acid	
D-Erythro-Pentitol	
Mannitol	
Glycerol	
meso-Erythritol	
Arabinitol	
Erythritol	
<u>Arabitol</u>	
Arabinofuranose	
Dihydroxyacetone	
Levoglucozan	
Myo-Inositol	
Trehalose-6-phosphate	
Mannopyranose	
2-Hydroxyisocaproic acid	
4-Hydroxybutanoic acid	Fatty acids and analogues
Butanoic acid	

Table S2. Main classes of shared metabolites of *L.fermentum* U-21 and *L.fermentum* 279 detected in the lipid-containing phase of culture supernatant.

Metabolite	Class
Alanine (Ala)	
Asparagine (Asn)	
Proline (Pro)	
Tryptophan (Trp)	Amino acids and derivatives
1-Aminocyclopentanecarboxylic	
Pyroglutamic acid	
Oxalic acid	
Phthalic acid	
Ritalinic acid	Organic acids
4-Hydroxybenzoic acid	
Lyxose	Saccharides
Heptadecanoic acid	
Undecanoic acid	Fatty acids and analogues
Butanoic acid	

Oleic acid

Table S3. Main classes of *L.fermentum* 279 metabolites detected in the aqueous phase of culture supernatant.

Metabolite ¹	Class
Glycine (Gly)	Amino acids and derivatives
Alanine (Ala)	
Valine (Val)	
Leucine (Leu)	
Isoleucine (Ile)	
Aspartic acid (Asp)	
Asparagine (Asn)	
Glutamic acid (Glu)	
Glutamine (Gln)	
Serine (Ser)	
Threonine (Thr)	
Methionine (Met)	
Lysine (Lys)	
Histidine (His)	
Proline (Pro)	
Phenylalanine (Phe)	
Tyrosine (Tyr)	
Tryptophan (Trp)	
2-Aminocaprylic acid	
<u>5-Aminovaleric acid</u>	
<u>6-Aminocaproic acid</u>	
<u>Cystathionine</u>	
<u>7-Azatryptophan</u>	
Norleucine	
Homocysteine	
Homoserine	
Norvaline	
Ornithine	
N-Methyl- α -aminoisobutyric acid	
β -Alanine	
5-Hydroxytryptophan	
Pyroglutamic acid	
Aceturic acid	
α -Methyl-L-tyrosine	
N,N-Dimethylglycine	
N-Acetyl-L-glutamic acid	
<u>N-α-Acetyl-L-Lysine</u>	
<u>N-Methyl-L-glutamic acid</u>	
<u>N-methyltryptophan</u>	
<u>Tranexamic acid</u>	
Carnitine	
<u>Aconitic acid</u>	
<u>Acrylic acid</u>	
<u>Citric acid</u>	
<u>Ethylphosphonic acid</u>	Organic acid
<u>β-Hydroxypyruvic acid</u>	
Propanoic acid	
Cinnamic acid	
Succinic acid	

Formic acid
Fumaric acid
Maleic acid
Malonic acid
Phthalic acid
Propanedioic acid
Oxalic acid
2-Aminobutanoic acid
2-Hydroxybutyric acid
3-Hydroxybutyric acid
Glycolic acid
Lactic Acid
Tartaric acid
Methylcitric acid
Malic acid
Allofuranose
Allose
Arabinose
Maltose
Melibiose
Mannobiose
Cellobiose
Lactose
Turanose
Erythrose
Xylose
Galactose
Glucose
Mannose
Tagatose
Fructose
Rhamnose
Tagatofuranose
Talofuranose
D-Trehalose
Sucrose
2-Keto-gluconic acid
Gluconic acid
Mannonic acid
Ribonic acid
Xylonic acid
Glyceraldehyde
Galactopyranose
Galactose oxime
Glucopyranose
β-D-Galactofuranose
D-Glucitol
Dulcitol
Xylitol
D-Erythro-Pentitol
Mannitol
Glycerol
meso-Erythritol

Saccharides

Arabinitol	
Erythritol	
<u>Arabitol</u>	
Arabinofuranose	
Dihydroxyacetone	
Levogluconan	
Myo-Inositol	
Trehalose-6-phosphate	
Mannopyranose	
<u>Methyl galactoside</u>	
2-Hydroxyisocaproic acid	
4-Hydroxybutanoic acid	
Butanoic acid	Fatty acids and analogues
<u>Decanoic acid</u>	
<u>Tiglic acid</u>	

¹Underline metabolites are unique for *L. fermentum* 279

Table S4. Main classes of *L.fermentum* 279 metabolite detected in the lipid-containing phase of culture supernatant.

Metabolite	Class
Alanine (Ala)	
Asparagine (Asn)	
Proline (Pro)	
Histidine (His)	
Tryptophan (Trp)	Amino acids and derivatives
1-Aminocyclopentanecarboxylic	
Pyroglutamic acid	
<u>L-Norleucine</u>	
<u>Cinnamic acid</u>	
Oxalic acid	
Phthalic acid	
Ritalinic acid	Organic acids
4-Hydroxybenzoic acid	
<u>Toluic acid</u>	
<u>L-Sorbofuranose</u>	
<u>β-Arabinopyranose</u>	Saccharides
Lyxose	
<u>Arachidic acid</u>	
Butanoic acid	
<u>Pentadecanoic acid</u>	
<u>Propanoic acid</u>	
<u>Hexanoic acid</u>	Fatty acids and analogues
Heptadecanoic acid	
Undecanoic acid	
Oleic acid	

Table S5. All shared metabolites of *L.fermentum* U-21 and *L.fermentum* 279 detected in the extracellular vesicles.

Metabolite	Class
Tryptophan (Trp)	
Phenylalanine (Phe)	
Alanine (Ala)	Amino acids and derivatives
Proline (Pro)	

Valine (Val)	
Aspartic acid (Asp)	
Asparagine (Asn)	
3-Amino-2-piperidone	
3-Methylpiperazine-2,5-dione	
Amino levulinic acid	
Norleucine	
L-2-Aminobutyric acid	
N-Methyl-a-aminoisobutyric acid	
Pyroglutamic acid	
Penicillamine	
Pyrrolidine-2-carboxamide	
Timonacic	
Tranexamic acid	
l-Norvaline	
2-Aminocaprylic acid	
Creatinine	
7-Azatryptophan	
Etidocaine	
Octadecanamide	
Oleamide	
Mercaptoacetic acid	
Methoxyacetic acid	
Glutarate	
Benzeneethanamine	
Acetic anhydride	Organic acid
Fumaric acid	
Pyrrole-2,5-dicarboxylic acid	
Succinic acid	
Pyrrole-2-carboxylic acid	
Citric acid	
Tricarballic acid	
Glucosamine	
Ribono-1,4-lactone	
Fucose	
3- α -Mannobiose	
Lactose	
Turanose	
Xylopyranose	
Galactose	
Lyxose	
Glucose	Saccharides
Erythrose	
Gulose	
Rhamnose	
Glyceraldehyde	
Arabinonic acid	
Gluconic acid	
Erythro-Pentitol	
1-Deoxypentitol	
Pentitol	
Erythritol	
Maltitol	

Levogluconan	
Furan	
2-Hydroxyisocaproic acid	
6-Aminocaproic acid	
Itaconic acid	
2-Hydroxy-3-methylbutyric acid	
4-Pentenoic acid	
1-Decanol	
2-Undecen-4-ol	
Dodecanamide	Fatty acids and analogues
(Z)-Docos-13-enamide	
Hexanoic acid	
Propanoic acid	
Erucic acid	
Pentanamide	
Glycylglycine	
Valylvaline	
1-(benzo[d][1,3]dioxol-5-yl)-2-(4-methylpiperidin-1-yl)pentan-1-one	
1,2,4-Butanetriol	
1,2-Bis(4-methoxyphenyl)ethane-1,2-diamine	
1,3-Cyclohexanebis(methylamine)	
1,3-Dioxolane	
1,3-Propanediol	
1,2,3-Butanetriol	
1,2-Benzenediol	
(R)-(-)-2-Pyrrolidinemethanol	
1,3-bis[(Trimethylsilyl)ethynyl]benzene	
1,3-Dioxolane	
1,3-Dioxolane-2-methanol	
1,4-Bis[2-[N-[6-methoxy-8-quinolyl]amino]propionyl]piperazine	
1,4-diazabicyclo[4.3.0]nonan-2,5-dione	
1,6-Bis(trimethylsilyl)-1,3,5-hexatriyne	
1-[2,4-Bis(trimethylsiloxy)phenyl]-2-[(4-trimethylsiloxy)phenyl]propan-1-one	
17a-Aza-D-homoandrostan-17-one	
1-butanamine	Other organic compound
1-Cyclohexyldimethylsilyloxy-4-methylpentane	
1-Dichloromethyl(dimethyl)silyloxyoctadecane	
Carbonic acid	
Disulfide	
1-Isobutylsulfanylmethyl-2,8,9-trioxa-5-aza-1-sila-bicyclo[3.3.3]undecane	
2-(1-Amino-2-1H-imidazol-1-ylethyl)-4-amino-6-dimethylamino-S-triazine	
2-(2,5-Dimethoxyphenyl)-7-methoxy-2,4,6-cycloheptatrien-1-one	
2-(2-Benzyldecahydroisoquinolin-3-yl)ethanol	
2-(4'-Methoxyphenyl)-2-(3'-methyl-4'methoxyphenyl)propane	
2-(4-Methyl-1,3-thiazol-5-yl)ethanamine	
2,3,4-Trimethoxymandelic acid	
2,4,4-Trimethyl-1-pentanol	
2,4-Pentadienenitrile	
2-[[2-[Dimethylamino]propyl]amino]-4-[trichloromethyl]-6-[a,a,a-trichloro-p-tolyl]-S-triazine	

2-[2-[2-Methoxyethoxy]ethoxy-1,3-dioxalane
2-Cyano-5-(4-fluorophenyl)pyrimidine
2-Ethyl-3-ketovalerate
2--Fluorobenzylamine
2-Morpholinomethyl-1,3-diphenyl-2-propanol
2-Propanone
2-t-Butyl-5-methyl-[1,3]dioxolane-4-carboxylic acid
2-Undecanethiol
3,5-Di(2-thienyl)pyridine
3,6-Dioxa-2,4,5,7-tetrasilaoctane
3-Ethylpentan-3-ol
3-Hydroxymethyl-2-trimethylsilyloxypentane
4-((5-Ethenyl-1-azabicyclo(2,2,2)octan-2-yl)oxymethyl)-6-methoxy-
quinoline
4,4'-Bitriazolyl
4-Benzyl-1-(1-methyl-2-[(trimethylsilyl)oxy]-2-{4-
[(trimethylsilyl)oxy]phenyl}ethyl)piperidine
4H-1,2,4-Triazol-4-amine
4-Hydroxy-5-methyl-1-(tetrahydrofuran-2-yl)pyrimidin-2(1H)-one
4-Pyrimidinamine
5a-Pregnane-3beta,20a-diamine
5F-PB-22
5-Hydroxy-2-methylpyridine
8-(4-Hydroxyphenyl)-1-methyl-3H,6H,7H-imidazo[1,2-g]purine-2,4-
dione
8-Heptadecene
Benzenamine
Benzo[1,2-c:3,4-c':5,6-c'']tris[1,2,5]oxadiazole
Disilane
Ethyl pipercolinate
Methyl (2R,3R,4S)-3-(tert-butyl dimethylsilyloxy)-2,4-
dimethylhexanoate
Methyl (Z)-10-pentadecenoate
Methyl 2,2-dimethyl-3,6,9,12,15-pentaoxa-2-silaheptadecan-17-oate
Methyl 2-hydroxy-4-methyl-4-nitroso-pentanoate
Methylmalonic monoamide
N(1)-[4-[4-Methoxyphenyl]-6-[trichloromethyl]-2-pyrimidinyl]-
N(2),N(2)-
N,N-Diethylheptylamine
N-Acetyl-veratramine
N-Dimethylaminomethyl-tert.-butyl-isopropylphosphine
N-Ethyldiethanolamine
Ortetamine
Tetratetracontane
Trifluoroacetamide
(1-Benzyl-3-phenyl-prop-2-ynyl)-dimethyl-amine
(S)-(+)-2-Pyrrolidinemethanol
(Z)-Methyl hexadec-11-enoate
[2-Pyrrolidinyl]methylamine
1,2,4,5-Tetrazine, 3,6-diphenyl-
1,2-Bis(1,4,7-trioxa-10-azacyclododec-10-yl)-ethane
1-Cyclohexyldimethylsilyloxy-2-phenylethane
1-Cyclohexylethanol

1-Phenyl-2-(2-trimethylsilylcyclopropen-1-yl)ethanol
 2,2,6,6-Tetramethyl-2,6-disilapiperidine
 2,3,4-Trifluorobenzoic acid
 2,5-Dimethoxy-4-nitrophenethylamine
 2,6,10-Trimethyltridecane
 2-[[2-[Dimethylamino]propyl]amino-4-[trichloromethyl]-6-[a,a,a-trichloro-m-tolyl]-S-triazine
 2-Methyl-2-(trimethylsilyloxy)-1-(4-(2-(trimethylsilyloxy)ethoxy)phenyl)propan-1-one
 2-Methyl-8-hydroxyquinoline
 2-Pentamethyldisilanyloxybutane
 2-Phenyl-1,3-oxazol-2-ine
 3,8-Dioxa-2,9-disiladecane
 3H-1,2,4-Triazol-3-one, 1,2-dihydro-
 3-Methoxyhex-1-ene
 3-Methyl-1,3-bis(trimethylsilyloxy)butane
 3-Propionyloxytridecane
 3-Trimethylsilylmethyl-4-hydroxy-2-methyl-1-hexene
 4-Ethyl-4-methyl-1-hexene
 4-methoxy-N,N-Dimethylcathinone
 5-fluoro PB-22 N-(2-fluoropentyl) isomer
 9-Acetylhydrazono-3,6-dichloro-2,7-bis-[2-(diethylamino)ethoxy]fluorene
 Benzimidazo[2,1-a]isoquinoline
 Bromosuccinic acid
 Desethylterbutylazine
 Ether
 Etonitazene
 Methyl 2-hydroxy-2-(4-hydroxyphenyl)propanoate
 Metoprolol
 N,O-Bis(tert-butyltrimethylsilyl)carbamate
 N-[beta-Hydroxy-beta-[4-[1-adamantyl-6,8-dichloro]quinolyl]ethyl]piperidine
 N-Benzhydrylidene-1-(2,4,6-trimethylphenyl)ethylamine N-oxide
 N-Ethylformamide
 Propanamide
 Propanolol
 Spiro[bicyclo[2.2.1]heptane-2,2'-[1,3]dioxolane]-3-one
 Tolycaine
 Trimethylsilyl 3-(3-chloro-4-[(trimethylsilyl)oxy]phenyl)-2-[(trimethylsilyl)amino]propanoate
 Tris(trimethylsilyl)carbamate
 (±)-N-Ethylcathinone ephedrine
 (5-methoxyindol-3-yl)-N,N-diisopropyl-glyoxylamide
 (Methoxymethyl)trimethylsilane
 (Z)-5-Methoxy-3,5-dimethyl-2-hexenyltrimethylsilane
 1-(2-(3-Cyclohexenyl)ethyl)silatrane
 1-(2-Methoxyethoxy)-2-methyl-2-propanol
 1-(3,4-Methylenedioxyphenyl)-2-methylamino-1-butanone
 1-(3-Methylbutyl)-2,3,4,6-tetramethylbenzene
 3-Furoic acid
 2-Propenoic acid
 Scyllo-Inositol

2-Butyne-1,4-diol
5-Octadecene
Eicosane
3-Hexadecene
Ethane
Nonane
Heptane
Decane
Benzoin
3-Methylpiperazine-2,5-dione
Benzene
4-Hydroxybenzoic acid
1-Naphthylamine
Phenanthrene
Flecainide
Phthalic acid
Dibutyl phthalate
Benzyl thiocyanate
Butylone
Pentylone
1-Butanone
2,4-Pentanedione
4-Methylethcathinone
2-Butanone
2-Cyclohexen-1-one
Octadecanamide
Oleamide
Cloricromen
Cyclohexane
Cyclopropane
Cyclopropene
Cyclohexanamine
Mevalonolactone
Triethylene glycol
2(3H)-Furanone
2-Furoic Acid
Boron
1,3-Butadiyne
Melatonin
indole-3-acetamide 3
Phthalimide
Isoquinolinium
4-(2-Aminoethyl)-2-methoxyphenol
Adrenaline
Butalamine
1-Hexanamine
3-Amino-2,4-dimethylpentane
Diisopropylamine
Isopropylamine, N-trimethylsilyl-
spermidine
Ethylamine
Terbutaline
(R)-(-)-Phenylephrine

Hydroquinone
Piperidine
2-Piperidinone
5-Hydroxymaltol
Pyrazine
Isonicotinic Acid
Picolinic acid
2-hydroxypyridine
Pyridine
2(1H)-Pyridinone
Cytosine
Pyrrole-2-carboxylic acid
1-Methyl-5-mercaptopotrazole
Undecene
1-Heptadecene
Dodecene
N,N'-Dimethylurea
