Table S1 Classification of differential metabolites

Ion mode	SuperClass	Class	SubClass	description	VIP	Fold change
Positive	Organic acids and derivatives	Keto acids and derivatives	Short-chain keto acids and derivatives	Dihydroxyfumarate	2.03	144.01
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	L-Fucose-1-phosphate	2.15	52.37
	Benzenoids	Phenols	Methoxyphenols	Vanillin	2.29	21.00
	Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	D-Alanyl-D-alanine (D-Ala-D-Ala)	1.24	11.21
	Organic nitrogen compounds	Organonitrogen compounds	Quaternary ammonium salts	Acetylcholine	20.04	7.54
	Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine ribonucleotides	Guanosine 5'-diphosphate (GDP)	1.07	7.39
	Organic nitrogen compounds	Organonitrogen compounds	Quaternary ammonium salts	Phosphorylcholine	5.50	7.12
	Lipids and lipid-like molecules	Glycerophospholipids	Glycerophosphates	Glycerol 3-phosphate	4.28	6.62
	Organic oxygen compounds	Organooxygen compounds	Carbonyl compounds	Diacetyl	8.90	6.47
	Organic nitrogen compounds	Organonitrogen compounds	Cyclohexylamines	Cyclohexylamine	12.77	5.98

Organic nitrogen compounds	Organonitrogen compounds	Quaternary ammonium salts	Choline	1.86	5.77
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	alpha-D-Glucose 1-phosphate	1.83	5.47
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Glyceraldehyde 3-phosphate	4.36	4.84
Lipids and lipid-like molecules	Glycerophospholipids	Glycerophosphocholines	Glycerophosphocholine	1.04	4.71
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	D-Glucose 6-phosphate	1.04	4.53
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	gamma-L-Glutamyl-L-glutamic acid	2.82	4.44
Nucleosides, nucleotides, and analogues	5'-deoxyribonucleosides	5'-deoxy-5'-thionucleosides	S-Methyl-5'-thioadenosine	16.87	4.05
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Citrulline	5.43	3.98
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Glutamate	1.32	3.82
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	gamma-L-Glutamyl-L-valine	1.34	3.75
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Pipecolic acid	3.00	3.71
Nucleosides, nucleotides, and analogues	Pyrimidine nucleotides	Pyrimidine ribonucleotides	Uridine 5'-diphosphate (UDP)	1.09	3.59
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Proline	1.42	3.57
Organoheterocyclic compounds	Indoles and derivatives	Indolyl carboxylic acids and derivatives	L-Tryptophan	3.05	3.54

Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Arginine	8.22	3.53
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	N6,N6,N6-Trimethyl-L-lysine	2.55	3.52
Lipids and lipid-like molecules	Fatty Acyls	Fatty acid esters	Acetylcarnitine	1.96	2.90
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	Creatinine	4.77	2.81
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Aspartate	3.05	2.71
Organic nitrogen compounds	Organonitrogen compounds	Quaternary ammonium salts	L-Carnitine	4.29	2.70
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Histidine	2.42	2.47
Nucleosides, nucleotides, and analogues	5'-deoxyribonucleosides	5'-deoxy-5'-thionucleosides	S-Adenosylmethionine	2.89	2.39
Benzenoids	Phenols	Benzenediols	Dopamine	1.53	2.39
Organonitrogen compounds	Amines	Alkanolamines	Triethanolamine	4.69	2.30
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	1-Aminocyclopropanecarboxylic acid	2.69	2.23
Nucleosides, nucleotides, and analogues	(5'->5')-dinucleotides		Nicotinamide adenine dinucleotide (NAD)	8.13	2.10

Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	Creatine	1.14	2.08
Nucleosides, nucleotides, and analogues	Pyrimidine nucleotides	Pyrimidine ribonucleotides	Uridine 5'-monophosphate (UMP)	1.83	1.94
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	Betaine	4.91	1.86
Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine nucleotide sugars	ADP-ribose	1.59	1.78
Organoheterocyclic compounds	Diazines	Pyrimidines and pyrimidine derivatives	Uracil	1.06	1.74
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Methionine	1.01	1.68
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	3-Aminobutanoic acid	7.27	1.66
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	4-Aminobutyric acid	1.01	1.64
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	N6-Methyl-L-lysine	1.13	1.63
Organoheterocyclic compounds	Pyridines and derivatives	Pyridinecarboxylic acids and derivatives	Nicotinamide	1.13	1.50
Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine ribonucleotides	Adenosine monophosphate (AMP)	1.79	1.49
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Phenylalanine	2.65	1.42
Benzenoids	Benzene and substituted derivatives	Phenethylamines	Tyramine	3.50	1.41

Nucleosides, nucleotides, and analogues	Pyrimidine nucleotides	Pyrimidine ribonucleotides	Cytidine 5'-monophosphate (CMP)	1.26	1.34
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Leucine	1.36	1.24
Organoheterocyclic compounds	Diazines	Pyrimidines and pyrimidine derivatives	Cytosine	2.89	1.23
Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine ribonucleotides	Adenosine 5'-diphosphate (ADP)	1.08	1.22
Organoheterocyclic compounds	Imidazopyrimidines	Purines and purine derivatives	2-Hydroxyadenine	2.93	0.95
Nucleosides, nucleotides, and analogues	Purine nucleosides	Purine 2'-deoxyribonucleosides	Deoxyadenosine	6.22	0.24
Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine deoxyribonucleotides	2'-Deoxyadenosine 5'-monophosphate (dAMP)	1.10	0.66
Phenylpropanoids and polyketides	Isoflavonoids	Isoflav-2-enes	Daidzein	1.57	0.61
Organic acids and derivatives	Peptidomimetics	Hybrid peptides	L-Carnosine	1.04	0.59
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	Diaminopimelic acid	6.46	0.56
Organic acids and derivatives	Organic phosphoric acids and derivatives	Phosphate esters	Phosphoenolpyruvate	2.12	0.40
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	D-Proline	1.95	0.28

	Organic acids and derivatives	Carboxylic acids and derivatives	Carboxylic acid derivatives	N-Acetylcadaverine	3.30	0.28
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	3-Phospho-D-glycerate	2.79	0.44
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Isomaltose	11.41	0.17
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Flavin adenine dinucleotide (FAD)	1.84	0.75
Negtive	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	D-Ribulose 5-phosphate	4.39	103.88
	Organic acids and derivatives	Keto acids and derivatives	Short-chain keto acids and derivatives	Dihydroxyfumarate	1.19	80.53
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	L-Rhamnose	1.91	57.80
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	2-Deoxyribose 5-phosphate	1.23	23.38
	Lipids and lipid-like molecules	Fatty Acyls	Fatty acids and conjugates	16-Hydroxypalmitic acid	14.16	18.16
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	D-Mannose	12.82	13.08
	Organic acids and derivatives	Carboxylic acids and derivatives	Dicarboxylic acids and derivatives	Succinate	3.17	12.34
	Organic acids and derivatives	Carboxylic acids and derivatives	Tricarboxylic acids and derivatives	Citrate	7.60	12.13
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Alpha-D-Glucose	4.77	10.95
	Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	D-Tagatose	3.52	9.70

Nucleosides, nucleotides, and analogues	Flavin nucleotides		Flavin mononucleotide (FMN)	1.06	8.48
Organic acids and derivatives	Hydroxy acids and derivatives	Medium-chain hydroxy acids and derivatives	Galactonic acid	1.25	8.30
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Maltotriose	1.07	8.21
Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine nucleotide sugars	ADP-glucose	1.14	8.08
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	1-Deoxy-D-xylulose 5-phosphate	1.43	7.10
Lipids and lipid-like molecules	Fatty Acyls	Fatty acids and conjugates	cis-9-Palmitoleic acid	9.81	6.44
Organic acids and derivatives	Hydroxy acids and derivatives	Short-chain hydroxy acids and derivatives	(S)-2-Hydroxyglutarate	2.95	6.26
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	5-L-Glutamyl-L-alanine	1.40	5.85
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	D-Mannose 1-phosphate	2.39	5.67
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	L-Threonate	2.05	5.57
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	N-Formylmethionine	2.93	5.54
Lipids and lipid-like molecules	Fatty Acyls	Eicosanoids	Guanosine 5'-monophosphate (GMP)	1.09	5.34
Organic nitrogen compounds	Organonitrogen compounds	Quaternary ammonium salts	Phosphorylcholine	5.30	5.15

Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Pyroglutamic acid	1.27	4.93
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	N-Acetyl-L-glutamate	1.77	4.89
Organoheterocyclic compounds	Pyridines and derivatives	Pyridinecarboxylic acids and derivatives	Nicotinate	1.19	4.88
Lipids and lipid-like molecules	Fatty Acyls	Fatty acids and conjugates	3-Hydorxy-3-methylglutaric acid	1.58	4.85
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Histidine	2.73	4.81
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	gamma-L-Glutamyl-L-glutamic acid	1.22	4.49
Organic acids and derivatives	Hydroxy acids and derivatives	Beta hydroxy acids and derivatives	3-Hydroxypropionic acid (beta-lactic acid)	1.29	4.47
Lipids and lipid-like molecules	Glycerophospholipids	Glycerophosphates	Glycerol 3-phosphate	7.42	4.38
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	D-Erythrose 4-phosphate	2.06	3.98
Organoheterocyclic compounds	Indoles and derivatives	Indolyl carboxylic acids and derivatives	L-Tryptophan	3.62	3.90
Organoheterocyclic compounds	Indoles and derivatives	Indolyl carboxylic acids and derivatives	Indolelactic acid	3.64	3.88
Nucleosides, nucleotides, and analogues	5'-deoxyribonucleosides	5'-deoxy-5'-thionucleosides	S-Methyl-5'-thioadenosine	7.82	3.71

Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	Creatinine	1.16	3.15
Lipids and lipid-like molecules	Fatty Acyls	Fatty acids and conjugates	Dodecanoic acid	3.96	2.97
Lipids and lipid-like molecules	Fatty Acyls	Fatty acids and conjugates	Myristic acid	2.47	2.97
Organic acids and derivatives	Hydroxy acids and derivatives	Medium-chain hydroxy acids and derivatives	3-Hydroxydodecanoic acid	1.51	2.91
Lipids and lipid-like molecules	Fatty Acyls	Fatty acids and conjugates	Palmitic acid	22.88	2.90
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Ribitol	2.16	2.78
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Glutamate	12.48	2.64
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Alanine	3.81	2.57
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	L-Fucose-1-phosphate	1.13	2.53
Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine ribonucleotides	Adenosine monophosphate (AMP)	6.27	2.44
Organic nitrogen compounds	Organonitrogen compounds	Quaternary ammonium salts	L-Carnitine	1.09	2.40
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	D-Aspartic acid	6.33	2.12
Phenylpropanoids and polyketides	Phenylpropanoic acids		Hydroxyphenyllactic acid	2.53	1.98
Nucleosides, nucleotides, and analogues	(5'->5')-dinucleotides		Nicotinamide adenine	4.55	1.96

			dinucleotide (NAD)		
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	N-Acetyl-L-aspartic acid	1.54	1.87
Nucleosides, nucleotides, and analogues	Pyrimidine nucleotides	Pyrimidine ribonucleotides	Uridine 5'-monophosphate (UMP)	2.60	1.84
Nucleosides, nucleotides, and analogues	Pyrimidine nucleotides	Pyrimidine ribonucleotides	Uridine 5'-diphosphate (UDP)	1.46	1.80
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Valine	1.81	1.63
Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine ribonucleotides	Adenosine 3',5'-diphosphate (PAP)	2.15	1.60
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Phenylalanine	2.76	1.60
Organoheterocyclic compounds	Diazines	Pyrimidines and pyrimidine derivatives	Uracil	6.14	1.48
Nucleosides, nucleotides, and analogues	Pyrimidine nucleotides	Pyrimidine nucleotide sugars	UDP-N-acetylglucosamine	2.10	1.43
Organic acids and derivatives	Keto acids and derivatives	Medium-chain keto acids and derivatives	2-Oxoadipic acid	4.28	1.07
Organoheterocyclic compounds	Lactones	Gamma butyrolactones	L-Gulonic gamma-lactone	1.21	0.82
Lipids and lipid-like molecules	Fatty Acyls	Lineolic acids and derivatives	Linoleic acid	25.09	0.75
Organoheterocyclic compounds	Diazines	Pyrimidines and pyrimidine derivatives	Dihydrouracil	1.03	0.59

Organic acids and derivatives	Hydroxy acids and derivatives	Alpha hydroxy acids and derivatives	DL-lactate	1.09	0.57
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	Diaminopimelic acid	7.61	0.56
Nucleosides, nucleotides, and analogues	Purine nucleotides	Purine deoxyribonucleotides	Deoxyguanosine triphosphate (dGTP)	1.52	0.48
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	L-Glutamine	2.27	0.45
Organic acids and derivatives	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	Acetylglycine	1.05	0.45
Organic acids and derivatives	Organic phosphoric acids and derivatives	Phosphate esters	Phosphoenolpyruvate	2.78	0.43
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Dihydroxyacetone phosphate	2.77	0.40
Nucleosides, nucleotides, and analogues	Pyrimidine nucleotides	Pyrimidine nucleotide sugars	Uridine diphosphate glucose(UDP-D-Glucose)	2.72	0.33
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Fructose 1-phosphate	1.12	0.27
Organoheterocyclic compounds	Diazines	Pyrimidines and pyrimidine derivatives	Thymine	3.53	0.20
Organic oxygen compounds	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	Galactinol	19.42	0.18
Lipids and lipid-like molecules	Fatty Acyls	Fatty acids and conjugates	2-Methyl-3-hydroxybutyric acid	2.53	0.17