

Supplemental Table S1: Complete association results of a serum metabolomics of dry eye disease[†], ordered by *P*-value.

Metabolite	Pathway	Super-pathway	P-value	Beta
androsterone sulfate	Sterol/Steroid	Lipid	0.000297316	-0.2041044
epiandrosterone sulfate	Sterol/Steroid	Lipid	0.000361852	-0.200962718
4-androsten-3beta,17beta-diol disulfate 1*	Sterol/Steroid	Lipid	0.002269213	-0.194854716
dehydroisoandrosterone sulfate (DHEA-S)	Sterol/Steroid	Lipid	0.002292265	-0.183184893
4-androsten-3beta,17beta-diol disulfate 2*	Sterol/Steroid	Lipid	0.007706761	-0.170728093
theophylline	Xanthine metabolism	Xenobiotics	0.015834425	0.136858493
N1-methyladenosine	Purine metabolism, adenine containing	Nucleotide	0.015994007	-0.131957949
1-palmitoylglycerophosphocholine	Lysolipid	Lipid	0.022084951	-0.115056477
caffeine	Xanthine metabolism	Xenobiotics	0.03414392	0.119333957
1,7-dimethylurate	Xanthine metabolism	Xenobiotics	0.037368642	0.123718145
serine	Glycine, serine and threonine metabolism	Amino acid	0.045928814	0.107144048
2-palmitoylglycerophosphocholine*	Lysolipid	Lipid	0.04960331	-0.10247175
2-linoleoylglycerophosphocholine*	Lysolipid	Lipid	0.06188007	-0.111619635
1-stearoylglycerophosphocholine	Lysolipid	Lipid	0.062772945	-0.098793907
alanine	Alanine and aspartate metabolism	Amino acid	0.077530092	0.095822933
paraxanthine	Xanthine metabolism	Xenobiotics	0.082859665	0.096549293
dimethylarginine (SDMA + ADMA)	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.091851929	-0.092115118
glutaroyl carnitine	Lysine metabolism	Amino acid	0.094314986	-0.090797295
1-oleoylglycerophosphocholine	Lysolipid	Lipid	0.095911529	-0.085506307
1-linoleoylglycerophosphocholine	Lysolipid	Lipid	0.096647366	-0.087239888
3-(4-hydroxyphenyl)lactate	Phenylalanine & tyrosine metabolism	Amino acid	0.103865832	-0.087975507
4-acetamidobutanoate	Guanidino and acetamido metabolism	Amino acid	0.105887511	-0.099800894
cortisone	Sterol/Steroid	Lipid	0.108947555	-0.090315331
margarate (17:0)	Long chain fatty acid	Lipid	0.130789043	-0.082233552
glycochenodeoxycholate	Bile acid metabolism	Lipid	0.131173423	0.085727513
2-hydroxypalmitate	Fatty acid, monohydroxy	Lipid	0.134686294	-0.079234034
1-myristoylglycerophosphocholine	Lysolipid	Lipid	0.14078931	-0.078505588
citrulline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.142493558	-0.083696976
alpha-ketoglutarate	Krebs cycle	Energy	0.14269881	0.090091213
undecanoate (11:0)	Medium chain fatty acid	Lipid	0.149265523	-0.07792308
myristate (14:0)	Long chain fatty acid	Lipid	0.152353854	-0.081971551
creatinine	Creatine metabolism	Amino acid	0.156549545	-0.076132487
10-nonadecenoate (19:1n9)	Long chain fatty acid	Lipid	0.159163315	-0.07954789
5-dodecenoate (12:1n7)	Medium chain fatty acid	Lipid	0.159739927	-0.07776334

myristoleate (14:1n5)	Long chain fatty acid	Lipid	0.161910634	-0.078871062
methionine	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.166727918	0.078479352
glycerophosphorylcholine (GPC)	Glycerolipid metabolism	Lipid	0.167555302	-0.078791482
glycine	Glycine, serine and threonine metabolism	Amino acid	0.1713396	0.073328547
choline	Glycerolipid metabolism	Lipid	0.178565355	0.072535276
palmitoyl sphingomyelin	Sphingolipid	Lipid	0.192440424	-0.080677902
gamma-glutamyltyrosine	gamma-glutamyl	Peptide	0.198335937	-0.077684322
1-palmitoleoylglycerophosphocholine*	Lysolipid	Lipid	0.205070661	-0.067646853
2-stearoylglycerophosphocholine*	Lysolipid	Lipid	0.219916464	-0.064436571
2-aminobutyrate	Butanoate metabolism	Amino acid	0.236077011	-0.064707593
1-palmitoylglycerophosphoethanolamine	Lysolipid	Lipid	0.237909906	0.062416077
palmitoleate (16:1n7)	Long chain fatty acid	Lipid	0.239635327	-0.066599471
indolelactate	Tryptophan metabolism	Amino acid	0.240045421	-0.064673206
isobutyrylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.24610178	0.063408215
dihomo-linoleate (20:2n6)	Long chain fatty acid	Lipid	0.251643326	-0.064412292
allantoin	Purine metabolism, urate metabolism	Nucleotide	0.253306214	0.068771481
2-hydroxyisobutyrate	Valine, leucine and isoleucine metabolism	Amino acid	0.254684558	0.071524921
alpha-hydroxyisovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.255386888	-0.062180012
pentadecanoate (15:0)	Long chain fatty acid	Lipid	0.257203924	-0.062595616
xanthine	Purine metabolism, (hypo)xanthine/inosine containing	Nucleotide	0.259870178	-0.068468108
ursodeoxycholate	Bile acid metabolism	Lipid	0.260964675	0.069924953
10-heptadecenoate (17:1n7)	Long chain fatty acid	Lipid	0.266768624	-0.063076119
p-cresol sulfate	Phenylalanine & tyrosine metabolism	Amino acid	0.267065905	0.062069858
cortisol	Sterol/Steroid	Lipid	0.267892563	-0.063593704
isovalerate	Fatty acid metabolism	Lipid	0.271591391	0.072640652
erythronate*	Aminosugars metabolism	Carbohydrate	0.277850279	0.060427458
1-stearoylglycerol (1-monostearin)	Monoacylglycerol	Lipid	0.279527018	0.060358523
2-methylbutyrylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.281734697	0.062257852
trans-4-hydroxyproline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.286471774	0.058291759
theobromine	Xanthine metabolism	Xenobiotics	0.302571175	0.055390214
arachidonate (20:4n6)	Long chain fatty acid	Lipid	0.305774884	-0.054748292
1-stearoylglycerophosphoethanolamine	Lysolipid	Lipid	0.309890726	0.054819378
stachydrine	Food component/Plant	Xenobiotics	0.331345838	0.052734035
pro-hydroxy-pro	Dipeptide	Peptide	0.332923	0.050567832
1-arachidonoylglycerophosphoethanolamine *	Lysolipid	Lipid	0.333289847	0.048895312
tyrosine	Phenylalanine & tyrosine metabolism	Amino acid	0.33993471	-0.05419382
threonine	Glycine, serine and threonine metabolism	Amino acid	0.342973328	0.058814501

butyrylcarnitine	Fatty acid metabolism (also BCAA metabolism)	Lipid	0.343055131	0.053620785
N-acetylthreonine	Glycine, serine and threonine metabolism	Amino acid	0.343902303	0.054688076
acetylcarnitine	Carnitine metabolism	Lipid	0.34413242	-0.052897454
pyruvate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.350074598	0.053558132
1-eicosadienoylglycerophosphocholine*	Lysolipid	Lipid	0.364921181	-0.051001882
eicosenoate (20:1n9 or 11)	Long chain fatty acid	Lipid	0.368934368	-0.050331998
cysteine	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.371055967	-0.047683242
decanoylcarnitine	Carnitine metabolism	Lipid	0.374862479	-0.050209885
pseudouridine	Pyrimidine metabolism, uracil containing	Nucleotide	0.379164413	-0.048865692
catechol sulfate	Benzoate metabolism	Xenobiotics	0.381844788	0.046626193
pantothenate	Pantothenate and CoA metabolism	Cofactors and vitamins	0.382664011	0.046475293
succinylcarnitine	Krebs cycle	Energy	0.387388928	-0.054715961
1,5-anhydroglucitol (1,5-AG)	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.389408807	-0.045416679
biliverdin	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.397173051	-0.051045255
HWESASXX*	Polypeptide	Peptide	0.402866695	0.048877855
palmitate (16:0)	Long chain fatty acid	Lipid	0.412146927	-0.04659182
hyodeoxycholate	Bile acid metabolism	Lipid	0.420840746	-0.047669305
2-tetradecenoyl carnitine	Carnitine metabolism	Lipid	0.422460725	-0.046856517
1-stearoylglycerophosphoinositol	Lysolipid	Lipid	0.425164246	-0.043088218
cis-4-decenoyl carnitine	Carnitine metabolism	Lipid	0.425891939	-0.050806963
2-oleoylglycerophosphocholine*	Lysolipid	Lipid	0.432156011	-0.041830755
oleate (18:1n9)	Long chain fatty acid	Lipid	0.435377667	-0.043483298
1-palmitoylglycerophosphoinositol*	Lysolipid	Lipid	0.440142924	-0.04891335
1-eicosatrienoylglycerophosphocholine*	Lysolipid	Lipid	0.441440602	-0.038931048
1-heptadecanoylglycerophosphocholine	Lysolipid	Lipid	0.442377528	-0.040872259
laurate (12:0)	Medium chain fatty acid	Lipid	0.442422218	-0.042857211
threonate	Ascorbate and aldarate metabolism	Cofactors and vitamins	0.443054123	0.041031389
indolepropionate	Tryptophan metabolism	Amino acid	0.444877164	-0.040885887
histidine	Histidine metabolism	Amino acid	0.451318977	-0.041114872
gamma-glutamylphenylalanine	gamma-glutamyl	Peptide	0.451338865	-0.041262317
5-oxoproline	Glutathione metabolism	Amino acid	0.458763756	-0.04121392
bilirubin (Z,Z)	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.460493211	0.043064972
glutamate	Glutamate metabolism	Amino acid	0.468719067	0.042395326
serotonin (5HT)	Tryptophan metabolism	Amino acid	0.470292753	-0.047866301
heptanoate (7:0)	Medium chain fatty acid	Lipid	0.47462611	-0.038418548
levulinate (4-oxovalerate)	Valine, leucine and isoleucine metabolism	Amino acid	0.476803062	0.038921477
isovalerylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.481173913	0.039750686
stearate (18:0)	Long chain fatty acid	Lipid	0.481600581	-0.040171806
3-methylhistidine	Histidine metabolism	Amino acid	0.482037753	-0.041399667

lysine	Lysine metabolism	Amino acid	0.484444516	0.037245064
1-docosahexaenoylglycerophosphocholine*	Lysolipid	Lipid	0.485829777	0.038117809
docosahexaenoate (DHA; 22:6n3)	Essential fatty acid	Lipid	0.501899068	0.037628006
hypoxanthine	Purine metabolism, (hypo)xanthine/inosine containing	Nucleotide	0.510205691	-0.038224626
ornithine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.510427648	-0.034782474
threitol	Nucleotide sugars, pentose metabolism	Carbohydrate	0.511490122	0.038612881
4-ethylphenylsulfate	Benzoate metabolism	Xenobiotics	0.512680318	0.037499288
3-phenylpropionate (hydrocinnamate)	Phenylalanine & tyrosine metabolism	Amino acid	0.5148475	0.039910953
trimethyl-N-aminovalerate	Carnitine metabolism	Lipid	0.517073763	0.036310775
linoleate (18:2n6)	Essential fatty acid	Lipid	0.522164138	-0.034797567
arginine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.527272102	0.03466151
taurochenodeoxycholate	Bile acid metabolism	Lipid	0.535689152	-0.039460286
glycerate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.538677279	0.033129508
phenyllactate (PLA)	Phenylalanine & tyrosine metabolism	Amino acid	0.540400968	0.037629961
dihomo-linolenate (20:3n3 or n6)	Essential fatty acid	Lipid	0.542381167	-0.03188376
1-palmitoylplasménylethanolamine*	Lysolipid	Lipid	0.544187917	-0.037045081
phosphate	Oxidative phosphorylation	Energy	0.546858576	-0.031925403
cholesterol	Sterol/Steroid	Lipid	0.552821624	-0.033403311
gamma-glutamylleucine	gamma-glutamyl	Peptide	0.553398009	0.036119125
piperine	Food component/Plant	Xenobiotics	0.556855156	-0.033952432
uridine	Pyrimidine metabolism, uracil containing	Nucleotide	0.557271735	-0.030194849
aspartate	Alanine and aspartate metabolism	Amino acid	0.558207828	-0.030913471
lathosterol	Sterol/Steroid	Lipid	0.564815923	-0.036490057
4-methyl-2-oxopentanoate	Valine, leucine and isoleucine metabolism	Amino acid	0.571915286	-0.033430175
nonadecanoate (19:0)	Long chain fatty acid	Lipid	0.572447166	-0.031327349
isoleucine	Valine, leucine and isoleucine metabolism	Amino acid	0.591227499	0.029550091
asparagine	Alanine and aspartate metabolism	Amino acid	0.591329543	0.029478063
pyroglutamine*	Glutamate metabolism	Amino acid	0.594283823	-0.030646401
scyllo-inositol	Inositol metabolism	Lipid	0.595463246	0.031837045
glycerol	Glycerolipid metabolism	Lipid	0.596711799	0.029691386
proline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.603548346	0.028376391
arabinose	Nucleotide sugars, pentose metabolism	Carbohydrate	0.625793402	-0.03072093
stearidonate (18:4n3)	Long chain fatty acid	Lipid	0.628066231	-0.025792191
creatine	Creatine metabolism	Amino acid	0.63244339	-0.02688376
1-arachidonoylglycerophosphoinositol*	Lysolipid	Lipid	0.645524614	0.025770567
7-methylxanthine	Xanthine metabolism	Xenobiotics	0.658463514	-0.028156381
3-indoxyl sulfate	Tryptophan metabolism	Amino acid	0.667442924	0.022771236

bilirubin (E,E)*	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.672040382	0.024658998
palmitoylcarnitine	Carnitine metabolism	Lipid	0.676688125	-0.023219917
4-vinylphenol sulfate	Benzoate metabolism	Xenobiotics	0.680986633	0.023366158
dodecanedioate	Fatty acid, dicarboxylate	Lipid	0.682616841	0.022731036
heme*	Hemoglobin and porphyrin	Cofactors and vitamins	0.68780922	0.023514134
erythrose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.687943887	-0.022584289
C-glycosyltryptophan*	Tryptophan metabolism	Amino acid	0.695265726	-0.024005052
erythritol	Sugar, sugar substitute, starch	Xenobiotics	0.696231609	0.021828683
1-palmitoylglycerol (1-monopalmitin)	Monoacylglycerol	Lipid	0.701581816	-0.020542877
glycerol 2-phosphate	Chemical	Xenobiotics	0.704724451	0.023547074
linolenate [alpha or gamma; (18:3n3 or 6)]	Essential fatty acid	Lipid	0.712534296	0.021660618
N-acetylmethionine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.714668109	-0.020059166
stearoylcarnitine	Carnitine metabolism	Lipid	0.720504178	-0.021398213
quininate	Food component/Plant	Xenobiotics	0.721750633	0.021173345
urate	Purine metabolism, urate metabolism	Nucleotide	0.724171041	0.021194773
10-undecenoate (11:1n1)	Medium chain fatty acid	Lipid	0.740205551	-0.018264575
N-acetylalanine	Alanine and aspartate metabolism	Amino acid	0.742052382	-0.017810098
3-hydroxybutyrate (BHBA)	Ketone bodies	Lipid	0.74893887	-0.017417759
betaine	Glycine, serine and threonine metabolism	Amino acid	0.752950889	0.01793887
glycocholate	Bile acid metabolism	Lipid	0.758473539	0.018140113
adrenate (22:4n6)	Long chain fatty acid	Lipid	0.762734295	0.016065189
tryptophan	Tryptophan metabolism	Amino acid	0.764912482	-0.016501241
tetradecanedioate	Fatty acid, dicarboxylate	Lipid	0.768371863	-0.017098768
glucose	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.771020673	0.015667547
gamma-glutamylvaline	gamma-glutamyl	Peptide	0.781749195	0.017419478
1-oleoylglycerophosphoethanolamine	Lysolipid	Lipid	0.79209251	0.014141893
pelargonate (9:0)	Medium chain fatty acid	Lipid	0.798105093	-0.014266462
alpha-tocopherol	Tocopherol metabolism	Cofactors and vitamins	0.801781147	-0.015678054
propionylcarnitine	Fatty acid metabolism (also BCAA metabolism)	Lipid	0.810326606	0.013997157
mannose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.813625279	-0.013218581
malate	Krebs cycle	Energy	0.814050246	-0.013495514
octadecanedioate	Fatty acid, dicarboxylate	Lipid	0.817037034	-0.013361316
indoleacetate	Tryptophan metabolism	Amino acid	0.819213184	-0.011903944
octanoylcarnitine	Carnitine metabolism	Lipid	0.822925222	-0.012250609
3-methyl-2-oxobutyrate	Valine, leucine and isoleucine metabolism	Amino acid	0.823789309	-0.012951928
oleoylcarnitine	Carnitine metabolism	Lipid	0.823828058	-0.012095744
docosapentaenoate (n3 DPA; 22:5n3)	Essential fatty acid	Lipid	0.829106224	-0.011922278

2-hydroxystearate	Fatty acid, monohydroxy	Lipid	0.835045167	-0.010533662
leucine	Valine, leucine and isoleucine metabolism	Amino acid	0.835382886	0.011861082
phenol sulfate	Phenylalanine & tyrosine metabolism	Amino acid	0.846037703	0.009714127
pipecolate	Lysine metabolism	Amino acid	0.846887905	0.010504288
1-arachidonoylglycerophosphocholine*	Lysolipid	Lipid	0.84753598	-0.009723492
N-acetylglycine	Glycine, serine and threonine metabolism	Amino acid	0.847774167	-0.011619825
kynurenine	Tryptophan metabolism	Amino acid	0.854307341	0.009924531
3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	Fatty acid, dicarboxylate	Lipid	0.854388077	0.010305839
phenylalanine	Phenylalanine & tyrosine metabolism	Amino acid	0.856336154	-0.009501841
tryptophan betaine	Tryptophan metabolism	Amino acid	0.857933466	-0.011421185
phenylacetylglutamine	Phenylalanine & tyrosine metabolism	Amino acid	0.86083473	-0.009342407
gamma-tocopherol	Tocopherol metabolism	Cofactors and vitamins	0.862594691	0.010477243
pyridoxate	Vitamin B6 metabolism	Cofactors and vitamins	0.869814223	0.008249855
urea	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.882521425	0.009222705
2-hydroxybutyrate (AHB)	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.883011116	0.008556371
beta-hydroxyisovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.887061962	-0.00747623
acetylphosphate	Oxidative phosphorylation	Energy	0.889691872	0.007592362
eicosapentaenoate (EPA; 20:5n3)	Essential fatty acid	Lipid	0.889978048	0.007883795
citrate	Krebs cycle	Energy	0.890338893	-0.008412569
hexadecanedioate	Fatty acid, dicarboxylate	Lipid	0.898356068	-0.007673929
carnitine	Carnitine metabolism	Lipid	0.901492565	0.006912125
glutamine	Glutamate metabolism	Amino acid	0.90243775	-0.00713302
hexanoylcarnitine	Carnitine metabolism	Lipid	0.909772933	-0.006272453
caproate (6:0)	Medium chain fatty acid	Lipid	0.911672791	0.005958997
hippurate	Benzoate metabolism	Xenobiotics	0.915795835	0.005938247
tauroolithocholate 3-sulfate	Bile acid metabolism	Lipid	0.937177972	-0.00532227
1-linoleoylglycerophosphoethanolamine*	Lysolipid	Lipid	0.93745325	0.003959016
valine	Valine, leucine and isoleucine metabolism	Amino acid	0.941161477	-0.003527071
fructose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.941174988	-0.004596127
glycerol 3-phosphate (G3P)	Glycerolipid metabolism	Lipid	0.94341736	-0.003083935
lactate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.950458279	0.003481271
caprylate (8:0)	Medium chain fatty acid	Lipid	0.953243953	-0.003834028
cholate	Bile acid metabolism	Lipid	0.957583023	0.003431784
7-alpha-hydroxy-3-oxo-4-cholestenoate (7-Hoca)	Sterol/Steroid	Lipid	0.983701322	0.000653765
gamma-glutamylglutamine	gamma-glutamyl	Peptide	0.988870552	0.000843416
benzoate	Benzoate metabolism	Xenobiotics	0.989528191	-0.000725936
3-methyl-2-oxovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.991396295	-0.000545361

myo-inositol	Inositol metabolism	Lipid	1	0.000648873
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[†]A subject was considered as having dry eye disease if there was presence of both dryness and irritation symptoms either constantly or often, and/or a report of a previous clinical diagnosis of dry eye disease.

Supplemental Table S2: Complete association results of a serum metabolomics study with outcome variable dryness and irritation symptoms, ordered by *P*-value.

Metabolite	Pathway	Super-pathway	P-value	Beta
4-androsten-3beta,17beta-diol disulfate 2*	Sterol/Steroid	Lipid	2.89E-08	-0.156457853
androsterone sulfate	Sterol/Steroid	Lipid	0.0000401	-0.112958237
epiandrosterone sulfate	Sterol/Steroid	Lipid	0.0000157	-0.106112773
4-androsten-3beta,17beta-diol disulfate 1*	Sterol/Steroid	Lipid	0.0000641	-0.112597307
dehydroepiandrosterone sulfate (DHEA-S)	Sterol/Steroid	Lipid	0.000113533	-0.101490182
3-(4-hydroxyphenyl)lactate	Phenylalanine & tyrosine metabolism	Amino acid	0.002105103	-0.073368453
glycerol	Glycerolipid metabolism	Lipid	0.003937188	0.069676049
erythronate*	Aminosugars metabolism	Carbohydrate	0.02488977	0.054207175
heptanoate (7:0)	Medium chain fatty acid	Lipid	0.027106437	0.051533273
allantoin	Purine metabolism, urate metabolism	Nucleotide	0.02821878	0.058169696
1,7-dimethylurate	Xanthine metabolism	Xenobiotics	0.031144017	0.056524589
linolenate [alpha or gamma; (18:3n3 or 6)]	Essential fatty acid	Lipid	0.031441255	0.051806801
1-oleoylglycerophosphoethanolamine	Lysolipid	Lipid	0.036388271	0.047298226
caproate (6:0)	Medium chain fatty acid	Lipid	0.041681723	0.047520952
linoleate (18:2n6)	Essential fatty acid	Lipid	0.042565811	0.049001082
caprylate (8:0)	Medium chain fatty acid	Lipid	0.045301506	0.047254214
10-heptadecenoate (17:1n7)	Long chain fatty acid	Lipid	0.046530063	0.049918098
phenol sulfate	Phenylalanine & tyrosine metabolism	Amino acid	0.05030169	0.045728954
trans-4-hydroxyproline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.050850146	0.045272664
1-arachidonoylglycerophosphoinositol*	Lysolipid	Lipid	0.056733674	0.044672193
theophylline	Xanthine metabolism	Xenobiotics	0.056978801	0.046921003
alpha-ketoglutarate	Krebs cycle	Energy	0.057445637	0.050316778
palmitoleate (16:1n7)	Long chain fatty acid	Lipid	0.06035818	0.047077701
pantothenate	Pantothenate and CoA metabolism	Cofactors and vitamins	0.061799215	0.04391447

ornithine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.066088399	-0.041609034
phosphate	Oxidative phosphorylation	Energy	0.073505005	0.041847262
cortisol	Sterol/Steroid	Lipid	0.075569705	-0.04292455
choline	Glycerolipid metabolism	Lipid	0.08268641	0.040756017
myristoleate (14:1n5)	Long chain fatty acid	Lipid	0.093724608	0.041643592
butyrylcarnitine	Fatty acid metabolism (also BCAA metabolism)	Lipid	0.093826337	0.041780486
urate	Purine metabolism, urate metabolism	Nucleotide	0.095898492	0.04253841
glycine	Glycine, serine and threonine metabolism	Amino acid	0.096300292	0.039335634
methionine	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.105132091	0.039366133
pelargonate (9:0)	Medium chain fatty acid	Lipid	0.10578073	0.038305285
myristate (14:0)	Long chain fatty acid	Lipid	0.108092465	0.040013303
caffeine	Xanthine metabolism	Xenobiotics	0.112517576	0.038886321
biliverdin	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.112613458	-0.041466041
2-hydroxyisobutyrate	Valine, leucine and isoleucine metabolism	Amino acid	0.113047531	0.043567455
dimethylarginine (SDMA + ADMA)	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.115004345	-0.037225927
2-aminobutyrate	Butanoate metabolism	Amino acid	0.120981871	-0.036670649
cholesterol	Sterol/Steroid	Lipid	0.124770269	0.03770056
2-linoleoylglycerophosphocholine*	Lysolipid	Lipid	0.125648408	-0.03882312
1- arachidonoylglycerophosphoethanolamine*	Lysolipid	Lipid	0.130816826	0.033534003
alanine	Alanine and aspartate metabolism	Amino acid	0.132939619	0.035243967
catechol sulfate	Benzoate metabolism	Xenobiotics	0.138003958	0.03506565
arginine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.140604654	0.035217626
piperine	Food component/Plant	Xenobiotics	0.142118671	-0.036083878

threitol	Nucleotide sugars, pentose metabolism	Carbohydrate	0.148347924	0.036808225
5-dodecenoate (12:1n7)	Medium chain fatty acid	Lipid	0.149920541	0.034813767
arabinose	Nucleotide sugars, pentose metabolism	Carbohydrate	0.150910999	-0.038882093
alpha-hydroxyisovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.153761354	-0.034273899
heme*	Hemoglobin and porphyrin	Cofactors and vitamins	0.159887691	0.035879571
oleate (18:1n9)	Long chain fatty acid	Lipid	0.163725552	0.034113705
palmitate (16:0)	Long chain fatty acid	Lipid	0.170999135	0.033644319
glutamate	Glutamate metabolism	Amino acid	0.173785343	0.034167627
pipecolate	Lysine metabolism	Amino acid	0.182621926	0.032023776
4-vinylphenol sulfate	Benzoate metabolism	Xenobiotics	0.184230196	0.032909947
levulinate (4-oxovalerate)	Valine, leucine and isoleucine metabolism	Amino acid	0.195313113	0.030118917
paraxanthine	Xanthine metabolism	Xenobiotics	0.205110569	0.030758603
cortisone	Sterol/Steroid	Lipid	0.21142851	-0.030368514
alpha-tocopherol	Tocopherol metabolism	Cofactors and vitamins	0.215695161	0.031907754
pro-hydroxy-pro	Dipeptide	Peptide	0.22101517	0.028387623
citrate	Krebs cycle	Energy	0.227954443	-0.029386023
1-palmitoylglycerophosphoethanolamine	Lysolipid	Lipid	0.248840203	0.02643905
1-linoleoylglycerophosphoethanolamine*	Lysolipid	Lipid	0.2512417	0.025792389
serine	Glycine, serine and threonine metabolism	Amino acid	0.252526872	0.026619431
N1-methyladenosine	Purine metabolism, adenine containing	Nucleotide	0.26073776	-0.026570542
undecanoate (11:0)	Medium chain fatty acid	Lipid	0.263897309	0.02597011
1-stearoylglycerol (1-monostearin)	Monoacylglycerol	Lipid	0.278251822	0.0263217
serotonin (5HT)	Tryptophan metabolism	Amino acid	0.282730205	0.029137924
quininate	Food component/Plant	Xenobiotics	0.290529098	0.028498437
glycerol 2-phosphate	Chemical	Xenobiotics	0.296833851	0.027336186
adrenate (22:4n6)	Long chain fatty acid	Lipid	0.299467085	0.023806739

threonine	Glycine, serine and threonine metabolism	Amino acid	0.301018632	0.028247454
indolepropionate	Tryptophan metabolism	Amino acid	0.31408542	-0.023584879
glycochenodeoxycholate	Bile acid metabolism	Lipid	0.316091018	0.024159502
mannose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.323102058	-0.02389909
gamma-glutamyltyrosine	gamma-glutamyl	Peptide	0.331288456	-0.025779559
isovalerate	Fatty acid metabolism	Lipid	0.333186439	0.026411631
glutaroyl carnitine	Lysine metabolism	Amino acid	0.333885813	-0.022797585
4-methyl-2-oxopentanoate	Valine, leucine and isoleucine metabolism	Amino acid	0.334313636	-0.024367802
glycerol 3-phosphate (G3P)	Glycerolipid metabolism	Lipid	0.338438552	0.021691568
gamma-glutamylglutamine	gamma-glutamyl	Peptide	0.341204462	-0.02339507
tryptophan	Tryptophan metabolism	Amino acid	0.345465415	-0.021679206
1-palmitoylglycerophosphocholine	Lysolipid	Lipid	0.349333249	-0.020451864
3-phenylpropionate (hydrocinnamate)	Phenylalanine & tyrosine metabolism	Amino acid	0.351513274	0.024120981
benzoate	Benzoate metabolism	Xenobiotics	0.353464348	0.021439854
hexanoylcarnitine	Carnitine metabolism	Lipid	0.3544301	0.022780004
histidine	Histidine metabolism	Amino acid	0.357838613	0.022131095
laurate (12:0)	Medium chain fatty acid	Lipid	0.361056796	0.021970257
10-nonadecenoate (19:1n9)	Long chain fatty acid	Lipid	0.363352041	0.022342239
glycerate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.371799218	0.021067406
stearoylcarnitine	Carnitine metabolism	Lipid	0.389173495	-0.021798344
1-linoleoylglycerophosphocholine	Lysolipid	Lipid	0.39207502	-0.019378179
N-acetylmethionine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.394541864	-0.02025398
glutamine	Glutamate metabolism	Amino acid	0.396615795	0.020334493
phenyllactate (PLA)	Phenylalanine & tyrosine metabolism	Amino acid	0.402532654	-0.022670416
theobromine	Xanthine metabolism	Xenobiotics	0.409135803	0.019162045

malate	Krebs cycle	Energy	0.415719825	-0.019568889
7-methylxanthine	Xanthine metabolism	Xenobiotics	0.416707285	-0.021925986
pyridoxate	Vitamin B6 metabolism	Cofactors and vitamins	0.428181502	0.018614354
acetylphosphate	Oxidative phosphorylation	Energy	0.431972889	0.018200945
lathosterol	Sterol/Steroid	Lipid	0.433751589	0.02190005
citrulline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.437086734	-0.019033929
4-ethylphenylsulfate	Benzoate metabolism	Xenobiotics	0.439195468	0.019730093
1-stearoylglycerophosphoinositol	Lysolipid	Lipid	0.44763556	0.017659581
1-oleoylglycerophosphocholine	Lysolipid	Lipid	0.46005958	-0.016611961
isovalerylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.469018649	-0.017381441
hyodeoxycholate	Bile acid metabolism	Lipid	0.471314831	-0.01891697
beta-hydroxyisovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.474635789	0.016882565
docosapentaenoate (n3 DPA; 22:5n3)	Essential fatty acid	Lipid	0.47764182	0.017649077
tyrosine	Phenylalanine & tyrosine metabolism	Amino acid	0.503207556	-0.016495103
creatinine	Creatine metabolism	Amino acid	0.504686468	-0.015536941
cysteine	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.517722539	0.015057553
2-tetradecenoyl carnitine	Carnitine metabolism	Lipid	0.528188553	-0.015976425
2-hydroxypalmitate	Fatty acid, monohydroxy	Lipid	0.538472853	0.013935477
threonate	Ascorbate and aldarate metabolism	Cofactors and vitamins	0.538607484	0.01440131
xanthine	Purine metabolism, (hypo)xanthine/inosine containing	Nucleotide	0.543080738	-0.015665194
2-hydroxystearate	Fatty acid, monohydroxy	Lipid	0.548724013	0.013599068
dodecanedioate	Fatty acid, dicarboxylate	Lipid	0.555206643	0.014468271
cholate	Bile acid metabolism	Lipid	0.563338788	0.015042533
3-hydroxybutyrate (BHBA)	Ketone bodies	Lipid	0.572920208	0.013340236

p-cresol sulfate	Phenylalanine & tyrosine metabolism	Amino acid	0.577421029	0.013418433
stearate (18:0)	Long chain fatty acid	Lipid	0.580206489	0.013471354
tryptophan betaine	Tryptophan metabolism	Amino acid	0.581737686	-0.015213343
bilirubin (Z,Z)	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.582914342	0.014246602
palmitoyl sphingomyelin	Sphingolipid	Lipid	0.589861218	0.014862477
tauroolithocholate 3-sulfate	Bile acid metabolism	Lipid	0.592767806	0.013317187
valine	Valine, leucine and isoleucine metabolism	Amino acid	0.593283698	0.012568538
asparagine	Alanine and aspartate metabolism	Amino acid	0.603889922	0.012132429
trimethyl-N-aminovalerate	Carnitine metabolism	Lipid	0.608242798	0.012293212
indolelactate	Tryptophan metabolism	Amino acid	0.609027345	-0.012316775
proline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.617646228	0.011986937
C-glycosyltryptophan*	Tryptophan metabolism	Amino acid	0.619502555	0.013029919
pyruvate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.624151144	0.011988989
1-palmitoleoylglycerophosphocholine*	Lysolipid	Lipid	0.626239728	0.011393959
7-alpha-hydroxy-3-oxo-4-cholestenoate (7-Hoca)	Sterol/Steroid	Lipid	0.626428693	0.011363333
pyroglutamine*	Glutamate metabolism	Amino acid	0.630720062	0.012130895
dihomo-linoleate (20:2n6)	Long chain fatty acid	Lipid	0.632871131	0.011690721
3-indoxyl sulfate	Tryptophan metabolism	Amino acid	0.633624805	0.011121922
propionylcarnitine	Fatty acid metabolism (also BCAA metabolism)	Lipid	0.643399103	0.011380731
2-palmitoylglycerophosphocholine*	Lysolipid	Lipid	0.649990767	-0.010286613
creatine	Creatine metabolism	Amino acid	0.650458644	0.011109857
gamma-glutamylphenylalanine	gamma-glutamyl	Peptide	0.653797019	-0.010789695
3-methyl-2-oxovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.668749421	-0.010613981
HWESASXX*	Polypeptide	Peptide	0.66885391	0.010886673

erythrose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.676989345	0.009558762
1-myristoylglycerophosphocholine	Lysolipid	Lipid	0.686004412	-0.009353266
lysine	Lysine metabolism	Amino acid	0.688467689	0.009294329
bilirubin (E,E)*	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.693287558	-0.009821971
dihomo-linolenate (20:3n3 or n6)	Essential fatty acid	Lipid	0.702709098	0.008875571
margarate (17:0)	Long chain fatty acid	Lipid	0.704596201	0.009025515
1-heptadecanoylglycerophosphocholine	Lysolipid	Lipid	0.717536388	0.008546542
acetylcarnitine	Carnitine metabolism	Lipid	0.722426521	-0.008591249
palmitoylcarnitine	Carnitine metabolism	Lipid	0.726698525	-0.008433654
carnitine	Carnitine metabolism	Lipid	0.729682635	0.008238981
1-palmitoylplasmeneylethanolamine*	Lysolipid	Lipid	0.736177055	-0.008895685
isoleucine	Valine, leucine and isoleucine metabolism	Amino acid	0.739583933	0.007960969
glycerophosphorylcholine (GPC)	Glycerolipid metabolism	Lipid	0.740278297	-0.008223929
1-stearoylglycerophosphoethanolamine	Lysolipid	Lipid	0.741913814	0.007660921
scyllo-inositol	Inositol metabolism	Lipid	0.759537556	0.007776367
5-oxoproline	Glutathione metabolism	Amino acid	0.763643694	-0.007270488
taurochenodeoxycholate	Bile acid metabolism	Lipid	0.770039452	-0.007889676
1-arachidonoylglycerophosphocholine*	Lysolipid	Lipid	0.773710063	-0.006532771
eicosapentaenoate (EPA; 20:5n3)	Essential fatty acid	Lipid	0.779185388	0.006706841
1-palmitoylglycerophosphoinositol*	Lysolipid	Lipid	0.782122186	0.00738449
1-palmitoylglycerol (1-monopalmitin)	Monoacylglycerol	Lipid	0.788177333	-0.006203129
kynurenine	Tryptophan metabolism	Amino acid	0.788628549	0.006526953
succinylcarnitine	Krebs cycle	Energy	0.791300732	-0.007270961
ursodeoxycholate	Bile acid metabolism	Lipid	0.795353541	0.007169043
octadecanedioate	Fatty acid, dicarboxylate	Lipid	0.797465402	0.006311575
1-eicosadienoylglycerophosphocholine*	Lysolipid	Lipid	0.801808466	0.006168369
eicosenoate (20:1n9 or 11)	Long chain fatty acid	Lipid	0.802126557	-0.006143784
phenylacetylglutamine	Phenylalanine & tyrosine metabolism	Amino acid	0.80813789	0.005733632

erythritol	Sugar, sugar substitute, starch	Xenobiotics	0.81875158	0.005652444
2-oleoylglycerophosphocholine*	Lysolipid	Lipid	0.818826456	0.005371761
hexadecanedioate	Fatty acid, dicarboxylate	Lipid	0.830517131	0.005189027
gamma-glutamylvaline	gamma-glutamyl	Peptide	0.833371647	0.005500857
nonadecanoate (19:0)	Long chain fatty acid	Lipid	0.848401933	0.004643742
glycocholate	Bile acid metabolism	Lipid	0.849062751	0.004917798
N-acetyllalanine	Alanine and aspartate metabolism	Amino acid	0.853153329	0.004442957
urea	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.855033819	0.004611736
gamma-tocopherol	Tocopherol metabolism	Cofactors and vitamins	0.860358966	0.004520972
tetradecanedioate	Fatty acid, dicarboxylate	Lipid	0.867071059	0.004212792
uridine	Pyrimidine metabolism, uracil containing	Nucleotide	0.87047397	0.003808338
N-acetylthreonine	Glycine, serine and threonine metabolism	Amino acid	0.875546022	-0.003951552
stearidonate (18:4n3)	Long chain fatty acid	Lipid	0.877372777	0.003698204
leucine	Valine, leucine and isoleucine metabolism	Amino acid	0.88553179	0.00347746
1,5-anhydroglucitol (1,5-AG)	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.88883396	0.003275727
2-methylbutyrylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.89065836	0.003504567
docosahexaenoate (DHA; 22:6n3)	Essential fatty acid	Lipid	0.891446175	0.003314176
fructose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.891657073	0.003101015
gamma-glutamylleucine	gamma-glutamyl	Peptide	0.8964108	0.003365708
hippurate	Benzoate metabolism	Xenobiotics	0.897561353	-0.003054962
1-eicosatrienoylglycerophosphocholine*	Lysolipid	Lipid	0.910003784	-0.002524681
1-stearoylglycerophosphocholine	Lysolipid	Lipid	0.911990684	-0.002547298

3-methyl-2-oxobutyrate	Valine, leucine and isoleucine metabolism	Amino acid	0.914701925	0.002671074
stachydrine	Food component/Plant	Xenobiotics	0.915619571	-0.002488631
2-stearoylglycerophosphocholine*	Lysolipid	Lipid	0.920504326	-0.002277895
2-hydroxybutyrate (AHB)	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.922278269	-0.002407243
pentadecanoate (15:0)	Long chain fatty acid	Lipid	0.926496605	0.002230508
hypoxanthine	Purine metabolism, (hypo)xanthine/inosine containing	Nucleotide	0.93076749	-0.00215609
lactate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.931862287	0.002090325
oleoylcarnitine	Carnitine metabolism	Lipid	0.933074768	-0.00203911
decanoylcarnitine	Carnitine metabolism	Lipid	0.936282985	-0.001979502
phenylalanine	Phenylalanine & tyrosine metabolism	Amino acid	0.944070016	0.001656388
cis-4-decenoyl carnitine	Carnitine metabolism	Lipid	0.946433831	-0.001850358
4-acetamidobutanoate	Guanidino and acetamido metabolism	Amino acid	0.946599851	0.001754025
betaine	Glycine, serine and threonine metabolism	Amino acid	0.948607463	-0.001567674
glucose	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.952786466	0.001394911
aspartate	Alanine and aspartate metabolism	Amino acid	0.956143409	-0.001297755
3-methylhistidine	Histidine metabolism	Amino acid	0.956640194	0.001371583
arachidonate (20:4n6)	Long chain fatty acid	Lipid	0.961374702	0.001134838
indoleacetate	Tryptophan metabolism	Amino acid	0.973998267	-0.000756547
octanoylcarnitine	Carnitine metabolism	Lipid	0.975292684	0.000760718
pseudouridine	Pyrimidine metabolism, uracil containing	Nucleotide	0.982131887	0.000539096

isobutyrylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.98348493	0.00049283
10-undecenoate (11:1n1)	Medium chain fatty acid	Lipid	0.983768659	-0.000485292
3-carboxy-4-methyl-5-propyl-2- furanpropanoate (CMPF)	Fatty acid, dicarboxylate	Lipid	0.984451046	0.000472605
1-docosahexaenoylglycerophosphocholine*	Lysolipid	Lipid	0.985815093	0.000420415
myo-inositol	Inositol metabolism	Lipid	0.993135601	0.00020664
N-acetylglycine	Glycine, serine and threonine metabolism	Amino acid	0.99954432	-0.0000137

Supplemental Table S3: Complete association results of a serum metabolomics study with outcome variable a clinical diagnosis of dry eye disease, ordered by *P*-value.

Metabolite	Pathway	Super-pathway	P-value	Beta
epiandrosterone sulfate	Sterol/Steroid	Lipid	0.000290781	-0.218742145
androsterone sulfate	Sterol/Steroid	Lipid	0.001104212	-0.197012358
dehydroepiandrosterone sulfate (DHEA-S)	Sterol/Steroid	Lipid	0.004142316	-0.184956199
4-androsten-3beta,17beta-diol disulfate 1*	Sterol/Steroid	Lipid	0.014212261	-0.167036805
N1-methyladenosine	Purine metabolism, adenine containing	Nucleotide	0.017275936	-0.13824799
serine	Glycine, serine and threonine metabolism	Amino acid	0.026238815	0.127350162
1-palmitoylglycerophosphocholine	Lysolipid	Lipid	0.03016996	-0.115627256
4-androsten-3beta,17beta-diol disulfate 2*	Sterol/Steroid	Lipid	0.034445636	-0.144149327
5-dodecenoate (12:1n7)	Medium chain fatty acid	Lipid	0.047602388	-0.117446655
xanthine	Purine metabolism, (hypo)xanthine/inosine containing	Nucleotide	0.050596437	-0.127492496
theophylline	Xanthine metabolism	Xenobiotics	0.051194421	0.117954641
myristoleate (14:1n5)	Long chain fatty acid	Lipid	0.053999497	-0.116881498
indolelactate	Tryptophan metabolism	Amino acid	0.056961617	-0.112295144
myristate (14:0)	Long chain fatty acid	Lipid	0.059435335	-0.115677335
1-stearoylglycerophosphocholine	Lysolipid	Lipid	0.062941142	-0.105528287
cortisone	Sterol/Steroid	Lipid	0.064647435	-0.11005104
4-acetamidobutanoate	Guanidino and acetamido metabolism	Amino acid	0.06558337	-0.120745941
3-(4-hydroxyphenyl)lactate	Phenylalanine & tyrosine metabolism	Amino acid	0.065787535	-0.105814394
10-nonadecenoate (19:1n9)	Long chain fatty acid	Lipid	0.067760925	-0.110282031
margarate (17:0)	Long chain fatty acid	Lipid	0.068897575	-0.10503999
glutaroyl carnitine	Lysine metabolism	Amino acid	0.078007201	-0.102140674
pseudouridine	Pyrimidine metabolism, uracil containing	Nucleotide	0.078431152	-0.103804979
caffeine	Xanthine metabolism	Xenobiotics	0.079084632	0.105777112

alanine	Alanine and aspartate metabolism	Amino acid	0.089776142	0.098233781
dimethylarginine (SDMA + ADMA)	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.093910649	-0.09787477
1-oleoylglycerophosphocholine	Lysolipid	Lipid	0.094931291	-0.091224798
hyodeoxycholate	Bile acid metabolism	Lipid	0.096235159	-0.104247446
10-heptadecenoate (17:1n7)	Long chain fatty acid	Lipid	0.09713237	-0.101266698
creatinine	Creatine metabolism	Amino acid	0.102915811	-0.093017703
1,7-dimethylurate	Xanthine metabolism	Xenobiotics	0.104831172	0.103063908
palmitoleate (16:1n7)	Long chain fatty acid	Lipid	0.117018708	-0.095321855
pyruvate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.118273434	0.096809683
gamma-glutamyltyrosine	gamma-glutamyl	Peptide	0.12114197	-0.100090497
undecanoate (11:0)	Medium chain fatty acid	Lipid	0.126904758	-0.087855618
methionine	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.134751188	0.090577756
alpha-ketoglutarate	Krebs cycle	Energy	0.135654691	0.098108444
arachidonate (20:4n6)	Long chain fatty acid	Lipid	0.144806365	-0.08333226
dihomo-linoleate (20:2n6)	Long chain fatty acid	Lipid	0.154770956	-0.085493566
paraxanthine	Xanthine metabolism	Xenobiotics	0.157509864	0.084085086
2-palmitoylglycerophosphocholine*	Lysolipid	Lipid	0.158996244	-0.077985304
2-hydroxypalmitate	Fatty acid, monohydroxy	Lipid	0.170787969	-0.077388357
1-linoleoylglycerophosphocholine	Lysolipid	Lipid	0.175627455	-0.075662268
laurate (12:0)	Medium chain fatty acid	Lipid	0.176852667	-0.080301739
choline	Glycerolipid metabolism	Lipid	0.186020283	0.075575013
pentadecanoate (15:0)	Long chain fatty acid	Lipid	0.200553692	-0.075716223
threonine	Glycine, serine and threonine metabolism	Amino acid	0.201824402	0.084285645
palmitoyl sphingomyelin	Sphingolipid	Lipid	0.202348651	-0.084106699
1-eicosadienoylglycerophosphocholine*	Lysolipid	Lipid	0.219428522	-0.07411916
oleate (18:1n9)	Long chain fatty acid	Lipid	0.22484671	-0.072806468
palmitate (16:0)	Long chain fatty acid	Lipid	0.228400124	-0.073504593
1-palmitoleoylglycerophosphocholine*	Lysolipid	Lipid	0.237496791	-0.067061977
glycochenodeoxycholate	Bile acid metabolism	Lipid	0.239276837	0.071154015
1-myristoylglycerophosphocholine	Lysolipid	Lipid	0.247535543	-0.065604981

1-stearoylglycerol (1-monostearin)	Monoacylglycerol	Lipid	0.249605311	0.068652254
arginine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.257809594	0.066241429
stearate (18:0)	Long chain fatty acid	Lipid	0.258101281	-0.068520439
1-palmitoylglycerophosphoethanolamine	Lysolipid	Lipid	0.259835857	0.063176676
2-stearoylglycerophosphocholine*	Lysolipid	Lipid	0.266476282	-0.062343175
succinylcarnitine	Krebs cycle	Energy	0.267035681	-0.074940177
isovalerate	Fatty acid metabolism	Lipid	0.269739105	0.0780315
tyrosine	Phenylalanine & tyrosine metabolism	Amino acid	0.280199458	-0.06536347
aspartate	Alanine and aspartate metabolism	Amino acid	0.294362477	-0.060150477
eicosenoate (20:1n9 or 11)	Long chain fatty acid	Lipid	0.295038148	-0.062732131
indoleacetate	Tryptophan metabolism	Amino acid	0.301003461	-0.058637472
citrulline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.302827972	-0.06241031
bilirubin (Z,Z)	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.303434235	0.064667736
1-stearoylglycerophosphoethanolamine	Lysolipid	Lipid	0.30462107	0.059201259
theobromine	Xanthine metabolism	Xenobiotics	0.305595702	0.058838234
1-heptadecanoylglycerophosphocholine	Lysolipid	Lipid	0.309580515	-0.058127945
phosphate	Oxidative phosphorylation	Energy	0.311671029	-0.057351894
cortisol	Sterol/Steroid	Lipid	0.333152767	-0.059133617
cysteine	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.335529842	-0.054752263
glycine	Glycine, serine and threonine metabolism	Amino acid	0.339937937	0.054657052
2-oleoylglycerophosphocholine*	Lysolipid	Lipid	0.341152765	-0.053808122
taurochenodeoxycholate	Bile acid metabolism	Lipid	0.347432992	-0.063954724
alpha-hydroxyisovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.35064945	-0.054304998
gamma-glutamylglutamine	gamma-glutamyl	Peptide	0.350995997	0.057540149
threonate	Ascorbate and aldarate metabolism	Cofactors and vitamins	0.363096201	0.051878793
serotonin (5HT)	Tryptophan metabolism	Amino acid	0.366247529	-0.063937695

linoleate (18:2n6)	Essential fatty acid	Lipid	0.370272478	-0.052638849
bilirubin (E,E)*	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.37777186	0.055143537
C-glycosyltryptophan*	Tryptophan metabolism	Amino acid	0.381847866	-0.056172654
1-palmitoylplasmylethanolamine*	Lysolipid	Lipid	0.386280988	-0.05654387
glycerophosphorylcholine (GPC)	Glycerolipid metabolism	Lipid	0.386788825	-0.052969326
2-linoleoylglycerophosphocholine*	Lysolipid	Lipid	0.400935951	-0.053846124
glutamate	Glutamate metabolism	Amino acid	0.401448469	0.05234801
asparagine	Alanine and aspartate metabolism	Amino acid	0.402243558	0.049047728
gamma-glutamylphenylalanine	gamma-glutamyl	Peptide	0.40302834	-0.048761842
stearidonate (18:4n3)	Long chain fatty acid	Lipid	0.415863586	-0.046973876
decanoylcarnitine	Carnitine metabolism	Lipid	0.421308052	-0.048632379
phenylacetylglutamine	Phenylalanine & tyrosine metabolism	Amino acid	0.429323651	-0.044650467
pyroglutamine*	Glutamate metabolism	Amino acid	0.436302447	-0.047686836
isoleucine	Valine, leucine and isoleucine metabolism	Amino acid	0.442050346	0.045033858
2-tetradecenoyl carnitine	Carnitine metabolism	Lipid	0.443311091	-0.047970447
1,5-anhydroglucitol (1,5-AG)	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.447966612	-0.042238066
gamma-glutamylleucine	gamma-glutamyl	Peptide	0.454995113	0.048052456
butyrylcarnitine	Fatty acid metabolism (also BCAA metabolism)	Lipid	0.456535998	0.044891514
hippurate	Benzoate metabolism	Xenobiotics	0.464806863	-0.04160419
nonadecanoate (19:0)	Long chain fatty acid	Lipid	0.471975652	-0.042811212
lathosterol	Sterol/Steroid	Lipid	0.487762993	-0.046828288
myo-inositol	Inositol metabolism	Lipid	0.492979274	-0.039924102
2-hydroxybutyrate (AHB)	Cysteine, methionine, SAM, taurine metabolism	Amino acid	0.494636406	0.041355078
N-acetylthreonine	Glycine, serine and threonine metabolism	Amino acid	0.501013211	0.041642793
1-docosahexaenoylglycerophosphocholine*	Lysolipid	Lipid	0.504073288	0.038681534
erythritol	Sugar, sugar substitute, starch	Xenobiotics	0.504273249	-0.040920452
1-arachidonoylglycerophosphoinositol*	Lysolipid	Lipid	0.506008835	0.038832311

hypoxanthine	Purine metabolism, (hypo)xanthine/inosine containing	Nucleotide	0.506689948	-0.041504647
N-acetylornithine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.507989681	-0.039015485
proline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.510933148	0.038324022
pipecolate	Lysine metabolism	Amino acid	0.511214614	0.038712195
biliverdin	Hemoglobin and porphyrin metabolism	Cofactors and vitamins	0.513576937	-0.041996496
heptanoate (7:0)	Medium chain fatty acid	Lipid	0.515905704	-0.03750956
heme*	Hemoglobin and porphyrin	Cofactors and vitamins	0.516265494	0.040454297
1-arachidonoylglycerophosphoethanolamine*	Lysolipid	Lipid	0.517165282	0.034635495
acetylcarnitine	Carnitine metabolism	Lipid	0.526979852	-0.037742648
3-methylhistidine	Histidine metabolism	Amino acid	0.527075108	-0.039815141
fructose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.536318919	-0.034709346
urate	Purine metabolism, urate metabolism	Nucleotide	0.538578514	-0.036892242
isovalerylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.540981941	0.036173178
phenyllactate (PLA)	Phenylalanine & tyrosine metabolism	Amino acid	0.546296164	0.040030297
1-eicosatrienoylglycerophosphocholine*	Lysolipid	Lipid	0.556717797	-0.031557187
creatine	Creatine metabolism	Amino acid	0.557417519	-0.034884732
threitol	Nucleotide sugars, pentose metabolism	Carbohydrate	0.567061379	0.036204913
10-undecenoate (11:1n1)	Medium chain fatty acid	Lipid	0.568501409	-0.033674985
dihomo-linolenate (20:3n3 or n6)	Essential fatty acid	Lipid	0.570249251	-0.032024724
piperine	Food component/Plant	Xenobiotics	0.57462635	-0.03454624
3-phenylpropionate (hydrocinnamate)	Phenylalanine & tyrosine metabolism	Amino acid	0.59532188	0.034557428
HWESASXX*	Polypeptide	Peptide	0.600257377	0.032659339

pantothenate	Pantothenate and CoA metabolism	Cofactors and vitamins	0.600786388	0.029913106
arabinose	Nucleotide sugars, pentose metabolism	Carbohydrate	0.604622176	-0.034496325
malate	Krebs cycle	Energy	0.605820052	-0.030793994
2-methylbutyrylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.609418527	0.03134199
trimethyl-N-aminovalerate	Carnitine metabolism	Lipid	0.611929477	0.030294397
2-aminobutyrate	Butanoate metabolism	Amino acid	0.616437861	-0.028989775
docosapentaenoate (n3 DPA; 22:5n3)	Essential fatty acid	Lipid	0.620637989	-0.029666529
erythrose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.620704066	-0.028794522
gamma-glutamylvaline	gamma-glutamyl	Peptide	0.624233771	0.032031735
isobutyrylcarnitine	Valine, leucine and isoleucine metabolism	Amino acid	0.626874601	0.02850456
lysine	Lysine metabolism	Amino acid	0.629164721	0.027509215
uridine	Pyrimidine metabolism, uracil containing	Nucleotide	0.639425419	-0.025561525
ursodeoxycholate	Bile acid metabolism	Lipid	0.641617042	0.030680153
beta-hydroxyisovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.643680958	-0.026421585
p-cresol sulfate	Phenylalanine & tyrosine metabolism	Amino acid	0.648956732	0.027717284
quininate	Food component/Plant	Xenobiotics	0.651600708	0.028468533
leucine	Valine, leucine and isoleucine metabolism	Amino acid	0.661164279	0.02618625
stachydrine	Food component/Plant	Xenobiotics	0.66279498	0.024885199
citrate	Krebs cycle	Energy	0.665816808	-0.026428367
7-methylxanthine	Xanthine metabolism	Xenobiotics	0.667848407	-0.029461488
alpha-tocopherol	Tocopherol metabolism	Cofactors and vitamins	0.683161671	0.0264513
levulinate (4-oxovalerate)	Valine, leucine and isoleucine metabolism	Amino acid	0.689413123	0.023468372
cholesterol	Sterol/Steroid	Lipid	0.69119319	-0.024058929

stearoylcarnitine	Carnitine metabolism	Lipid	0.696627755	0.025051237
glycerol 2-phosphate	Chemical	Xenobiotics	0.705638198	0.025245225
1-oleoylglycerophosphoethanolamine	Lysolipid	Lipid	0.705806142	-0.020440552
5-oxoproline	Glutathione metabolism	Amino acid	0.707700086	-0.022046981
3-methyl-2-oxovalerate	Valine, leucine and isoleucine metabolism	Amino acid	0.708979647	0.023181994
propionylcarnitine	Fatty acid metabolism (also BCAA metabolism)	Lipid	0.713099385	-0.021460154
histidine	Histidine metabolism	Amino acid	0.715233191	-0.020942969
phenol sulfate	Phenylalanine & tyrosine metabolism	Amino acid	0.717169003	0.020114814
2-hydroxyisobutyrate	Valine, leucine and isoleucine metabolism	Amino acid	0.726024473	0.023359786
gamma-tocopherol	Tocopherol metabolism	Cofactors and vitamins	0.731312327	0.022187068
caproate (6:0)	Medium chain fatty acid	Lipid	0.733005356	0.019580302
indolepropionate	Tryptophan metabolism	Amino acid	0.736357193	-0.018992919
1-stearoylglycerophosphoinositol	Lysolipid	Lipid	0.73983159	-0.019447589
betaine	Glycine, serine and threonine metabolism	Amino acid	0.740691245	0.020232405
hexadecanedioate	Fatty acid, dicarboxylate	Lipid	0.76176838	0.01736582
allantoin	Purine metabolism, urate metabolism	Nucleotide	0.772327284	0.018445636
pyridoxate	Vitamin B6 metabolism	Cofactors and vitamins	0.773679178	0.016164233
docosahexaenoate (DHA; 22:6n3)	Essential fatty acid	Lipid	0.777859495	0.016840937
N-acetylalanine	Alanine and aspartate metabolism	Amino acid	0.782930259	-0.015871974
trans-4-hydroxyproline	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.786623177	0.016193905
mannose	Fructose, mannose, galactose, starch, and sucrose metabolism	Carbohydrate	0.797845963	0.015033588
acetylphosphate	Oxidative phosphorylation	Energy	0.803652291	0.014422192
octadecanedioate	Fatty acid, dicarboxylate	Lipid	0.805675771	0.014785057
palmitoylcarnitine	Carnitine metabolism	Lipid	0.806553112	0.015236648

glycerate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.807922561	0.013952507
kynurenine	Tryptophan metabolism	Amino acid	0.816852119	-0.013601649
valine	Valine, leucine and isoleucine metabolism	Amino acid	0.822365296	0.013067289
cholate	Bile acid metabolism	Lipid	0.823006759	0.014443729
cis-4-decenoyl carnitine	Carnitine metabolism	Lipid	0.83171795	-0.01489421
1-arachidonoylglycerophosphocholine*	Lysolipid	Lipid	0.851170359	-0.010214372
4-vinylphenol sulfate	Benzoate metabolism	Xenobiotics	0.854044156	0.011241448
erythronate*	Aminosugars metabolism	Carbohydrate	0.855544355	0.010574788
linolenate [alpha or gamma; (18:3n3 or 6)]	Essential fatty acid	Lipid	0.856771133	-0.01004328
taurothocholate 3-sulfate	Bile acid metabolism	Lipid	0.860883795	0.009949856
3-methyl-2-oxobutyrate	Valine, leucine and isoleucine metabolism	Amino acid	0.861617288	0.011106901
scyllo-inositol	Inositol metabolism	Lipid	0.867239239	-0.011313734
glycocholate	Bile acid metabolism	Lipid	0.873174703	0.009899393
ornithine	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.876325411	0.008774025
glycerol	Glycerolipid metabolism	Lipid	0.877508655	0.00945334
lactate	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.877583215	0.009231647
caprylate (8:0)	Medium chain fatty acid	Lipid	0.884490135	-0.009237127
tryptophan	Tryptophan metabolism	Amino acid	0.88903922	0.007214791
glutamine	Glutamate metabolism	Amino acid	0.894603784	-0.007886051
tetradecanedioate	Fatty acid, dicarboxylate	Lipid	0.895100641	-0.008360181
adrenate (22:4n6)	Long chain fatty acid	Lipid	0.895454801	0.007353593
urea	Urea cycle; arginine-, proline-, metabolism	Amino acid	0.895630464	-0.007780102
octanoylcarnitine	Carnitine metabolism	Lipid	0.896083838	-0.007645623
catechol sulfate	Benzoate metabolism	Xenobiotics	0.899970581	0.007115516
dodecanedioate	Fatty acid, dicarboxylate	Lipid	0.902395873	0.007199001
1-palmitoylglycerophosphoinositol*	Lysolipid	Lipid	0.907065383	-0.008186688
3-hydroxybutyrate (BHBA)	Ketone bodies	Lipid	0.909389092	-0.006835149
pelargonate (9:0)	Medium chain fatty acid	Lipid	0.921051245	-0.006192266

tryptophan betaine	Tryptophan metabolism	Amino acid	0.921975247	0.006740114
4-methyl-2-oxopentanoate	Valine, leucine and isoleucine metabolism	Amino acid	0.92230276	-0.006119761
glycerol 3-phosphate (G3P)	Glycerolipid metabolism	Lipid	0.923359305	0.006141396
carnitine	Carnitine metabolism	Lipid	0.923569427	0.005721227
4-ethylphenylsulfate	Benzoate metabolism	Xenobiotics	0.923754881	-0.006568308
1-linoleoylglycerophosphoethanolamine*	Lysolipid	Lipid	0.926538171	-0.005371443
2-hydroxystearate	Fatty acid, monohydroxy	Lipid	0.932667255	-0.004356958
N-acetylglycine	Glycine, serine and threonine metabolism	Amino acid	0.932743716	-0.006084948
1-palmitoylglycerol (1-monopalmitin)	Monoacylglycerol	Lipid	0.933762073	-0.004766886
7-alpha-hydroxy-3-oxo-4-cholestenoate (7-Hoca)	Sterol/Steroid	Lipid	0.933879719	-0.005018504
eicosapentaenoate (EPA; 20:5n3)	Essential fatty acid	Lipid	0.935924715	0.00487171
3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	Fatty acid, dicarboxylate	Lipid	0.953413774	0.003645768
phenylalanine	Phenylalanine & tyrosine metabolism	Amino acid	0.957426884	-0.002758028
hexanoylcarnitine	Carnitine metabolism	Lipid	0.958405703	0.003261256
pro-hydroxy-pro	Dipeptide	Peptide	0.968192839	0.001555603
benzoate	Benzoate metabolism	Xenobiotics	0.982064166	0.001150327
glucose	Glycolysis, gluconeogenesis, pyruvate metabolism	Carbohydrate	0.986789188	0.001080741
3-indoxyl sulfate	Tryptophan metabolism	Amino acid	0.989460695	-0.00070736
oleoylcarnitine	Carnitine metabolism	Lipid	1	0.000161859