








ORIGINAL RESEARCH

Serum Metabolites Are Associated With HFpEF in Biopsy-Proven Nonalcoholic Fatty Liver Disease

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BACKGROUND: Nonalcoholic fatty liver disease (NAFLD) and heart failure with preserved ejection fraction (HFpEF) share common risk factors, including obesity and diabetes. They are also thought to be mechanistically linked. The aim of this study was to define serum metabolites associated with HFpEF in a cohort of patients with biopsy-proven NAFLD to identify common mechanisms.

METHODS AND RESULTS: We performed a retrospective, single-center study of 89 adult patients with biopsy-proven NAFLD who had transthoracic echocardiography performed for any indication. Metabolomic analysis was performed on serum using ultrahigh performance liquid and gas chromatography/tandem mass spectrometry. HFpEF was defined as ejection fraction >50% plus at least 1 echocardiographic feature of HFpEF (diastolic dysfunction, abnormal left atrial size) and at least 1 heart failure sign or symptom. We performed generalized linear models to evaluate associations between individual metabolites, NAFLD, and HFpEF. Thirty-seven out of 89 (41.6%) patients met criteria for HFpEF. A total of 1151 metabolites were detected; 656 were analyzed after exclusion of unnamed metabolites and those with >30% missing values. Fifty-three metabolites were associated with the presence of HFpEF with unadjusted *P* value <0.05; none met statistical significance after adjustment for multiple comparisons. The majority (39/53, 73.6%) were lipid metabolites, and levels were generally increased. Two cysteine metabolites (cysteine s-sulfate and s-methylcysteine) were present at significantly lower levels in patients with HFpEF.

CONCLUSIONS: We identified serum metabolites associated with HFpEF in patients with biopsy-proven NAFLD, with increased levels of multiple lipid metabolites. Lipid metabolism could be an important pathway linking HFpEF to NAFLD.

Key Words: heart failure ■ metabolic syndrome ■ metabolomics ■ nonalcoholic fatty liver disease

Nonalcoholic fatty liver disease (NAFLD), which is estimated to affect one-quarter of the world's population and the prevalence of which is projected to increase, is strongly linked to cardiovascular disease.¹⁻³ Common risk factors include diabetes, hyperlipidemia, and obesity. Not surprising, therefore, is the fact that cardiovascular disease and complications of cirrhosis represent the top causes of mortality in patients with NAFLD.^{1,4} The link between NAFLD and coronary artery

disease and related events such as myocardial infarction is well established.⁵ Further, advanced fibrosis in NAFLD is independently associated with multiple forms of incident cardiovascular disease, including coronary artery disease, peripheral vascular disease, and congestive heart failure.⁶

Interestingly, NAFLD appears to be more strongly associated with heart failure with preserved ejection fraction (HFpEF) than with heart failure with reduced

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CLINICAL PERSPECTIVE

What Is New?

- Serum metabolites including lipid and amino acid metabolites are associated with the presence of heart failure with preserved ejection fraction in patients with biopsy-proven nonalcoholic fatty liver disease.

What Are the Clinical Implications?

- Although nonalcoholic fatty liver disease and heart failure with preserved ejection fraction are known to share risk factors, the pathogenic mechanisms linking the 2 diseases are unknown.
- Our work points toward lipid metabolism as a potentially significant pathway.

Nonstandard Abbreviations and Acronyms

HFpEF	heart failure with preserved ejection fraction
NAFLD	nonalcoholic fatty liver disease
NASH	nonalcoholic steatohepatitis
TTE	transthoracic echocardiogram

ejection fraction.⁷ The association between NAFLD and HFpEF has been explored, but it remains poorly understood.^{8,9} Patients with HFpEF have signs or symptoms of heart failure despite normal ejection fraction.¹⁰ Up to half of patients with HFpEF are thought to have NAFLD,¹¹ and among those with both HFpEF and NAFLD, advanced fibrosis may be present in up to 37.5%.¹² The prevalence of HFpEF in patients with NAFLD is less clear. As with other forms of cardiovascular disease, NAFLD and HFpEF share multiple risk factors, but the relationship between the 2 is complex. Large cohort studies have identified an independent association between NAFLD and echocardiographic features of HFpEF, including myocardial remodeling and diastolic dysfunction.¹³ The longitudinal CARDIA (Coronary Artery Risk Development in Young Adults) study found that NAFLD was associated with left ventricular hypertrophy, but the association did not persist after adjustment for obesity.¹⁴ Liver fibrosis stage is a strong predictor of overall clinical outcomes, liver-related decompensation, and cardiovascular events in NAFLD, and may have prognostic significance in HFpEF, suggesting shared pathways of progression.^{15–18} Elucidating common mechanisms between NAFLD and HFpEF, particularly through noninvasive

means, would have important diagnostic and therapeutic implications. Metabolomics is the analysis of small molecules (metabolites) in body fluids or tissues. Metabolites are intermediates or end products of cellular processes and can include lipids, amino acids, and products of energy generation such as the tricarboxylic acid cycle. Measuring metabolites can provide a window into alterations in metabolism associated with disease states. In the context of NAFLD and HFpEF, metabolomics could further our understanding of the molecular similarities between the 2 diseases, identify biomarkers to diagnose patients with overlapping disease, and guide the development of new therapies. This is particularly important because therapeutic options are limited for HFpEF, and NAFLD has no FDA-approved treatments.

To our knowledge, there are no published studies evaluating serum metabolites in patients with biopsy-proven NAFLD and HFpEF. The objective of this study was to evaluate metabolites associated with the presence of HFpEF in a cohort of patients with biopsy-proven NAFLD.

METHODS

Study Population and Clinical Phenotyping

We performed a retrospective, single-center cohort study of adults (aged ≥ 18 years) with biopsy-proven NAFLD enrolled in the Duke University Health System NAFLD Biorepository and Clinical Database. The biorepository is approved by the institutional review board and contains clinical information and biospecimens including frozen liver tissue and serum from patients who underwent standard of care diagnostic liver biopsy between 2007 and 2013. Further details regarding the biorepository and its enrollment criteria have been published.¹⁹ Participants specifically consented for genomic and metabolomic analysis of their specimens through the NAFLD biorepository. All authors had access to the study data and approved the final manuscript. The data that support the findings of this study are available from the corresponding author upon reasonable request.

For this study, we defined NAFLD as: (1) presence of $>5\%$ hepatic steatosis on liver biopsy, (2) absence of histologic and serologic evidence for other forms of chronic liver disease, and (3) little or no alcohol consumption (<20 g/d for women and <30 g/d for men). Demographic and clinical data were obtained at the time of liver biopsy. Serum samples were collected from participants at the time of liver biopsy following a 12-hour fast. The study cohort was selected for inclusion into the metabolomic cohort based on severity of hepatic fibrosis at the time of biopsy and included

participants with biopsy-proven NAFLD at different stages of fibrosis (mild, Metavir fibrosis stage F0–1, n=50; intermediate, stage F2, n=100; advanced, stage F3–4, n=50²⁰) and included only those participants who had high quality serum and liver biopsy tissue collected at the same time. Fibrosis groups were matched for sex, age (+/– 5 years), and body mass index (BMI) (+/– 3 points). Liver biopsy specimens were independently reviewed and scored by 1 pathologist (C.G.) using nonalcoholic steatohepatitis (NASH) Clinical Research Network scoring criteria.²¹

To identify patients with HFpEF, we limited the analysis to those who had transthoracic echocardiography (TTE) performed for any indication, at any time before or after liver biopsy. If >1 TTE was available for a given participant, we used the most recent exam. We established 3 definitions of HFpEF based on clinical guidelines describing heart failure as signs or symptoms of heart failure attributable to structural and functional abnormalities of the heart.^{22,23} First, “HFpEF” was defined as ejection fraction >50% on TTE plus the presence of at least 1 echocardiographic feature of HFpEF (diastolic dysfunction, abnormal left atrial size) and at least 1 of the following heart failure signs or symptoms: jugular venous pressure >8 cm, loop diuretic treatment, peripheral or pulmonary edema, exertional symptoms, fatigue, or HFpEF on problem list. Second, “HFpEF-no fatigue” included the same echocardiographic criteria as “HFpEF” but excluded fatigue from the heart failure signs or symptoms, given the high prevalence of fatigue among patients with chronic liver disease.²⁴ Finally, we defined “diastolic dysfunction” as solely echocardiographic criteria (ie, ejection fraction >50% plus either diastolic dysfunction or abnormal left atrial size). All echocardiographic criteria were ascertained based on TTE reports in the electronic medical record using manual chart review.

Clinical Data

Demographics including age, sex, BMI, smoking status, medical comorbidities, and medications were collected as part of the clinical database at the time of liver biopsy.

Metabolomics Analysis

Sample Handling and Processing

All samples were stored at –80 °C until processed on the metabolomics platform at Metabolon, Inc. (Durham, NC). Patient serum samples underwent metabolomic analysis with ultrahigh performance liquid chromatography/tandem mass spectrometry optimized for acidic species, ultrahigh performance liquid chromatography/tandem mass spectrometry for basic species, and gas chromatography/mass spectrometry. Metabolites

were then identified using automated comparison of the ion features in the experimental samples to a reference library of chemical standard entries that included retention time, molecular weight (m/z), preferred adducts, and in-source fragments as well as their associated tandem mass spectrometry spectra. This library allowed for rapid identification of metabolites in the experimental samples with high confidence. A detailed explanation of the metabolite analysis procedure and quality control process has been published,^{25,26} and quality control details appear in Data S1.

Lipidomics Panel

Lipids were extracted in the presence of authentic internal standards using chloroform:methanol. Lipids were trans-esterified in 1% sulfuric acid in methanol in a sealed vial under a nitrogen atmosphere at 100°C for 45 minutes. The resulting fatty acid methyl esters were extracted from the mixture with hexane containing 0.05% butylated hydroxytoluene and prepared for gas chromatography by sealing the hexane extracts under nitrogen. Fatty acid methyl esters were separated and quantified by capillary gas chromatography (Agilent Technologies 6890 Series GC) equipped with a 30-m DB 88 capillary column (Agilent Technologies) and a flame ionization detector.

Statistical Analysis

Patient demographic, clinical, biochemical, and histologic characteristics were summarized. Categorical variables were shown as counts and percentages and comparisons between HFpEF phenotypes tested using chi-squared test or Fisher exact test while continuous variables were analyzed using Wilcoxon test. We performed a logit link for a generalized linear model with binomial likelihood performed to evaluate the association between NAFLD without HFpEF and NAFLD with each HFpEF phenotype by metabolite while controlling for covariates: age, sex, diabetes, hypertension, BMI, and liver fibrosis stage. For each definition of HFpEF, we compared patients meeting the definition to those with TTE not meeting the definition. Statistical significance was defined as *P* value <0.05, and *P* values were subsequently adjusted for multiple comparisons using the Benjamini-Hochberg procedure.²⁷ All analyses were done using R (v4.1.0).

RESULTS

Study Participant Characteristics

Of the 200 participants with biopsy-proven NAFLD and serum metabolite results, 187 had available clinical data. Of those, 89 had a TTE and were included in

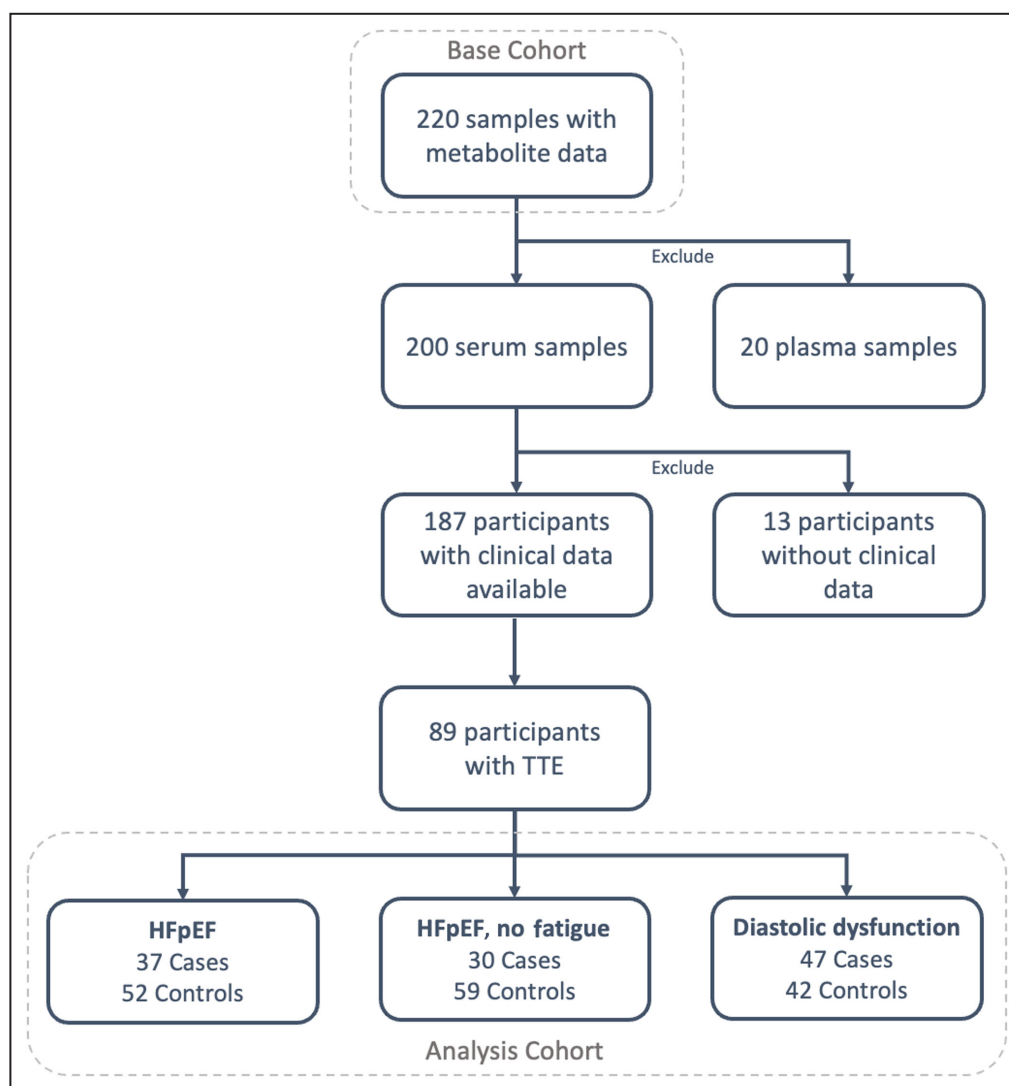


Figure 1. Cohort diagram.

HFpEF indicates heart failure with preserved ejection fraction; and TTE, transthoracic echocardiogram.

the final analyses (Figure 1). Thirty-eight (42.7%) participants were women, and the mean age at liver biopsy was 50.4 years. The mean BMI was 36.4 kg/m², and 36% of participants had diabetes. Four participants had evidence of significant coronary artery disease, with prior myocardial infarction, coronary artery bypass, or percutaneous coronary intervention, and 6 had documented atrial fibrillation or atrial flutter.

Regarding HFpEF phenotypes, 37 met the “HFpEF” definition, 30 were classified as “HFpEF-no fatigue,” and 47 were classified as “diastolic dysfunction.” Table 1 presents detailed demographics by HFpEF definition, and a Venn diagram depicting the number of patients who met each definition appears in Figure S1. Because only a proportion of the participants with serum metabolites had TTE information, we compared the cohort included in the final analyses to those excluded. Details are shown in Table S1. Overall,

the cohorts were not statistically different by age, race, liver fibrosis stage, NAFLD Activity Score, liver blood tests, or diagnosis of hyperlipidemia. Those patients with TTE were more likely to be men, have a diagnosis of hypertension, and have a higher mean BMI and mean hemoglobin A1c.

Metabolites Detected

Serum from the cohort yielded 1151 metabolites (760 identified and 361 unnamed). These metabolites derived from 8 super-pathways: amino acids (n=157), peptides (n=55), carbohydrates (n=28), energy related (n=7), lipids (n=307), nucleotides (n=34), cofactors/vitamins (n=34), and xenobiotics (n=67). The unnamed metabolites were excluded. We also excluded metabolites for which >30% of values were missing, which was presumably attributable to levels below the limit of

Table 1. Patient Characteristics

	HFpEF			HFpEF, no fatigue			Diastolic dysfunction		
	No (n=52)	Yes (n=37)	P value	No (n=59)	Yes (n=30)	P value	No (n=42)	Yes (n=47)	P value
Age (mean, SD)	49.0 (9.7)	52.4 (8.7)	0.10	48.9 (9.5)	53.6 (8.4)	0.02	48.6 (9.3)	52.1 (9.3)	0.08
Women (n, %)	22 (42.3)	16 (43.2)	1	24 (40.7)	14 (46.7)	0.75	17 (40.5)	21 (44.7)	0.85
White race (n, %)	46 (88.5)	36 (97.3)	0.13	53 (89.8)	29 (96.7)	0.26	36 (85.7)	46 (97.9)	0.03
BMI (mean, SD)	35.5 (6.4)	37.5 (7.6)	0.18	35.4 (6.7)	38.3 (7.2)	0.07	35.9 (6.5)	36.8 (7.4)	0.53
Diabetes (n, %)	21 (40.4)	11 (29.7)	0.42	24 (40.7)	8 (26.7)	0.29	17 (40.5)	15 (31.9)	0.54
Hypertension (n, %)	36 (69.2)	31 (83.8)	0.19	42 (71.2)	25 (83.3)	0.32	28 (66.7)	39 (83.0)	0.13
Total cholesterol (mean, SD)	181.6 (45.5)	187.7 (44.6)	0.55	186.5 (46.9)	179.7 (41.2)	0.53	187.8 (43.6)	181.1 (46.3)	0.52
LDL (mean, SD)	113.27 (39.2)	108.56 (39.2)	0.61	114.04 (38.4)	105.64 (40.5)	0.38	118.56 (38.5)	104.95 (38.8)	0.13
HDL (mean, SD)	37.4 (9.2)	38.5 (18.5)	0.71	38.9 (15.4)	35.6 (9.3)	0.32	37.7 (9.0)	37.9 (17.0)	0.95
Statin prescribed (n, %)	11 (21.2)	18 (48.6)	0.006	15 (25.4)	14 (46.7)	0.04	8 (19.0)	21 (44.7)	0.01
Fibrosis stage (n, %)			0.14			0.45			0.08
Stage 0	0 (0.0)	3 (8.1)		1 (1.7)	2 (6.7)		0 (0.0)	3 (6.4)	
Stage 1	9 (17.3)	7 (18.9)		10 (16.9)	6 (20.0)		6 (14.3)	10 (21.3)	
Stage 2	24 (46.2)	15 (40.5)		25 (42.4)	14 (46.7)		17 (40.5)	22 (46.8)	
Stage 3	18 (34.6)	9 (24.3)		21 (35.6)	6 (20.0)		18 (42.9)	9 (19.1)	
Stage 4	1 (1.9)	3 (8.1)		2 (3.4)	2 (6.7)		1 (2.4)	3 (6.4)	

BMI indicates body mass index; HDL, high-density lipoprotein; and LDL, low-density lipoprotein.

detection, and resulted in exclusion of 27 metabolites, or 3% of the total, as shown in [Figure S2](#). For the remaining 656 metabolites, missing values (2.4%–2.6%, see [Table S2](#)) were imputed to half of the observed minimum value for each metabolite, and batch effects were corrected by removing mean day-wise effects from each analyte independently after log-transformation.²⁸

Association of Metabolites With NAFLD and HFpEF Phenotypes

We assessed metabolites across the 3 HFpEF phenotypes to identify metabolites unique or similar across these definitions. For the “HFpEF” phenotype, 53 metabolites were associated with the presence of HFpEF with P value <0.05 . None remained significant after adjustment for multiple comparisons. The majority (39/53, 73.6%) of the significant metabolites were in lipid metabolism, and levels of these metabolites were generally increased in patients with HFpEF. Multiple glycerophosphorylcholines (GPCs, $n=20$) and glycerophosphorylethanolamines (GPEs, $n=9$) were among the most significant metabolites, and these were quantified at higher levels in patients with HFpEF compared with those without. Two metabolites of cysteine (cysteine s-sulfate and s-methylcysteine) were both present at significantly lower levels in patients with HFpEF. A heatmap of significant metabolites appears in [Figure 2](#), full results are in [Table S3](#), and a volcano plot appears in [Figure S3](#).

For “HFpEF-no fatigue,” 50 metabolites were significant to the $P<0.05$ level. None remained significant

after adjustment for multiple comparisons. Overall, the results were similar to “HFpEF,” with robust representation of lipids (34/50, 68%), particularly GPCs and GPEs. However, lower levels of taurochenolate sulfate, a conjugated secondary bile acid, were associated with “HFpEF-no fatigue.” Full results appear in [Table S4](#), and a volcano plot appears in [Figure S4](#).

For the echocardiographic definition, “diastolic dysfunction,” 39 metabolites were significantly associated with HFpEF. None remained significant after adjustment for multiple comparisons. Many metabolites overlapped with results from the other 2 HFpEF definitions and, again, most significant metabolites related to lipid metabolism (29/39, 74.3%). Several metabolites unique to this definition included biliverdin ($P=0.02$) and xylitol ($P=0.01$). Nucleotide family metabolites such as orotidine, 2'-deoxyuridine, and orotate, precursors of pyrimidine biosynthesis, were also uniquely significant for this phenotype. Full results appear in [Table S5](#), and a volcano plot appears in [Figure S5](#).

Fifteen metabolites were associated with all 3 definitions of HFpEF. These included 10 lipids, 1 cysteine metabolite (S-methylcysteine), and citrate ([Table 2](#) and [Figure 3](#)).

DISCUSSION

NAFLD and cardiovascular disease have both reached epidemic proportions. Links between NAFLD and HFpEF have been increasingly recognized because of shared risk factors and pathophysiologic



Figure 2. Heat map of metabolites associated with HFpEF definition.

Each column is 1 subject, with the top row showing HFpEF (orange) or no HFpEF (teal). Fibrosis stage is shown in the second row. Each subsequent row represents 1 metabolite, with pathways indicated by color in the leftmost column. Increased/decreased levels (HFpEF vs no HFpEF) are shown by the colors of each box in the matrix. Negative Z-scores are red to orange, positive Z-scores are blue. HFpEF indicates heart failure with preserved ejection fraction.

characteristics.⁷ Despite this, common mechanisms and biomarkers able to identify patients with NAFLD at risk for, or already afflicted with, HFpEF remain unknown. Here we investigated the association between serum metabolites and HFpEF in a cohort of patients with biopsy-proven NAFLD to identify both unique and common metabolic pathways between these diseases. To our knowledge, this is the first such analysis published. While no individual metabolites unique to those

patients with NAFLD with HFpEF phenotypes survived adjustment for multiple comparisons, presumably driven by the large number of metabolites evaluated, many were significant to the $P < 0.05$ level, and several themes persisted. First, lipid metabolism represented the most common (>65%) pathway associated with HFpEF among participants with biopsy-proven NAFLD. Lipid metabolites were generally increased in patients with HFpEF compared with those without. Of

Table 2. Metabolites Significantly Associated With All 3 Definitions of HFpEF*

Pathway	Subpathway	Metabolite
Lipid	Lysolipid	1-arachidonoyl-GPE* (20:4)*
		1-docosahexaenoylglycerophosphoethanolamine*
		2-stearoylglycerophosphoethanolamine*
		1-stearoyl-GPE (18:0)
		2-arachidonoyl-GPE* (20:4)*
		1-myristoyl-GPC (14:0)
	Fatty acid, dicarboxylate	azelate (nonanedioate; C9)
	Mole % total fatty acid	TL18:3n6 (g-linolenic acid)
	Monoacylglycerol	2-docosahexaenoylglycerol*
		1-arachidonoylglycerol
Energy	TCA cycle	citrate
		alpha-ketoglutarate
Amino acid	Methionine, cysteine, SAM, and taurine metabolism	S-methylcysteine
	Lysine metabolism	N6-acetyllysine
Xenobiotics	Food component/plant	methyl glucopyranoside (alpha+beta)

GPC indicates glycerophosphocholine; GPE, glycerophosphoethanolamine; SAM, S-Adenosyl methionine; and TCA, tricarboxylic acid cycle.
 *Covariates: age, sex, diabetes, hypertension, body mass index, and liver fibrosis stage.

note, more patients with HFpEF by any definition were on statin medications at the time of liver biopsy compared with those without HFpEF.

While this is the first published study to investigate the overlap between biopsy-proven NAFLD and HFpEF, metabolomic analysis has been used in NAFLD and HFpEF alone to predict the presence and severity of disease. In NAFLD, levels of triglycerides^{29,30} and polyunsaturated fatty acids³¹ distinguished simple steatosis from NASH, and differences in bile acids separated

patients with NAFLD from healthy controls.³² Caussy et al previously reported that a combination of 10 serum metabolites in bile acid, amino acid, lipid, nucleotide, and peptide pathways could accurately identify the presence of advanced NAFLD fibrosis.³³ Additionally, our group previously found that vitamin E, serotonin, and bile acid metabolites associated with future liver-related events in a cohort of patients with biopsy proven NAFLD and NASH.²⁶ In heart failure, several small studies have assessed metabolomic signatures of HFpEF compared with heart failure with reduced ejection fraction (HFrEF) and patients without heart failure. In 1 study, patients with HFpEF had several metabolomic differences, including higher serum amino acids and lower levels of several lipids including sphingomyelins and phosphatidylcholines.³⁴ Another study examined 63 metabolites in 752 patients (282 HFpEF, 279 HFrEF, 191 control) and found differences in long-chain acylcarnitine levels among the groups, with higher levels seen in patients with HFpEF and patients with HFrEF compared with controls.³⁵ Animal models of HFpEF and metabolic syndrome demonstrate alterations in lipid metabolism with nicotinamide supplementation.³⁶ Overall, both NAFLD and HFpEF appear to be associated with changes in lipid and amino acid metabolism, consistent with our findings.

Several metabolites from our analysis point to areas meriting future investigation. GPCs and GPEs, both phospholipids, featured prominently in the significant metabolites associated with all 3 HFpEF definitions. GPC is a choline metabolite and acetylcholine precursor. In 1 small study of health adults, administration of GPC increased plasma growth hormone levels and increased hepatic fatty acid oxidation.³⁷ Choline

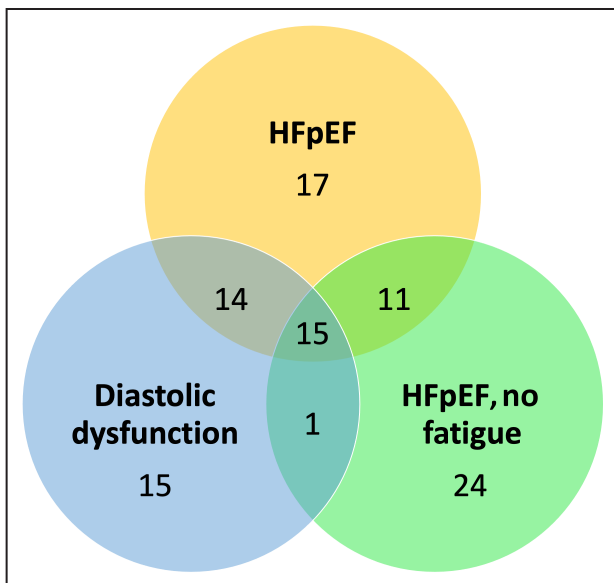


Figure 3. Venn diagram showing metabolites associated with each definition of HFpEF as well as metabolites that overlap between definitions.

HFpEF indicates heart failure with preserved ejection fraction.

metabolism has established links to NAFLD. A choline metabolism signature has previously been associated with steatosis severity,³⁸ and serum homocysteine (a choline metabolite) has been associated with histologic severity.³⁹ A high choline diet in an animal model of HFpEF resulted in increased myocardial fibrosis.⁴⁰ This suggests differential effects of derangements in choline metabolism in NAFLD versus HFpEF, given that choline restriction is a common method to induce steatosis in animal models of NAFLD. Although GPCs have not yet been linked to HFpEF in humans directly, 1 study of adolescents linked multiple GPCs to traditional cardiovascular risk factors including visceral adiposity.⁴¹ GPEs, also in the phospholipid biosynthesis pathway, also featured prominently among lipid metabolites associated with HFpEF. In 1 study, differences in these metabolites were found when obese patients with and without insulin resistance had serum metabolites compared.⁴² In addition, disruption of phosphoethanolamine synthesis in animal models has been shown to promote development of NASH.⁴³

Although fewer amino acid metabolites were associated with HFpEF relative to lipid metabolites, several are noteworthy. Cysteine metabolites (cysteine s-sulfate and s-methylcysteine) were present at lower levels in patients with HFpEF compared with those without. The liver metabolizes cysteine to glutathione, which is important in modulating oxidative stress. In 1 study, pediatric subjects with NAFLD had higher plasma levels of cysteine and homocysteine compared with healthy controls, but the subgroup with NASH had lower levels of cysteine and homocysteine compared with those with NAFLD not meeting histologic criteria for NASH,⁴⁴ consistent with our results. Increases in urinary cysteine excretion (specifically carboxyethyl cysteine and succinyl-cysteine) were found in an obese mouse model of HFpEF compared with control mice.⁴⁵ It is unclear why lower levels of cysteine have been associated with HFpEF and NASH, but our findings suggest that cysteine metabolism, with its key role in addressing oxidative stress, warrants further investigation. A branched chain amino acid (BCAA) metabolite, 2-hydroxy-3-methylvalerate, was also associated with HFpEF. We previously found that branched chain amino acid transaminase 1 (BCAT1) was overexpressed and hypomethylated in patients with NAFLD who experienced clinical decompensation.⁴⁶ Both human and animal data have linked BCAA to insulin resistance, and restriction of BCAA in the diet of obese mice resulted in a shift toward fatty acid metabolism in cardiac myocytes.^{47,48}

Multiple intermediates in the tricarboxylic acid cycle, including citrate (decreased) and alpha-ketoglutarate (increased), were associated with HFpEF. Previously, increased serum levels of citrate were associated with 3-month mortality in patients with acute heart failure,

attributed to increased fatty acid beta-oxidation.⁴⁹ Animal models have linked expression levels of liver pyruvate kinase, which makes pyruvate available for the tricarboxylic acid cycle, to steatosis severity and fibrosis in NAFLD in a sex-specific manner.⁵⁰ In addition, deletion of a cellular citrate transporter, SLC13A5, in mice fed a high-fat diet was found to prevent development of obesity and hepatic steatosis.⁵¹ Carbohydrate energy extraction may have far-reaching implications for metabolic syndrome, and derangements in this process could be 1 link between NAFLD and HFpEF.

Bile acid metabolism did not feature prominently in significant metabolites but was present. Taurocholate sulfate was decreased in subjects with “HFpEF-no fatigue.” Bile acids are thought to mediate the association between the gut microbiome and metabolic disease, and they may play a role in both NAFLD and HFpEF. Bile acid levels, and specifically the ratio of primary to secondary bile acids, have been associated with chronic heart failure.⁵² Bile acid metabolism has been associated with severity of NAFLD, and bile acids have been used as therapeutics in NAFLD.^{53,54} In addition, postprandial taurine-containing bile acid levels were increased in participants with NAFLD compared with healthy controls.⁵⁵

Given the increasing awareness of the clinical and physiologic links between NAFLD and HFpEF, our analysis is well positioned to provide new insights on relevant altered metabolites between these 2 populations that have not yet been studied (patients with biopsy-proven NAFLD and HFpEF by TTE and clinical parameters). Strengthening our results is the fact that identified metabolites overlap with those found in previous analyses of NAFLD and HFpEF independently. For example, a prospective cohort study of 156 participants with biopsy-proven NAFLD identified 32 metabolites significantly associated with advanced fibrosis.³³ That analysis highlighted taurine and taurocholate, suggesting that taurine-containing primary bile acids may be associated not only with progression of liver disease but also of HFpEF, as we found. In the previously mentioned metabolomic analysis of HFpEF, multiple phosphatidylcholines were significantly associated with HFpEF.³⁴

The limitations of this study include the small sample size, single center design, and our racially homogeneous population, a common limitation for NAFLD studies. Our ascertainment of HFpEF using retrospective chart review, particularly for clinical factors, leaves open the possibility that events or TTEs were not captured in our system or were missed due to incomplete documentation. About half of patients with serum metabolite data and clinical data available did not have TTE. Our comparison of participants with and without TTE found that participants who had TTE differed by sex, hemoglobin A1c, presence of hypertension, and BMI. Other unmeasured factors could differ between these groups. As serum metabolites were evaluated a single time at the

index liver biopsy, serial measurements to indicate metabolite trends were not available, and metabolites are thought to fluctuate based on numerous factors. If heart failure developed after liver biopsy, then metabolite measurement and onset of symptoms or TTE findings would be separated in time, further limiting assessment of this relationship. Limitations in the metabolite assay itself include the possible presence of unmeasured or unnamed metabolites that could be of mechanistic or prognostic significance. Despite these limitations, these findings can provide the first step in characterizing the underlying unique and common physiology in NAFLD and HFpEF. This will be essential for establishing effective diagnostics and therapeutics given the rising prevalence and common underlying factors in both.

In summary, we conducted the first evaluation of serum metabolites associated with the presence of HFpEF by TTE and clinical criteria in a cohort of patients with biopsy-proven NAFLD. Our findings point to the importance of lipid, amino acid, and carbohydrate metabolism in these patients. These pathways warrant further investigation to understand both the unique and overlapping features between these related disease processes, which could lend to improved development of biomarkers and treatments.

ARTICLE INFORMATION

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Disclosures

Dr Guy reports consulting for CymaBay Therapeutics and NGM Biopharmaceuticals. The remaining authors have no disclosures to report.

Supplemental Material

Data S1
Tables S1–S5
Figures S1–S5

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SUPPLEMENTAL MATERIAL

DATA S1: SUPPLEMENTAL METHODS

Quality Assurance and Control

Several types of controls were analyzed in concert with the experimental samples. Specifically, a pooled matrix sample generated by taking a small volume of each experimental sample served as a technical replicate throughout the data set. Extracted water samples served as process blanks and a cocktail of quality control (QC) standards chosen not to interfere with the measurement of endogenous compounds were spiked into every analyzed sample to allow for instrument performance monitoring and aided chromatographic alignment. Instrument variability was determined by calculating the median relative standard deviation (RSD) for the standards that were added to each sample prior to injection into the mass spectrometers. Process variability was determined by calculating the median RSD for all endogenous metabolites (*i.e.*, non-instrument standards) present in 100% of the pooled matrix samples. Experimental samples were randomized across the platform run with QC samples spaced evenly among the injections.

Table S1: TTE vs no TTE

	No TTE (N=98)	TTE (N=89)	p-value
Age (mean, SD)	50.0 (11.4)	50.4 (9.4)	0.77
Female (n, %)	61 (62.2)	38 (42.7)	0.01
Race (n, %)			0.56
White	84 (85.7)	82 (92.1)	
Black	8 (8.2)	4 (4.5)	
BMI (mean, SD)	34.2 (7.3)	36.4 (7.0)	0.04
Diabetes mellitus (%)	35 (35.7)	32 (36.0)	1
Hemoglobin A1c (mean, SD)	6.1 (0.9)	6.6 (1.6)	0.03
Hypertension	54 (55.1)	67 (75.3)	0.006
Total cholesterol (mean, SD)	201.0 (56.2)	184.2 (44.9)	0.04
LDL (mean, SD)	120.0 (34.6)	111.3 (39.0)	0.15
HDL (mean, SD)	42.47 (14.6)	37.84 (13.7)	0.04
Hyperlipidemia	36 (36.7)	37 (41.6)	0.60
Hypertriglyceridemia	18 (18.4)	12 (13.5)	0.48
AST (mean, SD)	70.5 (53.9)	64.5 (42.9)	0.41
ALT (mean, SD)	93.9 (73.2)	80.3 (50.3)	0.15
Fibrosis stage (n, %)			0.07
Stage 0	9 (9.2)	3 (3.4)	
Stage 1	20 (20.4)	16 (18.0)	
Stage 2	51 (52.0)	39 (43.8)	
Stage 3	14 (14.3)	27 (30.3)	
Stage 4	4 (4.1)	4 (4.5)	
NASH Activity Score			0.72
1	2 (2.2)	1 (1.2)	
2	11 (12.1)	6 (7.1)	
3	14 (15.4)	12 (14.1)	
4	19 (20.9)	27 (31.8)	
5	23 (25.3)	20 (23.5)	
6	13 (14.3)	12 (14.1)	
7	9 (9.9)	7 (8.2)	

TTE = transthoracic echocardiogram; SD = standard deviation; LDL = low-density lipoprotein; HDL = high-density lipoprotein; AST = aspartate aminotransferase; ALT = alanine aminotransferase; NASH = non-alcoholic steatohepatitis

Table S2: Missing metabolite values by HFpEF definition*

	HFpEF		HFpEF No Fatigue		Diastolic dysfunction	
	No	Yes	No	Yes	No	Yes
Missing values (%, IQR)	2.4% (1.8-3.2)	2.6% (1.8-3.0)	2.4% (1.8-3.2)	2.6% (1.8-2.7)	2.4% (1.8-3.3)	2.4% (1.8-3.0)

*For entire cohort of 89 patients: 2.4% (IQR: 1.8-3.0)

HFpEF = heart failure with preserved ejection fraction; IQR = interquartile range

Table S3: HFpEF full results*

Metabolite	Pathway	Sub-Pathway	log Fold change	Unadjusted p-value	Adjusted p-value
1-arachidonoyl-GPE* (20:4)*	Lipid	Lysolipid	0.28	0.0001	0.06
1-docosahexaenoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.37	0.0003	0.10
2-stearoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.33	0.001	0.16
1-stearoyl-GPE (18:0)	Lipid	Lysolipid	0.26	0.002	0.19
2-arachidonoyl-GPE* (20:4)*	Lipid	Lysolipid	0.58	0.002	0.19
1-arachidonoyl-GPC* (20:4)*	Lipid	Lysolipid	0.27	0.002	0.19
azelate (nonanedioate; C9)	Lipid	Fatty Acid, Dicarboxylate	-0.31	0.003	0.19
2-arachidonoyl-GPC* (20:4)*	Lipid	Lysolipid	0.32	0.003	0.19
alpha-ketoglutarate	Energy	TCA Cycle	0.32	0.003	0.19
1-palmitoyl-GPC (16:0)	Lipid	Lysolipid	0.23	0.003	0.19
TL18:3n6 (g-linolenic acid)	Lipid	Mole % Total Fatty Acid	0.24	0.004	0.19
1-myristoyl-GPC (14:0)	Lipid	Lysolipid	0.40	0.004	0.19
1-oleoyl-GPE (18:1)	Lipid	Lysolipid	0.24	0.004	0.19
2-oleoyl-GPE* (18:1)*	Lipid	Lysolipid	0.85	0.004	0.19
2-palmitoleoyl-GPC* (16:1)*	Lipid	Lysolipid	0.53	0.005	0.19
1-palmitoyl-GPE (16:0)	Lipid	Lysolipid	0.24	0.005	0.19
palmitoyl-arachidonoylglycerophosphocholine (2)*	Lipid	Lysolipid	0.17	0.005	0.19
2-hydroxy-3-methylvalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.27	0.006	0.19
2-myristoyl-GPC* (14:0)*	Lipid	Lysolipid	0.55	0.006	0.19
1-oleoyl-GPC (18:1)	Lipid	Lysolipid	0.28	0.006	0.19
1-arachidonoylglycerol	Lipid	Monoacylglycerol	0.24	0.006	0.20
1-linolenoylglycerophosphocholine (18:3n3)*	Lipid	Lysolipid	0.34	0.007	0.20
citrate	Energy	TCA Cycle	-0.18	0.008	0.21
cysteine s-sulfate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.20	0.008	0.21
2-docosahexaenoyl-GPC* (22:6)*	Lipid	Lysolipid	0.40	0.008	0.21
caproate (6:0)	Lipid	Medium Chain Fatty Acid	-0.16	0.009	0.22
2-palmitoyl-GPC* (16:0)*	Lipid	Lysolipid	0.25	0.009	0.22
1-eicosapentaenoylglycerophosphocholine (20:5n3)*	Lipid	Lysolipid	0.47	0.009	0.22
1-stearoyl-GPC (18:0)	Lipid	Lysolipid	0.29	0.01	0.23

glucose	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.14	0.01	0.25
2-palmitoyl-GPE* (16:0)*	Lipid	Lysolipid	0.28	0.01	0.25
1-palmitoleoyl-GPC* (16:1)*	Lipid	Lysolipid	0.32	0.01	0.25
N6-acetyllysine	Amino Acid	Lysine Metabolism	0.12	0.01	0.27
1-pentadecanoylglycerophosphocholine (15:0)*	Lipid	Lysolipid	0.25	0.01	0.27
methyl glucopyranoside (alpha + beta)	Xenobiotics	Food Component/Plant	-0.72	0.02	0.29
1-docosahexaenoyl-GPC* (22:6)*	Lipid	Lysolipid	0.28	0.02	0.29
2-eicosatrienoyl-GPC* (20:3)*	Lipid	Lysolipid	0.21	0.02	0.32
1-docosahexaenoylglycerol	Lipid	Monoacylglycerol	0.32	0.02	0.32
1-eicosatrienoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.55	0.02	0.35
1-eicosatrienoyl-GPC* (20:3)*	Lipid	Lysolipid	0.23	0.02	0.35
1-docosapentaenoyl-GPC* (22:5n3)*	Lipid	Lysolipid	0.26	0.02	0.35
ribitol	Carbohydrate	Pentose Metabolism	0.14	0.02	0.38
propionylglycine (C3)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	0.26	0.03	0.40
phenylpyruvate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.17	0.03	0.40
1-linolenoylglycerol	Lipid	Monoacylglycerol	0.25	0.03	0.41
N2-methylguanosine	Nucleotide	Purine Metabolism, Guanine containing	0.22	0.03	0.44
2-stearoyl-GPC* (18:0)*	Lipid	Lysolipid	0.29	0.03	0.44
1-palmitoylplasmylethanolamine*	Lipid	Lysolipid	0.17	0.03	0.44
eugenol sulfate	Xenobiotics	Food Component/Plant	0.87	0.03	0.45
N-acetyltryptophan	Amino Acid	Tryptophan Metabolism	0.23	0.04	0.46
2-docosahexaenoylglycerol*	Lipid	Monoacylglycerol	0.69	0.04	0.48
2-hydroxyisobutyrate	Xenobiotics	Chemical	0.20	0.04	0.49
adrenate (22:4n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.18	0.04	0.51
benzoate	Xenobiotics	Benzoate Metabolism	-0.14	0.04	0.53
S-methylcysteine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.20	0.04	0.53
3-methoxytyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.13	0.05	0.53
mannose	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.14	0.05	0.55
methionine sulfone	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.29	0.05	0.57
3b-hydroxy-5-cholenoic acid	Lipid	Secondary Bile Acid Metabolism	-0.48	0.06	0.61

1-stearoylplasménylethanolamine*	Lipid	Lysolipid	0.22	0.06	0.61
3-methyl-2-oxobutyrate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.11	0.06	0.61
N6-succinyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.14	0.06	0.61
2-linoleoyl-GPC* (18:2)*	Lipid	Lysolipid	0.19	0.06	0.61
2-arachidonoyl glycerol	Lipid	Monoacylglycerol	0.20	0.06	0.61
1-oleoylplasménylethanolamine*	Lipid	Lysolipid	0.19	0.06	0.61
beta-hydroxyisovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.18	0.06	0.61
malonate (propanedioate)	Lipid	Fatty Acid Synthesis	-0.29	0.06	0.61
7-alpha-hydroxycholesterol	Lipid	Sterol	0.33	0.06	0.61
fucose	Carbohydrate	Pentose Metabolism	0.19	0.07	0.61
2-oleoyl-GPC* (18:1)*	Lipid	Lysolipid	0.17	0.07	0.61
phenylalanylleucine	Peptide	Dipeptide	0.55	0.07	0.61
stearoyl-arachidonoyl-glycerophosphoethanolamine (1)*	Lipid	Lysolipid	0.20	0.07	0.61
cytidine	Nucleotide	Pyrimidine Metabolism, Cytidine containing	0.16	0.07	0.61
docosahexaenoate (DHA; 22:6n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.19	0.07	0.61
xylitol	Carbohydrate	Pentose Metabolism	0.28	0.07	0.61
pyruvate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.26	0.07	0.61
sulfate*	Xenobiotics	Chemical	0.07	0.07	0.61
1-methyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.09	0.07	0.61
TL20:3n9 (mead acid)	Lipid	Mole % Total Fatty Acid	0.24	0.08	0.61
alpha-hydroxyisovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.21	0.08	0.61
stearidonate (18:4n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.23	0.08	0.61
serylleucine	Peptide	Dipeptide	-0.67	0.08	0.61
3-methylglutaconate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.27	0.08	0.61
1-heptadecanoyl-GPC (17:0)	Lipid	Lysolipid	0.32	0.08	0.62
3-hydroxy-3-methylglutarate	Lipid	Mevalonate Metabolism	0.12	0.08	0.64
TL18:4n3 (stearidonic acid)	Lipid	Mole % Total Fatty Acid	0.34	0.09	0.64
1-eicosenoylglycerophosphocholine (20:1n9)*	Lipid	Lysolipid	0.25	0.09	0.64
indoleacetylglutamine	Amino Acid	Tryptophan Metabolism	0.55	0.09	0.65
3-methylglutaryl carnitine (2)	Amino Acid	Lysine Metabolism	0.27	0.09	0.65
2-ethylhexanoic acid	Xenobiotics	Chemical	-0.14	0.09	0.65

hexanoylglycine (C6)	Lipid	Fatty Acid Metabolism(Acyl Glycine)	0.53	0.09	0.65
orotate	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.28	0.09	0.65
1-linoleoyl-GPC (18:2)	Lipid	Lysolipid	0.14	0.09	0.65
betaine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.10	0.10	0.68
N-acetylputrescine	Amino Acid	Polyamine Metabolism	0.16	0.10	0.68
ethylmalonate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.18	0.10	0.68
2-palmitoylglycerol (16:0)	Lipid	Monoacylglycerol	0.26	0.10	0.68
stearylcarntine (C18)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.19	0.10	0.69
glutamine	Amino Acid	Glutamate Metabolism	-0.06	0.11	0.69
1-methylnicotinamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	-0.43	0.11	0.69
tetradecanedioate (C14)	Lipid	Fatty Acid, Dicarboxylate	-0.21	0.11	0.69
hexadecanedioate (C16)	Lipid	Fatty Acid, Dicarboxylate	-0.20	0.11	0.69
TL20:5n3 (eicosapentaenoic acid)	Lipid	Mole % Total Fatty Acid	0.24	0.11	0.69
eicosapentaenoate (EPA; 20:5n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.25	0.11	0.69
1-arachidoyl-GPC (20:0)	Lipid	Lysolipid	0.51	0.11	0.69
stearyl-arachidonoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.11	0.11	0.69
3-hydroxyoctanoate	Lipid	Fatty Acid, Monohydroxy	-0.18	0.11	0.70
dimethylarginine (ADMA + SDMA)	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.05	0.12	0.72
sphinganine	Lipid	Sphingolipid Metabolism	0.51	0.12	0.73
arachidonate (20:4n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.09	0.12	0.73
6-oxopiperidine-2-carboxylic acid	Xenobiotics	Drug	0.14	0.12	0.73
TL22:5n3 (docosapentaenoic acid)	Lipid	Mole % Total Fatty Acid	0.11	0.13	0.74
alpha-hydroxycaproate	Lipid	Fatty Acid, Monohydroxy	0.13	0.13	0.74
5,6-dihydrothymine	Nucleotide	Pyrimidine Metabolism, Thymine containing	-0.12	0.13	0.74
3-hydroxy-2-ethylpropionate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.12	0.13	0.74
stearate (18:0)	Lipid	Long Chain Fatty Acid	0.07	0.13	0.74
1-eicosadienoyl-GPC* (20:2)*	Lipid	Lysolipid	0.20	0.13	0.74
3-methyl catechol sulfate (1)	Xenobiotics	Benzoate Metabolism	0.47	0.13	0.74
glutamate	Amino Acid	Glutamate Metabolism	0.12	0.14	0.74
trimethylamine N-oxide	Lipid	Phospholipid Metabolism	0.67	0.14	0.75
dopamine sulfate (2)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.16	0.14	0.75
myristoylcarnitine	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.20	0.14	0.75
phenyllactate (PLA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.11	0.14	0.75

gamma-glutamylalanine	Peptide	Gamma-glutamyl Amino Acid	0.14	0.14	0.75
2-aminooctanoate	Lipid	Fatty Acid, Amino	0.19	0.14	0.75
N-acetylglycine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.18	0.14	0.75
TL20:1n9 (eicosanoic acid)	Lipid	Mole % Total Fatty Acid	-0.07	0.14	0.75
1,2,3-benzenetriol sulfate (2)	Xenobiotics	Chemical	-0.67	0.15	0.75
xanthosine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.16	0.15	0.75
TL16:1n7 (palmitoleic acid)	Lipid	Mole % Total Fatty Acid	0.14	0.16	0.75
4-hydroxyhippurate	Xenobiotics	Benzoate Metabolism	-0.28	0.16	0.75
2-linoleoyl-GPE* (18:2)*	Lipid	Lysolipid	0.17	0.16	0.75
9,10-DiHOME	Lipid	Fatty Acid, Dihydroxy	-0.30	0.16	0.75
palmitoylcarnitine (C16)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.15	0.16	0.75
TL18:2n6 (linoleic acid)	Lipid	Mole % Total Fatty Acid	-0.07	0.16	0.75
indolepropionate	Amino Acid	Tryptophan Metabolism	-0.28	0.16	0.75
3-ureidopropionate	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.14	0.16	0.75
1-stearoylglycerol (18:0)	Lipid	Monoacylglycerol	0.42	0.16	0.75
N-acetylleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.12	0.16	0.75
myristoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.07	0.16	0.75
alpha-ketobutyrate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.29	0.16	0.75
dodecanedioate (C12)	Lipid	Fatty Acid, Dicarboxylate	-0.18	0.17	0.76
cysteine-glutathione disulfide	Amino Acid	Glutathione Metabolism	-0.38	0.17	0.76
4-imidazoleacetate	Amino Acid	Histidine Metabolism	-0.36	0.17	0.76
TL14:0 (myristic acid)	Lipid	Mole % Total Fatty Acid	0.14	0.17	0.76
2-hydroxybutyrate (AHB)	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.14	0.17	0.76
gamma-glutamylisoleucine*	Peptide	Gamma-glutamyl Amino Acid	0.09	0.17	0.76
homocitrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.18	0.17	0.76
gamma-glutamyl-2-aminobutyrate	Peptide	Gamma-glutamyl Amino Acid	0.25	0.18	0.76
1,6-anhydroglucose	Xenobiotics	Food Component/Plant	-0.30	0.18	0.76
gamma-glutamylvaline	Peptide	Gamma-glutamyl Amino Acid	0.07	0.18	0.76
inosine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	-0.41	0.18	0.76
2-aminoheptanoate	Lipid	Fatty Acid, Amino	0.13	0.18	0.76
creatine	Amino Acid	Creatine Metabolism	0.15	0.18	0.76
3-(4-hydroxyphenyl)propionate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.51	0.18	0.76
docosapentaenoate (DPA; 22:5n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.14	0.18	0.76

5-oxoproline	Amino Acid	Glutathione Metabolism	-0.11	0.18	0.76
1-myristoylglycerol (14:0)	Lipid	Monoacylglycerol	0.20	0.18	0.76
2-methylmalonyl carnitine	Lipid	Fatty Acid Synthesis	-0.11	0.19	0.76
oxalate (ethanedioate)	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	-0.21	0.19	0.76
2-keto-3-deoxy-gluconate	Xenobiotics	Food Component/Plant	0.17	0.19	0.76
1,5-anhydroglucitol (1,5-AG)	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	-0.19	0.19	0.76
hydantoin-5-propionic acid	Amino Acid	Histidine Metabolism	0.30	0.19	0.76
homostachydrine*	Xenobiotics	Food Component/Plant	-0.17	0.19	0.76
butyrylcarnitine (C4)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	0.15	0.19	0.76
N-methylproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.33	0.20	0.77
orotidine	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.29	0.20	0.77
aspartylphenylalanine	Peptide	Dipeptide	0.29	0.20	0.77
sorbitol	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.21	0.20	0.77
taurocholate sulfate	Lipid	Secondary Bile Acid Metabolism	-0.22	0.20	0.77
thyroxine	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.35	0.20	0.77
arabinose	Carbohydrate	Pentose Metabolism	0.28	0.20	0.77
N-acetylmethionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.20	0.20	0.77
methyl indole-3-acetate	Xenobiotics	Food Component/Plant	0.19	0.21	0.77
methylsuccinate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.09	0.21	0.77
oleamide	Lipid	Fatty Acid, Amide	0.23	0.21	0.77
gamma-CEHC glucuronide*	Cofactors and Vitamins	Tocopherol Metabolism	0.39	0.21	0.77
2'-deoxyuridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.17	0.21	0.77
prolylhydroxyproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.16	0.21	0.77
pyridoxine (Vitamin B6)	Cofactors and Vitamins	Vitamin B6 Metabolism	-0.11	0.21	0.77
5-HETE	Lipid	Eicosanoid	0.22	0.21	0.78
5-methylthioadenosine (MTA)	Amino Acid	Polyamine Metabolism	0.38	0.22	0.78
7-dehydro-cholesterol	Lipid	Sterol	0.44	0.22	0.78
4-methyl-2-oxopentanoate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.08	0.22	0.78
stearoyl-arachidonoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.24	0.22	0.78
oleoylcarnitine (C18)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.15	0.22	0.78
1-linoleoylglycerol (18:2)	Lipid	Monoacylglycerol	0.13	0.22	0.78
gluconate	Xenobiotics	Food Component/Plant	0.10	0.22	0.78
pyroglutamine*	Amino Acid	Glutamate Metabolism	-0.18	0.23	0.78

N-oleoyltaurine	Lipid	Endocannabinoid	0.29	0.23	0.79
1-palmitoylglycerol (16:0)	Lipid	Monoacylglycerol	0.11	0.23	0.79
tyrosylglutamate	Peptide	Dipeptide	0.32	0.23	0.79
beta-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.26	0.23	0.79
alanine	Amino Acid	Alanine and Aspartate Metabolism	0.06	0.23	0.79
inositol 1-phosphate (I1P)	Lipid	Inositol Metabolism	0.13	0.24	0.79
TLTL (Total Total Lipid)	Lipid	Quantitative Total Fatty Acid	0.10	0.24	0.79
N6-methyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.12	0.24	0.79
N-acetyl-aspartyl-glutamate (NAAG)	Amino Acid	Glutamate Metabolism	-0.09	0.24	0.80
3-methoxycatechol sulfate (1)	Xenobiotics	Benzoate Metabolism	-0.43	0.24	0.80
leucylalanine	Peptide	Dipeptide	0.28	0.25	0.81
glutaryl carnitine (C5)	Amino Acid	Lysine Metabolism	0.08	0.25	0.81
indolebutyrate	Amino Acid	Tryptophan Metabolism	0.24	0.25	0.81
caprylate (8:0)	Lipid	Medium Chain Fatty Acid	-0.07	0.25	0.81
desmosterol	Lipid	Sterol	-0.20	0.25	0.81
4-hydroxyphenylpyruvate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.15	0.25	0.81
erythronate*	Carbohydrate	Aminosugar Metabolism	0.07	0.25	0.81
allo-isoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.08	0.26	0.81
gamma-glutamylleucine	Peptide	Gamma-glutamyl Amino Acid	0.06	0.26	0.81
tartronate (hydroxymalonate)	Xenobiotics	Bacterial/Fungal	-0.17	0.26	0.81
catechol sulfate	Xenobiotics	Benzoate Metabolism	-0.24	0.26	0.81
1,2-propanediol	Xenobiotics	Chemical	0.25	0.26	0.81
threonate	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	-0.18	0.26	0.81
gamma-glutamyllysine	Peptide	Gamma-glutamyl Amino Acid	0.09	0.26	0.81
arabonate	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	0.11	0.26	0.81
N-delta-acetylornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.16	0.27	0.81
3-methoxytyramine sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.13	0.27	0.81
histidyltryptophan	Peptide	Dipeptide	-0.23	0.27	0.81
TL14:1n5 (mystoleic acid)	Lipid	Mole % Total Fatty Acid	0.18	0.27	0.82
gamma-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.16	0.27	0.82
12-HETE	Lipid	Eicosanoid	-0.28	0.28	0.82
docosadienoate (22:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.09	0.28	0.82
cyclo(pro-pro)	Peptide	Dipeptide	0.13	0.28	0.82
4-acetamidobutanoate	Amino Acid	Polyamine Metabolism	0.08	0.28	0.82

1-dihomo-linolenylglycerol (alpha, gamma)	Lipid	Monoacylglycerol	0.11	0.28	0.82
glycolithocholate sulfate*	Lipid	Secondary Bile Acid Metabolism	-0.29	0.28	0.82
dopamine sulfate (1)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.18	0.28	0.82
5alpha-pregnan-3beta,20beta-diol monosulfate (1)	Lipid	Steroid	-0.25	0.29	0.82
glycylvaline	Peptide	Dipeptide	0.41	0.29	0.82
isobutyrylglycine (C4)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.12	0.29	0.82
10-nonadecenoate (19:1n9)	Lipid	Long Chain Fatty Acid	0.10	0.29	0.82
TL22:6n3 (docosahexaenoic acid)	Lipid	Mole % Total Fatty Acid	0.10	0.29	0.82
2-arachidonoylglycerophosphoinositol*	Lipid	Lysolipid	0.23	0.29	0.82
alpha-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.11	0.29	0.82
threonylphenylalanine	Peptide	Dipeptide	-0.42	0.29	0.82
3-hydroxydecanoate	Lipid	Fatty Acid, Monohydroxy	-0.10	0.29	0.82
glycerophosphoethanolamine	Lipid	Phospholipid Metabolism	0.16	0.30	0.82
isovalerate (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.09	0.30	0.82
TL24:1n9 (nervonic acid)	Lipid	Mole % Total Fatty Acid	-0.10	0.30	0.82
phenylalanylserine	Peptide	Dipeptide	-0.35	0.30	0.82
octadecanedioate (C18)	Lipid	Fatty Acid, Dicarboxylate	-0.13	0.30	0.82
10-undecenoate (11:1n1)	Lipid	Medium Chain Fatty Acid	-0.10	0.30	0.82
maleate (cis-Butenedioate)	Lipid	Fatty Acid, Dicarboxylate	0.15	0.31	0.82
4-methylcatechol sulfate	Xenobiotics	Benzoate Metabolism	-0.25	0.31	0.82
N-acetylcarnosine	Peptide	Dipeptide Derivative	-0.08	0.31	0.82
2-hydroxypalmitate	Lipid	Fatty Acid, Monohydroxy	-0.06	0.31	0.83
adenosine	Nucleotide	Purine Metabolism, Adenine containing	-0.18	0.31	0.83
paraxanthine	Xenobiotics	Xanthine Metabolism	-0.49	0.32	0.83
1-linoleoyl-GPE (18:2)*	Lipid	Lysolipid	0.09	0.32	0.83
biliverdin	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	-0.20	0.32	0.83
bilirubin (E,E)*	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	0.17	0.32	0.83
tryptophylglutamate	Peptide	Dipeptide	-0.39	0.32	0.83
3-hydroxybutyrate (BHBA)	Lipid	Ketone Bodies	-0.20	0.32	0.83
delta-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.23	0.32	0.84
hydroquinone sulfate	Xenobiotics	Drug	-0.28	0.32	0.84
oleoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.05	0.33	0.84
seryltyrosine	Peptide	Dipeptide	0.23	0.33	0.84
nonadecanoate (19:0)	Lipid	Long Chain Fatty Acid	0.06	0.33	0.84

methionine sulfoxide	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.08	0.33	0.84
17-methylstearate	Lipid	Fatty Acid, Branched	0.10	0.33	0.84
palmitate (16:0)	Lipid	Long Chain Fatty Acid	0.05	0.34	0.85
o-cresol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.54	0.34	0.85
docosapentaenoate (n6 DPA; 22:5n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.07	0.34	0.85
mannitol	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.29	0.35	0.86
N-acetylisoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.14	0.35	0.86
N-acetylneuraminate	Carbohydrate	Aminosugar Metabolism	0.10	0.35	0.86
1-arachidonoylglycerophosphate	Lipid	Lysolipid	0.11	0.35	0.86
TL20:4n6 (arachidonic acid)	Lipid	Mole % Total Fatty Acid	0.06	0.35	0.86
3-(3-hydroxyphenyl)propionate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.37	0.36	0.87
dimethyl sulfone	Xenobiotics	Chemical	0.30	0.36	0.87
12,13-DiHOME	Lipid	Fatty Acid, Dihydroxy	-0.13	0.36	0.88
lysine	Amino Acid	Lysine Metabolism	0.04	0.36	0.88
hypotaurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.19	0.36	0.88
3-hydroxyisobutyrate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.08	0.37	0.88
16a-hydroxy DHEA 3-sulfate	Lipid	Steroid	-0.17	0.37	0.88
3-methyl-2-oxovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.05	0.37	0.88
cyclohexanebutanoic acid	Xenobiotics	Chemical	-0.10	0.37	0.88
glucuronate	Carbohydrate	Aminosugar Metabolism	0.09	0.37	0.88
methyl-4-hydroxybenzoate sulfate	Xenobiotics	Benzoate Metabolism	-0.37	0.37	0.88
16-hydroxypalmitate	Lipid	Fatty Acid, Monohydroxy	-0.06	0.37	0.88
5alpha-androstan-3beta,17beta-diol disulfate	Lipid	Steroid	-0.23	0.37	0.88
1-methylhistidine	Amino Acid	Histidine Metabolism	0.09	0.38	0.88
indolelactate	Amino Acid	Tryptophan Metabolism	0.06	0.38	0.88
betonicine	Xenobiotics	Food Component/Plant	-0.45	0.38	0.88
glycocholate	Lipid	Primary Bile Acid Metabolism	0.24	0.38	0.88
7-HOCA	Lipid	Sterol	0.09	0.39	0.89
gamma-glutamylphenylalanine	Peptide	Gamma-glutamyl Amino Acid	0.05	0.39	0.89
lactate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.05	0.39	0.89
arachidate (20:0)	Lipid	Long Chain Fatty Acid	0.05	0.39	0.89
TL22:1n9 (erucic acid)	Lipid	Mole % Total Fatty Acid	-0.18	0.39	0.89
eicosenoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.07	0.39	0.89
succinate	Energy	TCA Cycle	-0.04	0.40	0.89

N-acetyl-3-methylhistidine*	Amino Acid	Histidine Metabolism	0.24	0.40	0.89
serine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.05	0.40	0.89
cyclo(gly-pro)	Peptide	Dipeptide	0.13	0.40	0.89
2-piperidinone	Xenobiotics	Food Component/Plant	0.23	0.41	0.89
1,3,7-trimethylurate	Xenobiotics	Xanthine Metabolism	-0.28	0.41	0.89
prolylglycine	Peptide	Dipeptide	-0.15	0.41	0.89
TL18:1n9 (oleic acid)	Lipid	Mole % Total Fatty Acid	0.03	0.41	0.89
methylpalmitate (15 or 2)	Lipid	Fatty Acid, Branched	0.07	0.41	0.89
linoleoylcarnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.11	0.41	0.89
glycylphenylalanine	Peptide	Dipeptide	-0.22	0.41	0.89
valylarginine	Peptide	Dipeptide	0.21	0.41	0.89
TL18:3n3 (a-linolenic acid)	Lipid	Mole % Total Fatty Acid	0.06	0.41	0.89
pregnenolone sulfate	Lipid	Steroid	0.17	0.42	0.89
palmitoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.06	0.42	0.89
theobromine	Xenobiotics	Xanthine Metabolism	-0.25	0.42	0.89
saccharin	Xenobiotics	Food Component/Plant	0.48	0.42	0.89
3beta,7alpha-dihydroxy-5-cholestenoate	Lipid	Secondary Bile Acid Metabolism	0.25	0.42	0.89
N-formylmethionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.04	0.43	0.89
homovanillate (HVA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.09	0.43	0.89
I-urobilinogen	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	0.35	0.43	0.89
ribose	Carbohydrate	Pentose Metabolism	-0.13	0.43	0.89
gamma-CEHC	Cofactors and Vitamins	Tocopherol Metabolism	0.11	0.43	0.89
dihomolinoleate (20:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.07	0.43	0.89
N-acetylglutamine	Amino Acid	Glutamate Metabolism	-0.09	0.43	0.89
3-hydroxyhippurate	Xenobiotics	Benzoate Metabolism	-0.27	0.43	0.89
7-methylurate	Xenobiotics	Xanthine Metabolism	-0.36	0.44	0.89
palmitoyl-linoleoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	-0.05	0.44	0.89
glycerol 3-phosphate (G3P)	Lipid	Glycerolipid Metabolism	0.18	0.44	0.89
N-acetylaspartate (NAA)	Amino Acid	Alanine and Aspartate Metabolism	-0.05	0.44	0.89
kynurenate	Amino Acid	Tryptophan Metabolism	-0.08	0.44	0.89
octanoylcarnitine (C8)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.07	0.44	0.89
asparagine	Amino Acid	Alanine and Aspartate Metabolism	-0.03	0.44	0.89
cis-Cyclo[L-ala-L-Pro]	Peptide	Dipeptide	0.07	0.44	0.89

3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	Lipid	Fatty Acid, Dicarboxylate	0.28	0.45	0.89
tauroolithocholate 3-sulfate	Lipid	Secondary Bile Acid Metabolism	-0.26	0.45	0.89
trigonelline (N'-methylnicotinate)	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	-0.18	0.45	0.89
pantothenate (Vitamin B5)	Cofactors and Vitamins	Pantothenate and CoA Metabolism	0.09	0.45	0.89
acisoga	Amino Acid	Polyamine Metabolism	0.07	0.45	0.89
glycine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.06	0.45	0.89
malate	Energy	TCA Cycle	-0.06	0.45	0.89
1-palmitoleoyl-GPI* (16:1)*	Lipid	Lysolipid	0.33	0.45	0.89
pseudouridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.04	0.46	0.90
erythritol	Xenobiotics	Food Component/Plant	0.09	0.47	0.90
4-androsten-3beta,17beta-diol monosulfate (1)	Lipid	Steroid	0.15	0.47	0.90
cis-4-decenoyl carnitine	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.07	0.47	0.90
TL18:0 (stearic acid)	Lipid	Mole % Total Fatty Acid	-0.03	0.47	0.90
urea	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.06	0.47	0.90
eicosenoate (20:1n9 or 1n11)	Lipid	Long Chain Fatty Acid	0.07	0.47	0.90
gamma-glutamylmethionine	Peptide	Gamma-glutamyl Amino Acid	0.07	0.47	0.90
androsterone sulfate	Lipid	Steroid	-0.18	0.47	0.90
1-palmitoylglycerophosphate	Lipid	Lysolipid	0.11	0.48	0.90
TL22:4n6 (adrenic acid)	Lipid	Mole % Total Fatty Acid	0.06	0.48	0.90
1,3-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.30	0.48	0.90
dihydroorotate	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.17	0.48	0.90
palmitoyl-linoleoyl-glycerophosphoinositol (1)*	Lipid	Lysolipid	0.14	0.48	0.90
cyclo(L-phe-L-pro)	Peptide	Dipeptide	-0.15	0.48	0.90
maltose	Carbohydrate	Glycogen Metabolism	0.18	0.48	0.90
caffeine	Xenobiotics	Xanthine Metabolism	-0.32	0.48	0.90
ornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.06	0.49	0.90
TL22:5n6 (osbond acid)	Lipid	Mole % Total Fatty Acid	0.07	0.49	0.90
salicyluric glucuronide*	Xenobiotics	Drug	0.37	0.49	0.90
margarate (17:0)	Lipid	Long Chain Fatty Acid	0.06	0.49	0.90
2-hydroxyoctanoate	Lipid	Fatty Acid, Monohydroxy	0.08	0.49	0.90
alpha-glutamyltyrosine	Peptide	Dipeptide	-0.23	0.49	0.90
lanosterol	Lipid	Sterol	-0.18	0.49	0.90
5alpha-pregnan-3beta,20alpha-diol disulfate	Lipid	Steroid	0.14	0.49	0.90
1-linoleoyl-GPI* (18:2)*	Lipid	Lysolipid	0.07	0.49	0.90

leucylglycine	Peptide	Dipeptide	-0.24	0.49	0.90
3-(4-hydroxyphenyl)lactate (HPLA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.04	0.50	0.90
isoleucylglycine	Peptide	Dipeptide	-0.15	0.50	0.90
10-heptadecenoate (17:1n7)	Lipid	Long Chain Fatty Acid	0.07	0.50	0.90
serylalanine	Peptide	Dipeptide	0.11	0.50	0.90
xanthine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.07	0.50	0.90
arabitol	Carbohydrate	Pentose Metabolism	0.05	0.50	0.90
5alpha-androstan-3beta,17alpha-diol disulfate	Lipid	Steroid	-0.20	0.50	0.90
2-linolenoylglycerophosphocholine (18:3n3)*	Lipid	Lysolipid	-0.21	0.51	0.90
palmitoyl-oleoyl-glycerophosphoglycerol (2)*	Lipid	Lysolipid	0.22	0.51	0.90
3beta,7beta-dihydroxy-5-cholestenoate	Lipid	Sterol	-0.06	0.51	0.90
TL20:2n6 (eicosadienoic acid)	Lipid	Mole % Total Fatty Acid	0.05	0.51	0.90
1-oleoyl-GPI (18:1)*	Lipid	Lysolipid	0.08	0.51	0.90
3-methylhistidine	Amino Acid	Histidine Metabolism	0.16	0.51	0.91
threitol	Carbohydrate	Pentose Metabolism	-0.08	0.52	0.91
1-arachidonoyl-GPI* (20:4)*	Lipid	Lysolipid	0.05	0.52	0.91
taurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.06	0.52	0.91
theophylline	Xenobiotics	Xanthine Metabolism	-0.26	0.52	0.91
methionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.03	0.52	0.91
N-palmitoyl glycine	Lipid	Fatty Acid Metabolism(Acyl Glycine)	-0.08	0.52	0.91
5-methyluridine (ribothymidine)	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.04	0.52	0.91
gamma-glutamylglutamate	Peptide	Gamma-glutamyl Amino Acid	0.10	0.53	0.91
O-methylcatechol sulfate	Xenobiotics	Benzoate Metabolism	-0.13	0.53	0.91
2-hydroxystearate	Lipid	Fatty Acid, Monohydroxy	-0.03	0.54	0.91
palmitoyl-palmitoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.07	0.54	0.91
ergothioneine	Xenobiotics	Food Component/Plant	0.12	0.54	0.91
3-indoxyl sulfate	Amino Acid	Tryptophan Metabolism	0.10	0.54	0.91
uridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.03	0.54	0.91
linolenate (18:3n3 or 3n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.06	0.54	0.91
TL20:0 (arachidic acid)	Lipid	Mole % Total Fatty Acid	-0.04	0.54	0.91
pyroglutamylglutamine	Peptide	Dipeptide	0.10	0.54	0.91
4-androsten-3beta,17beta-diol disulfate (2)	Lipid	Steroid	-0.09	0.54	0.91

1,7-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.24	0.54	0.91
vanillylmandelate (VMA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.07	0.55	0.92
beta-alanine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.06	0.55	0.92
hydroxybutyrylcarnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.11	0.55	0.92
myristate (14:0)	Lipid	Long Chain Fatty Acid	0.05	0.56	0.92
stearoyl-arachidonoyl-glycerophosphoinositol (1)*	Lipid	Lysolipid	0.04	0.56	0.93
fructose	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.05	0.57	0.93
N-acetylserine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.03	0.57	0.93
1-methylimidazoleacetate	Amino Acid	Histidine Metabolism	0.10	0.57	0.93
2-aminoadipate	Amino Acid	Lysine Metabolism	0.05	0.57	0.93
imidazole lactate	Amino Acid	Histidine Metabolism	0.05	0.57	0.93
phenylacetate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.09	0.57	0.93
glycylproline	Peptide	Dipeptide	0.14	0.57	0.93
phenylcarnitine*	Xenobiotics	Chemical	-0.18	0.57	0.93
pyroglutamylvaline	Peptide	Dipeptide	-0.05	0.58	0.93
oleic ethanolamide	Lipid	Endocannabinoid	-0.05	0.58	0.93
tryptophan betaine	Amino Acid	Tryptophan Metabolism	-0.15	0.58	0.93
glycylglycine	Peptide	Dipeptide	-0.24	0.58	0.93
N-methylpipercolate	Xenobiotics	Chemical	-0.10	0.58	0.93
2-oleoylglycerol (18:1)	Lipid	Monoacylglycerol	0.06	0.58	0.93
4-hydroxychlorothalonil	Xenobiotics	Chemical	0.08	0.58	0.93
2-aminobutyrate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.05	0.59	0.93
HWESASXX*	Peptide	Polypeptide	-0.12	0.59	0.93
TL20:3n6 (di-homo-g-linoleic acid)	Lipid	Mole % Total Fatty Acid	-0.03	0.59	0.93
glycochenodeoxycholate	Lipid	Primary Bile Acid Metabolism	0.13	0.59	0.93
fumarate	Energy	TCA Cycle	-0.05	0.59	0.93
cyclo(leu-pro)	Peptide	Dipeptide	-0.10	0.59	0.93
cholestanol	Lipid	Sterol	-0.05	0.60	0.94
5alpha-androstan-3alpha,17beta-diol disulfate	Lipid	Steroid	-0.18	0.60	0.94
choline	Lipid	Phospholipid Metabolism	0.03	0.60	0.94
phenylacetylglutamine	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.09	0.60	0.94
4-androsten-3beta,17beta-diol monosulfate (2)	Lipid	Steroid	-0.13	0.60	0.94
1-oleoylglycerol (18:1)	Lipid	Monoacylglycerol	0.06	0.61	0.94
4-guanidinobutanoate	Amino Acid	Guanidino and Acetamido Metabolism	-0.16	0.61	0.94

5alpha-pregnan-3beta,20alpha-diol monosulfate (2)	Lipid	Steroid	0.19	0.61	0.94
erucate (22:1n9)	Lipid	Long Chain Fatty Acid	0.05	0.61	0.94
N-acetyltaurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.06	0.61	0.94
sphingomyelin	Lipid	Sphingolipid Metabolism	0.04	0.61	0.94
3-methoxycatechol sulfate (2)	Xenobiotics	Benzoate Metabolism	-0.14	0.62	0.94
2,3-dihydroxyisovalerate	Xenobiotics	Food Component/Plant	0.17	0.62	0.94
glycocholenate sulfate*	Lipid	Secondary Bile Acid Metabolism	-0.05	0.62	0.94
3-[3-(sulfooxy)phenyl]propanoic acid	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.23	0.62	0.94
5,6-dihydrouracil	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.04	0.62	0.94
allantoin	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	-0.08	0.62	0.94
oleoyl sphingomyelin	Lipid	Sphingolipid Metabolism	0.03	0.62	0.94
cysteine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.05	0.62	0.94
tyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.03	0.62	0.94
2-pyrrolidinone	Xenobiotics	Chemical	0.09	0.63	0.94
isobutyrylcarnitine (C4)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.06	0.63	0.94
4-androsten-3beta,17beta-diol disulfate (1)	Lipid	Steroid	0.10	0.63	0.94
pyridoxal	Cofactors and Vitamins	Vitamin B6 Metabolism	-0.17	0.63	0.94
TLdm18:1n7 (plasmalogen vaccenic acid)	Lipid	Mole % Total Fatty Acid	0.10	0.64	0.94
N2,N5-diacetylornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.10	0.64	0.94
1-methylguanosine	Nucleotide	Purine Metabolism, Guanine containing	-0.02	0.64	0.94
threonine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.03	0.64	0.94
isovalerylglycine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.06	0.65	0.95
N-acetylalanine	Amino Acid	Alanine and Aspartate Metabolism	0.02	0.65	0.95
aspartylleucine	Peptide	Dipeptide	-0.07	0.65	0.95
aspartate	Amino Acid	Alanine and Aspartate Metabolism	0.05	0.65	0.95
decanoylcarnitine (C10)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.04	0.65	0.95
gamma-glutamylglutamine	Peptide	Gamma-glutamyl Amino Acid	-0.04	0.65	0.95
valerylcarnitine (C5)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.17	0.66	0.95
ADSGEGDFXAEGGGVR*	Peptide	Fibrinogen Cleavage Peptide	0.04	0.66	0.95
cinnamoylglycine	Xenobiotics	Food Component/Plant	0.22	0.66	0.95
myristoleoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	-0.05	0.66	0.95

1-methylurate	Xenobiotics	Xanthine Metabolism	-0.11	0.67	0.95
andro steroid monosulfate (1)*	Lipid	Steroid	-0.12	0.67	0.95
phenol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.12	0.67	0.95
palmitoleate (16:1n7)	Lipid	Long Chain Fatty Acid	0.05	0.67	0.95
N-acetylhistidine	Amino Acid	Histidine Metabolism	-0.09	0.67	0.95
N-acetylcitrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.11	0.67	0.95
pregnen-diol disulfate*	Lipid	Steroid	0.07	0.67	0.95
3-hydroxylaurate	Lipid	Fatty Acid, Monohydroxy	-0.04	0.67	0.95
indoleacetate	Amino Acid	Tryptophan Metabolism	0.05	0.68	0.95
5alpha-pregnan-3(alpha or beta),20beta-diol disulfate	Lipid	Steroid	-0.21	0.68	0.95
pelargonate (9:0)	Lipid	Medium Chain Fatty Acid	-0.02	0.68	0.95
deoxycarnitine	Lipid	Carnitine Metabolism	-0.02	0.68	0.95
glucarate 1,4-lactone	Carbohydrate	Disaccharides and Oligosaccharides	-0.29	0.68	0.95
guanosine	Nucleotide	Purine Metabolism, Guanine containing	-0.14	0.68	0.95
proline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.02	0.68	0.95
1-palmitoyl-GPI* (16:0)*	Lipid	Lysolipid	0.06	0.68	0.95
glycerophosphorylcholine (GPC)	Lipid	Phospholipid Metabolism	0.03	0.69	0.95
taurocholate	Lipid	Primary Bile Acid Metabolism	0.15	0.69	0.95
2-hydroxyhippurate (salicylurate)	Xenobiotics	Benzoate Metabolism	0.16	0.69	0.95
TL22:0 (behenic acid)	Lipid	Mole % Total Fatty Acid	-0.04	0.69	0.96
hydroxyproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.05	0.70	0.96
3-hydroxypyridine sulfate	Xenobiotics	Chemical	0.11	0.70	0.96
4-ethylphenyl sulfate	Xenobiotics	Benzoate Metabolism	0.09	0.70	0.96
myristoleoylcarnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.06	0.70	0.96
isovalerylcarnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.04	0.71	0.96
citrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.03	0.71	0.96
glycerol	Lipid	Glycerolipid Metabolism	0.03	0.71	0.96
lathosterol	Lipid	Sterol	0.06	0.71	0.96
beta-hydroxyisovaleroylcarnitine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.03	0.71	0.96
TL24:0 (lignoceric acid)	Lipid	Mole % Total Fatty Acid	0.05	0.71	0.96
campesterol	Lipid	Sterol	0.05	0.72	0.96
ursodeoxycholate	Lipid	Secondary Bile Acid Metabolism	0.14	0.72	0.96
gamma-glutamyltryptophan	Peptide	Gamma-glutamyl Amino Acid	0.03	0.72	0.96
TLdm18:1n9 (plasmalogen oleic acid)	Lipid	Mole % Total Fatty Acid	0.04	0.72	0.96

2-hydroxydecanoate	Lipid	Fatty Acid, Monohydroxy	0.04	0.72	0.96
N2-acetyllysine	Amino Acid	Lysine Metabolism	-0.06	0.72	0.96
acetoacetate	Lipid	Ketone Bodies	-0.05	0.73	0.96
kynurenine	Amino Acid	Tryptophan Metabolism	0.02	0.73	0.96
myo-inositol	Lipid	Inositol Metabolism	0.02	0.73	0.96
guanidinoacetate	Amino Acid	Creatine Metabolism	0.03	0.73	0.96
linoleate (18:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.02	0.73	0.96
glycolate (hydroxyacetate)	Xenobiotics	Chemical	-0.02	0.73	0.96
dihomolinolenate (20:3n3 or 3n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.02	0.73	0.96
pipecolate	Amino Acid	Lysine Metabolism	-0.05	0.73	0.96
valine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.01	0.74	0.96
ectoine	Xenobiotics	Chemical	0.09	0.74	0.96
hypoxanthine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	-0.06	0.74	0.96
squalene	Lipid	Sterol	0.10	0.74	0.96
C-glycosyltryptophan	Amino Acid	Tryptophan Metabolism	0.02	0.74	0.96
TL16:0 (palmitic acid)	Lipid	Mole % Total Fatty Acid	0.01	0.74	0.96
quinolate	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	0.05	0.74	0.96
3,7-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.11	0.74	0.96
alpha-hydroxyisocaproate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.03	0.74	0.96
coprostanol	Lipid	Sterol	0.10	0.75	0.96
glycoursodeoxycholate	Lipid	Secondary Bile Acid Metabolism	0.11	0.75	0.96
stachydrine	Xenobiotics	Food Component/Plant	-0.10	0.75	0.96
quinat	Xenobiotics	Food Component/Plant	0.16	0.75	0.96
bilirubin	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	0.09	0.75	0.96
acetylcarnitine (C2)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.03	0.75	0.96
cys-gly, oxidized	Amino Acid	Glutathione Metabolism	-0.06	0.75	0.96
TL20:4n3 (eicosatetraoic acid)	Lipid	Mole % Total Fatty Acid	0.04	0.75	0.96
eicosanodioate	Lipid	Fatty Acid, Dicarboxylate	-0.04	0.76	0.96
indole-3-carboxylic acid	Amino Acid	Tryptophan Metabolism	-0.02	0.76	0.96
adenosine 3',5'-cyclic monophosphate (cAMP)	Nucleotide	Purine Metabolism, Adenine containing	-0.07	0.76	0.96
glutarate (pentanedioate)	Amino Acid	Lysine Metabolism	0.05	0.76	0.96
etiocholanolone glucuronide	Lipid	Steroid	-0.08	0.77	0.96
N2,N2-dimethylguanosine	Nucleotide	Purine Metabolism, Guanine containing	0.02	0.77	0.96
xylose	Carbohydrate	Pentose Metabolism	0.06	0.77	0.96

4-allylphenol sulfate	Xenobiotics	Food Component/Plant	0.07	0.77	0.96
palmitoyl-oleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.02	0.77	0.96
taurodeoxycholate	Lipid	Secondary Bile Acid Metabolism	0.13	0.77	0.96
docosatienoate (22:3n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.03	0.77	0.96
adenine	Nucleotide	Purine Metabolism, Adenine containing	0.04	0.77	0.96
hexanoylcarnitine (C6)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.02	0.78	0.96
3-hydroxymyristate	Lipid	Fatty Acid, Monohydroxy	-0.03	0.78	0.96
salicylate	Xenobiotics	Drug	0.12	0.78	0.96
3-methylglutaryl carnitine (1)	Amino Acid	Lysine Metabolism	-0.04	0.78	0.96
palmitoyl ethanolamide	Lipid	Endocannabinoid	-0.02	0.78	0.96
1-docosapentaenoyl-GPC* (22:5n6)*	Lipid	Lysolipid	-0.09	0.78	0.96
palmitoleoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.01	0.79	0.96
1-pentadecanoylglycerol (1-monopentadecanoin)	Lipid	Monoacylglycerol	-0.03	0.79	0.96
pentadecanoate (15:0)	Lipid	Long Chain Fatty Acid	0.02	0.79	0.97
glycodeoxycholate	Lipid	Secondary Bile Acid Metabolism	0.11	0.79	0.97
gamma-glutamylhistidine	Peptide	Gamma-glutamyl Amino Acid	0.06	0.80	0.97
scyllo-inositol	Lipid	Inositol Metabolism	-0.04	0.80	0.97
2-stearoylglycerophosphoinositol*	Lipid	Lysolipid	-0.04	0.80	0.97
cystine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.01	0.81	0.97
cortisone	Lipid	Steroid	-0.04	0.81	0.97
glycerate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	-0.02	0.81	0.97
4-ureidobutyrate	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.04	0.81	0.97
histidine	Amino Acid	Histidine Metabolism	-0.02	0.81	0.97
stearoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.02	0.82	0.97
imidazole propionate	Amino Acid	Histidine Metabolism	0.04	0.82	0.97
pregn steroid monosulfate*	Lipid	Steroid	0.03	0.82	0.97
creatinine	Amino Acid	Creatine Metabolism	0.01	0.82	0.97
2-hydroxyglutarate	Lipid	Fatty Acid, Dicarboxylate	-0.02	0.82	0.97
phenylalanyltryptophan	Peptide	Dipeptide	0.04	0.82	0.97
13-HODE + 9-HODE	Lipid	Fatty Acid, Monohydroxy	-0.03	0.83	0.97
N-(2-furoyl)glycine	Xenobiotics	Food Component/Plant	0.04	0.83	0.97
21-hydroxypregnenolone disulfate	Lipid	Steroid	0.04	0.83	0.97
beta-sitosterol	Lipid	Sterol	0.03	0.83	0.97
TLdm16:0 (plasmalogen palmitic acid)	Lipid	Mole % Total Fatty Acid	-0.02	0.83	0.97

caprate (10:0)	Lipid	Medium Chain Fatty Acid	-0.02	0.83	0.97
xylonate	Carbohydrate	Pentose Metabolism	0.04	0.83	0.97
p-cresol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.06	0.84	0.97
N3-methyluridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.03	0.84	0.97
arginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.01	0.84	0.97
TL15:0 (pentadecanoic acid)	Lipid	Mole % Total Fatty Acid	-0.01	0.84	0.97
2-methylbutyrocarnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.02	0.84	0.97
thymol sulfate	Xenobiotics	Food Component/Plant	0.09	0.84	0.97
gamma-glutamyltyrosine	Peptide	Gamma-glutamyl Amino Acid	-0.01	0.84	0.97
dehydroisoandrosterone sulfate (DHEA-S)	Lipid	Steroid	0.04	0.84	0.97
stearoyl-linoleoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	-0.02	0.84	0.97
O-sulfo-L-tyrosine	Xenobiotics	Chemical	0.01	0.84	0.97
3-phenylpropionate (hydrocinnamate)	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.06	0.85	0.97
cholate	Lipid	Primary Bile Acid Metabolism	0.07	0.85	0.97
stearoyl-linoleoyl-glycerophosphoethanolamine (1)*	Lipid	Lysolipid	-0.02	0.85	0.97
pregnanediol-3-glucuronide	Lipid	Steroid	-0.06	0.85	0.97
glycolithocholate	Lipid	Secondary Bile Acid Metabolism	-0.08	0.85	0.98
tryptophan	Amino Acid	Tryptophan Metabolism	0.01	0.86	0.98
N-acetylarginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.02	0.86	0.98
tiglyl carnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.02	0.86	0.98
palmitoyl-palmitoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.02	0.87	0.98
vaccenate (18:1n7)	Lipid	Long Chain Fatty Acid	0.01	0.87	0.98
taurochenodeoxycholate	Lipid	Primary Bile Acid Metabolism	0.05	0.87	0.98
cholesterol	Lipid	Sterol	-0.01	0.87	0.98
serotonin (5HT)	Amino Acid	Tryptophan Metabolism	0.04	0.87	0.98
palmitoyl-arachidonoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.02	0.87	0.98
urate	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	-0.01	0.87	0.98
tyramine O-sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.04	0.87	0.98
pyrraline	Xenobiotics	Food Component/Plant	-0.04	0.88	0.98
N-acetyltyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.02	0.88	0.98
pyridoxate	Cofactors and Vitamins	Vitamin B6 Metabolism	-0.03	0.88	0.98

dimethylglycine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.01	0.88	0.98
7-methylguanine	Nucleotide	Purine Metabolism, Guanine containing	-0.01	0.88	0.98
phenylalanylglutamate	Peptide	Dipeptide	0.07	0.89	0.98
13-methylmyristic acid	Lipid	Fatty Acid, Branched	0.01	0.89	0.98
N-acetyl-beta-alanine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.01	0.89	0.98
4-hydroxybenzoate	Xenobiotics	Benzoate Metabolism	0.06	0.89	0.98
phenylalanylphenylalanine	Peptide	Dipeptide	0.02	0.89	0.98
levulinate (4-oxoalate)	Xenobiotics	Food Component/Plant	-0.01	0.89	0.98
N-acetyl-1-methylhistidine*	Amino Acid	Histidine Metabolism	-0.02	0.90	0.98
7-methylxanthine	Xenobiotics	Xanthine Metabolism	-0.04	0.90	0.98
propionylcarnitine (C3)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	0.01	0.90	0.98
TL18:1n7 (avaccenic acid)	Lipid	Mole % Total Fatty Acid	0.01	0.90	0.99
S-adenosylhomocysteine (SAH)	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.02	0.90	0.99
5-acetylamino-6-amino-3-methyluracil	Xenobiotics	Xanthine Metabolism	0.05	0.91	0.99
homoarginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.03	0.91	0.99
chenodeoxycholate	Lipid	Primary Bile Acid Metabolism	0.03	0.91	0.99
5-dodecenoate (12:1n7)	Lipid	Medium Chain Fatty Acid	-0.01	0.91	0.99
2-linoleoylglycerol (2-monolinolein)	Lipid	Monoacylglycerol	0.02	0.92	0.99
laurylcarnitine (C12)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.01	0.92	0.99
gamma-glutamylthreonine*	Peptide	Gamma-glutamyl Amino Acid	0.01	0.92	0.99
myristoleate (14:1n5)	Lipid	Long Chain Fatty Acid	-0.02	0.92	0.99
oleoyl-linoleoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.01	0.92	0.99
4-androsten-3alpha,17alpha-diol monosulfate (3)	Lipid	Steroid	-0.02	0.92	0.99
N1-Methyl-2-pyridone-5-carboxamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	0.01	0.92	0.99
gentisate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.04	0.93	0.99
p-cresol-glucuronide*	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.04	0.93	0.99
N-acetylkynurenine (2)	Amino Acid	Tryptophan Metabolism	0.03	0.93	0.99
ribonate (ribonolactone)	Carbohydrate	Pentose Metabolism	0.01	0.93	0.99
oleate (18:1n9)	Lipid	Long Chain Fatty Acid	0.01	0.93	0.99
isoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.004	0.93	0.99
pyroglutamylglycine	Peptide	Dipeptide	0.02	0.94	0.99
N-acetylphenylalanine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.01	0.94	0.99
hippurate	Xenobiotics	Benzoate Metabolism	0.02	0.94	0.99

palmitoyl sphingomyelin	Lipid	Sphingolipid Metabolism	0.003	0.94	0.99
cortisol	Lipid	Steroid	0.01	0.94	0.99
2-aminophenol sulfate	Xenobiotics	Chemical	-0.02	0.94	0.99
nicotinamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	0.01	0.94	0.99
succinylcarnitine (C4)	Energy	TCA Cycle	0.01	0.95	0.99
laurate (12:0)	Lipid	Medium Chain Fatty Acid	0.01	0.95	0.99
tartarate	Xenobiotics	Food Component/Plant	-0.02	0.95	0.99
histidylphenylalanine	Peptide	Dipeptide	0.02	0.95	0.99
N-acetylglutamate	Amino Acid	Glutamate Metabolism	0.01	0.95	0.99
phenylalanine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.002	0.95	0.99
4-androsten-3alpha,17alpha-diol monosulfate (2)	Lipid	Steroid	-0.01	0.96	0.99
3-methylxanthine	Xenobiotics	Xanthine Metabolism	-0.02	0.96	0.99
trans-urocanate	Amino Acid	Histidine Metabolism	0.01	0.96	0.99
5alpha-androstan-3alpha,17beta-diol monosulfate (1)	Lipid	Steroid	0.02	0.96	0.99
DSGEGDFXAEGGGVR*	Peptide	Fibrinogen Cleavage Peptide	-0.01	0.97	1.00
N-6-trimethyllysine	Amino Acid	Lysine Metabolism	-0.004	0.97	1.00
piperine	Xenobiotics	Food Component/Plant	-0.01	0.97	1.00
5-hydroxyindoleacetate	Amino Acid	Tryptophan Metabolism	-0.003	0.97	1.00
deoxycholate	Lipid	Secondary Bile Acid Metabolism	0.01	0.98	1.00
phosphate	Energy	Oxidative Phosphorylation	-0.001	0.98	1.00
TLdm18:0 (plasmalogen stearic acid)	Lipid	Mole % Total Fatty Acid	-0.002	0.98	1.00
1-methylxanthine	Xenobiotics	Xanthine Metabolism	-0.01	0.98	1.00
N6-carbamoylthreonyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.002	0.98	1.00
leucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.001	0.98	1.00
1-stearoyl-GPI (18:0)	Lipid	Lysolipid	0.002	0.99	1.00
sphingosine 1-phosphate	Lipid	Sphingolipid Metabolism	0.001	0.99	1.00
carnitine	Lipid	Carnitine Metabolism	-0.001	0.99	1.00
epiandrosterone sulfate	Lipid	Steroid	0.004	0.99	1.00
galactonate	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.01	0.99	1.00
N-acetylalliin	Xenobiotics	Food Component/Plant	-0.01	0.99	1.00
4-vinylphenol sulfate	Xenobiotics	Benzoate Metabolism	-0.003	0.99	1.00
tyrosylglutamine	Peptide	Dipeptide	0.002	0.99	1.00
N-acetylthreonine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.001	0.99	1.00
stigmasterol	Lipid	Sterol	-0.001	0.99	1.00

N-acetylvaline	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.0003	1.00	1.00
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*Covariates: age, sex, diabetes, hypertension, BMI, and liver fibrosis stage
TCA = tricarboxylic acid cycle; GPE = Glycerophosphoethanolamine; GPC = Glycerophosphocholine; SAM = S-Adenosyl methionine

Table S4: HFpEF-no fatigue full results*

Metabolite	Pathway	Sub-Pathway	log Fold change	Unadjusted p-value	Adjusted p-value
1-arachidonoyl-GPE* (20:4)*	Lipid	Lysolipid	0.27	0.0004	0.13
azelate (nonanedioate; C9)	Lipid	Fatty Acid, Dicarboxylate	-0.37	0.0006	0.13
taurocholenate sulfate	Lipid	Secondary Bile Acid Metabolism	-0.60	0.0008	0.13
1-stearoyl-GPE (18:0)	Lipid	Lysolipid	0.28	0.001	0.13
1-arachidonylglycerol	Lipid	Monoacylglycerol	0.30	0.001	0.13
1-docosahexaenoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.35	0.001	0.13
2-stearoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.33	0.001	0.13
1-oleoyl-GPE (18:1)	Lipid	Lysolipid	0.27	0.002	0.15
1-palmitoyl-GPE (16:0)	Lipid	Lysolipid	0.27	0.002	0.18
2-arachidonoyl glycerol	Lipid	Monoacylglycerol	0.32	0.003	0.20
1-linolenylglycerol	Lipid	Monoacylglycerol	0.34	0.004	0.25
citrate	Energy	TCA Cycle	-0.20	0.005	0.26
2-oleoyl-GPE* (18:1)*	Lipid	Lysolipid	0.85	0.007	0.37
7-alpha-hydroxycholesterol	Lipid	Sterol	0.50	0.009	0.37
2-palmitoyl-GPE* (16:0)*	Lipid	Lysolipid	0.31	0.009	0.37
1-eicosatrienoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.65	0.009	0.37
N2-methylguanosine	Nucleotide	Purine Metabolism, Guanine containing	0.28	0.01	0.37
alpha-ketoglutarate	Energy	TCA Cycle	0.29	0.01	0.37
2-arachidonoyl-GPE* (20:4)*	Lipid	Lysolipid	0.50	0.01	0.39
1-docosahexaenoylglycerol	Lipid	Monoacylglycerol	0.36	0.01	0.39
TL18:3n6 (g-linolenic acid)	Lipid	Mole % Total Fatty Acid	0.22	0.01	0.41
2-docosahexaenoylglycerol*	Lipid	Monoacylglycerol	0.85	0.01	0.44
glycerophosphoethanolamine	Lipid	Phospholipid Metabolism	0.38	0.02	0.52
hexanoylglycine (C6)	Lipid	Fatty Acid Metabolism(Acyl Glycine)	0.76	0.02	0.53
N6-acetyllysine	Amino Acid	Lysine Metabolism	0.12	0.02	0.54
methyl glucopyranoside (alpha + beta)	Xenobiotics	Food Component/Plant	-0.72	0.02	0.59
glutamine	Amino Acid	Glutamate Metabolism	-0.09	0.02	0.59
5alpha-pregnan-3beta,20beta-diol monosulfate (1)	Lipid	Steroid	-0.54	0.03	0.59
2-palmitoylglycerol (16:0)	Lipid	Monoacylglycerol	0.36	0.03	0.59
TL14:0 (myristic acid)	Lipid	Mole % Total Fatty Acid	0.23	0.03	0.59

pyruvate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.33	0.03	0.59
N-delta-acetylornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.33	0.03	0.59
1-linoleoylglycerol (18:2)	Lipid	Monoacylglycerol	0.24	0.03	0.59
1-myristoyl-GPC (14:0)	Lipid	Lysolipid	0.32	0.03	0.59
3b-hydroxy-5-choleonoic acid	Lipid	Secondary Bile Acid Metabolism	-0.57	0.03	0.59
arabinose	Carbohydrate	Pentose Metabolism	0.49	0.03	0.59
benzoate	Xenobiotics	Benzoate Metabolism	-0.16	0.04	0.59
1-palmitoylglycerol (16:0)	Lipid	Monoacylglycerol	0.21	0.04	0.59
phenylpyruvate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.17	0.04	0.59
3beta,7alpha-dihydroxy-5-cholestenoate	Lipid	Secondary Bile Acid Metabolism	0.68	0.04	0.59
2-keto-3-deoxy-gluconate	Xenobiotics	Food Component/Plant	0.29	0.04	0.59
1-myristoylglycerol (14:0)	Lipid	Monoacylglycerol	0.32	0.04	0.59
pyridoxine (Vitamin B6)	Cofactors and Vitamins	Vitamin B6 Metabolism	-0.19	0.04	0.59
S-methylcysteine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.21	0.04	0.59
3-methoxytyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.14	0.04	0.60
threonine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.12	0.04	0.60
stearoyl-arachidonoyl-glycerophosphoethanolamine (1)*	Lipid	Lysolipid	0.23	0.04	0.60
1-dihomo-linolenylglycerol (alpha, gamma)	Lipid	Monoacylglycerol	0.22	0.04	0.60
butyrylcarnitine (C4)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	0.24	0.05	0.60
orotate	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.34	0.05	0.60
2-oleoylglycerol (18:1)	Lipid	Monoacylglycerol	0.24	0.05	0.64
gamma-CEHC glucuronide*	Cofactors and Vitamins	Tocopherol Metabolism	0.63	0.05	0.64
3-methyl catechol sulfate (1)	Xenobiotics	Benzoate Metabolism	0.63	0.05	0.65
eugenol sulfate	Xenobiotics	Food Component/Plant	0.83	0.05	0.65
methionine sulfone	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.30	0.06	0.65
caproate (6:0)	Lipid	Medium Chain Fatty Acid	-0.12	0.06	0.65
16a-hydroxy DHEA 3-sulfate	Lipid	Steroid	-0.37	0.06	0.65
2-myristoyl-GPC* (14:0)*	Lipid	Lysolipid	0.40	0.06	0.65
4-androsten-3beta,17beta-diol disulfate (2)	Lipid	Steroid	-0.28	0.06	0.65
indoleacetylglutamine	Amino Acid	Tryptophan Metabolism	0.64	0.06	0.65
1-pentadecanoylglycerophosphocholine (15:0)*	Lipid	Lysolipid	0.20	0.06	0.65

alpha-hydroxycaproate	Lipid	Fatty Acid, Monohydroxy	0.16	0.06	0.65
cytidine	Nucleotide	Pyrimidine Metabolism, Cytidine containing	0.18	0.06	0.65
1-oleoylglycerol (18:1)	Lipid	Monoacylglycerol	0.22	0.07	0.66
2-linoleoylglycerol (2-monolinolein)	Lipid	Monoacylglycerol	0.29	0.07	0.66
3-hydroxybutyrate (BHBA)	Lipid	Ketone Bodies	-0.38	0.07	0.66
indolebutyrate	Amino Acid	Tryptophan Metabolism	0.39	0.07	0.66
beta-alanine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.19	0.07	0.66
TL20:3n9 (mead acid)	Lipid	Mole % Total Fatty Acid	0.26	0.07	0.66
5alpha-pregnan-3(alpha or beta),20beta-diol disulfate	Lipid	Steroid	-0.94	0.07	0.66
N-acetylleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.16	0.07	0.66
palmitoyl-linoleoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	-0.12	0.08	0.66
gluconate	Xenobiotics	Food Component/Plant	0.15	0.08	0.66
methionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.09	0.08	0.66
3-(4-hydroxyphenyl)propionate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.70	0.08	0.66
2-docosahexaenoyl-GPC* (22:6)*	Lipid	Lysolipid	0.28	0.08	0.66
gamma-glutamylglutamine	Peptide	Gamma-glutamyl Amino Acid	-0.16	0.08	0.66
biliverdin	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	-0.36	0.08	0.66
1-eicosapentaenoylglycerophosphocholine (20:5n3)*	Lipid	Lysolipid	0.33	0.08	0.66
indolepropionate	Amino Acid	Tryptophan Metabolism	-0.35	0.09	0.66
orotidine	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.40	0.09	0.66
propionylglycine (C3)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	0.21	0.09	0.66
2-aminobutyrate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.15	0.09	0.66
methyl indole-3-acetate	Xenobiotics	Food Component/Plant	0.26	0.09	0.66
2-hydroxyglutarate	Lipid	Fatty Acid, Dicarboxylate	-0.16	0.09	0.66
9,10-DiHOME	Lipid	Fatty Acid, Dihydroxy	-0.38	0.09	0.66
isobutyrylglycine (C4)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.20	0.09	0.66
methionine sulfoxide	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.15	0.09	0.66
7-dehydro-cholesterol	Lipid	Sterol	0.63	0.09	0.66
4-imidazoleacetate	Amino Acid	Histidine Metabolism	-0.46	0.09	0.66
isovalerylglycine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.22	0.09	0.66
betaine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.11	0.09	0.66
TL18:2n6 (linoleic acid)	Lipid	Mole % Total Fatty Acid	-0.08	0.09	0.66

1-arachidonoyl-GPC* (20:4)*	Lipid	Lysolipid	0.16	0.10	0.66
2-ethylhexanoic acid	Xenobiotics	Chemical	-0.15	0.10	0.66
TLdm16:0 (plasmalogen palmitic acid)	Lipid	Mole % Total Fatty Acid	-0.14	0.10	0.66
1-linolenoylglycerophosphocholine (18:3n3)*	Lipid	Lysolipid	0.22	0.10	0.66
tauroolithocholate 3-sulfate	Lipid	Secondary Bile Acid Metabolism	-0.58	0.10	0.66
o-cresol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.97	0.10	0.66
glucose	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.10	0.10	0.66
oleamide	Lipid	Fatty Acid, Amide	0.31	0.10	0.66
dimethylarginine (ADMA + SDMA)	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.06	0.10	0.66
pyroglutamylglutamine	Peptide	Dipeptide	0.29	0.10	0.66
N-acetyl-aspartyl-glutamate (NAAG)	Amino Acid	Glutamate Metabolism	-0.13	0.10	0.66
phenylalanylleucine	Peptide	Dipeptide	0.52	0.11	0.67
2-hydroxy-3-methylvalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.17	0.11	0.67
homostachydrine*	Xenobiotics	Food Component/Plant	-0.21	0.11	0.69
malonate (propanedioate)	Lipid	Fatty Acid Synthesis	-0.26	0.11	0.69
2-palmitoleoyl-GPC* (16:1)*	Lipid	Lysolipid	0.31	0.12	0.71
TL18:4n3 (stearidonic acid)	Lipid	Mole % Total Fatty Acid	0.32	0.12	0.73
TL18:1n9 (oleic acid)	Lipid	Mole % Total Fatty Acid	0.06	0.12	0.73
1,2,3-benzenetriol sulfate (2)	Xenobiotics	Chemical	-0.75	0.12	0.73
glycolithocholate sulfate*	Lipid	Secondary Bile Acid Metabolism	-0.44	0.12	0.73
N-acetylglutamate	Amino Acid	Glutamate Metabolism	-0.41	0.13	0.73
TLdm18:0 (plasmalogen stearic acid)	Lipid	Mole % Total Fatty Acid	-0.14	0.13	0.73
TLTL (Total Total Lipid)	Lipid	Quantitative Total Fatty Acid	0.13	0.13	0.73
N-acetylglutamine	Amino Acid	Glutamate Metabolism	-0.18	0.13	0.73
stearidonate (18:4n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.20	0.13	0.73
galactonate	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.72	0.13	0.73
gamma-glutamyltyrosine	Peptide	Gamma-glutamyl Amino Acid	-0.11	0.13	0.73
xylitol	Carbohydrate	Pentose Metabolism	0.25	0.13	0.73
tyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.08	0.14	0.73
4-guanidinobutanoate	Amino Acid	Guanidino and Acetamido Metabolism	-0.49	0.14	0.74
N-acetyltryptophan	Amino Acid	Tryptophan Metabolism	0.17	0.14	0.74
1-palmitoyl-GPC (16:0)	Lipid	Lysolipid	0.12	0.14	0.74
2-arachidonoyl-GPC* (20:4)*	Lipid	Lysolipid	0.16	0.15	0.74

3-methyl-2-oxobutyrate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.09	0.15	0.74
N2,N5-diacetylornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.31	0.15	0.74
alanine	Amino Acid	Alanine and Aspartate Metabolism	0.07	0.15	0.74
glycolate (hydroxyacetate)	Xenobiotics	Chemical	-0.09	0.15	0.74
uridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.08	0.15	0.74
xanthosine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.17	0.15	0.74
pregnen-diol disulfate*	Lipid	Steroid	-0.23	0.15	0.75
inositol 1-phosphate (I1P)	Lipid	Inositol Metabolism	0.17	0.15	0.75
N-acetylglycine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.18	0.16	0.75
2-linoleoyl-GPE* (18:2)*	Lipid	Lysolipid	0.18	0.16	0.75
stearoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.10	0.16	0.75
stearate (18:0)	Lipid	Long Chain Fatty Acid	0.07	0.16	0.75
gamma-glutamylthreonine*	Peptide	Gamma-glutamyl Amino Acid	-0.14	0.16	0.75
homoarginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.42	0.16	0.75
O-sulfo-L-tyrosine	Xenobiotics	Chemical	0.10	0.16	0.75
2-palmitoyl-GPC* (16:0)*	Lipid	Lysolipid	0.14	0.16	0.75
N2-acetyllysine	Amino Acid	Lysine Metabolism	-0.23	0.17	0.75
16-hydroxypalmitate	Lipid	Fatty Acid, Monohydroxy	-0.10	0.17	0.75
gentisate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.63	0.17	0.75
ribitol	Carbohydrate	Pentose Metabolism	0.09	0.17	0.75
stearoylcarnitine (C18)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.17	0.17	0.75
TL14:1n5 (myristoleic acid)	Lipid	Mole % Total Fatty Acid	0.24	0.17	0.75
glycocholate sulfate*	Lipid	Secondary Bile Acid Metabolism	-0.15	0.17	0.75
N-acetyltaurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.17	0.17	0.75
gamma-CEHC	Cofactors and Vitamins	Tocopherol Metabolism	0.20	0.18	0.75
homocitrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.18	0.18	0.75
trans-urocanate	Amino Acid	Histidine Metabolism	0.18	0.18	0.75
1-palmitoleoyl-GPC* (16:1)*	Lipid	Lysolipid	0.18	0.18	0.75
sphingomyelin	Lipid	Sphingolipid Metabolism	0.11	0.18	0.75
4-androsten-3beta,17beta-diol monosulfate (2)	Lipid	Steroid	-0.34	0.18	0.75
proline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.08	0.18	0.75
cysteine-glutathione disulfide	Amino Acid	Glutathione Metabolism	-0.38	0.18	0.75

1-docosahexaenoyl-GPC* (22:6)*	Lipid	Lysolipid	0.17	0.18	0.76
7-methylguanine	Nucleotide	Purine Metabolism, Guanine containing	-0.08	0.19	0.76
palmitoyl-oleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.10	0.19	0.76
hydroxybutyrylcarnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.25	0.19	0.76
4-hydroxyphenylpyruvate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.18	0.19	0.76
kynurenate	Amino Acid	Tryptophan Metabolism	-0.14	0.19	0.76
3-methylglutarylcarnitine (2)	Amino Acid	Lysine Metabolism	0.22	0.19	0.76
3-methoxytyramine sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.16	0.19	0.76
allo-isoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.09	0.19	0.76
tetradecanedioate (C14)	Lipid	Fatty Acid, Dicarboxylate	-0.17	0.20	0.76
TL18:0 (stearic acid)	Lipid	Mole % Total Fatty Acid	-0.05	0.20	0.76
arginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.10	0.20	0.76
pipecolate	Amino Acid	Lysine Metabolism	-0.19	0.20	0.76
N-acetylcitrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.35	0.20	0.77
phenylalanine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.05	0.20	0.77
TLdm18:1n9 (plasmalogen oleic acid)	Lipid	Mole % Total Fatty Acid	-0.13	0.21	0.77
7-HOCA	Lipid	Sterol	0.13	0.21	0.77
hydroquinone sulfate	Xenobiotics	Drug	-0.37	0.21	0.77
N-acetylaspartate (NAA)	Amino Acid	Alanine and Aspartate Metabolism	-0.08	0.21	0.77
N-acetylarginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.15	0.21	0.77
1-stearoylplasmeneylethanolamine *	Lipid	Lysolipid	0.15	0.21	0.77
cyclohexanebutanoic acid	Xenobiotics	Chemical	-0.15	0.21	0.77
pyroglutamine*	Amino Acid	Glutamate Metabolism	-0.19	0.21	0.77
cys-gly, oxidized	Amino Acid	Glutathione Metabolism	0.24	0.22	0.77
4-methyl-2-oxopentanoate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.08	0.22	0.77
3beta,7beta-dihydroxy-5-cholestenoate	Lipid	Sterol	-0.11	0.22	0.77
1,6-anhydroglucose	Xenobiotics	Food Component/Plant	-0.29	0.22	0.77
arachidate (20:0)	Lipid	Long Chain Fatty Acid	0.08	0.22	0.77
hexadecanedioate (C16)	Lipid	Fatty Acid, Dicarboxylate	-0.16	0.22	0.77
5alpha-androstan-3beta,17beta-diol disulfate	Lipid	Steroid	-0.33	0.22	0.77
seryltyrosine	Peptide	Dipeptide	0.31	0.22	0.77
octadecanedioate (C18)	Lipid	Fatty Acid, Dicarboxylate	-0.16	0.23	0.77

4-hydroxyhippurate	Xenobiotics	Benzoate Metabolism	-0.25	0.23	0.77
dopamine sulfate (2)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.14	0.23	0.77
docosahexaenoate (DHA; 22:6n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.14	0.23	0.77
N-acetylthreonine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.12	0.23	0.77
alpha-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.13	0.23	0.77
N-methylpipecolate	Xenobiotics	Chemical	-0.22	0.23	0.77
beta-hydroxyisovaleroylcarnitine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.11	0.23	0.78
prolylhydroxyproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.16	0.23	0.78
N-acetylcarnosine	Peptide	Dipeptide Derivative	-0.09	0.24	0.78
trimethylamine N-oxide	Lipid	Phospholipid Metabolism	0.56	0.24	0.79
aspartylphenylalanine	Peptide	Dipeptide	0.28	0.24	0.79
andro steroid monosulfate (1)*	Lipid	Steroid	-0.32	0.25	0.80
3-methylglutaconate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.18	0.25	0.80
cysteine s-sulfate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.09	0.25	0.80
2-eicosatrienoyl-GPC* (20:3)*	Lipid	Lysolipid	0.11	0.26	0.80
asparagine	Amino Acid	Alanine and Aspartate Metabolism	-0.05	0.26	0.80
pregn steroid monosulfate*	Lipid	Steroid	-0.18	0.26	0.80
1-oleoyl-GPC (18:1)	Lipid	Lysolipid	0.12	0.26	0.80
TL16:1n7 (palmitoleic acid)	Lipid	Mole % Total Fatty Acid	0.11	0.26	0.80
TL24:1n9 (nervonic acid)	Lipid	Mole % Total Fatty Acid	-0.12	0.26	0.80
quinat	Xenobiotics	Food Component/Plant	0.59	0.26	0.80
21-hydroxypregnenolone disulfate	Lipid	Steroid	-0.19	0.26	0.80
deoxycarnitine	Lipid	Carnitine Metabolism	-0.06	0.26	0.80
paraxanthine	Xenobiotics	Xanthine Metabolism	-0.57	0.26	0.80
1-methylnicotinamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	-0.32	0.26	0.80
4-ethylphenyl sulfate	Xenobiotics	Benzoate Metabolism	0.27	0.27	0.80
inosine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	-0.35	0.27	0.80
mannose	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.08	0.27	0.80
ethylmalonate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.13	0.27	0.80
eicosapentaenoate (EPA; 20:5n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.18	0.27	0.80
N6-succinyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.09	0.27	0.80
creatine	Amino Acid	Creatine Metabolism	0.13	0.27	0.80

1-pentadecanoylglycerol (1-monopentadecanoin)	Lipid	Monoacylglycerol	0.15	0.27	0.80
methyl-4-hydroxybenzoate sulfate	Xenobiotics	Benzoate Metabolism	-0.48	0.27	0.80
5,6-dihydrothymine	Nucleotide	Pyrimidine Metabolism, Thymine containing	-0.09	0.28	0.80
adrenate (22:4n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.10	0.28	0.80
acetoacetate	Lipid	Ketone Bodies	-0.17	0.28	0.80
TL20:5n3 (eicosapentaenoic acid)	Lipid	Mole % Total Fatty Acid	0.17	0.28	0.80
1-eicosatrienoyl-GPC* (20:3)*	Lipid	Lysolipid	0.12	0.28	0.80
piperine	Xenobiotics	Food Component/Plant	-0.24	0.28	0.80
nonadecanoate (19:0)	Lipid	Long Chain Fatty Acid	0.06	0.28	0.80
5alpha-androstan-3alpha,17beta-diol disulfate	Lipid	Steroid	-0.38	0.28	0.81
glucarate 1,4-lactone	Carbohydrate	Disaccharides and Oligosaccharides	-0.78	0.29	0.81
TL22:5n3 (docosapentaenoic acid)	Lipid	Mole % Total Fatty Acid	0.08	0.29	0.81
TL20:1n9 (eicoasenoic acid)	Lipid	Mole % Total Fatty Acid	-0.05	0.30	0.81
ectoine	Xenobiotics	Chemical	-0.29	0.30	0.81
3-hydroxy-3-methylglutarate	Lipid	Mevalonate Metabolism	0.08	0.30	0.81
valine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.04	0.30	0.81
sulfate*	Xenobiotics	Chemical	0.04	0.30	0.81
indoleacetate	Amino Acid	Tryptophan Metabolism	0.14	0.30	0.81
palmitoylcarnitine (C16)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.12	0.30	0.81
cyclo(L-phe-L-pro)	Peptide	Dipeptide	-0.23	0.31	0.81
1-stearoyl-GPC (18:0)	Lipid	Lysolipid	0.12	0.31	0.81
fucose	Carbohydrate	Pentose Metabolism	0.11	0.31	0.81
N-acetylputrescine	Amino Acid	Polyamine Metabolism	0.11	0.31	0.81
cortisone	Lipid	Steroid	-0.16	0.31	0.81
12,13-DiHOME	Lipid	Fatty Acid, Dihydroxy	-0.15	0.31	0.81
oleoyl-linoleoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.08	0.31	0.81
gamma-glutamylmethionine	Peptide	Gamma-glutamyl Amino Acid	-0.11	0.31	0.81
histidylphenylalanine	Peptide	Dipeptide	0.31	0.31	0.81
caffeine	Xenobiotics	Xanthine Metabolism	-0.48	0.32	0.81
ornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.08	0.32	0.81
N-acetyl-1-methylhistidine*	Amino Acid	Histidine Metabolism	-0.15	0.32	0.81
7-methylurate	Xenobiotics	Xanthine Metabolism	-0.49	0.32	0.81
lactate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.06	0.32	0.81
citrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.10	0.32	0.81

leucylalanine	Peptide	Dipeptide	0.26	0.32	0.81
alpha-ketobutyrate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.21	0.32	0.81
arachidonate (20:4n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.06	0.32	0.81
androsterone sulfate	Lipid	Steroid	-0.27	0.32	0.81
3-hydroxypyridine sulfate	Xenobiotics	Chemical	0.31	0.32	0.81
glutamate	Amino Acid	Glutamate Metabolism	0.08	0.33	0.81
lanosterol	Lipid	Sterol	0.27	0.33	0.81
2-aminooctanoate	Lipid	Fatty Acid, Amino	0.14	0.33	0.82
histidine	Amino Acid	Histidine Metabolism	0.09	0.33	0.82
N-acetylneuraminate	Carbohydrate	Aminosugar Metabolism	0.11	0.34	0.82
TL18:3n3 (a-linolenic acid)	Lipid	Mole % Total Fatty Acid	0.07	0.34	0.82
docosapentaenoate (n6 DPA; 22:5n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.08	0.34	0.82
dehydroisoandrosterone sulfate (DHEA-S)	Lipid	Steroid	-0.19	0.34	0.82
1-palmitoylplasmeneylethanolamine*	Lipid	Lysolipid	0.08	0.34	0.82
1-docosapentaenoyl-GPC* (22:5n3)*	Lipid	Lysolipid	0.11	0.34	0.82
3-indoxyl sulfate	Amino Acid	Tryptophan Metabolism	0.15	0.34	0.82
desmosterol	Lipid	Sterol	-0.17	0.35	0.82
cholestanol	Lipid	Sterol	-0.09	0.35	0.82
pyridoxate	Cofactors and Vitamins	Vitamin B6 Metabolism	0.19	0.35	0.82
palmitoyl-arachidonoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.06	0.35	0.82
10-undecenoate (11:1n1)	Lipid	Medium Chain Fatty Acid	-0.10	0.35	0.83
dodecanedioate (C12)	Lipid	Fatty Acid, Dicarboxylate	-0.12	0.35	0.83
3-hydroxyoctanoate	Lipid	Fatty Acid, Monohydroxy	-0.11	0.35	0.83
imidazole lactate	Amino Acid	Histidine Metabolism	-0.09	0.36	0.83
oxalate (ethanedioate)	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	-0.16	0.36	0.83
isoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.04	0.36	0.83
taurochenodeoxycholate	Lipid	Primary Bile Acid Metabolism	-0.29	0.36	0.83
N6-methyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.10	0.36	0.83
alpha-hydroxyisovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.11	0.37	0.84
stachydrine	Xenobiotics	Food Component/Plant	0.29	0.37	0.84
palmitoyl-arachidonoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.11	0.37	0.84
5-hydroxyindoleacetate	Amino Acid	Tryptophan Metabolism	0.09	0.37	0.84
palmitate (16:0)	Lipid	Long Chain Fatty Acid	0.05	0.37	0.84

4-ureidobutyrate	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.14	0.37	0.84
myristoylcarnitine	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.13	0.37	0.84
eicosenoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.08	0.37	0.84
myristoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.05	0.38	0.84
ursodeoxycholate	Lipid	Secondary Bile Acid Metabolism	0.37	0.38	0.84
leucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.04	0.38	0.84
theophylline	Xenobiotics	Xanthine Metabolism	-0.36	0.38	0.85
serotonin (5HT)	Amino Acid	Tryptophan Metabolism	0.23	0.39	0.85
oleoylcarnitine (C18)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.11	0.39	0.85
cis-4-decenoyl carnitine	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.09	0.39	0.85
glycerophosphorylcholine (GPC)	Lipid	Phospholipid Metabolism	0.06	0.39	0.85
TL22:0 (behenic acid)	Lipid	Mole % Total Fatty Acid	-0.09	0.39	0.85
maleate (cis-Butenedioate)	Lipid	Fatty Acid, Dicarboxylate	0.13	0.39	0.85
TL16:0 (palmitic acid)	Lipid	Mole % Total Fatty Acid	0.03	0.39	0.85
1-linoleoyl-GPE (18:2)*	Lipid	Lysolipid	0.08	0.40	0.85
acetylcarnitine (C2)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.08	0.40	0.85
lathosterol	Lipid	Sterol	0.15	0.41	0.85
glycylproline	Peptide	Dipeptide	0.22	0.41	0.85
12-HETE	Lipid	Eicosanoid	-0.23	0.41	0.85
docosapentaenoate (DPA; 22:5n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.09	0.41	0.85
serine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.05	0.41	0.85
threonate	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	-0.14	0.41	0.85
mannitol	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.27	0.41	0.85
2-linoleoyl-GPC* (18:2)*	Lipid	Lysolipid	0.09	0.41	0.85
5-oxoproline	Amino Acid	Glutathione Metabolism	-0.07	0.41	0.85
theobromine	Xenobiotics	Xanthine Metabolism	-0.27	0.41	0.85
10-nonadecenoate (19:1n9)	Lipid	Long Chain Fatty Acid	0.08	0.41	0.85
cyclo(leu-pro)	Peptide	Dipeptide	-0.15	0.41	0.85
succinate	Energy	TCA Cycle	-0.04	0.41	0.85
quinolinate	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	0.14	0.42	0.86
methylsuccinate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.06	0.42	0.86
pyroglutamylglycine	Peptide	Dipeptide	0.19	0.42	0.86
hydroxyproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.10	0.42	0.86
3-(3-hydroxyphenyl)propionate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.34	0.42	0.86

urea	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.07	0.42	0.86
TLdm18:1n7 (plasmalogen vaccenic acid)	Lipid	Mole % Total Fatty Acid	-0.17	0.43	0.86
pregnenediol-3-glucuronide	Lipid	Steroid	-0.27	0.43	0.86
nicotinamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	0.11	0.43	0.86
sphinganine	Lipid	Sphingolipid Metabolism	0.28	0.43	0.86
myristoleoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	-0.10	0.43	0.86
caprylate (8:0)	Lipid	Medium Chain Fatty Acid	-0.05	0.43	0.86
urate	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.05	0.44	0.86
pseudouridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.04	0.44	0.86
dimethyl sulfone	Xenobiotics	Chemical	0.26	0.44	0.86
palmitoleoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	-0.04	0.44	0.86
3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	Lipid	Fatty Acid, Dicarboxylate	0.30	0.44	0.86
1-methylguanosine	Nucleotide	Purine Metabolism, Guanine containing	0.04	0.44	0.86
N-acetylphenylalanine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.09	0.44	0.86
1-palmitoylglycerophosphate	Lipid	Lysolipid	0.13	0.45	0.86
2-hydroxystearate	Lipid	Fatty Acid, Monohydroxy	-0.04	0.45	0.86
4-androsten-3alpha,17alpha-diol monosulfate (3)	Lipid	Steroid	-0.20	0.45	0.86
1,7-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.32	0.45	0.86
3-methyl-2-oxovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.05	0.45	0.87
kynurenine	Amino Acid	Tryptophan Metabolism	0.05	0.46	0.87
tartarate	Xenobiotics	Food Component/Plant	-0.23	0.46	0.87
N-palmitoyl glycine	Lipid	Fatty Acid Metabolism(Acyl Glycine)	-0.10	0.46	0.87
beta-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.17	0.46	0.87
N-acetyltyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.08	0.46	0.87
4-vinylphenol sulfate	Xenobiotics	Benzoate Metabolism	-0.23	0.46	0.87
glycolithocholate	Lipid	Secondary Bile Acid Metabolism	-0.32	0.46	0.87
17-methylstearate	Lipid	Fatty Acid, Branched	0.08	0.46	0.87
ribonate (ribonolactone)	Carbohydrate	Pentose Metabolism	-0.07	0.46	0.87
erythritol	Xenobiotics	Food Component/Plant	0.10	0.47	0.87
phenylalanylphenylalanine	Peptide	Dipeptide	0.11	0.47	0.87
stearoyl-linoleoyl-glycerophosphoethanolamine (1)*	Lipid	Lysolipid	0.10	0.47	0.87
4-acetamidobutanoate	Amino Acid	Polyamine Metabolism	0.06	0.47	0.87

pentadecanoate (15:0)	Lipid	Long Chain Fatty Acid	0.05	0.47	0.87
bilirubin	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	-0.21	0.48	0.87
2-aminoheptanoate	Lipid	Fatty Acid, Amino	0.07	0.48	0.87
4-androsten-3beta,17beta-diol disulfate (1)	Lipid	Steroid	-0.16	0.48	0.87
taurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.07	0.48	0.88
2-hydroxyoctanoate	Lipid	Fatty Acid, Monohydroxy	0.08	0.48	0.88
4-androsten-3alpha,17alpha-diol monosulfate (2)	Lipid	Steroid	-0.17	0.49	0.88
5-methylthioadenosine (MTA)	Amino Acid	Polyamine Metabolism	0.23	0.49	0.88
tiglyl carnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.08	0.49	0.88
tyrosylglutamate	Peptide	Dipeptide	0.19	0.49	0.88
5alpha-pregnan-3beta,20alpha-diol disulfate	Lipid	Steroid	-0.15	0.49	0.88
2-linolenoylglycerophosphocholine (18:3n3)*	Lipid	Lysolipid	-0.23	0.49	0.88
pantothenate (Vitamin B5)	Cofactors and Vitamins	Pantothenate and CoA Metabolism	0.08	0.49	0.88
dopamine sulfate (1)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.12	0.50	0.88
pyrraline	Xenobiotics	Food Component/Plant	0.17	0.50	0.88
TL22:4n6 (adrenic acid)	Lipid	Mole % Total Fatty Acid	0.06	0.50	0.88
tartronate (hydroxymalonate)	Xenobiotics	Bacterial/Fungal	-0.11	0.50	0.88
1,3-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.30	0.50	0.89
alpha-hydroxyisocaproate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.06	0.50	0.89
5-dodecenoate (12:1n7)	Lipid	Medium Chain Fatty Acid	-0.08	0.51	0.89
erythronate*	Carbohydrate	Aminosugar Metabolism	0.04	0.51	0.89
TL15:0 (pentadecanoic acid)	Lipid	Mole % Total Fatty Acid	0.03	0.52	0.90
N-acetylkynurenine (2)	Amino Acid	Tryptophan Metabolism	-0.21	0.52	0.90
2-aminophenol sulfate	Xenobiotics	Chemical	0.19	0.52	0.90
2-pyrrolidinone	Xenobiotics	Chemical	-0.12	0.52	0.90
homovanillate (HVA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.08	0.52	0.90
malate	Energy	TCA Cycle	-0.05	0.52	0.90
glycylvaline	Peptide	Dipeptide	0.26	0.53	0.90
stearoyl-arachidonoylglycerophosphoinositol (1)*	Lipid	Lysolipid	0.05	0.53	0.90
phenyllactate (PLA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.05	0.53	0.90
TL22:1n9 (erucic acid)	Lipid	Mole % Total Fatty Acid	-0.14	0.54	0.91
squalene	Lipid	Sterol	0.19	0.54	0.91
TL22:6n3 (docosahexaenoic acid)	Lipid	Mole % Total Fatty Acid	0.06	0.54	0.91

1-eicosenoylglycerophosphocholine (20:1n9)*	Lipid	Lysolipid	0.09	0.54	0.91
myristoleate (14:1n5)	Lipid	Long Chain Fatty Acid	-0.16	0.54	0.91
leucylglycine	Peptide	Dipeptide	0.22	0.54	0.91
stearoyl-arachidonoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.13	0.54	0.91
glycerol 3-phosphate (G3P)	Lipid	Glycerolipid Metabolism	-0.15	0.54	0.91
glucuronate	Carbohydrate	Aminosugar Metabolism	0.06	0.54	0.91
3-hydroxydecanoate	Lipid	Fatty Acid, Monohydroxy	-0.06	0.55	0.91
3-hydroxyhippurate	Xenobiotics	Benzoate Metabolism	-0.22	0.55	0.91
5,6-dihydrouracil	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.05	0.55	0.91
N-acetylisoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.09	0.55	0.91
HWESASXX*	Peptide	Polypeptide	-0.14	0.55	0.91
octanoylcarnitine (C8)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.05	0.56	0.91
1,3,7-trimethylurate	Xenobiotics	Xanthine Metabolism	-0.21	0.56	0.91
indole-3-carboxylic acid	Amino Acid	Tryptophan Metabolism	0.04	0.56	0.91
2-stearoyl-GPC* (18:0)*	Lipid	Lysolipid	0.08	0.56	0.91
cortisol	Lipid	Steroid	-0.08	0.56	0.91
vanillylmandelate (VMA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.07	0.56	0.91
tryptophan	Amino Acid	Tryptophan Metabolism	-0.03	0.56	0.91
1-palmitoyl-GPI* (16:0)*	Lipid	Lysolipid	0.09	0.56	0.91
S-adenosylhomocysteine (SAH)	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.08	0.57	0.91
allantoin	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.09	0.57	0.91
prolylglycine	Peptide	Dipeptide	-0.11	0.57	0.91
palmitoyl-oleoyl-glycerophosphoglycerol (2)*	Lipid	Lysolipid	-0.20	0.57	0.91
margarate (17:0)	Lipid	Long Chain Fatty Acid	0.05	0.58	0.92
eicosanodioate	Lipid	Fatty Acid, Dicarboxylate	-0.08	0.58	0.92
adenine	Nucleotide	Purine Metabolism, Adenine containing	-0.07	0.58	0.92
I-urobilinogen	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	0.25	0.58	0.92
cholate	Lipid	Primary Bile Acid Metabolism	0.22	0.59	0.92
p-cresol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.16	0.59	0.92
arabonate	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	0.05	0.59	0.92
beta-sitosterol	Lipid	Sterol	0.07	0.59	0.92
gamma-glutamylphenylalanine	Peptide	Gamma-glutamyl Amino Acid	-0.03	0.59	0.92

isovalerate (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.05	0.59	0.92
phenol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.16	0.59	0.92
choline	Lipid	Phospholipid Metabolism	0.03	0.60	0.92
oleic ethanolamide	Lipid	Endocannabinoid	-0.05	0.60	0.93
levulinate (4-oxovalerate)	Xenobiotics	Food Component/Plant	-0.06	0.60	0.93
3-hydroxymyristate	Lipid	Fatty Acid, Monohydroxy	-0.05	0.60	0.93
phenylalanylglutamate	Peptide	Dipeptide	0.27	0.61	0.93
palmitoyl-linoleoyl-glycerophosphoinositol (1)*	Lipid	Lysolipid	0.11	0.61	0.93
cystine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.03	0.61	0.93
hypoxanthine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.10	0.61	0.93
2-hydroxypalmitate	Lipid	Fatty Acid, Monohydroxy	-0.03	0.61	0.93
TL20:3n6 (di-homo-g-linoleic acid)	Lipid	Mole % Total Fatty Acid	-0.03	0.61	0.93
1,5-anhydroglucitol (1,5-AG)	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	-0.08	0.62	0.93
1-methylimidazoleacetate	Amino Acid	Histidine Metabolism	-0.09	0.62	0.93
salicylate	Xenobiotics	Drug	-0.22	0.62	0.93
1,2-propanediol	Xenobiotics	Chemical	0.12	0.62	0.93
saccharin	Xenobiotics	Food Component/Plant	0.31	0.62	0.93
phenylalanylserine	Peptide	Dipeptide	-0.18	0.62	0.93
1-linoleoyl-GPC (18:2)	Lipid	Lysolipid	0.04	0.62	0.93
aspartate	Amino Acid	Alanine and Aspartate Metabolism	0.05	0.62	0.93
N-acetyl-beta-alanine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.04	0.62	0.93
2-methylbutyrylcarnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.04	0.62	0.93
cyclo(pro-pro)	Peptide	Dipeptide	0.06	0.63	0.93
TL20:4n3 (eicosatetranoic acid)	Lipid	Mole % Total Fatty Acid	0.06	0.63	0.93
docosadienoate (22:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.04	0.63	0.93
5alpha-androstan-3beta,17alpha-diol disulfate	Lipid	Steroid	-0.15	0.63	0.93
gamma-glutamyltryptophan	Peptide	Gamma-glutamyl Amino Acid	-0.04	0.63	0.93
phosphate	Energy	Oxidative Phosphorylation	-0.02	0.63	0.93
guanidinoacetate	Amino Acid	Creatine Metabolism	-0.05	0.64	0.93
3-methoxycatechol sulfate (1)	Xenobiotics	Benzoate Metabolism	-0.18	0.64	0.93
gamma-glutamylhistidine	Peptide	Gamma-glutamyl Amino Acid	-0.11	0.64	0.93
phenylacetylglutamine	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.08	0.64	0.93
vaccenate (18:1n7)	Lipid	Long Chain Fatty Acid	-0.04	0.64	0.93

C-glycosyltryptophan	Amino Acid	Tryptophan Metabolism	0.02	0.65	0.93
cholesterol	Lipid	Sterol	-0.03	0.65	0.93
taurodeoxycholate	Lipid	Secondary Bile Acid Metabolism	-0.22	0.65	0.93
2-piperidinone	Xenobiotics	Food Component/Plant	0.13	0.65	0.93
cinnamoylglycine	Xenobiotics	Food Component/Plant	0.24	0.65	0.93
4-allylphenol sulfate	Xenobiotics	Food Component/Plant	0.12	0.65	0.93
scyllo-inositol	Lipid	Inositol Metabolism	-0.08	0.66	0.93
stigmasterol	Lipid	Sterol	-0.09	0.66	0.93
3-[3-(sulfooxy)phenyl]propanoic acid	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.22	0.66	0.93
2-methylmalonyl carnitine	Lipid	Fatty Acid Synthesis	-0.04	0.66	0.93
cyclo(gly-pro)	Peptide	Dipeptide	0.07	0.66	0.93
glycerol	Lipid	Glycerolipid Metabolism	0.04	0.66	0.93
N-acetyl-3-methylhistidine*	Amino Acid	Histidine Metabolism	-0.13	0.66	0.93
guanosine	Nucleotide	Purine Metabolism, Guanine containing	-0.16	0.66	0.93
N-methylproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.12	0.66	0.93
gamma-glutamylalanine	Peptide	Gamma-glutamyl Amino Acid	0.04	0.66	0.93
1-stearoyl-GPI (18:0)	Lipid	Lysolipid	-0.04	0.67	0.93
myristate (14:0)	Lipid	Long Chain Fatty Acid	0.04	0.67	0.93
hippurate	Xenobiotics	Benzoate Metabolism	0.10	0.67	0.93
1-stearoylglycerol (18:0)	Lipid	Monoacylglycerol	0.13	0.67	0.93
arabitol	Carbohydrate	Pentose Metabolism	0.04	0.67	0.93
glycocholate	Lipid	Primary Bile Acid Metabolism	0.12	0.68	0.93
isoleucylglycine	Peptide	Dipeptide	0.10	0.68	0.93
O-methylcatechol sulfate	Xenobiotics	Benzoate Metabolism	0.09	0.68	0.93
dimethylglycine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.04	0.68	0.93
1-arachidonoyl-GPI* (20:4)*	Lipid	Lysolipid	0.03	0.68	0.93
thyroxine	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.12	0.68	0.93
4-androsten-3beta,17beta-diol monosulfate (1)	Lipid	Steroid	-0.09	0.69	0.93
hypotaurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.09	0.69	0.93
methylpalmitate (15 or 2)	Lipid	Fatty Acid, Branched	0.04	0.69	0.93
hydantoin-5-propionic acid	Amino Acid	Histidine Metabolism	0.10	0.69	0.93
dihomolinolenate (20:3n3 or 3n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.02	0.70	0.94
1-arachidoyl-GPC (20:0)	Lipid	Lysolipid	0.13	0.70	0.94
2-hydroxybutyrate (AHB)	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.04	0.70	0.94
tyramine O-sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.11	0.70	0.94

pelargonate (9:0)	Lipid	Medium Chain Fatty Acid	-0.02	0.71	0.94
valylarginine	Peptide	Dipeptide	0.10	0.71	0.94
histidyltryptophan	Peptide	Dipeptide	-0.08	0.71	0.94
4-hydroxychlorothalonil	Xenobiotics	Chemical	0.06	0.71	0.94
propionylcarnitine (C3)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	0.03	0.71	0.94
palmitoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.03	0.71	0.94
glycerate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.03	0.71	0.94
5-methyluridine (ribothymidine)	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.02	0.71	0.94
5-HETE	Lipid	Eicosanoid	0.07	0.72	0.94
N2,N2-dimethylguanosine	Nucleotide	Purine Metabolism, Guanine containing	0.02	0.72	0.94
2-oleoyl-GPC* (18:1)*	Lipid	Lysolipid	0.04	0.72	0.94
indolelactate	Amino Acid	Tryptophan Metabolism	0.03	0.72	0.94
TL20:0 (arachidic acid)	Lipid	Mole % Total Fatty Acid	-0.03	0.72	0.94
3-hydroxyisobutyrate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.04	0.72	0.94
phenylalanyltryptophan	Peptide	Dipeptide	0.06	0.72	0.94
ADSGEGDFXAEGGGVR*	Peptide	Fibrinogen Cleavage Peptide	0.04	0.72	0.94
4-methylcatechol sulfate	Xenobiotics	Benzoate Metabolism	-0.09	0.72	0.94
3,7-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.12	0.72	0.94
4-hydroxybenzoate	Xenobiotics	Benzoate Metabolism	0.16	0.72	0.94
TL20:2n6 (eicosadienoic acid)	Lipid	Mole % Total Fatty Acid	0.03	0.73	0.94
fumarate	Energy	TCA Cycle	-0.03	0.73	0.95
2'-deoxyuridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.05	0.74	0.95
linoleoylcarnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.05	0.74	0.95
isobutyrylcarnitine (C4)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.04	0.74	0.95
trigonelline (N'-methylnicotinate)	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	-0.08	0.75	0.95
chenodeoxycholate	Lipid	Primary Bile Acid Metabolism	0.09	0.75	0.95
phenylcarnitine*	Xenobiotics	Chemical	0.11	0.75	0.95
3-methylxanthine	Xenobiotics	Xanthine Metabolism	0.11	0.75	0.95
N-formylmethionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.02	0.75	0.95
serylalanine	Peptide	Dipeptide	0.05	0.75	0.95
sphingosine 1-phosphate	Lipid	Sphingolipid Metabolism	-0.02	0.76	0.95
campesterol	Lipid	Sterol	0.05	0.76	0.95
catechol sulfate	Xenobiotics	Benzoate Metabolism	-0.07	0.76	0.95
3-hydroxylaurate	Lipid	Fatty Acid, Monohydroxy	-0.03	0.76	0.95
oleate (18:1n9)	Lipid	Long Chain Fatty Acid	-0.03	0.76	0.95

palmitoyl-palmitoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.04	0.76	0.95
adenosine 3',5'-cyclic monophosphate (cAMP)	Nucleotide	Purine Metabolism, Adenine containing	-0.07	0.76	0.95
5alpha-pregnan-3beta,20alpha-diol monosulfate (2)	Lipid	Steroid	-0.11	0.76	0.95
1-eicosadienoyl-GPC* (20:2)*	Lipid	Lysolipid	-0.04	0.77	0.95
N-acetylalanine	Amino Acid	Alanine and Aspartate Metabolism	0.01	0.77	0.95
stearoyl-arachidonoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	-0.02	0.77	0.95
carnitine	Lipid	Carnitine Metabolism	-0.01	0.77	0.95
pyroglutamylvaline	Peptide	Dipeptide	0.03	0.77	0.95
2-hydroxydecanoate	Lipid	Fatty Acid, Monohydroxy	0.04	0.78	0.95
pregnenolone sulfate	Lipid	Steroid	-0.06	0.78	0.95
salicyluric glucuronide*	Xenobiotics	Drug	0.16	0.78	0.95
TL22:5n6 (osbond acid)	Lipid	Mole % Total Fatty Acid	0.03	0.78	0.95
laurylcarnitine (C12)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.03	0.79	0.95
N1-Methyl-2-pyridone-5-carboxamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	0.04	0.79	0.95
2-stearoylglycerophosphoinositol*	Lipid	Lysolipid	-0.05	0.79	0.95
cysteine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.03	0.79	0.95
eicosenoate (20:1n9 or 1n11)	Lipid	Long Chain Fatty Acid	0.03	0.79	0.95
oleoyl sphingomyelin	Lipid	Sphingolipid Metabolism	0.02	0.79	0.95
phenylacetate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.04	0.79	0.95
N-acetylalliin	Xenobiotics	Food Component/Plant	0.11	0.79	0.95
1-methylurate	Xenobiotics	Xanthine Metabolism	-0.07	0.79	0.95
3-ureidopropionate	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.03	0.79	0.95
N-acetylvaline	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.01	0.80	0.95
erucate (22:1n9)	Lipid	Long Chain Fatty Acid	0.03	0.80	0.95
isovalerylcarnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.03	0.80	0.95
taurocholate	Lipid	Primary Bile Acid Metabolism	-0.10	0.80	0.95
dihydroorotate	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.06	0.80	0.96
gamma-glutamylisoleucine*	Peptide	Gamma-glutamyl Amino Acid	0.02	0.80	0.96
gamma-glutamylglutamate	Peptide	Gamma-glutamyl Amino Acid	0.04	0.81	0.96
aspartylleucine	Peptide	Dipeptide	0.04	0.81	0.96
decanoylcarnitine (C10)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.02	0.82	0.97
hexanoylcarnitine (C6)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.02	0.82	0.97
2-hydroxyisobutyrate	Xenobiotics	Chemical	0.02	0.82	0.97

1-arachidonoyl glycerophosphate	Lipid	Lysolipid	0.03	0.82	0.97
tyrosylglutamine	Peptide	Dipeptide	0.04	0.84	0.97
gamma-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.03	0.84	0.97
thymol sulfate	Xenobiotics	Food Component/Plant	0.09	0.84	0.97
N3-methyluridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.03	0.84	0.97
glycodeoxycholate	Lipid	Secondary Bile Acid Metabolism	0.09	0.84	0.97
13-methylmyristic acid	Lipid	Fatty Acid, Branched	0.02	0.84	0.97
2,3-dihydroxyisovalerate	Xenobiotics	Food Component/Plant	0.07	0.84	0.97
3-methoxycatechol sulfate (2)	Xenobiotics	Benzoate Metabolism	-0.06	0.85	0.97
tryptophylglutamate	Peptide	Dipeptide	0.08	0.85	0.97
glycine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.02	0.85	0.97
fructose	Carbohydrate	Fructose, Mannose and Galactose Metabolism	-0.02	0.85	0.97
threitol	Carbohydrate	Pentose Metabolism	0.02	0.85	0.97
1-docosapentaenoyl-GPC* (22:5n6)*	Lipid	Lysolipid	-0.06	0.85	0.97
2-hydroxyhippurate (salicylurate)	Xenobiotics	Benzoate Metabolism	-0.08	0.85	0.97
glycylglycine	Peptide	Dipeptide	-0.09	0.85	0.97
epiandrosterone sulfate	Lipid	Steroid	-0.05	0.85	0.97
threonylphenylalanine	Peptide	Dipeptide	0.08	0.85	0.97
alpha-glutamyltyrosine	Peptide	Dipeptide	0.06	0.85	0.97
glycochenodeoxycholate	Lipid	Primary Bile Acid Metabolism	-0.05	0.85	0.97
imidazole propionate	Amino Acid	Histidine Metabolism	-0.04	0.86	0.98
serylleucine	Peptide	Dipeptide	-0.07	0.86	0.98
10-heptadecenoate (17:1n7)	Lipid	Long Chain Fatty Acid	0.02	0.86	0.98
glycoursodeoxycholate	Lipid	Secondary Bile Acid Metabolism	-0.06	0.87	0.98
TL20:4n6 (arachidonic acid)	Lipid	Mole % Total Fatty Acid	0.01	0.87	0.98
1-methylhistidine	Amino Acid	Histidine Metabolism	-0.02	0.88	0.98
N-acetylhistidine	Amino Acid	Histidine Metabolism	0.03	0.88	0.98
tryptophan betaine	Amino Acid	Tryptophan Metabolism	-0.04	0.88	0.98
valerylcarnitine (C5)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.06	0.88	0.98
ribose	Carbohydrate	Pentose Metabolism	0.03	0.88	0.98
myo-inositol	Lipid	Inositol Metabolism	0.01	0.89	0.98
stearoyl-linoleoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.01	0.89	0.98
gamma-glutamylleucine	Peptide	Gamma-glutamyl Amino Acid	-0.01	0.89	0.98
3-hydroxy-2-ethylpropionate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.01	0.89	0.98
cis-Cyclo[L-ala-L-Pro]	Peptide	Dipeptide	0.01	0.89	0.98

N6-carbamoylthreonyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.01	0.89	0.98
N-6-trimethyllysine	Amino Acid	Lysine Metabolism	-0.02	0.90	0.98
N-acetylmethionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.02	0.90	0.98
5-acetylamino-6-amino-3-methyluracil	Xenobiotics	Xanthine Metabolism	0.06	0.90	0.98
3-phenylpropionate (hydrocinnamate)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.04	0.90	0.98
7-methylxanthine	Xenobiotics	Xanthine Metabolism	-0.04	0.90	0.98
1-heptadecanoyl-GPC (17:0)	Lipid	Lysolipid	0.02	0.90	0.98
betonicine	Xenobiotics	Food Component/Plant	0.07	0.90	0.98
bilirubin (E,E)*	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	-0.02	0.91	0.98
13-HODE + 9-HODE	Lipid	Fatty Acid, Monohydroxy	0.02	0.91	0.98
glutarate (pentanedioate)	Amino Acid	Lysine Metabolism	-0.02	0.91	0.98
glycylphenylalanine	Peptide	Dipeptide	0.03	0.91	0.98
laurate (12:0)	Lipid	Medium Chain Fatty Acid	-0.01	0.91	0.98
maltose	Carbohydrate	Glycogen Metabolism	0.03	0.91	0.98
N-oleoyltaurine	Lipid	Endocannabinoid	-0.03	0.91	0.98
ergothioneine	Xenobiotics	Food Component/Plant	0.02	0.91	0.98
delta-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.03	0.92	0.98
caprate (10:0)	Lipid	Medium Chain Fatty Acid	0.01	0.92	0.98
2-arachidonoylglycerophosphoinositol*	Lipid	Lysolipid	-0.02	0.92	0.98
xanthine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.01	0.92	0.98
1-oleoyl-GPI (18:1)*	Lipid	Lysolipid	0.01	0.92	0.98
acisoga	Amino Acid	Polyamine Metabolism	0.01	0.92	0.98
2-aminoadipate	Amino Acid	Lysine Metabolism	0.01	0.92	0.98
1-oleoylplasmylethanolamine*	Lipid	Lysolipid	0.01	0.92	0.98
deoxycholate	Lipid	Secondary Bile Acid Metabolism	0.02	0.92	0.98
pyridoxal	Cofactors and Vitamins	Vitamin B6 Metabolism	-0.04	0.92	0.98
linoleate (18:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	-0.01	0.94	0.99
N-(2-furoyl)glycine	Xenobiotics	Food Component/Plant	-0.01	0.94	0.99
docosatrienoate (22:3n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	-0.01	0.94	0.99
glutaroylcarnitine (C5)	Amino Acid	Lysine Metabolism	0.01	0.94	0.99
TL18:1n7 (avaccenic acid)	Lipid	Mole % Total Fatty Acid	0.003	0.94	0.99
succinylcarnitine (C4)	Energy	TCA Cycle	-0.01	0.94	0.99
1-palmitoleoyl-GPI* (16:1)*	Lipid	Lysolipid	0.03	0.94	0.99

palmitoyl sphingomyelin	Lipid	Sphingolipid Metabolism	0.003	0.95	0.99
gamma-glutamyllysine	Peptide	Gamma-glutamyl Amino Acid	-0.01	0.95	0.99
1-linoleoyl-GPI* (18:2)*	Lipid	Lysolipid	-0.01	0.95	0.99
3-methylglutaryl carnitine (1)	Amino Acid	Lysine Metabolism	0.01	0.95	0.99
N-acetylserine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.003	0.96	0.99
3-methylhistidine	Amino Acid	Histidine Metabolism	0.01	0.96	0.99
gamma-glutamyl-2-aminobutyrate	Peptide	Gamma-glutamyl Amino Acid	0.01	0.96	0.99
gamma-glutamylvaline	Peptide	Gamma-glutamyl Amino Acid	0.003	0.96	0.99
DSGEGDFXAEGGGVR*	Peptide	Fibrinogen Cleavage Peptide	-0.01	0.96	0.99
dihomolinoleate (20:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.004	0.97	0.99
TL24:0 (lignoceric acid)	Lipid	Mole % Total Fatty Acid	0.01	0.97	0.99
3-(4-hydroxyphenyl)lactate (HPLA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.003	0.97	0.99
p-cresol-glucuronide*	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.02	0.97	0.99
1-methyladenosine	Nucleotide	Purine Metabolism, Adenine containing	-0.002	0.97	0.99
5alpha-androstan-3alpha,17beta-diol monosulfate (1)	Lipid	Steroid	0.01	0.97	0.99
xylose	Carbohydrate	Pentose Metabolism	0.01	0.97	0.99
linolenate (18:3n3 or 3n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	-0.004	0.97	0.99
creatinine	Amino Acid	Creatine Metabolism	-0.002	0.97	0.99
adenosine	Nucleotide	Purine Metabolism, Adenine containing	-0.01	0.97	0.99
xylonate	Carbohydrate	Pentose Metabolism	-0.01	0.97	0.99
1-methylxanthine	Xenobiotics	Xanthine Metabolism	-0.01	0.97	0.99
lysine	Amino Acid	Lysine Metabolism	0.002	0.97	0.99
coprostanol	Lipid	Sterol	-0.01	0.97	0.99
palmitoleate (16:1n7)	Lipid	Long Chain Fatty Acid	-0.004	0.98	0.99
beta-hydroxyisovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.003	0.98	0.99
oleoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.001	0.99	0.99
6-oxopiperidine-2-carboxylic acid	Xenobiotics	Drug	0.001	0.99	0.99
palmitoyl ethanolamide	Lipid	Endocannabinoid	-0.001	0.99	0.99
etiocholanolone glucuronide	Lipid	Steroid	-0.004	0.99	0.99
myristoleoyl carnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.002	0.99	0.99
sorbitol	Carbohydrate	Fructose, Mannose and Galactose Metabolism	-0.001	1.00	1.00
palmitoyl-palmitoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.0003	0.97	1.00

*Covariates: age, sex, diabetes, hypertension, BMI, and liver fibrosis stage

TCA = tricarboxylic acid cycle; GPE = Glycerophosphoethanolamine; GPC = Glycerophosphocholine; SAM = S-Adenosyl methionine

Table S5: Diastolic dysfunction full results*

Metabolite	Pathway	Sub-Pathway	Log Fold change	Unadjusted p-value	Adjusted p-value
azelate (nonanedioate; C9)	Lipid	Fatty Acid, Dicarboxylate	-0.33	0.001	0.49
1-arachidonoyl-GPE* (20:4)*	Lipid	Lysolipid	0.21	0.003	0.49
1-arachidonylglycerol	Lipid	Monoacylglycerol	0.25	0.004	0.49
2-arachidonoyl-GPC* (20:4)*	Lipid	Lysolipid	0.29	0.01	0.49
1-arachidonoyl-GPC* (20:4)*	Lipid	Lysolipid	0.24	0.01	0.49
palmitoyl-arachidonoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.17	0.01	0.49
TL18:3n6 (g-linolenic acid)	Lipid	Mole % Total Fatty Acid	0.22	0.01	0.49
citrate	Energy	TCA Cycle	-0.17	0.01	0.49
1-docosahexaenoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.26	0.01	0.49
2-palmitoleoyl-GPC* (16:1)*	Lipid	Lysolipid	0.48	0.01	0.49
N6-acetyllsine	Amino Acid	Lysine Metabolism	0.13	0.01	0.49
2-arachidonoyl-GPE* (20:4)*	Lipid	Lysolipid	0.47	0.01	0.49
xylitol	Carbohydrate	Pentose Metabolism	0.40	0.01	0.49
sulfate*	Xenobiotics	Chemical	0.09	0.01	0.59
myristoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.12	0.01	0.59
1-palmitoyl-GPC (16:0)	Lipid	Lysolipid	0.19	0.01	0.59
cysteine s-sulfate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.18	0.02	0.59
S-methylcysteine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.23	0.02	0.59
ethylmalonate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.25	0.02	0.64
orotate	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.37	0.02	0.64
orotidine	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.50	0.02	0.65
2-myristoyl-GPC* (14:0)*	Lipid	Lysolipid	0.44	0.02	0.67
1-myristoyl-GPC (14:0)	Lipid	Lysolipid	0.31	0.02	0.67
TL20:3n9 (mead acid)	Lipid	Mole % Total Fatty Acid	0.30	0.03	0.67
1-stearoyl-GPE (18:0)	Lipid	Lysolipid	0.18	0.03	0.67
adrenate (22:4n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.18	0.03	0.67
1-linolenylglycerophosphocholine (18:3n3)*	Lipid	Lysolipid	0.27	0.03	0.67
arachidonate (20:4n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.12	0.03	0.67
biliverdin	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	-0.41	0.03	0.67
2-hydroxy-3-methylvalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.20	0.03	0.67

alpha-ketoglutarate	Energy	TCA Cycle	0.22	0.04	0.67
fucose	Carbohydrate	Pentose Metabolism	0.21	0.04	0.67
1-oleoyl-GPC (18:1)	Lipid	Lysolipid	0.21	0.04	0.67
2-stearoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.21	0.04	0.67
3-methylglutaconate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.31	0.04	0.67
1-palmitoleoyl-GPC* (16:1)*	Lipid	Lysolipid	0.26	0.04	0.67
2-palmitoyl-GPC* (16:0)*	Lipid	Lysolipid	0.20	0.04	0.67
hexadecanedioate (C16)	Lipid	Fatty Acid, Dicarboxylate	-0.25	0.04	0.67
1-stearoylglycerol (18:0)	Lipid	Monoacylglycerol	0.59	0.04	0.67
2'-deoxyuridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.27	0.04	0.67
2-docosahexaenoylglycerol*	Lipid	Monoacylglycerol	0.66	0.04	0.68
xanthosine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.21	0.04	0.68
1-eicosapentaenoylglycerophosphocholine (20:5n3)*	Lipid	Lysolipid	0.36	0.05	0.68
3-methylglutaryl carnitine (2)	Amino Acid	Lysine Metabolism	0.31	0.05	0.68
methyl glucopyranoside (alpha + beta)	Xenobiotics	Food Component/Plant	-0.58	0.05	0.70
N6-succinyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.15	0.05	0.70
sphinganine	Lipid	Sphingolipid Metabolism	0.63	0.05	0.70
1-stearoyl-GPC (18:0)	Lipid	Lysolipid	0.22	0.05	0.70
2-arachidonoyl glycerol	Lipid	Monoacylglycerol	0.20	0.05	0.70
5,6-dihydrothymine	Nucleotide	Pyrimidine Metabolism, Thymine containing	-0.15	0.06	0.72
phenylalanyl leucine	Peptide	Dipeptide	0.57	0.06	0.72
1-oleoyl-GPE (18:1)	Lipid	Lysolipid	0.16	0.06	0.72
3b-hydroxy-5-cholenoic acid	Lipid	Secondary Bile Acid Metabolism	-0.47	0.06	0.72
methionine sulfone	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.27	0.06	0.72
stearoyl-arachidonoyl-glycerophosphoethanolamine (1)*	Lipid	Lysolipid	0.20	0.06	0.72
1-palmitoyl-GPE (16:0)	Lipid	Lysolipid	0.16	0.06	0.72
2-palmitoylglycerol (16:0)	Lipid	Monoacylglycerol	0.29	0.06	0.72
stearoyl-arachidonoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.13	0.07	0.72
1-stearoylplasmylethanolamine*	Lipid	Lysolipid	0.21	0.07	0.72
1-docosapentaenoyl-GPC* (22:5n3)*	Lipid	Lysolipid	0.20	0.07	0.72
N-acetylputrescine	Amino Acid	Polyamine Metabolism	0.18	0.07	0.72

lanosterol	Lipid	Sterol	-0.46	0.07	0.72
1-pentadecanoylglycerophosphocholine (15:0)*	Lipid	Lysolipid	0.18	0.07	0.72
myristoylcarnitine	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.24	0.07	0.72
1-docosahexaenoylglycerol	Lipid	Monoacylglycerol	0.24	0.07	0.72
tetradecanedioate (C14)	Lipid	Fatty Acid, Dicarboxylate	-0.22	0.08	0.72
eugenol sulfate	Xenobiotics	Food Component/Plant	0.71	0.08	0.72
2-oleoyl-GPC* (18:1)*	Lipid	Lysolipid	0.17	0.08	0.72
2-hydroxyisobutyrate	Xenobiotics	Chemical	0.17	0.08	0.72
propionylglycine (C3)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	0.21	0.08	0.72
2-stearoyl-GPC* (18:0)*	Lipid	Lysolipid	0.23	0.08	0.72
1-linolenoylglycerol	Lipid	Monoacylglycerol	0.20	0.08	0.74
1-docosahexaenoyl-GPC* (22:6)*	Lipid	Lysolipid	0.20	0.08	0.74
1-palmitoylplasmenylethanolamine *	Lipid	Lysolipid	0.13	0.08	0.74
3-hydroxy-3-methylglutarate	Lipid	Mevalonate Metabolism	0.12	0.09	0.74
leucylalanine	Peptide	Dipeptide	0.41	0.09	0.74
caprylate (8:0)	Lipid	Medium Chain Fatty Acid	-0.11	0.09	0.74
indoleacetylglutamine	Amino Acid	Tryptophan Metabolism	0.54	0.09	0.74
palmitoyl-linoleoylglycerophosphocholine (2)*	Lipid	Lysolipid	-0.11	0.09	0.74
3-methoxytyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.11	0.09	0.74
malonate (propanedioate)	Lipid	Fatty Acid Synthesis	-0.26	0.09	0.74
ribitol	Carbohydrate	Pentose Metabolism	0.10	0.09	0.74
serylleucine	Peptide	Dipeptide	-0.62	0.09	0.74
benzoate	Xenobiotics	Benzoate Metabolism	-0.11	0.10	0.79
1,2,3-benzenetriol sulfate (2)	Xenobiotics	Chemical	-0.74	0.10	0.79
erythronate*	Carbohydrate	Aminosugar Metabolism	0.10	0.11	0.82
1-eicosatrienoyl-GPC* (20:3)*	Lipid	Lysolipid	0.16	0.11	0.84
2-eicosatrienoyl-GPC* (20:3)*	Lipid	Lysolipid	0.14	0.11	0.84
adenosine	Nucleotide	Purine Metabolism, Adenine containing	-0.28	0.12	0.84
3-methoxycatechol sulfate (1)	Xenobiotics	Benzoate Metabolism	-0.57	0.12	0.84
N-acetyltryptophan	Amino Acid	Tryptophan Metabolism	0.17	0.12	0.84
glycylvaline	Peptide	Dipeptide	0.58	0.12	0.84
phenyllactate (PLA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.12	0.12	0.84
glutamine	Amino Acid	Glutamate Metabolism	-0.06	0.12	0.84
dimethyl sulfone	Xenobiotics	Chemical	0.48	0.12	0.84

cytidine	Nucleotide	Pyrimidine Metabolism, Cytidine containing	0.14	0.12	0.84
alpha-hydroxyisovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.18	0.13	0.85
1-oleoylplasménylethanolamine*	Lipid	Lysolipid	0.15	0.13	0.86
phenylalanylserine	Peptide	Dipeptide	-0.50	0.13	0.87
2-palmitoyl-GPE* (16:0)*	Lipid	Lysolipid	0.17	0.14	0.87
1-methyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.08	0.14	0.87
docosahexaenoate (DHA; 22:6n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.16	0.14	0.87
3-methyl catechol sulfate (1)	Xenobiotics	Benzoate Metabolism	0.45	0.14	0.87
inositol 1-phosphate (I1P)	Lipid	Inositol Metabolism	0.16	0.14	0.87
caproate (6:0)	Lipid	Medium Chain Fatty Acid	-0.09	0.14	0.87
eicosenoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.12	0.14	0.87
tyrosylglutamate	Peptide	Dipeptide	0.38	0.14	0.87
3-hydroxy-2-ethylpropionate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.11	0.14	0.87
palmitoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.10	0.14	0.87
stearoylcarnitine (C18)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.17	0.15	0.87
2-docosahexaenoyl-GPC* (22:6)*	Lipid	Lysolipid	0.21	0.16	0.89
pyroglutamylglutamine	Peptide	Dipeptide	0.24	0.16	0.89
3-indoxyl sulfate	Amino Acid	Tryptophan Metabolism	0.21	0.16	0.89
eicosapentaenoate (EPA; 20:5n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.21	0.16	0.89
cyclo(pro-pro)	Peptide	Dipeptide	0.16	0.16	0.89
methyl indole-3-acetate	Xenobiotics	Food Component/Plant	0.20	0.16	0.89
12-HETE	Lipid	Eicosanoid	-0.36	0.16	0.89
glutamate	Amino Acid	Glutamate Metabolism	0.11	0.17	0.89
aspartylphenylalanine	Peptide	Dipeptide	0.31	0.17	0.89
tyramine O-sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.38	0.17	0.89
2-arachidonoylglycerophosphoinositol*	Lipid	Lysolipid	0.29	0.17	0.89
3-methoxytyramine sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.16	0.17	0.89
cysteine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.14	0.18	0.89
glycolithocholate sulfate*	Lipid	Secondary Bile Acid Metabolism	-0.36	0.18	0.89
mannose	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.10	0.18	0.89
3-ureidopropionate	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.13	0.18	0.89
dodecanedioate (C12)	Lipid	Fatty Acid, Dicarboxylate	-0.17	0.18	0.89

N-methylproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.33	0.18	0.89
1,3-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.55	0.18	0.89
1-arachidoyl-GPC (20:0)	Lipid	Lysolipid	0.42	0.19	0.89
1-eicosenoylglycerophosphocholine (20:1n9)*	Lipid	Lysolipid	0.19	0.19	0.89
phenylpyruvate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.10	0.19	0.89
palmitoylcarnitine (C16)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.14	0.19	0.89
docosapentaenoate (DPA; 22:5n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.13	0.19	0.89
betaine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.08	0.19	0.89
TL20:4n6 (arachidonic acid)	Lipid	Mole % Total Fatty Acid	0.09	0.19	0.89
kynurenate	Amino Acid	Tryptophan Metabolism	-0.13	0.19	0.89
oleoylcarnitine (C18)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.16	0.19	0.89
octadecanedioate (C18)	Lipid	Fatty Acid, Dicarboxylate	-0.16	0.20	0.89
N2-methylguanosine	Nucleotide	Purine Metabolism, Guanine containing	0.13	0.20	0.89
TL20:2n6 (eicosadienoic acid)	Lipid	Mole % Total Fatty Acid	0.10	0.20	0.89
1-heptadecanoyl-GPC (17:0)	Lipid	Lysolipid	0.23	0.20	0.89
N6-methyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.13	0.20	0.89
5-HETE	Lipid	Eicosanoid	0.22	0.20	0.89
dimethylarginine (ADMA + SDMA)	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.04	0.20	0.89
cis-Cyclo[L-ala-L-Pro]	Peptide	Dipeptide	0.12	0.20	0.89
N-acetylmethionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.20	0.20	0.89
gamma-glutamyllysine	Peptide	Gamma-glutamyl Amino Acid	0.10	0.21	0.89
stearate (18:0)	Lipid	Long Chain Fatty Acid	0.06	0.21	0.89
histidyltryptophan	Peptide	Dipeptide	-0.26	0.21	0.89
TL20:5n3 (eicosapentaenoic acid)	Lipid	Mole % Total Fatty Acid	0.19	0.21	0.89
imidazole propionate	Amino Acid	Histidine Metabolism	0.24	0.21	0.89
C-glycosyltryptophan	Amino Acid	Tryptophan Metabolism	0.06	0.21	0.89
phenylacetylglutamine	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.21	0.21	0.89
desmosterol	Lipid	Sterol	-0.21	0.21	0.89
glucuronate	Carbohydrate	Aminosugar Metabolism	0.12	0.21	0.89
cyclo(gly-pro)	Peptide	Dipeptide	0.19	0.21	0.89
sphingomyelin	Lipid	Sphingolipid Metabolism	0.09	0.21	0.89
4-hydroxyhippurate	Xenobiotics	Benzoate Metabolism	-0.24	0.22	0.89
TL18:2n6 (linoleic acid)	Lipid	Mole % Total Fatty Acid	-0.06	0.22	0.90

16-hydroxypalmitate	Lipid	Fatty Acid, Monohydroxy	-0.09	0.22	0.92
allo-isoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.08	0.23	0.92
2-oleoyl-GPE* (18:1)*	Lipid	Lysolipid	0.36	0.23	0.92
docosapentaenoate (n6 DPA; 22:5n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.09	0.23	0.92
9,10-DiHOME	Lipid	Fatty Acid, Dihydroxy	-0.25	0.23	0.92
TL22:5n3 (docosapentaenoic acid)	Lipid	Mole % Total Fatty Acid	0.08	0.23	0.92
2-aminooctanoate	Lipid	Fatty Acid, Amino	0.15	0.24	0.92
7-alpha-hydroxycholesterol	Lipid	Sterol	0.21	0.24	0.92
thyroxine	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.32	0.24	0.92
gamma-glutamylvaline	Peptide	Gamma-glutamyl Amino Acid	0.06	0.24	0.92
saccharin	Xenobiotics	Food Component/Plant	0.70	0.24	0.92
glucose	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.06	0.24	0.92
hypotaurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.24	0.25	0.93
10-undecenoate (11:1n1)	Lipid	Medium Chain Fatty Acid	-0.11	0.25	0.93
1-palmitoylglycerophosphate	Lipid	Lysolipid	0.18	0.25	0.93
salicylic glucuronide*	Xenobiotics	Drug	0.60	0.25	0.93
gamma-glutamylalanine	Peptide	Gamma-glutamyl Amino Acid	0.11	0.25	0.93
cholesterol	Lipid	Sterol	-0.07	0.25	0.93
taurothiocholate 3-sulfate	Lipid	Secondary Bile Acid Metabolism	-0.38	0.25	0.93
alanine	Amino Acid	Alanine and Aspartate Metabolism	0.05	0.26	0.93
taurocholate sulfate	Lipid	Secondary Bile Acid Metabolism	-0.19	0.26	0.93
stearidonate (18:4n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.14	0.26	0.93
7-methylurate	Xenobiotics	Xanthine Metabolism	-0.51	0.26	0.93
serine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.07	0.26	0.93
glutaryl carnitine (C5)	Amino Acid	Lysine Metabolism	0.08	0.26	0.93
1-dihomo-linolenylglycerol (alpha, gamma)	Lipid	Monoacylglycerol	0.11	0.27	0.93
lactate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.06	0.27	0.93
pseudouridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.05	0.27	0.93
taurochenodeoxycholate	Lipid	Primary Bile Acid Metabolism	-0.33	0.27	0.93
N-acetyl-3-methylhistidine*	Amino Acid	Histidine Metabolism	0.30	0.27	0.93
oleoyl sphingomyelin	Lipid	Sphingolipid Metabolism	0.07	0.28	0.93

phenylacetate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.17	0.28	0.93
delta-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.25	0.28	0.93
1-arachidonoylglycerophosphate	Lipid	Lysolipid	0.12	0.28	0.93
4-acetamidobutanoate	Amino Acid	Polyamine Metabolism	0.08	0.28	0.93
theobromine	Xenobiotics	Xanthine Metabolism	-0.33	0.28	0.93
indolepropionate	Amino Acid	Tryptophan Metabolism	-0.20	0.29	0.93
butyrylcarnitine (C4)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	0.12	0.29	0.93
salicylate	Xenobiotics	Drug	0.43	0.29	0.93
1,2-propanediol	Xenobiotics	Chemical	0.23	0.29	0.93
N-acetyl-1-methylhistidine*	Amino Acid	Histidine Metabolism	0.15	0.29	0.93
TL18:1n9 (oleic acid)	Lipid	Mole % Total Fatty Acid	0.04	0.29	0.93
1-eicosadienoyl-GPC* (20:2)*	Lipid	Lysolipid	0.14	0.29	0.93
N3-methyluridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.14	0.29	0.93
N-oleoyltaurine	Lipid	Endocannabinoid	0.25	0.29	0.93
N-acetylcarnosine	Peptide	Dipeptide Derivative	-0.08	0.29	0.93
pregnen-diol disulfate*	Lipid	Steroid	0.16	0.30	0.93
methionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.05	0.30	0.93
2-ethylhexanoic acid	Xenobiotics	Chemical	-0.09	0.30	0.93
gamma-CEHC glucuronide*	Cofactors and Vitamins	Tocopherol Metabolism	0.31	0.30	0.93
caprate (10:0)	Lipid	Medium Chain Fatty Acid	-0.10	0.30	0.93
1-myristoylglycerol (14:0)	Lipid	Monoacylglycerol	0.15	0.30	0.93
gamma-glutamylisoleucine*	Peptide	Gamma-glutamyl Amino Acid	0.07	0.31	0.93
3-hydroxypyridine sulfate	Xenobiotics	Chemical	0.29	0.31	0.93
2-piperidinone	Xenobiotics	Food Component/Plant	0.27	0.31	0.93
2-linoleoyl-GPC* (18:2)*	Lipid	Lysolipid	0.10	0.31	0.93
12,13-DiHOME	Lipid	Fatty Acid, Dihydroxy	-0.14	0.32	0.93
4-methylcatechol sulfate	Xenobiotics	Benzoate Metabolism	-0.24	0.32	0.93
dopamine sulfate (2)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.11	0.32	0.93
palmitoyl-arachidonoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.11	0.32	0.93
N2-acetyllysine	Amino Acid	Lysine Metabolism	0.15	0.32	0.93
indolelactate	Amino Acid	Tryptophan Metabolism	0.07	0.32	0.93
arabonate	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	0.09	0.32	0.93
N-palmitoyl glycine	Lipid	Fatty Acid Metabolism(Acyl Glycine)	-0.12	0.32	0.93
6-oxopiperidine-2-carboxylic acid	Xenobiotics	Drug	0.08	0.33	0.93
arabitol	Carbohydrate	Pentose Metabolism	0.08	0.33	0.93

tryptophan betaine	Amino Acid	Tryptophan Metabolism	0.25	0.33	0.93
2-hydroxyhippurate (salicylurate)	Xenobiotics	Benzoate Metabolism	0.39	0.33	0.93
glycylphenylalanine	Peptide	Dipeptide	-0.25	0.33	0.93
5alpha-pregnan-3beta,20alpha-diol monosulfate (2)	Lipid	Steroid	0.34	0.33	0.93
myo-inositol	Lipid	Inositol Metabolism	0.05	0.33	0.93
2-stearoylglycerophosphoinositol*	Lipid	Lysolipid	-0.16	0.34	0.93
glycylproline	Peptide	Dipeptide	-0.24	0.34	0.93
5-methylthioadenosine (MTA)	Amino Acid	Polyamine Metabolism	0.29	0.34	0.93
adenosine 3',5'-cyclic monophosphate (cAMP)	Nucleotide	Purine Metabolism, Adenine containing	0.21	0.34	0.93
palmitoleoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.05	0.34	0.93
5alpha-pregnan-3beta,20alpha-diol disulfate	Lipid	Steroid	0.19	0.34	0.93
erythritol	Xenobiotics	Food Component/Plant	0.12	0.34	0.93
methysuccinate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.07	0.34	0.93
prolylhydroxyproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.12	0.34	0.93
gamma-glutamyl-2-aminobutyrate	Peptide	Gamma-glutamyl Amino Acid	0.17	0.34	0.93
p-cresol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.26	0.35	0.93
TL22:6n3 (docosahexaenoic acid)	Lipid	Mole % Total Fatty Acid	0.09	0.35	0.93
hydroquinone sulfate	Xenobiotics	Drug	-0.26	0.35	0.93
2,3-dihydroxyisovalerate	Xenobiotics	Food Component/Plant	0.32	0.35	0.93
myristoleoylcarnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.14	0.35	0.93
pantothenate (Vitamin B5)	Cofactors and Vitamins	Pantothenate and CoA Metabolism	0.11	0.35	0.93
dihomolinolenate (20:3n3 or 3n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.05	0.35	0.93
dihomolinoleate (20:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.09	0.35	0.93
5,6-dihydrouracil	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.07	0.36	0.93
1-linoleoyl-GPC (18:2)	Lipid	Lysolipid	0.07	0.36	0.93
paraxanthine	Xenobiotics	Xanthine Metabolism	-0.44	0.36	0.93
3-hydroxymyristate	Lipid	Fatty Acid, Monohydroxy	0.08	0.36	0.93
valylarginine	Peptide	Dipeptide	0.23	0.36	0.93
coprostanol	Lipid	Sterol	0.28	0.36	0.93
imidazole lactate	Amino Acid	Histidine Metabolism	0.08	0.36	0.93
pregnenolone sulfate	Lipid	Steroid	0.19	0.36	0.93
TL15:0 (pentadecanoic acid)	Lipid	Mole % Total Fatty Acid	-0.04	0.37	0.93
alpha-hydroxyisocaproate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.08	0.37	0.93

docosadienoate (22:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.08	0.37	0.93
N-acetylneuramate	Carbohydrate	Aminosugar Metabolism	0.10	0.37	0.93
N-acetyltaurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.11	0.38	0.93
laurylcarnitine (C12)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.10	0.38	0.93
7-dehydro-cholesterol	Lipid	Sterol	0.31	0.38	0.93
2-aminobutyrate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.07	0.38	0.93
1-palmitoylglycerol (16:0)	Lipid	Monoacylglycerol	0.08	0.38	0.93
N-acetylaspartate (NAA)	Amino Acid	Alanine and Aspartate Metabolism	-0.05	0.38	0.93
1-linoleoylglycerol (18:2)	Lipid	Monoacylglycerol	0.09	0.38	0.93
N-acetyl-aspartyl-glutamate (NAAG)	Amino Acid	Glutamate Metabolism	-0.06	0.38	0.93
5-oxoproline	Amino Acid	Glutathione Metabolism	-0.07	0.39	0.93
glycochenodeoxycholate	Lipid	Primary Bile Acid Metabolism	-0.21	0.39	0.93
glycocholenate sulfate*	Lipid	Secondary Bile Acid Metabolism	-0.09	0.39	0.93
hippurate	Xenobiotics	Benzoate Metabolism	-0.18	0.39	0.94
1-methylnicotinamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	-0.23	0.39	0.94
N-6-trimethyllysine	Amino Acid	Lysine Metabolism	-0.09	0.39	0.94
10-nonadecenoate (19:1n9)	Lipid	Long Chain Fatty Acid	0.08	0.40	0.94
dihydroorotate	Nucleotide	Pyrimidine Metabolism, Orotate containing	0.20	0.40	0.94
tyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.04	0.40	0.94
21-hydroxypregnenolone disulfate	Lipid	Steroid	0.14	0.40	0.94
glycoursodeoxycholate	Lipid	Secondary Bile Acid Metabolism	-0.29	0.40	0.94
4-hydroxychlorothalonil	Xenobiotics	Chemical	0.11	0.41	0.95
oxalate (ethanedioate)	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	-0.13	0.41	0.95
catechol sulfate	Xenobiotics	Benzoate Metabolism	-0.17	0.41	0.95
glycolate (hydroxyacetate)	Xenobiotics	Chemical	-0.05	0.41	0.95
2-methylmalonyl carnitine	Lipid	Fatty Acid Synthesis	-0.07	0.42	0.95
isovalerylcarnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.08	0.42	0.95
stigmasterol	Lipid	Sterol	-0.15	0.42	0.95
dopamine sulfate (1)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.13	0.42	0.95
alpha-glutamyltyrosine	Peptide	Dipeptide	-0.26	0.42	0.95
arachidate (20:0)	Lipid	Long Chain Fatty Acid	0.05	0.43	0.95
beta-hydroxyisovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.08	0.43	0.95
palmitoyl sphingomyelin	Lipid	Sphingolipid Metabolism	0.03	0.43	0.95

asparagine	Amino Acid	Alanine and Aspartate Metabolism	-0.03	0.43	0.95
piperine	Xenobiotics	Food Component/Plant	0.17	0.43	0.95
oleoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	0.04	0.43	0.95
cholestanol	Lipid	Sterol	-0.07	0.43	0.95
alpha-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.08	0.43	0.95
cyclohexanebutanoic acid	Xenobiotics	Chemical	-0.09	0.43	0.95
inosine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	-0.23	0.43	0.95
eicosanodioate	Lipid	Fatty Acid, Dicarboxylate	-0.10	0.44	0.95
3beta,7alpha-dihydroxy-5-cholestenoate	Lipid	Secondary Bile Acid Metabolism	0.24	0.44	0.95
xanthine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.08	0.44	0.95
eicosenoate (20:1n9 or 1n11)	Lipid	Long Chain Fatty Acid	0.07	0.44	0.95
isobutyrylglycine (C4)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.09	0.44	0.95
2-hydroxyoctanoate	Lipid	Fatty Acid, Monohydroxy	0.08	0.44	0.95
proline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.04	0.44	0.95
ribonate (ribonolactone)	Carbohydrate	Pentose Metabolism	-0.07	0.45	0.95
3-methyl-2-oxobutyrate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.04	0.45	0.95
ectoine	Xenobiotics	Chemical	0.20	0.45	0.95
linoleoylcarnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.10	0.45	0.95
pyruvate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.11	0.46	0.95
hydantoin-5-propionic acid	Amino Acid	Histidine Metabolism	0.17	0.46	0.95
cysteine-glutathione disulfide	Amino Acid	Glutathione Metabolism	-0.20	0.46	0.95
3-hydroxybutyrate (BHBA)	Lipid	Ketone Bodies	-0.14	0.46	0.95
histidylphenylalanine	Peptide	Dipeptide	0.21	0.47	0.95
allantoin	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	-0.11	0.47	0.95
1,3,7-trimethylurate	Xenobiotics	Xanthine Metabolism	-0.24	0.47	0.95
mannitol	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.22	0.47	0.95
alpha-ketobutyrate	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.14	0.47	0.95
squalene	Lipid	Sterol	0.20	0.47	0.95
3-(4-hydroxyphenyl)propionate	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.27	0.47	0.95
pyridoxine (Vitamin B6)	Cofactors and Vitamins	Vitamin B6 Metabolism	-0.06	0.47	0.95

TL16:1n7 (palmitoleic acid)	Lipid	Mole % Total Fatty Acid	0.07	0.47	0.95
ornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.06	0.47	0.95
pelargonate (9:0)	Lipid	Medium Chain Fatty Acid	-0.04	0.47	0.95
beta-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	-0.15	0.48	0.95
taurine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.07	0.48	0.95
aspartate	Amino Acid	Alanine and Aspartate Metabolism	0.07	0.48	0.95
TL20:1n9 (eicosaenoic acid)	Lipid	Mole % Total Fatty Acid	-0.03	0.48	0.95
1-methylhistidine	Amino Acid	Histidine Metabolism	0.07	0.48	0.95
taurocholate	Lipid	Primary Bile Acid Metabolism	-0.25	0.48	0.95
5alpha-androstan-3beta,17beta-diol disulfate	Lipid	Steroid	-0.18	0.48	0.95
N-formylmethionine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.03	0.49	0.95
4-androsten-3beta,17beta-diol disulfate (1)	Lipid	Steroid	0.15	0.49	0.95
tryptophylglutamate	Peptide	Dipeptide	-0.27	0.49	0.95
4-allylphenol sulfate	Xenobiotics	Food Component/Plant	0.17	0.49	0.96
chenodeoxycholate	Lipid	Primary Bile Acid Metabolism	-0.17	0.49	0.96
arginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.05	0.50	0.96
palmitate (16:0)	Lipid	Long Chain Fatty Acid	0.03	0.50	0.96
ADSGEGDFXAEGGGVR*	Peptide	Fibrinogen Cleavage Peptide	-0.06	0.50	0.96
phenol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.18	0.50	0.96
1,5-anhydroglucitol (1,5-AG)	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	-0.09	0.50	0.97
O-sulfo-L-tyrosine	Xenobiotics	Chemical	0.05	0.51	0.97
valine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.03	0.51	0.97
gamma-glutamylleucine	Peptide	Gamma-glutamyl Amino Acid	0.04	0.51	0.97
N-acetylphenylalanine	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.07	0.51	0.97
seryltyrosine	Peptide	Dipeptide	0.15	0.51	0.97
serylalanine	Peptide	Dipeptide	0.10	0.51	0.97
glycylglycine	Peptide	Dipeptide	-0.28	0.52	0.97
N-acetylglutamate	Amino Acid	Glutamate Metabolism	0.16	0.52	0.97
5alpha-pregnan-3beta,20beta-diol monosulfate (1)	Lipid	Steroid	-0.15	0.52	0.97
TLdm18:1n9 (plasmalogen oleic acid)	Lipid	Mole % Total Fatty Acid	0.06	0.52	0.97
indolebutyrate	Amino Acid	Tryptophan Metabolism	0.13	0.52	0.97
3-hydroxyoctanoate	Lipid	Fatty Acid, Monohydroxy	-0.07	0.52	0.97

4-hydroxyphenylpyruvate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.08	0.53	0.97
5-hydroxyindoleacetate	Amino Acid	Tryptophan Metabolism	0.06	0.53	0.97
urea	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.05	0.53	0.97
homovanillate (HVA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.07	0.53	0.97
3-methylhistidine	Amino Acid	Histidine Metabolism	0.15	0.53	0.97
threonate	Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	-0.10	0.53	0.97
N-acetyl glycine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.08	0.53	0.97
citrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.06	0.54	0.97
fructose	Carbohydrate	Fructose, Mannose and Galactose Metabolism	-0.05	0.54	0.97
caffeine	Xenobiotics	Xanthine Metabolism	-0.27	0.54	0.97
theophylline	Xenobiotics	Xanthine Metabolism	-0.24	0.54	0.97
beta-hydroxyisovalerylcarnitine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.05	0.54	0.97
hexanoylcarnitine (C6)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.05	0.54	0.97
1-arachidonoyl-GPI* (20:4)*	Lipid	Lysolipid	0.04	0.54	0.97
indoleacetate	Amino Acid	Tryptophan Metabolism	0.07	0.55	0.97
2-aminoheptanoate	Lipid	Fatty Acid, Amino	0.06	0.55	0.97
sorbitol	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.10	0.55	0.97
4-androsten-3beta,17beta-diol monosulfate (1)	Lipid	Steroid	0.12	0.55	0.97
N-acetylalanine	Amino Acid	Alanine and Aspartate Metabolism	0.02	0.55	0.97
palmitoyl-oleoyl-glycerophosphoglycerol (2)*	Lipid	Lysolipid	0.19	0.56	0.97
N-acetyltyrosine	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.06	0.56	0.97
1-eicosatrienoylglycerophosphoethanolamine*	Lipid	Lysolipid	0.14	0.56	0.97
adenine	Nucleotide	Purine Metabolism, Adenine containing	0.07	0.56	0.98
3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	Lipid	Fatty Acid, Dicarboxylate	0.21	0.56	0.98
glycine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.04	0.57	0.98
1,7-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.22	0.57	0.98
galactonate	Carbohydrate	Fructose, Mannose and Galactose Metabolism	0.25	0.57	0.98
homostachydrine*	Xenobiotics	Food Component/Plant	0.07	0.57	0.98
1-methylxanthine	Xenobiotics	Xanthine Metabolism	0.18	0.57	0.98
methionine sulfoxide	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	-0.05	0.57	0.98
2-hydroxydecanoate	Lipid	Fatty Acid, Monohydroxy	0.07	0.58	0.98

quinolinate	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	0.09	0.58	0.98
isoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.02	0.58	0.98
3-hydroxyisobutyrate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.05	0.58	0.98
threonine	Amino Acid	Glycine, Serine and Threonine Metabolism	-0.03	0.59	0.98
malate	Energy	TCA Cycle	-0.04	0.59	0.98
isoleucylglycine	Peptide	Dipeptide	-0.12	0.59	0.98
N-(2-furoyl)glycine	Xenobiotics	Food Component/Plant	0.10	0.59	0.98
lathosterol	Lipid	Sterol	-0.09	0.59	0.98
phenylalanine	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.02	0.59	0.98
andro steroid monosulfate (1)*	Lipid	Steroid	0.14	0.59	0.98
stearoyl-arachidonoyl-glycerophosphoinositol (1)*	Lipid	Lysolipid	0.04	0.59	0.98
1-oleoyl-GPI (18:1)*	Lipid	Lysolipid	0.07	0.59	0.98
stearoyl-linoleoyl-glycerophosphoethanolamine (1)*	Lipid	Lysolipid	-0.07	0.60	0.99
gamma-glutamyltryptophan	Peptide	Gamma-glutamyl Amino Acid	0.04	0.60	0.99
1-oleoylglycerol (18:1)	Lipid	Monoacylglycerol	0.06	0.61	0.99
13-HODE + 9-HODE	Lipid	Fatty Acid, Monohydroxy	-0.07	0.61	0.99
guanosine	Nucleotide	Purine Metabolism, Guanine containing	-0.17	0.61	0.99
3-(4-hydroxyphenyl)lactate (HPLA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.03	0.61	0.99
3-hydroxylaurate	Lipid	Fatty Acid, Monohydroxy	0.05	0.61	0.99
phenylalanyltryptophan	Peptide	Dipeptide	0.08	0.62	0.99
TL22:1n9 (erucic acid)	Lipid	Mole % Total Fatty Acid	-0.10	0.62	0.99
5-methyluridine (ribothymidine)	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.03	0.62	0.99
4-androsten-3beta,17beta-diol disulfate (2)	Lipid	Steroid	0.07	0.63	0.99
acisoga	Amino Acid	Polyamine Metabolism	0.04	0.63	0.99
TL14:0 (myristic acid)	Lipid	Mole % Total Fatty Acid	0.05	0.63	0.99
gamma-tocopherol	Cofactors and Vitamins	Tocopherol Metabolism	0.07	0.63	0.99
4-guanidinobutanoate	Amino Acid	Guanidino and Acetamido Metabolism	0.15	0.63	0.99
3-phenylpropionate (hydrocinnamate)	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.13	0.63	0.99
N-acetylserine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.02	0.63	0.99
pregn steroid monosulfate*	Lipid	Steroid	0.07	0.64	0.99
TLdm18:1n7 (plasmalogen vaccenic acid)	Lipid	Mole % Total Fatty Acid	-0.10	0.64	0.99
isovalerylglycine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.06	0.64	0.99

O-methylcatechol sulfate	Xenobiotics	Benzoate Metabolism	-0.10	0.64	0.99
TL22:5n6 (osbond acid)	Lipid	Mole % Total Fatty Acid	0.04	0.64	0.99
serotonin (5HT)	Amino Acid	Tryptophan Metabolism	0.12	0.64	0.99
beta-alanine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.05	0.64	0.99
homocitrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.06	0.65	0.99
quinat	Xenobiotics	Food Component/Plant	0.22	0.65	0.99
dimethylglycine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.04	0.65	0.99
gamma-CEHC	Cofactors and Vitamins	Tocopherol Metabolism	0.06	0.65	0.99
creatine	Amino Acid	Creatine Metabolism	0.05	0.65	0.99
palmitoyl ethanolamide	Lipid	Endocannabinoid	0.03	0.65	0.99
gentisate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.19	0.65	0.99
7-methylguanine	Nucleotide	Purine Metabolism, Guanine containing	-0.02	0.65	0.99
stearoyl-linoleoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	-0.03	0.66	0.99
2-linoleoyl-GPE* (18:2)*	Lipid	Lysolipid	0.05	0.66	0.99
N2,N5-diacetylornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.09	0.66	0.99
cholate	Lipid	Primary Bile Acid Metabolism	-0.17	0.66	0.99
N-acetylvaline	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.02	0.66	0.99
octanoylcarnitine (C8)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.04	0.66	0.99
isobutyrylcarnitine (C4)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.05	0.66	0.99
lysine	Amino Acid	Lysine Metabolism	0.02	0.66	0.99
trans-urocanate	Amino Acid	Histidine Metabolism	-0.05	0.67	0.99
tiglyl carnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.04	0.67	0.99
phenylcarnitine*	Xenobiotics	Chemical	-0.13	0.67	0.99
uridine	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.02	0.68	0.99
4-androsten-3alpha,17alpha-diol monosulfate (2)	Lipid	Steroid	0.10	0.68	0.99
gamma-glutamylphenylalanine	Peptide	Gamma-glutamyl Amino Acid	0.02	0.68	0.99
stearoyl-arachidonoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.08	0.68	0.99
xylose	Carbohydrate	Pentose Metabolism	0.08	0.69	0.99
gamma-glutamylglutamate	Peptide	Gamma-glutamyl Amino Acid	0.06	0.69	0.99
TL18:1n7 (avaccenic acid)	Lipid	Mole % Total Fatty Acid	0.02	0.69	0.99
myristate (14:0)	Lipid	Long Chain Fatty Acid	0.03	0.69	0.99
tartronate (hydroxymalonate)	Xenobiotics	Bacterial/Fungal	-0.06	0.69	0.99

1-methylimidazoleacetate	Amino Acid	Histidine Metabolism	0.07	0.70	0.99
bilirubin (E,E)*	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	0.07	0.70	0.99
prolylglycine	Peptide	Dipeptide	-0.07	0.70	0.99
glycocholate	Lipid	Primary Bile Acid Metabolism	-0.10	0.70	0.99
gamma-glutamylthreonine*	Peptide	Gamma-glutamyl Amino Acid	0.03	0.70	0.99
gamma-glutamylglutamine	Peptide	Gamma-glutamyl Amino Acid	-0.03	0.70	0.99
N-acetylleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.03	0.70	0.99
TL22:4n6 (adrenic acid)	Lipid	Mole % Total Fatty Acid	0.03	0.70	0.99
arabinose	Carbohydrate	Pentose Metabolism	0.08	0.70	0.99
S-adenosylhomocysteine (SAH)	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.05	0.71	0.99
androsterone sulfate	Lipid	Steroid	-0.09	0.71	0.99
docosatrienoate (22:3n3)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.04	0.71	0.99
nicotinamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	-0.05	0.71	0.99
trimethylamine N-oxide	Lipid	Phospholipid Metabolism	0.16	0.71	0.99
dehydroisoandrosterone sulfate (DHEA-S)	Lipid	Steroid	0.07	0.72	0.99
1,6-anhydroglucose	Xenobiotics	Food Component/Plant	-0.08	0.72	0.99
acetoacetate	Lipid	Ketone Bodies	-0.05	0.72	0.99
alpha-hydroxycaproate	Lipid	Fatty Acid, Monohydroxy	0.03	0.72	0.99
oleic ethanolamide	Lipid	Endocannabinoid	0.03	0.72	0.99
DSGEGDFXAEGGGVR*	Peptide	Fibrinogen Cleavage Peptide	-0.09	0.72	0.99
4-methyl-2-oxopentanoate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.02	0.72	0.99
pregnanediol-3-glucuronide	Lipid	Steroid	0.11	0.73	0.99
3beta,7beta-dihydroxy-5-cholestenoate	Lipid	Sterol	-0.03	0.73	0.99
1-methylguanosine	Nucleotide	Purine Metabolism, Guanine containing	-0.02	0.73	0.99
N-acetylcitrulline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.09	0.73	0.99
1-palmitoleoyl-GPI* (16:1)*	Lipid	Lysolipid	0.14	0.73	0.99
valerylcarnitine (C5)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.13	0.74	0.99
10-heptadecenoate (17:1n7)	Lipid	Long Chain Fatty Acid	0.04	0.74	0.99
4-vinylphenol sulfate	Xenobiotics	Benzoate Metabolism	0.10	0.74	0.99
2-methylbutyrylcarnitine (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.03	0.74	0.99
TL14:1n5 (myristoleic acid)	Lipid	Mole % Total Fatty Acid	0.05	0.74	0.99
3,7-dimethylurate	Xenobiotics	Xanthine Metabolism	-0.10	0.74	0.99
nonadecanoate (19:0)	Lipid	Long Chain Fatty Acid	0.02	0.74	0.99

cyclo(leu-pro)	Peptide	Dipeptide	0.06	0.75	0.99
hexanoylglycine (C6)	Lipid	Fatty Acid Metabolism(Acyl Glycine)	0.10	0.75	0.99
3-methylglutaryl carnitine (1)	Amino Acid	Lysine Metabolism	0.05	0.75	0.99
stachydrine	Xenobiotics	Food Component/Plant	0.09	0.75	0.99
cortisol	Lipid	Steroid	-0.04	0.75	0.99
N-acetylarginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.04	0.75	0.99
tryptophan	Amino Acid	Tryptophan Metabolism	-0.01	0.76	0.99
2-hydroxystearate	Lipid	Fatty Acid, Monohydroxy	0.02	0.76	0.99
N-acetylisoleucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.04	0.76	0.99
N2,N2-dimethylguanosine	Nucleotide	Purine Metabolism, Guanine containing	0.02	0.76	0.99
gamma-glutamylmethionine	Peptide	Gamma-glutamyl Amino Acid	0.03	0.77	0.99
methylpalmitate (15 or 2)	Lipid	Fatty Acid, Branched	0.02	0.77	0.99
succinate	Energy	TCA Cycle	0.01	0.77	0.99
4-ureidobutyrate	Nucleotide	Pyrimidine Metabolism, Uracil containing	0.04	0.77	0.99
phenylalanylphenylalanine	Peptide	Dipeptide	-0.04	0.77	0.99
levulinate (4-oxoalverate)	Xenobiotics	Food Component/Plant	0.03	0.77	0.99
leucine	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.01	0.77	0.99
3-hydroxyhippurate	Xenobiotics	Benzoate Metabolism	-0.10	0.78	0.99
2-linolenoylglycerophosphocholine(18:3n3)*	Lipid	Lysolipid	-0.09	0.78	0.99
cis-4-decenoyl carnitine	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.03	0.78	0.99
homoarginine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	-0.08	0.78	0.99
1-pentadecanoylglycerol (1-monopentadecanoin)	Lipid	Monoacylglycerol	-0.03	0.78	0.99
pyridoxal	Cofactors and Vitamins	Vitamin B6 Metabolism	-0.10	0.79	0.99
maleate (cis-Butenedioate)	Lipid	Fatty Acid, Dicarboxylate	0.04	0.79	0.99
p-cresol-glucuronide*	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.12	0.79	0.99
urate	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	-0.02	0.79	0.99
N-acetylglutamine	Amino Acid	Glutamate Metabolism	0.03	0.79	0.99
4-ethylphenyl sulfate	Xenobiotics	Benzoate Metabolism	0.06	0.80	0.99
isovalerate (C5)	Amino Acid	Leucine, Isoleucine and Valine Metabolism	-0.02	0.80	0.99
pentadecanoate (15:0)	Lipid	Long Chain Fatty Acid	-0.02	0.80	0.99
TL20:0 (arachidic acid)	Lipid	Mole % Total Fatty Acid	-0.02	0.80	0.99
etiocholanolone glucuronide	Lipid	Steroid	-0.07	0.80	0.99

thymol sulfate	Xenobiotics	Food Component/Plant	-0.11	0.80	0.99
TL24:0 (lignoceric acid)	Lipid	Mole % Total Fatty Acid	0.03	0.80	0.99
campesterol	Lipid	Sterol	-0.03	0.80	0.99
5alpha-pregnan-3(alpha or beta),20beta-diol disulfate	Lipid	Steroid	0.12	0.80	0.99
o-cresol sulfate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.14	0.80	0.99
2-linoleoylglycerol (2-monolinolein)	Lipid	Monoacylglycerol	-0.04	0.81	0.99
tyrosylglutamine	Peptide	Dipeptide	-0.04	0.81	0.99
succinylcarnitine (C4)	Energy	TCA Cycle	-0.02	0.81	0.99
N-acetyl-beta-alanine	Nucleotide	Pyrimidine Metabolism, Uracil containing	-0.02	0.81	0.99
1-methylurate	Xenobiotics	Xanthine Metabolism	-0.06	0.81	0.99
glycerol 3-phosphate (G3P)	Lipid	Glycerolipid Metabolism	-0.05	0.82	0.99
7-methylxanthine	Xenobiotics	Xanthine Metabolism	-0.07	0.82	0.99
7-HOCA	Lipid	Sterol	-0.02	0.82	0.99
trigonelline (N'-methylnicotinate)	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	-0.05	0.82	0.99
TL24:1n9 (nervonic acid)	Lipid	Mole % Total Fatty Acid	0.02	0.82	0.99
guanidinoacetate	Amino Acid	Creatine Metabolism	0.02	0.82	0.99
5-acetylamino-6-amino-3-methyluracil	Xenobiotics	Xanthine Metabolism	0.09	0.83	0.99
maltose	Carbohydrate	Glycogen Metabolism	0.05	0.83	0.99
glucarate 1,4-lactone	Carbohydrate	Disaccharides and Oligosaccharides	0.15	0.83	0.99
margarate (17:0)	Lipid	Long Chain Fatty Acid	0.02	0.83	0.99
TL18:3n3 (a-linolenic acid)	Lipid	Mole % Total Fatty Acid	-0.02	0.83	0.99
propionylcarnitine (C3)	Lipid	Fatty Acid Metabolism (also BCAA Metabolism)	-0.02	0.83	0.99
acetylcarnitine (C2)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.02	0.83	0.99
threonylphenylalanine	Peptide	Dipeptide	-0.08	0.83	0.99
1-docosapentaenoyl-GPC* (22:5n6)*	Lipid	Lysolipid	0.06	0.83	0.99
ursodeoxycholate	Lipid	Secondary Bile Acid Metabolism	-0.08	0.84	0.99
2-hydroxybutyrate (AHB)	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.02	0.84	0.99
palmitoleate (16:1n7)	Lipid	Long Chain Fatty Acid	0.02	0.84	0.99
creatinine	Amino Acid	Creatine Metabolism	0.01	0.85	0.99
TL20:4n3 (eicosatetraoic acid)	Lipid	Mole % Total Fatty Acid	0.02	0.85	0.99
threitol	Carbohydrate	Pentose Metabolism	-0.02	0.85	0.99
2-oleoylglycerol (18:1)	Lipid	Monoacylglycerol	0.02	0.85	0.99
indole-3-carboxylic acid	Amino Acid	Tryptophan Metabolism	-0.01	0.85	0.99
TLdm16:0 (plasmalogen palmitic acid)	Lipid	Mole % Total Fatty Acid	-0.01	0.86	0.99

histidine	Amino Acid	Histidine Metabolism	-0.02	0.86	0.99
glycerol	Lipid	Glycerolipid Metabolism	0.01	0.86	0.99
pyroglutamine*	Amino Acid	Glutamate Metabolism	-0.03	0.86	0.99
N-acetylthreonine	Amino Acid	Glycine, Serine and Threonine Metabolism	0.02	0.86	0.99
pyroglutamylglycine	Peptide	Dipeptide	-0.04	0.87	0.99
N6-carbamoylthreonyladenosine	Nucleotide	Purine Metabolism, Adenine containing	0.01	0.87	0.99
myristoleoyl sphingomyelin*	Lipid	Sphingolipid Metabolism	0.02	0.87	0.99
5-dodecenoate (12:1n7)	Lipid	Medium Chain Fatty Acid	-0.02	0.87	0.99
5alpha-androstan-3beta,17alpha-diol disulfate	Lipid	Steroid	0.05	0.87	0.99
ribose	Carbohydrate	Pentose Metabolism	0.03	0.87	0.99
5alpha-androstan-3alpha,17beta-diol monosulfate (1)	Lipid	Steroid	0.06	0.87	0.99
gamma-glutamylhistidine	Peptide	Gamma-glutamyl Amino Acid	-0.04	0.87	0.99
N-delta-acetylornithine	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.02	0.87	0.99
vaccenate (18:1n7)	Lipid	Long Chain Fatty Acid	0.01	0.87	0.99
decanoylcarnitine (C10)	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	0.01	0.87	0.99
N-acetylhistidine	Amino Acid	Histidine Metabolism	0.03	0.88	0.99
17-methylstearate	Lipid	Fatty Acid, Branched	0.02	0.88	0.99
16a-hydroxy DHEA 3-sulfate	Lipid	Steroid	0.03	0.88	0.99
erucate (22:1n9)	Lipid	Long Chain Fatty Acid	0.01	0.88	0.99
xylonate	Carbohydrate	Pentose Metabolism	0.03	0.88	0.99
1-linoleoyl-GPI* (18:2)*	Lipid	Lysolipid	0.01	0.88	0.99
palmitoyl-linoleoyl-glycerophosphoinositol (1)*	Lipid	Lysolipid	-0.03	0.88	0.99
phosphate	Energy	Oxidative Phosphorylation	-0.01	0.88	0.99
cyclo(L-phe-L-pro)	Peptide	Dipeptide	0.03	0.89	0.99
myristoleate (14:1n5)	Lipid	Long Chain Fatty Acid	-0.04	0.89	0.99
glycerophosphoethanolamine	Lipid	Phospholipid Metabolism	0.02	0.89	0.99
kynurenine	Amino Acid	Tryptophan Metabolism	0.01	0.89	0.99
tartarate	Xenobiotics	Food Component/Plant	0.04	0.89	0.99
beta-sitosterol	Lipid	Sterol	-0.02	0.90	0.99
linoleate (18:2n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	0.01	0.90	0.99
glycolithocholate	Lipid	Secondary Bile Acid Metabolism	-0.05	0.90	0.99
glycerate	Carbohydrate	Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	0.01	0.91	0.99
glutarate (pentanedioate)	Amino Acid	Lysine Metabolism	0.02	0.91	0.99
fumarate	Energy	TCA Cycle	-0.01	0.91	0.99

oleate (18:1n9)	Lipid	Long Chain Fatty Acid	0.01	0.91	0.99
epiandrosterone sulfate	Lipid	Steroid	0.03	0.91	0.99
oleamide	Lipid	Fatty Acid, Amide	0.02	0.91	0.99
carnitine	Lipid	Carnitine Metabolism	-0.004	0.92	0.99
2-pyrrolidinone	Xenobiotics	Chemical	-0.02	0.92	0.99
2-keto-3-deoxy-gluconate	Xenobiotics	Food Component/Plant	0.01	0.92	0.99
3-methoxycatechol sulfate (2)	Xenobiotics	Benzoate Metabolism	-0.03	0.92	0.99
phenylalanylglutamate	Peptide	Dipeptide	0.05	0.92	0.99
TL20:3n6 (di-homo-g-linoleic acid)	Lipid	Mole % Total Fatty Acid	-0.01	0.93	0.99
3-[3-(sulfooxy)phenyl]propanoic acid	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.04	0.93	0.99
N-methylpipercolate	Xenobiotics	Chemical	-0.02	0.93	0.99
N-acetyllaiiin	Xenobiotics	Food Component/Plant	0.03	0.93	0.99
deoxycarnitine	Lipid	Carnitine Metabolism	-0.004	0.93	0.99
stearoyl-linoleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.01	0.93	0.99
HWESASXX*	Peptide	Polypeptide	-0.02	0.93	0.99
3-hydroxydecanoate	Lipid	Fatty Acid, Monohydroxy	0.01	0.93	0.99
1-linoleoyl-GPE (18:2)*	Lipid	Lysolipid	-0.01	0.94	0.99
2-aminophenol sulfate	Xenobiotics	Chemical	-0.02	0.94	0.99
choline	Lipid	Phospholipid Metabolism	-0.004	0.94	0.99
gluconate	Xenobiotics	Food Component/Plant	0.01	0.94	0.99
betonidine	Xenobiotics	Food Component/Plant	0.04	0.94	0.99
aspartylleucine	Peptide	Dipeptide	-0.01	0.94	0.99
l-urobilinogen	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	0.03	0.94	0.99
deoxycholate	Lipid	Secondary Bile Acid Metabolism	-0.01	0.94	0.99
hydroxybutyrylcarnitine*	Lipid	Fatty Acid Metabolism(Acyl Carnitine)	-0.01	0.94	0.99
oleoyl-linoleoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	-0.01	0.94	0.99
hydroxyproline	Amino Acid	Urea cycle; Arginine and Proline Metabolism	0.01	0.94	0.99
TL18:4n3 (stearidonic acid)	Lipid	Mole % Total Fatty Acid	0.01	0.94	0.99
N-acetylkynurenine (2)	Amino Acid	Tryptophan Metabolism	0.02	0.94	0.99
pyroglutamylvaline	Peptide	Dipeptide	-0.01	0.94	0.99
cys-gly, oxidized	Amino Acid	Glutathione Metabolism	-0.01	0.95	0.99
pyrraline	Xenobiotics	Food Component/Plant	0.02	0.95	0.99
glycerophosphorylcholine (GPC)	Lipid	Phospholipid Metabolism	0.004	0.95	0.99
TL22:0 (behenic acid)	Lipid	Mole % Total Fatty Acid	0.01	0.95	0.99
palmitoyl-palmitoyl-glycerophosphocholine (2)*	Lipid	Lysolipid	0.01	0.95	0.99

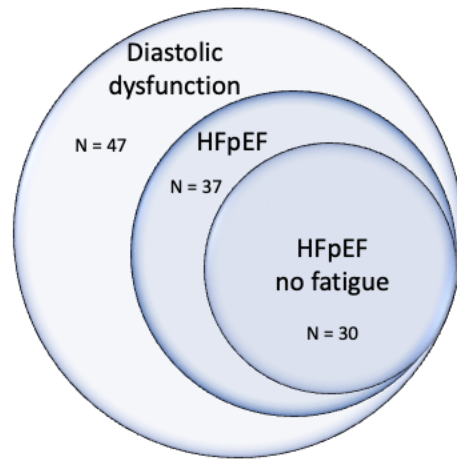
TLTL (Total Total Lipid)	Lipid	Quantitative Total Fatty Acid	0.005	0.95	0.99
pyridoxate	Cofactors and Vitamins	Vitamin B6 Metabolism	0.01	0.95	0.99
linolenate (18:3n3 or 3n6)	Lipid	Polyunsaturated Fatty Acid (n3 and n6)	-0.01	0.96	0.99
2-aminoadipate	Amino Acid	Lysine Metabolism	-0.005	0.96	0.99
4-androsten-3alpha,17alpha-diol monosulfate (3)	Lipid	Steroid	-0.01	0.96	0.99
cystine	Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	0.003	0.96	0.99
taurodeoxycholate	Lipid	Secondary Bile Acid Metabolism	0.02	0.96	0.99
TLdm18:0 (plasmalogen stearic acid)	Lipid	Mole % Total Fatty Acid	-0.004	0.96	0.99
palmitoyl-oleoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.004	0.96	0.99
TL16:0 (palmitic acid)	Lipid	Mole % Total Fatty Acid	-0.001	0.96	0.99
scyllo-inositol	Lipid	Inositol Metabolism	0.01	0.96	0.99
2-hydroxyglutarate	Lipid	Fatty Acid, Dicarboxylate	0.004	0.96	0.99
leucylglycine	Peptide	Dipeptide	0.01	0.97	0.99
hypoxanthine	Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	0.01	0.97	0.99
bilirubin	Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	0.01	0.97	0.99
sphingosine 1-phosphate	Lipid	Sphingolipid Metabolism	-0.003	0.97	0.99
laurate (12:0)	Lipid	Medium Chain Fatty Acid	0.004	0.97	0.99
ergothioneine	Xenobiotics	Food Component/Plant	0.01	0.97	0.99
1-palmitoyl-GPI* (16:0)*	Lipid	Lysolipid	-0.01	0.97	0.99
N1-Methyl-2-pyridone-5-carboxamide	Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	0.005	0.97	0.99
TL18:0 (stearic acid)	Lipid	Mole % Total Fatty Acid	0.001	0.97	0.99
methyl-4-hydroxybenzoate sulfate	Xenobiotics	Benzoate Metabolism	-0.01	0.97	0.99
5alpha-androstan-3alpha,17beta-diol disulfate	Lipid	Steroid	-0.01	0.97	0.99
4-imidazoleacetate	Amino Acid	Histidine Metabolism	-0.01	0.98	0.99
pipecolate	Amino Acid	Lysine Metabolism	-0.004	0.98	0.99
cinnamoylglycine	Xenobiotics	Food Component/Plant	0.01	0.98	0.99
2-hydroxypalmitate	Lipid	Fatty Acid, Monohydroxy	0.001	0.98	0.99
glycodeoxycholate	Lipid	Secondary Bile Acid Metabolism	0.01	0.98	0.99
3-methylxanthine	Xenobiotics	Xanthine Metabolism	0.01	0.98	0.99
vanillylmandelate (VMA)	Amino Acid	Phenylalanine and Tyrosine Metabolism	-0.002	0.98	0.99
4-androsten-3beta,17beta-diol monosulfate (2)	Lipid	Steroid	-0.005	0.98	0.99
gamma-glutamyltyrosine	Peptide	Gamma-glutamyl Amino Acid	-0.001	0.98	0.99

4-hydroxybenzoate	Xenobiotics	Benzoate Metabolism	-0.01	0.98	0.99
palmitoyl-palmitoyl-glycerophosphocholine (1)*	Lipid	Lysolipid	-0.002	0.99	1.00
3-(3-hydroxyphenyl)propionate	Amino Acid	Phenylalanine and Tyrosine Metabolism	0.003	0.99	1.00
3-methyl-2-oxovalerate	Amino Acid	Leucine, Isoleucine and Valine Metabolism	0.0005	0.99	1.00
1-stearoyl-GPI (18:0)	Lipid	Lysolipid	0.0002	1.00	1.00
13-methylmyristic acid	Lipid	Fatty Acid, Branched	0.0002	1.00	1.00
cortisone	Lipid	Steroid	0.0001	1.00	1.00

*Covariates: age, sex, diabetes, hypertension, BMI, and liver fibrosis stage

TCA = tricarboxylic acid cycle; GPE = Glycerophosphoethanolamine; GPC = Glycerophosphocholine; SAM = S-Adenosyl methionine

Figure S1: Venn diagram showing number of patients meeting each definition of HFpEF and overlap between definitions



HFpEF = heart failure with preserved ejection fraction

Figure S2: Metabolite missingness

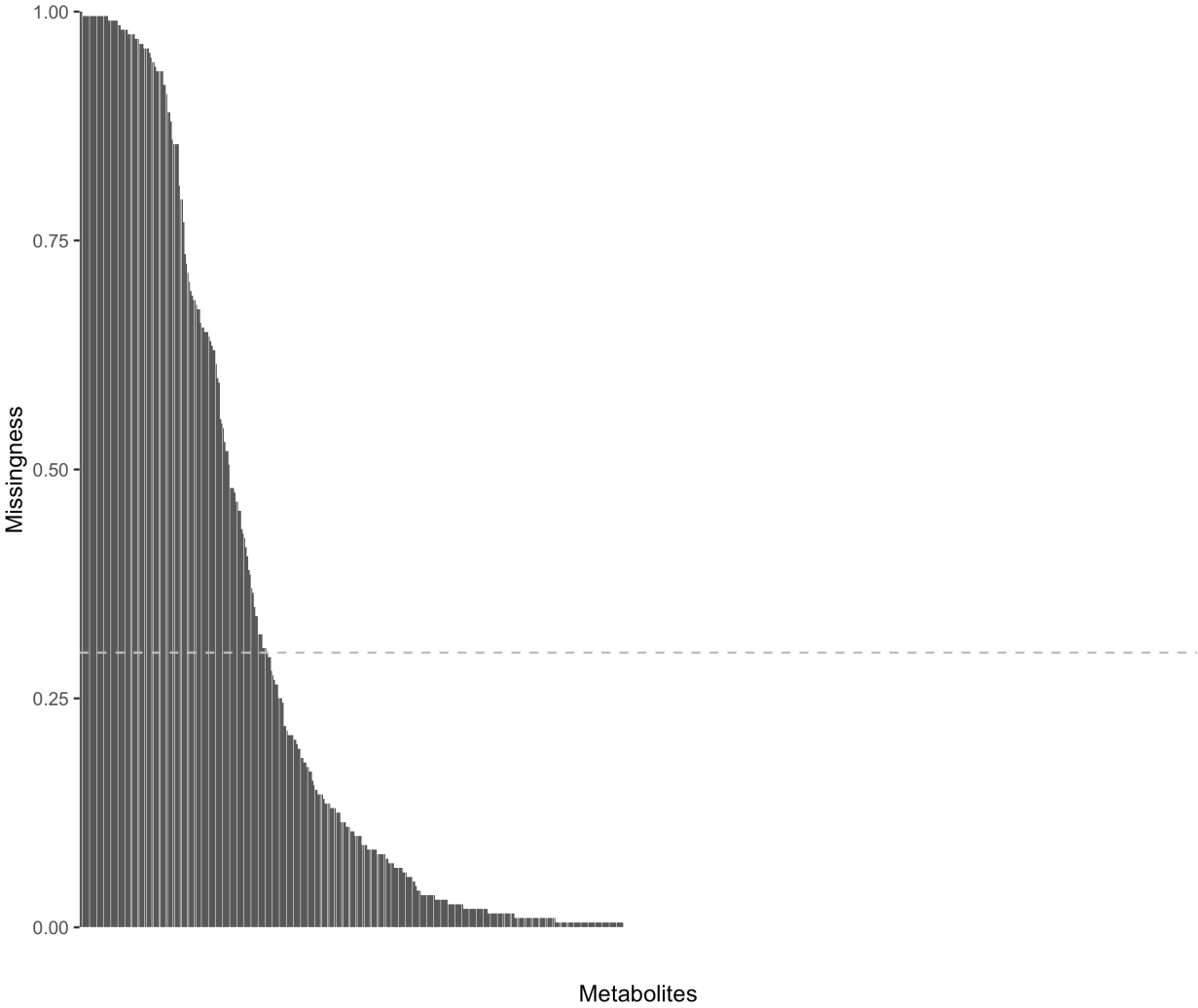
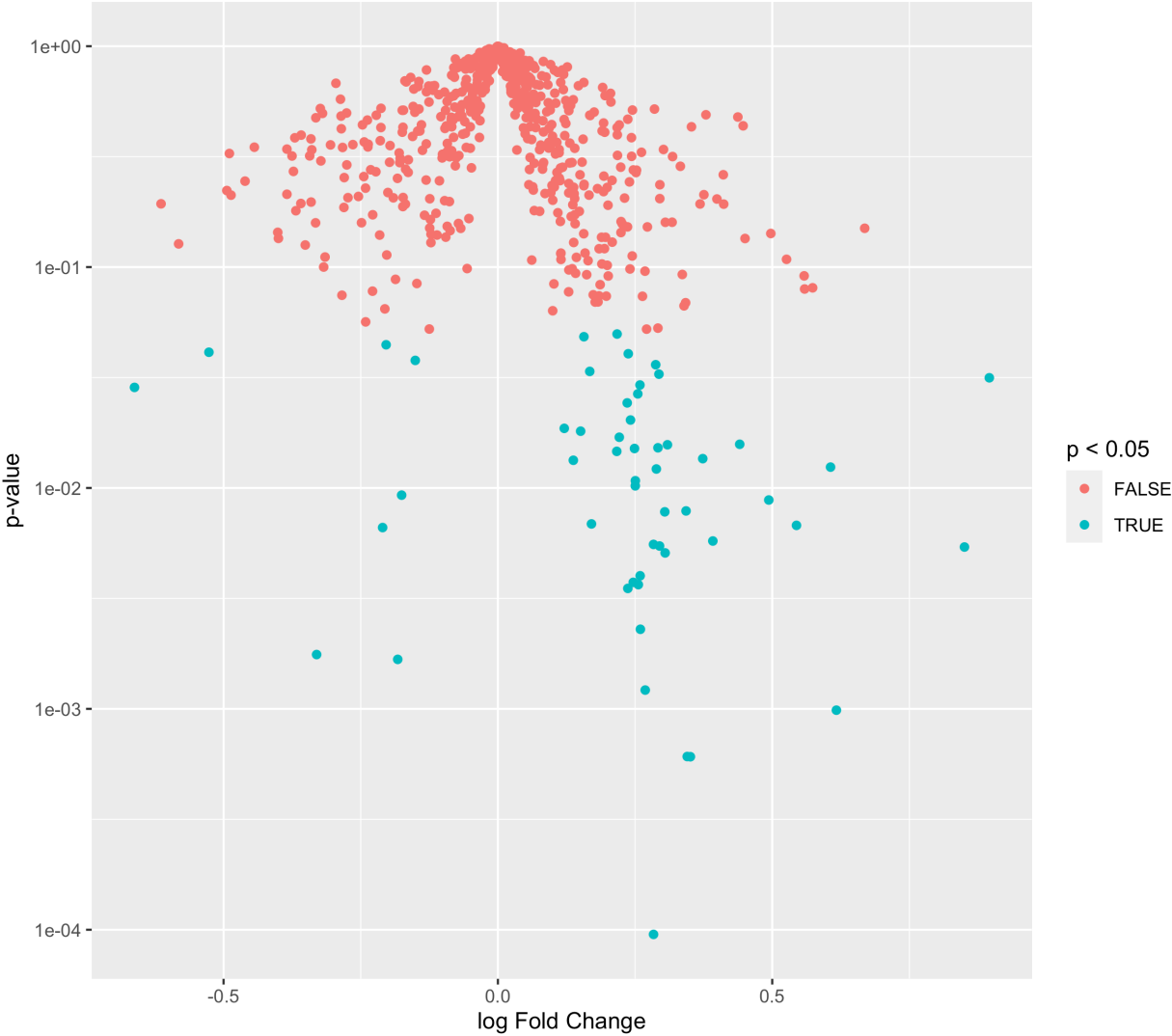
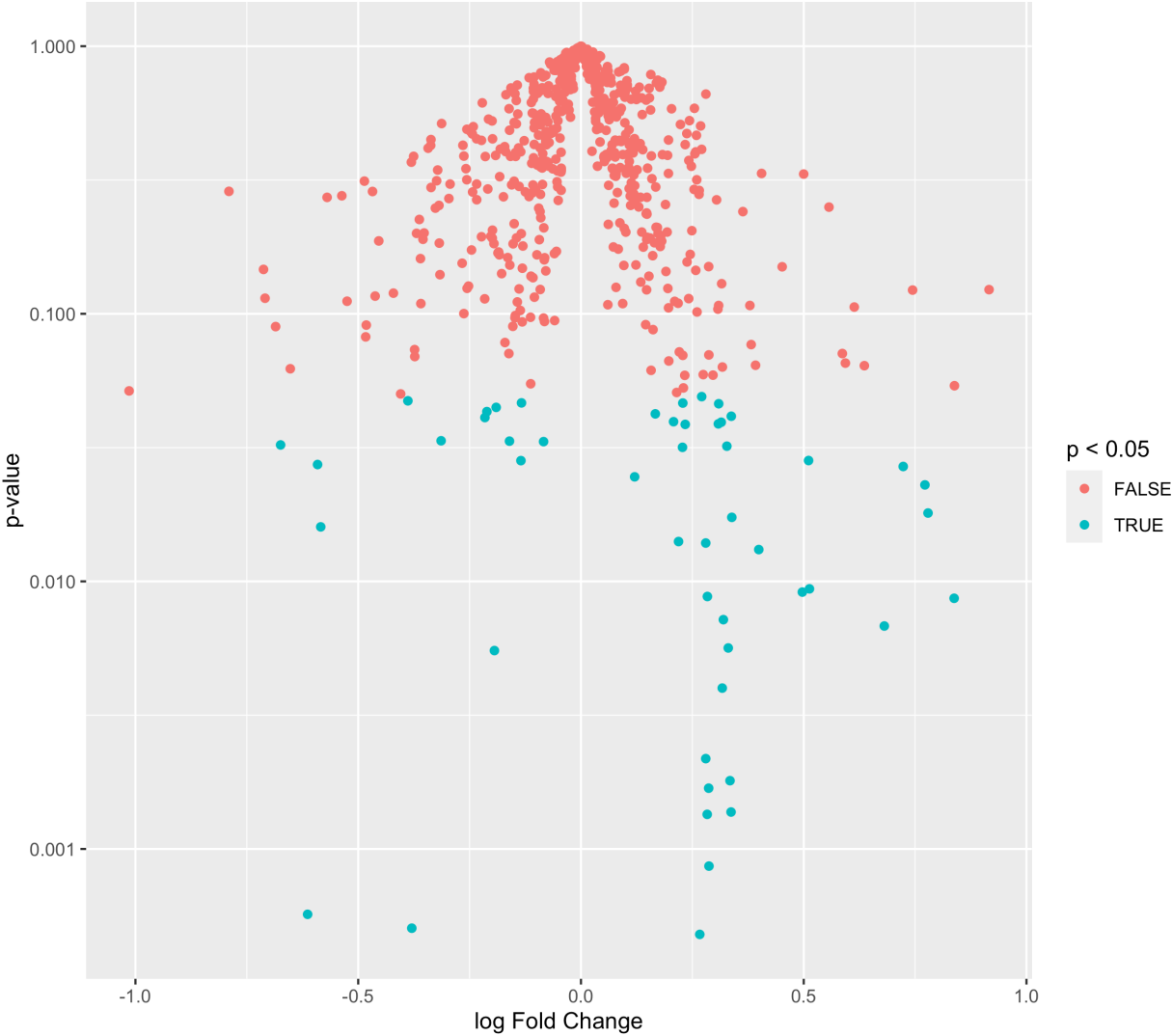


Figure S3: Volcano plot for HFpEF



HFpEF = heart failure with preserved ejection fraction

Figure S4: Volcano plot for HFpEF-no fatigue



HFpEF = heart failure with preserved ejection fraction

Figure S5: Volcano plot for diastolic dysfunction

