Plasma Metabolomic Profiles in Different Stages of CKD

Vallabh O. Shah, Raymond R. Townsend,† Harold I. Feldman,† Kirk L. Pappan,‡ Elizabeth Kensicki,‡ and David L. Vander Jagt**

Summary

Background and objectives CKD is a common public health problem. Identifying biomarkers adds prognostic/diagnostic value by contributing to an understanding of CKD at the molecular level and possibly defining new drug targets. Metabolomics provides a snapshot of biochemical events at a particular time in the progression of CKD. This cross-sectional metabolomics study ascertained whether plasma metabolite profiles are significantly different in CKD stages 2, 3, and 4.

Design, setting, participants, & measurements An analysis of plasma metabolites, using gas and liquid chromatography coupled to mass spectrometry, was conducted on 30 nondiabetic men ages 40–52 years, with 10 participants each in CKD stages 2, 3, and 4 based on their estimated GFR (calculated by the Modified Diet in Renal Disease formula). Participants were recruited in late 2008, and plasma samples were tested at Metabolon Inc and analyzed in 2012.

Results Comparison of stage 3/stage 2 identified 62 metabolites that differed ($P \leq 0.05$), with 39 higher and 23 lower in stage 3 compared with stage 2; comparisons of stage 4/stage 2 identified 111 metabolites, with 66 higher and 45 lower; and comparisons of stage 4/stage 3 identified 11 metabolites, with 7 higher and 4 lower. Major differences in metabolite profiles with increasing stage of CKD were observed, including altered arginine metabolism, elevated coagulation/inflammation, impaired carboxylate anion transport, and decreased adrenal steroid hormone production.

Conclusions Global metabolite profiling of plasma uncovered potential biomarkers of stages of CKD. Moreover, these biomarkers provide insight into possible pathophysiologic processes that may contribute to progression of CKD.

Clin J Am Soc Nephrol 8: 363–370, 2013. doi: 10.2215/CJN.05540512

*University of New Mexico Health Sciences Center, Albuquerque, New Mexico; †Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; and ‡Metabolon Inc., Durham, North Carolina

Correspondence: Dr. Vallabh O. Shah, Department of Biochemistry and Molecular Biology, School of Medicine, University of New Mexico Health Sciences Center, 1 University of New Mexico, MSC08 4670, Albuquerque, NM 87131. Email: vshah@salud.unm.edu

Introduction

CKD encompasses a spectrum of kidney diseases, ranging from kidney damage with normal kidney function to ESRD. The National Kidney Foundation has devised a five-stage classification system for CKD based on the level of GFR (1). Cardiovascular disease (CVD) is a major cause of morbidity and mortality in patients with all forms of CKD and contributes to the complexity of CKD (2–6). This complexity introduces new challenges in predicting and treating patients sufficiently early in the course of CKD to positively alter patient outcome. Until recently, most risk factor analysis of kidney diseases has focused on ESRD. Little is known about the effect of various risk factors at each stage of disease and how these contribute to the rate of progression to ESRD. In addition, there has been little study of the potential differences in risk factors for transition from one stage to the next and whether the risk factors for onset and transition from stage 1 to stage 2 may differ from those for transition to stage 3 and stage 4 CKD or for final development of ESRD. Currently, both the incidence and prevalence of CKD leading to ESRD continue to increase at an alarming rate in the United States. There are at least 19 million people in the United States with some degree of CKD (7), with enormous costs to society (8), prompting the Surgeon General to include CKD as a focus area for improving the nation's health in Healthy People 2010. An understanding of the characteristics of early stage CKD, as well as the factors that differentially affect the progression of CKD from one stage to the next, is essential for determining appropriate therapy and predicting long-term outcomes.

Metabolomics, which is the most recent systems-biology approach to complement the genomic, transcriptomic, and proteomic efforts to characterize an entire biologic system, is increasingly being used to study kidney function (9–11). Because metabolites represent the end products of the genome and proteome, metabolomics holds the promise of providing an integrated physiologic phenotype of a system. Such metabolic profiling involves a comprehensive measurement of the types and concentrations of metabolites in a system at a specified time, such as each stage of CKD. Metabolomics also provides insight into metabolic pathways and networks downstream of gene expression. Complex metabolite profiles may

provide the data required to enable the diagnosis, risk stratification, treatment, and evaluation of treatment response of patients. This may be through the identification of single biomarkers as in the more traditional methods or more likely by identification of patterns across many metabolites.

In this cross-sectional study, we determined plasma metabolite profiles of 30 participants; these were nondiabetic men aged 40–52 years, with 10 each in CKD stages 2, 3, and 4 based on their estimated GFR. Our goal was to determine whether there are significant differences in specific metabolites by stage of CKD and whether these may be useful stage-specific biomarkers. A related goal was to consider whether these differences might offer insight into potential pathophysiologic mechanisms that contribute to progression of CKD.

Materials and Methods

Study Participants

Plasma samples, which were obtained from the University of Pennsylvania from patients recruited in late 2008, were stored at −80°C for this study. Samples from 30 participants with CKD, 10 each in stages 2, 3 and 4, were selected for metabolite analysis at Metabolon Inc in 2012. Informed consent was obtained from all participants. Descriptions of the participants are summarized in Table 1.

Sample Accessioning/Preparation

All mass spectrometry data were collected at Metabolon Inc. Each plasma sample was accessioned into the Metabolon LIMS system and was assigned by the LIMS unique identifier, which was associated with the original source identifier only. The nontargeted metabolic profiling platform utilized for this analysis combined three independent platforms: ultrahigh performance liquid chromatography–tandem mass spectrometry (UHPLC–MS/MS^2) optimized for basic species, UHPLC–MS/MS^2 optimized for acidic species, and gas chromatography/mass spectrometry (GC/MS). Samples were processed essentially as described previously (12,13). For each sample, 100 μl was used for analyses. Using an automated liquid handler (Hamilton LabStar, Salt Lake City, UT), protein was precipitated from the plasma with methanol that contained four standards to report on extraction efficiency. The resulting supernatant was split into equal aliquots for analysis on the three platforms. Aliquots, dried under nitrogen and vacuum-desiccated, were subsequently either reconstituted in 50 μl 0.1% formic acid in water (acidic conditions) or in 50 μl 6.5 mM ammonium bicarbonate in water, pH 8 (basic conditions) for the two UHPLC–MS/MS^2 analyses, or were derivatized to a final volume of 50 μl for GC/MS analysis using equal parts bistrimethyl-silyl-trifluoroacetamide and solvent mixture acetonitrile:dichloromethane:cyclohexane (5:4:1) with 5% triethylamine at 60°C for 1 hour. In addition, three types of controls were analyzed in concert with the experimental samples: aliquots of a well characterized human plasma pool served as technical replicates throughout the data set, extracted water samples served as process blanks, and a cocktail of standards spiked into every analyzed sample allowed instrument performance monitoring. Experimental samples and controls were randomized across platform run days.

LC/MS, LC/MS^2

For UHLC–MS/MS^2 analysis, aliquots were separated using a Waters Acquity UPLC (Waters, Millford, MA) and were analyzed using an LTQ mass spectrometer (Thermo Fisher Scientific Inc, Waltham, MA) that consisted of an electrospray ionization source and linear ion-trap mass analyzer. The MS instrument scanned 99–1000 *m/z* and alternated between MS and MS^2 scans using dynamic exclusion with approximately six scans per second.

GC/MS

Derivatized samples for GC/MS were separated on a 5% phenyldimethyl silicone column with helium as the carrier gas and a temperature ramp from 60°C to 340°C and then analyzed on a Thermo-Finnigan Trace DSQ MS (Thermo Fisher Scientific Inc.) operated at unit mass resolving power with electron impact ionization and a 50–750 atomic mass unit scan range.

Compound Identification

Compounds were identified by automated comparison of the ion features in the experimental samples with a reference library of chemical standard entries that included retention time, molecular weight (*m/z*), preferred adducts,

Table 1. Study participant baseline characteristics

	Kidney Disease Progression		
	CKD Stage 2	CKD Stage 3	CKD Stage 4
Number of patients	10	10	10
Sex	Male	Male	Male
Ethnicity	NHW	NHW	NHW
Age (yr)	51.4±3.3	58.2±2.6	61.5±4.7
Height (cm)	168.1±6.9	174.5±5.3	175.5±6.1
Weight (kg)	92.9±9.6	97.3±7.9	100.5±10.0
Body mass index	32.8±2.6	31.9±2.2	32.5±1.8
Estimated GFR (ml/min per 1.73 m^2)	63.6±13.2	37.9±9.9	27.4±4.4

Data are presented as mean ± SD. NHW, non-Hispanic white.

and in-source fragments as well as associated MS spectra, and were curated by visual inspection for quality control using software developed at Metabolon (14). At present, >2500 commercially available purified standards are registered into LIMS for distribution to both the LC and GC platforms for determination of their analytical characteristics. Compound abundance was quantified by calculating the area under the curve for the quantification ion of the compound.

Statistical Analyses

To aid data visualization, the raw area counts for each biochemical were rescaled by dividing each sample value by the median value for that specific biochemical. For statistical analyses, any missing values were assumed to be below the limits of detection and these values were imputed with the compound minimum (minimum value imputation). Statistical analyses of log-transformed data were performed using "R" (http://cran.r-project.org/), which is a freely available, open-source software package. Welch's *t* tests were performed to compare data between experimental groups. Multiple comparisons were accounted for by estimating the false discovery rate (FDR) using *q* values (15). CKD groups were classified using Random Forest analyses. Random Forests give an estimate of how well we can classify *individuals* in a *new* data set into each group, in contrast to a *t* test, which tests whether the unknown means for two populations are different or not. Random Forests create a set of classification trees based on continual sampling of the experimental units and compounds. Each observation is then classified based on the majority votes from all of the classification trees (16,17).

Results

Global Metabolite Determination

Initially, metabolites were measured in all plasma samples and were then evaluated by comparing values from CKD stage 3 with stage 2, CKD stage 4 with stage 2, and CKD stage 4 with stage 3. In total, 258 metabolites were identified. A subset of these metabolites was identified, with significant differences in one or more of these CKD stage comparisons ($P \leq 0.05$); an additional set of metabolites was identified that approached significance ($0.05 < P < 0.10$). Supplemental Table 1 lists the fold of the differences and statistical test results, including the *q*-value statistic, which is an estimate of the FDR in multiparametric datasets, for every metabolite detected in this study. Supplemental Table 2 shows the median re-scaled raw area counts with missing values imputed with the observed minimum detection value and represents the individual sample values that contributed to the statistical results in Supplemental Table 1. A total of 62 metabolites were identified that were significantly higher or lower in comparisons of CKD stage 3 with stage 2, with 39 higher and 23 lower; in comparisons of CKD stage 4 with stage 2, a total of 111 metabolites differed significantly, with 66 higher and 45 lower; and in comparisons of CKD stage 4 with stage 3, 11 metabolites were identified, with 7 higher and 4 lower. The number of different metabolites that differed significantly was 117. The raw data for all 258 metabolites are presented in the Supplemental Material.

Identification of Thematic Changes

Differences in level of a specific metabolite among a large number may be significant by chance. Therefore, it was of interest to search for thematic differences in which multiple metabolites are significantly higher or lower, which would unlikely be due to chance. Random Forest classification of CKD stage 2 compared with stage 3 and of CKD stage 4 compared with stage 2 identified metabolites based upon their abilities to identify groups. The 30 top-ranking metabolites for the Random Forest classification that compared CKD stages 2 and 4 are listed in Figure 1, denoted as the biochemical importance plot. These metabolites were evaluated, along with related metabolites beyond the top 30, to identify thematic differences. These differences may reveal CKD stage-specific biomarkers. They may also reflect significant alterations of pathophysiology that promote progression from CKD stage 2 to higher stages. Several themes were identified.

Altered Arginine Metabolism

A large difference in relative metabolite concentration was observed for dimethylarginine, as shown in Table 2, as a combination of asymmetric and symmetric dimethylarginine. Dimethylarginine in CKD stage 3 is higher compared with stage 2 (8.1-fold) and in CKD stage 4 compared with stage 2 (4.8-fold). This represents one of the larger metabolite fold increases that were observed in this cross-sectional comparison of CKD stage 2 with higher stages. Other metabolites related to arginine metabolism that were also significantly different in CKD stages 3 and 4 compared with stage 2 include ornithine and citrulline. Ornithine was markedly lower in CKD stages 3 and 4 compared with CKD stage 2.

Elevated Coagulation/Inflammation

The largest fold difference that was observed in comparisons of CKD stage 2 with stage 3, which remained elevated in stage 4, was the increase in coagulation/inflammation factor fibrinopeptide-A and phosphorylated fibrinopeptide-A (Table 2). The higher level of fibrinopeptide-A in CKD stage 3 compared with stage 2 (689-fold) is maintained in CKD stage 4 compared with stage 2 (827-fold). The higher level of phosphorylated fibrinopeptide-A (phosphorylated at serine-3) in CKD stage 3 compared with stage 2 (18-fold) remained elevated in stage 4 compared with stage 2 (45-fold) and was significantly higher in CKD stage 4 compared with stage 3 (2.5-fold). Proline-hydroxyproline dipeptide was significantly higher in CKD stage 3 compared with stage 2 (2.5-fold) and in stage 4 compared with stage 2 (4.5-fold), which may reflect matrix degradation in response to increased coagulation/inflammation.

Impaired Carboxylate Anion Transport

Numerous mono-and di-carboxylate anions are higher in CKD stages 3 and 4 compared with CKD stage 2 (Table 2). A number of these are γ-glutamyl amino acid dipeptides. γ-glutamylglutamine, for example, is higher in CKD stage 3 compared with stage 2 (3.8-fold) and in stage 4 compared with stage 2 (4.8-fold). The γ-glutamyl amino acid dipeptides in Table 2 are involved in the γ-glutamyl cycle,

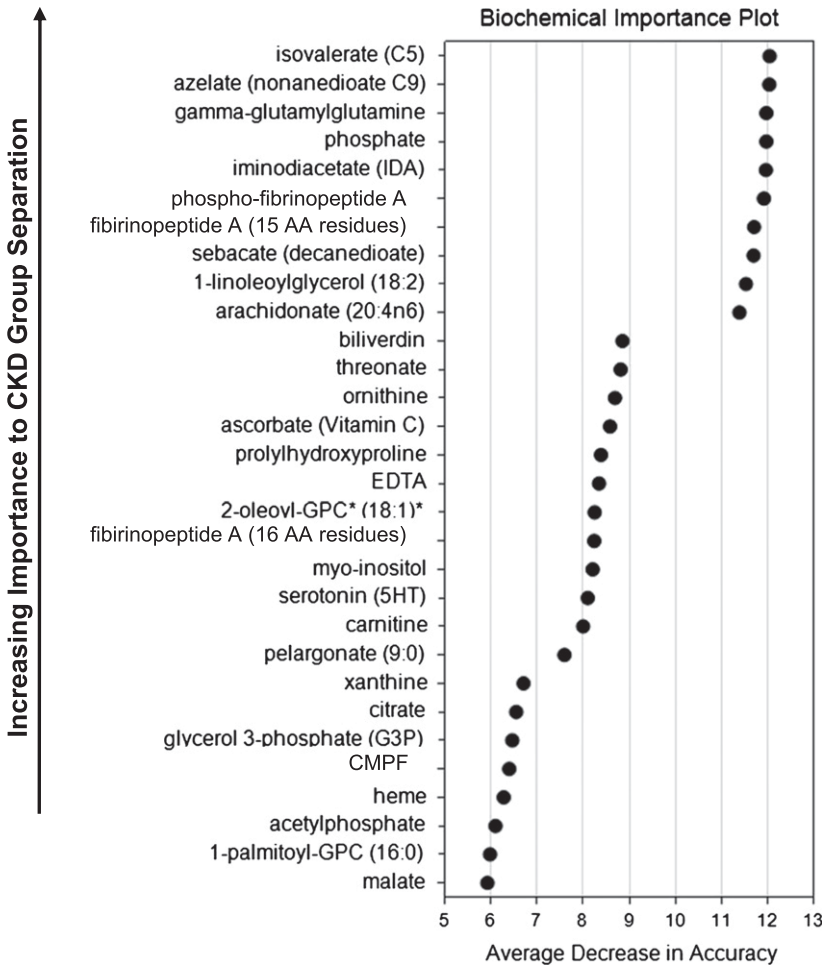

Figure 1. | **Top 30 metabolites important to CKD stage 2 versus stage 4 separation by Random Forest classification.** Random Forest multivariate classification was conducted by randomly choosing CDK stage 2 and CDK stage 4 samples ("in-bag"), randomly choosing variables (metabolites) to build classification and regression trees (CART) based on the in-bag samples, and then using several CART trees (50,000) to classify the remaining "out-of-bag" samples between CDK stage 2 and CDK stage 4 (17). The final prediction is based on an aggregation of the predictions across all trees for which the observation was part of the out-of-bag samples. Average decrease in accuracy was obtained by computing the classification error, based on out-of-bag samples, for each CART tree, permuting each variable, and re-computing the error for each permuted tree. The average difference between the two errors was computed and scaled by dividing the SD of these differences yielding a relationship of the more important the variable to the classification, the higher its average decrease in accuracy.

which is involved in glutathione homeostasis. These increases may reflect increased oxidative stress related to depletion of glutathione. Other carboxylate anions also are increased. 3-Carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF), a known uremic toxin that accumulates in ESRD, is higher in CKD stage 3 compared with stage 2 (18.3-fold) and in stage 4 compared with stage 2 (23.6-fold).

Decreased Adrenal Steroid Hormone Production

A number of adrenal steroid hormones, especially sulfated metabolites, were significantly lower in CKD stage 4 compared with stage 2 (Table 2). These are also anions. However, unlike the situation with carboxylate anions, in which higher levels were observed in higher stages of CKD, the sulfated metabolites were lower in the higher stages of CKD. Cortisol was also significantly lower in CKD stage 4 compared with stage 2 (0.62-fold). This suggests that a decrease in production of adrenal steroid hormones may explain these data.

Discussion

Major differences in metabolite profiles in the various stages of CKD were observed, consistent with altered arginine metabolism, elevated coagulation/inflammation, impaired carboxylate anion transport, and decreased adrenal steroid hormone production. These differences may reveal stage-specific biomarkers of CKD. Of particular interest are the major differences in metabolite profiles related to arginine metabolism and the significance of these changes with respect to impaired production of NO and the effect that this may have on endothelial function. Also of particular interest are the large fold increases in the levels of fibrinopeptide-A in comparisons of CKD stages 3 and 4 with CKD stage 2 and the significance of these increases with respect to development of a procoagulation/proinflammation state.

Arginine Metabolism

There are extensive data on the possible role of asymmetric dimethylarginine in kidney disease owing to its

Table 2. Ratios of significant changes of specific metabolites by stage of CKD ($P \leq 0.05$), mean values, and *P* values

	Fold of Change			Mean ± SD			*P* Value		
	Stages 3/2	Stages 4/2	Stages 4/3	CKD Stage 2	CKD Stage 3	CKD Stage 4	Stages 3/2	Stages 4/2	Stages 4/3
Altered arginine metabolism									
Dimethylarginine (SDMA + ADMA)	8.1	4.8		0.497±0.133	4.01±2.27	2.40±1.77	7.9E-05	0.01	0.17
Citrulline	1.6	1.3[a]		0.825±0.194	1.30±0.586	1.08±0.362	0.03	0.08	
Ornithine	0.28	0.16		4.33±1.39	1.19±1.32	0.683±0.334	2.0E-4	1.4E-06	
Arginine	1.5[a]	1.5[a]		0.675±0.238	1.02±0.480	1.03±0.559	0.06	0.10	
Elevated coagulation/inflammation									
Fibrinopeptide A	689	827		0.002±0.001	1.03±0.765	1.24±0.795	3.0E-4	1.1E-14	
Phosphorylated fibrinopeptide A	18	45	2.5	0.045±0.017	0.818±0.683	2.06±2.62	0.002	4.4E-08	0.04
Proline-hydroxyproline	2.5	4.5		0.466±0.251	1.16±1.26	2.08±1.68	0.03	8.3E-05	
Impaired carboxylate anion transport									
γ-Glutamylleucine		1.3		0.821±0.283		1.07±0.161		0.03	
γ-Glutamylisoleucine	1.6	1.7		0.670±0.196	1.12±0.440	1.18±0.510	0.01	0.01	
γ-Glutamylglutamine	3.8	4.8		0.275±0.166	1.05±0.417	1.31±0.349	5.5E-05	8.9E-06	
γ-Glutamylphenylalanine	1.5	1.3		0.903±0.240	1.31±0.480	1.17±0.181	0.03	0.01	
CMPF	18.3[a]	23.6		0.307±0.279	5.61±11.9	7.23±7.20	0.06	5.0E-4	
Decreased adrenal steroid hormone production									
Dehydroisoandrosterone sulfate		0.55		1.48±0.878		0.819±0.685		0.04	
4-androsten-3-β,17-β-diol disulfate		0.26		3.91±3.76		1.02±0.958		0.01	

ADMA, asymmetric dimethylarginine; SDMA, symmetric dimethylarginine; CMPF, 3-Carboxy-4-methyl-5-propyl-2- furanpropanoate.
[a]$0.1 > P > 0.05$.

ability to inhibit nitric oxide synthase (NOS) and limit production of NO, thereby contributing to vascular complications associated with CKD (18,19). The presence of asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) in human urine was first reported in 1970 (20). Inhibition of NOS by ADMA but not by SDMA was reported in 1992, with the observation that plasma levels of SDMA and ADMA were markedly elevated in CKD and ESRD and the suggestion that inhibition of NOS by ADMA may contribute to CVD, hypertension, and immune dysfunction associated with kidney disease (21). ADMA and SDMA are produced as post-translational modifications of selected arginine residues in specific proteins by methyl transfer from *S*-adenosylmethionine, which is catalyzed by protein arginine methyltransferases (PRMTs) (22,23). In turnover of proteins with methylated arginine residues, ADMA and SDMA, as well as mono-methylated arginine residues, are released. Most of the SDMA is released into plasma for clearance by the kidney. ADMA, however, is primarily converted into dimethylamine and citrulline, catalyzed by dimethylarginine dimethylaminohydrolases (DDAH-1 and DDAH-2) with distinct tissue distribution and regulation (24). Hydrolysis catalyzed by DDAH accounts for about 80% of the fate of ADMA. The remaining ADMA is excreted into the urine. It has been suggested that the plasma concentrations of ADMA are determined primarily by DDAH-1, which is highly expressed in kidney (25) and is colocalized with NOS (26). Thus, impaired kidney function may directly dictate the plasma concentrations of ADMA, which can inhibit endothelial NOS (eNOS) at low micromolar concentrations. In addition, methylarginines and dimethylarginines reduce uptake of arginine and other cationic amino acids by inhibition of amino acid transporters CAT-1 and CAT-2, which may also contribute to diminished production of NO (27).

Coagulation/Inflammation

Damage to the endothelium normally exposes collagen and other subendothelial proteins that are recognized by platelet receptors to initiate platelet activation. In addition, tissue factor is exposed on the damaged endothelium and can form a complex with factor VII to initiate the proteolysis cascades that produce thrombin. The activated platelets bind thrombin, which results in release of additional factors to recruit platelets to the site of clot formation. Platelet-bound thrombin also catalyzes the degradation of fibrinogen to form fibrin at the surface of the aggregated platelets, which is then cross-linked to form the clot. Patients with CKD can exhibit defects with any of these aspects of hemostasis, suggesting that CKD is a procoagulation state (28). Impaired platelet activation has been reported in CKD patients with mild-to-moderate CKD (29).

Fibrinopeptide-A is a 16 amino acid peptide derived from the thrombin-catalyzed proteolysis of the N-terminal end of the Aα-chain in fibrinogen. Accumulation of fibrinopeptide-A may reflect diminished capacity to clear this metabolite concomitant with a decrease in estimated GFR or may indicate development of a procoagulation state in the progression of CKD stage 2 to stages 3 and 4. Fibrinopeptide-A is a proinflammatory peptide (30), which suggests that this potential development of a procoagulation state is accompanied by the development of inflammation. Fibrinopeptide-A may be a useful stage-specific biomarker. However, the marked differences in levels of fibrinopeptide-A with stage of CKD may also reflect the development of a procoagulation/proinflammation state and may define the critical point of progression of CKD to states that eventually lead to ESRD. In support of this suggestion, recent studies of several animal models of CKD demonstrated the involvement of coagulation factor Xa and the ability of inhibitors of factor Xa to suppress development of some of the pathologic factors associated with CKD (31).

A critical component of endothelial control of hemostasis is the generation of NO at the appropriate time and levels. In experimental animal studies, eNOS production of NO regulates expression of tissue factor, suggesting that impairment of NO production will result in elevated tissue factor and promotion of coagulation (32). In addition, NO produced by the endothelium acts locally to inhibit platelet aggregation and therefore is essential for dampening the procoagulation response (33). The differences in levels of dimethylarginines (Table 2) observed in comparisons of CKD stage 2 with stage 3 suggests impaired NO production, which therefore may exacerbate the development of a procoagulation/proinflammation state in early stage CKD and enhance its progression (34).

Carboxylate Anions

CMPF is one of a number of uremic toxins that accumulate in ESRD, due to tight binding to albumin, and present problems in removal during hemodialysis (35). CMPF is toxic both to endothelial cells and to proximal tubular cells (36,37). CMPF was higher in CKD stage 3 compared with stage 2 and higher in stage 4 compared with stage 3.

In summary, in this cross-sectional metabolomics study, we determined metabolite patterns in different stages of CKD. The results demonstrated that, for the specific population that was studied, significant differences in metabolite patterns occur. Specifically, markedly higher levels of dimethylarginine and fibrinopeptide-A in comparisons of CKD stage 3 with CKD stage 2 suggest that these may be stage-specific biomarkers. These differences also point to endothelial dysfunction and suggest that a convergence of impaired NO production and enhanced production of coagulation/inflammation factor fibrinopeptide-A may collectively act to enhance progression of CKD beyond stage 2. These are testable hypotheses.

Study Limitations

This was an initial proof-of-concept study in which to address the question whether metabolomics might provide meaningful data for comparison of differences in CKD by stage. As such, it was a cross-sectional study with a limited study population. The results, although interesting and potentially meaningful for identification of stage-specific biomarkers and for insight into CKD progression, are preliminary to a longitudinal study of metabolite changes in CKD progression. The approved future longitudinal study will utilize the Chronic Renal Insufficiency Cohort population in order to compare CKD progression in diabetic and nondiabetic CKD populations that are further divided by age, sex, and ethnicity.

Acknowledgments

This project was supported in part by an Innovative Pilot Grant from the National Center for Research Resources and the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH) (8UL1TR000041) and the University of New Mexico (UNM) Clinical and Translational Science Center. We also acknowledge support from grants from the National Center for Research Resources (5P20RR016480-12) and the National Institute of General Medical Sciences (8P20GM103451-12) of the NIH. The cost for clinical phenotyping was supported under a UNM Health Sciences-based Cardiovascular and Metabolic Diseases Signature Program. Portions of this work with R.R.T were supported under Grants DK-060984 and UL1RR024134 from NIH.

This work was presented in poster form at the American Society of Nephrology Kidney Week 2012, San Diego, CA, November 3, 2012.

Disclosures

E.K. and K.L.P. are employees of Metabolon Inc and, as such, have affiliations with or financial involvement with Metabolon Inc.

References

1. National Kidney Foundation: K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Am J Kidney Dis* 39[Suppl 1]: S1–S266, 2002
2. Anakevar NS, Pfeffer MA: Cardiovascular risk in chronic kidney disease. *Kidney Int Suppl* 92: S11–S15, 2004
3. Dries DL, Exner DV, Domanski MJ, Greenberg B, Stevenson LW: The prognostic implications of renal insufficiency in asymptomatic and symptomatic patients with left ventricular systolic dysfunction. *J Am Coll Cardiol* 35: 681–689, 2000
4. Ruilope LM, Salvetti A, Jamerson K, Hansson L, Warnold I, Wedel H, Zanchetti A: Renal function and intensive lowering of blood pressure in hypertensive participants of the hypertension optimal treatment (HOT) study. *J Am Soc Nephrol* 12: 218–225, 2001
5. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 351: 1296–1305, 2004
6. Muntner P, He J, Hamm L, Loria C, Whelton PK: Renal insufficiency and subsequent death resulting from cardiovascular disease in the United States. *J Am Soc Nephrol* 13: 745–753, 2002
7. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS: Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 41: 1–12, 2003
8. Xue JL, Ma JZ, Louis TA, Collins AJ: Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. *J Am Soc Nephrol* 12: 2753–2758, 2001
9. Portilla D, Schnackenberg L, Beger RD: Metabolomics as an extension of proteomic analysis: Study of acute kidney injury. *Semin Nephrol* 27: 609–620, 2007
10. Toyohara T, Akiyama Y, Suzuki T, Takeuchi Y, Mishima E, Tanemoto M, Momose A, Toki N, Sato H, Nakayama M, Hozawa A, Tsuji I, Ito S, Soga T, Abe T: Metabolomic profiling of uremic solutes in CKD patients. *Hypertens Res* 33: 944–952, 2010
11. Rhee EP, Thadhani R: New insights into uremia-induced alterations in metabolic pathways. *Curr Opin Nephrol Hypertens* 20: 593–598, 2011
12. Ohta T, Masutomi N, Tsutsui N, Sakairi T, Mitchell M, Milburn MV, Ryals JA, Beebe KD, Guo L: Untargeted metabolomic profiling as an evaluative tool of fenofibrate-induced toxicology in Fischer 344 male rats. *Toxicol Pathol* 37: 521–535, 2009
13. Evans AM, DeHaven CD, Barrett T, Mitchell M, Milgram E: Integrated, nontargeted ultrahigh performance liquid chromatography/electrospray ionization tandem mass spectrometry platform for the identification and relative quantification of the small-molecule complement of biological systems. *Anal Chem* 81: 6656–6667, 2009
14. Dehaven CD, Evans AM, Dai H, Lawton KA: Organization of GC/MS and LC/MS metabolomics data into chemical libraries. *J Cheminform* 2: 9, 2010
15. Storey JD, Tibshirani R: Statistical significance for genomewide studies. *Proc Natl Acad Sci U S A* 100: 9440–9445, 2003
16. Breiman L: Random Forests. *Mach Learn* 45: 5–32, 2001
17. Goldstein BA, Hubbard AE, Cutler A, Barcellos LF: An application of Random Forests to a genome-wide association dataset: methodological considerations & new findings. *BMC Genet* 11: 49, 2010
18. Schwedhelm E, Böger RH: The role of asymmetric and symmetric dimethylarginines in renal disease. *Nat Rev Nephrol* 7: 275–285, 2011
19. Wilcox CS: Asymmetric dimethylarginine and reactive oxygen species. *Hypertension* 59: 375–381, 2012
20. Kakimoto Y, Akazawa S: Isolation and identification of N-G,N-G- and N-G,N′-G-dimethyl-arginine, N-ε-mono-, di-, and trimethyllysine, and glucosylgalactosyl- and galactosyl-delta-hydroxylysine from human urine. *J Biol Chem* 245: 5751–5758, 1970
21. Vallance P, Leone A, Calver A, Collier J, Moncada S: Accumulation of an endogenous inhibitor of nitric oxide synthesis in chronic renal failure. *Lancet* 339: 572–575, 1992
22. Durban E, Lee HW, Kim S, Paik WK: Purification and characterization of protein methylase I (S-adenosylmethionine: Protein-arginine methyltransferase; EC 2.1.1.23) from calf brain. *Methods Cell Biol* 19: 59–67, 1978
23. Rawal N, Rajpurohit R, Lischwe MA, Williams KR, Paik WK, Kim S: Structural specificity of substrate for S-adenosylmethionine: protein arginine N-methyltransferases. *Biochim Biophys Acta* 1248: 11–18, 1995
24. Leiper JM, Santa Maria J, Chubb A, MacAllister RJ, Charles IG, Whitley GS, Vallance P: Identification of two human dimethylarginine dimethylaminohydrolases with distinct tissue distributions and homology with microbial arginine deiminases. *Biochem J* 343: 209–214, 1999
25. Kimoto M, Whitley GS, Tsuji H, Ogawa T: Detection of N^G, N^G-dimethylarginine dimethylaminohydrolase in human tissues using a monoclonal antibody. *J Biochem* 117: 237–238, 1995
26. Tojo A, Welch WJ, Bremer V, Kimoto M, Kimura K, Omata M, Ogawa T, Vallance P, Wilcox CS: Colocalization of demethylating enzymes and NOS and functional effects of methylarginines in rat kidney. *Kidney Int* 52: 1593–1601, 1997
27. Closs EI, Simon A, Vékony N, Rotmann A: Plasma membrane transporters for arginine. *J Nutr* 134[Suppl]: 2752S–2759S, discussion 2765S–2767S, 2004
28. Jalal DI, Chonchol M, Targher G: Disorders of hemostasis associated with chronic kidney disease. *Semin Thromb Hemost* 36: 34–40, 2010
29. Thijs A, Nanayakkara PW, Ter Wee PM, Huijgens PC, van Guldener C, Stehouwer CD: Mild-to-moderate renal impairment is associated with platelet activation: A cross-sectional study. *Clin Nephrol* 70: 325–331, 2008
30. Jennewein C, Tran N, Paulus P, Ellinghaus P, Eble JA, Zacharowski K: Novel aspects of fibrin(ogen) fragments during inflammation. *Mol Med* 17: 568–573, 2011
31. Ono T: [Roles of coagulation pathway and factor Xa in chronic kidney disease (CKD)]. *Yakugaku Zasshi* 132: 449–453, 2012
32. van Hinsbergh VWM: Endothelium—role in regulation of coagulation and inflammation. *Semin Immunopathol* 34: 93–106, 2012
33. Solovey A, Kollander R, Milbauer LC, Abdulla F, Chen YIE, Kelm RJ Jr, Hebbel RP: Endothelial nitric oxide synthase and nitric oxide regulate endothelial tissue factor expression in vivo in the sickle transgenic mouse. *Am J Hematol* 85: 41–45, 2010
34. Moncada S, Higgs A: The L-arginine-nitric oxide pathway. *N Engl J Med* 329: 2002–2012, 1993
35. Jourde-Chiche N, Dou L, Cerini C, Dignat-George F, Vanholder R, Brunet P: Protein-bound toxins—update 2009. *Semin Dial* 22: 334–339, 2009
36. Itoh Y, Ezawa A, Kikuchi K, Tsuruta Y, Niwa T: Protein-bound uremic toxins in hemodialysis patients measured by liquid

chromatography/tandem mass spectrometry and their effects on endothelial ROS production. *Anal Bioanal Chem* 403: 1841–1850, 2012
37. Miyamoto Y, Iwao Y, Mera K, Watanabe H, Kadowaki D, Ishima Y, Chuang VT, Sato K, Otagiri M, Maruyama T: A uremic toxin, 3-carboxy-4-methyl-5-propyl-2-furanpropionate induces cell damage to proximal tubular cells via the generation of a radical intermediate. *Biochem Pharmacol* 84: 1207–1214, 2012

Received: May 31, 2012 **Accepted:** October 19, 2012

Published online ahead of print. Publication date available at www.cjasn.org.

This article contains supplemental material online at http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.05540512/-/DCSupplemental.

Supplemental Data Table 1
UNNM-01-12VW

Biochemical Name	Platform	Fold of Change			Statistical Values						Mean Values			Standard Deviation		
		CKD3 / CKD2	CKD4 / CKD2	CKD4 / CKD3	CKD3 / CKD2		CKD4 / CKD2		CKD4 / CKD3		CKD2	CKD3	CKD4	CKD2	CKD3	CKD4
					p-value	q-value	p-value	q-value	p-value	q-value						
glycine	GC/MS	1.3	1.36	1.04	0.08	0.08	0.04	0.03	0.73	0.98	0.845	1.100	1.147	0.341	0.344	0.333
N-acetylglycine	GC/MS	1.45	1.21	0.84	0.02	0.04	0.30	0.14	0.24	0.88	0.641	0.929	0.777	0.125	0.320	0.336
serine	GC/MS	1.31	1.31	1	0.02	0.04	0.01	0.01	0.96	0.99	0.812	1.063	1.063	0.239	0.180	0.154
threonine	GC/MS	1.15	1.21	1.06	0.41	0.20	0.10	0.06	0.58	0.92	0.898	1.028	1.088	0.194	0.327	0.264
betaine	LC/MS pos	0.82	0.54	0.66	0.15	0.12	0.00	0.00	0.13	0.88	1.478	1.209	0.793	0.410	0.802	0.402
aspartate	GC/MS	1.15	1.22	1.06	0.33	0.18	0.28	0.13	0.83	0.98	0.869	0.998	1.057	0.387	0.331	0.434
asparagine	GC/MS	1.36	1.58	1.16	0.09	0.09	0.01	0.01	0.29	0.88	0.798	1.087	1.261	0.302	0.435	0.475
alanine	GC/MS	1.31	1.42	1.09	0.02	0.04	0.01	0.01	0.32	0.88	0.803	1.051	1.144	0.253	0.175	0.216
N-acetylalanine	LC/MS neg	1.38	1.54	1.12	0.13	0.11	0.06	0.05	0.68	0.98	0.815	1.127	1.258	0.314	0.594	0.833
glutamate	GC/MS	0.8	1.07	1.34	0.43	0.21	0.79	0.29	0.32	0.88	1.188	0.950	1.276	0.746	0.245	0.676
glutamine	LC/MS pos	0.98	0.92	0.94	0.69	0.26	0.22	0.11	0.53	0.92	1.043	1.024	0.963	0.127	0.212	0.178
pyroglutamine*	LC/MS pos	2.03	1.33	0.65	0.11	0.10	0.58	0.22	0.30	0.88	0.825	1.677	1.095	0.462	1.325	0.813
histidine	LC/MS neg	1.09	1.09	1	0.16	0.12	0.16	0.09	0.98	0.99	0.918	1.004	1.003	0.132	0.128	0.134
3-methylhistidine	LC/MS neg	1.65	2.66	1.61	0.46	0.21	0.44	0.18	0.88	0.98	1.013	1.674	2.693	0.886	1.952	4.134
lysine	LC/MS pos	0.66	0.59	0.9	0.02	0.04	0.00	0.00	0.79	0.98	1.270	0.834	0.751	0.286	0.454	0.342
pipecolate	LC/MS pos	1.1	0.96	0.87	0.96	0.31	0.84	0.29	0.82	0.98	1.395	1.538	1.337	1.149	1.344	1.133
N6-acetyllysine	LC/MS pos	1.47	1.56	1.06	0.03	0.04	0.13	0.07	0.86	0.98	0.902	1.328	1.406	0.266	0.541	0.967
glutaroyl carnitine	LC/MS pos	1.57	1.63	1.04	0.04	0.06	0.30	0.14	0.59	0.92	0.813	1.275	1.329	0.429	0.585	1.199
phenylalanine	LC/MS pos	1.3	1.21	0.92	0.02	0.04	0.01	0.01	0.55	0.92	0.853	1.112	1.029	0.124	0.320	0.140
phenylacetate	LC/MS neg	1.39	1	0.72	0.07	0.07			0.07	0.88	0.507	0.707	0.507	0.000	0.311	0.000
p-cresol sulfate	LC/MS neg	1.91	1.61	0.84	0.22	0.15	0.31	0.14	0.82	0.98	0.945	1.802	1.521	0.860	1.939	1.288
tyrosine	LC/MS pos	1.26	0.91	0.72	0.52	0.23	0.34	0.15	0.27	0.88	1.049	1.327	0.956	0.212	0.776	0.175
3-(4-hydroxyphenyl)lactate	GC/MS	1.5	0.99	0.66	0.51	0.22	0.79	0.29	0.41	0.90	0.901	1.353	0.892	0.373	1.261	0.574
3-methoxytyrosine	LC/MS pos	1.42	1.43	1.01	0.00	0.01	0.01	0.01	0.97	0.99	0.697	0.987	0.995	0.144	0.212	0.279
phenylacetylglutamine	LC/MS pos	2.31	1.62	0.7	0.28	0.17	0.39	0.16	0.69	0.98	0.817	1.885	1.322	0.608	2.027	1.724
phenol sulfate	LC/MS neg	1.32	1.78	1.35	0.83	0.28	0.12	0.07	0.24	0.88	1.040	1.370	1.847	0.709	1.566	1.393
kynurenine	LC/MS pos	1.16	1.24	1.07	0.37	0.19	0.10	0.06	0.55	0.92	0.944	1.093	1.171	0.234	0.391	0.337
tryptophan	LC/MS pos	1	0.88	0.88	0.70	0.26	0.29	0.14	0.78	0.98	1.064	1.060	0.933	0.254	0.426	0.186
indolelactate	LC/MS pos	0.98	1.28	1.3	0.69	0.26	0.46	0.19	0.33	0.88	1.017	0.998	1.300	0.357	0.538	0.800
indoleacetate	LC/MS pos	0.65	0.55	0.85	0.03	0.04	0.01	0.01	0.25	0.88	1.572	1.015	0.859	0.731	0.384	0.428
tryptophan betaine	LC/MS pos	1.36	1.34	0.98	0.63	0.25	0.59	0.22	0.95	0.99	1.215	1.656	1.631	1.434	1.751	1.439
serotonin (5HT)	LC/MS pos	1.48	1.8	1.21	0.01	0.04	0.00	0.01	0.35	0.88	0.592	0.877	1.065	0.001	0.318	0.482
C-glycosyltryptophan*	LC/MS pos	1.78	2.31	1.3	0.04	0.06	0.01	0.01	0.44	0.91	0.734	1.306	1.694	0.314	1.076	1.771

Supplemental Data Table 1
UNNM-01-12VW

Biochemical Name	Platform	Fold of Change			Statistical Values						Mean Values			Standard Deviation		
		CKD3 / CKD2	CKD4 / CKD2	CKD4 / CKD3	CKD3 / CKD2		CKD4 / CKD2		CKD4 / CKD3		CKD2	CKD3	CKD4	CKD2	CKD3	CKD4
					p-value	q-value	p-value	q-value	p-value	q-value						
3-indoxyl sulfate	LC/MS neg	1.35	1.35	1	0.56	0.23	0.29	0.14	0.67	0.98	1.186	1.595	1.600	0.914	1.499	1.414
indolepropionate	LC/MS pos	1.44	0.78	0.54	0.57	0.23	0.40	0.17	0.18	0.88	1.179	1.703	0.920	0.620	1.802	0.603
3-methyl-2-oxobutyrate	LC/MS neg	1.07	1.08	1.02	0.91	0.29	0.65	0.24	0.81	0.98	0.954	1.018	1.033	0.207	0.349	0.296
3-methyl-2-oxovalerate	LC/MS neg	0.97	1.1	1.13	0.87	0.28	0.42	0.17	0.33	0.88	0.961	0.933	1.058	0.305	0.302	0.284
beta-hydroxyisovalerate	LC/MS neg	0.97	0.96	1	0.82	0.28	0.81	0.29	0.99	0.99	0.779	0.752	0.751	0.283	0.281	0.280
alpha-hydroxyisocaproate	LC/MS neg	1.1	1.24	1.13	0.72	0.26	0.60	0.23	0.83	0.98	0.580	0.635	0.718	0.148	0.321	0.585
isoleucine	LC/MS pos	0.95	1.08	1.15	0.79	0.27	0.32	0.14	0.07	0.88	1.004	0.950	1.088	0.279	0.185	0.161
leucine	LC/MS pos	0.96	0.98	1.02	0.64	0.25	0.92	0.31	0.66	0.98	1.029	0.989	1.009	0.212	0.280	0.150
valine	LC/MS pos	0.98	1.02	1.04	0.84	0.28	0.68	0.25	0.51	0.92	0.991	0.970	1.011	0.222	0.210	0.128
3-hydroxyisobutyrate	GC/MS	1.37	1.16	0.85	0.21	0.14	0.56	0.22	0.51	0.92	0.792	1.087	0.920	0.251	0.569	0.418
4-methyl-2-oxopentanoate	LC/MS neg	0.99	1.07	1.09	0.71	0.26	0.58	0.22	0.44	0.91	0.974	0.961	1.045	0.269	0.395	0.277
alpha-hydroxyisovalerate	LC/MS neg	1.05	0.85	0.81	0.27	0.17	0.12	0.07	0.77	0.98	2.256	2.360	1.920	1.314	3.850	3.316
isobutyrylcarnitine	LC/MS pos	1.44	1.59	1.1	0.32	0.18	0.14	0.08	0.66	0.98	1.066	1.534	1.693	1.030	1.283	1.554
2-methylbutyroylcarnitine	LC/MS pos	1.31	1.12	0.86	0.52	0.23	0.85	0.29	0.46	0.91	0.843	1.103	0.946	0.438	0.733	0.950
isovalerylcarnitine	LC/MS pos	1.07	1.16	1.09	0.77	0.27	0.60	0.23	0.80	0.98	1.039	1.109	1.206	0.438	0.479	0.570
cysteine	GC/MS	1.03	0.85	0.82	0.99	0.31	0.27	0.13	0.31	0.88	1.052	1.078	0.890	0.297	0.408	0.322
methionine	LC/MS neg	1.36	1.09	0.8	0.15	0.12	0.13	0.07	0.35	0.88	0.943	1.285	1.025	0.128	0.660	0.101
2-hydroxybutyrate (AHB)	GC/MS	1.4	1.37	0.98	0.25	0.17	0.28	0.13	0.94	0.99	0.832	1.164	1.136	0.454	0.732	0.689
dimethylarginine (SDMA + ADMA)	LC/MS pos	8.06	4.84	0.6	0.00	0.00	0.01	0.01	0.17	0.88	0.497	4.006	2.403	0.133	2.273	1.774
arginine	LC/MS neg	1.51	1.53	1.01	0.06	0.07	0.10	0.06	0.93	0.99	0.675	1.020	1.032	0.238	0.480	0.559
ornithine	LC/MS pos	0.28	0.16	0.57	0.00	0.00	0.00	0.00	0.34	0.88	4.327	1.195	0.683	1.387	1.316	0.334
urea	GC/MS	1.32	1.51	1.14	0.17	0.13	0.09	0.06	0.67	0.98	0.803	1.062	1.210	0.351	0.474	0.772
proline	LC/MS pos	1.28	0.97	0.76	0.21	0.14	0.84	0.29	0.15	0.88	0.966	1.239	0.936	0.260	0.518	0.246
citrulline	LC/MS pos	1.58	1.31	0.83	0.03	0.05	0.08	0.05	0.42	0.90	0.825	1.304	1.082	0.194	0.586	0.362
N-acetylornithine	LC/MS pos	1.66	1.39	0.84	0.09	0.09	0.07	0.05	0.87	0.98	0.905	1.501	1.257	0.762	0.999	0.400
trans-4-hydroxyproline	GC/MS	1.23	1.4	1.14	0.44	0.21	0.25	0.12	0.71	0.98	0.973	1.199	1.361	0.362	0.581	0.937
creatine	LC/MS pos	0.97	1.22	1.25	0.64	0.25	0.85	0.29	0.58	0.92	0.978	0.952	1.192	0.460	0.752	0.694
creatinine	LC/MS pos	1.16	1.23	1.06	0.75	0.26	0.98	0.33	0.82	0.98	1.085	1.264	1.337	0.296	0.655	1.344
2-aminobutyrate	LC/MS pos	1.14	1.28	1.13	0.59	0.24	0.05	0.04	0.28	0.88	0.889	1.010	1.140	0.262	0.401	0.237
4-acetamidobutanoate	LC/MS pos	2.17	1.71	0.79	0.17	0.13	0.15	0.08	0.85	0.98	0.866	1.876	1.483	0.232	2.613	1.542
5-oxoproline	LC/MS pos	1.46	1.42	0.97	0.03	0.04	0.09	0.06	0.74	0.98	0.806	1.180	1.140	0.309	0.388	0.391
aspartylphenylalanine	LC/MS pos	2	3.56	1.78	0.02	0.04	0.00	0.00	0.07	0.88	0.354	0.710	1.261	0.000	0.496	0.798
pro-hydroxy-pro	LC/MS pos	2.49	4.46	1.79	0.03	0.05	0.00	0.00	0.05	0.88	0.466	1.162	2.079	0.251	1.268	1.677

Supplemental Data Table 1 UNNM-01-12VW		Fold of Change			Statistical Values						Mean Values			Standard Deviation		
		CKD3 CKD2	CKD4 CKD2	CKD4 CKD3	CKD3 CKD2		CKD4 CKD2		CKD4 CKD3		CKD2	CKD3	CKD4	CKD2	CKD3	CKD4
Biochemical Name	Platform				p-value	q-value	p-value	q-value	p-value	q-value						
cyclo(leu-pro)	LC/MS pos	0.55	0.36	0.65	0.42	0.21	0.11	0.07	0.33	0.88	1.971	1.093	0.716	2.732	1.073	0.516
phenylalanyltryptophan	LC/MS pos	1.11	2.39	2.16	0.74	0.26	0.02	0.02	0.04	0.88	0.736	0.817	1.762	0.543	0.570	1.150
gamma-glutamylvaline	LC/MS pos	1.17	1.22	1.04	0.27	0.17	0.07	0.05	0.62	0.95	0.912	1.065	1.108	0.236	0.311	0.250
gamma-glutamylleucine	LC/MS pos	1.12	1.3	1.16	0.51	0.22	0.03	0.02	0.15	0.88	0.821	0.921	1.070	0.283	0.310	0.161
gamma-glutamylisoleucine*	LC/MS pos	1.61	1.7	1.06	0.01	0.03	0.01	0.01	0.78	0.98	0.695	1.117	1.184	0.196	0.440	0.510
gamma-glutamylmethionine	LC/MS pos	1.09	0.85	0.78	0.70	0.26	0.37	0.16	0.21	0.88	1.044	1.138	0.887	0.387	0.474	0.291
gamma-glutamylglutamine	LC/MS pos	3.83	4.78	1.25	0.00	0.00	0.00	0.00	0.13	0.88	0.275	1.053	1.313	0.166	0.417	0.349
gamma-glutamylphenylalanine	LC/MS pos	1.45	1.29	0.89	0.03	0.04	0.01	0.01	0.59	0.92	0.903	1.311	1.165	0.240	0.480	0.181
gamma-glutamyltyrosine	LC/MS pos	1.19	0.97	0.82	0.55	0.23	0.95	0.32	0.53	0.92	0.993	1.179	0.966	0.366	0.631	0.193
bradykinin, des-arg(9)	LC/MS pos	4.95	1.42	0.29	0.26	0.17	0.17	0.09	0.60	0.92	0.764	3.779	1.083	0.306	7.550	0.651
ADSGEGDFXAEGGGVR*	LC/MS pos	2.06	2.82	1.37	0.01	0.03	0.00	0.00	0.24	0.88	0.465	0.957	1.311	0.000	0.516	0.761
DSGEGDFXAEGGGVR*	LC/MS pos	689.13	826.73	1.2	0.00	0.00	0.00	0.00	0.21	0.88	0.002	1.034	1.240	0.001	0.765	0.795
ADpSGEGDFXAEGGGVR*	LC/MS pos	18.01	45.27	2.51	0.00	0.01	0.00	0.00	0.04	0.88	0.045	0.818	2.055	0.017	0.683	2.624
erythronate*	GC/MS	1.61	1.45	0.9	0.31	0.18	0.28	0.13	0.95	0.99	0.992	1.597	1.438	0.393	1.737	1.299
fructose	GC/MS	2.83	1.76	0.62	0.03	0.04	0.00	0.01	0.50	0.92	0.763	2.157	1.343	0.346	1.695	0.534
mannitol	GC/MS	6.94	3.8	0.55	0.08	0.09	0.02	0.02	0.98	0.99	0.216	1.495	0.819	0.059	2.326	0.745
mannose	GC/MS	0.67	0.68	1.02	0.19	0.14	0.24	0.12	0.78	0.98	1.572	1.046	1.070	1.004	0.444	0.365
1,5-anhydroglucitol (1,5-AG)	LC/MS neg	0.76	0.62	0.82	0.54	0.23	0.26	0.13	0.53	0.92	1.291	0.978	0.801	0.711	0.487	0.295
glycerate	GC/MS	0.69	0.51	0.74	0.04	0.05	0.00	0.00	0.02	0.88	1.185	0.823	0.608	0.378	0.225	0.163
glucose	GC/MS	0.69	0.71	1.02	0.09	0.09	0.11	0.06	0.83	0.98	1.422	0.984	1.003	0.697	0.307	0.293
1,6-anhydroglucose	GC/MS	0.55	0.49	0.89	0.33	0.18	0.29	0.14	0.96	0.99	1.391	0.759	0.675	1.891	0.751	0.510
pyruvate	GC/MS	0.48	0.39	0.8	0.01	0.03	0.00	0.00	0.33	0.88	1.921	0.925	0.744	1.014	0.526	0.453
lactate	GC/MS	0.91	0.93	1.02	0.63	0.25	0.58	0.22	0.86	0.98	1.210	1.100	1.127	0.434	0.310	0.558
arabitol	GC/MS	1.3	1.75	1.35	0.24	0.16	0.01	0.01	0.19	0.88	0.826	1.073	1.450	0.206	0.557	0.904
gluconate	GC/MS	1.43	1.01	0.7	0.99	0.31	0.69	0.25	0.73	0.98	0.859	1.232	0.866	0.663	2.085	0.462
arabinose	GC/MS	0.8	0.68	0.84	0.61	0.24	0.32	0.14	0.56	0.92	0.787	0.631	0.531	0.656	0.421	0.165
xylonate	GC/MS	1.8	2.35	1.3	0.13	0.11	0.05	0.04	0.56	0.92	0.636	1.145	1.493	0.025	1.131	1.648
citrate	GC/MS	0.76	0.51	0.67	0.08	0.08	0.00	0.00	0.04	0.88	1.506	1.147	0.773	0.499	0.501	0.218
alpha-ketoglutarate	GC/MS	1.34	0.95	0.71	0.51	0.22	0.84	0.29	0.41	0.90	0.625	0.839	0.593	0.253	0.755	0.172
succinate	GC/MS	1.15	1.23	1.07	0.31	0.18	0.04	0.03	0.45	0.91	0.824	0.951	1.015	0.170	0.314	0.209
malate	GC/MS	0.68	0.51	0.75	0.06	0.07	0.00	0.00	0.23	0.88	1.344	0.918	0.690	0.471	0.486	0.162
acetylphosphate	GC/MS	1.7	1.92	1.13	0.00	0.00	0.00	0.00	0.40	0.90	0.630	1.073	1.213	0.169	0.280	0.332
phosphate	GC/MS	0.44	0.3	0.69	0.00	0.00	0.00	0.00	0.41	0.90	2.679	1.167	0.804	0.452	0.910	0.190

Supplemental Data Table 1 UNNM-01-12VW		Fold of Change			Statistical Values						Mean Values			Standard Deviation		
		CKD3 CKD2	CKD4 CKD2	CKD4 CKD3	CKD3 CKD2		CKD4 CKD2		CKD4 CKD3		CKD2	CKD3	CKD4	CKD2	CKD3	CKD4
Biochemical Name	Platform				p-value	q-value	p-value	q-value	p-value	q-value						
linoleate (18:2n6)	LC/MS neg	1.42	1.63	1.15	0.38	0.19	0.00	0.00	0.30	0.88	0.740	1.050	1.210	0.195	0.485	0.364
linolenate [alpha or gamma; (18:3n3 or 6)]	LC/MS neg	1.64	2.11	1.29	0.33	0.18	0.00	0.00	0.22	0.88	0.661	1.085	1.398	0.238	0.525	0.559
dihomo-linolenate (20:3n3 or n6)	LC/MS neg	1.3	1.48	1.14	0.42	0.21	0.01	0.01	0.29	0.88	0.870	1.128	1.290	0.284	0.545	0.359
eicosapentaenoate (EPA; 20:5n3)	LC/MS neg	2.37	3.73	1.57	0.16	0.13	0.00	0.00	0.12	0.88	0.607	1.438	2.262	0.365	1.432	1.490
docosapentaenoate (n3 DPA; 22:5n3)	LC/MS neg	1.84	2.55	1.39	0.13	0.11	0.00	0.00	0.11	0.88	0.623	1.143	1.590	0.288	0.641	0.552
docosahexaenoate (DHA; 22:6n3)	LC/MS neg	2.08	2.3	1.1	0.10	0.09	0.00	0.00	0.46	0.91	0.671	1.399	1.542	0.229	0.847	0.705
caproate (6:0)	LC/MS neg	1.67	2.11	1.26	0.06	0.07	0.00	0.00	0.17	0.88	0.562	0.940	1.186	0.374	0.435	0.383
heptanoate (7:0)	LC/MS neg	1.39	1.72	1.23	0.07	0.08	0.00	0.00	0.10	0.88	0.598	0.834	1.027	0.258	0.313	0.201
caprylate (8:0)	LC/MS neg	1.41	1.31	0.93	0.11	0.10	0.05	0.04	0.95	0.99	0.751	1.058	0.980	0.372	0.381	0.178
pelargonate (9:0)	LC/MS neg	1.3	1.5	1.15	0.04	0.05	0.00	0.00	0.10	0.88	0.744	0.970	1.112	0.172	0.217	0.114
caprate (10:0)	LC/MS neg	1.14	1.04	0.91	0.45	0.21	0.52	0.21	0.73	0.98	1.002	1.147	1.046	0.256	0.463	0.150
undecanoate (11:0)	LC/MS neg	1.44	1.57	1.09	0.01	0.03	0.00	0.00	0.48	0.92	0.818	1.178	1.283	0.194	0.356	0.371
laurate (12:0)	LC/MS neg	1.03	1.01	0.98	0.82	0.28	0.82	0.29	0.98	0.99	1.049	1.079	1.055	0.353	0.343	0.214
5-dodecenoate (12:1n7)	LC/MS neg	2.46	0.71	0.29	0.09	0.09	0.16	0.09	0.01	0.88	1.084	2.663	0.767	0.629	2.585	0.309
myristate (14:0)	LC/MS neg	1.09	1.13	1.04	0.94	0.30	0.32	0.14	0.48	0.92	1.038	1.127	1.174	0.425	0.670	0.343
myristoleate (14:1n5)	LC/MS neg	1.2	0.91	0.76	0.62	0.25	0.63	0.23	0.89	0.98	1.463	1.756	1.331	1.409	1.773	0.544
palmitate (16:0)	LC/MS neg	1.2	1.25	1.04	0.64	0.25	0.08	0.05	0.50	0.92	0.920	1.104	1.150	0.315	0.528	0.313
palmitoleate (16:1n7)	LC/MS neg	1.14	1.07	0.94	0.87	0.28	0.36	0.16	0.40	0.90	1.263	1.440	1.357	1.006	1.394	0.555
margarate (17:0)	LC/MS neg	1.54	1.49	0.97	0.25	0.17	0.03	0.03	0.70	0.98	0.804	1.237	1.194	0.375	0.633	0.414
10-heptadecenoate (17:1n7)	LC/MS neg	1.21	1.28	1.05	0.83	0.28	0.10	0.06	0.36	0.89	0.898	1.090	1.145	0.509	0.738	0.342
stearate (18:0)	LC/MS neg	1.2	1.25	1.04	0.53	0.23	0.11	0.06	0.59	0.92	0.938	1.123	1.171	0.294	0.441	0.367
oleate (18:1n9)	LC/MS neg	1.34	1.39	1.04	0.48	0.22	0.03	0.03	0.45	0.91	0.871	1.164	1.212	0.399	0.685	0.355
cis-vaccenate (18:1n7)	GC/MS	0.23	0.64	2.73	0.09	0.09	0.62	0.23	0.19	0.88	1.181	0.277	0.757	1.524	0.187	0.839
stearidonate (18:4n3)	LC/MS neg	2.42	2.38	0.98	0.07	0.07	0.01	0.01	0.57	0.92	0.511	1.237	1.215	0.511	1.221	0.599
nonadecanoate (19:0)	LC/MS neg	1.58	1.59	1.01	0.11	0.10	0.01	0.01	0.59	0.92	0.705	1.115	1.124	0.263	0.668	0.345
10-nonadecenoate (19:1n9)	LC/MS neg	1.61	1.37	0.85	0.50	0.22	0.05	0.04	0.57	0.92	0.909	1.461	1.248	0.712	1.338	0.419
eicosenoate (20:1n9 or 11)	LC/MS neg	1.72	1.39	0.81	0.45	0.21	0.08	0.05	0.70	0.98	0.980	1.686	1.365	0.655	1.755	0.575
dihomo-linoleate (20:2n6)	LC/MS neg	1.66	1.39	0.83	0.32	0.18	0.07	0.05	0.88	0.98	0.783	1.303	1.086	0.444	0.965	0.422
dihomo-alpha-linolenate (20:3n3)	LC/MS neg	1.3	1.48	1.14	0.42	0.21	0.01	0.01	0.29	0.88	0.870	1.128	1.290	0.284	0.545	0.359
arachidonate (20:4n6)	LC/MS neg	1.86	2.2	1.18	0.01	0.03	0.00	0.00	0.19	0.88	0.631	1.176	1.386	0.180	0.501	0.304
adrenate (22:4n6)	LC/MS neg	1.39	1.41	1.01	0.34	0.18	0.02	0.02	0.52	0.92	0.869	1.210	1.221	0.403	0.625	0.291
3-hydroxydecanoate	LC/MS neg	1.18	0.72	0.61	0.83	0.28	0.39	0.16	0.34	0.88	1.193	1.407	0.857	0.931	1.349	0.261
16-hydroxypalmitate	LC/MS neg	0.95	0.63	0.67	0.73	0.26	0.07	0.05	0.20	0.88	1.491	1.422	0.946	0.859	0.935	0.229

Supplemental Data Table 1 UNNM-01-12VW		Fold of Change			Statistical Values						Mean Values			Standard Deviation		
		CKD3 / CKD2	CKD4 / CKD2	CKD4 / CKD3	CKD3 / CKD2		CKD4 / CKD2		CKD4 / CKD3		CKD2	CKD3	CKD4	CKD2	CKD3	CKD4
Biochemical Name	Platform				p-value	q-value	p-value	q-value	p-value	q-value						
2-hydroxystearate	LC/MS neg	1.57	1.29	0.82	0.28	0.18	0.01	0.01	0.96	0.99	0.791	1.245	1.020	0.226	0.661	0.130
2-hydroxypalmitate	LC/MS neg	1.35	1.18	0.87	0.75	0.26	0.08	0.05	0.69	0.98	0.920	1.240	1.082	0.253	1.000	0.160
sebacate (decanedioate)	LC/MS pos	4.87	8.13	1.67	0.00	0.02	0.00	0.00	0.03	0.88	0.155	0.756	1.263	0.019	0.570	0.445
azelate (nonanedioate)	LC/MS neg	8.58	17.95	2.09	0.01	0.03	0.00	0.00	0.02	0.88	0.127	1.087	2.272	0.021	0.972	1.286
octadecanedioate	LC/MS neg	0.98	0.67	0.69	0.14	0.12	0.05	0.04	0.87	0.98	1.215	1.195	0.819	0.532	1.897	0.703
3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	LC/MS neg	18.28	23.58	1.29	0.06	0.07	0.00	0.00	0.17	0.88	0.307	5.608	7.234	0.279	11.864	7.195
oleamide	LC/MS pos	1.03	1.28	1.24	0.73	0.26	0.87	0.30	0.64	0.96	1.029	1.061	1.313	0.727	1.201	1.174
propionylcarnitine	LC/MS pos	0.86	0.81	0.95	0.36	0.19	0.21	0.11	0.72	0.98	1.126	0.968	0.917	0.418	0.336	0.376
butyrylcarnitine	LC/MS pos	0.49	0.38	0.76	0.02	0.04	0.00	0.00	0.86	0.98	2.492	1.229	0.936	1.803	1.319	0.774
isovalerate	LC/MS neg	2.03	2.43	1.2	0.01	0.03	0.00	0.00	0.16	0.88	0.481	0.975	1.168	0.148	0.421	0.211
carnitine	LC/MS pos	0.62	0.61	0.97	0.00	0.01	0.00	0.00	0.87	0.98	1.390	0.867	0.844	0.185	0.372	0.207
3-dehydrocarnitine*	LC/MS pos	1.08	1.53	1.41	0.52	0.23	0.13	0.07	0.26	0.88	1.023	1.105	1.563	0.469	0.409	1.167
acetylcarnitine	LC/MS pos	0.95	0.88	0.92	0.61	0.24	0.37	0.16	0.73	0.98	1.219	1.156	1.069	0.428	0.581	0.487
hexanoylcarnitine	LC/MS pos	0.88	0.97	1.1	0.58	0.24	0.95	0.32	0.52	0.92	1.234	1.085	1.194	0.791	0.549	0.507
octanoylcarnitine	LC/MS pos	0.88	0.84	0.96	0.91	0.29	0.97	0.32	0.85	0.98	1.369	1.201	1.151	1.279	0.769	0.663
decanoylcarnitine	LC/MS pos	0.71	0.62	0.87	0.54	0.23	0.30	0.14	0.63	0.96	1.712	1.216	1.056	1.794	0.696	0.583
laurylcarnitine	LC/MS pos	0.82	0.56	0.68	0.75	0.26	0.35	0.15	0.58	0.92	2.043	1.683	1.143	2.256	1.323	0.675
palmitoylcarnitine	LC/MS pos	0.93	0.55	0.59	0.50	0.22	0.02	0.02	0.19	0.88	1.511	1.412	0.837	0.746	1.112	0.386
oleoylcarnitine	LC/MS pos	0.87	0.66	0.76	0.33	0.18	0.11	0.07	0.76	0.98	1.749	1.514	1.147	1.334	1.525	0.959
cholate	LC/MS neg	0.55	1.4	2.54	0.62	0.25	0.89	0.30	0.55	0.92	2.633	1.454	3.696	4.482	2.108	6.210
glycocholate	LC/MS pos	1.96	0.13	0.07	0.45	0.21	0.01	0.01	0.14	0.88	4.207	8.244	0.549	4.058	20.881	0.310
taurocholate	LC/MS neg	14.75	0.36	0.02	0.58	0.24	0.05	0.04	0.15	0.88	1.346	19.863	0.491	1.163	44.588	0.189
taurochenodeoxycholate	LC/MS neg	12.48	0.19	0.01	0.83	0.28	0.04	0.03	0.29	0.88	2.078	25.940	0.386	2.057	62.115	0.351
ursodeoxycholate	LC/MS neg	1.23	1.12	0.91	0.68	0.26	0.83	0.29	0.85	0.98	1.016	1.250	1.138	0.452	1.606	1.089
hyodeoxycholate	LC/MS neg	0.24	0.36	1.51	0.00	0.00	0.00	0.00	0.07	0.88	2.681	0.641	0.967	1.772	0.549	0.596
glycochenodeoxycholate	LC/MS neg	2.92	0.11	0.04	0.20	0.14	0.00	0.00	0.21	0.88	12.067	35.263	1.339	12.006	99.211	1.991
glycolithocholate sulfate*	LC/MS neg	0.64	0.7	1.1	0.48	0.22	0.41	0.17	0.80	0.98	1.459	0.933	1.022	1.220	0.533	0.803
taurolithocholate 3-sulfate	LC/MS neg	1.68	0.89	0.53	0.53	0.23	0.88	0.30	0.44	0.91	1.002	1.684	0.896	0.741	1.675	0.604
glycocholenate sulfate*	LC/MS neg	0.76	1.05	1.38	0.28	0.17	0.77	0.28	0.16	0.88	1.091	0.832	1.147	0.524	0.436	0.538
taurocholenate sulfate*	LC/MS neg	2.68	1.76	0.66	0.02	0.04	0.03	0.03	0.42	0.90	0.678	1.816	1.193	0.376	1.586	0.755
glycerol	GC/MS	0.74	0.79	1.06	0.03	0.05	0.08	0.05	0.83	0.98	1.153	0.856	0.906	0.290	0.331	0.375
choline	LC/MS pos	1.38	1.32	0.95	0.05	0.06	0.08	0.05	0.73	0.98	0.836	1.157	1.100	0.334	0.344	0.376

Supplemental Data Table 1 UNNM-01-12VW		Fold of Change			Statistical Values						Mean Values			Standard Deviation		
		CKD3 CKD2	CKD4 CKD2	CKD4 CKD3	CKD3 CKD2		CKD4 CKD2		CKD4 CKD3		CKD2	CKD3	CKD4	CKD2	CKD3	CKD4
Biochemical Name	Platform				p-value	q-value	p-value	q-value	p-value	q-value						
glycerol 3-phosphate (G3P)	GC/MS	1.36	1.76	1.29	0.06	0.07	0.00	0.00	0.04	0.88	0.791	1.080	1.395	0.221	0.385	0.297
glycerophosphorylcholine (GPC)	LC/MS pos	1.72	2.54	1.48	0.32	0.18	0.00	0.00	0.08	0.88	0.557	0.959	1.416	0.254	0.974	0.835
myo-inositol	GC/MS	2.27	2.01	0.89	0.03	0.05	0.01	0.01	0.98	0.99	0.810	1.841	1.631	0.340	1.671	1.157
scyllo-inositol	GC/MS	1.97	1.27	0.64	0.15	0.12	0.34	0.15	0.45	0.91	0.586	1.156	0.742	0.335	1.214	0.467
3-hydroxybutyrate (BHBA)	GC/MS	1.56	1.3	0.84	0.36	0.19	0.34	0.15	0.96	0.99	1.258	1.958	1.641	1.174	2.082	1.290
1-oleoylglycerophosphoethanolamine	LC/MS neg	0.69	0.46	0.66	0.09	0.09	0.01	0.01	0.40	0.90	1.702	1.172	0.779	0.943	1.106	0.422
1-linoleoylglycerophosphoethanolamine*	LC/MS neg	0.66	0.61	0.93	0.04	0.05	0.02	0.02	0.82	0.98	1.534	1.012	0.940	0.742	0.560	0.397
1-arachidonoylglycerophosphoethanolamine*	LC/MS neg	0.83	0.93	1.12	0.15	0.12	0.49	0.20	0.40	0.90	1.104	0.912	1.025	0.288	0.294	0.302
2-arachidonoylglycerophosphoethanolamine*	LC/MS neg	0.74	0.95	1.29	0.06	0.07	0.55	0.21	0.36	0.89	1.061	0.783	1.008	0.367	0.277	0.528
1-myristoylglycerophosphocholine	LC/MS pos	0.53	0.46	0.86	0.03	0.05	0.01	0.01	0.89	0.98	1.741	0.931	0.805	0.785	0.651	0.492
1-palmitoylglycerophosphocholine	LC/MS pos	0.73	0.69	0.94	0.01	0.03	0.00	0.00	0.78	0.98	1.266	0.923	0.870	0.241	0.287	0.194
2-palmitoylglycerophosphocholine*	LC/MS pos	0.56	0.53	0.95	0.00	0.01	0.00	0.00	0.82	0.98	1.519	0.843	0.802	0.378	0.431	0.428
1-palmitoleoylglycerophosphocholine*	LC/MS pos	0.33	0.36	1.11	0.01	0.03	0.04	0.03	0.51	0.92	2.690	0.882	0.976	1.815	1.057	0.668
1-heptadecanoylglycerophosphocholine	LC/MS pos	0.87	0.55	0.63	0.52	0.23	0.01	0.01	0.02	0.88	1.349	1.173	0.741	0.536	0.545	0.255
1-stearoylglycerophosphocholine	LC/MS pos	0.88	0.75	0.85	0.29	0.18	0.05	0.04	0.58	0.92	1.243	1.096	0.928	0.328	0.544	0.359
2-stearoylglycerophosphocholine*	LC/MS pos	0.67	0.61	0.91	0.11	0.10	0.05	0.04	0.71	0.98	1.426	0.956	0.869	0.703	0.609	0.591
1-oleoylglycerophosphocholine	LC/MS pos	0.6	0.57	0.95	0.03	0.04	0.02	0.02	0.84	0.98	1.591	0.962	0.911	0.635	0.440	0.351
2-oleoylglycerophosphocholine*	LC/MS pos	0.58	0.43	0.73	0.01	0.03	0.00	0.00	0.33	0.88	1.764	1.030	0.756	0.714	0.628	0.269
1-linoleoylglycerophosphocholine	LC/MS pos	0.75	0.68	0.91	0.03	0.04	0.00	0.01	0.52	0.92	1.270	0.948	0.866	0.323	0.259	0.232
1-eicosatrienoylglycerophosphocholine*	LC/MS pos	0.69	0.75	1.1	0.18	0.13	0.35	0.15	0.50	0.92	1.457	1.004	1.100	0.768	0.474	0.422
1-arachidonoylglycerophosphocholine*	LC/MS pos	1.26	1.47	1.17	0.68	0.26	0.01	0.01	0.23	0.88	0.905	1.139	1.333	0.227	0.613	0.394
1-docosahexaenoylglycerophosphocholine*	LC/MS pos	1.18	1.46	1.23	0.21	0.14	0.00	0.01	0.11	0.88	0.863	1.019	1.256	0.163	0.284	0.341
1-palmitoylglycerol (1-monopalmitin)	GC/MS	0.67	0.43	0.64	0.21	0.15	0.01	0.01	0.09	0.88	1.287	0.866	0.556	0.793	0.532	0.188
1-linoleoylglycerol (1-monolinolein)	LC/MS neg	4.79	6.73	1.41	0.00	0.00	0.00	0.00	0.09	0.88	0.310	1.481	2.084	0.193	0.923	0.762
stearoyl sphingomyelin	GC/MS	2.14	2.07	0.96	0.34	0.18	0.29	0.14	0.97	0.99	0.574	1.232	1.187	0.416	1.097	1.034
lathosterol	GC/MS	1.14	0.82	0.72	0.65	0.25	0.53	0.21	0.28	0.88	0.524	0.596	0.428	0.386	0.409	0.201
cholesterol	GC/MS	1.03	1.01	0.97	1.00	0.31	0.98	0.32	0.99	0.99	1.017	1.051	1.022	0.160	0.328	0.210
dehydroisoandrosterone sulfate (DHEA-S)	LC/MS neg	0.87	0.55	0.64	0.32	0.18	0.04	0.03	0.52	0.92	1.478	1.280	0.819	0.878	0.933	0.685
epiandrosterone sulfate	LC/MS neg	0.51	0.77	1.5	0.06	0.07	0.15	0.08	0.94	0.99	1.594	0.819	1.232	1.022	0.481	1.267
androsterone sulfate	LC/MS neg	0.45	0.53	1.18	0.05	0.07	0.06	0.05	0.95	0.99	2.135	0.956	1.124	1.846	0.709	1.180
cortisol	LC/MS pos	0.68	0.62	0.9	0.10	0.09	0.03	0.03	0.79	0.98	1.449	0.992	0.894	0.718	0.469	0.379
cortisone	LC/MS pos	0.86	0.59	0.69	0.20	0.14	0.00	0.01	0.08	0.88	1.059	0.907	0.628	0.203	0.320	0.276
7-alpha-hydroxy-3-oxo-4-cholestenoate (7-Hoca)	LC/MS neg	0.78	0.86	1.09	0.30	0.18	0.43	0.18	0.86	0.98	1.550	1.214	1.326	1.084	1.102	1.122

Supplemental Data Table 1
UNNM-01-12VW

Biochemical Name	Platform	Fold of Change			Statistical Values						Mean Values			Standard Deviation		
		CKD3 / CKD2	CKD4 / CKD2	CKD4 / CKD3	CKD3 / CKD2		CKD4 / CKD2		CKD4 / CKD3		CKD2	CKD3	CKD4	CKD2	CKD3	CKD4
					p-value	q-value	p-value	q-value	p-value	q-value						
4-androsten-3beta,17beta-diol disulfate 1*	LC/MS neg	0.55	0.26	0.47	0.09	0.09	0.01	0.01	0.54	0.92	3.909	2.164	1.020	3.756	3.462	0.958
4-androsten-3beta,17beta-diol disulfate 2*	LC/MS neg	0.97	0.54	0.55	0.52	0.23	0.01	0.01	0.11	0.88	1.254	1.219	0.675	0.535	0.802	0.452
5alpha-androstan-3beta,17beta-diol disulfate	LC/MS neg	0.39	0.27	0.7	0.02	0.04	0.00	0.00	0.42	0.90	2.602	1.008	0.710	1.989	1.040	0.848
pregnen-diol disulfate*	LC/MS neg	0.67	0.34	0.5	0.17	0.13	0.00	0.00	0.13	0.88	2.035	1.360	0.682	1.725	1.112	0.483
xanthine	LC/MS pos	2.37	4.27	1.8	0.04	0.06	0.00	0.01	0.18	0.88	0.502	1.189	2.146	0.118	1.196	2.334
hypoxanthine	LC/MS neg	1.01	1.03	1.02	0.34	0.18	0.26	0.13	0.48	0.92	0.938	0.947	0.964	0.000	0.026	0.068
inosine	LC/MS neg	2.91	4.72	1.62	0.02	0.04	0.00	0.00	0.14	0.88	0.300	0.873	1.416	0.000	0.817	0.931
N1-methyladenosine	LC/MS pos	0.93	0.78	0.84	0.38	0.19	0.02	0.02	0.39	0.90	1.087	1.013	0.851	0.202	0.422	0.216
adenosine 5'-monophosphate (AMP)	LC/MS pos	0.55	0.54	0.98	0.02	0.04	0.02	0.02	0.34	0.88	1.350	0.742	0.729	0.964	0.039	0.000
guanosine	LC/MS neg	1.52	2	1.32	0.06	0.07	0.01	0.01	0.22	0.88	0.505	0.765	1.007	0.000	0.436	0.492
urate	LC/MS neg	1.11	1.06	0.95	0.28	0.17	0.44	0.18	0.64	0.96	0.978	1.085	1.034	0.191	0.221	0.161
uridine	LC/MS neg	1.05	1.31	1.25	0.75	0.26	0.04	0.03	0.07	0.88	0.906	0.948	1.184	0.289	0.258	0.238
pseudouridine	LC/MS neg	1.48	1.64	1.11	0.11	0.10	0.07	0.05	0.76	0.98	0.946	1.403	1.554	0.256	0.993	1.274
ascorbate (Vitamin C)	GC/MS	7.15	11.46	1.6	0.00	0.01	0.00	0.00	0.19	0.88	0.114	0.811	1.301	0.000	0.668	0.999
threonate	GC/MS	2.65	3.27	1.23	0.03	0.04	0.00	0.00	0.18	0.88	0.453	1.203	1.483	0.296	0.711	0.439
heme	LC/MS pos	0.34	0.1	0.3	0.01	0.03	0.00	0.00	0.23	0.88	5.139	1.747	0.529	4.173	2.381	0.492
bilirubin (Z,Z)	LC/MS neg	2.01	1.43	0.71	0.33	0.18	0.08	0.05	0.97	0.99	0.901	1.814	1.291	0.312	1.979	0.521
bilirubin (E,E)*	LC/MS neg	1.29	1.07	0.83	0.72	0.26	0.57	0.22	0.97	0.99	1.058	1.368	1.129	0.428	0.848	0.353
bilirubin (E,Z or Z,E)*	LC/MS pos	1.02	0.74	0.73	0.44	0.21	0.25	0.12	0.87	0.98	1.288	1.319	0.958	0.862	1.312	0.458
biliverdin	LC/MS pos	0.92	0.33	0.36	0.14	0.12	0.00	0.00	0.62	0.95	1.729	1.595	0.568	1.245	1.879	0.295
nicotinamide	LC/MS pos	0.86	0.65	0.76	0.37	0.19	0.04	0.03	0.35	0.88	1.240	1.064	0.810	0.539	0.594	0.408
pantothenate	LC/MS pos	0.95	1.44	1.52	0.73	0.26	0.47	0.19	0.34	0.88	0.847	0.804	1.220	0.407	0.472	1.031
alpha-tocopherol	GC/MS	1.31	1.79	1.36	0.16	0.12	0.03	0.03	0.03	0.88	0.782	1.026	1.397	0.428	0.331	0.472
gamma-tocopherol	GC/MS	1.02	1.81	1.77	0.82	0.28	0.04	0.03	0.05	0.88	0.502	0.512	0.908	0.059	0.089	0.552
pyridoxate	LC/MS neg	1.55	1.81	1.17	0.59	0.24	0.01	0.01	0.14	0.88	0.818	1.270	1.485	0.525	1.797	0.753
hippurate	LC/MS neg	2.88	1.62	0.56	0.34	0.18	0.92	0.31	0.42	0.90	1.092	3.145	1.765	0.936	5.985	3.096
2-hydroxyhippurate (salicylurate)	LC/MS neg	1.11	4.34	3.92	0.84	0.28	0.34	0.15	0.42	0.90	0.524	0.581	2.275	0.437	0.508	5.448
catechol sulfate	LC/MS neg	1.44	1.24	0.86	0.78	0.27	0.29	0.14	0.48	0.92	1.089	1.573	1.352	1.007	2.604	0.806
4-vinylphenol sulfate	LC/MS neg	1.32	2.18	1.65	0.92	0.29	0.25	0.12	0.34	0.88	1.059	1.403	2.310	0.788	1.524	2.576
glycolate (hydroxyacetate)	GC/MS	0.85	0.83	0.98	0.18	0.13	0.12	0.07	0.81	0.98	0.850	0.721	0.706	0.247	0.139	0.096
iminodiacetate (IDA)	GC/MS	0.32	0.15	0.45	0.00	0.00	0.00	0.00	0.20	0.88	4.452	1.439	0.655	2.340	1.630	0.266
salicylate	LC/MS neg	0.46	0.63	1.38	0.70	0.26	0.61	0.23	0.28	0.88	1.509	0.692	0.958	3.378	0.873	0.736
salicyluric glucuronide*	LC/MS neg	1.72	4.67	2.71	0.33	0.18	0.18	0.09	0.49	0.92	0.397	0.684	1.855	0.248	0.890	3.931

Supplemental Data Table 1
UNNM-01-12VW

Biochemical Name	Platform	Fold of Change			Statistical Values						Mean Values			Standard Deviation		
		CKD3 / CKD2	CKD4 / CKD2	CKD4 / CKD3	CKD3 / CKD2		CKD4 / CKD2		CKD4 / CKD3		CKD2	CKD3	CKD4	CKD2	CKD3	CKD4
					p-value	q-value	p-value	q-value	p-value	q-value						
4-acetamidophenol	LC/MS pos	1.37	1.24	0.91	0.69	0.26	0.85	0.29	0.84	0.98	0.414	0.568	0.514	0.281	0.607	0.605
p-acetamidophenylglucuronide	LC/MS neg	1.61	1.32	0.82	0.40	0.20	0.37	0.16	0.91	0.99	0.387	0.624	0.510	0.192	0.733	0.363
2-propylpentanoate (valproate)	LC/MS neg	2.32	2.29	0.98	0.00	0.00	0.00	0.00	0.91	0.99	0.541	1.257	1.238	0.251	0.561	0.394
pioglitazone*	LC/MS pos	1	1	1							1.000	1.000	1.000	0.000	0.000	0.000
hydroxypioglitazone*	LC/MS pos	1	1	1							1.000	1.000	1.000	0.000	0.000	0.000
naproxen	GC/MS	1	1	1							1.000	1.000	1.000	0.000	0.000	0.000
metformin	LC/MS pos	1	1	1							1.000	1.000	1.000	0.000	0.000	0.000
metoprolol	LC/MS pos	1	2.04	2.04			0.17	0.09	0.17	0.88	0.190	0.190	0.388	0.000	0.000	0.427
metoprolol acid metabolite*	LC/MS pos	9.28	64.82	6.98	0.29	0.18	0.16	0.09	0.48	0.92	0.454	4.216	29.440	0.046	11.746	75.934
hydrochlorothiazide	LC/MS neg	1	1	1							1.000	1.000	1.000	0.000	0.000	0.000
EDTA	LC/MS neg	0.67	0.55	0.83	0.00	0.02	0.00	0.00	0.17	0.88	0.933	0.621	0.514	0.232	0.227	0.000
quinate	GC/MS	1.25	3.03	2.42	0.74	0.26	0.12	0.07	0.21	0.88	0.451	0.564	1.368	0.267	0.517	2.202
piperine	LC/MS pos	2.65	3.61	1.36	0.04	0.06	0.01	0.01	0.43	0.91	0.460	1.217	1.658	0.459	0.830	1.495
thymol sulfate	LC/MS neg	1.03	2.46	2.38	0.75	0.26	0.51	0.20	0.37	0.90	0.925	0.957	2.278	0.981	1.295	3.941
N-(2-furoyl)glycine	LC/MS neg	0.76	0.75	0.98	0.59	0.24	0.55	0.21	0.92	0.99	0.770	0.585	0.576	0.746	0.163	0.132
stachydrine	LC/MS pos	2.07	0.58	0.28	0.36	0.19	0.95	0.32	0.26	0.88	2.383	4.932	1.384	3.495	8.117	1.796
homostachydrine*	LC/MS pos	0.86	0.72	0.83	0.45	0.21	0.08	0.05	0.27	0.88	1.206	1.043	0.867	0.463	0.380	0.299
caffeine	LC/MS pos	0.92	0.17	0.19	0.17	0.13	0.00	0.00	0.29	0.88	3.474	3.202	0.606	2.179	4.686	0.319
paraxanthine	LC/MS pos	0.78	0.37	0.48	0.29	0.18	0.03	0.03	0.38	0.90	1.693	1.318	0.626	1.165	1.723	0.341
theobromine	LC/MS pos	0.45	0.36	0.81	0.21	0.14	0.14	0.08	0.82	0.98	2.499	1.125	0.908	2.701	0.962	0.473
theophylline	LC/MS pos	0.85	0.54	0.63	0.56	0.23	0.07	0.05	0.24	0.88	1.348	1.150	0.727	0.816	0.859	0.255
1-methylurate	LC/MS pos	2.05	0.94	0.46	0.50	0.22	0.74	0.27	0.38	0.90	0.652	1.336	0.613	0.321	2.258	0.342
1,7-dimethylurate	LC/MS pos	1.51	0.79	0.52	0.70	0.26	0.10	0.06	0.24	0.88	0.701	1.059	0.553	0.264	1.442	0.000
1-methylxanthine	LC/MS pos	1.03	1	0.97	0.86	0.28	0.89	0.30	0.95	0.99	0.749	0.774	0.749	0.163	0.418	0.237
3-methylxanthine	LC/MS pos	0.87	0.7	0.8	0.40	0.20	0.38	0.16	0.87	0.98	0.836	0.729	0.586	0.652	0.931	0.218
5-acetylamino-6-amino-3-methyluracil	LC/MS neg	1.8	1	0.55	0.34	0.18			0.34	0.88	0.199	0.360	0.199	0.000	0.506	0.000
cotinine	LC/MS pos	1	1.05	1.05			0.34	0.15	0.34	0.88	0.785	0.785	0.828	0.000	0.000	0.136
erythritol	GC/MS	1.53	1.55	1.02	0.29	0.18	0.15	0.08	0.80	0.98	0.986	1.508	1.533	0.376	1.390	1.228

Supplementary Data Table 2

SUPER PATHWAY	SUB PATHWAY	BIOCHEMICAL NAME	PLATFORM	CKD2-01	CKD2-02	CKD2-03	CKD2-04	CKD2-05	CKD2-06	CKD2-07	CKD2-08	CKD2-09	CKD2-10	CKD3-01	CKD3-02	CKD3-03	CKD3-04	CKD3-05	CKD3-06	CKD3-07	CKD3-08	CKD3-09	CKD3-10	CKD4-01	CKD4-02	CKD4-03	CKD4-04	CKD4-05	CKD4-06	CKD4-07	CKD4-08	CKD4-09	CKD4-10	% Filled Values CKD2	% Filled Values CKD3	% Filled Values CKD4
			GROUP	CKD2										CKD3										CKD4												
Amino acid	Glycine, serine and threonine metabolism	glycine	GC/MS	0.828	0.885	0.467	0.818	0.650	0.586	0.689	1.003	1.708	0.819	0.587	0.716	1.451	1.101	1.188	1.147	1.084	1.061	0.881	1.789	1.283	0.997	0.700	0.806	0.784	1.207	1.379	1.449	1.749	1.119	100	100	100
		N-acetylglycine	GC/MS	0.582	0.582	0.905	0.582	0.582	0.582	0.582	0.582	0.848	0.582	0.582	0.834	1.000	1.022	1.499	1.368	0.582	0.818	0.582	1.002	0.582	0.582	0.582	1.296	0.582	0.582	0.582	0.946	1.449	0.582	30	70	30
		serine	GC/MS	1.268	1.020	0.539	0.836	0.645	0.678	0.782	1.005	0.851	0.490	0.907	0.885	1.208	1.324	1.194	0.772	1.180	1.180	0.934	1.043	1.223	0.959	1.014	0.905	0.805	1.226	0.995	1.282	1.111	1.113	100	100	100
		threonine	GC/MS	0.853	1.314	0.999	1.020	0.715	0.770	0.709	0.904	1.001	0.689	1.216	0.855	0.505	1.030	1.194	0.730	1.082	1.288	0.752	1.630	1.249	0.909	0.599	1.001	0.998	1.056	1.112	1.485	0.999	1.474	100	100	100
		betaine	LC/MS Pos	1.891	1.438	2.084	1.791	1.711	1.525	0.979	1.318	0.770	1.268	3.290	1.021	1.259	1.636	0.925	0.333	0.919	0.831	1.038	0.842	1.720	0.432	0.427	0.534	0.413	0.752	0.731	0.904	1.062	0.954	100	100	100
	Alanine and aspartate metabolism	aspartate	GC/MS	0.512	0.512	0.757	0.512	1.383	1.588	0.889	0.827	0.564	1.144	1.041	0.985	1.101	0.512	1.215	0.655	1.132	0.890	0.752	1.691	0.512	1.904	1.090	1.015	1.594	0.797	0.801	0.861	1.319	0.673	80	90	90
		asparagine	GC/MS	1.101	0.513	0.849	1.186	0.534	0.791	0.513	0.680	1.294	0.513	0.984	0.877	0.914	0.513	1.104	0.792	1.591	1.367	0.763	1.963	1.438	1.108	1.000	1.273	1.063	0.958	2.512	1.374	0.977	0.912	80	90	100
		alanine	GC/MS	0.890	1.122	0.422	1.179	0.775	0.748	0.604	0.613	1.062	0.621	1.150	0.790	1.372	0.855	0.992	1.053	1.165	0.987	1.206	0.936	1.531	1.180	0.992	1.340	1.082	1.161	0.977	1.355	1.008	0.808	100	100	100
		N-acetylalanine	LC/MS Neg	1.052	0.431	0.559	0.733	0.955	1.192	1.342	0.431	0.663	0.789	0.642	0.540	2.669	0.931	1.225	1.121	1.325	1.011	0.826	0.975	1.249	1.223	0.806	1.098	1.091	0.909	3.562	0.589	1.000	1.053	90	100	100
	Glutamate metabolism	glutamate	GC/MS	0.920	3.213	1.183	1.135	1.027	1.298	0.545	0.688	0.985	0.883	1.154	1.237	0.870	0.478	0.589	1.116	1.015	0.924	1.091	1.024	0.904	2.174	2.068	1.937	2.022	0.820	0.567	0.800	0.622	0.849	100	100	100
		glutamine	LC/MS Pos	1.000	1.060	0.926	1.279	0.868	1.006	1.240	1.017	1.000	1.029	1.450	1.083	0.899	0.972	0.845	0.675	0.923	1.086	1.127	1.175	1.135	0.952	0.884	0.723	0.969	0.918	0.796	1.306	1.118	0.829	100	100	100
		pyroglutamine*	LC/MS Pos	1.268	1.633	0.539	0.334	1.289	0.897	0.789	0.464	0.196	0.839	1.018	0.182	0.848	1.165	2.427	1.104	1.043	4.466	1.159	3.359	1.561	0.982	0.388	1.778	0.793	0.388	2.758	0.429	1.608	0.264	100	100	100
	Histidine metabolism	histidine	LC/MS Neg	0.911	1.171	0.861	0.992	0.742	0.727	0.862	0.937	0.953	1.025	1.100	0.773	1.067	1.045	0.873	0.888	1.220	1.056	1.008	1.012	1.026	1.022	0.813	0.939	1.049	1.065	1.036	1.297	0.861	0.918	100	100	100
		3-methylhistidine	LC/MS Neg	0.332	0.356	0.332	0.880	1.852	2.611	2.270	0.484	0.683	0.332	0.332	0.332	3.384	0.332	0.590	6.417	0.946	2.506	1.054	0.850	1.383	0.926	0.332	0.399	2.994	0.458	12.920	0.332	6.856	0.332	70	80	70
	Lysine metabolism	lysine	LC/MS Pos	1.404	1.249	1.035	1.740	1.397	0.723	1.067	1.506	1.173	1.405	1.649	1.334	0.492	0.384	0.679	0.977	0.577	1.292	0.326	0.625	0.467	1.261	0.551	0.550	1.023	0.332	0.484	0.734	1.304	0.804	100	100	100
		pipecolate	LC/MS Pos	0.808	0.410	4.123	0.808	0.847	1.204	1.386	1.068	0.598	2.695	4.383	0.472	3.447	1.732	0.309	1.400	1.242	0.932	0.582	0.878	2.129	1.550	0.423	1.102	1.528	0.688	4.146	0.684	0.581	0.537	100	100	100
		N6-acetyllysine	LC/MS Pos	1.011	0.866	0.964	0.899	1.316	0.774	1.302	0.595	0.798	0.493	0.786	0.869	2.652	1.314	0.892	1.607	1.470	1.299	1.030	1.362	1.819	1.790	1.223	0.619	0.989	0.863	3.879	0.640	1.349	0.885	100	100	100
		glutaroyl carnitine	LC/MS Pos	1.078	0.922	0.524	1.137	0.555	1.801	0.589	0.577	0.537	0.409	0.610	0.489	1.254	1.143	1.616	1.119	1.181	1.341	1.369	2.631	1.951	2.321	0.767	0.881	0.547	0.374	4.209	0.559	0.563	1.113	100	100	100
	Phenylalanine & tyrosine metabolism	phenylalanine	LC/MS Pos	0.819	0.840	0.704	0.961	0.992	1.020	0.627	0.829	0.921	0.822	1.105	0.824	1.030	1.400	1.024	0.814	1.899	0.990	1.009	1.026	1.008	1.041	1.243	1.203	0.892	0.825	1.089	1.086	0.853	1.045	100	100	100
		phenylacetate	LC/MS Neg	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.587	1.167	1.000	1.274	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	0.507	10	40	0
		p-cresol sulfate	LC/MS Neg	1.214	0.012	0.053	0.722	1.481	1.896	2.636	0.296	0.339	0.795	0.226	0.130	2.982	0.609	2.948	6.493	0.611	1.124	1.064	1.833	2.235	0.105	0.440	1.863	0.147	1.850	3.766	0.629	3.238	0.936	100	100	100
		tyrosine	LC/MS Pos	0.979	1.346	1.135	1.063	1.090	0.960	0.676	1.318	1.143	0.779	1.626	0.915	0.557	2.583	0.799	0.686	2.786	1.221	0.975	1.118	1.021	1.208	0.858	1.102	0.870	0.921	0.751	1.211	0.713	0.906	100	100	100
		3-(4-hydroxyphenyl)lactate	GC/MS	0.811	1.276	1.205	0.958	1.382	0.476	0.476	0.476	0.642	1.312	1.572	0.476	0.801	4.447	0.649	0.476	2.451	1.439	0.738	0.476	0.898	2.386	0.540	1.073	0.832	0.724	0.476	1.042	0.476	0.476	70	70	80
		3-methoxytyrosine	LC/MS Pos	0.652	0.681	0.612	0.644	0.612	0.996	0.612	0.612	0.935	0.612	1.000	0.694	1.121	0.806	1.147	0.612	1.055	1.255	1.142	1.039	1.203	0.612	0.889	1.024	0.612	1.147	1.534	0.868	0.928	1.131	50	90	90
		phenylacetylglutamine	LC/MS Pos	1.089	0.125	0.956	0.617	1.287	1.156	2.059	0.343	0.190	0.347	0.339	0.127	4.824	0.304	2.397	6.054	1.321	1.044	0.590	1.850	1.074	0.294	0.240	1.230	0.504	0.841	6.118	1.062	1.236	0.619	100	100	100
		phenol sulfate	LC/MS Neg	0.592	1.629	0.283	0.483	0.979	0.864	1.647	2.540	1.000	0.381	0.388	0.668	1.872	0.207	1.626	0.878	5.574	1.000	0.500	0.991	1.341	2.159	1.042	2.550	5.247	1.666	2.272	0.530	1.273	0.389	100	100	100
	Tryptophan metabolism	kynurenine	LC/MS Pos	1.313	0.631	0.708	1.015	1.302	0.868	0.942	0.996	0.699	0.964	0.768	0.768	1.360	1.340	0.997	0.633	1.969	0.891	1.161	1.043	1.348	1.281	0.644	1.217	1.179	0.906	1.908	1.277	1.003	0.947	100	100	100
		tryptophan	LC/MS Pos	1.093	1.051	1.319	1.076	1.031	0.828	0.544	1.284	1.428	0.981	1.495	1.245	0.341	1.355	0.962	0.461	1.685	0.904	1.185	0.968	0.863	0.997	0.959	1.003	1.222	0.873	0.561	1.159	0.799	0.890	100	100	100
		indolelactate	LC/MS Pos	1.031	0.669	1.619	0.720	1.245	1.475	0.581	0.759	0.861	1.205	1.281	0.595	1.302	0.994	0.498	0.624	2.244	0.476	0.822	1.140	0.917	3.081	0.737	1.006	1.024	0.805	2.233	1.096	1.631	0.467	100	100	100
		indoleacetate	LC/MS Pos	2.226	1.141	1.805	0.881	3.264	0.881	1.014	1.533	1.472	1.503	1.078	0.830	1.177	0.779	0.986	1.177	1.956	0.625	0.658	0.887	0.577	0.885	0.362	1.483	1.544	0.715	1.262	0.597	0.748	0.413	100	100	100
		tryptophan betaine	LC/MS Pos	0.839	1.001	5.116	0.592	0.385	1.628	0.629	1.251	0.238	0.475	0.541	0.722	2.045	3.446	1.839	0.220	1.252	0.355	0.407	5.733	1.195	2.132	2.532	0.999	3.506	0.449	0.220	4.329	0.220	0.730	100	100	80
		serotonin (5HT)	LC/MS Pos	0.592	0.592	0.592	0.592	0.592	0.592	0.592	0.592	0.592	0.594	0.592	0.592	1.209	1.220	0.694	0.658	0.592	1.373	1.151	0.692	0.611	0.720	0.685	1.128	1.132	0.872	0.592	1.603	2.084	1.228	20	70	90
		C-glycosyltryptophan*	LC/MS Pos	1.027	0.466	0.414	0.748	0.895	1.341	0.973	0.488	0.495	0.497	0.626	0.727	4.277	0.715	0.965	1.347	1.219	1.209	0.763	1.208	1.339	1.311	0.791	1.170	1.151	0.873	6.706	1.090	1.337	1.167	100	100	100
		3-indoxyl sulfate	LC/MS Neg	1.830	0.215	0.147	0.922	2.110	0.861	3.099	0.919	0.627	1.127	0.394	0.844	3.483	0.318	4.590	2.890	0.905	1.213	0.631	0.682	1.285	0.774	0.434	1.078	1.125	1.622	5.407	1.440	2.038	0.798	100	100	100
		indolepropionate	LC/MS Pos	1.258	0.293	1.637	0.829	1.605	1.132	1.566	0.293	2.253	0.926	1.242	0.600	1.916	0.788	1.297	0.827	0.345	2.659	6.457	0.903	1.919	0.812	0.293	0.377	0.764	0.770	1.000	0.293	1.982	0.993	80	100	90
	Valine, leucine and isoleucine metabolism	3-methyl-2-oxobutyrate	LC/MS Neg	1.173	0.917	1.002	1.184	0.963	0.854	0.460	1.114	0.910	0.963	1.295	1.607	0.305	1.248	0.931	0.815	0.881	1.056	1.165	0.876	0.714	1.058	1.363	1.443	1.146	0.811	0.474	1.170	0.998	1.158	100	100	100
		3-methyl-2-oxovalerate	LC/MS Neg	1.021	0.384	1.087	1.123	1.021	0.944	0.513	1.072	1.452	0.990	1.499	1.108	0.336	0.971	0.948	0.640	0.925	0.869	1.086	0.950	0.760	1.029	1.611	1.190	1.225	0.895	0.646	0.909	1.310	1.010	100	100	100
		beta-hydroxyisovalerate	LC/MS Neg	1.000	0.520	0.734	1.278	1.146	0.520	0.520	0.872	0.520	0.683	0.520	0.520	0.520	0.520	0.773	0.804	1.029	1.277	1.042	0.520	0.520	0.520	0.520	1.076	0.865	0.520	1.229	0.697	0.520	1.051	60	60	50
		alpha-hydroxyisocaproate	LC/MS Neg	0.533	0.533	1.000	0.533	0.533	0.533	0.533	0.533	0.533	0.533	0.542	0.533	0.533	1.549	0.533	0.533	0.533	0.533	0.533	0.533	0.533	2.382	0.533	0.533	0.533	0.533	0.533	0.533	0.533	0.533	10	30	10
		isoleucine	LC/MS Pos	1.118	0.556	1.062	1.214	1.355	1.348	0.974	0.909	0.927	0.575	0.900	0.761	0.701	0.967	1.199	0.774	1.243	0.951	1.107	0.894	0.901	0.961	1.461	1.030	1.113	1.048	1.223	1.011	0.989	1.146	100	100	100
		leucine	LC/MS Pos	1.155	1.177	0.914	1.334	1.148	1.151	0.720	0.994	1.031	0.661	1.519	0.986	0.521	0.707	1.006	0.880	1.169	0.945	1.260	0.898	1.143	1.039	1.111	1.231	0.975	0.789	0.909	1.133	0.795	0.961	100	100	100
		valine	LC/MS Pos	1.203	1.133	0.766	1.279	1.260	0.978	0.808	1.019	0.780	0.684	1.217	1.036	0.583	0.768	0.918	0.981	1.178	0.892	1.251	0.874	0.945	1.098	1.108	0.984	1.192	1.099	0.837	1.016	0.780	1.048	100	100	100
		3-hydroxyisobutyrate	GC/MS	1.178	0.831	0.905	0.948	0.519	0.970	0.519	1.015	0.519	0.519	1.193	1.046	1.142	2.074	0.650	0.746	2.059	0.519	0.519	0.920	0.519	1.695	0.519	1.179	1.293	0.659	1.245	0.519	0.590	0.985	70	80	70
		4-methyl-2-oxopentanoate	LC/MS Neg	1.122	0.964	0.927	1.150	0.910	0.775	0.340	1.188	1.276	1.093	1.672	1.159	0.171	0.948	0.929	0.643	0.840	1.036	1.295	0.916	0.889	1.038	1.420	1.399	1.271	0.790	0.528	1.131	1.042	0.940	100	100	100
		alpha-hydroxyisovalerate	LC/MS Neg	1.450	3.931	5.079	1.604	2.170	1.899	0.430	2.011	2.094	1.894	3.614	0.841	0.524	12.972	0.602	0.735	1.989	0.566	1.039	0.715	0.410	11.326	0.961	1.441	0.927	0.946	0.961	0.854	0.745	0.624	100	100	100
		isobutyrylcarnitine	LC/MS Pos	1.328	0.221	0.225	0.907	3.280	2.479	0.807	0.453	0.468	0.486	0.461	0.400	3.162	0.302	1.781	4.203	1.737	0.694	1.017	1.585	0.920	1.114	0.359	1.545	2.482	0.983	5.792	0.724	1.319	1.691	100	100	100
		2-methylbutyroylcarnitine	LC/MS Pos	1.395	0.810	0.597	1.000	1.275	1.393	0.305	0.353	0.997	0.305	0.790	0.473	2.563	0.776	0.305	1.471	1.920	1.221	0.305	1.209	0.660	0.305	0.801	0.305	1.145	0.305	3.441	0.919	0.305	1.271	80	80	70
		isovalerylcarnitine	LC/MS Pos	1.188	0.768	1.582	1.002	0.995	1.954	0.803	0.766	0.867	0.461	0.923	1.000	0.461	1.330	1.007	1.239	1.592	0.610	0.838	2.090	0.563	1.946	0.933	1.731	1.290	0.794	1.563	0.788	0.476	1.979	100	90	100
	Cysteine, methionine, SAM, taurine metabolism	cysteine	GC/MS	0.438	0.970	1.228	1.024	1.411	1.041	1.016	1.181	0.771	1.440	1.240	0.894	0.438	0.747	0.823	1.088	1.144	1.624	0.971	1.811	0.882	1.622	0.752	0.984	1.131	0.804	0.583	0.438	0.892	0.807	90	100	90
		methionine	LC/MS Neg	0.876	0.961	1.050	1.004	0.966	0.919	0.847	1.168	0.955	0.683	1.233	0.825	0.734	2.614	1.023	0.862	2.388	1.101	0.940	1.127	1.169	0.988	0.842	1.021	1.118	0.891	1.078	0.996	1.053	1.093	100	100	100
		2-hydroxybutyrate (AHB)	GC/MS	1.068	0.791	1.857	1.008	0.776	1.086	0.380	0.430	0.547	0.380	1.944	1.391	0.380	2.798	0.571	1.146	0.643	0.992	1.074	0.697	0.399	1.183	2.355	2.300	1.237	0.946	0.557	1.096	0.551	0.737	90	90	100
	Urea cycle; arginine-, proline-, metabolism	dimethylarginine (SDMA + ADMA)	LC/MS Pos	0.317	0.726	0.338	0.631	0.491	0.510	0.431	0.456	0.433	0.638	0.635	0.931	6.273	4.274	1.025	4.502	5.630	4.946	6.397	5.451	0.975	4.453	0.317	0.611	3.059	0.317	2.097	3.470	3.736	4.999	100	100	80
		arginine	LC/MS Neg	0.544	0.566	0.700	0.537	1.081	1.149	0.558	0.537	0.537	0.537	0.806	0.537	1.025	0.840	1.824	1.738	1.379	0.975	0.537	0.537	1.749	0.537	0.537	0.537	0.537	1.058	1.873	0.870	0.850	1.773	70	70	60
		ornithine	LC/MS Pos	5.330	0.656	5.535	5.376	4.529	4.677	4.315	4.065	4.269	4.520	4.700	1.737	0.376	0.710	0.357	0.440	0.368	1.107	0.846	1.306	1.053	0.420	0.769	0.353	0.947	0.352	1.249	0.507	0.849	0.333	100	100	100
		urea	GC/MS	1.007	0.440	0.505	0.685	1.060	1.372	1.301	0.495	0.527	0.636	0.834	0.484	1.678	0.604	0.993	2.008	1.131	1.105	0.692	1.087	0.999	1.421	0.605	1.094	1.310	0.653	3.262	0.652	1.001	1.101	100	100	100
		proline	LC/MS Pos	0.761	0.907	1.401	1.029	1.160	1.257	0.862	0.717	1.017	0.549	1.187	0.700	2.020	1.787	0.779	0.685	2.005	1.020	1.211	0.996	0.928	1.004	0.649	0.662	1.502	0.952	1.049	1.024	0.777	0.819	100	100	100
		citrulline	LC/MS Pos	1.195	0.714	0.880	0.891	0.796	1.075	0.789	0.568	0.701	0.638	1.115	0.504	1.402	1.658	0.955	1.253	2.587	1.098	0.757	1.710	1.283	1.075	0.712	0.593	0.698	1.045	1.521	0.943	1.692	1.258	100	100	100
		N-acetylornithine	LC/MS Pos	0.867	0.352	0.666	0.520	0.469	2.097	2.511	0.352	0.469	0.744	2.326	0.469	3.638	0.875	0.816	1.000	1.787	2.191	1.405	0.505	1.795	1.189	1.225	1.474	0.978	0.414	1.538	1.557	1.461	0.936	90	100	100
		trans-4-hydroxyproline	GC/MS	1.570	0.684	0.360	1.276	1.190	1.218	1.099	0.824	0.876	0.631	1.110	0.394	1.687	0.718	0.972	1.281	2.301	0.700	1.023	1.803	0.921	0.752	0.753	0.902	1.043	0.977	3.525	0.872	1.251	2.619	100	100	100
	Creatine metabolism	creatine	LC/MS Pos	0.436	0.443	1.600	1.368	1.217	1.499	0.907	0.976	1.026	0.308	0.610	2.600	0.334	0.370	0.360	1.870	0.499	1.181	1.024	0.672	0.169	0.862	1.561	1.715	1.531	2.170	0.560	1.825	0.248	1.277	100	100	100
		creatinine	LC/MS Pos	1.009	0.771	0.664	1.221	1.344	1.581	1.424	0.962	0.934	0.936	1.161	0.378	2.823	0.579	1.376	1.415	1.124	1.359	0.991	1.432	0.950	1.454	0.701	0.755	0.701	0.906	5.079	0.645	1.377	0.804	100	100	100
	Butanoate metabolism	2-aminobutyrate	LC/MS Pos	0.804	0.865	1.231	1.302	0.923	0.953	1.037	0.694	0.625	0.456	1.399	1.087	0.420	1.807	0.859	0.889	1.027	0.903	1.182	0.529	0.973	1.306	1.317	1.377	1.233	1.186	1.345	1.153	0.668	0.843	100	100	100
	Guanidino and acetamido metabolism	4-acetamidobutanoate	LC/MS Pos	0.841	0.898	1.106	0.641	1.128	1.099	1.057	0.459	0.763	0.666	0.752	0.675	9.242	0.459	1.163	1.254	1.166	1.447	0.974	1.631	1.128	1.592	0.851	1.229	0.900	0.770	5.808	0.670	0.882	1.000	90	100	100
	Glutathione metabolism	5-oxoproline	LC/MS Pos	0.398	1.297	0.554	0.506	0.991	0.576	1.014	0.793	0.718	1.208	0.698	0.979	1.816	1.620	0.981	1.139	0.959	1.299	1.585	0.718	1.319	1.547	0.947	0.632	1.392	1.278	1.500	1.009	1.404	0.374	100	100	100
Peptide	Dipeptide	aspartylphenylalanine	LC/MS Pos	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.671	1.549	0.354	0.469	0.592	0.449	1.698	0.606	1.043	2.551	1.006	2.633	0.354	0.752	0.354	1.538	1.386	0.994	0	70	90
		pro-hydroxy-pro	LC/MS Pos	0.636	0.286	0.331	0.286	0.286	0.286	0.930	0.334	0.860	0.422	0.761	0.626	4.626	0.286	0.331	1.157	1.392	0.810	0.542	1.090	1.975	1.070	1.223	0.563	2.068	1.309	4.122	1.202	1.292	5.965	60	100	100
		cyclo(leu-pro)	LC/MS Pos	0.552	4.912	8.775	0.552	0.552	0.906	1.040	0.552	0.960	0.906	2.545	0.552	0.786	3.593	0.552	0.552	0.696	0.552	0.552	0.552	0.552	0.552	0.552	2.185	0.552	0.552	0.552	0.552	0.552	0.552	60	40	20
		phenylalanyltryptophan	LC/MS Pos	0.704	1.976	1.125	0.672	1.135	0.266	0.266	0.486	0.468	0.266	1.031	1.052	0.266	1.841	0.312	0.356	0.766	0.477	1.661	0.404	1.395	3.523	0.413	3.394	1.000	2.058	0.667	2.215	0.492	2.463	80	90	100
	gamma-glutamyl	gamma-glutamylvaline	LC/MS Pos	0.943	1.348	0.944	1.029	0.922	1.169	0.627	0.725	0.831	0.585	1.195	0.813	1.032	0.632	0.724	1.417	1.498	1.353	0.791	1.193	0.822	1.323	0.959	1.144	1.204	0.971	1.647	1.101	0.806	1.107	100	100	100
		gamma-glutamylleucine	LC/MS Pos	1.079	1.324	0.700	0.957	0.685	1.063	0.592	0.530	0.857	0.427	1.269	0.700	0.506	0.468	0.950	0.700	1.347	1.106	1.116	1.043	0.894	1.206	0.840	1.211	1.196	0.816	1.061	1.186	1.092	1.201	100	100	100
		gamma-glutamylisoleucine*	LC/MS Pos	0.583	0.583	0.853	0.878	0.583	1.141	0.583	0.583	0.583	0.583	0.895	1.020	1.360	0.583	0.729	1.240	1.691	1.942	0.745	0.961	0.879	0.698	0.960	1.427	0.980	0.583	2.342	1.194	1.578	1.200	40	90	90
		gamma-glutamylmethionine	LC/MS Pos	0.614	1.259	1.503	1.058	1.700	0.898	0.614	1.294	0.887	0.614	1.469	0.876	0.614	1.695	0.695	0.614	1.973	0.907	1.215	1.327	1.166	0.883	0.614	0.942	0.834	0.614	0.649	0.759	1.560	0.846	80	80	80
		gamma-glutamylglutamine	LC/MS Pos	0.256	0.533	0.366	0.543	0.093	0.091	0.269	0.100	0.213	0.284	0.500	0.335	1.012	1.196	1.112	0.725	1.245	1.331	1.413	1.656	1.696	1.148	0.873	1.314	1.144	1.391	0.988	1.504	2.011	1.061	100	100	100
		gamma-glutamylphenylalanine	LC/MS Pos	0.877	1.461	0.655	0.968	0.784	1.022	0.587	0.811	0.978	0.891	1.130	0.753	2.006	1.427	0.935	0.824	2.109	1.464	0.928	1.534	0.934	1.143	1.274	1.234	1.168	0.934	1.423	1.326	0.918	1.300	100	100	100
		gamma-glutamyltyrosine	LC/MS Pos	0.735	1.860	0.733	0.852	1.038	1.139	0.533	1.046	1.177	0.817	1.285	0.616	0.806	1.796	0.675	0.666	2.595	1.390	0.770	1.195	0.842	1.306	0.677	1.012	1.011	0.735	0.989	1.178	0.856	1.053	100	100	100
	Polypeptide	bradykinin, des-arg(9)	LC/MS Pos	0.614	0.614	0.614	0.908	0.686	0.614	0.614	1.589	0.614	0.771	0.614	0.614	0.614	0.614	0.614	8.263	0.614	0.614	24.160	1.064	0.903	0.936	0.614	1.225	2.472	0.614	2.011	0.614	0.614	0.825	50	30	60
	Fibrinogen cleavage peptide	ADSGEGDFXAEGGGVR*	LC/MS Pos	0.465	0.465	0.465	0.465	0.465	0.465	0.465	0.465	0.465	0.465	0.465	0.465	1.818	0.668	1.588	1.589	0.717	0.906	0.483	0.867	0.465	0.657	2.948	1.134	1.440	1.094	1.740	0.695	0.883	2.050	0	80	100
		DSGEGDFXAEGGGVR*	LC/MS Pos	0.001	0.001	0.001	0.005	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	1.702	0.858	2.271	1.826	0.977	1.158	0.355	1.188	0.928	0.329	1.262	1.290	1.023	0.420	2.126	1.280	0.762	2.981	40	80	100
		ADpSGEGDFXAEGGGVR*	LC/MS Pos	0.039	0.039	0.039	0.094	0.045	0.039	0.039	0.040	0.039	0.039	0.039	0.039	1.137	0.043	1.086	1.241	0.280	2.051	1.248	1.013	0.987	1.403	0.941	0.860	0.839	1.893	9.333	1.161	0.571	2.563	40	80	100
Carbohydrate	Aminosugars metabolism	erythronate*	GC/MS	1.108	0.709	0.625	0.746	1.782	1.308	1.262	0.545	0.706	1.131	1.197	0.532	6.435	0.676	0.871	1.707	0.963	1.368	0.849	1.370	0.997	1.510	1.003	0.947	1.030	0.732	5.058	0.852	1.479	0.768	100	100	100
	Fructose, mannose, galactose, starch, and sucrose metabolism	fructose	GC/MS	0.880	0.447	0.516	0.734	0.895	0.696	0.893	0.546	0.420	1.597	0.368	0.417	4.972	0.994	1.932	1.441	1.280	4.480	4.000	1.685	1.006	1.306	1.976	1.030	0.963	1.525	0.754	0.769	1.813	2.282	100	100	100
		mannitol	GC/MS	0.190	0.190	0.190	0.190	0.261	0.190	0.371	0.190	0.190	0.190	0.190	0.190	5.956	0.190	1.662	5.688	0.190	0.506	0.190	0.190	2.331	0.947	0.190	0.190	0.190	0.190	1.387	1.000	1.493	0.265	20	40	70
		mannose	GC/MS	2.743	1.264	0.996	1.003	1.025	3.409	2.773	1.212	0.686	0.611	0.839	1.212	2.249	0.909	1.007	0.883	0.707	0.997	0.834	0.821	0.973	1.013	2.029	0.954	1.006	1.182	1.072	0.842	0.653	0.980	100	100	100
	Glycolysis, gluconeogenesis, pyruvate metabolism	1,5-anhydroglucitol (1,5-AG)	LC/MS Neg	0.382	2.148	1.894	1.079	1.689	0.340	0.329	1.712	1.925	1.408	1.543	1.862	0.329	0.988	1.018	0.438	0.551	1.282	1.000	0.765	1.134	0.672	0.525	1.268	0.571	0.950	0.408	0.930	0.540	1.014	90	100	100
		glycerate	GC/MS	1.721	1.013	0.599	0.553	1.538	1.095	1.368	1.348	1.245	1.367	0.813	0.775	0.886	1.081	0.662	0.509	1.158	1.042	0.796	0.509	0.509	1.000	0.509	0.509	0.509	0.586	0.509	0.509	0.724	0.718	100	90	40
		glucose	GC/MS	2.234	1.152	1.042	0.938	1.321	2.218	2.709	1.026	0.861	0.720	1.120	1.012	1.757	0.886	0.693	0.839	0.673	0.845	1.014	0.997	0.848	1.003	1.772	0.849	1.059	1.107	0.783	0.786	0.986	0.841	100	100	100
		1,6-anhydroglucose	GC/MS	0.420	0.331	6.452	0.331	0.331	0.811	0.677	0.673	1.567	2.319	0.331	0.331	2.396	0.331	0.331	1.864	0.331	0.490	0.331	0.852	0.601	0.331	0.331	0.331	0.331	0.331	1.592	0.331	1.148	1.424	70	50	40
		pyruvate	GC/MS	1.901	1.053	0.901	1.472	3.592	3.123	2.022	1.600	0.575	2.965	1.558	2.101	0.922	1.000	0.562	0.663	0.551	0.499	0.891	0.499	0.499	0.984	1.926	0.499	0.499	0.499	0.499	0.885	0.646	0.499	100	80	50
		lactate	GC/MS	0.842	1.454	0.825	1.028	1.810	1.321	0.707	0.766	1.488	1.855	1.440	1.406	0.854	1.124	0.684	0.953	0.785	1.003	1.637	1.110	0.795	1.677	2.414	1.435	0.997	0.922	0.685	0.798	0.866	0.676	100	100	100
	Nucleotide sugars, pentose metabolism	arabitol	GC/MS	0.574	0.953	0.919	0.918	0.889	0.574	1.173	0.718	0.972	0.574	1.028	0.574	2.469	0.831	0.574	0.831	0.968	1.198	0.816	1.434	1.523	1.241	0.634	1.310	1.047	0.892	3.903	1.086	1.391	1.474	70	90	100
		gluconate	GC/MS	1.832	0.390	0.390	0.403	0.798	1.474	2.041	0.390	0.481	0.390	0.390	0.390	7.098	0.390	0.390	0.390	0.390	1.241	0.561	1.084	0.538	1.298	0.840	0.390	0.913	0.916	1.770	0.390	1.213	0.390	60	40	80
		arabinose	GC/MS	0.479	0.479	2.232	0.479	0.479	0.479	1.799	0.481	0.479	0.479	0.479	0.479	1.817	0.479	0.479	0.479	0.479	0.654	0.479	0.479	1.000	0.479	0.479	0.479	0.479	0.479	0.479	0.479	0.479	0.479	30	30	10
		xylonate	GC/MS	0.706	0.628	0.628	0.628	0.628	0.628	0.628	0.628	0.628	0.628	0.694	0.628	4.205	0.628	1.062	0.628	0.628	1.721	0.628	0.628	1.656	0.628	0.628	0.938	0.935	0.683	5.909	0.628	2.299	0.628	20	40	60
Energy	Krebs cycle	citrate	GC/MS	2.616	0.999	1.049	1.932	1.639	1.611	1.349	0.979	1.343	1.547	2.013	1.566	0.599	1.894	0.670	0.797	0.883	0.972	1.060	1.019	1.001	0.857	0.564	0.949	0.489	0.822	0.584	1.154	0.622	0.694	100	100	100
		alpha-ketoglutarate	GC/MS	1.059	0.505	0.505	1.148	0.505	0.505	0.505	0.505	0.505	0.505	0.505	1.257	0.505	2.879	0.505	0.505	0.719	0.505	0.505	0.505	0.505	1.000	0.583	0.505	0.505	0.505	0.505	0.810	0.505	0.505	20	30	40
		succinate	GC/MS	0.690	0.690	0.690	0.914	1.146	0.690	0.881	0.690	0.789	1.059	0.690	0.972	0.690	1.656	0.690	1.021	1.235	1.050	0.690	0.810	1.069	0.690	1.258	0.772	0.920	0.989	0.894	1.000	1.297	1.262	50	70	90
		malate	GC/MS	1.742	1.481	1.577	1.593	1.908	1.260	0.559	0.559	1.114	1.651	1.989	0.982	1.000	1.508	0.559	0.559	0.860	0.604	0.559	0.559	0.785	0.559	0.564	0.813	0.559	0.932	0.945	0.559	0.621	0.559	80	70	60
	Oxidative phosphorylation	acetylphosphate	GC/MS	0.626	0.566	0.428	1.050	0.694	0.593	0.522	0.506	0.632	0.688	0.751	0.980	1.219	1.098	1.373	1.397	1.020	1.062	1.317	0.512	1.136	1.229	0.877	0.595	0.935	1.386	1.515	1.503	1.290	1.664	100	100	100
		phosphate	GC/MS	2.721	2.105	2.684	2.862	2.737	2.438	3.794	2.666	2.367	2.415	3.008	2.694	0.752	0.766	0.770	0.985	0.606	0.634	1.059	0.391	0.689	0.845	0.626	0.460	0.657	1.005	1.027	0.917	0.822	0.995	100	100	100
	Essential fatty acid	linoleate (18:2n6)	LC/MS Neg	0.778	1.093	0.945	0.525	0.693	0.837	0.526	0.562	0.857	0.586	1.340	1.406	0.160	1.851	1.131	1.133	0.695	1.108	1.183	0.494	0.903	1.194	1.043	1.229	0.666	1.279	0.957	1.537	1.320	1.974	100	100	100
		linolenate [alpha or gamma; (18:3n3 or 6)]	LC/MS Neg	0.643	0.979	1.021	0.423	0.907	0.651	0.402	0.409	0.687	0.491	1.240	1.189	0.085	1.520	1.315	1.534	0.511	1.484	1.483	0.492	0.624	1.833	1.281	1.420	0.775	1.425	0.944	1.614	1.502	2.562	100	100	100
		dihomo-linolenate (20:3n3 or n6)	LC/MS Neg	0.767	1.561	1.001	0.741	0.816	0.806	0.532	0.899	0.977	0.600	0.955	1.392	0.274	2.199	1.180	1.449	0.685	0.994	1.510	0.646	1.114	1.243	0.999	1.753	1.211	1.765	0.699	1.656	1.001	1.459	100	100	100
		eicosapentaenoate (EPA; 20:5n3)	LC/MS Neg	0.354	1.100	0.464	0.844	0.451	0.094	0.094	0.805	0.836	1.026	0.451	0.974	0.094	0.886	1.429	4.850	0.296	1.440	2.876	1.077	1.046	2.599	3.336	3.912	4.931	1.554	0.920	0.711	0.740	2.866	90	90	100
		docosapentaenoate (n3 DPA; 22:5n3)	LC/MS Neg	0.584	1.114	0.904	0.527	0.337	0.367	0.236	0.530	0.950	0.680	1.033	0.937	0.131	1.148	1.071	2.111	0.425	1.443	2.161	0.968	0.943	1.344	1.823	2.417	2.171	2.005	0.766	1.734	1.032	1.670	100	100	100
		docosahexaenoate (DHA; 22:6n3)	LC/MS Neg	0.897	1.056	0.696	0.547	0.326	0.823	0.350	0.748	0.684	0.585	1.005	0.660	0.127	0.831	1.457	3.137	1.249	1.911	2.102	1.508	0.995	1.565	2.339	2.128	2.705	1.185	0.927	1.047	0.581	1.952	100	100	100
	Medium chain fatty acid	caproate (6:0)	LC/MS Neg	0.524	1.018	0.417	1.213	0.255	0.343	0.170	0.304	1.011	0.366	0.509	0.693	0.203	0.775	1.266	1.557	1.029	0.755	1.520	1.090	0.783	1.281	0.989	1.479	1.511	1.899	0.592	1.038	1.017	1.271	100	100	100
		heptanoate (7:0)	LC/MS Neg	0.502	0.852	0.535	1.187	0.427	0.427	0.427	0.427	0.770	0.427	0.545	0.693	0.427	0.427	0.896	1.332	1.064	0.773	1.146	1.033	0.637	1.089	1.062	1.326	1.182	1.172	0.762	1.009	0.991	1.041	50	90	100
		caprylate (8:0)	LC/MS Neg	0.770	1.552	0.707	1.091	0.547	0.538	0.292	0.535	1.001	0.474	0.999	0.904	0.289	1.502	1.044	1.026	1.623	0.747	1.320	1.130	0.761	0.983	0.958	1.150	1.019	1.188	0.599	1.003	1.043	1.101	100	100	100
		pelargonate (9:0)	LC/MS Neg	0.755	1.013	0.615	0.931	0.649	0.724	0.407	0.716	0.872	0.755	0.794	0.828	0.502	0.910	1.077	1.086	1.077	1.019	1.241	1.165	0.987	1.140	1.055	1.273	1.213	1.176	0.880	1.119	1.113	1.167	100	100	100
		caprate (10:0)	LC/MS Neg	1.193	1.588	1.070	0.978	0.918	0.874	0.606	1.010	0.856	0.929	1.163	0.883	0.616	2.318	0.904	0.970	1.421	0.955	1.127	1.109	0.868	1.115	0.813	1.130	0.990	1.129	0.861	1.196	1.210	1.146	100	100	100
		undecanoate (11:0)	LC/MS Neg	0.943	0.945	0.507	0.937	0.749	0.593	0.984	0.976	0.565	0.976	0.962	0.728	1.527	1.020	2.006	1.124	1.168	0.938	1.145	1.164	1.056	1.946	0.932	0.969	1.089	1.016	1.883	1.409	1.127	1.402	100	100	100
		laurate (12:0)	LC/MS Neg	1.032	1.260	0.993	0.807	0.759	0.930	0.844	1.969	0.887	1.008	1.265	0.836	0.727	1.866	0.930	1.398	1.007	0.857	1.027	0.877	0.901	1.119	0.720	1.279	0.848	1.071	0.846	1.342	1.179	1.245	100	100	100
		5-dodecenoate (12:1n7)	LC/MS Neg	0.588	2.542	1.049	1.831	0.802	0.453	0.865	0.947	0.879	0.886	7.929	3.109	1.358	6.631	1.660	0.978	1.369	2.559	0.453	0.583	1.000	1.212	0.453	0.453	0.760	0.453	0.453	0.897	0.780	1.208	100	90	60
		myristate (14:0)	LC/MS Neg	1.256	1.990	1.293	0.708	0.633	1.068	0.493	0.993	1.088	0.853	1.668	1.119	0.357	2.756	0.985	1.007	0.831	0.768	1.142	0.633	1.248	1.257	0.865	1.854	0.836	0.981	0.854	1.547	0.933	1.368	100	100	100
		myristoleate (14:1n5)	LC/MS Neg	1.367	4.989	2.673	0.678	0.604	0.851	0.546	0.631	1.650	0.641	3.208	1.768	0.436	6.306	0.862	1.171	0.908	1.048	1.035	0.821	0.937	1.331	0.869	2.338	0.834	0.965	0.827	2.045	1.502	1.661	100	100	100
		palmitate (16:0)	LC/MS Neg	1.020	1.542	1.322	0.587	0.726	0.890	0.610	0.735	1.048	0.719	1.837	1.404	0.267	1.968	1.029	1.083	0.860	0.809	1.199	0.584	0.965	1.111	0.980	1.602	0.837	1.068	0.913	1.382	0.908	1.733	100	100	100
		palmitoleate (16:1n7)	LC/MS Neg	1.208	3.386	2.745	0.504	0.583	0.750	0.369	0.913	1.332	0.835	3.405	2.235	0.168	4.254	0.903	0.931	0.579	0.579	1.036	0.310	0.997	1.599	1.007	2.360	0.819	1.003	0.808	1.916	1.106	1.955	100	100	100
		margarate (17:0)	LC/MS Neg	1.503	1.121	0.690	0.688	0.674	0.886	0.421	0.404	1.226	0.427	1.698	2.013	0.169	2.084	1.439	1.243	0.671	0.944	1.514	0.593	0.810	1.056	1.283	1.558	0.722	1.206	0.859	1.859	0.824	1.764	100	100	100
		10-heptadecenoate (17:1n7)	LC/MS Neg	1.185	2.025	1.336	0.551	0.536	0.767	0.388	0.560	1.073	0.555	1.722	1.939	0.155	2.485	0.928	1.011	0.653	0.608	1.018	0.381	0.980	1.283	1.065	1.837	0.778	1.034	0.713	1.538	0.989	1.235	100	100	100

Lipid	Long chain fatty acid	stearate (18:0)	LC/MS Neg	1.325	1.416	0.986	0.709	0.732	1.051	0.530	0.893	1.109	0.631	1.533	1.428	0.283	1.827	1.249	1.202	0.768	0.902	1.207	0.829	0.934	0.946	1.014	1.589	0.883	1.151	0.890	1.390	0.942	1.971	100	100	100
		oleate (18:1n9)	LC/MS Neg	0.998	1.815	1.195	0.593	0.564	0.780	0.541	0.688	0.960	0.575	1.808	1.754	0.220	2.530	1.002	1.094	0.787	0.802	1.101	0.537	1.074	1.396	1.035	1.604	0.813	1.011	0.823	1.623	0.963	1.774	100	100	100
		cis-vaccenate (18:1n7)	GC/MS	1.221	4.332	3.576	0.173	0.817	0.173	0.173	1.000	0.173	0.173	0.173	0.173	0.173	0.173	0.173	0.173	0.173	0.709	0.369	0.484	0.173	1.738	0.173	0.173	0.173	1.385	0.947	0.173	0.173	2.461	50	40	40
		stearidonate (18:4n3)	LC/MS Neg	0.269	1.447	1.482	0.170	0.244	0.353	0.170	0.404	0.405	0.170	0.987	0.790	0.170	2.335	0.810	4.167	0.245	1.013	1.558	0.289	0.170	1.273	1.352	1.892	1.253	1.158	0.511	1.540	0.834	2.167	80	90	90
		nonadecanoate (19:0)	LC/MS Neg	1.061	0.789	0.713	0.538	0.514	0.775	0.445	0.773	1.138	0.306	1.366	1.338	0.306	2.758	1.005	0.856	1.000	0.610	1.238	0.678	1.003	1.234	0.659	1.133	0.853	1.068	0.827	1.661	1.062	1.736	100	90	100
		10-nonadecenoate (19:1n9)	LC/MS Neg	1.346	2.741	1.082	0.522	0.443	0.655	0.398	0.529	0.837	0.531	2.105	2.609	0.146	4.582	0.826	1.380	0.617	0.898	1.167	0.281	0.918	1.176	1.122	2.110	0.843	1.158	0.671	1.595	1.389	1.496	100	100	100
		eicosenoate (20:1n9 or 11)	LC/MS Neg	1.163	2.481	1.593	0.454	0.494	0.965	0.447	0.725	1.071	0.407	2.613	2.206	0.157	6.176	0.925	1.652	0.762	0.745	1.159	0.462	0.963	1.444	1.214	2.285	0.983	1.017	0.665	2.008	0.942	2.129	100	100	100
		dihomo-linoleate (20:2n6)	LC/MS Neg	0.958	1.816	1.080	0.411	0.484	0.699	0.346	0.566	0.966	0.501	1.875	1.637	0.136	3.581	1.184	1.242	0.523	1.191	1.219	0.440	0.633	1.034	0.842	1.460	0.677	1.152	0.653	1.406	1.056	1.944	100	100	100
		dihomo-alpha-linolenate (20:3n3)	LC/MS Neg	0.767	1.561	1.001	0.741	0.816	0.806	0.532	0.899	0.977	0.600	0.955	1.392	0.274	2.199	1.180	1.449	0.685	0.994	1.510	0.646	1.114	1.243	0.999	1.753	1.211	1.765	0.699	1.656	1.001	1.459	100	100	100
		arachidonate (20:4n6)	LC/MS Neg	0.634	0.991	0.553	0.765	0.403	0.548	0.368	0.664	0.712	0.670	0.843	0.700	0.319	1.273	1.850	1.519	0.990	1.002	1.882	1.377	1.383	1.131	1.103	1.870	1.382	1.800	1.178	1.331	0.998	1.678	100	100	100
		adrenate (22:4n6)	LC/MS Neg	0.825	1.793	0.986	0.409	0.598	0.724	0.477	0.793	1.218	0.869	1.591	1.204	0.205	2.485	1.296	1.490	0.680	0.978	1.464	0.709	1.014	1.127	0.964	1.790	0.975	1.346	0.960	1.514	1.051	1.473	100	100	100
	Fatty acid, monohydroxy	3-hydroxydecanoate	LC/MS Neg	2.062	3.521	0.707	0.834	1.272	0.763	0.615	0.615	0.925	0.615	2.632	1.662	0.615	4.761	0.615	1.106	0.615	0.615	0.829	0.619	0.615	0.779	0.615	1.008	0.615	1.400	0.873	0.615	0.992	1.054	70	60	70
		16-hydroxypalmitate	LC/MS Neg	3.074	2.977	1.355	0.897	0.777	0.967	0.738	1.590	1.477	1.054	3.024	1.439	0.728	3.167	0.660	0.612	1.221	1.506	0.970	0.890	1.111	1.030	0.820	1.305	0.911	0.669	0.967	0.965	0.529	1.151	100	100	100
		2-hydroxystearate	LC/MS Neg	1.325	0.639	0.873	0.784	0.754	0.692	0.481	0.851	0.887	0.628	1.009	1.149	0.142	2.575	1.971	1.277	1.196	0.724	1.395	1.007	1.010	0.855	0.835	1.014	1.109	1.104	0.993	0.913	1.107	1.258	100	100	100
		2-hydroxypalmitate	LC/MS Neg	1.344	0.750	1.036	0.800	0.746	0.842	0.571	1.094	1.271	0.750	0.826	0.808	0.182	3.848	1.288	0.709	1.618	0.744	1.323	1.053	1.062	0.943	1.001	1.298	1.058	0.941	1.166	0.999	0.946	1.407	100	100	100
	Fatty acid, dicarboxylate	sebacate (decanedioate)	LC/MS Pos	0.144	0.144	0.144	0.144	0.189	0.144	0.144	0.189	0.162	0.144	0.144	0.144	0.144	0.228	0.709	1.198	1.131	0.873	1.707	1.278	0.917	0.993	1.793	2.204	1.000	0.708	1.195	1.269	1.417	1.129	40	70	100
		azelate (nonanedioate)	LC/MS Neg	0.144	0.127	0.128	0.154	0.100	0.145	0.130	0.083	0.121	0.134	0.088	0.140	0.106	0.176	0.932	1.069	2.026	1.840	2.821	1.667	1.068	1.857	4.921	4.255	2.246	1.374	1.332	2.218	1.831	1.620	100	100	100
		octadecanedioate	LC/MS Neg	2.169	1.311	0.622	1.000	1.376	1.000	2.082	0.785	1.004	0.800	1.096	0.858	0.276	6.502	0.276	0.276	1.165	0.276	0.761	0.467	0.276	0.276	0.642	1.034	2.356	0.316	0.649	0.650	1.720	0.276	100	70	70
		3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	LC/MS Neg	0.349	0.106	0.221	0.106	0.106	0.216	0.810	0.229	0.106	0.821	0.198	0.106	0.106	0.106	0.904	38.714	0.790	3.386	6.310	5.458	1.000	13.874	13.440	20.573	4.053	2.528	3.467	0.106	0.797	12.505	60	70	100
	Fatty acid, amide	oleamide	LC/MS Pos	2.101	0.215	1.828	0.296	1.448	1.000	0.224	1.256	1.628	0.299	0.784	3.553	0.284	2.948	0.572	0.179	0.721	1.107	0.221	0.238	0.179	1.116	1.620	3.537	2.399	0.179	0.765	2.537	0.179	0.614	100	90	80
	Fatty acid metabolism (also BCAA metabolism)	propionylcarnitine	LC/MS Pos	1.398	1.012	0.796	1.203	1.595	1.965	0.988	0.788	0.614	0.904	1.116	1.048	0.622	1.126	0.792	1.201	1.578	0.356	0.851	0.988	0.425	1.059	0.836	1.140	1.096	0.600	1.564	0.658	0.483	1.304	100	100	100
		butyrylcarnitine	LC/MS Pos	2.533	6.945	1.026	3.510	3.067	1.197	1.191	0.997	2.512	1.937	3.575	3.735	0.413	1.444	0.434	0.488	0.696	0.244	0.535	0.728	0.372	2.888	0.458	1.545	0.557	0.520	1.003	0.505	0.540	0.977	100	100	100
	Fatty acid metabolism	isovalerate	LC/MS Neg	0.681	0.554	0.505	0.596	0.289	0.425	0.289	0.565	0.612	0.289	0.377	0.552	0.289	1.074	1.359	1.115	1.455	1.000	1.330	1.200	0.980	1.140	1.026	1.357	1.338	1.380	0.824	1.247	0.956	1.427	80	90	100
	Carnitine metabolism	carnitine	LC/MS Pos	1.443	1.493	1.571	1.397	1.199	1.666	1.301	1.519	1.251	1.064	1.552	1.441	0.367	0.890	0.676	0.684	0.610	0.759	0.696	0.994	0.622	1.204	1.006	0.868	0.789	1.102	0.615	0.886	0.652	0.699	100	100	100
		3-dehydrocarnitine*	LC/MS Pos	1.008	1.059	0.630	1.092	0.895	1.439	2.122	0.755	0.519	0.709	0.897	0.849	1.004	0.951	0.878	1.795	0.854	1.119	0.779	1.923	0.996	4.672	1.603	0.916	1.575	0.677	2.060	1.125	0.972	1.030	100	100	100
		acetylcarnitine	LC/MS Pos	1.484	1.903	1.906	0.981	1.143	1.286	1.061	0.962	0.785	0.680	1.456	1.290	0.894	2.600	0.784	1.134	0.688	0.665	0.754	1.299	0.739	1.365	0.756	1.467	0.752	0.651	2.218	0.885	0.838	1.019	100	100	100
		hexanoylcarnitine	LC/MS Pos	1.064	3.272	0.619	1.073	0.892	1.864	0.973	0.690	0.919	0.969	1.720	1.300	0.402	1.432	0.973	1.192	0.522	0.476	0.805	2.027	0.511	1.174	0.721	2.011	0.908	0.972	2.040	1.027	1.115	1.460	100	100	100
		octanoylcarnitine	LC/MS Pos	1.315	4.572	0.411	1.409	0.521	2.388	1.024	0.458	1.093	0.494	1.478	1.047	0.605	0.951	1.237	0.959	0.459	0.802	1.262	3.209	0.904	1.328	0.713	1.492	0.424	0.715	2.486	0.530	1.947	0.976	100	100	100
		decanoylcarnitine	LC/MS Pos	2.094	6.563	0.536	1.278	0.656	2.141	1.281	0.804	1.012	0.754	2.166	0.901	0.331	1.318	0.944	1.045	0.572	0.988	1.268	2.627	0.792	1.614	0.518	1.059	0.517	0.806	2.004	0.496	1.933	0.824	100	100	100
		laurylcarnitine	LC/MS Pos	4.051	7.690	0.432	0.868	0.597	1.930	1.661	1.790	0.699	0.708	3.063	1.000	0.236	4.208	0.792	1.868	0.420	2.548	0.477	2.216	0.814	1.956	0.236	1.422	0.795	0.702	1.828	0.699	2.267	0.715	100	100	90
		palmitoylcarnitine	LC/MS Pos	2.147	2.893	0.805	1.091	1.712	0.861	1.748	2.186	0.581	1.087	3.281	0.958	0.363	3.600	1.042	0.817	0.492	1.125	1.049	1.394	0.675	1.791	0.570	1.198	0.706	0.784	0.788	0.749	0.483	0.623	100	100	100
		oleoylcarnitine	LC/MS Pos	2.426	5.252	0.897	1.285	1.542	0.712	1.468	1.901	0.926	1.085	3.441	1.312	0.424	5.031	0.602	0.442	0.653	1.131	0.655	1.449	1.074	3.798	0.832	1.385	0.606	0.772	0.788	0.751	0.599	0.867	100	100	100
	Bile acid metabolism	cholate	LC/MS Neg	13.656	1.423	7.702	0.310	0.994	0.310	0.310	0.310	0.768	0.547	0.310	0.310	0.310	6.444	0.310	0.310	4.121	0.954	1.006	0.465	13.458	0.615	3.519	0.310	0.610	0.310	0.521	0.310	0.310	16.992	60	50	70
		glycocholate	LC/MS Pos	1.000	8.830	11.770	0.265	5.034	0.726	0.265	1.648	6.739	5.793	0.579	0.502	0.735	67.057	1.436	0.265	10.124	1.059	0.265	0.418	0.524	0.969	0.265	0.560	0.265	0.265	0.265	1.144	0.610	0.620	90	80	60
		taurocholate	LC/MS Neg	0.380	2.142	3.561	0.380	1.133	0.380	0.391	0.465	1.986	2.647	0.380	0.380	0.380	137.150	3.883	0.380	54.884	0.392	0.380	0.428	0.380	0.766	0.380	0.618	0.380	0.380	0.380	0.380	0.380	0.867	70	60	30
		taurochenodeoxycholate	LC/MS Neg	0.721	3.574	5.782	0.123	2.135	0.510	0.123	0.242	3.078	4.490	0.123	0.123	0.123	194.194	2.350	0.123	61.114	0.123	0.123	1.000	0.123	0.331	0.123	0.522	0.520	0.123	0.219	0.123	0.530	1.248	80	50	60
		ursodeoxycholate	LC/MS Neg	1.089	1.871	0.529	0.529	0.861	0.645	0.636	1.313	1.230	1.453	0.529	0.529	0.529	5.502	0.529	2.418	0.839	0.529	0.562	0.529	0.581	0.529	0.638	0.529	0.529	2.014	0.610	1.067	0.933	3.951	80	40	80
		hyodeoxycholate	LC/MS Neg	2.212	6.700	1.789	0.564	4.106	3.092	1.638	1.419	1.720	3.572	0.529	0.270	0.344	0.270	0.499	1.718	0.539	0.363	1.607	0.270	0.667	2.509	0.402	0.753	0.485	0.765	1.211	0.891	0.876	1.109	100	80	100
		glycochenodeoxycholate	LC/MS Neg	4.371	27.231	33.265	0.379	16.001	3.475	0.512	3.896	23.021	8.517	0.129	0.482	0.279	316.903	10.287	0.596	22.025	0.537	0.928	0.467	0.612	0.354	1.000	0.129	0.161	0.129	0.129	0.892	5.836	4.146	100	90	80
		glycolithocholate sulfate*	LC/MS Neg	1.334	0.180	0.694	0.284	0.759	1.560	1.114	4.272	1.901	2.486	0.870	1.573	0.549	1.462	1.849	0.824	0.180	0.718	0.435	0.868	0.418	0.180	1.000	0.477	0.180	2.099	1.708	0.403	2.231	1.526	90	90	90
		taurolithocholate 3-sulfate	LC/MS Neg	1.583	0.247	0.727	0.219	0.187	1.009	0.757	2.165	1.000	2.127	0.375	2.030	0.520	5.320	3.237	0.679	0.187	1.556	0.234	2.705	0.718	0.187	0.483	0.737	0.458	1.552	1.767	0.187	1.647	1.222	90	90	90
		glycocholenate sulfate*	LC/MS Neg	1.863	1.136	1.155	0.802	0.525	0.636	0.345	1.812	1.515	1.116	1.491	0.769	0.206	1.568	0.423	0.992	0.538	0.959	0.644	0.734	1.235	1.177	1.399	0.733	0.333	1.020	2.425	0.969	1.008	1.171	100	100	100
		taurocholenate sulfate*	LC/MS Neg	0.623	0.972	1.247	0.319	0.319	0.408	0.363	1.327	0.605	0.595	1.469	1.390	0.319	5.813	1.181	0.970	2.843	2.139	0.484	1.555	1.028	1.472	0.762	1.207	1.441	0.872	3.135	0.466	0.896	0.654	90	90	100
	Glycerolipid metabolism	glycerol	GC/MS	1.129	1.572	1.655	0.972	1.424	0.948	0.997	0.821	1.009	1.003	1.347	1.298	0.466	1.193	0.518	1.007	0.655	0.675	0.805	0.592	0.638	1.303	0.741	1.038	0.559	1.048	0.360	1.595	0.694	1.079	100	100	100
		choline	LC/MS Pos	0.708	1.216	0.443	0.691	1.544	0.676	0.987	0.719	0.510	0.863	0.805	0.523	1.640	0.945	1.069	1.299	1.185	1.240	1.248	1.621	1.333	1.360	0.762	1.013	0.655	0.942	1.955	0.837	1.103	1.042	100	100	100
		glycerol 3-phosphate (G3P)	GC/MS	0.439	0.679	0.803	0.775	1.017	0.601	0.892	0.646	1.217	0.845	0.621	0.655	0.813	1.074	1.241	1.460	0.943	1.380	1.802	0.813	1.266	0.983	1.596	1.428	0.935	1.215	1.461	1.546	1.645	1.878	100	100	100
		glycerophosphorylcholine (GPC)	LC/MS Pos	0.644	0.433	0.433	1.246	0.433	0.487	0.433	0.433	0.433	0.595	0.997	0.433	0.469	0.439	0.433	0.433	0.441	0.433	3.068	2.445	2.291	0.851	3.189	1.252	0.635	1.348	0.433	1.003	1.255	1.901	40	70	90
	Inositol metabolism	myo-inositol	GC/MS	0.913	0.613	0.593	0.429	0.897	0.846	1.659	0.826	0.547	0.777	0.594	0.587	6.187	0.912	0.974	1.426	1.575	2.675	1.214	2.268	1.349	2.006	1.009	1.347	0.921	0.996	4.789	1.329	1.564	1.004	100	100	100
		scyllo-inositol	GC/MS	0.478	0.497	0.478	0.478	0.478	0.478	1.540	0.478	0.478	0.478	0.478	0.478	2.512	1.000	0.478	0.478	0.528	4.104	0.478	1.031	0.478	1.877	0.545	0.515	0.478	0.478	1.196	0.902	0.478	0.478	20	50	60
	Ketone bodies	3-hydroxybutyrate (BHBA)	GC/MS	2.582	3.855	1.991	0.471	0.958	0.709	0.403	0.669	0.582	0.356	2.343	4.489	0.408	6.771	1.042	0.783	0.551	1.446	1.078	0.670	0.613	0.529	2.213	4.326	0.655	1.126	3.311	0.747	1.097	1.793	100	100	100
	Lysolipid	1-oleoylglycerophosphoethanolamine	LC/MS Neg	1.183	1.694	2.076	0.921	2.132	0.540	1.238	1.508	3.983	1.743	1.584	0.797	0.975	1.655	0.274	0.385	4.025	0.398	0.796	0.830	0.746	0.567	1.025	1.045	0.395	0.140	0.292	0.934	1.220	1.420	100	100	100
		1-linoleoylglycerophosphoethanolamine*	LC/MS Neg	1.149	0.905	1.288	1.009	2.592	1.374	0.985	1.391	3.149	1.503	1.643	1.064	0.790	0.788	0.628	0.664	2.320	0.497	0.991	0.734	0.811	0.779	1.221	0.827	0.446	0.577	0.592	1.062	1.376	1.704	100	100	100
		1-arachidonoylglycerophosphoethanolamine*	LC/MS Neg	0.879	1.011	0.950	1.050	1.375	1.278	0.722	1.050	1.732	0.989	1.185	0.928	0.767	0.348	1.153	1.032	1.021	0.545	1.287	0.855	1.453	0.925	0.789	1.236	0.605	0.662	1.412	0.936	0.965	1.263	100	100	100
		2-arachidonoylglycerophosphoethanolamine*	LC/MS Neg	0.905	1.008	1.191	0.626	0.992	1.784	0.630	1.191	1.483	0.796	1.250	1.128	0.506	0.506	0.801	0.506	0.506	0.772	0.899	0.954	1.107	0.506	0.784	1.784	0.506	0.590	1.087	0.506	1.298	1.915	100	70	70
		1-myristoylglycerophosphocholine	LC/MS Pos	1.411	2.435	2.227	1.258	2.814	0.481	0.642	2.444	1.969	1.731	2.403	0.720	0.228	1.377	0.171	0.646	0.539	1.042	0.958	1.231	0.538	1.053	0.363	1.896	0.785	0.682	0.292	1.313	0.510	0.614	100	100	100
		1-palmitoylglycerophosphocholine	LC/MS Pos	1.222	1.373	1.044	1.244	1.837	0.918	1.223	1.194	1.347	1.255	1.410	1.110	0.564	1.096	0.602	0.823	0.637	0.987	0.777	1.227	0.702	0.993	0.898	1.311	0.722	0.692	0.816	1.007	0.718	0.840	100	100	100
		2-palmitoylglycerophosphocholine*	LC/MS Pos	1.239	1.701	1.890	1.134	2.093	1.000	1.182	1.597	1.924	1.427	1.758	0.974	0.335	0.806	0.449	0.926	0.543	0.756	0.568	1.313	0.480	1.132	0.668	1.780	0.494	0.796	0.762	1.061	0.514	0.335	100	100	90
		1-palmitoleoylglycerophosphocholine*	LC/MS Pos	1.006	5.860	4.181	1.625	3.634	0.178	1.249	3.159	4.365	1.641	3.761	0.897	0.209	0.967	0.133	0.432	0.244	0.697	0.898	0.576	1.019	1.831	0.994	2.172	0.187	0.218	0.427	1.353	0.517	1.045	100	100	100
		1-heptadecanoylglycerophosphocholine	LC/MS Pos	1.439	1.975	0.560	1.047	1.814	0.545	1.785	1.955	1.189	1.180	1.008	0.888	0.891	1.321	1.537	0.831	0.515	0.985	1.261	2.492	0.708	1.040	1.079	0.992	0.482	0.368	0.544	0.584	0.672	0.945	100	100	100
		1-stearoylglycerophosphocholine	LC/MS Pos	1.465	1.697	1.420	1.345	1.545	0.911	0.833	1.108	1.378	0.729	1.664	1.023	0.410	1.779	0.767	0.953	0.525	1.005	0.816	2.019	0.497	1.416	0.915	1.621	0.756	0.610	0.599	0.995	0.862	1.010	100	100	100
		2-stearoylglycerophosphocholine*	LC/MS Pos	1.137	1.588	1.956	1.490	1.728	0.959	0.371	1.395	2.898	0.741	1.275	1.156	0.469	2.099	0.496	0.390	0.578	0.892	0.421	1.787	0.405	1.332	1.041	2.203	0.518	0.391	0.438	0.813	0.360	1.188	100	100	100
		1-oleoylglycerophosphocholine	LC/MS Pos	1.580	2.836	1.646	1.443	2.186	0.448	1.453	1.519	1.778	1.018	1.720	0.907	0.680	1.413	0.495	0.546	0.751	0.709	0.826	1.568	0.930	1.377	0.982	1.527	0.404	0.577	0.567	1.027	0.856	0.859	100	100	100
		2-oleoylglycerophosphocholine*	LC/MS Pos	1.378	3.395	1.679	1.642	2.372	0.694	1.463	1.792	1.835	1.389	1.940	1.000	0.633	1.935	0.524	0.627	0.591	0.645	0.522	1.883	0.806	0.796	0.635	1.223	0.442	0.442	0.529	1.149	0.848	0.684	100	100	90
		1-linoleoylglycerophosphocholine	LC/MS Pos	1.298	1.104	1.466	1.171	1.816	0.804	0.961	1.352	1.700	1.030	1.344	1.000	0.466	1.049	0.745	0.849	1.036	0.934	0.771	1.283	0.562	0.774	1.083	0.953	0.679	0.741	0.600	0.982	1.287	1.000	100	100	100
		1-eicosatrienoylglycerophosphocholine*	LC/MS Pos	0.859	2.573	1.037	1.798	2.559	0.488	0.721	1.465	2.130	0.941	1.974	0.653	0.272	0.960	0.707	1.121	0.774	1.283	0.884	1.414	0.978	1.178	1.022	1.805	0.695	1.220	0.592	1.812	0.777	0.922	100	100	100
		1-arachidonoylglycerophosphocholine*	LC/MS Pos	0.998	1.124	0.836	1.071	0.865	0.625	0.590	0.922	1.305	0.716	0.870	0.801	0.250	0.519	1.913	1.580	0.795	1.756	0.940	1.968	1.327	0.993	2.112	1.845	1.002	1.235	1.512	0.858	1.137	1.312	100	100	100
		1-docosahexaenoylglycerophosphocholine*	LC/MS Pos	1.042	0.703	0.889	0.960	0.905	0.956	0.546	0.764	1.077	0.781	0.692	0.974	0.627	0.696	1.073	1.161	1.000	1.384	1.131	1.457	0.860	1.507	1.661	1.787	1.252	1.000	1.002	1.130	0.843	1.515	100	100	100
	Monoacylglycerol	1-palmitoylglycerol (1-monopalmitin)	GC/MS	1.502	2.633	0.807	1.056	1.953	2.329	0.539	0.447	0.447	1.163	0.486	2.138	0.447	0.571	0.559	1.030	1.127	0.654	1.204	0.447	0.447	0.760	0.447	0.447	0.447	0.970	0.447	0.705	0.447	0.447	90	80	30
		1-linoleoylglycerol (1-monolinolein)	LC/MS Neg	0.159	0.225	0.264	0.273	0.328	0.736	0.556	0.101	0.262	0.192	0.328	0.340	0.846	0.977	2.319	2.293	2.784	1.023	2.528	1.374	1.591	2.036	1.668	0.832	1.795	1.965	1.946	2.536	3.608	2.859	100	100	100
	Sphingolipid	stearoyl sphingomyelin	GC/MS	1.000	0.422	0.141	0.832	1.286	0.141	0.141	0.381	0.968	0.431	0.319	1.734	0.141	0.718	2.372	3.145	1.417	0.141	2.187	0.141	0.202	0.141	1.160	0.888	0.141	2.671	1.449	0.354	2.042	2.822	80	70	80
	Sterol/Steroid	lathosterol	GC/MS	0.364	0.765	0.364	0.364	1.561	0.364	0.364	0.364	0.364	0.364	0.364	1.271	0.364	0.364	0.364	0.729	0.364	0.364	1.407	0.364	0.364	1.000	0.364	0.364	0.364	0.364	0.364	0.364	0.364	0.364	20	30	20
		cholesterol	GC/MS	0.897	1.047	0.998	1.210	1.050	1.001	1.024	0.692	1.277	0.971	0.909	0.973	1.224	1.267	0.923	1.533	0.898	0.660	1.531	0.594	0.756	0.999	0.938	0.734	0.806	1.229	1.224	1.276	1.039	1.220	100	100	100
		dehydroisoandrosterone sulfate (DHEA-S)	LC/MS Neg	0.970	0.605	2.428	0.760	0.609	1.030	1.344	1.498	2.457	3.080	2.342	2.641	0.046	1.881	1.999	0.614	0.281	1.539	1.132	0.323	0.173	0.395	0.189	1.705	0.512	1.463	0.914	0.234	2.051	0.559	100	100	100
		epiandrosterone sulfate	LC/MS Neg	1.238	0.595	2.137	1.029	1.000	0.739	2.825	0.534	3.374	2.470	1.186	1.183	0.081	0.598	0.953	0.856	0.199	1.008	1.639	0.492	0.193	0.372	0.209	2.980	0.994	2.426	1.274	0.081	3.448	0.340	100	100	90
		androsterone sulfate	LC/MS Neg	1.987	0.841	0.981	1.231	1.000	0.511	3.409	0.892	5.640	4.862	1.841	1.514	0.082	1.398	0.402	0.598	0.171	1.278	1.930	0.345	0.082	0.325	0.279	1.921	1.136	3.251	0.788	0.276	2.944	0.239	100	90	100
		cortisol	LC/MS Pos	0.997	2.369	2.258	0.834	1.003	0.864	1.114	0.855	2.690	1.510	0.886	1.962	0.760	0.233	1.023	1.195	1.363	0.703	0.659	1.140	1.241	0.773	0.633	1.147	0.600	0.520	0.770	0.480	1.130	1.642	100	100	100
		cortisone	LC/MS Pos	1.215	1.208	1.298	0.905	0.886	1.030	1.000	0.648	1.228	1.175	1.017	1.218	0.302	1.048	0.577	0.624	1.184	0.803	1.017	1.284	0.917	0.863	0.302	0.778	0.668	0.522	0.302	0.302	0.565	1.062	100	90	80
		7-alpha-hydroxy-3-oxo-4-cholestenoate (7-Hoca)	LC/MS Neg	4.188	1.488	0.936	0.454	1.533	0.664	1.824	0.943	1.130	2.340	0.968	2.205	0.282	3.993	0.622	0.801	0.893	1.000	0.859	0.515	0.523	0.384	1.098	1.224	1.044	1.124	3.148	0.870	0.282	3.561	100	90	100
		4-androsten-3beta,17beta-diol disulfate 1*	LC/MS Neg	1.272	7.312	3.954	0.601	1.121	0.512	2.190	5.587	4.121	12.416	11.431	4.057	0.238	0.902	0.913	0.478	0.342	2.215	0.653	0.408	0.292	0.899	0.243	3.427	0.608	1.087	1.652	0.367	1.150	0.475	100	100	100
		4-androsten-3beta,17beta-diol disulfate 2*	LC/MS Neg	1.239	1.257	0.938	0.575	0.603	1.062	1.171	1.727	1.630	2.339	2.001	2.244	0.332	2.305	1.178	0.292	0.682	1.836	0.665	0.656	0.427	0.250	0.347	1.125	0.411	0.826	1.549	0.182	1.088	0.546	100	100	100
		5alpha-androstan-3beta,17beta-diol disulfate	LC/MS Neg	1.183	5.736	2.636	0.608	1.068	0.731	2.442	1.583	4.239	5.796	3.575	1.698	0.232	0.932	0.171	0.171	0.497	1.423	0.773	0.609	0.171	0.314	0.345	2.923	0.321	1.186	0.862	0.171	0.637	0.171	100	80	80
		pregnen-diol disulfate*	LC/MS Neg	1.542	2.111	1.760	0.588	0.912	1.006	1.268	3.252	1.443	6.467	2.994	2.964	0.528	0.994	1.509	0.232	0.626	2.707	0.563	0.479	0.273	0.427	0.498	1.026	0.285	0.761	1.769	0.183	1.010	0.583	100	100	100
Nucleotide	Purine metabolism, (hypo)xanthine/inosine containing	xanthine	LC/MS Pos	0.460	0.460	0.490	0.460	0.460	0.460	0.460	0.471	0.837	0.460	0.460	0.741	0.460	1.628	0.672	0.982	0.460	4.316	1.711	0.460	3.024	1.750	0.939	8.233	3.140	0.548	0.460	1.000	1.316	1.051	40	60	90
		hypoxanthine	LC/MS Neg	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	0.938	1.022	0.938	0.938	0.938	0.978	0.938	1.154	0.938	0.938	0.938	0.938	0.938	0.938	0	20	20
		inosine	LC/MS Neg	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	2.469	0.598	0.573	2.262	0.300	1.006	0.355	0.571	0.300	0.994	0.300	2.333	1.459	1.786	2.154	0.851	0.846	3.136	0	70	90
	Purine metabolism, adenine containing	N1-methyladenosine	LC/MS Pos	1.032	0.769	0.902	1.142	1.360	1.349	1.269	0.891	1.153	1.003	1.389	0.813	1.978	0.749	1.002	1.125	1.006	0.444	0.777	0.848	0.484	0.815	1.054	0.811	0.998	0.759	1.169	0.640	0.712	1.071	100	100	100
		adenosine 5'-monophosphate (AMP)	LC/MS Pos	1.028	0.921	0.908	0.729	0.972	1.043	1.966	1.309	0.729	3.897	0.729	0.852	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	0.729	90	10	0
	Purine metabolism, guanine containing	guanosine	LC/MS Neg	0.505	0.505	0.505	0.505	0.505	0.505	0.505	0.505	0.505	0.505	0.505	0.505	1.577	0.643	0.583	1.580	0.505	0.743	0.505	0.505	0.505	0.516	0.505	1.460	1.239	1.141	1.328	0.859	0.587	1.929	0	60	80
	Purine metabolism, urate metabolism	urate	LC/MS Neg	0.827	0.994	0.651	0.984	0.847	1.185	1.302	0.868	1.118	1.003	1.112	1.041	0.804	0.838	1.356	1.209	1.276	0.822	0.997	1.393	0.777	1.087	0.922	1.140	0.996	1.079	1.340	0.922	1.167	0.913	100	100	100
	Pyrimidine metabolism, uracil containing	uridine	LC/MS Neg	0.897	0.364	1.140	1.421	0.705	1.119	0.909	0.698	0.837	0.972	1.082	0.894	0.813	1.189	0.968	1.058	0.371	1.094	1.258	0.752	0.971	1.371	1.502	1.328	1.198	1.247	0.893	1.463	1.028	0.840	100	100	100
		pseudouridine	LC/MS Neg	0.982	0.597	0.669	0.817	0.947	1.359	1.343	0.750	0.996	1.004	0.753	0.846	4.150	0.995	1.333	1.471	1.185	1.215	0.856	1.224	1.338	1.590	0.751	1.285	1.240	0.946	5.110	0.974	1.338	0.964	100	100	100
Cofactors and vitamins	Ascorbate and aldarate metabolism	ascorbate (Vitamin C)	GC/MS	0.113	0.113	0.113	0.113	0.113	0.113	0.113	0.113	0.113	0.113	0.113	0.113	0.937	1.819	0.892	0.245	1.000	1.873	1.004	0.113	1.771	0.734	3.712	1.433	1.481	0.856	0.113	1.615	0.631	0.657	0	80	90
		threonate	GC/MS	1.000	0.064	0.064	0.172	0.499	0.370	0.689	0.495	0.636	0.545	0.266	0.147	1.877	1.552	1.608	0.709	1.493	2.224	1.527	0.623	1.182	1.552	1.562	1.816	1.749	0.856	1.595	2.208	1.546	0.765	90	100	100
	Hemoglobin and porphyrin metabolism	heme	LC/MS Pos	0.726	2.112	0.860	3.037	10.107	13.837	3.619	5.090	5.211	6.790	7.656	4.017	0.105	1.599	0.182	0.094	0.397	0.851	1.318	1.251	0.263	0.180	0.202	0.918	0.138	0.294	0.213	0.426	1.578	1.082	100	100	100
		bilirubin (Z,Z)	LC/MS Neg	0.976	1.460	1.007	0.683	0.365	0.672	0.945	1.225	0.993	0.688	1.186	0.929	0.298	4.303	1.061	0.333	1.248	1.393	6.458	0.934	1.640	0.775	1.379	2.056	1.704	1.928	1.096	0.754	0.949	0.626	100	100	100
		bilirubin (E,E)*	LC/MS Neg	1.083	2.143	1.235	0.875	0.516	0.888	0.924	0.928	1.130	0.853	2.081	1.662	0.240	2.800	0.887	0.448	0.892	1.228	2.420	1.018	1.329	0.894	0.957	1.782	1.093	1.651	0.754	1.080	0.982	0.763	100	100	100
		bilirubin (E,Z or Z,E)*	LC/MS Pos	1.130	3.594	1.397	0.768	0.574	0.909	1.528	1.026	1.189	0.765	1.708	1.082	0.087	4.611	0.523	0.319	0.335	1.129	1.669	1.723	0.602	0.557	0.574	1.482	0.974	1.890	0.561	1.293	0.800	0.843	100	100	100
		biliverdin	LC/MS Pos	1.485	5.157	1.393	1.041	1.328	1.538	1.187	2.073	1.000	1.085	3.244	2.337	0.084	5.676	0.084	0.155	0.362	0.535	2.862	0.611	0.393	0.630	0.328	0.697	0.201	1.231	0.339	0.763	0.478	0.622	100	90	100
	Nicotinate and nicotinamide	nicotinamide	LC/MS Pos	1.008	2.060	1.388	0.581	0.769	0.736	1.017	1.986	1.803	1.056	1.781	0.406	0.670	1.279	1.357	0.841	1.079	0.406	2.193	0.632	0.406	0.992	0.600	0.716	1.050	1.780	0.491	0.857	0.434	0.770	100	80	100
	Pantothenate and CoA metabolism	pantothenate	LC/MS Pos	0.469	0.969	0.720	1.214	1.052	1.685	0.469	0.469	0.950	0.469	1.376	1.031	1.847	0.656	0.469	0.469	0.469	0.665	0.590	0.469	0.469	3.547	2.475	1.435	0.806	0.469	1.187	0.469	0.498	0.848	70	60	70
	Tocopherol metabolism	alpha-tocopherol	GC/MS	0.558	0.635	0.044	0.913	0.596	1.180	1.625	0.554	1.015	0.700	0.993	0.743	0.842	0.823	0.909	1.414	0.824	1.111	1.785	0.818	1.289	1.533	1.372	1.227	1.628	1.240	1.284	2.568	0.820	1.007	100	100	100
		gamma-tocopherol	GC/MS	0.483	0.483	0.483	0.483	0.483	0.483	0.483	0.483	0.670	0.483	0.483	0.483	0.483	0.483	0.483	0.483	0.765	0.483	0.483	0.483	0.483	0.564	1.235	0.483	0.483	0.483	1.793	0.483	1.687	1.382	20	10	50
	Vitamin B6 metabolism	pyridoxate	LC/MS Neg	0.566	0.566	0.566	0.566	2.276	0.863	0.661	0.566	0.729	0.823	0.566	0.566	6.353	0.566	0.566	0.681	0.566	1.178	0.796	0.859	1.923	1.411	2.064	1.800	1.215	0.566	3.087	1.120	0.785	0.880	50	60	90
Xenobiotics	Benzoate metabolism	hippurate	LC/MS Neg	1.432	0.167	0.167	0.970	1.158	2.981	2.282	0.228	0.538	1.000	0.462	0.216	20.004	0.192	1.719	2.250	0.872	1.372	1.604	2.763	2.181	0.201	0.167	0.492	0.290	1.074	10.377	0.388	0.934	1.549	90	100	100
		2-hydroxyhippurate (salicylurate)	LC/MS Neg	0.295	0.295	0.295	0.295	0.295	1.159	1.498	0.295	0.295	0.522	0.295	0.295	1.604	0.295	0.737	0.295	1.404	0.295	0.295	0.295	1.591	0.295	0.841	0.295	0.295	0.295	17.736	0.295	0.647	0.464	30	40	50
		catechol sulfate	LC/MS Neg	0.448	0.182	0.208	0.182	1.267	1.412	2.037	0.580	1.250	3.321	0.202	0.400	8.884	0.182	0.778	1.244	0.803	0.994	1.527	0.716	1.776	1.891	0.222	0.500	1.006	0.774	2.856	1.618	1.969	0.902	90	90	100
		4-vinylphenol sulfate	LC/MS Neg	0.428	0.255	0.893	0.255	2.001	0.418	1.107	1.299	1.312	2.624	0.333	0.586	4.114	0.255	1.219	0.419	4.070	0.282	0.646	2.101	7.934	0.403	0.449	0.797	1.404	2.464	5.652	2.928	0.549	0.520	90	90	100
	Chemical	glycolate (hydroxyacetate)	GC/MS	0.668	0.668	1.030	1.059	0.668	1.094	1.313	0.668	0.668	0.668	0.668	0.668	0.668	0.668	0.676	0.668	1.111	0.750	0.668	0.668	0.747	0.668	0.668	0.668	0.668	0.668	0.668	0.668	0.668	0.970	40	30	30
		iminodiacetate (IDA)	GC/MS	3.586	3.559	4.942	4.250	6.949	9.960	2.501	2.969	2.707	3.099	5.071	3.813	0.604	1.026	0.415	0.992	0.644	0.535	1.008	0.282	0.644	0.752	0.523	0.574	0.979	0.685	0.268	0.362	1.162	0.597	100	100	100
	Drug	salicylate	LC/MS Neg	0.305	0.305	0.420	0.305	0.305	1.000	11.100	0.305	0.305	0.744	0.305	0.305	0.494	0.305	1.213	0.343	3.042	0.305	0.305	0.305	1.898	0.305	1.875	0.305	0.305	0.416	1.912	0.305	1.434	0.828	40	50	60
		salicyluric glucuronide*	LC/MS Neg	0.319	0.319	0.319	0.319	0.319	1.104	0.319	0.319	0.319	0.319	0.319	0.319	0.435	0.319	0.432	3.166	0.896	0.319	0.319	0.319	1.523	0.319	0.397	0.319	0.319	0.319	12.929	0.319	1.793	0.319	20	40	40
		4-acetamidophenol	LC/MS Pos	0.282	0.282	0.282	0.282	0.282	1.000	0.889	0.282	0.282	0.282	0.282	0.282	1.868	0.282	0.282	1.553	0.282	0.282	0.282	0.282	0.282	0.688	0.282	0.282	2.196	0.282	0.282	0.282	0.282	0.282	20	20	30
		p-acetamidophenylglucuronide	LC/MS Neg	0.326	0.326	0.326	0.326	0.326	0.326	0.934	0.326	0.326	0.326	0.326	0.326	1.009	0.326	0.326	2.617	0.326	0.326	0.326	0.326	0.326	1.000	0.326	0.326	1.351	0.326	0.326	0.326	0.463	0.326	20	20	30
		2-propylpentanoate (valproate)	LC/MS Neg	0.449	0.780	0.419	1.034	0.332	0.426	0.335	0.427	0.853	0.357	0.583	0.575	1.811	2.350	1.197	1.585	1.090	0.902	1.508	0.966	0.716	1.697	1.035	1.494	1.375	1.743	0.556	1.045	1.361	1.354	100	100	100
		pioglitazone*	LC/MS Pos	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	10	0	0
		hydroxypioglitazone*	LC/MS Pos	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	10	0	0
		naproxen	GC/MS	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	0	0	10
		metformin	LC/MS Pos	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	0	0	10
		metoprolol	LC/MS Pos	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	0.190	1.364	0.190	0.190	0.190	0.190	0.190	1.000	0.190	0.190	0.190	0	10	20
		metoprolol acid metabolite*	LC/MS Pos	0.440	0.440	0.440	0.440	0.440	0.440	0.585	0.440	0.440	0.440	0.440	0.440	0.440	0.440	0.440	0.440	0.440	1.000	0.440	37.640	49.499	0.440	0.762	0.440	0.440	0.440	241.059	0.440	0.440	0.440	10	20	40
		hydrochlorothiazide	LC/MS Neg	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	10	0	0
	EDTA	EDTA	LC/MS Neg	0.751	0.634	0.938	1.052	1.048	1.165	0.514	0.994	0.989	1.243	1.095	1.006	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	0.514	100	20	0
		quinate	GC/MS	0.327	0.327	0.327	0.327	0.459	0.327	0.602	0.327	0.327	1.166	0.327	0.327	1.791	0.327	0.327	1.238	0.327	0.327	0.327	0.327	0.938	0.971	0.327	0.327	0.347	0.327	7.514	1.029	1.578	0.327	30	30	60

	Food component/Plant	piperine	LC/MS Pos	0.072	0.099	1.000	1.217	0.407	0.478	0.072	1.045	0.072	0.134	2.235	0.292	1.592	0.072	1.844	1.925	1.332	0.281	2.029	0.568	0.416	3.075	2.009	0.833	0.402	1.487	0.786	0.474	5.107	1.990	80	90	100
		thymol sulfate	LC/MS Neg	2.385	1.000	0.349	0.185	2.900	0.185	0.185	0.185	1.170	0.707	0.185	0.185	0.276	0.310	1.343	0.260	3.627	0.219	2.983	0.185	0.535	4.651	0.185	0.185	0.284	0.185	1.919	1.147	0.890	12.797	60	80	70
		N-(2-furoyl)glycine	LC/MS Neg	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.534	2.891	0.534	0.534	1.048	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.534	0.952	0.534	0.534	0.534	20	10	10
		stachydrine	LC/MS Pos	7.259	1.048	0.075	0.200	0.059	0.613	10.306	1.308	1.186	1.780	0.309	0.072	8.191	2.959	0.486	3.903	2.824	26.986	0.764	2.820	0.952	6.033	0.366	1.315	0.766	0.096	2.761	0.512	0.535	0.501	100	100	100
		homostachydrine*	LC/MS Pos	0.908	1.284	1.938	1.000	0.616	1.401	1.420	0.590	1.049	1.853	1.693	0.614	1.406	0.664	0.738	1.203	1.409	1.157	0.746	0.796	0.823	0.590	0.796	0.816	0.885	0.590	1.199	0.836	0.590	1.540	90	100	80
	Xanthine metabolism	caffeine	LC/MS Pos	5.582	4.183	2.769	2.913	3.899	2.223	4.745	0.545	0.436	7.447	2.921	0.414	7.791	14.670	0.080	1.000	3.647	0.080	1.071	0.352	0.767	0.449	1.131	0.286	0.487	0.517	0.136	0.433	0.861	0.991	100	90	100
		paraxanthine	LC/MS Pos	3.560	1.514	0.365	1.780	2.428	1.103	2.080	0.582	0.231	3.282	1.068	0.346	5.900	0.600	0.206	1.392	2.190	0.206	0.760	0.512	1.000	0.510	0.635	0.206	0.483	0.477	0.206	0.512	1.150	1.085	100	80	90
		theobromine	LC/MS Pos	4.815	1.230	0.454	0.903	8.722	4.187	2.661	0.655	0.265	1.096	2.773	0.569	2.874	0.743	0.265	0.748	1.501	0.265	0.941	0.572	0.897	0.271	0.344	1.381	1.235	1.587	0.265	0.926	1.000	1.175	100	80	90
		theophylline	LC/MS Pos	2.945	2.078	0.390	1.073	1.519	0.947	1.845	0.656	0.390	1.632	1.025	0.589	3.081	1.519	0.390	0.975	2.089	0.390	0.749	0.688	1.026	0.390	1.038	0.728	0.820	0.390	0.390	0.756	0.788	0.942	80	80	80
		1-methylurate	LC/MS Pos	0.512	0.445	0.445	0.445	1.112	0.445	1.018	0.445	0.445	1.205	0.445	0.445	7.697	0.445	0.445	1.422	0.638	0.445	0.445	0.934	0.568	0.445	0.445	0.445	0.445	0.445	1.459	0.445	0.982	0.445	40	40	40
		1,7-dimethylurate	LC/MS Pos	0.553	0.553	0.553	0.553	0.851	0.553	0.975	0.553	0.553	1.317	0.553	0.553	5.140	0.553	0.553	0.553	1.025	0.553	0.553	0.553	0.553	0.553	0.553	0.553	0.553	0.553	0.553	0.553	0.553	0.553	40	20	0
		1-methylxanthine	LC/MS Pos	0.703	0.642	0.642	0.642	1.061	0.642	0.898	0.642	0.642	0.972	0.642	0.642	1.965	0.642	0.642	0.642	0.642	0.642	0.642	0.642	1.330	0.642	0.642	0.642	0.642	0.642	0.642	0.642	1.028	0.642	40	20	20
		3-methylxanthine	LC/MS Pos	1.013	0.435	0.435	0.435	1.284	1.000	2.449	0.435	0.435	0.435	0.435	0.435	3.378	0.435	0.435	0.435	0.435	0.435	0.435	0.435	0.635	0.435	0.435	0.443	0.435	0.435	1.038	0.708	0.857	0.435	40	10	60
		5-acetylamino-6-amino-3-methyluracil	LC/MS Neg	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	1.801	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0	10	10
	Tobacco metabolite	cotinine	LC/MS Pos	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	0.785	1.215	0.785	0.785	0.785	10	0	10
	Sugar, sugar substitute, starch	erythritol	GC/MS	0.941	0.571	0.746	0.678	1.309	1.512	1.595	0.608	0.800	1.100	0.963	0.533	5.308	0.620	0.986	1.660	1.014	1.426	0.911	1.655	1.177	1.686	0.786	0.975	1.107	0.731	4.843	0.843	1.964	1.214	100	100	100