

Supplementary Methods

Metabolite peak integration

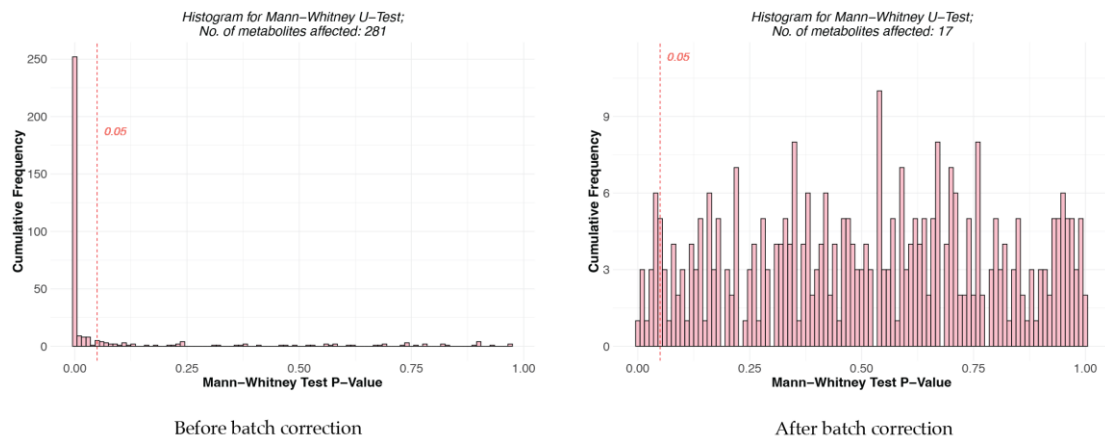
During peak integration, all analytes were normalized to the peak height of their mapping ISTD. To perform this, in MRMKit parameter setting, “ISTD_trace_all” was set to 1, “normalize” was set to 1 [1]. MRMKit would then scale the analyte peak to the corresponding ISTD peak, the intensity output of each analyte was calculated as below:

$$\text{Analyte Intensity} = \frac{\text{Analyte peak height}}{\text{ISTD peak height}} \quad (1)$$

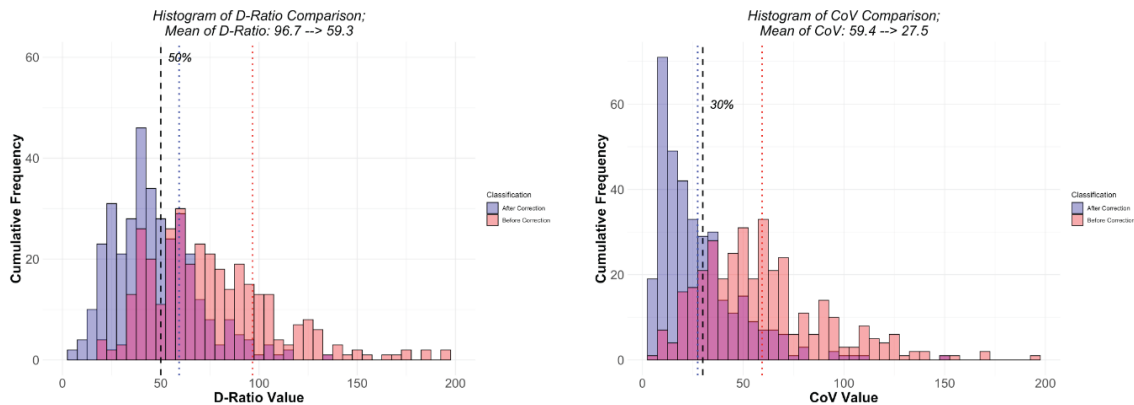
The intensity values would then be included in the initial data for down-stream statistical analysis.

Column-specific batch correction

Our assay was performed by using 2 columns with column-switching mode, therefore column-specific batch effect would exist in addition to common batch effect. We hereby applied column-specific batch correction, during which each column would be treated as a separate batch. There would be different initial batches for different runs, while within each initial batch/run, there would also be 2 different batches because they were measured by 2 columns. Finally, the number of batches input to MRMKit for processing would be double the number of actual runs. Then with “batch_correction” set to 1 in MRMKit, the column-specific batch correction would be performed.



(a). *p*-value distribution of average intensity comparison for metabolites measured in 2 columns (left: before batch correction; right: after batch).



(b). Distribution of metabolites' CoV and D-ratio before and after batch correction (left: D-ratio distribution; right: CoV distribution).

Figure S1 (a). *p*-value distribution of average intensity comparison for metabolites measured in 2 columns (left: before batch correction; right: after batch). **(b).** Distribution of metabolites' CoV and D-ratio before and after batch correction (left: D-ratio distribution; right: CoV distribution).

To check whether this batch correction method improved data quality, we observed the average intensity comparison result of same analytes measured by the 2 columns before and after batch correction. As shown in Figure S1 (a), before batch correction, most of the *p*-values were less than 0.05, indicating that there're significant difference between the 2 columns. While after the correction, the *p*-values were more evenly distributed, showing that this column-specific batch correction did decrease the batch effect caused by using different columns. Analytes' CoV and D-ratio also improved after correction (Figure S1 (b)).

Quality control by CoV and D-ratio

Data quality control was performed by (1) calculating coefficient of variation (CoV), dispersion ratio (D-ratio) [2] (2) filtering out low-quality data based on CoV and D-ratio threshold. For each indicated batch, CoV was calculated as:

$$CoV = \frac{\text{Standard Deviation (SD) across all pooled samples}}{\text{Mean across all pooled samples}} \quad (2)$$

which indicates the internal variance of repeated measurements.

D-ratio was calculated as:

$$D - ratio = \frac{\text{Standard Deviation (SD) across all pooled samples}}{\text{Standard Deviation (SD) across all subjects samples}} = \frac{\text{Non - biological variance}}{\text{Biological variance}} \quad (3)$$

which shows the departure of non-biological variance from biological variance. Hence, analytes with smaller CoV and D-ratio were expected to have better and more reliable data quality. In our assay, analytes with CoV > 30% and D-Ratio > 50% were removed.

Table S1. SRM Table of analytes and Internal standard (ISTD)

Name	Precursor Ion (m/z)	Product Ion (m/z)	Ret. Time (s)	Collision Energy (V)	Cell Acc. Voltage (V)	Polarity	Remark
Analyte							
(S)-Malate/Glutaric acid	133.1	115.1	360	10	5	Pos	
1-Methyladenosine	281.8	150	196.5	27	5	Pos	
1-Methylhistidine	170.1	124.1	321.1	14	5	Pos	
11-Deoxycortisol	347.3	97.1	312	30	5	Pos	
12-Deoxycortisol	347.4	311.3	46	13	5	Pos	Removed after QC
17alpha-Hydroxyprogesterone	331.2	109.1	46	30	5	Pos	
2-Amino-2-methylpropanoate	104.1	45.1	135.6	10	5	Pos	
2-Aminobutyrate/Dimethylglycine	104.1	58.1	134.4	10	5	Pos	
2-Aminoisbutyric acid	104.1	58.1	134.4	10	5	Pos	
2-Aminooctanoic acid	160	55.3	159.8	21	5	Pos	Removed after QC
2-Aminopimelic acid/4-Aminopimelic acid	174.1	130	207	12	5	Neg	Removed after manual review
2-Hydrobenzoic acid/4- Hydrobenzoic acid	137	93.2	72.6	12	5	Neg	
2-hydroxyisobutyric acid	105.1	77	168	10	5	Pos	
2-Oxoglutarate/Phenylpropionic acid	145	101	269.6	13	5	Neg	
2,3-dihydroxybenzoic acid	153	109	120	19	5	Neg	
3-Amino-2-methylpropanoic acid (BAIBA)	103.9	86	210	3	5	Pos	
3-Aminoisobutanoate	104.2	86.1	145.8	10	5	Pos	
3-Carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF) (feature 1)	239	195	52.1	10	5	Neg	
3-Carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF) (feature 2)	239	195	65	10	5	Neg	Removed after QC
3-Chlorotyrosine	216.1	170	175.8	12	5	Pos	
3-Hydroxybutyrate/Hydroxypyruvate	103	59	72	5	5	Neg	
3-Hydroxyisovalerylcarnitine	262.1	84.9	160.8	22	5	Pos	

Table S1. Continued.

3-Indolepropionate	189.9	129.9	48.6	20	5	Pos	Removed after QC
3-Methoxytyramine	303.1	151.1	44.4	25	5	Pos	Removed after QC
3-Methylhistamine	126.2	96.1	342	21	5	Pos	
3-Methylhistidine	170.1	126	348.6	12	5	Pos	
3-Nitrotyrosine (feature 1)	227.1	168.1	150	16	5	Pos	
3-Nitrotyrosine (feature 2)	227.1	181.8	156	16	5	Pos	
3-Nitrotyrosine (feature 3)	227.1	180.8	216	12	5	Neg	
3-Phosphoserine	186	88	87	15	5	Pos	Removed after QC
4-Aminobutyric Acid	104.01	69	198	22	5	Pos	Removed after QC
4-Guanidinobutyric acid	146.1	86	20.6	25	5	Pos	
4-Hydroxy-L-Proline	130.1	87.9	207.2	10	5	Neg	
4-Pyridoxic acid//Epinephrine	182.4	138.1	108	10	5	Neg	
5-Aminopentanoate	118.2	55.1	207.2	16	5	Pos	
5-Hydroxyindoleacetate	192.1	146	169.3	15	5	Pos	
5-Hydroxytryptophan/Serotonin	177.1	160.1	274.8	20	5	Pos	
5-Methylcytosine hydrochloride	126.2	109	354.9	20	5	Pos	
6-Aminouracil	127.9	67.8	201.6	20	5	Pos	
6'-Hydroxynicotinate	140.1	94	213	22	5	Pos	Removed after manual review
7-Methylguanosine	298	166	163.2	24	5	Pos	
7alpha-Hydroxy-4-cholesten-3-one (7-HCO)	401.5	177	45	24	5	Pos	Removed after manual review
7alpha,12alpha-Dihydroxycholest-4-en-3-one (7,12-DHCO)	417.1	381.2	47.3	20	5	Pos	
8-Hydroxydeoxyguanosine	284.3	168.1	4	10	5	Pos	Removed after QC
8-Isoprostane	353.4	193.2	54	30	5	Neg	
Absciscic acid	265.1	247.1	212.9	10	5	Pos	
Acadesine	259	110	153	24	5	Pos	Removed after QC

Table S1. Continued.

Acetaminophen	152	110	228.6	20	5	Pos	
Acetylcarnitine (C2)	260	85.1	76.7	26	5	Pos	Removed after manual review
Acetylcholine	146.1	87	189.7	14	5	Pos	
Acetylglycine/Guanidineacetate	118	76	263.6	10	5	Pos	
Acetylphosphate	139	79	168	24	5	Neg	
Acetylputrescine (feature 1)	131.1	114.1	168	10	5	Pos	detected RT:150
Acetylputrescine (feature 2)	131.1	114.1	168	10	5	Pos	detected RT:197
Aconitate	173	85	228	10	5	Neg	
Adenine	136	92	209.3	30	5	Pos	
Adenosine	268	136	166.2	19	5	Pos	Removed after QC
Adipoylcarnitine (C6DC)	290	85.1	47	35	5	Pos	
ADMA	203.2	46.2	294.9	17	5	Pos	
Agmatine	131	72	210	15	5	Pos	
Alanine	90.1	44	257.5	6	5	Pos	
Allantoic acid	177	61	360	10	5	Pos	
Allantoin (feature1)	157	96.9	164.6	10	3	Neg	
Allantoin (feature2)	157	114	166	8	3	Neg	
Allantoin (feature3)	159.1	116	137.6	5	5	Pos	Removed after QC
Alpha-Aminoadipate	162.2	127	213	20	5	Pos	
Alpha-Tocopherol (Vitamin E)	431.4	165	37	17	5	Pos	
Aminoisobutyrate	104.1	86	149.4	16	5	Pos	
Androstenedione	287.1	97.1	60	22	5	Pos	
Arachidic carnitine (C20:0)	456.7	85	53.4	25	5	Pos	
Arginine	175	70	363.6	25	5	Pos	
Argininosuccinate	289.1	271.1	209.8	10	5	Neg	
Asparagine	133	74	267.6	13	5	Pos	
Behenic carnitine (C22:0)	484.7	85	40	25	5	Pos	
Betaine	118	58	190	25	5	Pos	

Table S1. Continued.

Betaine aldehyde	102	58	218.4	21	5	Pos	Removed after QC
Bilirubin	583.3	285	40.8	36	5	Neg	
Biotin	243	42	171	55	5	Neg	Removed after QC
Butyrylcarnitine	232.1	84.9	105	20	5	Pos	
Caffeine	195.2	138.1	49.8	20	5	Pos	
CDP-ethanolamine	445	273	41.4	29	5	Neg	Removed after QC
Cervonyl carnitine (C22:6)	472.7	85	114	25	5	Pos	
Cholesteryl sulfate	465.2	97	54.4	39	5	Neg	Removed after QC
Cholic acid (CA)	407.2	345.2	42.9	32	5	Neg	
Choline	104	60	150	17	5	Pos	
Cis-5-tetradecenoylcarnitine	370.3	85	66	15	5	Pos	
Citramalate	149.1	93.1	36.7	18	5	Pos	
Citrulline	176.1	70.1	370.8	15	5	Pos	
Corticosterone	347.2	121.2	47.4	22	5	Pos	Removed after QC
Cortisone	361.2	163	48	22	5	Pos	Removed after manual review
Creatine (feature 1)	132.1	44.3	176.4	21	5	Pos	detected RT: 174
Creatine (feature 2)	132.1	44.3	176.4	21	5	Pos	detected RT: 183; Removed after manual review
Creatinine	114	44.3	151	19	5	Pos	Removed after manual review
Cyanocobalamin	678.3	147	97.8	32	5	Pos	Removed after QC
Cys-Gly, oxidized	355.1	176.8	37.2	20	5	Pos	Removed after QC
Cystathionine	221.1	120.1	132	12	5	Pos	
Cysteine	122.1	76.1	295.8	13	5	Pos	
Cysteine-sulfinic acid	154.1	136	251.8	5	5	Pos	
Cystine	241.2	151.9	338.5	9	7	Pos	
Cytosine (feature 1)	112	95	138	20	5	Pos	
Cytosine (feature 2)	112	95	155	20	5	Pos	Removed after QC
D-Erythrose-4-phosphate	199	97	193.3	19	5	Neg	Removed after manual review

Table S1. Continued.

D-Glucosamine/S-carboxymethyl-L-cysteine	180.1	163	158.4	10	5	Pos	Removed after QC
D-Glyceraldehyde 3-phosphate	169.1	97	210.6	14	5	Neg	
D-Glyceric acid	107	79	166.8	10	5	Pos	
D-Pantothenic acid	220.2	90.1	92.4	10	5	Pos	
Decenoylcarnitine	314.5	85	60	24	5	Pos	
Deoxyadenosine	252	136	150.6	22	5	Pos	
Deoxycarnitine	146.2	87	183	16	5	Pos	Removed after manual review
Deoxycholic acid (DCA)	391.2	345.2	48.6	36	5	Neg	Removed after QC
Dihydroorotate	157	113	210	14	5	Neg	
Dihydroxyacetone phosphate	183.2	165.1	39	10	5	Pos	
Dimethylarginine	203.2	70.1	293.4	20	5	Pos	
Dityrosine	361.3	315.1	49.8	25	5	Pos	
Dodecenoylcarnitine (C12:1)	342.5	85	58.8	25	5	Pos	Removed after manual review
Dopamine	154.2	91.2	94.8	22	5	Pos	Removed after QC
dUMP	307	195	52	18	5	Neg	Removed after QC
Epinephrine	184.1	166	69	11	5	Pos	
Ergothioneine	230	127	246	20	5	Pos	
Ethyl-3-ureidopropionate	161.1	120	165.3	10	5	Pos	
Flavone	223	121	52.2	29	5	Pos	
Free carnitine (C0)	162	103	217.8	22	5	Pos	
Fumarate/Maleic acid	115	71	360	13	5	Neg	Removed after QC
Galactitol	183.1	165.1	204	10	5	Pos	Removed after QC
Gluconolactone	177	99	225	10	5	Neg	
Glutaconic acid	129	85	163.6	11	5	Neg	
Glutamic acid	148.1	84.1	282	17	5	Pos	
Glutamine	147.1	84.1	360	17	5	Pos	
Glutaryl carnitine (C5DC)/Glutaryl carnitine (C6-OH)	276	85.1	201.8	40	5	Pos	

Table S1. Continued.

Glutathione-oxidized (GSSG)	613.2	355.2	37	22	5	Pos	Removed after QC
Glutathione-reduced (GSH)	308.1	84	43.2	18	5	Pos	
Glycerophosphocholine	258.1	104	270	16	5	Pos	
Glycine	76.4	58.1	192	10	5	Pos	
Glycochenodeoxycholic acid (GCDCA)/Glycodeoxycholic acid (GDCA)/Glycoursodeoxycholic acid (GUDCA)	448.3	74	85.6	10	5	Neg	Removed after manual review
Glycocholic acid (GCA)	464.4	74.2	111	30	5	Neg	
Glycolaldehyde dimer	121.1	77.1	166.8	21	5	Pos	
Glycolate/Propylene glycol (feature 1)	77.1	59	208.1	10	5	Pos	
Glycolate/Propylene glycol (feature 2)	77.2	59.1	207.4	10	5	Pos	
Glyoxylate	73	45	198	8	5	Pos	
Guanosine	284.1	151.9	197.9	23	5	Pos	
Heptanoyl-L-carnitine (C7:0)	274.3	85	76	20	5	Pos	
Hercynine	198	154.1	292.8	9	4	Pos	
Hexadecenoyl carnitine (C16:1)	398.3	85	66	15	5	Pos	
Hexenoylcarnitine (C6:1)/Hexenoylcarnitine (C6)	258	85.1	96	35	5	Pos	
Hippurate	178	77	120	20	5	Neg	
Histamine	112.1	95	360	15	5	Pos	
Histidine	156.1	110.1	367.2	14	5	Pos	
Homoarginine (hArg) (feature 1)	189.2	144	321.6	15	5	Pos	
Homoarginine (hArg) (feature 2)	189.2	144	351	15	5	Pos	
Homocysteine (feature 1)	136.1	91	108	19	5	Pos	Removed after QC
Homocysteine (feature 2)	136.1	91	162	19	5	Pos	
Homocysteine (feature 3)	136.1	90.2	204	19	5	Pos	
Hydroxybutyryl-carnitine (C4-OH)	248	85.1	177.3	30	5	Pos	Removed after manual review
Hydroxydodecenoylcarnitine	358.5	85	60.3	25	5	Pos	
Hydroxyhexadeceneoylcarnitine	414.3	85	29.1	25	5	Pos	

Table S1. Continued.

Hydroxyproline	132	68.2	252	19	5	Pos	Removed after QC
Hypotaurine	110.1	82.1	360	12	5	Pos	
Hypoxanthine	134.9	91.9	125.4	18	5	Neg	
Imidazole	69	41.4	184.8	10	5	Pos	
Indole	118	91	177.3	26	5	Pos	
Isovaleryl-carnitine (3-M-C4:0)	246.1	85	92.9	15	5	Pos	
Kynurenate	190.1	144.1	345	15	5	Pos	
Kynurenine	209.2	192	167.8	10	5	Pos	
L-Aspartic Acid	134	74	212.1	12	5	Pos	
L-DOPA	198.1	152.1	48	8	5	Pos	Removed after QC
L-homocysteine thiolactone	118.2	100	128.9	14	5	Pos	Removed after QC
L-Ornithine	133.1	70.1	374.2	16	5	Pos	
Lactate	89	43.2	100.9	16	5	Neg	
Lauroylcarnitine	344.2	285	72.7	16	5	Pos	Removed after manual review
Leucine/Isoleucine (feature 1)	132.1	86	183	13	5	Pos	detected RT: 174
Leucine/Isoleucine (feature 2)	132.1	86	183	13	5	Pos	detected RT: 183
Linoleate (feature 1)	279.2	279.2	41.4	2	5	Neg	
Linoleate (feature 2)	279.2	279.2	69	2	5	Neg	
Lithocholic acid (LCA)	498.3	80	127.4	70	5	Neg	
LPC 20:0	552.4	184	103.6	25	5	Pos	Removed after QC
LPC 20:1	550.4	184	104.8	25	5	Pos	
LPC 20:3	546.4	184	106.1	25	5	Pos	Removed after manual review
LPC 20:4	544.3	184	106.1	25	5	Pos	Removed after QC
LPC 20:5	542.3	184	109.8	25	5	Pos	
LPC 22:2	576.4	184	102	25	5	Pos	Removed after QC
LPC 22:6	568.3	184	104.8	25	5	Pos	Removed after manual review
LPC 24:0	608.5	184	98.5	25	5	Pos	Removed after QC
LPC 26:0	636.5	184	90	25	5	Pos	Removed after QC

Table S1. Continued.

LPC 28:1	662.5	184	72	25	5	Pos	Removed after QC
Lysine	147	84	361.8	14	5	Pos	
Maleic acid	115	71	120	13	5	Neg	
Malonylcarnitine (C3-DC)	248.1	84.8	177.6	18	5	Pos	
Mannitol/Sorbitol	181.1	59	225	8	5	Neg	
Melatonin	233.2	174.1	105.2	12	5	Pos	
Mesoxalate	119.1	91.1	43.8	16	5	Pos	
Metanephrene	179.9	148.2	45.6	20	3	Pos	
Metanephrene/Selenomethionine	198.2	180.9	280	12	5	Pos	
Methionine	150.1	133	195.9	12	5	Pos	
Methionine sulfoxide (feature 1)	166.1	74	167	10	5	Pos	Removed after QC
Methionine sulfoxide (feature 2)	166.1	103	166.2	15	5	Pos	
Methylcrotonylcarnitine (C5:1)	244.1	85	105	18	5	Pos	
Methylcrotonylcarnitine (C5:1)	244	85.1	101.2	30	5	Pos	
Methylcysteine (feature 1)	136	119	207	12	5	Pos	
Methylcysteine (feature 2)	136	119	223	12	5	Pos	
Methylguanidine	74.2	42.2	181.9	10	5	Pos	
Methylhistidine (feature 1)	170.1	96	347.2	22	5	Pos	
Methylhistidine (feature 2)	170.1	96	320	22	5	Pos	
Methylmalonic acid	117	73.1	116.9	13	5	Neg	
Methylnicotinamide	137	94	165	20	5	Pos	
Monosaccharide	198	163	237	6	5	Pos	
Myo-inositol	179	59.8	226.6	10	5	Neg	
N-Acetyl-D-glucosamine	222	138	202.6	18	5	Pos	Removed after QC
N-Acetyl-DL-methionine	190.2	147.9	178.2	12	5	Pos	
N-Acetyl-L-alanine	130	88.2	117.6	12	5	Pos	
N-Acetyl-L-asparagine	173.1	154.9	209.9	8	5	Neg	
N-Acetyl-L-aspartic acid	174	88	207.1	12	5	Neg	

Table S1. Continued.

N-Acetyl-L-Cysteine	163.1	43.2	213.2	17	5	Pos	
N-Acetylasparagine	175.2	133	367.2	11	5	Pos	
N-Acetylaspartate/N-Amidino-L-aspartate	176.1	134	251.3	10	5	Pos	
N-Acetylglucosamine phosphate	300	79	169.8	34	5	Neg	Removed after QC
N-Acetylglutamic acid	190.2	130.1	327	12	5	Pos	
N-Acetylglutamine (feature 1)	189.1	130	339.6	17	5	Pos	detected RT: 326
N-Acetylglutamine (feature 2)	189.1	130	339.6	17	5	Pos	detected RT: 351
N-Acetylglycine	118.2	72.1	204.6	16	5	Pos	
N-acetylmethionine	175.1	115.1	363	10	5	Pos	
N-Acetylserine	146	116	204	4	5	Neg	Removed after QC
N-Alpha-Acetyl-L-lysine	187.1	144.9	234	8	5	Neg	Removed after QC
N-carbamoyl-L-aspartate	175	132	277.8	13	5	Neg	
N-monomethylarginine (NMMA)	189.2	74	326.2	15	5	Pos	
N6-acetyl-L-lysine	189.1	126.1	343.8	10	5	Pos	
N6, N6, N6-Trimethyllysine (feature 1)	189.2	130.1	321	14	5	Pos	
N6, N6, N6-Trimethyllysine (feature 2)	189.2	130.1	343.8	14	5	Pos	
NAADP	745.1	604	70.7	20	5	Pos	Removed after QC
NADH	666.1	514	111	28	5	Pos	Removed after QC
NG,NG-Dimethylarginine	203	70	293.6	24	5	Pos	
Nicotinamide	123	79.9	210.8	18	5	Pos	
Nicotinamide riboside	255.1	56.9	94.1	24	5	Pos	
Nicotinamide ribotide	335	123	48	30	5	Pos	Removed after QC
Nicotinic acid	124	80.1	321.4	18	5	Pos	
Nitroarginine	220.1	59.1	180	35	5	Pos	
NMN (-H ₂ O)	301.1	134.1	39.4	35	5	Pos	Removed after QC
Noradrenaline	170.2	93	321	26	5	Pos	
Norleucine	132.2	69.1	183.1	16	5	Pos	Removed after manual review
Norvaline	118.2	72.1	208	16	5	Pos	

Table S1. Continued.

O-Acetyl-L-serine	148.1	106	186	10	5	Pos	Removed after QC
O-succinyl-L-homoserine	220.1	102.1	210	11	5	Pos	Removed after QC
Octadecenoyl carnitine (C18:1)	426.3	85	67	15	5	Pos	
Octadecadienoylcarnitine	424.3	85	58.9	32	5	Pos	
Octenoylcarnitine (C8:1)	286.1	85	73.6	24	5	Pos	
Orotate	155	111	186	10	5	Neg	Removed after QC
Orotidine-5-phosphate	367	323	46.9	18	5	Neg	
Orotidylic acid	367	97	65.1	10	5	Neg	Removed after QC
Oxalate	89	45	102	8	5	Neg	
Oxaloacetate	131	87	104.4	8	5	Neg	
Oxoguanine/3-Methoxytyramine	168	151	120	20	5	Pos	
Oxypurinol	153	136	67.2	20	5	Pos	
Palmitoylcarnitine	400.3	85	56.3	15	5	Pos	
Pantothenic acid (Vitamin B5)	218	146	90	21	5	Neg	Removed after QC
Paraxanthine	181.2	124.1	58	21	5	Pos	Removed after QC
Phenylacetylglycine	194.1	76	197.1	10	5	Pos	
Phenylalanine	166	120	168	10	5	Pos	
Phenylpyruvate	163	91	105.6	13	5	Neg	Removed after QC
Phospho(enol) pyruvic acid	167	79	120	10	5	Pos	Removed after QC
Phosphocreatine	212	43.9	201	24	5	Pos	
Phosphoglycerates	185	97	156	10	5	Neg	Removed after QC
Phosphorylcholine	183	125	87	23	5	Pos	
Pipecolic acid (feature 1)	138	84	174.6	18	5	Pos	
Pipecolic acid (feature 2)	138	84	202.8	18	5	Pos	
Progesterone	313.2	276.8	211.1	25	5	Neg	
Proline	116.1	70.1	214.1	13	5	Pos	
Propionylcarnitine (C3)	218.1	85	132.3	15	5	Pos	Removed after manual review
Purine	121.1	94	166.8	21	5	Pos	

Table S1. Continued.

Putrescine	89	72	296.1	12	5	Pos	Removed after manual review
Pyrazole	68	41.2	212.4	19	5	Pos	
Pyridoxamine (Vitamin B6)	169	152	200	11	5	Pos	
Pyridoxine (Vitamin B6)	170	134	39	18	5	Pos	
Pyrrolidinone	86.1	69.1	183.4	10	5	Pos	
Ribose	149	59.1	222	8	5	Neg	Removed after manual review
S-methyl ergothioneine	244.1	141	210	20	5	Pos	
S-methyl-5-thioadenosine	298	136	156.6	29	5	Pos	Removed after QC
S-Nitrosoglutathione	337.1	307.1	57.6	5	5	Pos	
Sarcosine	90	44.1	251.8	20	5	Pos	
Sedoheptulose 1,7-bisphosphate	369	166	73.4	20	5	Neg	Removed after QC
Serine	106	60	149.7	15	5	Pos	
Shikimate	173	93.1	69.2	18	5	Neg	
Spermidine	146.2	72	201.6	22	5	Pos	
Spermine	202.1	129.1	114	19	5	Pos	
Stearoyl-L-carnitine	428.4	85	53.4	15	5	Pos	
Succinate	116.9	73	104.4	10	5	Neg	
Succinylcarnitine (C4-DC)/3-hydroxyisovaleryl carnitine (C5-OH)	262	85.1	160.9	22	5	Pos	
Symmetrical dimethylarginine (SDMA)	203.2	171.9	293.4	9	5	Pos	
Taurine	124	80	245.8	18	5	Neg	Removed after QC
Taurochenodeoxycholic Acid (TCDCA)/Taurodeoxycholic Acid (TDCA)/Tauroursodeoxycholic acid (TUDCA) (feature 1)	498.3	498.3	124.2	20	5	Neg	detected RT: 40
Taurochenodeoxycholic Acid (TCDCA)/Taurodeoxycholic Acid (TDCA)/Tauroursodeoxycholic acid (TUDCA) (feature 2)	498.3	498.3	124.2	20	5	Neg	detected RT: 118; Removed after manual review

Table S1. Continued.

Taurochenodeoxycholic Acid (TCDCA)/Taurodeoxycholic Acid (TDCA)/Tauroursodeoxycholic acid (TUDCA) (feature 3)	498.3	498.3	126	20	5	Neg	
Taurocholate (TCA)	514.3	514.3	42.8	20	5	Neg	
Taurolithocholic acid (TLCA)	498.3	80	122.9	70	5	Neg	
Testosterone	289.1	109	42.6	22	5	Pos	Removed after QC
Tetrahydrofolate	446.1	430.1	37.8	11	5	Pos	Removed after QC
Theobromine	181.2	138	56.4	17	5	Pos	
Theophylline	181.1	124.1	57.6	19	5	Pos	Removed after QC
Thiamine (Vitamin B1)	265	122	170.5	19	5	Pos	
Thiourea	77	60	196.4	10	5	Pos	
Thymine	127.1	110	350.3	19	5	Pos	
Trans-4-hydroxyproline (feature 1)	132	85.9	175.1	14	5	Pos	
Trans-4-hydroxyproline (feature 2)	132	85.9	183.5	14	5	Pos	Removed after QC
Trigonelline	138.1	92.1	195	19	5	Pos	
Trimethylamine (TMA)	144.1	55.1	180	30	6	Pos	
Trimethylamine oxide (TMAO)	76	58	197.4	25	5	Pos	
Triuret (feature 1)	146.9	86.9	162	6	5	Pos	
Triuret (feature 2)	146.9	86.9	198	6	5	Pos	Removed after QC
Tryptophan	205.1	188.1	177.5	10	5	Pos	
Tyrosine	182	136	223.2	8	5	Pos	
Uracil	113	70	125	20	5	Pos	
Urea	61.1	44.2	105.2	25	5	Pos	
Urea/Ethanolamine	62.1	44.2	180	12	5	Pos	
Uric acid	167	123.9	204.5	13	3	Neg	
Uridine	245.1	113	127.2	8	5	Pos	
Valine	118	72	207.2	8	5	Pos	

Table S1. Continued.

Vitamin D2 (feature 1)	397.3	397.3	42.5	5	5	Pos	detected RT: 39
Vitamin D2 (feature 2)	397.3	397.3	42.5	5	5	Pos	detected RT: 45; Removed after QC
Vitamin D3	383.3	339.1	48	13	5	Neg	Removed after manual review
Vitamin K1	451.4	187	110.8	25	5	Pos	Removed after QC
Xanthine	151	108	123	16	5	Neg	
Xanthosine	285	153	165	10	5	Pos	
Xanthurenic acid	204	160	216	19	5	Neg	Removed after QC
ISTD							
7-HCO ISTD	408.1	97.2	42	32	5	Pos	
7,12-DHCO ISTD	425.2	398.3	42	15	5	Pos	
8- F2 isop ISTD	357.4	197.1	48	30	5	Neg	
ADMA ISTD	210.4	77.1	299.5	21	5	Pos	
Allantoin ISTD	162.9	117.8	166	20	5	Neg	
Arginine ISTD	185.1	122.1	366	25	5	Pos	
Aspartic acid ISTD	139.1	92.1	179.8	12	5	Pos	
BAIBA ISTD	107.2	89	234	5	5	Pos	
butyryl carnithine ISTD	235.1	84.9	108	20	5	Pos	
CDCADCA-UDCA-D4	395.3	395.3	48	30	5	Neg	
Creatinine ISTD	117.1	47.1	149.7	19	5	Pos	
Ergo ISTD	239.3	127	234	20	5	Pos	
GCA-D4 ISTD	468.3	74	96	70	5	Neg	
GCDCA-D4 ISTD	452.3	74	58.8	72	5	Neg	
glutamic acid ISTD	154.1	89.1	277.8	10	7	Pos	
glutamine ISTD	152.1	88.1	258	15	5	Pos	
Hercynine ISTD	207.2	163.2	288	9	4	Pos	
Histidine ISTD	165.2	118.2	354	15	5	Pos	
Homocysteine ISTD	140.2	94.2	362.4	15	5	Pos	

Table S1. Continued.

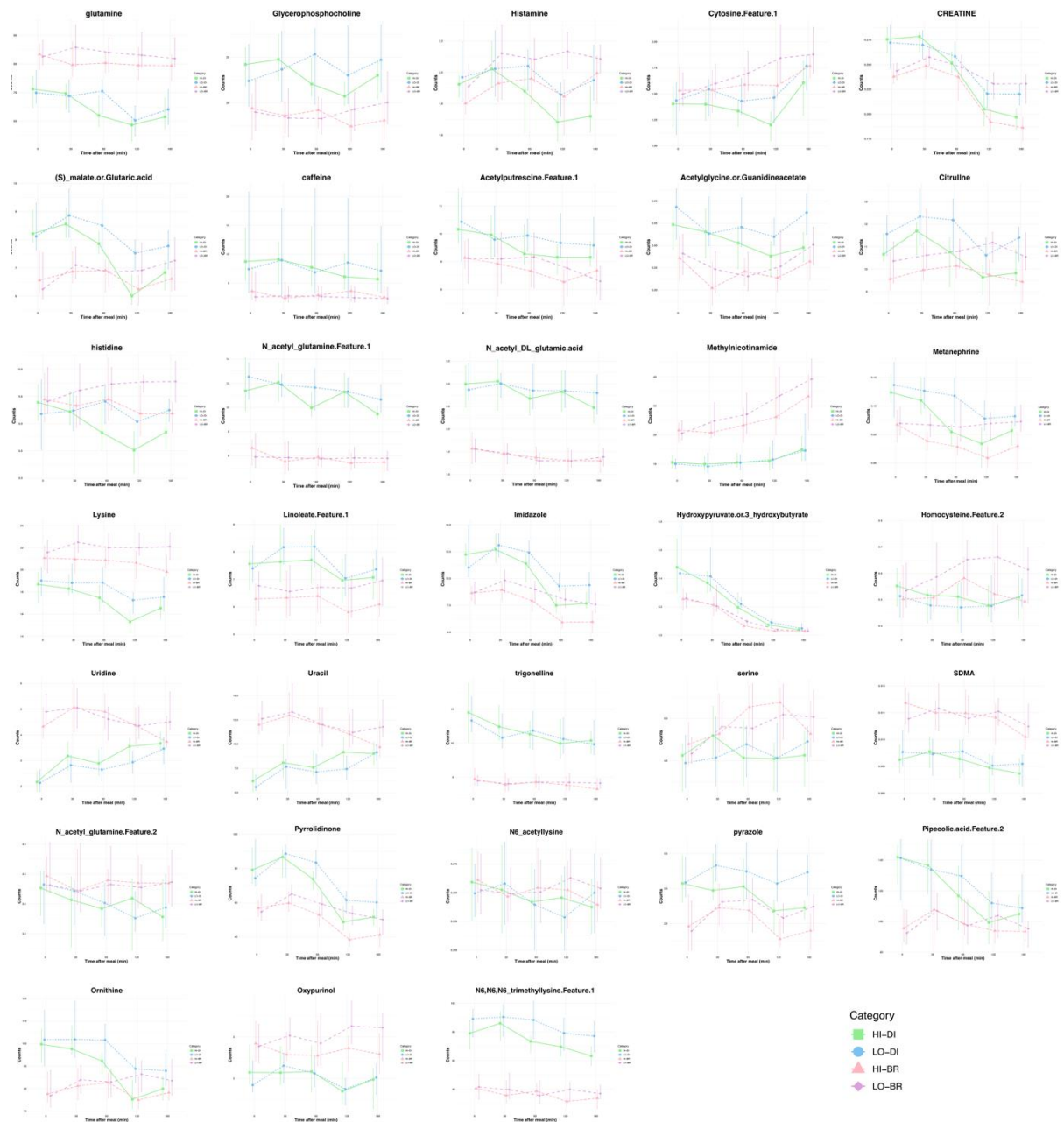
Isoleucine ISTD	139	74.1	180	20	5	Pos
Isovalerylcarnitine ISTD	255.2	85.1	91.8	20	5	Pos
LCA D4	379.3	379.3	45.6	30	5	Neg
leucine ISTD	138.1	91.2	195.6	10	5	Pos
Lysine ISTD	155.2	90.1	36.72	18	7	Pos
Methionine ISTD	156.2	109	194.4	15	5	Pos
Phenylalanine ISTD	176.1	129.1	168.6	10	5	Pos
Proline ISTD	122.1	75.1	208.8	14	5	Pos
Propionylcarnitine ISTD	221.2	85.1	120	20	5	Pos
Serine ISTD	110.2	63.1	279.6	8	3	Pos
Spermidine ISTD	150.2	76.1	201.6	15	5	Pos
TDCA ISTD	502.2	124.2	103.2	57	7	Neg
Threonine ISTD	125.1	78.1	259	10	7	Pos
Tyrosine ISTD	192.1	98.1	224.4	30	7	Pos
UA ISTD	169	125.1	214.8	13	3	Neg
Valine ISTD	123.1	76.1	208.8	15	5	Pos
Xanthine ISTD	153.1	109.1	126	18	5	Neg

Table S2: Detailed composition of the test meals (TM) and standardized meals (SM).

	Quantity (g)	Energy (kcal)	Protein (g)	Fat (g)	CHO (g)	Fiber (g)	Available CHO (g)
TM High GI (92)							
Glutinous rice	100.7	356.6	7.7	2.3	76.1	1.0	75.1
Chicken seasoning	2.0	4.5	0.3	0.1	0.7	0	0.7
Green leafy vegetables	20.0	6.9	0.6	0.4	0.3	0.1	0.2
TOTAL	122.7	368.0	8.5	2.7	77.1	1.1	76.0
TM Low GI (55)							
Parboiled Basmati rice	99.8	349.1	9.4	0.7	76.4	1.4	75.0
Chicken seasoning	2.0	4.5	0.3	0.1	0.7	0	0.7
Green leafy vegetables	20.0	6.9	0.6	0.4	0.3	0.1	0.2
TOTAL	121.8	360.5	10.2	1.1	77.4	1.5	75.9
SM							
Shrimp wanton soup	145.0	132.0	8.1	3.0	18.0	2.8	15.2
Soya milk	300.0	162.0	6.3	3.3	26.4	1.8	24.6
Soybeans- based snack	27.0	111.0	4.3	5.5	11.0	2.5	8.5
Almond nuts	40.0	233.0	9.2	19.5	5.3	4.3	1.1
Banana	125.0	110.0	1.0	0.0	30.0	3.0	27.0
TOTAL	637.0	748.0	28.9	31.3	90.7	14.4	76.4

The meals immediately prior to the test meals were standardized, i.e. the dinner prior to the breakfast test sessions and the lunch prior to the dinner test sessions. CHO: carbohydrate; GI: glycemic index; TM: test meal; SM: standard meal.

Figure S2. Level-time line plots of the metabolites with significant p -values (HI-DI: high-GI dinner; LO-DI: low-GI dinner; HI-BR: high-GI breakfast; LO-BR: low-GI breakfast).



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2. Broadhurst, D.; Goodacre, R.; Reinke, S.N.; Kuligowski, J.; Wilson, I.D.; Lewis, M.R.; Dunn, W.B. Guidelines and considerations for the use of system suitability and quality control samples in mass spectrometry assays applied in untargeted clinical metabolomic studies. *Metabolomics* **2018**, *14*, 72, doi:10.1007/s11306-018-1367-3.