

Supplementary description 1 Confidence Scoring Mechanism

We implemented the following scoring mechanism: if a full match with all above sources was achieved, a score of 5 for MzCloud, 4 for Chempider, 3 for Metabolika, and 3 for Masslist, was assigned to the feature; if partial match, a score of 2 was assigned; if no match, then a score of 0 was assigned; a score of 2 was assigned if the mass difference was less than 5 ppm and a score of 0 was assigned if the mass difference was greater than 5 ppm. Consequently, each feature had 5 scores and the sum of them was interpreted as the overall annotation confidence in this case. We categorized scores into the following categories: ≤ 3 was considered low confidence, $\geq 4 - 9$ are acceptable, and ≥ 10 was considered high confidence.

Supplementary Table 1 List Of All Features Identified in Linear Regression with FDR $q < 0.05$

Metabolite	Est	FDR	Conf.	Mol Wt	Ret. Time	Formula	Mode
Acesulfame potassium	1.009	0.013	0	162.99391	1.435	C4 H4 N O4 S	H
Taurine	0.796	0.004	16	125.01464	1.104	C2 H7 N O3 S	RP
Pulcherrimic acid	0.784	0.004	4	256.1423	12.053	C12 H20 N2 O4	RP
2949	0.745	0.001	4	258.15795	12.918	C12 H22 N2 O4	RP
8-Hydroxy-4-methoxy-7-methyl-7,8-dihydro-5H-furo[2,3-g]isochromen-5-one	0.697	0.001	4	248.06846	11.188	C13 H12 O5	RP
N-Phenylacetylglutamic acid.1	0.664	<0.001	4	265.09502	10.997	C13 H15 N O5	RP
4-Hydroxyphenylacetyl glycine.1	0.664	0.012	5	209.0688	10.764	C10 H11 N O4	RP
Europine	0.64	0.001	4	329.18397	9.883	C16 H27 N O6	RP
methyl 2-(benzoylamino)acetate	0.636	0.009	9	193.07389	11.22	C10 H11 N O3	RP
Epinephrine 4-sulfate	0.625	0.006	4	263.04644	9.869	C9 H13 N O6 S	RP
1-Pyrroline-4-hydroxy-2-carboxylate	0.622	0.002	6	129.04256	6.746	C5 H7 N O3	RP
O-sebacoylcarnitine.1	0.616	<0.001	4	345.2152	11.935	C17 H31 N O6	RP
tyr-thr	0.613	<0.001	4	282.12157	11.671	C13 H18 N2 O5	RP
Volkenin	0.606	0.001	4	287.10052	9.219	C12 H17 N O7	RP
4'-ethyl-N-(1-ethynylcyclohexyl)[1,1'-biphenyl]-4-carboxamide	0.605	0.004	0	331.19956	10.788	C23 H25 N O	RP
5,6,7-Trimethoxy-2H-chromen-2-one.1	0.593	<0.001	0	236.06605	11.916	C12 H12 O5	RP
Hypoxanthine	0.592	0.028	9	136.03855	3.893	C5 H4 N4 O	H
Taurine	0.587	0.016	16	125.01469	9.673	C2 H7 N O3 S	H
4-Methylhippuric acid	0.586	<0.001	7	193.07389	11.888	C10 H11 N O3	RP
4-Hydroxyprolylleucine	0.584	0.011	4	244.1423	11.375	C11 H20 N2 O4	RP
1-(2-Furylmethyl)-5-oxopyrrolidine-3-carboxylic acid	0.582	0.015	8	209.06878	3.095	C10 H11 N O4	H
Hexanoylglycine.1	0.578	0.043	5	173.1052	10.339	C8 H15 N O3	RP
(4E)-2-Oxohexenoic acid	0.571	0.001	6	128.04729	9.107	C6 H8 O3	RP
Ethopabate.1	0.566	0.001	4	237.1001	11.232	C12 H15 N O4	RP
Alliin	0.557	0.002	7	177.04598	1.311	C6 H11 N O3 S	RP
O-sebacoylcarnitine	0.555	0.002	4	345.21517	11.966	C17 H31 N O6	RP
2-Acetamido-N-fl-aspartyl-2-deoxyhexopyranosylamine	0.553	0.002	9	335.13302	1.105	C12 H21 N3 O8	RP
(5-methyl-3-isoxazolyl)[4-(5-propyl-2-pyrimidinyl)piperazino]methanone	0.538	<0.001	6	315.16822	9.047	C16 H21 N5 O2	RP
5-Aminonicotinic acid	0.535	0.013	8	138.04293	2.093	C6 H6 N2 O2	H
NP-011223.1	0.534	<0.001	0	208.10993	16.839	C10 H18 O3	RP
3,5-dibenzylpyridine-2,6-diamine	0.533	0.003	0	289.15256	7.049	C19 H19 N3	RP
NP-016455	0.528	0.035	5	242.12667	10.55	C11 H18 N2 O4	RP
Nitrilotriacetic acid.1	0.521	0.001	5	191.04301	1.125	C6 H9 N O6	RP
syringol	0.519	<0.001	4	154.063	9.002	C8 H10 O3	RP
1,7-Dimethyluric acid	0.517	0.035	11	196.05966	8.881	C7 H8 N4 O3	RP
4-Aminohippuric acid	0.514	0.01	5	194.06917	7.857	C9 H10 N2 O3	RP
4-Aminohippuric acid	0.513	0.011	9	194.06913	3.217	C9 H10 N2 O3	H
2-imino-3a-methylperhydro-5lambda~6~-thieno[3,4-d][1,3]thiazole-5,5-dione	0.512	0.001	5	206.01933	9.746	C6 H10 N2 O2	RP
O-(11-carboxyundecanoyl)carnitine	0.498	0.019	4	373.24647	12.937	C19 H35 N O6	RP
ophthalmic acid	0.497	0.008	4	289.12742	6.402	C11 H19 N3 O6	RP
(4S)-4-[(6-Carboxyhexanoyl)oxy]-4-(trimethylammonio)butanoate	0.484	0.01	4	303.16822	8.3	C14 H25 N O6	RP
(5alpha,6beta)-3-Hydroxy-17-methyl-4,5-epoxymorphinan-6-yl beta-L-glucopyranosiduronic acid	0.477	0.035	4	463.18424	14.471	C23 H29 N O9	RP
4-Phenylbutyric acid	0.473	0.007	10	164.08372	10.493	C10 H12 O2	RP
Hydantoin-5-propionate	0.472	0.014	5	172.04844	1.133	C6 H8 N2 O4	RP
N-Acetyl-L-phenylalanine	0.466	0.007	5	207.08953	11.731	C11 H13 N O3	RP
Nitrosoguvacoline	0.465	0.003	4	170.06924	1.39	C7 H10 N2 O3	RP
Phenylisocyanate	0.455	0.019	4	119.03707	7.857	C7 H5 N O	RP
4,7-Dioxooctanoic acid	0.452	0.006	4	172.07353	1.889	C8 H12 O4	H
[Similar to: Hippuric acid; <U+0394>Mass: 179.0585 Da]	0.45	0.015	2	358.11679	3.306	C18 H18 N2 O6	H
(1S_4S)-4-Hydroxy-3-oxocyclohexane-1-carboxylate	0.449	0.011	6	158.05786	2.361	C7 H10 O4	H
3_4-Dihydroxyphenylethyleneglycol	0.446	0.008	5	170.05791	9.126	C8 H10 O4	RP
Phthalaldehyde	0.441	0.045	6	134.03675	10.764	C8 H6 O2	RP
1_3_6_8-Naphthalenetetrol	0.439	<0.001	6	192.04226	12.637	C10 H8 O4	RP
Buspirone	0.437	0.022	7	385.24653	13.986	C21 H31 N5 O2	RP

Hippuric acid	0.435	0.028	9	179.05824	3.308	C9 H9 N O3	H
Indole-3-acetic acid.1	0.435	0.005	10	175.06334	10.801	C10 H9 N O2	RP
cis-2-Carboxycyclohexyl-acetic acid	0.433	0.011	4	186.08918	1.716	C9 H14 O4	H
3-amino-2-phenyl-2H-pyrazolo[4,3-c]pyridine-4,6-diol	0.433	0.022	0	242.07663	8.918	C12 H10 N4 O2	RP
N-[(2S)-2-Hydroxypropanoyl]methionine.2	0.43	0.029	4	221.07219	7.639	C8 H15 N O4 S	RP
Tetraacetylenethylenediamine	0.427	0.002	4	228.11111	1.398	C10 H16 N2 O4	RP
Methylimidazoleacetic acid	0.426	0.033	9	140.05857	1.322	C6 H8 N2 O2	RP
N(alpha)-Benzyloxycarbonyl-L-leucine	0.422	0.001	5	265.13141	9.17	C14 H19 N O4	RP
N-(6-methoxypyridin-3-yl)thiophene-2-carboxamide	0.421	0.002	0	234.05041	12.547	S	RP
4-(2,3-dihydro-1,4-benzodioxin-6-yl)butanoic acid	0.421	0.027	0	222.08676	10.496	C12 H14 O4	RP
N-[(2S)-2-Hydroxypropanoyl]methionine	0.421	0.012	4	221.07221	5.854	C8 H15 N O4 S	RP
4-oxododecanedioic acid.1	0.421	<0.001	0	266.11543	14.777	C12 H20 O5	RP
2_6-Dihydroxypseudoxynicotine	0.419	0.004	5	210.10044	7.371	C10 H14 N2 O3	RP
alpha-D-Xylose1-phosphate	0.418	0.006	6	230.01917	13.283	C5 H11 O8 P	H
XLR11 N-(2-fluoropentyl) isomer.3	0.417	0.033	0	329.22029	11.569	C21 H28 F N O	RP
O-sebacoylcarnitine.2	0.417	0.006	4	345.2152	9.449	C17 H31 N O6	RP
5-hydroxy-4-methoxy-5,6-dihydro-2H-pyran-2-one	0.414	0.024	9	144.04228	5.851	C6 H8 O4	RP
Pro-Hyp	0.41	0.004	4	228.111	8.418	C10 H16 N2 O4	RP
N6,N6,N6-Trimethyl-L-lysine	0.41	0.001	10	188.15251	1.076	C9 H20 N2 O2	RP
N-(4-Methoxybenzyl)glutamine	0.409	0.008	4	266.12666	6.755	C13 H18 N2 O4	RP
1-((3S,5S)-1-Methyl-5-[3-(4-pyridinyl)-1,2,4-oxadiazol-5-yl]-3-pyrrolidinyl)-3-phenylurea	0.409	<0.001	0	364.16694	5.301	C19 H20 N6 O2	RP
(5-Benzyl-3,6-dioxo-2-piperazinyl)acetic acid	0.408	0.047	4	262.09534	10.498	C13 H14 N2 O4	RP
thymol sulfate	0.404	0.007	4	230.06127	8.032	C10 H14 O4 S	RP
Ubiquinone-1(CoQ1).1	0.403	0.007	5	250.12049	16.839	C14 H18 O4	RP
Proacaciberin.1	0.402	0.007	4	391.14793	12.076	C16 H25 N O10	RP
N-Acetyl-D-glucosamine	0.4	0.015	5	237.08489	1.13	C8 H15 N O7	RP
Ecgonine	0.399	0.043	5	185.10515	2.956	C9 H15 N O3	H
3-Methylhistidine	0.398	0.01	7	169.08513	4.167	C7 H11 N3 O2	RP
Arenediol	0.397	0.012	5	112.05238	9.002	C6 H8 O2	RP
2-(6'-methylthio)hexylmalate.1	0.394	0.008	5	264.10332	11.456	C11 H20 O5 S	RP
NP-020902	0.393	0.006	0	224.06606	10.356	C9 H14 O5	RP
ON1225000	0.392	0.009	4	172.07357	10.938	C8 H12 O4	RP
4,7-Dioxooctanoic acid.1	0.387	0.006	4	172.07353	1.828	C8 H12 O4	H
Gentian violet	0.386	0.042	0	371.23086	12.012	C25 H29 N3	RP
3-Hydroxy-N-[(3S)-2-oxotetrahydro-3-furanyl]decanamide 3	0.384	0.005	4	271.17836	11.432	C14 H25 N O4	RP
NP-016344	0.381	0.002	0	244.03818	8.905	C11 H10 O5	RP
Succinyladenosine	0.38	0.005	4	383.10775	8.402	C14 H17 N5 O8	RP
3-Methylcrotonylglycine.1	0.38	<0.001	6	157.0739	4.887	C7 H11 N O3	RP
pentahomomethionine	0.38	0.042	6	219.1293	12.787	C10 H21 N O2 S	RP
1-(3_4-dimethoxyphenyl)ethane-1_2-diol.1	0.379	0.01	6	198.08922	12.425	C10 H14 O4	RP
NP-019445	0.378	0.015	9	194.05793	12.473	C10 H10 O4	RP
4-Hydroxyphenylacetic acid	0.376	0.002	9	152.04735	12.554	C8 H8 O3	RP
XLR11 N-(2-fluoropentyl) isomer.4	0.376	0.01	0	329.22028	13.856	C21 H28 F N O	RP
1,4:3,6-Dianhydro-2-[[4-(1,3-benzodioxol-5-yl)-2-pyrimidinyl]amino]-5-O-(benzylcarbamoyl)-2-deoxy-D-glucitol	0.374	0.019	0	476.166	14.632	C25 H24 N4 O6	RP
Hydantoin-5-propionate	0.374	0.019	5	172.04839	4.017	C6 H8 N2 O4	H
N2-(D-1-Carboxyethyl)-L-lysine	0.371	0.036	5	218.12668	1.097	C9 H18 N2 O4	RP
O-Propanoylcarnitine	0.371	0.021	5	217.13141	13.167	C10 H19 N O4	RP
5-Hydroxy-DL-tryptophan	0.371	0.021	6	220.08473	10.498	C11 H12 N2 O3	RP
N-(5-acetamidopentyl)acetamide.1	0.369	0.028	0	208.12116	8.501	C9 H18 N2 O2	RP
N1-[5-(tert-Butyl)-1,3-oxathiol-2-yliden]-2,4,5-trimethylaniline	0.368	0.008	0	275.1369	6.616	C16 H21 N O S	RP
4-oxododecanedioic acid	0.366	0.012	0	266.11542	13.58	C12 H20 O5	RP
His-His	0.366	0.007	4	292.12873	14.061	C12 H16 N6 O3	RP
4-oxododecanedioic acid.2	0.365	0.008	0	266.11435	13.018	C12 H20 O5	RP
thymol sulfate.1	0.363	0.007	4	230.06137	10.858	C10 H14 O4 S	RP
Propyl gallate	0.363	0.008	7	212.06847	1.806	C10 H12 O5	H

(5Z)-13-carboxytridec-5-enoylcarnitine	0.361	0.037	4	399.26211	13.043	C21 H37 N O6	RP
NP-011223	0.359	0.018	0	208.10993	17.095	C10 H18 O3	RP
N'-Cyano-N-[2-(trifluoromethyl)phenyl]							
pyrrolidine-1-carboximidamide	0.359	0.018	5	282.10793	11.786	C13 H13 F3 N4	RP
5-Valerolactone	0.358	0.001	5	100.05244	2.387	C5 H8 O2	H
Trimethylamine N-oxide	0.357	0.029	11	75.06844	1.162	C3 H9 N O	RP
Tetraacetylenethylenediamine.1	0.357	0.022	4	228.11111	1.726	C10 H16 N2 O4	RP
NP-021299	0.357	0.008	0	482.14025	13.579	C25 H24 N4 O4	RP
Pro-Hyp.1	0.354	0.001	4	228.11099	8.845	C10 H16 N2 O4	RP
6-Hydroxy-1-(hydroxymethyl)-5-{2-[2-(hydroxymethyl)-1-pyrrolidinyl]-2-oxoethyl}-1,4a-dimethyldecahydro-2-naphthalenyl							
phenylcarbamate	0.353	0.042	0	510.27642	15.191	C27 H40 N2 O6	RP
Isovalerylglutamic acid.1	0.352	0.015	4	231.11068	6.559	C10 H17 N O5	RP
Methohexital	0.351	0.001	4	262.13177	10.208	C14 H18 N2 O3	RP
3-Methoxy-4-hydroxyphenylethyleneglycol	0.35	0.014	6	184.07353	1.837	C9 H12 O4	H
						C14 H18 N4 O2	
metioprim	0.35	0.005	4	306.11511	6.444	S	RP
3-Hydroxy-N-[(3S)-2-oxotetrahydro-3-furanyl]octanamide	0.349	0.003	4	243.14704	8.437	C12 H21 N O4	RP
3-[(3-Hydroxydecanoyl)oxy]-4-(trimethylammonio)butanoate	0.349	0.021	4	331.23595	12.826	C17 H33 N O5	RP
NP-019374.2	0.348	0.029	0	224.10245	11.378	C10 H18 O4	RP
L-Aspartic acid fl-benzyl ester	0.347	0.015	8	223.08448	10.028	C11 H13 N O4	RP
NP-021018	0.346	0.012	0	208.10995	13.022	C12 H18 O4	RP
Phenylacetyl-L-glutamine	0.344	0.006	13	264.11097	9.953	C13 H16 N2 O4	RP
Valyl-4-hydroxyproline	0.34	0.01	4	230.12664	8.828	C10 H18 N2 O4	RP
5-Aminonicotinic acid.1	0.34	0.01	8	138.04293	3.193	C6 H6 N2 O2	H
Nicotianamine	0.339	0.002	5	303.14306	8.858	C12 H21 N3 O6	RP
1_6_6-Trimethyl-2_7-dioxabicyclo[3.2.2]nonan-3-one	0.339	0.007	5	184.10997	14.441	C10 H16 O3	RP
XLR11 N-(2-fluoropentyl) isomer	0.338	0.044	0	329.22028	13.005	C21 H28 F N O	RP
CEs-D-Ribofuranosylcreatine	0.336	0.022	4	263.11175	1.324	C9 H17 N3 O6	RP
Isovalerylglutamic acid.2	0.336	0.002	4	231.11068	11.486	C10 H17 N O5	RP
OxidizedRenillaluciferin	0.335	0.028	5	395.16143	12.486	C25 H21 N3 O2	RP
5-(acetylamino)-2-hydroxybenzoic acid	0.333	0.001	10	195.05316	9.67	C9 H9 N O4	RP
Procollagen5-(D-galactosyloxy)-L-lysine	0.331	0.027	6	324.15335	0.957	C12 H24 N2 O8	RP
1-Phenyl-1H-pyrazolo[3,4-d]pyrimidin-4-amine.1	0.33	0.018	0	211.08206	8.902	C11 H9 N5	RP
trans-Urocanic Acid.1	0.33	0.021	12	138.04291	2.308	C6 H6 N2 O2	RP
Hydantoin-5-propionate.1	0.33	0.015	5	172.04838	10.227	C6 H8 N2 O4	H
Hippuric acid	0.33	0.025	10	179.05832	9.792	C9 H9 N O3	RP
4-chloro-N~1~-(4-pyridinyl)-1,2-benzenediamine	0.329	0.004	0	219.05315	11.364	C11 H10 Cl N3	RP
N-Acetyl-L-carnosine	0.328	0.006	9	268.11722	11.348	C11 H16 N4 O4	H
N2-Acetyl-L-aminoadipate.3	0.327	0.025	5	203.07936	6.615	C8 H13 N O5	RP
1,5-Isoquinolinediol	0.324	0.019	9	161.04771	10.398	C9 H7 N O2	RP
6-(alpha-D-Glucosaminyl)-1D-myo-inositol	0.323	0.024	5	341.13236	7.647	C12 H23 N O10	H
2-Carboxy-2_3-dihydro-5_6-dihydroxyindole	0.322	0.045	6	195.05317	7.38	C9 H9 N O4	RP
4-Oxocyclohexanecarboxylate.1	0.321	0.048	5	142.06301	7.356	C7 H10 O3	RP
ionene	0.321	0.034	4	174.14086	10.45	C13 H18	RP
Pantothenicacid(VitaminB5).2	0.319	0.002	6	219.11067	1.338	C9 H17 N O5	RP
3-Hydroxy-N-[(3S)-2-oxotetrahydro-3-furanyl]decanamide.1	0.317	0.04	4	271.17836	10.648	C14 H25 N O4	RP
Genipin	0.315	0.043	4	226.08415	1.604	C11 H14 O5	H
trans-3-Hydroxycotinineglucuronide	0.314	0.013	5	368.12202	10.8	C16 H20 N2 O8	RP
formyl-isoglutamine.1	0.313	0.037	5	174.06409	1.295	C6 H10 N2 O4	RP
ON1225000.1	0.313	0.007	4	172.07358	9.001	C8 H12 O4	RP
3305	0.312	0.015	5	126.06804	9.003	C7 H10 O2	RP
2-(Hydroxymethyl)-1-methyl-3,4,5-piperidinetriol	0.312	0.004	4	177.10013	10.526	C7 H15 N O4	RP
Isopentenyladenosine	0.312	0.021	5	335.15818	14.187	C15 H21 N5 O4	RP
(5-Benzyl-3,6-dioxo-2-piperazinyl)							
acetic acid	0.311	0.034	4	262.09541	6.349	C13 H14 N2 O4	H
Guanidinosuccinic acid	0.311	0.009	9	175.05926	12.238	C5 H9 N3 O4	H
Ageratriol	0.308	0.019	0	234.16199	14.558	C15 H24 O3	RP
NP-001422.1	0.308	0.021	0	192.03982	10.106	C8 H10 O4	RP

N6-threonylcarbamoyladenine	0.307	0.021	4	412.13457	9.728	C15 H20 N6 O8	RP
ala-ser	0.306	0.001	4	176.07975	2.435	C6 H12 N2 O4	RP
Estrone	0.305	0.007	0	292.13991	12.909	C18 H22 O2	RP
8'-Hydroxyabscisate	0.305	0.006	5	280.13109	13.581	C15 H20 O5	RP
Neuraminic acid	0.304	0.021	5	267.09549	1.109	C9 H17 N O8	RP
N5-(L-1-Carboxyethyl)-L-ornithine	0.304	0.01	5	204.11109	1.383	C8 H16 N2 O4	RP
Linamarin.1	0.302	0.009	7	247.10557	11.325	C10 H17 N O6	RP
						C10 H14 N5 O6	
Deoxyadenosinemonophosphate	0.301	0.021	5	331.06689	9.037	P	RP
1-(3-Chlorophenyl)piperazine							
(m-CPP).1	0.297	0.013	0	196.07357	15.514	C10 H13 Cl N2	RP
2'-fluoro-N,N-diisopropyl[1,1'-biphenyl]-4-carboxamide	0.297	0.021	0	299.1733	9.475	C19 H22 F N O	RP
8'-Hydroxyabscisate.1	0.296	0.019	5	280.1311	14.776	C15 H20 O5	RP
(2S)-3-(1H-Imidazol-4-yl)-2-({[(3S,4S,5R)-2,3,4-trihydroxy-5-(hydroxymethyl)tetrahydro-2-furanyl]methyl}amino)propanoic acid (non-preferred name)	0.295	0.004	4	317.12253	1.396	C12 H19 N3 O7	RP
NP-016564	0.295	0.046	0	290.11306	14.982	C16 H20 O6	RP
Hexanoylglycine.3	0.294	0.012	5	173.10527	1.393	C8 H15 N O3	RP
N-Butyryl-L-homoserinelactone.1	0.293	0.037	5	171.08957	6.56	C8 H13 N O3	RP
						C15 H13 N3 O5	
5-Hydroxypiroxicam	0.293	0.021	0	347.06176	8.685	S	RP
Zalcitabine.1	0.293	0.013	4	211.09579	1.399	C9 H13 N3 O3	RP
N-Tigloylglycine	0.292	0.016	7	157.07387	3.47	C7 H11 N O3	H
(2R,3S,4S,5R,6R)-2-(hydroxymethyl)-6-(2-phenylethoxy)oxane-3,4,5-triol	0.291	0.01	0	306.108	14.776	C14 H20 O6	RP
JWH-175.1	0.291	0.014	0	327.20465	11.992	C24 H25 N	RP
4-Acetamidobutanoic acid	0.29	0.009	10	145.07387	2.418	C6 H11 N O3	H
3-Methylcrotonylglycine	0.289	0.028	9	157.07389	8.794	C7 H11 N O3	RP
Hexanoylcarnitine.1	0.287	0.012	9	259.17837	10.752	C13 H25 N O4	RP
(2S)-2-([1-(R)-Carboxyethyl]amino)pentanoate.2	0.287	0.01	5	189.10011	9.128	C8 H15 N O4	RP
Basic Red 9.1	0.282	0.033	0	287.13693	7.316	C19 H17 N3	RP
2-Oxoglutarate	0.282	0.038	8	145.03752	1.688	C5 H7 N O4	RP
2_6-Diaminoheptanedioic acid	0.281	0.023	6	190.09537	1.308	C7 H14 N2 O4	RP
L-Glutamic acid	0.277	0.008	11	147.05318	1.164	C5 H9 N O4	RP
3-Hydroxy-N-[(3S)-2-oxotetrahydro-3-furanyl]decanamide	0.276	0.043	4	271.17836	10.675	C14 H25 N O4	RP
Glycylprolylhydroxyproline	0.276	0.007	4	285.13247	8.809	C12 H19 N3 O5	RP
2-methoxyacetaminophen sulfate	0.275	0.026	4	261.0307	4.73	C9 H11 N O6 S	RP
Azelaic acid.2	0.274	0.022	5	188.10486	10.414	C9 H16 O4	RP
6-Acetamido-3-aminohexanoate	0.271	0.021	6	188.11609	11.136	C8 H16 N2 O3	H
Eugenol;4-Allylguaiacol	0.268	0.021	6	164.08373	16.893	C10 H12 O2	RP
(1-Ribosylimidazole)-4-acetate	0.266	0.022	5	258.08531	1.396	C10 H14 N2 O6	RP
Proline.1	0.266	0.021	11	115.06328	1.33	C5 H9 N O2	RP
fl-Cortolone	0.265	0.044	0	348.23016	16.502	C21 H34 O5	RP
3-indole carboxylic acid glucuronide	0.263	0.031	4	337.08014	8.152	C15 H15 N O8	H
[Similar to: N-Acetylneuraminic acid; <U+0394>Mass: -36.0211 Da]	0.262	0.019	2	273.08492	1.325	C11 H15 N O7	RP
NP-022068.1	0.262	0.021	0	210.05041	8.426	C8 H12 O5	RP
EUROPINE.1	0.262	0.021	4	329.18394	10.141	C16 H27 N O6	RP
Nitrilotriacetic acid	0.26	0.043	5	191.04297	3.503	C6 H9 N O6	RP
S-3-oxodecanoyl cysteamine	0.26	0.035	4	245.14492	14.183	C12 H23 N O2 S	RP
NP-016455.1	0.26	0.019	5	242.12664	10.988	C11 H18 N2 O4	RP
12,13-Dimethyl-5,14-dioxabicyclo[9.2.1]tetradeca-1(13),11-dien-4-one.1	0.259	0.011	4	236.14123	16.844	C14 H20 O3	RP
7-mercaptoheptanoylthreonine	0.258	0.033	5	263.11916	13.343	C11 H21 N O4 S	RP
2-amino-2,3,7-trideoxy-D-lyxo-hept-6-ulosonic acid	0.257	0.048	6	191.0794	8.001	C7 H13 N O5	RP
1-methyl-1H-benzimidazole-2-sulfonic acid	0.256	0.038	0	212.02967	4.126	C8 H8 N2 O3 S	RP
1-Nitrosopiperidine	0.256	0.005	4	114.07924	1.181	C5 H10 N2 O	RP
(8Z,11Z,14Z,17Z,20Z,23Z)-hexacosahexaenoic acid	0.254	0.015	4	384.3029	18.444	C26 H40 O2	RP
N-Acetyl-L-arginine dihydrate	0.254	0.011	12	216.12222	10.826	C8 H16 N4 O3	H
O-beta-D-Glucopyranosyl-cis-zeatin	0.252	0.017	5	381.16364	11.966	C16 H23 N5 O6	RP

Creatinine	0.252	0.012	13	113.05887	1.203	C4 H7 N3 O	RP
Dopamineglucuronide	0.251	0.045	5	329.11116	10.735	C14 H19 N O8	RP
D-2-Amino-hexano-6-lactam	0.245	0.012	5	128.095	1.398	C6 H12 N2 O	RP
4-hydroxy-3-(1-hydroxyiminoethyl)-1,6-diphenyl-1,2-dihydropyridin-2-one	0.244	0.031	0	320.11093	10.277	C19 H16 N2 O3	H
Guanidinosuccinic acid	0.243	0.021	9	175.05932	1.235	C5 H9 N3 O4	RP
N-[5-[(dimethylamino)sulfonyl]-2-methylphenyl]cyclohexane carboxamide	0.242	0.013	0	324.15351	15.738	C16 H24 N2 O3 S	H
Limonene-1_2-diol	0.241	0.034	5	170.13069	13.315	C10 H18 O2	RP
(1-Ribosylimidazole)-4-acetate.2	0.241	0.01	5	258.08524	5.166	C10 H14 N2 O6	RP
cis-2-Carboxycyclohexyl-acetic acid.1	0.241	0.031	4	186.08919	1.4	C9 H14 O4	H
N6-Acetyl-L-lysine	0.239	0.007	11	188.11618	1.392	C8 H16 N2 O3	RP
5-L-Glutamyl-L-tyrosine	0.238	0.047	5	254.05733	13.325	C7 H14 N2 O6 S	H
D-Arginine	0.237	0.021	6	174.11173	1.079	C6 H14 N4 O2	RP
N-Acetyl-1-aspartylglutamic acid	0.237	0.008	9	304.09067	4.592	C11 H16 N2 O8	RP
Kynurenic acid	0.234	0.033	10	189.0426	9.917	C10 H7 N O3	RP
2-imino-3a-methylperhydro-5lambda~6~-thieno[3,4-d][1,3]thiazole-5,5-dione.1	0.232	0.04	5	206.01915	10.161	C6 H10 N2 O2 S2	RP
2_3-Dimethylmaleate	0.23	0.037	6	144.04224	2.09	C6 H8 O4	H
N-Acetylputrescine	0.23	0.029	0	89.08411	1.394	C6 H14 N2 O	RP
6-(3Z)-3-Hexen-1-yltetrahydro-2H-Pyran-2-one	0.23	0.015	4	182.13069	13.604	C11 H18 O2	RP
carglumic acid	0.229	0.037	4	190.05898	1.172	C6 H10 N2 O5	RP
L(+)-Citrulline;2-Amino-5-uredovalerate.1	0.229	0.026	6	175.09577	1.396	C6 H13 N3 O3	RP
2271703	0.228	0.021	4	231.11069	11.281	C10 H17 N O5	RP
N-Feruloylglycine.3	0.228	0.043	5	251.07939	10.13	C12 H13 N O5	RP
(+/-)-6-Hydroxy-3-oxo-alpha-ionone	0.225	0.031	5	222.12558	17.094	C13 H18 O3	RP
N-[(2S)-2-Hydroxypropanoyl]-L-tyrosine	0.223	0.027	4	253.09501	9.101	C12 H15 N O5	RP
3-Morpholino-4-tetrahydro-1H-pyrrol-1-ylcyclobut-3-ene-1,2-dione	0.215	0.029	0	236.1137	8.729	C12 H16 N2 O3	RP
beta-Aspartylaspartic acid	0.213	0.049	4	248.06446	1.249	C8 H12 N2 O7	RP
MFCD02728197	0.212	0.04	4	280.14236	8.968	C14 H20 N2 O4	RP
Boc-Asn-ONp	0.21	0.019	4	353.12241	7.367	C15 H19 N3 O7	RP
Indole-3-acetaldoxime	0.207	0.034	5	174.07932	5.56	C10 H10 N2 O	RP
4,7-dimethylpyrazolo[5,1-c][1,2,4]triazine-3-carbonitrile	0.199	0.041	0	173.06879	2.59	C8 H7 N5	H
Ubiquinone-2(CoQ2)	0.199	0.019	5	318.18316	17.811	C19 H26 O4	RP
NP-020014.1	0.198	0.04	0	236.17762	16.985	C15 H26 O3	RP
7a-Hydroxytestosterone.1	0.196	0.01	10	304.20386	15.775	C19 H28 O3	RP
Cantharidin.1	0.183	0.044	9	196.07355	13.487	C10 H12 O4	RP
Deoxyadenosinemonophosphate.1	0.178	0.033	5	331.06695	7.737	C10 H14 N5 O6 P	RP
[Similar to: Uric acid; <U+0394>Mass: 192.0271 Da]	-0.18	0.021	2	360.05546	2.799	C5 H13 N8 O9 P	RP
Betaine	-0.29	0.001	14	117.07892	1.187	C5 H11 N O2	RP
20 fl-Dihydrocortisol.1	-0.29	0.021	8	364.22507	15.342	C21 H32 O5	RP
Stachydrine	-0.3	0.028	6	143.09463	7.831	C7 H13 N O2	RP
Choline	-0.31	0.001	7	103.09968	1.099	C5 H13 N O	RP
Capryloylglycine	-0.32	0.035	5	201.13646	15.199	C10 H19 N O3	RP
Capryloylglycine	-0.33	0.019	6	201.13648	1.929	C10 H19 N O3	H
Pyridoxamine;2-Methyl-4-aminomethyl-5-hydroxymethyl-3-Pyridinol	-0.34	0.027	6	168.08986	7.406	C8 H12 N2 O2	RP
fosfocreatinine	-0.35	0.007	4	193.02537	1.071	C4 H8 N3 O4 P	RP
Myristamide	-0.36	0.041	4	227.22491	20.297	C14 H29 N O	RP
3-(propan-2-yl)-octahydropyrrolo[1,2-a]pyrazine-1,4-dione	-0.41	0.009	6	196.12117	10.008	C10 H16 N2 O2	RP
Dihydrothymine	-0.47	0.013	9	128.05854	1.256	C5 H8 N2 O2	RP
hypaphorine	-0.47	0.007	4	246.1368	8.79	C14 H18 N2 O2	RP
PEG n6	-0.5	0.045	7	282.16792	9.715	C12 H26 O7	RP
PEG n7	-0.66	0.023	7	326.19414	10.338	C14 H30 O8	RP

(6R,7S)-6,7-Dihydroxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2E)-2-methyl-2-butenolate	-0.9	0.024	4	255.14706	12.842	C13 H21 N O4	RP
2-(4-Isobutylphenyl)acrylic acid	-0.91	0.045	4	204.11501	13.44	C13 H16 O2	RP
5,6-Dihydroxy-2-naphthalene sulfonic acid	-1.16	<0.001	4	240.00927	1.15	C10 H8 O5 S	H

Supplemental Table 2 In-depth Descriptions of Features from Table 2

Metabolite	Relevance
Taurine	The most abundant free amino acid in human cells; synthesized from other sulfonic amino acids such as methionine and cysteine, must also be provided by diet. It participates in bile acid formation, exerts antioxidant and anti-inflammatory actions as well as antiarrhythmic, ionotropic and chronotropic ones, is a central nervous system neuro-modulator, and is involved in retinal development and function. ⁵³
	There is an inverse association between taurine levels in urine and risk of mortality from coronary heart disease and stroke in adults aged 48-56. High urinary taurine/creatinine ratios were also inversely associated with cardiovascular disease risk factors, including BMI, BP, TC, obesity, hypertension and hypercholesterolemia. Taurine deficiency was associated with higher risk of hypertension. ⁵⁴
	Taurine is produced by the liver in response to exposure to toxins--increased concentration in plasma and urine can be used as a biomarker for paracetamol poisoning, and can also result from surgical trauma, X-radiation, muscle necrosis, or carbon tetrachloride-induced liver damage. ⁵⁵
1,7-Dimethyluric acid	conversion between caffeine metabolite 1,7-dimethylxanthine to 1,7-dimethyluric acid is being used to represent CYP2A6 activity which may represent a marker for susceptibility to dietary carcinogens; CYP2A6 bioactivates nitrosamines. ⁵⁶
4-Phenylbutyric acid	Benzene butyric acid may be potential biomarkers for early inflammation-stage pulmonary fibrosis. ⁵⁷
	Used clinically to treat urea cycle disorders, also prevents misfolded protein aggregation and alleviates endoplasmic reticulum stress. ⁵⁸
Indole-3-acetic acid	Indole-3-acetic acid is a naturally abundant auxin, a regulator of plant growth. It is found in human urine, plasma and the nervous system due to heavy consumption of vegetables, production by intestinal bacteria, or synthesis from tryptophan in tissues. ⁵⁹
	Indole-3-acetic acid concentration in urine correlates with liver damage and non-alcoholic steatohepatitis (NASH). It can also be used as a biomarker to differentiate between NASH and non-alcoholic fatty liver disease (NAFLD). ⁶⁰
	Testing for Indole-3-acetic acid in spot urine can be reliably used to diagnose acute appendicitis. ⁶¹
N6,N6,N6-Trimethyl-L-lysine	Non-protein amino acid, starting point for carnitine biosynthesis in mammals, essential for fatty acid transport and use in mitochondria. Produced by hydrolysis of proteins containing N6,N6,N6-Trimethyl-L-lysine as a post-translational modification of some lysine residues. ⁶²
	High concentration of N6, N6, N6-trimethyl-L-lysine in urine is a potential high-risk biomarker for bladder cancer. ⁶³
	N6,N6,N6-Trimethyl-L-lysine (TML) levels are independently associated with risk of incident (3-year) major adverse cardiovascular events and risk of incident (5-year) mortality. TML levels can be used as a nutrient precursor for gut microbiota-dependent generation of trimethylamine (TMA) and trimethylamine N-oxide (TMAO). ⁶⁴
Trimethylamine N-oxide	Increasing interest in understanding importance of TMAO relationships and dynamics with NOC formation, carcinogenic potential via DNA-methylation and direct mutagenic properties. ⁶⁵ Noted uremic toxin ²⁵
Phenylacetyl-L-glutamine	Phenylacetylglutamine is a colonic microbial metabolite from amino acid fermentation; it results from glutamine conjugation of phenylacetic acid. Higher concentrations of phenylacetyl-L-glutamine is found in serum of patients with advanced chronic kidney disease, and is a risk factor for cardiovascular disease and mortality. ⁶⁶

	Phenylacetylglutamine is a potential biomarker for ischemic stroke and is associated with unfavorable short-term outcomes. ⁶⁷ 5-(acetylamino)-2-hydroxybenzoic acid
5-(acetylamino)-2-hydroxybenzoic acid	Metabolite of 5-Aminosalicylic acid (mesalazine, 5-ASA, drug used to treat inflammatory bowel diseases); therapeutically inert, major metabolite present in blood, binds to proteins. ⁶⁸
trans-Urocanic Acid.1	following exposure to UVR, the naturally occurring trans-UCA is converted to cis-UCA, both of which have shown contributing to both health and disease; UV-induced cis-UCA is suggested to promote skin cancer by reducing cell-mediated immunity. ⁶⁹
Hippuric acid	Useful as a marker for bacterial overgrowth in the intestines, linked to polyphenol-rich diet; differences in green tea and black tea phenol production illustrate large interindividual variability between phenolic metabolite production and hippuric acid presence highlighting importance of individual microflora. ⁷⁰
4-Acetamidobutanoic acid	Predominant inhibitory neurotransmitter in central nervous system in mammals, also produced in plants to mitigate stress. It also plays a role in the induction of hypotension, and has tranquilizer and diuretic effects. Produced by decarboxylation of glutamic acid. ⁷¹ Used as a general biomarker for alcoholic liver injury, sepsis, malnutrition, multiple organ failure; linked to tuberculosis and pediatric metabolic diseases. May also be used as a biomarker for osteoporosis. ⁷²
L-Glutamic acid	discusses large set of urinary metabolites including glutamic acid, glutamine and derivatives that were observed to respond significantly after neoplasm. ⁷³ highlights glutamic acid's anticancer properties; cellular life and proliferation relies greatly on glutamine metabolic pathway and glutamic acid; endogenous levels of glutamic acid suggested to ameliorate cancerous side effects; in cancer patients, the deficiency of glutamate, glutamine, and other associated metabolites was suggested contribute to depletion of malignant cells. ⁷⁴
Proline	a precursor for hydroxyproline and used to produce collagen - proline and hydroxyproline urinary excretion can then be used as an index of collagen catabolism; collagen may promote cancer cell growth and migration during tumor-specific extracellular matrix remodeling. ⁷⁵
N-Acetyl-L-arginine dihydrate	known human metabolite; N-Acetylated-L-arginine (NALA) enhanced properties for arginine as an aggregation suppressor while minimizing disturbance of protein conformational stability. ⁷⁶
Creatinine	in addition to representing kidney health, serum creatinine levels may prove useful as a prognostic parameter predicting disease survival in vulvar cancer. ⁷⁷ renal monitoring for all cancer types is recommended measuring creatinine clearance through 24-hour urine collection. ⁷⁸
N6-Acetyl-L-lysine	role as human metabolite; lysine acetylation occurs for both histone and non-histone proteins throughout the cell and has great impact on protein functioning; article discusses implications of lysine acetylation in various cellular compartments associated with cancer biology and relevance of lysine acetylation as biomarkers for cancer prognosis. ⁷⁹ highlight novel potential cancer drivers for use as biomarkers and propose a new tumorigenesis mechanism tracking misregulation of lysine modifications in cancer-relevant pathways. ⁸⁰
Kynurenic acid	KYNA is a metabolite of L-tryptophan and is associated with non-recovery from acute renal failure. It is also involved in AhR pathway activation. KYNA may represent an important cancer marker: easily absorbed through digestive tract - can quickly concentrate serum and organs; pro-carcinogenic properties; endogenously produced by normal and cancer cells. ⁸¹

7a-Hydroxytestosterone	using urine metabolomics to conduct a biomarker exploration for gestational diabetes mellitus and spontaneous abortion, results show steroid hormone metabolites were significantly regulated and consistently upregulated in pregnant women. ⁸²
Betaine	Methyl derivative of glycine; functions as an organic osmolyte to protect cells under stress, acts as a catabolic source of methyl groups via transmethylation for use in various biochemical pathways. ⁸³
	Betaine in urine can be used as a dietary biomarker, especially of citrus fruit, and is associated with a decrease of inflammation. ⁸⁴
	Betaine concentration is inversely associated with risk of breast cancer. ⁸⁵