Analytical and Bioanalytical Chemistry

Electronic Supplementary Material

Monitoring metabolites consumption and secretion in cultured cells using ultra-performance liquid chromatography quadrupole-time of flight mass spectrometry (UPLC-Q-ToF-MS)

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Figure S1. Overlay extracted ion chromatograms obtained using mobile phases at different pHs. 1) SDMA, 2) ADMA, 3) Arginine, 4) Lysine, 5) Ornithine, 6) Cystine, 7) 5-MTA, 8) Deoxyadenosine, 9) Hypoxanthine, 10) Adenosine, 11) Xanthine 12) Inosine, 13) Deoxyguanosine, 14) Guanine, 15) Guanosine.

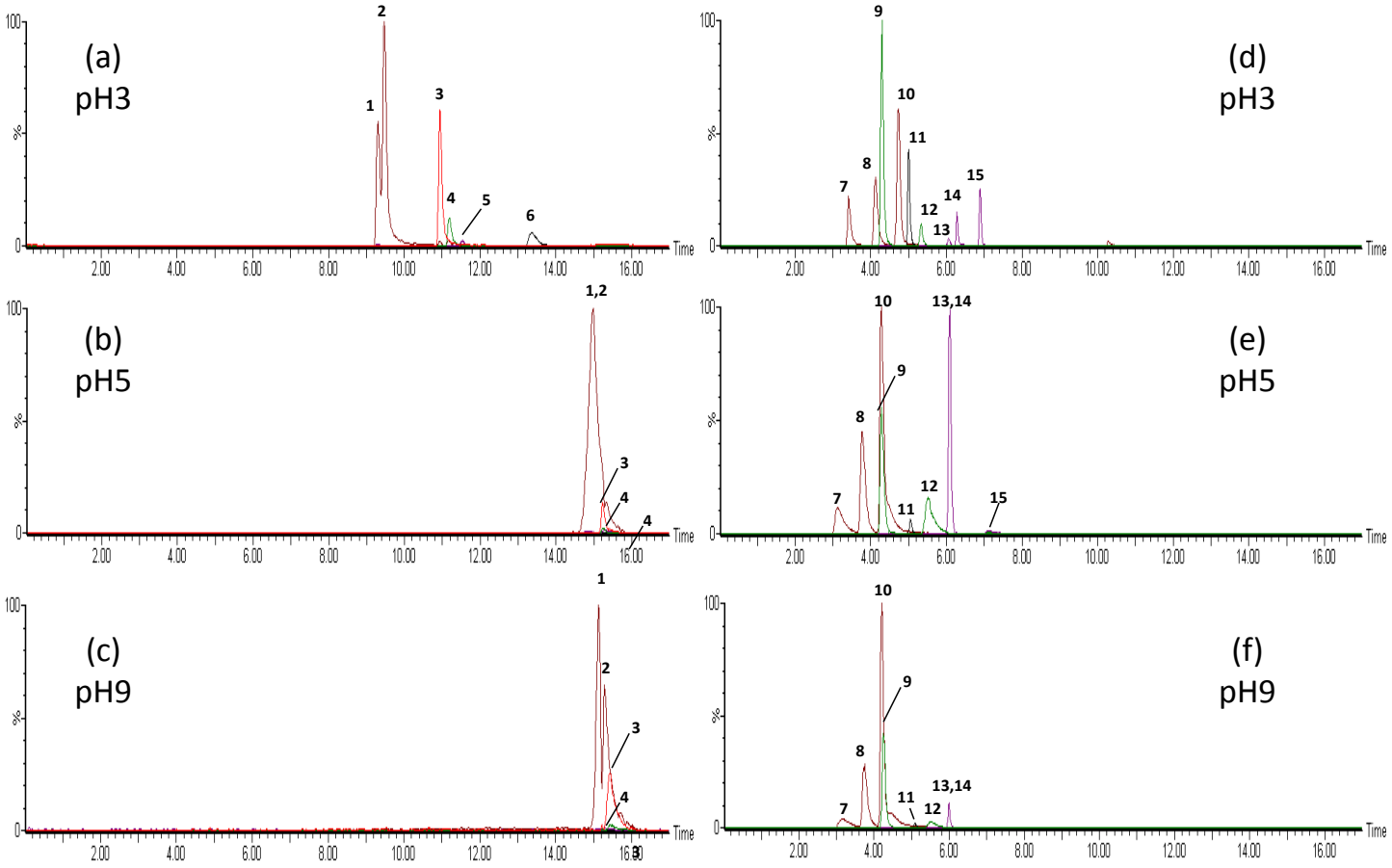

Figure S2. Growth and apoptosis of Molt-4 and CCRF-CEM treated with AMPK activators. Cells were resuspended in RPMI advanced media containing 0.5 mM AICAR, 0.1 mM A-769662 or DMSO (0.7%) and cultured at 37°C and 5% CO_2 in 24 well plates. Cells were counted using an automatic cell counter (Countess, Invitrogen). The graphs show fraction of viable cells (not stained with Trypan blue). Apoptosis was measured after 48 hrs using Annexin V binding and flow cytometry according to the manufactures instructions (Beckman Coulter). All apoptotic cells are shown, including cells undergoing necrosis (stained with Annexin V-PE and 7-AAD). Data from cells grown without DMSO and in RPMI, 10% FBS are also shown for comparison. Data shown represent the average and standard deviation of three independent experiments. Cells treated with the AMPK activators showed marked decrease in growth and increase in apoptosis. The concentration of viable cells was reduced by approximately 50% as compared to the controls after 48 hrs. Both AMPK activators increased the fraction of apoptotic cells for both cell lines, with Molt-4 showing more apoptosis.

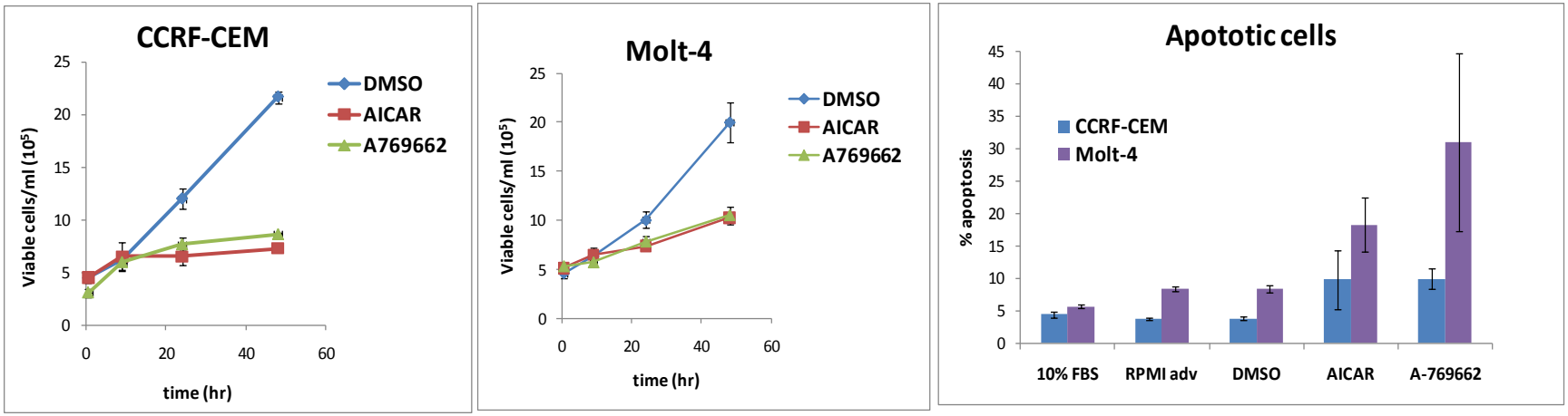

Figure S3. Total ATP in cells, treated as described for Fig. S2, was measured using a luminescent assay (CellTiter-Glo, Promega). Data were normalized to cell volume. For Molt-4 cells, concentrations were 6.1±0.7, 6.9±1.1 and 4.1±0.5 mM for DMSO, AICAR and A-769662, respectively. For CCRF-CEM cells, concentrations were 3.9±0.5, 9.1±0.8 and 3.5±0.3 mM for DMSO, AICAR and A-769662, respectively. Data shown represent average and standard deviation of three independent experiments. The total ATP, normalized to cell volume, was similar in cells treated with AMPK activators and control except in CCRF-CEM cells treated with AICAR, was it was increased 2 fold.

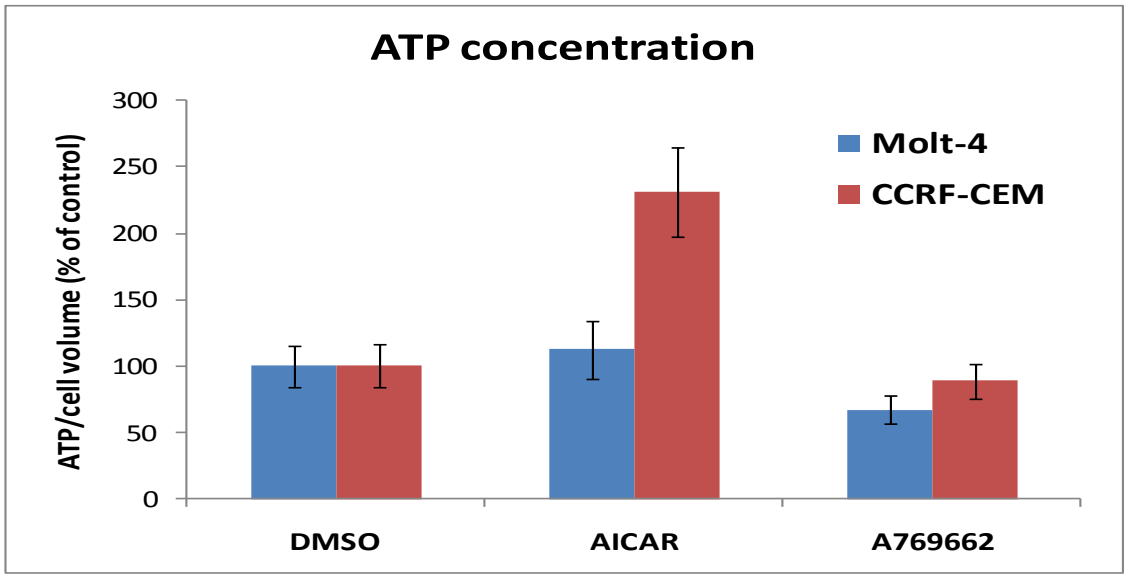

Figure S4. Metabolites secreted during the CCFR-CEM cells culture after 48 hours with AICAR treatments. The amount of compound secreted is given as log of pmoles/cells. Data from three biological replicates injected twice are shown. Concentration of carbamoyl-aspartate was calculated using dihydroorotic acid calibration curve.

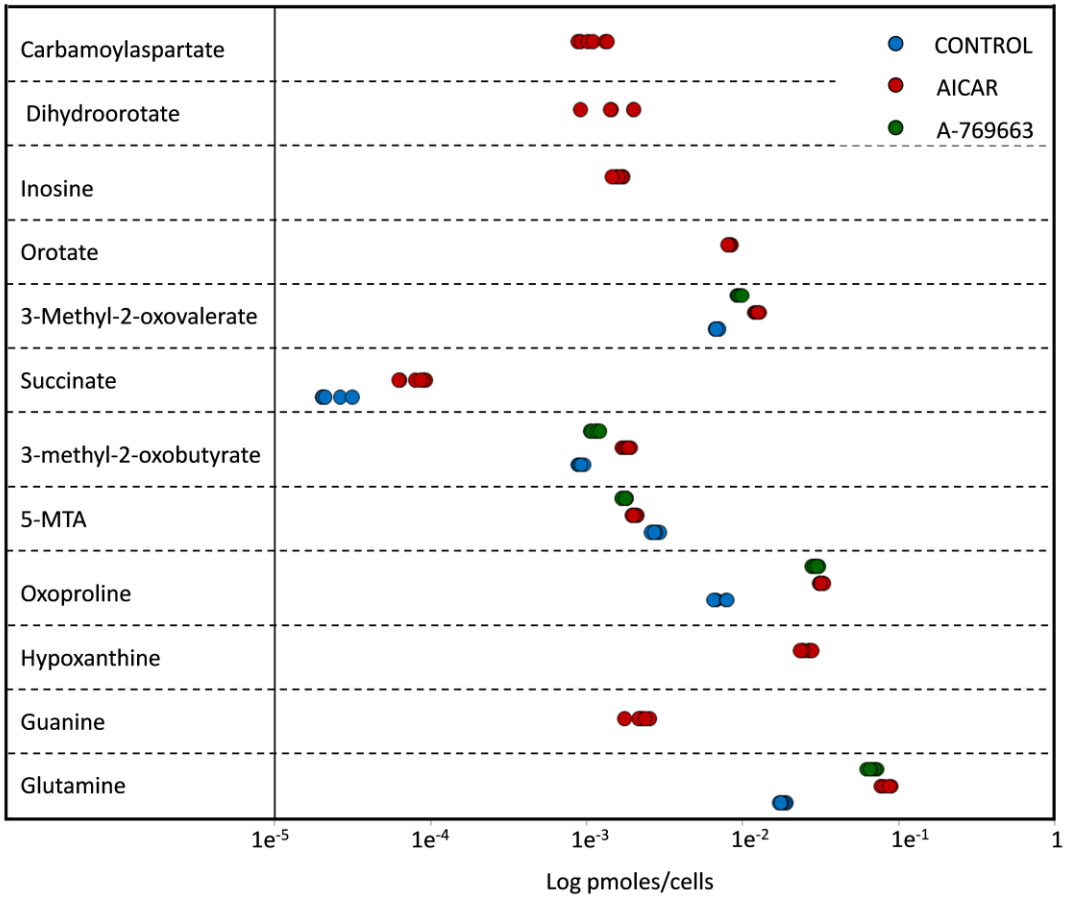

Table S1. List of metabolites investigated during the method development.

	Metabolite	*Kegg ID*	*Neutral Formula*	*RT [min]*	*ESI +*			*ESI -*		
					Theoretical mass	*Observed mass*	*Δ ppm*	*Theoretical mass*	*Observed mass*	*Δ ppm*
1	*2-deoxyadenosine*	HMDB00101	C10H13N5O3	4.04	252.1097	252.1096	-0.4	-	-	-
2	*2-deoxyguanosine*	HMDB00085	C10H13N5O4	6.01	268.1046	268.1065	7.1	266.0889	266.0883	-2.3
3	*2-hydroxybutyric acid*	HMDB00008	C4H8O3	1.68	-	-	-	103.0395	103.04	4.9
4	*2-ketobutyric acid*	HMDB00005	C4H6O3	1.26	-	-	-	101.0239	101.0236	-3
5	*3-methyl-2-oxobutyrate*	HMDB00019	C5H8O3	1.14	-	-	-	115.0395	115.0393	-1.7
6	*3-methyl-2-oxovalerate*	HMDB00491	C6H10O3	1.15	-	-	-	129.0552	129.0551	-0.8
7	*4-hydroxyphenylpiruvate*	HMDB00707	C9H8O4	2.61	-	-	-	179.0344	179.0376	17.9
8	*5-Methylthioadenosine (5-MTA)*	HMDB01173	C11H15N5O3S	3.33	298.0974	298.099	5.4	296.0817	296.0815	-0.7
9	*A769962*	-	C20H12N2O3S	3.89	361.0647	361.064	-1.9	359.049	359.0507	4.7
10	*Acetylalanine*	HMDB00766	C5H9NO3	2.1	132.0661	132.0671	7.6	130.0504	130.0516	9.2
11	*Acetylmethionine*	HMDB11745	C7H13NO3S	1.86	192.0694	192.0699	2.6	190.0538	190.0555	8.9
12	*Adenine*	HMDB00034	C5H5N5	4.04	136.0623	136.0625	1.5	134.0467	134.0469	1.5
13	*Adenosine*	HMDB00050	C10H13N5O4	4.61	268.1046	268.1049	1.1	266.0889	266.0895	2.3
14	*ADMA*	HMDB03334	C8H18N4O2	8.89	203.1508	203.1511	1.5	201.1352	201.1357	2.5
15	*AICAR*	-	C9H14N4O5	5.16	259.1042	259.105	3.1	257.0886	257.0898	4.7
16	*Allantoin*	HMDB00462	C4H6N4O3	4.9	-	-	-	157.0362	157.0372	6.4
17	*Alanine*	HMDB00161	C3H7NO2	6.61	90.0555	90.056	5.6	88.0399	88.0396	-3.4
18	*Alanyl-Glutamine*	-	C8H15N3O4	7.42	218.1141	218.1147	2.8	216.0984	216.0982	-0.9
19	*Arabinose*	HMDB11734	C5H10O5	5.07	-	-	-	149.045	149.0444	-4
20	*Arginine*	HMDB00517	C6H14N4O2	10.41	175.1195	175.1201	3.4	173.1039	173.1038	-0.6
21	*Asparagine*	HMDB00168	C4H8N2O3	6.14	133.0613	133.0602	-8.3	-	-	-
22	*Aspartic Acid*	HMDB00191	C4H7NO4	8.69	134.0453	134.0456	2.2	132.0297	132.0302	3.8
23	*Biotin*	HMDB00030	C10H16N2O3S	3.16	245.096	245.0978	7.3	243.0803	243.08	-1.2
24	*Choline*	HMDB00097	C5H14NO	1.62	104.1075	104.1082	6.7	-	-	-
25	*Citrate*	HMDB00094	C6H8O7	8.28	-	-	-	191.0192	191.0193	0.5
26	*Cysteine*	HMDB00574	C3H7NO2S	13.17	122.0276	122.028	3.3	120.0119	120.0129	8.3
27	*Cystine*	HMDB00192	C6H12N2O4S2	12.37	241.0317	241.0318	0.4	239.016	239.0164	1.7
28	*Dihydroorotic acid*	HMDB03349	C5H6N2O4	3.74	159.0406	159.0411	3.1	157.0249	157.0258	5.7

Table S1 (continued)										
29	*Dimethylglycine*	HMDB00092	C4H9NO2	6.29	104.0712	104.0718	5.8	102.0555	102.0556	1
30	*Folic Acid*	HMDB00121	C19H19N7O6	9.13	-	-	-	440.1319	440.1312	-1.6
31	*Fructose**	HMDB00660	C6H12O6	5.8	203.0532	203.0537	2.5	179.0556	179.0552	-2.2
32	*Galactose**	HMDB00143	C6H12O6	7.62	203.0532	203.0541	4.4	179.0556	179.0568	6.7
33	*Glucose**	HMDB00122	C6H12O6	7.29	203.0532	203.0534	1	179.0556	179.0558	1.1
34	*Glutamic Acid*	HMDB00148	C5H9NO4	7.98	148.061	148.0613	2	146.0453	146.046	4.8
35	*Glutamine*	HMDB00641	C5H10N2O3	8.65	147.077	147.0776	4.1	145.0613	145.0617	2.8
36	*Glycine*	HMDB00123	C2H5NO2	7.25	76.0399	76.0405	7.9	74.0242	74.0245	4.1
37	*Guanine*	HMDB00132	C5H5N5O	6.15	152.0572	152.0583	7.2	150.0416	150.0411	-3.3
38	*Guanosine*	HMDB00133	C10H13N5O5	6.86	284.0995	284.0998	1.1	282.0838	282.0835	-1.1
39	*Hippuric Acid*	HMDB00714	C9H9NO3	1.79	180.0661	180.0665	2.2	178.0504	178.052	9
40	*Histidine*	HMDB00177	C6H9N3O2	10.63	156.0773	156.0773	0	154.0617	154.0614	-1.9
41	*Hydroxyproline*	HMDB00725	C5H9NO3	7.91	132.0661	132.0664	2.3	130.0504	130.0516	9.2
42	*Hypoxanthine*	HMDB00157	C5H4N4O	4.28	137.0463	137.0466	2.2	135.0307	135.0312	3.7
43	*Inosine*	HMDB00195	C10H12N4O5	5.39	269.0886	269.0892	2.2	267.0729	267.0736	2.6
44	*Inositol**	HMDB00211	C6H12O6	9.92	203.0532	203.0537	2.5	179.0556	179.0563	3.9
45	*Isoleucine*	HMDB00172	C6H13NO2	5.67	132.1025	132.1031	4.5	130.0868	130.0878	7.7
46	*Lactate*	HMDB00190	C3H6O3	1.93	-	-	-	89.0239	89.0247	9
47	*Lactose**	HMDB00186	C12H22O11	10.35	365.106	365.1071	3	341.1084	341.1079	-1.5
48	*Leucine*	HMDB00687	C6H13NO2	5.81	132.1025	132.1032	5.3	130.0868	130.0872	3.1
49	*Lysine*	HMDB00182	C6H14N2O2	11.05	147.1134	147.1113	-14.3	145.0977	145.098	2.1
50	*Malate*	HMDB00744	C4H6O5	2.97	-	-	-	133.0137	133.0141	3
51	*Maltose**	HMDB00163	C12H22O11	10.55	365.106	365.1057	-0.8	341.1084	341.1087	0.9
52	*Mannose**	HMDB01163	C6H12O6	6.47	203.0532	203.0539	3.4	179.0556	179.0552	-2.2
53	*Methionine*	HMDB00696	C5H11NO2S	6.12	150.0589	150.0601	8	148.0432	148.043	-1.4
54	*Nicotinamide*	HMDB01406	C6H6N2O	1.99	123.0558	123.0564	4.9	-	-	-
55	*Ornithine*	HMDB00214	C5H12N2O2	11	133.0977	133.0974	-2.3	131.0821	131.0825	3.1
56	*Orotate*	HMDB00226	C5H4N2O4	6.24	157.0249	157.0255	3.8	155.0093	155.009	-1.9
57	*Oxoproline*	HMDB00267	C5H7NO3	2.89	130.0504	130.051	4.6	128.0348	128.0352	3.1
58	*p-Aminobenzoic acid (PABA)*	HMDB01392	C7H7NO2	1.31	138.0555	138.0562	5.1	-	-	-
59	*Panthothenate*	HMDB00210	C9H17NO5	2.74	220.1185	220.1191	2.7	218.1028	218.1031	1.4
60	*Phenol red*	-	C19H14O5S	4.43	355.064	355.0645	1.4	353.0484	353.0497	3.7
61	*Phenylalanine*	HMDB00159	C9H11NO2	5.97	166.0868	166.0878	6	164.0712	164.0705	-4.3
62	*Proline*	HMDB00162	C5H9NO2	6.31	116.0712	116.0714	1.7	-	-	-

Table S1 (continued)										
63	*Pyridoxal*	HMDB01545	C8H9NO3	3.25	168.0661	168.0667	3.6	166.0504	166.0506	1.2
64	*Pyridoxamine*	HMDB01431	C8H12N2O2	6.95	169.0977	169.0978	0.6	167.0821	167.0817	-2.4
65	*Pyridoxate*	HMDB00017	C8H9NO4	4.4	184.061	184.0613	1.6	182.0453	182.0459	3.3
66	*Pyridoxine*	HMDB00239	C8H11NO3	4.26	170.0817	170.0819	1.2	168.0661	168.0666	3
67	*Pyruvate*	HMDB00243	C3H4O3	1.35	-	-	-	87.0082	87.0089	8
68	*Raffinose**	HMDB03213	C18H32O16	12.37	527.1588	527.1594	1.1	503.1612	503.1632	4
69	*Riboflavin*	HMDB00244	C17H20N4O6	5.53	377.1461	377.1466	1.3	375.1305	375.1313	2.1
70	*S-Adenosylhomocysteine (SAH)*	HMDB04145	C14H20N6O5S	10.01	385.1294	385.1311	4.4	383.1138	383.114	0.5
71	*SDMA*	HMDB01539	C8H18N4O2	8.72	203.1508	203.1513	2.5	201.1352	201.1357	2.5
72	*Serine*	HMDB00187	C3H7NO3	8.68	106.0504	106.0508	3.8	104.0348	104.035	1.9
73	*Succinate*	HMDB00254	C4H6O4	2.46	-	-	-	117.0188	117.0196	6.8
74	*Sucrose**	HMDB00258	C12H22O11	10.11	365.106	365.107	2.7	341.1084	341.1089	1.5
75	*Thiamine*	HMDB00235	C12H17N4OS	5.98	265.1123	265.1137	5.3	-	-	-
76	*Threonine*	HMDB00167	C4H9NO3	7.74	120.0661	120.0666	4.2	118.0504	118.051	5.1
77	*Thymine*	HMDB00262	C5H6N2O2	2.45	127.0508	127.0511	2.4	125.0351	125.0359	6.4
78	*Trehalose**	HMDB00975	C12H22O11	10.82	365.106	365.1059	-0.3	341.1084	341.1078	-1.8
79	*Tryptophan*	HMDB00929	C11H12N2O2	6	205.0977	205.0986	4.4	203.0821	203.0807	-6.9
80	*Tyrosine*	HMDB00158	C9H11NO3	6.41	182.0817	182.0825	4.4	-	-	-
81	*Uracil*	HMDB00300	C4H4N2O2	2.62	113.0351	113.0355	3.5	111.0195	111.0193	-1.8
82	*Uric acid*	HMDB00289	C5H4N4O3	7.42	169.0362	169.0368	3.5	167.0205	167.0207	1.2
83	*Uridine*	HMDB00296	C9H12N2O6	3.95	-	-	-	243.0617	243.0626	3.7
84	*Valine*	HMDB00883	C5H11NO2	6.12	118.0868	118.0878	8.5	116.0712	116.0708	-3.4
85	*Xanthine*	HMDB00292	C5H4N4O2	4.99	153.0413	153.042	4.6	151.0256	151.0263	4.6
86	*Xanthosine*	HMDB00299	C10H12N4O6	5.93	285.0835	285.085	5.3	283.0679	283.0669	-3.5

** Na adducts in positive mode*

Table S2. RPMI advanced medium composition

Components	Concentration	
Amino Acids	mg/L	mM
Glycine	10	0.133
L-Alanine	8.9	0.1
L-Arginine	200	1.15
L-Asparagine	50	0.379
L-Aspartic acid	20	0.15
L-Cystine 2HCl	65	0.208
L-Glutamic Acid	20	0.136
L-Histidine	15	0.0968
L-Hydroxyproline	20	0.153
L-Isoleucine	50	0.382
L-Leucine	50	0.382
L-Lysine hydrochloride	40	0.274
L-Methionine	15	0.101
L-Phenylalanine	15	0.0909
L-Proline	20	0.174
L-Serine	30	0.286
L-Threonine	20	0.168
L-Tryptophan	5	0.0245
L-Tyrosine disodium salt	29	0.129
L-Valine	20	0.171
Vitamins	mg/L	mM
Ascorbic Acid phosphate	2.5	0.00863
Biotin	0.2	0.00082
Choline chloride	3	0.0214
D-Calcium pantothenate	0.25	0.000524
Folic Acid	1	0.00227
Niacinamide	1	0.0082
Para-Aminobenzoic Acid	1	0.0073
Pyridoxine hydrochloride	1	0.00485
Riboflavin	0.2	0.000532

Table S2 (continued)		
Thiamine hydrochloride	1	0.00297
Vitamin B12	0.005	0.0000037
Myo-inositol	35	0.194
Inorganic Salts	mg/L	mM
Calcium nitrate (Ca(NO3)2 4H2O)	100	0.424
Magnesium Sulfate (MgSO4) (anhyd.)	48.84	0.407
Potassium Chloride (KCl)	400	5.33
Sodium Bicarbonate (NaHCO3)	2000	23.81
Sodium Chloride (NaCl)	6000	103.45
Sodium Phosphate dibasic (Na2HPO4) anhydrous	800	5.63
Zinc sulfate (ZnSO4-7H2O)	0.874	0.00303
Proteins	mg/L	mM
AlbuMAX® II	400	∞
Human Transferrin (Holo)	7.5	∞
Insulin Recombinant Full Chain	10	∞
Trace Elements	mg/L	mM
Ammonium Metavanadate	0.0003	0.0000026
Cupric Sulfate	0.00125	0.000005
Manganous Chloride	0.00005	0.0000003
Sodium Selenite	0.005	0.0000289
Other Components	mg/L	mM
D-Glucose (Dextrose)	2000	11.11
Ethanolamine	1.9	0.0195
Glutathione (reduced)	1	0.00326
Phenol Red	5	0.0133
Sodium Pyruvate	110	1
L-Alanyl-Glutamine*	434.2	2

Table S3. Predicted exo-metabolome composition. We employed the published reconstruction of human metabolism, deemed Recon 1[1] and downloaded from the BiGG database [2]. This reconstruction represents the overall metabolic network encoded by the human genome but not of a specific cell type. Briefly, it accounts for 3400 intracellular metabolic and transport reactions located in eight different cellular compartments and 415 'exchange reactions' representing the exchange of metabolites with the environment, e.g., culture medium or biofluid. Therefore, the cell-specific exo-metabolome is expected to contain far less metabolites. Also it is expected that this initial list of 415 metabolites is incomplete, since not all metabolic pathways present in cells are known [3]. In this study, the cell lines were grown in RPMI advanced medium, therefore, we reduced this initial exo-metabolome list by computing the metabolites that could be secreted by an *in silico* (generic) cell grown on this defined medium. Therefore, the RPMI medium composition (Table S2) was mapped onto the reconstruction as uptake rates, assuming a cellular dry weight of $0.5*10^{-9}$ g_{DW}/cell. All metabolites, with an exchange reaction in Recon 1, were allowed to be secreted. The set of possible secreted metabolites, given the RPMI medium composition, was determined using flux variability analysis [4]. The results of this analysis are shown in this table (lower bound and upper bound on reaction constraints are listed as well as the minimally and maximally possible flux through each exchange reaction). This analysis resulted in a set of 225 metabolites predicted to be present in the exo-metabolome. All units are given in $mmol.g_{dw}^{-1}.h^{-1}$. Metabolites that were not predicted to be part of exo-metabolome but identified by mass spec are highlighted in red. All computations were carried out in Matlab (version 7.9.0.529 (R2009b)) using Tomlab (TomOpt, Inc.) as linear programming solver (Cobra Toolbox v2)[5].

Reaction abbreviation	Metabolite abbreviation	Metabolite name	Charged formula*	Lower bound	Upper bound	minFlux	maxFlux
EX_so4(e)	so4	sulfate	O4S	-100.000	1000.000	-100.000	0.515
EX_nh4(e)	nh4	ammonium	H4N	-100.000	1000.000	-100.000	427.419
EX_co2(e)	co2	carbon dioxide	CO2	-100.000	1000.000	-100.000	519.638
EX_h2o(e)	h2o	water	H2O	-100.000	1000.000	-100.000	599.556
EX_h(e)	h	proton	H	-100.000	1000.000	-100.000	1000.000
EX_o2(e)	o2	dioxygen	O2	-40.000	1000.000	-40.000	0.000
EX_hco3(e)	hco3	hydrogencarbonate	CHO3	-39.683	1000.000	-39.683	450.376
EX_glc(e)	glc-D	D-glucose	C6H12O6	-18.517	1000.000	-18.517	173.293
EX_pi(e)	pi	hydrogenphosphate	HO4P	-9.383	1000.000	-9.383	0.000
EX_arg-L(e)	arg-L	L-argininium(1+)	C6H15N4O2	-1.917	1000.000	-1.917	0.000
EX_pyr(e)	pyr	pyruvate	C3H3O3	-1.667	1000.000	-1.667	476.291
EX_ile-L(e)	ile-L	L-isoleucine	C6H13NO2	-0.637	1000.000	-0.637	0.000
EX_leu-L(e)	leu-L	L-leucine	C6H13NO2	-0.637	1000.000	-0.637	0.000
EX_asp-L(e)	asp-L	L-aspartate(1-)	C4H6NO4	-0.632	1000.000	-0.632	0.000
EX_ser-L(e)	ser-L	L-serine	C3H7NO3	-0.477	1000.000	-0.477	428.477
EX_lys-L(e)	lys-L	L-Lysine	C6H15N2O2	-0.457	1000.000	-0.457	0.000
EX_cys-L(e)	cys-L	L-cysteine	C3H7NO2S	-0.347	1000.000	-0.347	0.168
EX_inost(e)	inost	myo-inositol	C6H12O6	-0.323	1000.000	-0.323	190.725
EX_pro-L(e)	pro-L	L-proline	C5H9NO2	-0.290	1000.000	-0.290	1000.000
EX_val-L(e)	val-L	L-valine	C5H11NO2	-0.285	1000.000	-0.285	0.000
EX_thr-L(e)	thr-L	L-threonine	C4H9NO3	-0.280	1000.000	-0.280	0.000
EX_asn-L(e)	asn-L	L-asparagine	C4H8N2O3	-0.250	1000.000	-0.250	345.178

Table S3 (continued)							
EX_glu-L(e)	glu-L	L-glutamate(1-)	C5H8NO4	-0.227	1000.000	-0.227	296.511
EX_gly(e)	gly	glycine	C2H5NO2	-0.222	1000.000	-0.222	412.634
EX_tyr-L(e)	tyr-L	L-tyrosine	C9H11NO3	-0.215	1000.000	-0.215	0.152
EX_met-L(e)	met-L	L-methionine	C5H11NO2S	-0.168	1000.000	-0.168	0.000
EX_ala-L(e)	ala-L	L-alanine	C3H7NO2	-0.167	1000.000	-0.167	670.676
EX_his-L(e)	his-L	L-histidine	C6H9N3O2	-0.161	1000.000	-0.161	0.000
EX_phe-L(e)	phe-L	L-phenylalanine	C9H11NO2	-0.152	1000.000	-0.152	0.000
EX_ncam(e)	ncam	nicotinamide	C6H6N2O	-0.137	1000.000	-0.137	0.000
EX_trp-L(e)	trp-L	L-tryptophan	C11H12N2O2	-0.041	1000.000	-0.041	0.000
EX_chol(e)	chol	choline	C5H14NO	-0.036	1000.000	-0.036	139.450
EX_ascb-L(e)	ascb-L	L-ascorbic acid	C6H8O6	-0.014	1000.000	-0.014	0.000
EX_pydxn(e)	pydxn	pyridoxine	C8H11NO3	-0.008	1000.000	-0.008	0.000
EX_gthrd(e)	gthrd	Reduced glutathione	C10H16N3O6S	-0.005	1000.000	-0.005	0.000
EX_thm(e)	thm	thiamine(1+)	C12H17N4OS	-0.005	1000.000	-0.005	0.000
EX_fol(e)	fol	Folate	C19H18N7O6	-0.004	1000.000	-0.004	0.000
EX_pnto-R(e)	pnto-R	(R)-Pantothenate	C9H16NO5	-0.001	1000.000	-0.001	0.000
EX_gthox(e)	gthox	Oxidized glutathione	C20H30N6O12S2	0.000	1000.000	0.000	0.003
EX_thf(e)	thf	5,6,7,8-Tetrahydrofolate	C19H21N7O6	0.000	1000.000	0.000	0.004
EX_5mthf(e)	5mthf	5-Methyltetrahydrofolate	C20H24N7O6	0.000	1000.000	0.000	0.004
EX_thmtp(e)	thmtp	Thiamin triphosphate	C12H16N4O10P3S	0.000	1000.000	0.000	0.005
EX_thmmp(e)	thmmp	thiamine(1+) monophosphate(2-)	C12H16N4O4PS	0.000	1000.000	0.000	0.005
EX_4pyrdx(e)	4pyrdx	4-pyridoxic acid	C8H9NO4	0.000	1000.000	0.000	0.008
EX_pydx(e)	pydx	pyridoxal	C8H9NO3	0.000	1000.000	0.000	0.008
EX_pydam(e)	pydam	Pyridoxamine	C8H13N2O2	0.000	1000.000	0.000	0.008
EX_dhdascb(e)	dhdascb	dehydroascorbic acid	C6H6O6	0.000	1000.000	0.000	0.014
EX_srtn(e)	srtn	Serotonin	C10H13N2O	0.000	1000.000	0.000	0.041
EX_5htrp(e)	5htrp	5-hydroxy-L-tryptophan	C11H12N2O3	0.000	1000.000	0.000	0.041
EX_pheacgln(e)	pheacgln	N(2)-phenylacetyl-L-glutamine	C13H16N2O4	0.000	1000.000	0.000	0.152
EX_3mlda(e)	3mlda	3-Methylimidazoleacetic acid	C6H7N2O2	0.000	1000.000	0.000	0.161
EX_hista(e)	hista	Histamine	C5H10N3	0.000	1000.000	0.000	0.161
EX_1mncam(e)	1mncam	1-methylnicotinamide	C7H9N2O	0.000	1000.000	0.000	0.177
EX_mercplaccys(e)	mercplaccys	3-mercaptolactate-cysteine disulfide	C6H10O5S2N	0.000	1000.000	0.000	0.257
EX_3aib(e)	3aib	(S)-3-aminoisobutyric acid	C4H9NO2	0.000	1000.000	0.000	0.285
EX_nrpphr(e)	nrpphr	Norepinephrine	C8H12NO3	0.000	1000.000	0.000	0.366
EX_34dhoxpeg(e)	34dhoxpeg	3,4-Dihydroxyphenylethyleneglycol	C8H10O4	0.000	1000.000	0.000	0.367
EX_4hphac(e)	4hphac	4-Hydroxyphenylacetate	C8H7O3	0.000	1000.000	0.000	0.367
EX_adrnl(e)	adrnl	Adrenaline	C9H14NO3	0.000	1000.000	0.000	0.367
EX_dopasf(e)	dopasf	dopamine 3-O-sulfate	C8H11NO5S	0.000	1000.000	0.000	0.367
EX_34dhphe(e)	34dhphe	L-dopa	C9H11NO4	0.000	1000.000	0.000	0.367
EX_mepi(e)	mepi	Metanephrine	C10H16NO3	0.000	1000.000	0.000	0.367
EX_nrpphrsf(e)	nrpphrsf	Sulfate derivative of norepinephrine	C8H11NO6S	0.000	1000.000	0.000	0.367
EX_tymsf(e)	tymsf	Tyramine O-sulfate	C8H11NO4S	0.000	1000.000	0.000	0.367
EX_dopa(e)	dopa	Dopamine	C8H12NO2	0.000	1000.000	0.000	0.367
EX_2hb(e)	2hb	2-Hydroxybutyrate	C4H7O3	0.000	1000.000	0.000	0.448
EX_2mcit(e)	2mcit	2-methylcitrate(3-)	C7H7O7	0.000	1000.000	0.000	0.448
EX_cgly(e)	cgly	L-cysteinylglycine	C5H10N2O3S	0.000	1000.000	0.000	0.515
EX_o2s(e)	o2s	superoxide	O2	0.000	1000.000	0.000	0.800

Table S3 (continued)							
EX_ksii_core2(e)	ksii_core2	keratan sulfate II (core 2-linked)	C81H129N6O67S3X	0.000	1000.000	0.000	1.000
EX_ksii_core4(e)	ksii_core4	keratan sulfate II (core 4-linked)	C89H142N7O72S3X	0.000	1000.000	0.000	1.000
EX_hestratriol(e)	hestratriol	4,17 dihydroxy estradiol	C18H24O3	0.000	1000.000	0.000	2.581
EX_gchola(e)	gchola	glycocholic acid	C26H43NO6	0.000	1000.000	0.000	2.667
EX_tchola(e)	tchola	taurocholic acid	C26H45NO7S	0.000	1000.000	0.000	2.667
EX_dgchol(e)	dgchol	glycochenodeoxycholic acid	C26H43NO5	0.000	1000.000	0.000	2.667
EX_estradiolglc(e)	estradiolglc	17beta-estradiol 3-glucosiduronic acid	C24H32O8	0.000	1000.000	0.000	2.759
EX_estroneglc(e)	estroneglc	estrone 3-glucosiduronic acid	C24H30O8	0.000	1000.000	0.000	2.759
EX_estrones(e)	estrones	Estrone 3-sulfate	C18H21O5S	0.000	1000.000	0.000	2.759
EX_estradiol(e)	estradiol	estradiol	C18H24O2	0.000	1000.000	0.000	2.759
EX_aldstrn(e)	aldstrn	aldosterone	C21H28O5	0.000	1000.000	0.000	2.857
EX_crtsl(e)	crtsl	cortisol	C21H30O5	0.000	1000.000	0.000	2.857
EX_gdchola(e)	gdchola	glycochenodeoxycholic acid	C26H43NO5	0.000	1000.000	0.000	2.857
EX_tdchola(e)	tdchola	taurochenodeoxycholic acid	C26H45NO6S	0.000	1000.000	0.000	2.857
EX_6htststerone(e)	6htststerone	6 beta hydroxy testosterone	C19H28O3	0.000	1000.000	0.000	2.963
EX_crtstrn(e)	crtstrn	corticosterone	C21H30O4	0.000	1000.000	0.000	3.077
EX_5adtststerone(e)	5adtststerone	17beta-hydroxy-5alpha-androstan-3-one	C19H30O2	0.000	1000.000	0.000	3.200
EX_5adtststeroneglc(e)	5adtststeroneglc	5alpha-Dihydrotestosterone glucuronide	C25H38O8	0.000	1000.000	0.000	3.200
EX_5adtststerones(e)	5adtststerones	5alpha-Dihydrotestosterone sulfate	C19H29O5S	0.000	1000.000	0.000	3.200
EX_andrstrn(e)	andrstrn	androsterone	C19H30O2	0.000	1000.000	0.000	3.200
EX_andrstrnglc(e)	andrstrnglc	androsterone 3-glucosiduronic acid	C25H38O8	0.000	1000.000	0.000	3.200
EX_dheas(e)	dheas	Dehydroepiandrosterone sulfate	C19H27O5S	0.000	1000.000	0.000	3.200
EX_tststerone(e)	tststerone	testosterone	C19H28O2	0.000	1000.000	0.000	3.200
EX_tststeroneglc(e)	tststeroneglc	testosterone 3-glucosiduronic acid	C25H36O8	0.000	1000.000	0.000	3.200
EX_tststerones(e)	tststerones	testosterone sulfate	C19H27O5S	0.000	1000.000	0.000	3.200
EX_aprgstrn(e)	aprgstrn	(20S)-20-hydroxypregn-4-en-3-one	C21H32O2	0.000	1000.000	0.000	3.636
EX_2425dhvitd3(e)	2425dhvitd3	(24R)-24,25-dihydroxycalciol	C27H44O3	0.000	1000.000	0.000	3.636
EX_xoltri24(e)	xoltri24	(24S)-7alpha,24-dihydroxycholesterol	C27H46O3	0.000	1000.000	0.000	3.636
EX_4mptnl(e)	4mptnl	4-methylpentanal	C6H12O	0.000	1000.000	0.000	3.636
EX_xoltri25(e)	xoltri25	7alpha,25-dihydroxycholesterol	C27H46O3	0.000	1000.000	0.000	3.636
EX_xoltri27(e)	xoltri27	7alpha,26-dihydroxycholesterol	C27H46O3	0.000	1000.000	0.000	3.636
EX_prgstrn(e)	prgstrn	progesterone	C21H30O2	0.000	1000.000	0.000	3.636
EX_25hvitd3(e)	25hvitd3	calcidiol	C27H44O2	0.000	1000.000	0.000	4.000
EX_vitd3(e)	vitd3	calciol	C27H44O	0.000	1000.000	0.000	4.444
EX_chsterol(e)	chsterol	cholesterol	C27H46O	0.000	1000.000	0.000	4.444
EX_xolest_hs(e)	xolest_hs	cholesterol ester	C27H45XCO2	0.000	1000.000	0.000	4.444
EX_xolest2_hs(e)	xolest2_hs	cholesterol ester	C27H45FULLR2CO2	0.000	1000.000	0.000	4.444
EX_bildglcur(e)	bildglcur	Bilirubin beta-diglucuronide	C45H50N4O18	0.000	1000.000	0.000	7.273
EX_bilglcur(e)	bilglcur	mono(glucosyluronic acid)bilirubin	C39H44N4O12	0.000	1000.000	0.000	7.273
EX_bilirub(e)	bilirub	Bilirubin	C33H34N4O6	0.000	1000.000	0.000	7.273
EX_co(e)	co	carbon monoxide	CO	0.000	1000.000	0.000	7.273
EX_lpchol_hs(e)	lpchol_hs	lysophosphatidylcholine	C8H19NO5PFULLRCO2	0.000	1000.000	0.000	9.383
EX_pglyc_hs(e)	pglyc_hs	phosphatidylglycerol	C6H12O6PFULLRCO2FULLR2CO2	0.000	1000.000	0.000	9.383
EX_sphs1p(e)	sphs1p	Sphingosine 1-phosphate	C18H37NO5P	0.000	1000.000	0.000	9.383
EX_pe_hs(e)	pe_hs	phosphatidylethanolamine	C5H12NO4PFULLRCO2FULLR2CO2	0.000	1000.000	0.000	9.383
EX_camp(e)	camp	cAMP	C10H11N5O6P	0.000	1000.000	0.000	9.383
EX_pchol_hs(e)	pchol_hs	Phosphatidylcholine	C8H18NO4PFULLRCO2FULLR2CO2	0.000	1000.000	0.000	9.383

Table S3 (continued)							
EX_spc_hs(e)	spc_hs	sphingosylphosphorylcholine	C23H50N2O5P	0.000	1000.000	0.000	9.383
EX_sph1p(e)	sph1p	Sphinganine 1-phosphate	C18H39NO5P	0.000	1000.000	0.000	9.383
EX_35cgmp(e)	35cgmp	3,5-Cyclic GMP	C10H11N5O7P	0.000	1000.000	0.000	9.383
EX_1glyc_hs(e)	1glyc_hs	1 acyl phosphoglycerol	C6H13O7PFULLRCO2	0.000	1000.000	0.000	9.383
EX_crmp_hs(e)	crmp_hs	Ceramide 1-phosphate	C18H35NO5PFULLRCO	0.000	1000.000	0.000	9.383
EX_ps_hs(e)	ps_hs	phosphatidylserine	C6H11NO6PFULLRCO2FULLR2CO2	0.000	1000.000	0.000	9.383
EX_galgalfucfucgalacglcgalacglcgal14acglcgalgluside_hs(e)	galgalfucfucgalacglcgalacglcgal14acglcgalgluside_hs	(Gal)6 (Glc)1 (GlcNAc)3 (LFuc)2 (Cer)1	C96H165N4O60FULLRCO	0.000	1000.000	0.000	16.494
EX_acgalfucgalacgalfucgalacglcgal14acglcgalgluside_hs(e)	acgalfucgalacgalfucgalacglcgal14acglcgalgluside_hs	Type IIIAb	C92H158N5O55FULLRCO	0.000	1000.000	0.000	17.605
EX_gp1c_hs(e)	gp1c_hs	GP1c	C99H159N7O62FULLRCO	0.000	1000.000	0.000	17.730
EX_gp1calpha_hs(e)	gp1calpha_hs	GP1c alpha	C99H159N7O62FULLRCO	0.000	1000.000	0.000	17.730
EX_fucfucfucgalacglc13galacglcgal14acglcgalgluside_hs(e)	fucfucfucgalacglc13galacglcgal14acglcgalgluside_hs	(Gal)4 (Glc)1 (GlcNAc)3 (LFuc)3 (Cer)1	C90H155N4O54FULLRCO	0.000	1000.000	0.000	17.894
EX_gq1balpha_hs(e)	gq1balpha_hs	GQ1balpha	C88H143N6O54FULLRCO	0.000	1000.000	0.000	19.428
EX_gq1b_hs(e)	gq1b_hs	GQ1b	C88H143N6O54FULLRCO	0.000	1000.000	0.000	19.428
EX_lneldc(e)	lneldc	linoelaidic acid (all trans C18:2)	C18H31O2	0.000	1000.000	0.000	20.000
EX_no(e)	no	nitrosyl	NO	0.000	1000.000	0.000	20.000
EX_acgalfucgalacgalfuc12gal14acglcgalgluside_hs(e)	acgalfucgalacgalfuc12gal14acglcgalgluside_hs	Type IIIA glycolipid	C78H135N4O45FULLRCO	0.000	1000.000	0.000	20.324
EX_fucfucfucgalacglcgal14acglcgalgluside_hs(e)	fucfucfucgalacglcgal14acglcgalgluside_hs	(Gal)3 (Glc)1 (GlcNAc)2 (LFuc)3 (Cer)1	C76H132N3O44FULLRCO	0.000	1000.000	0.000	20.711
EX_gt1a_hs(e)	gt1a_hs	GT1a	C77H127N5O46FULLRCO	0.000	1000.000	0.000	21.443
EX_galfucgalacglcgal14acglcgalgluside_hs(e)	galfucgalacglcgal14acglcgalgluside_hs	(Gal)4 (Glc)1 (GlcNAc)2 (LFuc)1 (Cer)1	C70H122N3O41FULLRCO	0.000	1000.000	0.000	21.800
EX_acnacngalgbside_hs(e)	acnacngalgbside_hs	disialyl galactosylgloboside	C72H121N4O43FULLRCO	0.000	1000.000	0.000	22.081
EX_acn13acngalgbside_hs(e)	acn13acngalgbside_hs	sialyl (1,3) sialyl (2,6) galactosylgloboside	C72H121N4O43FULLRCO	0.000	1000.000	0.000	22.081
EX_acn23acngalgbside_hs(e)	acn23acngalgbside_hs	sialyl (2,3) sialyl (2,6) galactosylgloboside	C72H121N4O43FULLRCO	0.000	1000.000	0.000	22.081
EX_fucfuc132galacglcgal14acglcgalgluside_hs(e)	fucfuc132galacglcgal14acglcgalgluside_hs	V3Fuc,III3Fuc-nLc6Cer	C70H122N3O40FULLRCO	0.000	1000.000	0.000	22.099
EX_acngalacglcgal14acglcgalgluside_hs(e)	acngalacglcgal14acglcgalgluside_hs	VI3NeuAc-nLc6Cer	C69H118N4O40FULLRCO	0.000	1000.000	0.000	22.548
EX_galacglcgalgbside_hs(e)	galacglcgalgbside_hs	Gal-GlcNAc-Gal globoside	C64H112N3O37FULLRCO	0.000	1000.000	0.000	23.255
EX_fuc13galacglcgal14acglcgalgluside_hs(e)	fuc13galacglcgal14acglcgalgluside_hs	III3Fuc-nLc6Cer	C64H112N3O36FULLRCO	0.000	1000.000	0.000	23.595

Table S3 (continued)							
EX_acnacngal14acglcgalgluside_hs(e)	acnacngal14acglcgalgluside_hs	3,8-LD1	C66H111N4O38FULLRCO	0.000	1000.000	0.000	23.925
EX_gd1b2_hs(e)	gd1b2_hs	GD1beta	C66H111N4O38FULLRCO	0.000	1000.000	0.000	23.925
EX_gd1c_hs(e)	gd1c_hs	GD1c	C66H111N4O38FULLRCO	0.000	1000.000	0.000	23.925
EX_fucacgalfucgalacglcgalgluside_hs(e)	fucacgalfucgalacglcgalgluside_hs	(Gal)2 (GalNAc)1 (Glc)1 (GlcNAc)1 (LFuc)2 (Cer)1	C64H112N3O35FULLRCO	0.000	1000.000	0.000	23.946
EX_fucgalfucgalacglcgalgluside_hs(e)	fucgalfucgalacglcgalgluside_hs	(Gal)3 (Glc)1 (GlcNAc)1 (LFuc)2 (Cer)1	C62H109N2O35FULLRCO	0.000	1000.000	0.000	24.184
EX_oagt3_hs(e)	oagt3_hs	9-O-Acetylated GT3	C65H106N4O37FULLRCO	0.000	1000.000	0.000	25.104
EX_fucacngalacglcgalgluside_hs(e)	fucacngalacglcgalgluside_hs	IV3-a-Neu5Ac,III4-a-Fuc-Lc4Cer	C61H105N3O34FULLRCO	0.000	1000.000	0.000	25.108
EX_fucacngal14acglcgalgluside_hs(e)	fucacngal14acglcgalgluside_hs	IV3-a-NeuAc,III3-a-Fuc-nLc4Cer	C61H105N3O34FULLRCO	0.000	1000.000	0.000	25.108
EX_galgalgalthcrm_hs(e)	galgalgalthcrm_hs	Gal-Gal-Gal-Gal-Gal-Glc-Cer	C54H96NO32FULLRCO	0.000	1000.000	0.000	25.847
EX_fucgalgbside_hs(e)	fucgalgbside_hs	fucosyl galactosylgloboside	C56H99N2O31FULLRCO	0.000	1000.000	0.000	25.988
EX_galfuc12gal14acglcgalgluside_hs(e)	galfuc12gal14acglcgalgluside_hs	(Gal)3 (Glc)1 (GlcNAc)1 (LFuc)1 (Cer)1	C56H99N2O31FULLRCO	0.000	1000.000	0.000	25.988
EX_fucfucgalacglcgalgluside_hs(e)	fucfucgalacglcgalgluside_hs	Leb glycolipid	C56H99N2O30FULLRCO	0.000	1000.000	0.000	26.414
EX_fucfuc12gal14acglcgalgluside_hs(e)	fucfuc12gal14acglcgalgluside_hs	Ley glycolipid	C56H99N2O30FULLRCO	0.000	1000.000	0.000	26.414
EX_oagd3_hs(e)	oagd3_hs	9-O-Acetylated GD3	C54H90N3O29FULLRCO	0.000	1000.000	0.000	28.575
EX_fucgal14acglcgalgluside_hs(e)	fucgal14acglcgalgluside_hs	Lacto-N-fucopentaosyl III ceramide	C50H89N2O26FULLRCO	0.000	1000.000	0.000	28.580
EX_fuc14galacglcgalgluside_hs(e)	fuc14galacglcgalgluside_hs	Lea glycolipid	C50H89N2O26FULLRCO	0.000	1000.000	0.000	28.580
EX_gbside_hs(e)	gbside_hs	globoside	C44H79N2O22FULLRCO	0.000	1000.000	0.000	30.753
EX_tag_hs(e)	tag_hs	triglyceride	C3H5FULLRCO2FULLR2CO2FULLR3CO2	0.000	1000.000	0.000	35.675
EX_h2o2(e)	h2o2	hydrogen peroxide	H2O2	0.000	1000.000	0.000	40.000
EX_whhdca(e)	whhdca	omega hydroxy hexadecanoate (n-C16:0)	C16H31O3	0.000	1000.000	0.000	40.000
EX_elaid(e)	elaid	elaidate	C18H33O2	0.000	1000.000	0.000	40.000
EX_hdcea(e)	hdcea	palmitoleate	C16H29O2	0.000	1000.000	0.000	40.000
EX_vacc(e)	vacc	trans-vaccenate	C18H33O2	0.000	1000.000	0.000	40.000
EX_ha(e)	ha	hyaluronan	C28H40N2O22	0.000	1000.000	0.000	52.069
EX_dag_hs(e)	dag_hs	diglyceride	C3H6OFULLRCO2FULLR2CO2	0.000	1000.000	0.000	52.191
EX_fuc-L(e)	fuc-L	L-fucose	C6H12O5	0.000	1000.000	0.000	70.082
EX_oxa(e)	oxa	oxalate(2-)	C2O4	0.000	1000.000	0.000	80.000
EX_glyc-S(e)	glyc-S	(S)-Glycerate	C3H5O4	0.000	1000.000	0.000	80.000
EX_urate(e)	urate	7,9-dihydro-1H-purine-2,6,8(3H)-trione	C5H4N4O3	0.000	1000.000	0.000	80.000
EX_3aib-D(e)	3aib-D	D-3-Amino-isobutanoate	C4H9NO2	0.000	1000.000	0.000	81.218
EX_duri(e)	duri	2-deoxyuridine	C9H12N2O5	0.000	1000.000	0.000	81.218
EX_cytd(e)	cytd	cytidine	C9H13N3O5	0.000	1000.000	0.000	81.218
EX_thym(e)	thym	thymine	C5H6N2O2	0.000	1000.000	0.000	81.218
EX_ura(e)	ura	uracil	C4H4N2O2	0.000	1000.000	0.000	81.218
EX_dcyt(e)	dcyt	2-deoxycytidine	C9H13N3O4	0.000	1000.000	0.000	81.218
EX_uri(e)	uri	uridine	C9H12N2O6	0.000	1000.000	0.000	81.218

Table S3 (continued)							
EX_mag_hs(e)	mag_hs	monoacylglycerol 2	C3H7O2FULLR2CO2	0.000	1000.000	0.000	94.534
EX_gsn(e)	gsn	guanosine	C10H13N5O5	0.000	1000.000	0.000	94.589
EX_dgsn(e)	dgsn	2-deoxyguanosine	C10H13N5O4	0.000	1000.000	0.000	98.745
EX_lcts(e)	lcts	lactose	C12H22O11	0.000	1000.000	0.000	98.862
EX_sl-L(e)	sl-L	L-sulfolactate	C3H4O6S	0.000	1000.000	0.000	100.515
EX_taur(e)	taur	taurine	C2H7NO3S	0.000	1000.000	0.000	100.515
EX_ha_pre1(e)	ha_pre1	hyaluronan biosynthesis, precursor 1	C14H20NO11	0.000	1000.000	0.000	104.138
EX_adn(e)	adn	adenosine	C10H13N5O4	0.000	1000.000	0.000	107.143
EX_gua(e)	gua	guanine	C5H5N5O	0.000	1000.000	0.000	108.522
EX_dad-2(e)	dad-2	2-deoxyadenosine	C10H13N5O3	0.000	1000.000	0.000	111.901
EX_hdca(e)	hdca	palmitate	C16H31O2	0.000	1000.000	0.000	112.098
EX_Rtotal(e)	Rtotal	R total	CO2FULLR	0.000	1000.000	0.000	112.702
EX_Rtotal3(e)	Rtotal3	R total 3 position	CO2FULLR3	0.000	1000.000	0.000	112.702
EX_Rtotal2(e)	Rtotal2	R total 2 position	CO2FULLR2	0.000	1000.000	0.000	112.702
EX_ins(e)	ins	inosine	C10H12N4O5	0.000	1000.000	0.000	112.716
EX_din(e)	din	2-deoxyinosine	C10H12N4O4	0.000	1000.000	0.000	120.885
EX_ade(e)	ade	adenine	C5H5N5	0.000	1000.000	0.000	124.017
EX_glyb(e)	glyb	glycine betaine	C5H11NO2	0.000	1000.000	0.000	124.264
EX_ach(e)	ach	acetylcholine	C7H16NO2	0.000	1000.000	0.000	127.444
EX_hxan(e)	hxan	hypoxanthine	C5H4N4O	0.000	1000.000	0.000	138.455
EX_xylt(e)	xylt	xylitol	C5H12O5	0.000	1000.000	0.000	165.258
EX_abt(e)	abt	L-arabinitol	C5H12O5	0.000	1000.000	0.000	165.258
EX_man(e)	man	D-mannose	C6H12O6	0.000	1000.000	0.000	173.062
EX_gal(e)	gal	D-galactose	C6H12O6	0.000	1000.000	0.000	175.002
EX_fru(e)	fru	D-fructose	C6H12O6	0.000	1000.000	0.000	191.809
EX_glyc(e)	glyc	glycerol	C3H8O3	0.000	1000.000	0.000	195.568
EX_cit(e)	cit	citrate(3-)	C6H5O7	0.000	1000.000	0.000	215.534
EX_akg(e)	akg	2-oxoglutarate(2-)	C5H4O5	0.000	1000.000	0.000	217.312
EX_drib(e)	drib	2-deoxy-D-ribose	C5H10O4	0.000	1000.000	0.000	242.262
EX_gluala(e)	gluala	5-L-Glutamyl-L-alanine	C8H13N2O5	0.000	1000.000	0.000	288.874
EX_acac(e)	acac	acetoacetate	C4H5O3	0.000	1000.000	0.000	312.062
EX_acetone(e)	acetone	acetone	C3H6O	0.000	1000.000	0.000	312.062
EX_4abut(e)	4abut	gamma-aminobutyric acid	C4H9NO2	0.000	1000.000	0.000	318.266
EX_for(e)	for	formate	CH1O2	0.000	1000.000	0.000	346.395
EX_gln-L(e)	gln-L	L-glutamine	C5H10N2O3	0.000	1000.000	0.000	347.275
EX_bhb(e)	bhb	(R)-3-hydroxybutyrate	C4H7O3	0.000	1000.000	0.000	353.847
EX_succ(e)	succ	succinate(2-)	C4H4O4	0.000	1000.000	0.000	445.448
EX_lac-D(e)	lac-D	(R)-lactate	C3H5O3	0.000	1000.000	0.000	469.331
EX_lac-L(e)	lac-L	(S)-lactate	C3H5O3	0.000	1000.000	0.000	469.331
EX_creat(e)	creat	creatine	C4H9N3O2	0.000	1000.000	0.000	479.399
EX_ac(e)	ac	acetate	C2H3O2	0.000	1000.000	0.000	520.617
EX_mthgxl(e)	mthgxl	methylglyoxal	C3H4O2	0.000	1000.000	0.000	528.091
EX_acald(e)	acald	acetaldehyde	C2H4O	0.000	1000.000	0.000	535.261
EX_ala-B(e)	ala-B	beta-alanine	C3H7NO2	0.000	1000.000	0.000	621.633
EX_ala-D(e)	ala-D	D-alanine	C3H7NO2	0.000	1000.000	0.000	670.843
EX_meoh(e)	meoh	methanol	CH4O1	0.000	1000.000	0.000	671.593
EX_urea(e)	urea	urea	CH4N2O	0.000	1000.000	0.000	1000.000

Table S3 (continued)							
EX_carveol(e)	carveol	(-)-trans-carveol	C10H16O	0.000	1000.000	0.000	0.000
EX_appnn(e)	appnn	(+)-alpha-pinene	C10H16	0.000	1000.000	0.000	0.000
EX_avite1(e)	avite1	(+)-alpha-tocopherol	C29H50O2	0.000	1000.000	0.000	0.000
EX_crn(e)	crn	(R)-carnitine	C7H15NO3	0.000	1000.000	0.000	0.000
EX_10fthf(e)	10fthf	10-Formyltetrahydrofolate	C20H21N7O7	0.000	1000.000	0.000	0.000
EX_10fthf5glu(e)	10fthf5glu	10-formyltetrahydrofolate-[Glu](5)	C40H45N11O19	0.000	1000.000	0.000	0.000
EX_10fthf6glu(e)	10fthf6glu	10-formyltetrahydrofolate-[Glu](6)	C45H51N12O22	0.000	1000.000	0.000	0.000
EX_10fthf7glu(e)	10fthf7glu	10-formyltetrahydrofolate-[Glu](7)	C50H57N13O25	0.000	1000.000	0.000	0.000
EX_retinol-cis-11(e)	retinol-cis-11	11-cis-retinol	C20H30O	0.000	1000.000	0.000	0.000
EX_13-cis-retnglc(e)	13-cis-retnglc	13-cis-retinoyl glucuronide	C26H35O8	0.000	1000.000	0.000	0.000
EX_estriolglc(e)	estriolglc	16-Glucuronide-estriol	C24H32O9	0.000	1000.000	0.000	0.000
EX_paf_hs(e)	paf_hs	1-alkyl 2-acteylglycerol 3-phosphocholine	C11H23O4NPFULLRCO2	0.000	1000.000	0.000	0.000
EX_ak2lgchol_hs(e)	ak2lgchol_hs	1-alkyl 2-lysoglycerol 3-phosphocholine	C10H21O5NPFULLR	0.000	1000.000	0.000	0.000
EX_dmhptcrn(e)	dmhptcrn	2,6 dimethylheptanoyl carnitine	C16H35NO4	0.000	1000.000	0.000	0.000
EX_2425dhvitd2(e)	2425dhvitd2	24R,25-Dihyoxyvitamin D2	C28H44O3	0.000	1000.000	0.000	0.000
EX_25hvitd2(e)	25hvitd2	25-Hydroxyvitamin D2	C28H44O2	0.000	1000.000	0.000	0.000
EX_triodthy(e)	triodthy	3,3,5-triiodo-L-thyronine	C15H12I3NO4	0.000	1000.000	0.000	0.000
EX_ahandrostanglc(e)	ahandrostanglc	3alpha-hydroxy-5beta-androstan-17-one 3-glucosiduronic acid	C25H38O8	0.000	1000.000	0.000	0.000
EX_4hdebrisoquine(e)	4hdebrisoquine	4 hydroxy debrisoquine	C10H14N3O	0.000	1000.000	0.000	0.000
EX_4mtolbutamide(e)	4mtolbutamide	4 hydroxy tolbutamide	C12H18N2O4S	0.000	1000.000	0.000	0.000
EX_24nph(e)	24nph	4-nitrocatechol	C6H5NO4	0.000	1000.000	0.000	0.000
EX_4nph(e)	4nph	4-nitrophenol	C6H5NO3	0.000	1000.000	0.000	0.000
EX_4nphsf(e)	4nphsf	4-Nitrophenyl sulfate	C6H4NO6S	0.000	1000.000	0.000	0.000
EX_5homeprazole(e)	5homeprazole	5 hydroxy omeprazole	C17H19N3O4S	0.000	1000.000	0.000	0.000
EX_dad-5(e)	dad-5	5-deoxyadenosine	C10H13N5O3	0.000	1000.000	0.000	0.000
EX_5fthf(e)	5fthf	5-Formyltetrahydrofolate	C20H21N7O7	0.000	1000.000	0.000	0.000
EX_htaxol(e)	htaxol	6 alpha hydroxy taxol/ 6 alpha hydroxy paclitaxel	C47H31NO15	0.000	1000.000	0.000	0.000
EX_dhf(e)	dhf	7,8-Dihydrofolate	C19H19N7O6	0.000	1000.000	0.000	0.000
EX_retinol-9-cis(e)	retinol-9-cis	9-cis-retinol	C20H30O	0.000	1000.000	0.000	0.000
EX_adprib(e)	adprib	ADPribose	C15H21N5O14P2	0.000	1000.000	0.000	0.000
EX_adprbp(e)	adprbp	ADPribose 2-phosphate	C15H20N5O17P3	0.000	1000.000	0.000	0.000
EX_adrn(e)	adrn	adrenic acid	C22H35O2	0.000	1000.000	0.000	0.000
EX_aflatoxin(e)	aflatoxin	aflatoxin B1	C17H12O6	0.000	1000.000	0.000	0.000
EX_eaflatoxin(e)	eaflatoxin	aflatoxin B1 exo-8,9-epoxide	C17H12O7	0.000	1000.000	0.000	0.000
EX_xyl-D(e)	xyl-D	aldehydo-D-xylose	C5H10O5	0.000	1000.000	0.000	0.000
EX_retn(e)	retn	all-trans-retinoate	C20H27O2	0.000	1000.000	0.000	0.000
EX_retpalm(e)	retpalm	all-trans-retinyl palmitate		0.000	1000.000	0.000	0.000
EX_lnlnca(e)	lnlnca	alpha-linolenate	C18H29O2	0.000	1000.000	0.000	0.000
EX_apnnox(e)	apnnox	alpha-pinene oxide	C10H16O	0.000	1000.000	0.000	0.000
EX_avite2(e)	avite2	alpha-tocotrienol	C29H44O2	0.000	1000.000	0.000	0.000
EX_amp(e)	amp	AMP	C10H12N5O7P	0.000	1000.000	0.000	0.000
EX_antipyrene(e)	antipyrene	antipyrine	C11H12N2O	0.000	1000.000	0.000	0.000
EX_aqcobal(e)	aqcobal	Aquacob(III)alamin	C62H93CoN13O15P	0.000	1000.000	0.000	0.000
EX_arach(e)	arach	arachidate	C20H39O2	0.000	1000.000	0.000	0.000
EX_arachd(e)	arachd	arachidonate	C20H31O2	0.000	1000.000	0.000	0.000

Table S3 (continued)							
EX_atp(e)	atp	ATP(4-)	C10H12N5O13P3	0.000	1000.000	0.000	0.000
EX_bz(e)	bz	benzoate	C7H5O2	0.000	1000.000	0.000	0.000
EX_caro(e)	caro	beta-carotene	C40H56	0.000	1000.000	0.000	0.000
EX_bvite(e)	bvite	beta-tocopherol	C28H48O2	0.000	1000.000	0.000	0.000
EX_biocyt(e)	biocyt	Biocytin	C16H28N4O4S	0.000	1000.000	0.000	0.000
EX_btn(e)	**btn**	**Biotin**	**C10H15N2O3S**	**-0.001**	**1000.000**	**0.000**	**0.000**
EX_but(e)	but	butyrate	C4H7O2	0.000	1000.000	0.000	0.000
EX_cca_d3(e)	cca_d3	Calcitroic acid (D3)	C22H33O4	0.000	1000.000	0.000	0.000
EX_ca2(e)	ca2	calcium(2+)	Ca	-0.707	1000.000	0.000	0.000
EX_hexc(e)	hexc	cerotate	C26H51O2	0.000	1000.000	0.000	0.000
EX_crvnc(e)	crvnc	cervonic acid, C22:6 n-3	C22H31O2	0.000	1000.000	0.000	0.000
EX_chtn(e)	chtn	chitin	C24H41N3O16	0.000	1000.000	0.000	0.000
EX_cl(e)	cl	chloride	Cl	0.000	1000.000	0.000	0.000
EX_cholate(e)	cholate	cholate	C24H39O5	0.000	1000.000	0.000	0.000
EX_cspg_a(e)	cspg_a	chondroitin sulfate A (GalNAc4S-GlcA) proteoglycan	C45H66N2O45S3X	0.000	1000.000	0.000	0.000
EX_cspg_b(e)	cspg_b	chondroitin sulfate B / dermatan sulfate (IdoA2S-GalNAc4S) proteoglycan	C45H65N2O48S4X	0.000	1000.000	0.000	0.000
EX_cspg_c(e)	cspg_c	chondroitin sulfate C (GalNAc6S-GlcA) proteoglycan	C45H66N2O45S3X	0.000	1000.000	0.000	0.000
EX_cspg_d(e)	cspg_d	chondroitin sulfate D (GlcNAc6S-GlcA2S) proteoglycan	C45H64N2O51S5X	0.000	1000.000	0.000	0.000
EX_cspg_e(e)	cspg_e	chondroitin sulfate E (GalNAc4,6diS-GlcA) proteoglycan	C45H63N2O54S6X	0.000	1000.000	0.000	0.000
EX_cmp(e)	cmp	CMP	C9H12N3O8P	0.000	1000.000	0.000	0.000
EX_coumarin(e)	coumarin	coumarin	C9H6O2	0.000	1000.000	0.000	0.000
EX_csn(e)	csn	cytosine	C4H5N3O	0.000	1000.000	0.000	0.000
EX_asp-D(e)	asp-D	D-aspartate(1-)	C4H6NO4	0.000	1000.000	0.000	0.000
EX_debrisoquine(e)	debrisoquine	debrisoquine	C10H14N3	0.000	1000.000	0.000	0.000
EX_s2l2n2m2masn(e)	s2l2n2m2masn	de-Fuc form of PA6	C84H135N6O61X	0.000	1000.000	0.000	0.000
EX_dmantipyrine(e)	dmantipyrine	demethylated antipyrine	C10H10N2O	0.000	1000.000	0.000	0.000
EX_gam(e)	gam	D-Glucosamine	C6H14NO5	0.000	1000.000	0.000	0.000
EX_digalsgalside_hs(e)	digalsgalside_hs	Digalactosylceramidesulfate	C30H55NO15SFULLRCO	0.000	1000.000	0.000	0.000
EX_dlnlcg(e)	dlnlcg	dihomo-gamma-linolenic acid (n-6)	C20H33O2	0.000	1000.000	0.000	0.000
EX_dcsptn1(e)	dcsptn1	docosa-4,7,10,13,16-pentaenoic acid	C22H33O2	0.000	1000.000	0.000	0.000
EX_pro-D(e)	pro-D	D-proline	C5H9NO2	0.000	1000.000	0.000	0.000
EX_rbt(e)	rbt	D-ribitol	C5H12O5	0.000	1000.000	0.000	0.000
EX_rib-D(e)	rib-D	D-ribose	C5H10O5	0.000	1000.000	0.000	0.000
EX_ser-D(e)	ser-D	D-serine	C3H7NO3	0.000	1000.000	0.000	0.000
EX_tagat-D(e)	tagat-D	D-tagatose	C6H12O6	0.000	1000.000	0.000	0.000
EX_ebastine(e)	ebastine	ebastine	C32H39NO2	0.000	1000.000	0.000	0.000
EX_eicostet(e)	eicostet	eicosatetranoic acid	C20H31O2	0.000	1000.000	0.000	0.000
EX_etoh(e)	etoh	ethanol	C2H6O	0.000	1000.000	0.000	0.000
EX_11-cis-retfa(e)	11-cis-retfa	fatty acid 11-cis-retinol	C20H29OFULLR2CO	0.000	1000.000	0.000	0.000
EX_9-cis-retfa(e)	9-cis-retfa	fatty acid 9-cis-retinol	C20H29OFULLR2CO	0.000	1000.000	0.000	0.000
EX_retfa(e)	retfa	fatty acid retinol	C20H29OFULLR2CO	0.000	1000.000	0.000	0.000
EX_lnlncg(e)	lnlncg	gamma-linolenate	C18H29O2	0.000	1000.000	0.000	0.000

Table S3 (continued)							
EX_yvite(e)	yvite	gamma-tocopherol	C28H48O2	0.000	1000.000	0.000	0.000
EX_gdp(e)	gdp	GDP	C10H12N5O11P2	0.000	1000.000	0.000	0.000
EX_glygn2(e)	glygn2	glycogen, structure 2 (glycogenin-1,6-{7[1,4-Glc], 4[1,4-Glc]})	C66H111O56X	0.000	1000.000	0.000	0.000
EX_glygn4(e)	glygn4	glycogen, structure 4 (glycogenin-1,6-{2[1,4-Glc], [1,4-Glc]})	C18H31O16X	0.000	1000.000	0.000	0.000
EX_glygn5(e)	glygn5	glycogen, structure 5 (glycogenin-2[1,4-Glc])	C12H21O11X	0.000	1000.000	0.000	0.000
EX_gmp(e)	gmp	GMP	C10H12N5O8P	0.000	1000.000	0.000	0.000
EX_gtp(e)	gtp	GTP(4-)	C10H12N5O14P3	0.000	1000.000	0.000	0.000
EX_hspg(e)	hspg	heparan sulfate proteoglycan	C79H113N5O101S12X	0.000	1000.000	0.000	0.000
EX_7dhf(e)	7dhf	heptaglutamyl folate (DHF)	C49H55N13O24	0.000	1000.000	0.000	0.000
EX_7thf(e)	7thf	heptaglutamyl folate (THF)	C49H57N13O24	0.000	1000.000	0.000	0.000
EX_6thf(e)	6thf	hexaglutamyl folate (THF)	C44H51N12O21	0.000	1000.000	0.000	0.000
EX_6dhf(e)	6dhf	hexaglutamyl folate (DHF)	C44H49N12O21	0.000	1000.000	0.000	0.000
EX_cyan(e)	cyan	hydrogen cyanide	CHN	0.000	1000.000	0.000	0.000
EX_ebastineoh(e)	ebastineoh	hydroxylated ebastine	C32H39NO3	0.000	1000.000	0.000	0.000
EX_idp(e)	idp	IDP	C10H11N4O11P2	0.000	1000.000	0.000	0.000
EX_imp(e)	imp	IMP	C10H11N4O8P	0.000	1000.000	0.000	0.000
EX_i(e)	i	iodide	I	0.000	1000.000	0.000	0.000
EX_fe2(e)	fe2	iron(2+)	Fe	0.000	1000.000	0.000	0.000
EX_fe3(e)	fe3	iron(3+)	Fe	0.000	1000.000	0.000	0.000
EX_ksi(e)	ksi	keratan sulfate I	C247H393N17O213S12X	0.000	1000.000	0.000	0.000
EX_ksi_deg1(e)	ksi_deg1	keratan sulfate I, degradation product 1	C241H383N17O209S12X	0.000	1000.000	0.000	0.000
EX_arab-L(e)	arab-L	L-arabinose	C5H10O5	0.000	1000.000	0.000	0.000
EX_Lcystin(e)	Lcystin	L-cystine	C6H12N2O4S2	0.000	1000.000	0.000	0.000
EX_leuktrA4(e)	leuktrA4	Leukotriene A4	C20H29O3	0.000	1000.000	0.000	0.000
EX_leuktrB4(e)	leuktrB4	Leukotriene B4	C20H31O4	0.000	1000.000	0.000	0.000
EX_leuktrC4(e)	leuktrC4	Leukotriene C4	C30H45N3O9S	0.000	1000.000	0.000	0.000
EX_leuktrD4(e)	leuktrD4	Leukotriene D4	C25H39N2O6S	0.000	1000.000	0.000	0.000
EX_leuktrE4(e)	leuktrE4	leukotriene E4	C23H36NO5S	0.000	1000.000	0.000	0.000
EX_leuktrF4(e)	leuktrF4	leukotriene F4	C28H42N2O8S	0.000	1000.000	0.000	0.000
EX_hom-L(e)	hom-L	L-homoserine	C4H9NO3	0.000	1000.000	0.000	0.000
EX_lgnc(e)	lgnc	lignocerate	C24H47O2	0.000	1000.000	0.000	0.000
EX_limnen(e)	limnen	limonene	C10H16	0.000	1000.000	0.000	0.000
EX_lnlc(e)	lnlc	linoleate	C18H31O2	0.000	1000.000	0.000	0.000
EX_lipoate(e)	lipoate	lipoic acid	C8H14O2S2	0.000	1000.000	0.000	0.000
EX_thyox-L(e)	thyox-L	L-thyroxine	C15H11I4NO4	0.000	1000.000	0.000	0.000
EX_malt(e)	malt	maltose	C12H22O11	0.000	1000.000	0.000	0.000
EX_malttr(e)	malttr	maltotriose	C18H32O16	0.000	1000.000	0.000	0.000
EX_hpdca(e)	hpdca	margarate	C17H33O2	0.000	1000.000	0.000	0.000
EX_ttdca(e)	ttdca	myristate	C14H27O2	0.000	1000.000	0.000	0.000
EX_n2m2nmasn(e)	n2m2nmasn	N-Acetyl-beta-D-glucosaminyl-1,2-alpha-D-mannosyl-1,3-(N-acetyl-beta-D-glucosaminyl-1,2-alpha-D-mannosyl-1,6)-(N-acetyl-beta-D-glucosaminyl-1,4)-beta-D-mannosyl-1,4-N-acetyl-beta-D-glucosaminyl-R	C58H96N5O40X	0.000	1000.000	0.000	0.000
EX_acgam(e)	acgam	N-acetyl-D-glucosamine	C8H15NO6	0.000	1000.000	0.000	0.000

Table S3 (continued)							
EX_npthl(e)	npthl	naphthalene	C10H8	0.000	1000.000	0.000	0.000
EX_onpthl(e)	onpthl	naphthalene epoxide	C10H8O	0.000	1000.000	0.000	0.000
EX_nrvnc(e)	nrvnc	nervonate	C24H45O2	0.000	1000.000	0.000	0.000
EX_nad(e)	nad	Nicotinamide adenine dinucleotide	C21H26N7O14P2	0.000	1000.000	0.000	0.000
EX_nadp(e)	nadp	Nicotinamide adenine dinucleotide phosphate	C21H25N7O17P3	0.000	1000.000	0.000	0.000
EX_nac(e)	nac	nicotinate	C6H4NO2	0.000	1000.000	0.000	0.000
EX_nifedipine(e)	nifedipine	nifedipine	C17H18N2O6	0.000	1000.000	0.000	0.000
EX_octa(e)	octa	octanoate	C8H15O2	0.000	1000.000	0.000	0.000
EX_ocdcea(e)	ocdcea	oleate	C18H33O2	0.000	1000.000	0.000	0.000
EX_whddca(e)	whddca	omega hydroxy dodecanoate (n-C12:0)	C12H23O3	0.000	1000.000	0.000	0.000
EX_whttdca(e)	whttdca	omega hydroxy tetradecanoate (n-C14:0)	C14H27O3	0.000	1000.000	0.000	0.000
EX_omeprazole(e)	omeprazole	omeprazole	C17H19N3O3S	0.000	1000.000	0.000	0.000
EX_orn(e)	orn	ornithinium(1+)	C5H13N2O2	0.000	1000.000	0.000	0.000
EX_s2l2fn2m2masn(e)	s2l2fn2m2masn	PA6	C90H145N6O65X	0.000	1000.000	0.000	0.000
EX_taxol(e)	taxol	paclitaxel	C47H31NO14	0.000	1000.000	0.000	0.000
EX_ptdca(e)	ptdca	pentadecanoate	C15H29O2	0.000	1000.000	0.000	0.000
EX_5dhf(e)	5dhf	pentaglutamyl folate (DHF)	C39H43N11O18	0.000	1000.000	0.000	0.000
EX_5thf(e)	5thf	pentaglutamyl folate (THF)	C39H45N11O18	0.000	1000.000	0.000	0.000
EX_peplys(e)	peplys	Peptidyl-L-lysine	XH	0.000	1000.000	0.000	0.000
EX_perillyl(e)	perillyl	perillyl alcohol	C10H16O	0.000	1000.000	0.000	0.000
EX_phyQ(e)	phyQ	phylloquinone	C31H46O2	0.000	1000.000	0.000	0.000
EX_phyt(e)	phyt	phytanate	C20H39O2	0.000	1000.000	0.000	0.000
EX_k(e)	k	potassium(1+)	K	-8.883	1000.000	0.000	0.000
EX_ppa(e)	ppa	propionate	C3H5O2	0.000	1000.000	0.000	0.000
EX_prostgd2(e)	prostgd2	Prostaglandin D2	C20H31O5	0.000	1000.000	0.000	0.000
EX_prostge1(e)	prostge1	Prostaglandin E1	C20H33O5	0.000	1000.000	0.000	0.000
EX_prostge2(e)	prostge2	Prostaglandin E2	C20H31O5	0.000	1000.000	0.000	0.000
EX_prostgf2(e)	prostgf2	Prostaglandin F2alpha	C20H33O5	0.000	1000.000	0.000	0.000
EX_pheme(e)	pheme	Protoheme	C34H30FeN4O4	0.000	1000.000	0.000	0.000
EX_retinol(e)	retinol	retinol	C20H30O	0.000	1000.000	0.000	0.000
EX_retnglc(e)	retnglc	retinoyl glucuronide	C26H35O8	0.000	1000.000	0.000	0.000
EX_ribflv(e)	**Ribflv**	**riboflavin**	**C17H20N4O6**	**-0.001**	**1000.000**	**0.000**	**0.000**
EX_sarcs(e)	sarcs	sarcosine	C3H7NO2	0.000	1000.000	0.000	0.000
EX_sel(e)	sel	selenate	O4Se	0.000	1000.000	0.000	0.000
EX_na1(e)	na1	sodium(1+)	Na	-212.100	1000.000	0.000	0.000
EX_strch1(e)	strch1	starch, structure 1 (1,6-{7[1,4-Glc], 4[1,4-Glc]})	C66H112O56	0.000	1000.000	0.000	0.000
EX_strch2(e)	strch2	starch, structure 2 (1,6-{2[1,4-Glc], [1,4-Glc]})	C18H32O16	0.000	1000.000	0.000	0.000
EX_ocdca(e)	ocdca	stearate	C18H35O2	0.000	1000.000	0.000	0.000
EX_strdnc(e)	strdnc	stearidonic acid C18:4, n-3	C18H27O2	0.000	1000.000	0.000	0.000
EX_sucr(e)	sucr	sucrose	C12H22O11	0.000	1000.000	0.000	0.000
EX_tethex3(e)	tethex3	tetracosahexaenoic acid, n-3	C24H35O2	0.000	1000.000	0.000	0.000
EX_tetpent3(e)	tetpent3	tetracosapentaenoic acid, n-3	C24H37O2	0.000	1000.000	0.000	0.000
EX_tetpent6(e)	tetpent6	tetracosapentaenoic acid, n-6	C24H37O2	0.000	1000.000	0.000	0.000
EX_tettet6(e)	tettet6	tetracosatetraenoic acid n-6	C24H39O2	0.000	1000.000	0.000	0.000
EX_tcynt(e)	tcynt	thiocyanate	CNS	0.000	1000.000	0.000	0.000
EX_tsul(e)	tsul	thiosulfate(2-)	O3S2	0.000	1000.000	0.000	0.000
EX_txa2(e)	txa2	Thromboxane A2	C20H31O5	0.000	1000.000	0.000	0.000

Table S3 (continued)							
EX_thymd(e)	thymd	thymidine	C10H14N2O5	0.000	1000.000	0.000	0.000
EX_tmndnc(e)	tmndnc	timnodonic acid C20:5, n-3	C20H29O2	0.000	1000.000	0.000	0.000
EX_tolbutamide(e)	tolbutamide	tolbutamide	C12H18N2O3S	0.000	1000.000	0.000	0.000
EX_tre(e)	tre	Trehalose	C12H22O11	0.000	1000.000	0.000	0.000
EX_triodthysuf(e)	triodthysuf	Triiodothyronine sulfate	C15H11I3NO7S	0.000	1000.000	0.000	0.000
EX_Tyr-ggn(e)	Tyr-ggn	Tyr-194 of apo-glycogenin protein (primer for glycogen synthesis)	XOH	0.000	1000.000	0.000	0.000
EX_udp(e)	udp	UDP	C9H11N2O12P2	0.000	1000.000	0.000	0.000
EX_hcoumarin(e)	hcoumarin	umbelliferone	C9H6O3	0.000	1000.000	0.000	0.000
EX_ump(e)	ump	UMP	C9H11N2O9P	0.000	1000.000	0.000	0.000
EX_utp(e)	utp	UTP(4-)	C9H11N2O15P3	0.000	1000.000	0.000	0.000
EX_vitd2(e)	vitd2	vitamin D2	C28H44O	0.000	1000.000	0.000	0.000
EX_whtststerone(e)	whtststerone	w hydroxy testosterone	C19H28O3	0.000	1000.000	0.000	0.000
EX_adp	adp	ADP	C10H12N5O10P2	0.000	1000.000	0.000	0.000
EX_CLPND(e)	clpnd	clupanodonic acid	C22H33O2	0.000	1000.000	0.000	0.000
EX_oh1	oh1	hydroxide	HO	0.000	1000.000	0.000	0.000

*FULL is a generic formula for side chains of complex lipids.

Table S4. Coverage of the exo-metabolome at different ACN:sample dilutions

Dilutions	10:1	7:1	3:1
Features Detected	105	141	208
Metabolites Identified	32	40	45
Metabolites not identified	5-MTA Adenine ADMA Hypoxanthine Guanine Dimethylglycine SDMA Ornithine Oxoproline Aspartate* Cystine* Biotin* Tryptophan*	5-MTA Adenine Guanine SDMA Biotin*	

* present in the medium

Table S5. Samples order list

1	Pooled QC sample	Equilibration	11	Calibrator	POS	54	Calibrator	NEG
2	Pooled QC sample	Equilibration	12	Calibrator	POS	55	Calibrator	NEG
3	Pooled QC sample	Equilibration	13	Calibrator	POS	56	Calibrator	NEG
4	Pooled QC sample	Equilibration	14	Calibrator	POS	57	Calibrator	NEG
5	Pooled QC sample	Equilibration	15	Pooled QC sample	POS	58	Pooled QC sample	NEG
6	Pooled QC sample	Equilibration	16	Medium	POS	59	Medium	NEG
7	Pooled QC sample	Equilibration	17	Sample 1	POS	60	Sample 1	NEG
8	Pooled QC sample	Equilibration	18	Sample 2	POS	61	Sample 2	NEG
9	Pooled QC sample	Equilibration	19	Sample 3	POS	62	Sample 3	NEG
10	Pooled QC sample	Equilibration	20	Sample 4	POS	63	Sample 4	NEG
			21	Sample 5	POS	64	Sample 5	NEG
			22	Pooled QC sample	POS	65	Pooled QC sample	NEG
			23	Medium	POS	66	Medium	NEG
			24	Sample 6	POS	67	Sample 6	NEG
			25	Sample 7	POS	68	Sample 7	NEG
			26	Sample 8	POS	69	Sample 8	NEG
			27	Sample 9	POS	70	Sample 9	NEG
			28	Sample 10	POS	71	Sample 10	NEG
			29	Pooled QC sample	POS	72	Pooled QC sample	NEG
			30	Medium	POS	73	Medium	NEG
			31	Sample 11	POS	74	Sample 11	NEG
			32	Sample 12	POS	75	Sample 12	NEG
			33	Sample 13	POS	76	Sample 13	NEG
			34	Sample 14	POS	77	Sample 14	NEG
			35	Sample 15	POS	78	Sample 15	NEG
			36	Pooled QC sample	POS	79	Pooled QC sample	NEG
			37	Medium	POS	80	Medium	NEG
			38	Sample 16	POS	81	Sample 16	NEG
			39	Sample 17	POS	82	Sample 17	NEG
			40	Sample 18	POS	83	Sample 18	NEG
			41	Sample 19	POS	84	Sample 19	NEG
			42	Sample 20	POS	85	Sample 20	NEG
			43	Pooled QC sample	POS	86	Pooled QC sample	NEG
			44	Medium	POS	87	Medium	NEG
			45	Sample 21	POS	88	Sample 21	NEG
			46	Sample 22	POS	89	Sample 22	NEG
			47	Sample 23	POS	90	Sample 23	NEG
			48	Sample 24	POS	91	Sample 24	NEG
			49	Sample 25	POS	92	Sample 25	NEG
			50	Calibrator	POS	93	Calibrator	NEG
			51	Calibrator	POS	94	Calibrator	NEG
			52	Calibrator	POS	95	Calibrator	NEG
			53	Calibrator	POS	96	Calibrator	NEG

Table S6. Qualitative Comparison of detected compounds

	BIOCHEMICAL	HMDB ID	LC-MS & GC-MS	HILIC-MS
1	*3-methyl-2-oxobutyrate*	HMDB00019	√	√
2	*3-methyl-2-oxovalerate**	HMDB03736	√	√
3	*4-guanidinobutanoate*	HMDB03464	√	nd
4	*4-hydroxyphenylpyruvate*	HMDB00707	√	nd
5	*4-methyl-2-oxopentanoate**	HMDB00695	√	nd
6	*5-methylcytidine*	HMDB00982	nd	√
7	*5-methylthioadenosine (MTA)*	HMDB01173	√	√
8	*5-oxoproline*	HMDB00267	√	√
9	*adenine*	HMDB00034	√	√
10	*ADMA***	HMDB01539	√	√
11	*alanine*	HMDB00161	√	√
12	*alanylglutamine*	-	√	√
13	*arginine*	HMDB03416	√	√
14	*asparagine*	HMDB00168	√	√
15	*aspartate*	HMDB00191	√	√
16	*beta-hydroxyisovalerate*	HMDB00754	√	√
17	*betaine*	HMDB00043	√	√
18	*biotin*	HMDB00030	√	√
19	*caproate (6:0)*	HMDB00535	√	nd
20	*caprylate (8:0)*	HMDB00482	√	nd
21	*choline*	HMDB00097	√	√
22	*citrate*	HMDB00094	√	√
23	*cysteine*	HMDB00574	√	√
24	*cysteine-glutathione disulfide*	HMDB00656	√	nd
25	*cystine*	HMDB00192	√	√
26	*dihydroorotic acid*	HMDB03349	nd	√
27	*erythrose*	HMDB02649	√	nd
28	*folate*	HMDB00121	√	√
29	*fructose*	HMDB00660	√	nd
30	*glucose*	HMDB00122	√	√

Table S6 (continued)

31	*glutamate*	HMDB03339	√	√
32	*glutamine*	HMDB00641	√	√
33	*glycine*	HMDB00123	√	√
34	*guanine*	HMDB00132	√	√
35	*histidine*	HMDB00177	√	√
36	*hypoxanthine*	HMDB00157	√	√
37	*inosine*	HMDB00195	√	√
38	*isoleucine*	HMDB00172	√	√
39	*lactate*	HMDB00190	√	√
40	*leucine*	HMDB00687	√	√
41	*lysine*	HMDB00182	√	√
42	*malate*	HMDB00156	√	√
43	*methionine*	HMDB00696	√	√
44	*myo-inositol*	HMDB00211	√	√
45	*N-acetylalanine*	HMDB00766	√	√
46	*N-acetylisoleucine**	-	√	√
47	*N-acetylleucine**	HMDB11756	√	√
48	*N-acetylmethionine*	HMDB11745	√	√
49	*N-carbamoylaspartate*	HMDB00828	√	√
50	*nicotinamide*	HMDB01406	√	√
51	*O-acetylhomoserine*	-	√	nd
52	*ornithine*	HMDB03374	√	√
53	*orotate*	HMDB00226	√	√
54	*p-aminobenzoate (PABA)*	HMDB01392	√	√
55	*pantothenate*	HMDB00210	√	√
56	*p-cresol sulfate*	HMDB11635	√	nd
57	*phenol red*	-	√	√
58	*phenylalanine*	HMDB00159	√	√
59	*phosphate*	HMDB01429	√	nd
60	*proline*	HMDB00162	√	√
61	*pseudouridine**	HMDB00767	√	nd
62	*pyridoxate*	HMDB00017	√	√
63	*pyridoxine (Vitamin B6)*	HMDB02075	√	√

Table S6 (continued)

64	*pyruvate*	HMDB00243	√	√
65	*riboflavin (Vitamin B2)*	HMDB00244	√	√
66	*S-adenosylhomocysteine (SAH)*	HMDB00939	√	√
67	*SDMA***	HMDB03334	√	√
68	*serine*	HMDB03406	√	√
69	*succinate*	HMDB00254	√	√
70	*thiamin (Vitamin B1)*	HMDB00235	√	√
71	*threonine*	HMDB00167	√	√
72	*trans-4-hydroxyproline*	HMDB00725	√	√
73	*tryptophan*	HMDB00929	√	√
74	*tyrosine*	HMDB00158	√	√
75	*uracil*	HMDB00300	√	√
76	*uridine**	HMDB00296	√	√
77	*AICAR*	-	√	√
78	*A-769662*	-	√	√
79	*valine*	HMDB00883	√	√

* Isomers not separated during HILIC-MS analysis

** Isomers not separated during LC-MS and/or GC-MS analysis

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