

SUPPLEMENTARY MATERIALS

Supplementary Tables

Supplementary Table 1. Top 22 IC-specific serum metabolites out of more than 390 detected metabolites.

Supplementary Table 2. Top 4 differentially expressed analytes in serum.

Supplementary Table 3. Top 50 IC-specific urine metabolites out of more than 500 detected metabolites.

Table S1.

Metabolites	FC	FC (log2)	p value	p value (log 10)
ARACHIDONIC ACID	1.5359	0.61904	0.0092181	2.0354
HOMOCYSTEINE	0.56719	-0.8181	0.010477	1.9798
BETA-N-ACETYLGLUCOSAMINE	0.44663	-1.1628	0.010495	1.979
GUANINE	1.8883	0.91709	0.017327	1.7613
PHOSPHATE	0.60255	-0.73085	0.020363	1.6912
OXO-OCTADECANOIC ACID	1.549	0.63129	0.021275	1.6721
FRUCTOSE	0.51445	-0.9589	0.022772	1.6426
GALACTOSE	0.48342	-1.0486	0.025712	1.5899
CINNAMOYL-GLUCOSIDE	0.086894	-3.5246	0.02723	1.5649
5-AMINO-3-OXOHEXANOIC ACID	2.8031	1.487	0.02922	1.5343
ALPHA-KETOISOVALERIC ACID	0.52459	-0.93073	0.034539	1.4617
N1-ACETYL SPERMIDINE	2.4415	1.2878	0.035978	1.444
SUBERIC ACID	1.5113	0.59577	0.036209	1.4412
NONANEDIOIC ACID	1.5733	0.65379	0.036473	1.438
N-ACETYL-GLUTAMINE	1.6218	0.69759	0.052709	1.2781
LINOLEIC ACID	1.6795	0.74799	0.05497	1.2599
DIHYDROXYCHOLESTANOYL TAURINE	1.6197	0.6957	0.066038	1.1802
4-SULFOPHENOL	2.4622	1.2999	0.068482	1.1644
N-ACETYL-L-ORNITHINE	0.65571	-0.60888	0.074893	1.1256
OROTIDINE-5-PHOSPHATE	1.5619	0.64332	0.086729	1.0618
DIMETHYLSULFONE	2.0339	1.0242	0.097719	1.01
4-GUANIDINOBUTANOIC ACID	1.6081	0.68534	0.098591	1.0062

Table S2.

Metabolite	log₂FC	Permutation p-value	AUC
CINNAMOYL.GLUCOSIDE	1.467	0.485	0.77
BETA N ACETYLGLUCOSAMINE	-1.38	0.485	0.765
ARACHIDONIC ACID	0.758	0.485	0.773
ALPHA KETOISOVALERIC ACID	1.955	0.485	0.776

Not significant

Table S3.

Metabolites	FC	FC (log2)	p-value	p-value (log 10)
PURINE	2.1538	1.1069	4.29E-05	4.3672
PHENYLALANINE	2.1515	1.1053	0.00050223	3.2991
TETRADECADIENYLCARNITINE	0.45607	-1.1327	0.00099791	3.0009
5-OXOPROLINE	3.0523	1.6099	0.0011701	2.9318
ACETYLCARNITINE	2.0042	1.003	0.001236	2.908
GLYCINE	1.9094	0.93309	0.002303	2.6377
TAURINE	2.144	1.1003	0.0023347	2.6318
INDOXYL SULFATE	1.822	0.8655	0.0029447	2.531
CARNITINE	2.0245	1.0176	0.0031021	2.5083
RIBONO-1,4-LACTONE	0.56122	-0.83337	0.0032141	2.4929
BETA-N-ACETYLGLUCOSAMINE	1.8847	0.91433	0.0038099	2.4191
GLUCURONIC ACID	0.55165	-0.85817	0.0040161	2.3962
ASPARAGINE	5.1368	2.3609	0.0042038	2.3764
VALINE	1.7163	0.77934	0.0043871	2.3578
N-ACETYLASPARAGINE	1.8726	0.90505	0.0059014	2.229
DIHYDROXYPHENYLALANINE	1.7732	0.82632	0.0067172	2.1728
HIPPURIC ACID	1.5725	0.65304	0.0067535	2.1705
STEARAMIDE	1.6296	0.70449	0.0073044	2.1364
ARABINITOL	1.9886	0.99174	0.0078588	2.1046
GLU-ALA	1.7072	0.77162	0.0078722	2.1039
PYRIDOXAMINE	1.6971	0.76304	0.0082029	2.086
BETAINE	1.6012	0.67913	0.0082188	2.0852
AMP	0.6575	-0.60494	0.0087583	2.0576
2-PYRROLIDINONE	1.6041	0.68178	0.0089036	2.0504
1-DEOXYPENTITOL	1.6286	0.70362	0.0090406	2.0438
UREA	1.6604	0.73152	0.009694	2.0135
5-AMINO-3-OXOHXANOIC ACID	1.5473	0.62979	0.01089	1.963
CREATININE	1.7554	0.81182	0.010933	1.9613
3-HYDROXYHIPURIC ACID	0.53126	-0.9125	0.012119	1.9165
3,4-DIHYDROXYPHENYLACETIC ACID	0.43195	-1.2111	0.012696	1.8963
ALLANTOATE	1.5371	0.62019	0.014199	1.8478
PIPECOLIC ACID	1.7739	0.8269	0.014807	1.8295
INDOLE	2.1554	1.108	0.015201	1.8181
1-METHYLHISTIDINE	1.5527	0.63474	0.016059	1.7943
PROPIONYLCARNITINE	1.9799	0.98545	0.025254	1.5977
N-ACETYLANALANINE	2.2185	1.1496	0.025826	1.5879
PSEUDO URIDINE	0.5779	-0.7911	0.026075	1.5838
HYPOXANTHINE	0.60594	-0.72275	0.0293	1.5331
PREGNANOLONE SULFATE	0.50796	-0.97721	0.031206	1.5058
CHOLESTERYL SULFATE	2.0258	1.0185	0.03186	1.4968
HISTIDINE	1.5928	0.67153	0.032355	1.4901
3-PHOSPHOGLYCERATE	1.8826	0.91271	0.032936	1.4823
N6-ACETYL-L-LYSINE	2.3375	1.225	0.03459	1.461
SULFAMIC ACID	0.46064	-1.1183	0.036634	1.4361
ACETYLCHOLINE	2.0768	1.0544	0.037216	1.4293
RIBITOL	0.64391	-0.63506	0.04035	1.3942
GLUCURONIC ACID LACTONE	0.62234	-0.68423	0.041181	1.3853
3-DEHYDROXYCARNITINE	2.1009	1.071	0.044103	1.3555
ALANINE	2.5393	1.3444	0.049046	1.3094
2-AMINO BUTYRATE	1.6461	0.71902	0.050515	1.2966

Supplementary Figures

Supplementary Figure 1. Workflow of this study

Supplementary Figure 2. Biomarker analysis in serum samples. (A) A heatmap showing unsupervised clustering of the top 25 serum IC-specific metabolites out of more than 500 detected metabolites. (B) Top 15 discriminators by random forest analysis. (C) Enrichment overview of top 50 differentially expressed metabolites in IC compared to NC. Metabolic pathways associated with the metabolite sets are shown.

Supplementary Figure 3. Biomarker analysis in urine samples. (A) A heatmap showing unsupervised clustering of top urinary IC-specific metabolites. (B) Top 15 discriminators by random forest analysis. (C) Enrichment overview of top 50 differentially expressed metabolites in IC compared to NC. Metabolic sets that are predicted to be changed in the case of dysfunctional enzymes using genome-scale network model of human metabolism.

FIGURE S1.

Metabolomics Workflow

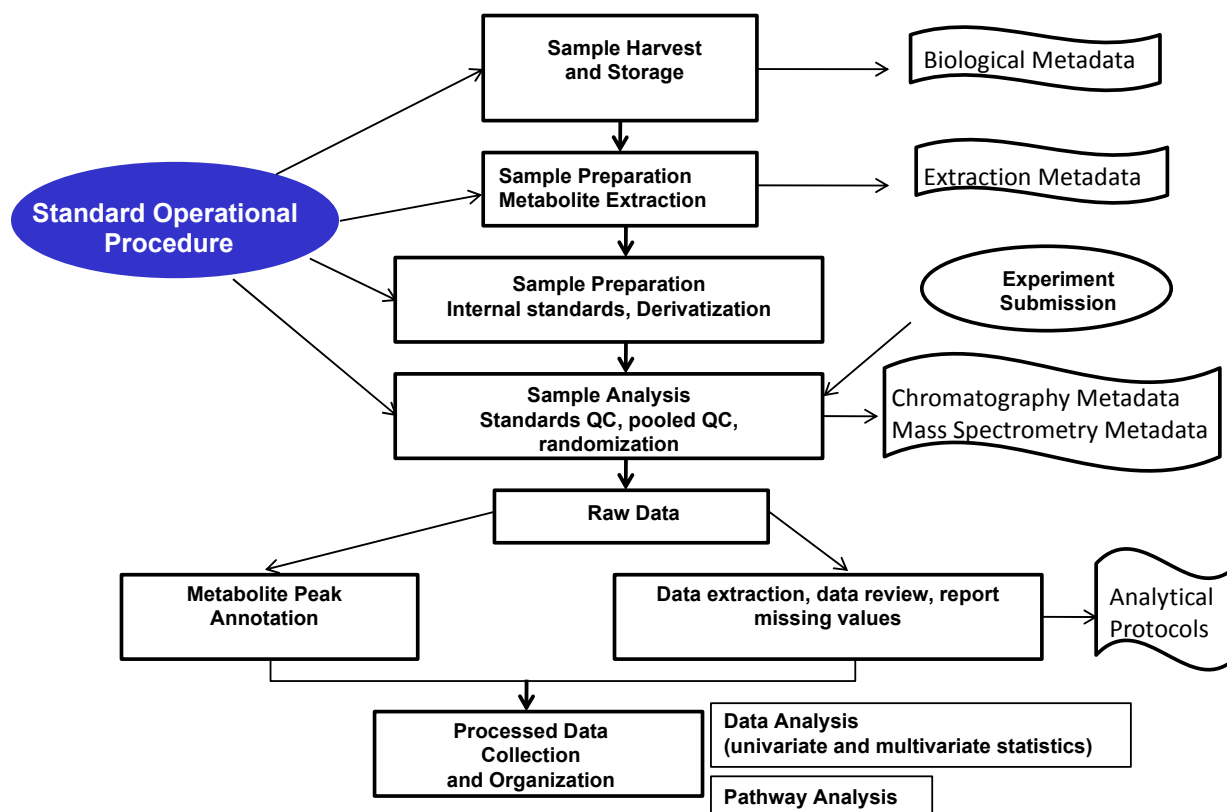


FIGURE S2.

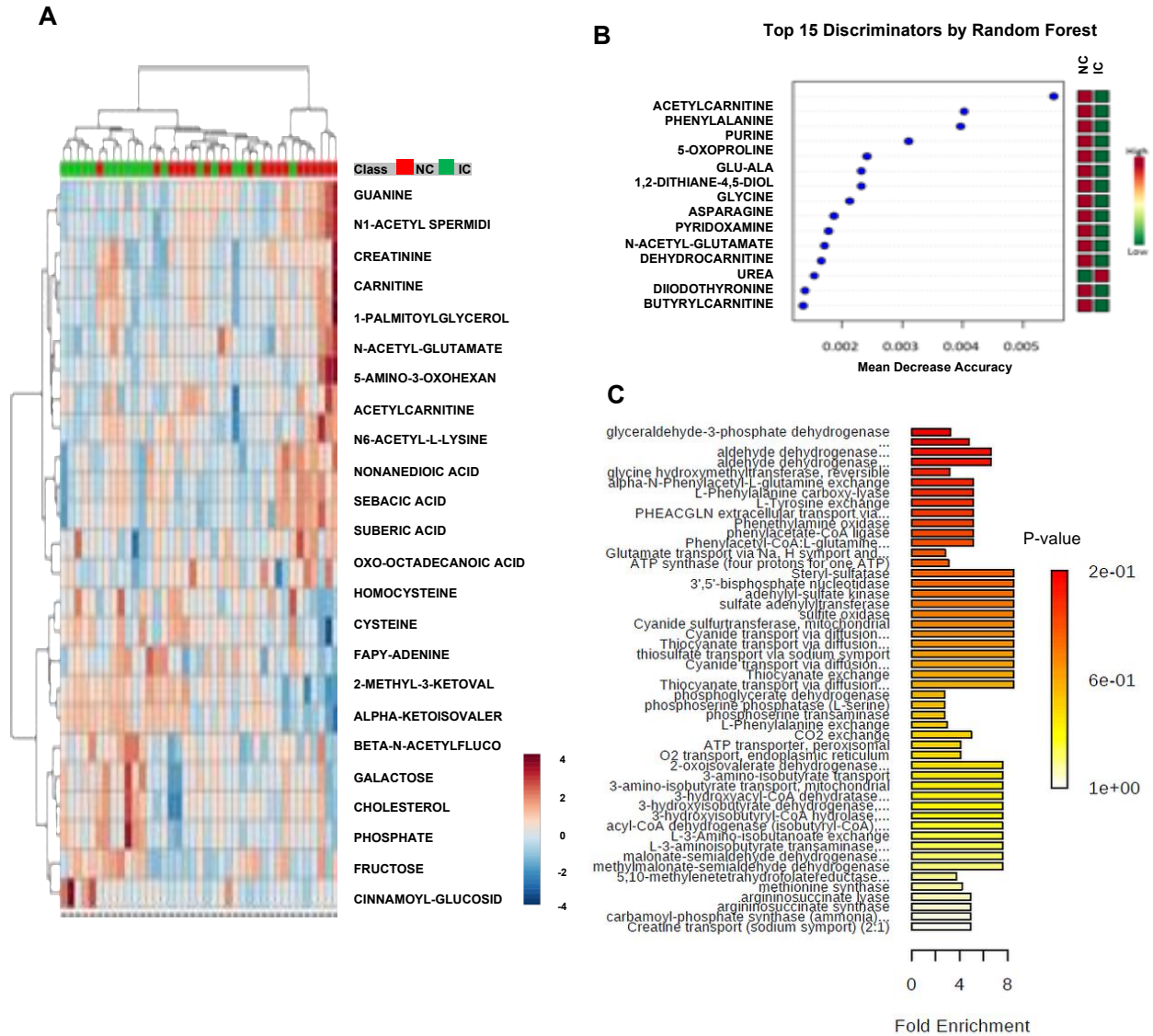


FIGURE S3.

