Metabolomic Data Analysis with MetaboAnalyst 5.0

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March 20, 2021

1 Background

MSEA or Metabolite Set Enrichment Analysis is a way to identify biologically meaningful patterns that are significantly enriched in quantitative metabolomic data. In conventional approaches, metabolites are evaluated individually for their significance under conditions of study. Those compounds that have passed certain significance level are then combined to see if any meaningful patterns can be discerned. In contrast, MSEA directly investigates if a set of functionally related metabolites without the need to preselect compounds based on some arbitrary cut-off threshold. It has the potential to identify subtle but consistent changes among a group of related compounds, which may go undetected with the conventional approaches.

Essentially, MSEA is a metabolomic version of the popular GSEA (Gene Set Enrichment Analysis) software with its own collection of metabolite set libraries as well as an implementation of user-friendly web-interfaces. GSEA is widely used in genomics data analysis and has proven to be a powerful alternative to conventional approaches. For more information, please refer to the original paper by Subramanian A, and a nice review paper by Nam D, Kim SY. [1]. [2]

2 MSEA Overview

Metabolite set enrichment analysis consists of four steps - data input, data processing, data analysis, and results download. Different analysis procedures are performed based on different input types. In addition, users can also browse and search the metabolite set libraries as well as upload their self-defined metabolite sets for enrichment analysis. Users can also perform metabolite name mapping between a variety of compound names, synonyms, and major database identifiers.

3 Data Input

There are three enrichment analysis algorithms offered by MSEA. Accordingly, three different types of data inputs are required by these three approaches:

- A list of important compound names - entered as a one column data (*Over Representation Analysis (ORA)*);
- A single measured biofluid (urine, blood, CSF) sample- entered as tab separated two-column data with the first column for compound name, and the second for concentration values (*Single Sample Profiling (SSP)*);

[1] Subramanian *Gene set enrichment analysis: A knowledge-based approach for interpreting genome-wide expression profiles.*, Proc Natl Acad Sci USA. 2005 102(43): 15545-50

[2] Nam D, Kim SY. *Gene-set approach for expression pattern analysis*, Briefings in Bioinformatics. 2008 9(3): 189-197.

- A compound concentration table - entered as a comma separated (.csv) file with the each sample per row and each metabolite concentration per column. The first column is sample names and the second column for sample phenotype labels (*Quantitative Enrichment Analysis (QEA)*)

You selected Over Representation Analysis (ORA) which requires a list of compound names as input.

4 Data Process

The first step is to standardize the compound labels. It is an essential step since the compound labels will be subsequently compared with compounds contained in the metabolite set library. MSEA has a built-in tool to convert between compound common names, synonyms, identifiers used in HMDB ID, PubChem, ChEBI, BiGG, METLIN, KEGG, or Reactome. **Table 1** shows the conversion results. Note: *1* indicates exact match, *2* indicates approximate match, and *0* indicates no match. A text file contain the result can be found the downloaded file *name_map.csv*

	Query	Match	HMDB	PubChem	KEGG	SMILES
1	HMDB0028907	Isoleucyl-Glycine	HMDB0028907	6992869		CCC(C)C(N)C(=O)NC(
2	HMDB0060018	NA	NA	NA	NA	NA
3	HMDB0000159	L-Phenylalanine	HMDB0000159	6140	C00079	C1=CC=C(C=C1)C[C@
4	HMDB0008138	PC(18:2(9Z,12Z)/18:2(9Z,12Z))	HMDB0008138	5288075	C00157	CCCCC/C=C\C/C=C\
5	HMDB0041724	NA	NA	NA	NA	NA
6	HMDB0000935	Uridine diphosphate glucuronic acid	HMDB0000935	17473	C00167	C1=CN(C(=O)NC1=O)
7	HMDB0028844	Glycyl-Isoleucine	HMDB0028844	88079		CCC(C)C(NC(=O)CN)C
8	HMDB0000929	L-Tryptophan	HMDB0000929	6305	C00078	C1=CC=C2C(=C1)C(=
9	HMDB0005322	NA	NA	NA	NA	NA
10	HMDB0059745	NA	NA	NA	NA	NA
11	HMDB0005808	Formononetin	HMDB0005808	5280378	C00858	COC1=CC=C(C=C1)C
12	HMDB0002917	D-Xylitol	HMDB0002917	6912	C00379	C([C@H](C([C@H](CO)O
13	HMDB0012102	SM(d18:1/20:0)	HMDB0012102	44260124	C00550	CCCCCCCCCCCCCCCC
14	HMDB0012085	SM(d18:0/14:0)	HMDB0012085	44260138	C00550	CCCCCCCCCCCCCCCC
15	HMDB0000749	Mesaconic acid	HMDB0000749	643798	C01732	C/C(=C\C(=O)O)/C(=
16	HMDB0008994	PE(18:0/18:2(9Z,12Z))	HMDB0008994	9546749	C00350	CCCCCCCCCCCCCCCC
17	HMDB0060649	NA	NA	NA	NA	NA
18	HMDB0013678	4-Hydroxyhippuric acid	HMDB0013678	151012		C1=CC(=CC=C1C(=O
19	HMDB0007218	DG(18:1(9Z)/18:1(9Z)/0:0)	HMDB0007218	9543716	C00165	CCCCCCCC/C=C\CC
20	HMDB0001008	Biliverdin	HMDB0001008	5353439	C00500	CC\1=C(/C(=C/C2=C
21	HMDB0062174	NA	NA	NA	NA	NA
22	HMDB0094710	3-[3-(Sulfooxy)phenyl]propanoic acid	HMDB0094710	187488		OC(=O)CCC1=CC(OS(
23	HMDB0013034	Palmitoylglycine	HMDB0013034	151008		CCCCCCCCCCCCCCCC
24	HMDB0001954	3-Hydroxyoctanoic acid	HMDB0001954	26613	C20793	CCCCCC(CC(=O)O)O
25	HMDB0010325	Ethyl glucuronide	HMDB0010325	18392195		CCO[C@H]1[C@@H]([C@
26	HMDB0007869	PC(14:0/16:0)	HMDB0007869	129657	C00157	CCCCCCCCCCCCCCCC
27	HMDB0000517	L-Arginine	HMDB0000517	6322	C00062	C(C[C@@H](C(=O)O)N
28	HMDB0002013	Butyrylcarnitine	HMDB0002013	439829	C02862	CCCC(=O)OC(CC(=O)
29	HMDB0001206	Acetyl-CoA	HMDB0001206	444493	C00024	CC(=O)SCCNC(=O)CC
30	HMDB0001043	Arachidonic acid	HMDB0001043	444899	C00219	CCCCC/C=C\C/C=C\
31	HMDB0000391	7-Ketodeoxycholic acid	HMDB0000391	188292	C04643	C[C@H](CCC(=O)O)[C
32	HMDB0003178	Heme	HMDB0003178	26945	C00032	CC1=C(CCC(O)=O)C2
33	HMDB0000696	L-Methionine	HMDB0000696	6137	C00073	CSCC[C@@H](C(=O)O)
34	HMDB0000279	Saccharopine	HMDB0000279	160556	C00449	C(CCN[C@@H](CCC(=O
35	HMDB0000959	Tiglylglycine	HMDB0000959	6441567		C/C=C(\C)/C(=O)NC(
36	HMDB0000827	Stearic acid	HMDB0000827	5281	C01530	CCCCCCCCCCCCCCCC
37	HMDB0028995	Phenylalanyl-Glycine	HMDB0028995	98207		NC(CC1=CC=CC=C1)C
38	HMDB0005765	Ophthalmic acid	HMDB0005765	7018721	C21016	CC[C@@H](C(=O)NCC
39	HMDB0011667	gamma-Glutamylglycine	HMDB0011667	165527		C(CC(=O)NCC(=O)O)[
40	HMDB0003869	Epsilon-(gamma-Glutamyl)-lysine	HMDB0003869	7015685		C(CCNC(=O)CC[C@@H
41	HMDB0011129	LysoPE(0:0/18:0)	HMDB0011129	53480667		CCCCCCCCCCCCCCCC
42	HMDB0000808	N-Butyrylglycine	HMDB0000808	88412		CCCC(=O)NCC(=O)O
43	HMDB0000641	L-Glutamine	HMDB0000641	5961	C00064	C(CC(=O)N)[C@@H](C
44	HMDB0002931	N-Acetylserine	HMDB0002931	65249		CC(=O)N[C@@H](CO)C
45	HMDB0004645	S-Nitrosoglutathione	HMDB0004645	104858		C(CC(=O)N[C@@H](CS
46	HMDB00653	Cholesterol sulfate	HMDB0000653	65076	C18043	C[C@H](CCCC(C)C)[C@
47	HMDB0001186	N1-Acetylspermine	HMDB0001186	916	C02567	CC(=O)NCCCNCCCCN
48	HMDB0012252	Linoleoyl ethanolamide	HMDB0012252	5283446		CCCCC/C=C\C/C=C\
49	HMDB0000682	Indoxyl sulfate	HMDB0000682	10258		C1=CC=C2C(=C1)C(=
50	HMDB0010388	LysoPC(18:3(9Z,12Z,15Z))	HMDB0010388	24779469	C04230	CC/C=C\C/C=C\C/C=
51	HMDB0000197	Indoleacetic acid	HMDB0000197	802	C00954	C1=CC=C2C(=C1)C(=
52	HMDB0000932	Tauro-b-muricholic acid	HMDB0000932	21124703		C[C@H](CCC(=O)NCCS
53	HMDB0000131	Glycerol	HMDB0000131	753	C00116	C(C(CO)O)O
54	HMDB0000679	Homocitrulline	HMDB0000679	65072	C02427	C(CCNC(=O)N)C[C@@
55	HMDB0000321	2-Hydroxyadipic acid	HMDB0000321	193530	C02360	C(CC(C(=O)O)O)CC(=
56	HMDB0004950	Ceramide (d18:1/18:0)	HMDB0004950	5283565	C00195	CCCCCCCCCCCCCCCC
57	HMDB0001296	Maltotetraose	HMDB0001296	439639	C02052	C([C@@H]1[C@H]([C@@
58	HMDB0002095	Malonylcarnitine	HMDB0002095	22833583		C[N+](C)(C)C[C@H](C
59	C02593	NA	NA	NA	NA	NA

60	HMDB0006455	Arachidonyl carnitine	HMDB0006455	53477832		CCCCCCCCC/C=C\C/
61	HMDB0059724	NA	NA	NA	NA	NA
62	HMDB0011621	Cinnamoylglycine	HMDB0011621	709625		C1=CC=C(C=C1)/C=C
63	HMDB0009012	PE(18:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	HMDB0009012	9546798	C00350	CCCCCCCCCCCCCCCC
64	HMDB0061714	Docosadienoate (22:2n6)	HMDB0061714	5282807	C16533	CCCCCC=CCC=CCCC
65	HMDB0000114	Glycerylphosphorylethanolamine	HMDB0000114	22833510	C01233	C(CO)N(CC(CO)O)P(=
66	HMDB0011517	LysoPE(20:4(5Z,8Z,11Z,14Z)/0:0)	HMDB0011517	42607465		CCCCC/C=C\C/C=C\
67	HMDB0240583	NA	NA	NA	NA	NA
68	HMDB0000201	L-Acetylcarnitine	HMDB0000201	7045767	C02571	CC(=O)OC(CC(=O)[O-
69	HMDB0010575	PG(16:0/18:2(9Z,12Z))	HMDB0010575	52927246		CCCCCCCCCCCCCCCC
70	HMDB0001155	Diadenosine triphosphate	HMDB0001155	14464643	C06197	C1=NC2=C(C(=N1)N)
71	HMDB0001890	Acetylcysteine	HMDB0001890	12035	C06809	CC(=O)N[C@@H](CS)C
72	HMDB0010382	LysoPC(16:0)	HMDB0010382	460602	C04230	CCCCCCCCCCCCCCCC
73	HMDB0240347	NA	NA	NA	NA	NA
74	HMDB0012101	SM(d18:1/18:1(9Z))	HMDB0012101	6443882	C00550	CCCCCCCCCCCCCC/C=
75	HMDB0240577	NA	NA	NA	NA	NA
76	HMDB0000271	Sarcosine	HMDB0000271	1088	C00213	CNCC(=O)O
77	HMDB0004029	11-Dehydrocorticosterone	HMDB0004029	13783449	C05490	C[C@]12CCC(=O)C=C1
78	HMDB0002100	Palmitoylethanolamide	HMDB0002100	4671	C16512	CCCCCCCCCCCCCCCC
79	HMDB0001893	Alpha-Tocopherol	HMDB0001893	14985	C02477	CC1=C(C(=C2CC[C@@
80	HMDB0001212	Hydantoin-5-propionic acid	HMDB0001212	782	C05565	C(CC(=O)O)C1C(=O)N
81	HMDB0011617	Adenosine 2'-phosphate	HMDB0011617	94136	C00946	C1=NC2=C(C(=N1)N)
82	HMDB0034879	1-[(5-Amino-5-carboxypentyl)amino]-1-deoxyfructose	HMDB0034879	9839580	C16488	NC(CCCCNCC1(O)OC(
83	HMDB0013128	Valerylcarnitine	HMDB0013128	53481619		CCCCC(=O)O[C@@H](
84	HMDB0001372	Thiamine pyrophosphate	HMDB0001372	1132	C00068	CC1=C(SC=[N+]1CC2=
85	HMDB0000158	L-Tyrosine	HMDB0000158	6057	C00082	C1=CC(=CC=C1C[C@
86	HMDB0000613	Erythronic acid	HMDB0000613	2781043		C([C@H]([C@H](C(=O)O
87	HMDB0003355	5-Aminopentanoic acid	HMDB0003355	138	C00431	C(CCN)CC(=O)O
88	HMDB0002092	Itaconic acid	HMDB0002092	811	C00490	C=C(CC(=O)O)C(=O)O
89	HMDB0000339	2-Methylbutyrylglycine	HMDB0000339	193872		CCC(C)C(=O)NCC(=O
90	HMDB0001316	6-Phosphogluconic acid	HMDB0001316	91493	C00345	C([C@H]([C@H]([C@@H
91	HMDB0008147	PC(18:2(9Z,12Z)/20:4(5Z,8Z,11Z,14Z))	HMDB0008147	24778979	C00157	CCCCC/C=C\C/C=C\
92	HMDB0000036	Taurocholic acid	HMDB0000036	6675	C05122	CC(CCC(=O)NCCS(=O
93	HMDB0000479	3-Methylhistidine	HMDB0000479	64969	C01152	CN1C=NC=C1C[C@@H
94	HMDB0002368	Nervonic acid	HMDB0002368	5281120	C08323	CCCCCCCC/C=C\CCC
95	HMDB0061652	3-hydroxyhexanoic acid	HMDB0061652	11829482		CCC[C@H](O)CC(O)=O
96	HMDB0240592	NA	NA	NA	NA	NA
97	HMDB0004949	Ceramide (d18:1/16:0)	HMDB0004949	5283564	C00195	CCCCCCCCCCCCCCCC
98	HMDB0002271	Imidazolepropionic acid	HMDB0002271	70630	C20522	C1=C(NC=N1)CCC(=O
99	HMDB11760	Cer(d18:0/16:0)	HMDB0011760	5283572		CCCCCCCCCCCCCCCC
100	HMDB0061705	6-Oxopiperidine-2-carboxylic acid	HMDB0061705	3014237		OC(=O)C1CCCC(O)=N
101	HMDB0007972	PC(16:0/18:1(9Z))	HMDB0007972	5497103	C00157	CCCCCCCCCCCCCCCC
102	HMDB0000497	5,6-Dihydrouridine	HMDB0000497	94312		C1CN(C(=O)NC1=O)[C
103	HMDB0010734	(R)-3-Hydroxy-hexadecanoic acid	HMDB0010734	15569776		CCCCCCCCCCCCCC[C@
104	HMDB0004704	9,10-DHOME	HMDB0004704	9966640	C14828	CCCCC/C=C\CC(C(C
105	HMDB0007969	PC(16:0/16:1(9Z))	HMDB0007969	6443788	C00157	CCCCCCCCCCCCCCCC
106	HMDB0240459	NA	NA	NA	NA	NA
107	HMDB00939	S-Adenosylhomocysteine	HMDB0000939	439155	C00021	C1=NC2=C(C(=N1)N)
108	HMDB0002203	3-Hydroxycapric acid	HMDB0002203	26612		CCCCCCCC(CC(=O)O
109	HMDB0013205	9-Decenoylcarnitine	HMDB0013205	53481651		C[N+](C)(C)CC(CC(=O
110	HMDB0012458	7alpha-Hydroxy-3-oxo-4-cholestenoate	HMDB0012458	3081085	C17337	C[C@H](CCCC(C)C(=O
111	HMDB0001413	Citicoline	HMDB0001413	13804	C00307	C[N+](C)(C)CCOP(=O
112	HMDB0000247	Sorbitol	HMDB0000247	5780	C00794	C([C@H]([C@H]([C@@H
113	HMDB0011691	Cytidine 2',3'-cyclic phosphate	HMDB0011691	53481030	C00127	C1=CN(C(=O)N=C1N)
114	HMDB0014903	Metyrosine	HMDB0014903	441350	C07921	C[C@](CC1=CC=C(C=
115	HMDB0000866	N-Acetyl-L-tyrosine	HMDB0000866	68310	C01657	CC(=O)N[C@@H](CC1=
116	HMDB0000860	Phenylpropionylglycine	HMDB0000860	1608347		C1=CC=C(C=C1)CCC(
117	HMDB0000715	Kynurenic acid	HMDB0000715	3845	C01717	C1=CC=C2C(=C1)C(=
118	HMDB0000672	Hexadecanedioic acid	HMDB0000672	10459	C19615	C(CCCCCCCC(=O)O)C
119	HMDB0001262	Maltotriose	HMDB0001262	439586	C01835	C([C@@H]1[C@H]([C@@
120	HMDB0000345	3-Hydroxyadipic acid	HMDB0000345	151913		C(CC(=O)O)C(CC(=O)
121	HMDB0000387	3-Hydroxydodecanoic acid	HMDB0000387	94216		CCCCCCCCCC(CC(=O
122	HMDB0000669	Ortho-Hydroxyphenylacetic acid	HMDB0000669	11970	C05852	C1=CC=C(C(=C1)CC(
123	HMDB0007883	PC(14:0/20:4(5Z,8Z,11Z,14Z))	HMDB0007883	24778634	C00157	CCCCCCCCCCCCCCC(=
124	HMDB0000138	Glycocholic acid	HMDB0000138	23617285	C01921	C[C@H](CCC(=O)NCC
125	HMDB0000832	Capryloylglycine	HMDB0000832	84290		CCCCCCCC(=O)NCC(
126	HMDB0002320	Imidazolelactic acid	HMDB0002320	459122	C05132	C1=CN(C=N1)CC(C(=
127	HMDB0011178	Prolylglycine	HMDB0011178	98206		C1CC(NC1)C(=O)NCC
128	HMDB0001487	NADH	HMDB0001487	928	C00004	C1C=CN(C=C1C(=O)N
129	HMDB10383	LysoPC(16:1(9Z))	HMDB0010383	24779461	C04230	CCCCCC/C=C\CCCC
130	HMDB0000225	Oxoadipic acid	HMDB0000225	71	C00322	C(CC(=O)C(=O)O)CC(
131	HMDB0003219	Sedoheptulose	HMDB0003219	439645	C08355	C(C(C(C(C(C(=O)CO)O
132	HMDB0007228	DG(18:1(9Z)/20:4(5Z,8Z,11Z,14Z)/0:0)	HMDB0007228	9543786	C00165	CCCCCCCC/C=C\CCC
133	HMDB0029965	Methyl beta-D-glucopyranoside	HMDB0029965	94214		COC1C(C(C(C(O1)CO)
134	HMDB0029131	Valyl-Leucine	HMDB0029131	6993118		CC(C)CC(NC(=O)C(N)
135	HMDB0006294	16-Hydroxy hexadecanoic acid	HMDB0006294	7058075	C18218	C(CCCCCCCC(=O)[O-
136	HMDB0000625	Gluconic acid	HMDB0000625	10690	C00257	C([C@H]([C@H]([C@@H
137	HMDB0000917	Ursocholic acid	HMDB0000917	122340	C17644	C[C@H](CCC(=O)O)[C
138	HMDB0029920	beta-D-3-Ribofuranosyluric acid	HMDB0029920	164933	C05513	OCC1OC(C(O)C1O)N1C
139	HMDB0010383	LysoPC(16:1(9Z))	HMDB0010383	24779461	C04230	CCCCCC/C=C\CCCC
140	HMDB0000510	Aminoadipic acid	HMDB0000510	469	C00956	C(CC(C(=O)O)N)CC(=
141	HMDB0000305	Vitamin A	HMDB0000305	445354	C17276	CC1=C(C(CCC1)(C)C)
142	HMDB0007112	DG(16:0/20:4(5Z,8Z,11Z,14Z)/0:0)	HMDB0007112	9543736	C00165	CCCCCCCCCCCCCCCC
143	HMDB0000848	Stearoylcarnitine	HMDB0000848	52922056		CCCCCCCCCCCCCCCC
144	HMDB0240316	NA	NA	NA	NA	NA
145	HMDB0003337	Oxidized glutathione	HMDB0003337	975	C00127	C(CC(=O)NC(CSSCC(C
146	HMDB0001276	N1-Acetylspermidine	HMDB0001276	496	C00612	CC(=O)NCCCNCCCCN

147	HMDB0003312	Daidzein	HMDB0003312	5281708	C10208	C1=CC(=CC=C1C2=C
148	HMDB0000224	O-Phosphoethanolamine	HMDB0000224	1015	C00346	C(COP(=O)(O)O)N
149	HMDB0002331	Imidazoleacetic acid riboside	HMDB0002331	440569	C05131	C1=C(N=CN1[C@H]2[C
150	HMDB0000791	L-Octanoylcarnitine	HMDB0000791	11953814	C02838	CCCCCCCC(=O)O[C@
151	HMDB0000626	Deoxycholic acid	HMDB0000626	222528	C04483	C[C@H](CCC(=O)O)[C
152	HMDB0009789	PI(16:0/20:4(5Z,8Z,11Z,14Z))	HMDB0009789		C00626	[H][C@@](COC(=O)CC
153	HMDB0001431	Pyridoxamine	HMDB0001431	1052	C00534	CC1=NC=C(C(=C1O)C
154	HMDB0000043	Betaine	HMDB0000043	247	C00719	C[N+](C)(C)CC(=O)[O-
155	HMDB0005320	NA	NA	NA	NA	NA
156	HMDB0000269	Sphinganine	HMDB0000269	91486	C00836	CCCCCCCCCCCCCCCC
157	HMDB0001068	D-Sedoheptulose 7-phosphate	HMDB0001068	22833559	C05382	C([C@@H]1[C@H]([C@H
158	HMDB0001520	Flavin Mononucleotide	HMDB0001520	643976	C00061	CC1=CC2=C(C=C1C)N
159	HMDB0012087	SM(d18:0/18:0)	HMDB0012087	44260130	C00550	CCCCCCCCCCCCCCCC
160	HMDB0011637	Taurohyocholate	HMDB0011637	0	C15516	[H][C@@]12C[C@H](O)C
161	HMDB0001494	Acetylphosphate	HMDB0001494	186	C00227	CC(=O)OP(=O)(O)O
162	HMDB0000208	Oxoglutaric acid	HMDB0000208	51	C00026	C(CC(=O)O)C(=O)C(=
163	HMDB0001396	5-Methyltetrahydrofolic acid	HMDB0001396	439234	C00440	CN1C(CNC2=C1C(=O)
164	HMDB13326	trans-2-Dodecenoylcarnitine	HMDB0013326	53481671		CCCCCCCCC/C=C/C(
165	HMDB0011756	N-Acetylleucine	HMDB0011756	70912	C02710	CC(C)C[C@@H](C(=O)
166	HMDB0029105	Tyrosyl-Glycine	HMDB0029105	7021854		NC(CC1=CC=C(O)C=C
167	HMDB0001511	Phosphocreatine	HMDB0001511	587	C02305	CN(CC(=O)O)C(=NP(=
168	HMDB0000360	2,4-Dihydroxybutanoic acid	HMDB0000360	192742		C(CO)C(C(=O)O)O
169	HMDB0000927	Valerylglycine	HMDB0000927	4737557		CCCCC(=O)NCC(=O)O
170	HMDB0010395	LysoPC(20:4(5Z,8Z,11Z,14Z))	HMDB0010395	24779476	C04230	CCCCC/C=C\C/C=C\
171	HMDB0000296	Uridine	HMDB0000296	6029	C00299	C1=CN(C(=O)NC1=O)
172	HMDB0240365	NA	NA	NA	NA	NA
173	HMDB0028929	Leucyl-Glycine	HMDB0028929	97364		CC(C)CC(N)C(=O)NCC
174	HMDB0004159	L-Urobilin	HMDB0004159	5280818	C05793	CCC1C(C(=O)NC1CC2
175	HMDB0000056	Beta-Alanine	HMDB0000056	239	C00099	C(CN)C(=O)O
176	HMDB0010168	SM(d18:0/16:0)	HMDB0010168	5283591	C00550	CCCCCCCCCCCCCCCC
177	HMDB0002302	Indole-3-propionic acid	HMDB0002302	3744		C1=CC=C2C(=C1)C(=
178	HMDB0000756	L-Hexanoylcarnitine	HMDB0000756	3246938		CCCCCC(=O)O[C@H](C
179	HMDB0061636	NA	NA	NA	NA	NA
180	HMDB0004980	cis-4-Decenoic acid	HMDB0004980	5312351		CCCCC/C=C\CCC(=C
181	HMDB0000163	D-Maltose	HMDB0000163	10991489	C00208	C([C@@H]1[C@H]([C@@
182	HMDB0000086	Glycerophosphocholine	HMDB0000086	71920	C00670	C[N+](C)(C)CCOP(=O
183	HMDB41718	NA	NA	NA	NA	NA
184	HMDB0005065	Oleoylcarnitine	HMDB0005065	46907933		CCCCCCCC/C=C\CCC
185	HMDB0000840	Salicyluric acid	HMDB0000840	10253	C07588	C1=CC=C(C(=C1)C(=
186	HMDB0000755	Hydroxyphenyllactic acid	HMDB0000755	9378	C03672	C1=CC(=CC=C1CC(C
187	HMDB0000205	Phenylpyruvic acid	HMDB0000205	997	C00166	C1=CC=C(C=C1)CC(=
188	HMDB0000874	Tauroursodeoxycholic acid	HMDB0000874	12443252		C[C@H](CCC(=O)NCCS
189	HMDB0000555	3-Methyladipic acid	HMDB0000555	6999745		C[C@@H](CCC(=O)O)C
190	HMDB0001015	N-Formyl-L-methionine	HMDB0001015	6995182	C03145	CSCC[C@H](C(=O)O)N
191	HMDB0009003	PE(18:0/20:4(5Z,8Z,11Z,14Z))	HMDB0009003	5289133	C00350	CCCCCCCCCCCCCCCC
192	HMDB0002024	Imidazoleacetic acid	HMDB0002024	96215	C02835	C1=C(NC=N1)CC(=O)
193	HMDB0000350	3-Hydroxysebacic acid	HMDB0000350	3017884		C(CCCC(=O)O)CCC(C
194	HMDB0000651	Decanoylcarnitine	HMDB0000651	10245190		CCCCCCCCCC(=O)OC
195	HMDB0001254	Glucosamine 6-phosphate	HMDB0001254	439217	C00352	C([C@@H]1[C@H]([C@@
196	HMDB0006028	N-Acetylasparagine	HMDB0006028	99715		CC(=O)N[C@@H](CC(=
197	HMDB0009093	PE(18:2(9Z,12Z)/18:2(9Z,12Z))	HMDB0009093	9546812	C00350	CCCCC/C=C\C/C=C\
198	HMDB0000782	Octadecanedioic acid	HMDB0000782	70095		C(CCCCCCCCC(=O)O
199	HMDB0001275	Propionyl-CoA	HMDB0001275	439164	C00100	CCC(=O)SCCNC(=O)C
200	HMDB0062551	4-ethylphenylsulfate	HMDB0062551	20822574		CCC1=CC=C(OS(O)(=
201	HMDB0001416	Pantetheine 4'-phosphate	HMDB0001416	987	C01134	CC(C)(COP(=O)(O)O)
202	HMDB0011732	2-Keto-L-gluconate	HMDB0011732	50	C03342	C(C(C(C(=O)C(=O)
203	HMDB0000061	Adenosine 3',5'-diphosphate	HMDB0000061	159296	C00054	C1=NC2=C(C(=N1)N)
204	HMDB0006469	Linoleyl carnitine	HMDB0006469	6450015		CCCCC/C=C\C/C=C\
205	HMDB0000958	trans-Aconitic acid	HMDB0000958	444212	C02341	C(/C(=C\C(=O)O)/C(
206	HMDB0000722	Lithocholyltaurine	HMDB0000722	53477716	C02592	C[C@H](CCC(=O)NCCS
207	HMDB0012097	SM(d18:1/14:0)	HMDB0012097	11433862		CCCCCCCCCCCCC/C=
208	HMDB0000512	N-Acetyl-L-phenylalanine	HMDB0000512	74839	C03519	CC(=O)N[C@@H](CC1=
209	HMDB0000691	Malonic acid	HMDB0000691	867	C04025	C(C(=O)O)C(=O)O
210	HMDB0000872	Tetradecanedioic acid	HMDB0000872	13185		C(CCCCCCC(=O)O)CC
211	HMDB0000299	Xanthosine	HMDB0000299	64959	C01762	C1=NC2=C(N1[C@H]3[
212	HMDB0004827	Proline betaine	HMDB0004827	7016563	C10172	C[N+]1(CCC[C@H]1C(=
213	HMDB0000623	Dodecanedioic acid	HMDB0000623	12736	C02678	C(CCCCCC(=O)O)CCC
214	HMDB0001874	D-threo-Isocitric acid	HMDB0001874	5318532	C00451	C([C@@H]([C@H](C(=C
215	HMDB0000044	Ascorbic acid	HMDB0000044	54670067	C01041	C([C@@H]([C@@H]1C(=
216	HMDB0002243	Picolinic acid	HMDB0002243	1018	C10164	C1=CC=NC(=C1)C(=O
217	HMDB10737	(R)-3-Hydroxy-Octadecanoic acid	HMDB0010737	5312838		CCCCCCCCCCCCCCCC
218	HMDB0000982	5-Methylcytidine	HMDB0000982	92918		CC1=CN(C(=O)N=C1N
219	HMDB0003148	Argininic acid	HMDB0003148	160437		C(C[C@@H](C(=O)O)O
220	HMDB0000071	Deoxyinosine	HMDB0000071	65058	C05512	C1[C@@H]([C@H](O[C@
221	HMDB61711	Methylphosphate	HMDB0061711	13130		COP(O)(O)=O
222	HMDB0240388	NA	NA	NA	NA	NA
223	HMDB0000017	4-Pyridoxic acid	HMDB0000017	6723	C00847	CC1=NC=C(C(=C1O)C
224	HMDB0061677	NA	NA	NA	NA	NA
225	HMDB0013287	Ne,Ne dimethyllysine	HMDB0013287	4478779	C05545	CN(C)CCCCC(C(=O)O
226	HMDB0000089	Cytidine	HMDB0000089	6253	C00475	C1=CN(C(=O)N=C1N)
227	HMDB0029200	Ferulic acid 4-sulfate	HMDB0029200	6305574		COC1=C(C=CC(=C1)/
228	HMDB0000893	Suberic acid	HMDB0000893	10457	C08278	C(CCCC(=O)O)CCC(=
229	HMDB0007121	DG(16:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	HMDB0007121	9543827		CCCCCCCCCCCCCCCC
230	HMDB0001401	Glucose 6-phosphate	HMDB0001401	5958	C00092	C([C@@H]1[C@H]([C@@
231	HMDB0000413	3-Hydroxydodecanedioic acid	HMDB0000413	16663321		C(CCCCC(=O)O)CCC(
232	HMDB0002815	LysoPC(18:1(9Z))	HMDB0002815	16081932	C04230	CCCCCCCC/C=C\CC
233	HMDB0001173	5'-Methylthioadenosine	HMDB0001173	439176	C00170	CSC[C@@H]1[C@H]([C@

234	HMDB0001564	CDP-Ethanolamine	HMDB0001564	123727	C00570	C1=CN(C(=O)N=C1N)
235	HMDB0013130	Glutarylcarnitine	HMDB0013130	71317118		C[N+](C)(C)C[C@@H](C
236	HMDB0000875	Trigonelline	HMDB0000875	5570	C01004	C[N+]1=CC=CC(=C1)C
237	HMDB0000169	D-Mannose	HMDB0000169	18950	C00936	C([C@@H]1[C@H]([C@@
238	HMDB0011640	Uridine 2',3'-cyclic phosphate	HMDB0011640	439715	C02355	C1=CN(C(=O)NC1=O)
239	HMDB0000267	Pyroglutamic acid	HMDB0000267	7405	C01879	C1CC(=O)N[C@@H]1C(
240	HMDB0006344	Alpha-N-Phenylacetyl-L-glutamine	HMDB0006344	92258	C04148	C1=CC=C(C=C1)CC(=
241	HMDB0240588	NA	NA	NA	NA	NA
242	HMDB0003426	Pantetheine	HMDB0003426	479	C00831	CC(C)(CO)C(C(=O)NC
243	HMDB0000094	Citric acid	HMDB0000094	311	C00158	C(C(=O)O)C(CC(=O)C
244	HMDB0003290	Gulonic acid	HMDB0003290	152304	C00800	C([C@H]([C@@H]([C@H
245	HMDB0000126	Glycerol 3-phosphate	HMDB0000126	439162	C00093	C([C@H](COP(=O)(O)C
246	HMDB0001078	Mannose 6-phosphate	HMDB0001078	439198	C00275	C([C@@H]1[C@H]([C@@
247	HMDB0006210	Heptadecanoyl carnitine	HMDB0006210	53477803		CCCCCCCCCCCCCCCC
248	HMDB0002166	(S)-b-aminoisobutyric acid	HMDB0002166	439434	C03284	C[C@@H](CN)C(=O)O
249	HMDB0000477	7Z,10Z-Hexadecadienoic acid	HMDB0000477	13932172		CCCCC/C=C\C/C=C\
250	HMDB0000896	Taurodeoxycholic acid	HMDB0000896	2733768	C05463	C[C@H](CCC(=O)NCCS
251	HMDB0002721	1-Methylinosine	HMDB0002721	65095		CN1C=NC2=C(C1=O)N
252	HMDB0038670	NA	NA	NA	NA	NA
253	HMDB0000665	Leucinic acid	HMDB0000665	92779		CC(C)CC(C(=O)O)O
254	HMDB0011130	LysoPE(18:0/0:0)	HMDB0011130	9547068	C21484	CCCCCCCCCCCCCCCC
255	HMDB0000235	Thiamine	HMDB0000235	1130	C00378	CC1=C(SC=[N+]1CC2=
256	HMDB0000206	N6-Acetyl-L-lysine	HMDB0000206	92832	C02727	CC(=O)NCCCC[C@@H]
257	HMDB000225	NA	NA	NA	NA	NA
258	HMDB04988	Pi-Methylimidazoleacetic acid	HMDB0004988	6451814		CN1C=NC=C1CC(=O)
259	HMDB0000122	D-Glucose	HMDB0000122	5793	C00221	C([C@@H]1[C@H]([C@@
260	HMDB0000951	Taurochenodesoxycholic acid	HMDB0000951	387316	C05465	C[C@H](CCC(=O)NCCS
261	HMDB0061684	N-Acetylisoleucine	HMDB0061684	7036275		CC[C@H](C)[C@H](NC(
262	HMDB0000529	5-Dodecenoic acid	HMDB0000529	5312378		CCCCCC/C=C\CCCC(
263	HMDB0000565	Galactonic acid	HMDB0000565	128869	C00880	C([C@H]([C@@H]([C@@
264	HMDB0240578	NA	NA	NA	NA	NA
265	HMDB0011686	p-Cresol glucuronide	HMDB0011686	154035		CC1=CC=C(C=C1)O[C
266	HMDB0011635	p-Cresol sulfate	HMDB0011635	4615423		CC1=CC=C(C=C1)OS(
267	HMDB0000671	Indolelactic acid	HMDB0000671	92904	C02043	C1=CC=C2C(=C1)C(=
268	HMDB0001264	Dehydroascorbic acid	HMDB0001264	7786	C05422	C([C@H]([C@@H]1C(=C
269	HMDB0001547	Corticosterone	HMDB0001547	5753	C02140	C[C@]12CCC(=O)C=C1
270	HMDB0000660	D-Fructose	HMDB0000660	439709	C02336	C([C@@H]1[C@H]([C@@
271	HMDB0000792	Sebacic acid	HMDB0000792	5192	C08277	C(CCCCC(=O)O)CCCC
272	HMDB0000821	Phenylacetylglycine	HMDB0000821	68144	C05598	C1=CC=C(C=C1)CC(=
273	HMDB0000288	Uridine 5'-monophosphate	HMDB0000288	6030	C00105	C1=CN(C(=O)NC1=O)
274	HMDB0002820	Methylimidazoleacetic acid	HMDB0002820	75810	C05828	CN1C=C(N=C1)CC(=O
275	HMDB000506	NA	NA	NA	NA	NA
276	HMDB0000892	Valeric acid	HMDB0000892	7991	C00803	CCCCC(=O)O
277	HMDB0000699	1-Methylnicotinamide	HMDB0000699	457	C02918	C[N+]1=CC=CC(=C1)C
278	HMDB0000355	3-Hydroxymethylglutaric acid	HMDB0000355	1662	C03761	CC(CC(=O)O)(CC(=O)
279	HMDB0013676	2,6-Dihydroxybenzoic acid	HMDB0013676	9338	C21298	C1=CC(=C(C(=C1)O)C
280	HMDB0001056	Dihydrofolic acid	HMDB0001056	98792	C00415	C1C(=NC2=C(N1)NC(=
281	HMDB0001049	gamma-Glutamylcysteine	HMDB0001049	123938	C00669	C(CC(=O)N[C@@H](CS
282	HMDB0004193	N1-Methyl-2-pyridone-5-carboxamide	HMDB0004193	69698	C05842	CN1C=C(C=CC1=O)C
283	HMDB0000638	Dodecanoic acid	HMDB0000638	3893	C02679	CCCCCCCCCCCC(=O)
284	HMDB0000767	Pseudouridine	HMDB0000767	15047	C02067	C1=C(C(=O)NC(=O)N
285	HMDB0000622	Ethylmalonic acid	HMDB0000622	11756		CCC(C(=O)O)C(=O)O
286	HMDB0003320	Indole-3-carboxylic acid	HMDB0003320	69867	C19837	C1=CC=C2C(=C1)C(=
287	HMDB0013127	Hydroxybutyrylcarnitine	HMDB0013127	53481617		CC(CC(=O)O[C@@H](C
288	HMDB0000560	5,8-Tetradecadienoic acid	HMDB0000560	5312409		CCCCC/C=C\C/C=C\
289	HMDB0000167	L-Threonine	HMDB0000167	6288	C00188	C[C@H]([C@@H](C(=O)
290	HMDB0003334	Symmetric dimethylarginine	HMDB0003334	169148		CNC(=NC)NCCC[C@@
291	HMDB0000222	L-Palmitoylcarnitine	HMDB0000222	11953816	C02990	CCCCCCCCCCCCCCCC
292	HMDB0000562	Creatinine	HMDB0000562	588	C00791	CN1CC(=O)N=C1N
293	HMDB0000779	Phenyllactic acid	HMDB0000779	3848	C01479	C1=CC=C(C=C1)CC(C
294	HMDB0013336	3-Hydroxyhexadecanoylcarnitine	HMDB0013336	53481691		CCCCCCCCCCCCCC(C
295	HMDB0000752	Methylglutaric acid	HMDB0000752	12284		CC(CC(=O)O)CC(=O)C
296	HMDB0002108	Methylcysteine	HMDB0002108	384585100	C22040	CSC[C@@H](C(=O)O)N
297	HMDB0003331	1-Methyladenosine	HMDB0003331	27476	C02494	CN1C=NC2=C(C1=N)N
298	HMDB0000448	Adipic acid	HMDB0000448	196	C06104	C(CCC(=O)O)CC(=O)O
299	HMDB0001348	SM(d18:1/18:0)	HMDB0001348	5283588	C00550	CCCCCCCCCCCCCCCC
300	HMDB0000078	Cysteinylglycine	HMDB0000078	439498	C01419	C([C@@H](C(=O)NCC(
301	HMDB0000023	(S)-3-Hydroxyisobutyric acid	HMDB0000023	87	C06001	C[C@@H](CO)C(=O)O
302	HMDB0001325	N6,N6,N6-Trimethyl-L-lysine	HMDB0001325	440120	C03793	C[N+](C)(C)CCCC[C@
303	HMDB0000897	7-Methylguanine	HMDB0000897	11361	C02242	CN1C=NC2=C1C(=O)N
304	HMDB0013133	Methylmalonylcarnitine	HMDB0013133	53481628		CC(C(=O)O)C(=O)O[C
305	HMDB0041623	N6-Carbamoyl-L-threonyladenosine	HMDB0041623	92021849		C[C@@H](O)[C@H](NC(
306	HMDB0002064	N-Acetylputrescine	HMDB0002064	122356	C02714	CC(=O)NCCCCN
307	HMDB0062557	N-Acetylthreonine	HMDB0062557	152204		C[C@@H](O)[C@H](NC(
308	HMDB0000005	2-Ketobutyric acid	HMDB0000005	58	C00109	CCC(=O)C(=O)O
309	HMDB0000462	Allantoin	HMDB0000462	204	C01551	C1(C(=O)NC(=O)N1)N
310	HMDB0002201	N-Carboxyethyl-g-aminobutyric acid	HMDB0002201	2572		C(CC(=O)O)CNCCC(=
311	HMDB0000210	Pantothenic acid	HMDB0000210	6613	C00864	CC(C)(CO)C(C(=O)NC
312	HMDB0000011	(R)-3-Hydroxybutyric acid	HMDB0000011	92135	C01089	C[C@H](CC(=O)O)O
313	HMDB0000687	L-Leucine	HMDB0000687	6106	C00123	CC(C)C[C@@H](C(=O)
314	HMDB0001373	Dephospho-CoA	HMDB0001373	439335	C00882	CC(C)(COP(=O)(O)OP
315	HMDB0000645	Galactose 1-phosphate	HMDB0000645	123912	C00446	C([C@@H]1[C@@H]([C@
316	HMDB0000211	myo-Inositol	HMDB0000211		C00137	O[C@H]1[C@H](O)[C@@
317	HMDB0000656	Cysteineglutathione disulfide	HMDB0000656	53477713		C(CC(=O)N[C@@H](CS
318	HMDB0002712	1,5-Anhydrosorbitol	HMDB0002712	64960	C07326	C1[C@@H]([C@H]([C@@
319	HMDB0004194	N1-Methyl-4-pyridone-3-carboxamide	HMDB0004194	440810	C05843	CN1C=CC(=O)C(=C1)
320	HMDB0000725	4-Hydroxyproline	HMDB0000725	5810	C01157	C1[C@H](CN[C@@H]1C

321	HMDB0061717	NA	NA	NA	NA	NA
322	HMDB0000125	NA	NA	NA	NA	NA
323	HMDB0011757	N-Acetylvaline	HMDB0011757	227752		CC(C)C(C(=O)O)NC(=
324	HMDB0000522	3-Methylglutaconic acid	HMDB0000522	1551553		C/C(=C\C(=O)O)/CC(
325	HMDB0012141	(R)-2,3-Dihydroxy-isovalerate	HMDB0012141	440279	C04272	CC(C)([C@H](C(=O)O)
326	HMDB0000172	L-Isoleucine	HMDB0000172	6306	C00407	CC[C@H](C)[C@@H](C(
327	HMDB0000630	Cytosine	HMDB0000630	597	C00380	C1=C(NC(=O)N=C1)N
328	HMDB0001423	Coenzyme A	HMDB0001423	87642	C00010	CC(C)(COP(=O)(O)OP
329	HMDB0001552	2-Keto-glutaramic acid	HMDB0001552	48	C00940	C(CC(=O)N)C(=O)C(=
330	HMDB0002329	Oxalic acid	HMDB0002329	971	C00209	C(=O)(C(=O)O)O
331	HMDB0000532	Acetylglycine	HMDB0000532	10972		CC(=O)NCC(=O)O
332	HMDB0000883	L-Valine	HMDB0000883	6287	C00183	CC(C)[C@@H](C(=O)O
333	HMDB0000064	Creatine	HMDB0000064	586	C00300	CN(CC(=O)O)C(=N)N
334	HMDB0001414	Putrescine	HMDB0001414	1045	C00134	C(CCN)CN
335	HMDB0000177	L-Histidine	HMDB0000177	6274	C00135	C1=C(NC=N1)C[C@@H
336	HMDB0000991	DL-2-Aminooctanoic acid	HMDB0000991	69522		CCCCCCC(C(=O)O)N
337	HMDB0000161	L-Alanine	HMDB0000161	5950	C00041	C[C@@H](C(=O)O)N
338	HMDB0000294	Urea	HMDB0000294	2447	C00086	C(=O)(N)N
339	HMDB01448	Sulfate	HMDB0001448	1117	C00059	[O-]S(=O)(=O)[O-]
340	HMDB0002000	Myristoleic acid	HMDB0002000	5281119	C08322	CCCC/C=C\CCCCCC
341	HMDB0240253	NA	NA	NA	NA	NA
342	HMDB0000729	Alpha-Hydroxyisobutyric acid	HMDB0000729	11671		CC(C)(C(=O)O)O
343	HMDB0000754	3-Hydroxyisovaleric acid	HMDB0000754	69362	C20827	CC(C)(CC(=O)O)O
344	HMDB0000498	4-Deoxyerythronic acid	HMDB0000498	13120901		C[C@H]([C@H](C(=O)C
345	HMDB0002453	4-Deoxythreonic acid	HMDB0002453	10964471		C[C@H]([C@@H](C(=O)
346	HMDB0000325	3-Hydroxysuberic acid	HMDB0000325	22328017		C(CCC(=O)O)CC(CC(=
347	HMDB0000317	2-Hydroxy-3-methylpentanoic acid	HMDB0000317	10796774		CC[C@@H](C)[C@H](C(
348	HMDB0000001	1-Methylhistidine	HMDB0000001	92105	C01152	CN1C=C(N=C1)C[C@@
349	HMDB0000190	L-Lactic acid	HMDB0000190	61503	C00186	C[C@@H](C(=O)O)O
350	HMDB0000407	2-Hydroxy-3-methylbutyric acid	HMDB0000407	99823		CC(C)C(C(=O)O)O

The second step is to check concentration values. For SSP analysis, the concentration must be measured in *umol* for blood and CSF samples. The urinary concentrations must be first converted to *umol/mmol_creatinine* in order to compare with reported concentrations in literature. No missing or negative values are allowed in SSP analysis. The concentration data for QEA analysis is more flexible. Users can upload either the original concentration data or normalized data. Missing or negative values are allowed (coded as *NA*) for QEA.

5 Selection of Metabolite Set Library

Before proceeding to enrichment analysis, a metabolite set library has to be chosen. There are seven built-in libraries offered by MSEA:

- Metabolic pathway associated metabolite sets (*currently contains 99 entries*);
- Disease associated metabolite sets (reported in blood) (*currently contains 344 entries*);
- Disease associated metabolite sets (reported in urine) (*currently contains 384 entries*)
- Disease associated metabolite sets (reported in CSF) (*currently contains 166 entries*)
- Metabolite sets associated with SNPs (*currently contains 4598 entries*)
- Predicted metabolite sets based on computational enzyme knockout model (*currently contains 912 entries*)
- Metabolite sets based on locations (*currently contains 73 entries*)
- Drug pathway associated metabolite sets (*currently contains 461 entries*)

In addition, MSEA also allows user-defined metabolite sets to be uploaded to perform enrichment analysis on arbitrary groups of compounds which researchers want to test. The metabolite set library is simply a two-column comma separated text file with the first column for metabolite set names and the second column for its compound names (**must use HMDB compound name**) separated by "; ". Please note, the built-in libraries are mainly from human studies. The functional grouping of metabolites may not be valid. Therefore, for data from subjects other than human being, users are suggested to upload their self-defined metabolite set libraries for enrichment analysis.

6 Enrichment Analysis

Over Representation Analysis (ORA) is performed when a list of compound names is provided. The list of compound list can be obtained through conventional feature selection methods, or from a clustering algorithm, or from the compounds with abnormal concentrations detected in SSP, to investigate if some biologically meaningful patterns can be identified.

ORA was implemented using the *hypergeometric test* to evaluate whether a particular metabolite set is represented more than expected by chance within the given compound list. One-tailed p values are provided after adjusting for multiple testing. **Figure 2** below summarizes the result.

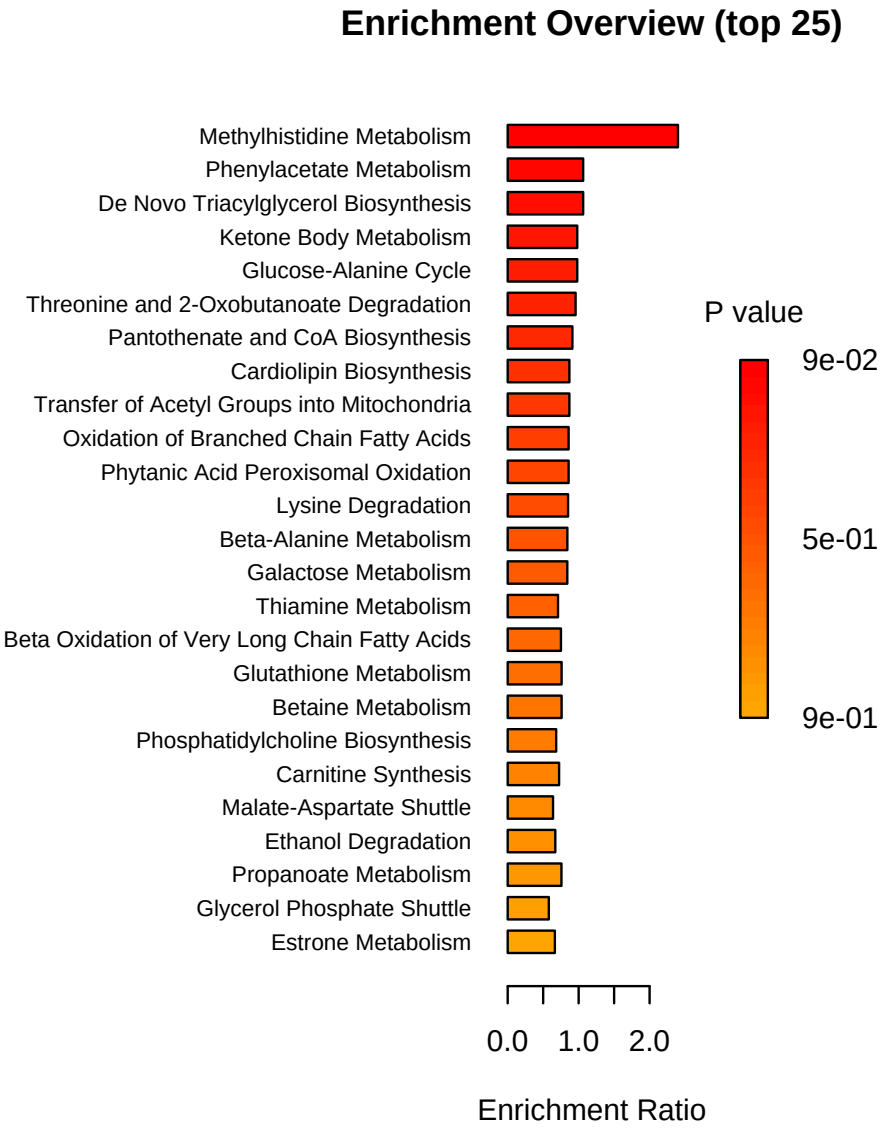

Figure 1: Summary Plot for Over Representation Analysis (ORA)

Table 2: Result from Over Representation Analysis

	total	expected	hits	Raw p	Holm p	FDR
Methylhistidine Metabolism	4	1.25	3	9.38E-02	1.00E+00	1.00E+00
Phenylacetate Metabolism	9	2.82	3	5.73E-01	1.00E+00	1.00E+00
De Novo Triacylglycerol Biosynthesis	9	2.82	3	5.73E-01	1.00E+00	1.00E+00
Ketone Body Metabolism	13	4.08	4	6.22E-01	1.00E+00	1.00E+00
Glucose-Alanine Cycle	13	4.08	4	6.22E-01	1.00E+00	1.00E+00
Threonine and 2-Oxobutanoate Degradation	20	6.27	6	6.36E-01	1.00E+00	1.00E+00
Pantothenate and CoA Biosynthesis	21	6.58	6	6.88E-01	1.00E+00	1.00E+00
Cardiolipin Biosynthesis	11	3.45	3	7.22E-01	1.00E+00	1.00E+00
Transfer of Acetyl Groups into Mitochondria	22	6.90	6	7.36E-01	1.00E+00	1.00E+00
Oxidation of Branched Chain Fatty Acids	26	8.15	7	7.56E-01	1.00E+00	1.00E+00
Phytanic Acid Peroxisomal Oxidation	26	8.15	7	7.56E-01	1.00E+00	1.00E+00
Lysine Degradation	30	9.40	8	7.73E-01	1.00E+00	1.00E+00
Beta-Alanine Metabolism	34	10.70	9	7.89E-01	1.00E+00	1.00E+00
Galactose Metabolism	38	11.90	10	8.03E-01	1.00E+00	1.00E+00
Thiamine Metabolism	9	2.82	2	8.28E-01	1.00E+00	1.00E+00
Beta Oxidation of Very Long Chain Fatty Acids	17	5.33	4	8.32E-01	1.00E+00	1.00E+00
Glutathione Metabolism	21	6.58	5	8.39E-01	1.00E+00	1.00E+00
Betaine Metabolism	21	6.58	5	8.39E-01	1.00E+00	1.00E+00
Phosphatidylcholine Biosynthesis	14	4.39	3	8.66E-01	1.00E+00	1.00E+00
Carnitine Synthesis	22	6.90	5	8.69E-01	1.00E+00	1.00E+00
Malate-Aspartate Shuttle	10	3.13	2	8.72E-01	1.00E+00	1.00E+00
Ethanol Degradation	19	5.96	4	8.94E-01	1.00E+00	1.00E+00
Propanoate Metabolism	42	13.20	10	8.96E-01	1.00E+00	1.00E+00
Glycerol Phosphate Shuttle	11	3.45	2	9.05E-01	1.00E+00	1.00E+00
Estrone Metabolism	24	7.52	5	9.16E-01	1.00E+00	1.00E+00
Nucleotide Sugars Metabolism	20	6.27	4	9.16E-01	1.00E+00	1.00E+00
Catecholamine Biosynthesis	20	6.27	4	9.16E-01	1.00E+00	1.00E+00
Phosphatidylethanolamine Biosynthesis	12	3.76	2	9.30E-01	1.00E+00	1.00E+00
Urea Cycle	29	9.09	6	9.32E-01	1.00E+00	1.00E+00
Plasmalogen Synthesis	26	8.15	5	9.47E-01	1.00E+00	1.00E+00
Thyroid hormone synthesis	13	4.08	2	9.49E-01	1.00E+00	1.00E+00
Spermidine and Spermine Biosynthesis	18	5.64	3	9.54E-01	1.00E+00	1.00E+00
Methionine Metabolism	43	13.50	9	9.57E-01	1.00E+00	1.00E+00
Glycine and Serine Metabolism	59	18.50	13	9.62E-01	1.00E+00	1.00E+00
Butyrate Metabolism	19	5.96	3	9.66E-01	1.00E+00	1.00E+00
Mitochondrial Electron Transport Chain	19	5.96	3	9.66E-01	1.00E+00	1.00E+00
Citric Acid Cycle	32	10.00	6	9.66E-01	1.00E+00	1.00E+00
Homocysteine Degradation	9	2.82	1	9.67E-01	1.00E+00	1.00E+00
Lactose Degradation	9	2.82	1	9.67E-01	1.00E+00	1.00E+00
Mitochondrial Beta-Oxidation of Long Chain Saturated Fatty Acids	28	8.78	5	9.67E-01	1.00E+00	1.00E+00
Caffeine Metabolism	24	7.52	4	9.70E-01	1.00E+00	1.00E+00
Vitamin B6 Metabolism	20	6.27	3	9.74E-01	1.00E+00	1.00E+00
Lactose Synthesis	20	6.27	3	9.74E-01	1.00E+00	1.00E+00
Phospholipid Biosynthesis	29	9.09	5	9.74E-01	1.00E+00	1.00E+00
Glycerolipid Metabolism	25	7.84	4	9.77E-01	1.00E+00	1.00E+00
Warburg Effect	58	18.20	12	9.78E-01	1.00E+00	1.00E+00
Histidine Metabolism	43	13.50	8	9.82E-01	1.00E+00	1.00E+00
D-Arginine and D-Ornithine Metabolism	11	3.45	1	9.84E-01	1.00E+00	1.00E+00
Degradation of Superoxides	11	3.45	1	9.84E-01	1.00E+00	1.00E+00
Starch and Sucrose Metabolism	31	9.72	5	9.85E-01	1.00E+00	1.00E+00
Sulfate/Sulfite Metabolism	22	6.90	3	9.86E-01	1.00E+00	1.00E+00
Alanine Metabolism	17	5.33	2	9.86E-01	1.00E+00	1.00E+00
Sphingolipid Metabolism	40	12.50	7	9.86E-01	1.00E+00	1.00E+00
Mitochondrial Beta-Oxidation of Short Chain Saturated Fatty Acids	27	8.46	4	9.87E-01	1.00E+00	1.00E+00
Mitochondrial Beta-Oxidation of Medium Chain Saturated Fatty Acids	27	8.46	4	9.87E-01	1.00E+00	1.00E+00
Glutamate Metabolism	49	15.40	9	9.88E-01	1.00E+00	1.00E+00
Fructose and Mannose Degradation	32	10.00	5	9.88E-01	1.00E+00	1.00E+00
Nicotinate and Nicotinamide Metabolism	37	11.60	6	9.90E-01	1.00E+00	1.00E+00
Retinol Metabolism	37	11.60	6	9.90E-01	1.00E+00	1.00E+00
Phenylalanine and Tyrosine Metabolism	28	8.78	4	9.90E-01	1.00E+00	1.00E+00
Amino Sugar Metabolism	33	10.30	5	9.91E-01	1.00E+00	1.00E+00
Androgen and Estrogen Metabolism	33	10.30	5	9.91E-01	1.00E+00	1.00E+00
Androstenedione Metabolism	24	7.52	3	9.92E-01	1.00E+00	1.00E+00
Valine, Leucine and Isoleucine Degradation	60	18.80	11	9.94E-01	1.00E+00	1.00E+00
Glycolysis	25	7.84	3	9.94E-01	1.00E+00	1.00E+00
Aspartate Metabolism	35	11.00	5	9.95E-01	1.00E+00	1.00E+00
Gluconeogenesis	35	11.00	5	9.95E-01	1.00E+00	1.00E+00
Fatty Acid Biosynthesis	35	11.00	5	9.95E-01	1.00E+00	1.00E+00
Arginine and Proline Metabolism	53	16.60	9	9.95E-01	1.00E+00	1.00E+00
Cysteine Metabolism	26	8.15	3	9.96E-01	1.00E+00	1.00E+00
Ammonia Recycling	32	10.00	4	9.97E-01	1.00E+00	1.00E+00
Tryptophan Metabolism	60	18.80	10	9.98E-01	1.00E+00	1.00E+00
Bile Acid Biosynthesis	65	20.40	11	9.98E-01	1.00E+00	1.00E+00
Pentose Phosphate Pathway	29	9.09	3	9.98E-01	1.00E+00	1.00E+00
Folate Metabolism	29	9.09	3	9.98E-01	1.00E+00	1.00E+00
Phosphatidylinositol Phosphate Metabolism	17	5.33	1	9.98E-01	1.00E+00	1.00E+00

Alpha Linolenic Acid and Linoleic Acid Metabolism	19	5.96	1	9.99E-01	1.00E+00	1.00E+00
Inositol Phosphate Metabolism	26	8.15	2	9.99E-01	1.00E+00	1.00E+00
Pyruvate Metabolism	48	15.00	6	9.99E-01	1.00E+00	1.00E+00
Ubiquinone Biosynthesis	20	6.27	1	1.00E+00	1.00E+00	1.00E+00
Riboflavin Metabolism	20	6.27	1	1.00E+00	1.00E+00	1.00E+00
Selenoamino Acid Metabolism	28	8.78	2	1.00E+00	1.00E+00	1.00E+00
Porphyrin Metabolism	40	12.50	4	1.00E+00	1.00E+00	1.00E+00
Pterine Biosynthesis	29	9.09	2	1.00E+00	1.00E+00	1.00E+00
Fatty Acid Elongation In Mitochondria	35	11.00	3	1.00E+00	1.00E+00	1.00E+00
Fatty acid Metabolism	43	13.50	4	1.00E+00	1.00E+00	1.00E+00
Steroidogenesis	43	13.50	4	1.00E+00	1.00E+00	1.00E+00
Pyrimidine Metabolism	59	18.50	7	1.00E+00	1.00E+00	1.00E+00
Inositol Metabolism	33	10.30	2	1.00E+00	1.00E+00	1.00E+00
Steroid Biosynthesis	48	15.00	3	1.00E+00	1.00E+00	1.00E+00
Tyrosine Metabolism	72	22.60	6	1.00E+00	1.00E+00	1.00E+00
Purine Metabolism	74	23.20	5	1.00E+00	1.00E+00	1.00E+00
Arachidonic Acid Metabolism	69	21.60	4	1.00E+00	1.00E+00	1.00E+00

7 Appendix: R Command History

```
 [1] "mSet<-InitDataObjects(\"conc\", \"msetora\", FALSE)"
 [2] "cmpd.vec<-c(\"HMDB0028907\",\"HMDB0060018\",\"HMDB0000159\",\"HMDB0008138\",\"HMDB0041724\",\"
 [3] "mSet<-Setup.MapData(mSet, cmpd.vec);"
 [4] "mSet<-CrossReferencing(mSet, \"hmdb\");"
 [5] "mSet<-CreateMappingResultTable(mSet)"
 [6] "mSet<-SetMetabolomeFilter(mSet, F);"
 [7] "mSet<-SetCurrentMsetLib(mSet, \"smpdb_pathway\", 2);"
 [8] "mSet<-CalculateHyperScore(mSet)"
 [9] "mSet<-PlotORA(mSet, \"ora_0_\", \"net\", \"png\", 72, width=NA)"
[10] "mSet<-PlotEnrichDotPlot(mSet, \"ora\", \"ora_dot_0_\", \"png\", 72, width=NA)"
[11] "mSet<-CalculateHyperScore(mSet)"
[12] "mSet<-PlotORA(mSet, \"ora_1_\", \"net\", \"png\", 72, width=NA)"
[13] "mSet<-PlotEnrichDotPlot(mSet, \"ora\", \"ora_dot_1_\", \"png\", 72, width=NA)"
[14] "mSet<-SaveTransformedData(mSet)"
[15] "mSet<-PreparePDFReport(mSet, \"guest4495850689290871210\")\n"
```

The report was generated on Sat Mar 20 21:29:24 2021 with R version 4.0.2 (2020-06-22).