Metabolomic Data Analysis with MetaboAnalyst 5.0

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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*

Table 1: Re

	Query	Match	HMDB	PubChem	KEGG	SMILES
1	1 3-Dimethyluric acid	1,3-Dimethyluric acid	HMDB0001857	70346		CN1C2=C(C(=O)N(C1
2	1-Methylhistidine	1-Methylhistidine	HMDB0000001	92105	C01152	CN1C=C(N=C1)C[C@
3	11a-Hydroxyprogesterone	11a-Hydroxyprogesterone	HMDB0000920	440105	C03747	CC(=O)C1CC[C@@H]2
4	3-Phenylbutyric acid	3-Phenylbutyric acid	HMDB0001955	20724		CC(CC(=O)O)C1=CC=
5	5-Hydroxytryptophan	5-Hydroxy-L-tryptophan	HMDB0000472	144	C00643	C1=CC2=C(C=C1O)C
6	5-Methoxytryptamine	5-Methoxytryptamine	HMDB0004095	1833	C05659	COC1=CC2=C(C=C1)
7	5-Methylcytosine	5-Methylcytosine	HMDB0002894	65040	C02376	CC1=C(NC(=O)N=C1
8	5-Phenylvaleric acid	5-Phenylvaleric acid	HMDB0002043	16757		C1=CC=C(C=C1)CCC
9	a-ketoglutarate	Oxoglutaric acid	HMDB0000208	51	C00026	C(CC(=O)O)C(=O)C(=
10	Acetyl glycine	Phenylacetylglycine	HMDB0000821	68144	C05598	C1=CC=C(C=C1)CC(
11	Acetyl-arginine	N-a-Acetyl-L-arginine	HMDB0004620	67427		CC(=O)N[C@@H](CCC
12	Acetyllysine	N-Alpha-acetyllysine	HMDB0000446	192590	C12989	CC(=O)NC(CCCCN)C
13	Aconitate	cis-Aconitic acid	HMDB0000072	643757	C00417	C(/C(=C/C(=O)O)/C(
14	Adenosine	Adenosine	HMDB0000050	60961	C00212	C1=NC2=C(C(=N1)N
15	ADP	ADP	HMDB0001341	6022	C00008	C1=NC2=C(C(=N1)N
16	ADP-D-Glucose	ADP-glucose	HMDB0006557	16500	C00498	C1=NC2=C(C(=N1)N
17	Aminoadipic acid	Aminoadipic acid	HMDB0000510	469	C00956	C(CC(C(=O)O)N)CC(=
18	AMP	Adenosine monophosphate	HMDB0000045	6083	C00020	C1=NC2=C(C(=N1)N
19	Androstenedione	Androstenedione	HMDB0000053	6128	C00280	C[C@]12CCC(=O)C=C
20	Arginine-Alanine	Arginyl-Alanine	HMDB0028702	7020333		CC(NC(=O)C(N)CCCN
21	Arginine-Glutamine	Arginyl-Glutamine	HMDB0028707	9857557		NC(CCCNC(N)=N)C(=
22	Arginine-Valine	Arginyl-Valine	HMDB0028722	6992654		CC(C)C(NC(=O)C(N)C
23	Ascorbic acid	Ascorbic acid	HMDB0000044	54670067	C01041	C([C@@H]([C@@H]1C(
24	Betaine	Betaine	HMDB0000043	247	C00719	C[N+](C)(C)CC(=O)[C
25	Carbamoyl phosphate	Carbamoyl phosphate	HMDB0001096	278	C00169	C(=O)(N)OP(=O)(O)O
26	Carnitine	L-Carnitine	HMDB0000062	2724480	C00318	C[N+](C)(C)C[C@H](C
27	Carnosine	Carnosine	HMDB0000033	439224	C00386	C1=C(NC=N1)C[C@@
28	Cholesteryl sulfate	Cholesterol sulfate	HMDB0000653	65076	C18043	C[C@H](CCCC(C)C)[C
29	Citramalic acid	Citramalic acid	HMDB0000426	441696	C00815	CC(CC(=O)O)(C(=O)
30	Citrate	Citric acid	HMDB0000094	311	C00158	C(C(=O)O)C(CC(=O)
31	Citrulline	Citrulline	HMDB0000904	9750	C00327	C(C[C@@H](C(=O)O)N
32	CMP	Cytidine monophosphate	HMDB0000095	8117	C00055	C1=CN(C(=O)N=C1N
33	Creatine	Creatine	HMDB0000064	586	C00300	CN(CC(=O)O)C(=N)N
34	Creatinine	Creatinine	HMDB0000562	588	C00791	CN1CC(=O)N=C1N
35	Cystine	L-Cystine	HMDB0000192	67678	C00491	C([C@@H](C(=O)O)N)
36	Cytidine	Cytidine	HMDB0000089	6253	C00475	C1=CN(C(=O)N=C1N
37	Cytosine	Cytosine	HMDB0000630	597	C00380	C1=C(NC(=O)N=C1)N
38	Deoxycytidine	Deoxycytidine	HMDB0000014	13711	C00881	C1[C@@H]([C@H](O[C
39	Deoxyguanosine	Deoxyguanosine	HMDB0000085	187790	C00330	C1[C@@H]([C@H](O[C
40	Dihydroorotate	4,5-Dihydroorotic acid	HMDB0000528	648	C00337	C1C(NC(=O)NC1=O)C
41	Dihydroxyacetone phosphate	Dihydroxyacetone phosphate	HMDB0001473	668	C00111	C(C(=O)COP(=O)(O)C
42	Dihydroxybenzeneacetic acid	3,4-Dihydroxybenzeneacetic acid	HMDB0001336	547	C01161	C1=CC(=C(C=C1CC(=
43	Feature 120	NA	NA	NA	NA	NA
44	Feature 121	NA	NA	NA	NA	NA
45	Feature 124	NA	NA	NA	NA	NA
46	Feature 21	NA	NA	NA	NA	NA
47	Feature 24	NA	NA	NA	NA	NA
48	Feature 30	NA	NA	NA	NA	NA
49	Feature 31	NA	NA	NA	NA	NA
50	Feature 33	NA	NA	NA	NA	NA
51	Feature 38	NA	NA	NA	NA	NA
52	Feature 48	NA	NA	NA	NA	NA
53	Feature 80	NA	NA	NA	NA	NA
54	Fructose	D-Fructose	HMDB0000660	439709	C02336	C([C@@H]1[C@H]([C@
55	Fructose-6-phosphate	Fructose 6-phosphate	HMDB0000124	69507	C00085	C([C@H]([C@H]([C@@H
56	gamma-amino butyrate	NA	NA	NA	NA	NA
57	Glucuronic acid	D-Glucuronic acid	HMDB0000127	94715	C00191	[C@@H]1([C@@H]([C@
58	Glutamate	L-Glutamic acid	HMDB0000148	33032	C00025	C(CC(=O)O)[C@@H](C
59	Glutaryl-carnitine	NA	NA	NA	NA	NA

60	Glutathione	Glutathione	HMDB0062697	745	C00051	NC(CCC(O)=NC(CS)C
61	Glutathione disulfide	Oxidized glutathione	HMDB0003337	975	C00127	C(CC(=O)NC(CSSCC(
62	Glycerate	Glyceric acid	HMDB0000139	439194	C00258	C([C@H](C(=O)O)O)O
63	Glycerol-3-phosphate	Glycerol 3-phosphate	HMDB0000126	439162	C00093	C([C@H](COP(=O)(O)
64	GMP	Guanosine monophosphate	HMDB0001397	6804	C00144	C1=NC2=C(N1[C@H]3
65	Guanosine	Guanosine	HMDB0000133	6802	C00387	C1=NC2=C(N1[C@H]3
66	Hippuric acid	Hippuric acid	HMDB0000714	464	C01586	C1=CC=C(C=C1)C(=
67	Histamine	Histamine	HMDB0000870	774	C00388	C1=C(NC=N1)CCN
68	Homocitrulline	Homocitrulline	HMDB0000679	65072	C02427	C(CCNC(=O)N)C[C@@
69	Homocysteine	Homocysteine	HMDB0000742	778	C00155	C(CS)C(C(=O)O)N
70	Hydroxyoctanoic acid	Hydroxyoctanoic acid	HMDB0000711	94180		CCCCCCC(C(=O)O)O
71	Hydroxyphenyl pyruvate	3-(3,4-Dihydroxyphenyl)pyruvate	METPA0460		C04045	
72	Hydroxyproline	4-Hydroxyproline	HMDB0000725	5810	C01157	C1[C@H](CN[C@@H]1C
73	Hypotaurine	Hypotaurine	HMDB0000965	107812	C00519	C(CS(=O)O)N
74	Indole	Indole	HMDB0000738	798	C00463	C1=CC=C2C(=C1)C=
75	Inosine	Inosine	HMDB0000195	6021	C00294	C1=NC(=O)C2=C(N1)
76	Inositol	myo-Inositol	HMDB0000211		C00137	O[C@H]1[C@H](O)[C@
77	Isocitrate	Isocitric acid	HMDB0000193	1198	C00311	C(C(C(C(=O)O)O)C(=
78	Itaconic acid	Itaconic acid	HMDB0002092	811	C00490	C=C(CC(=O)O)C(=O)
79	L-Octanoylcarnitine	L-Octanoylcarnitine	HMDB0000791	11953814	C02838	CCCCCCCC(=O)O[C@
80	Lactate	L-Lactic acid	HMDB0000190	61503	C00186	C[C@@H](C(=O)O)O
81	Leucic acid	D-Leucic acid	HMDB0000624	439960	C03264	CC(C)C[C@H](C(=O)O
82	Levulinic Acid	Levulinic acid	HMDB0000720	11579		CC(=O)CCC(=O)O
83	Lysine-Glutamine	Lysyl-Glutamine	HMDB0028949	196305		NCCCCC(N)C(=O)NC
84	Mandelic acid	Mandelic acid	HMDB0000703	439616	C01984	C1=CC=C(C=C1)[C@
85	Mannose-6-phosphate	Mannose 6-phosphate	HMDB0001078	439198	C00275	C([C@@H]1[C@H]([C@
86	Methionine sulfoxide	Methionine sulfoxide	HMDB0002005	847	C02989	CS(=O)CCC(C(=O)O)
87	Methyloxovaleric acid (Ketoleucine)	NA	NA	NA	NA	NA
88	Methylphenyllactate	3-Methylphenylacetic acid	HMDB0002222	12121		CC1=CC(=CC=C1)CC
89	N N N-Trimethyllysine	N6,N6,N6-Trimethyl-L-lysine	HMDB0001325	440120	C03793	C[N+](C)(C)CCCC[C@
90	N-acetyl-glutamate	N-Acetylglutamic acid	HMDB0001138	185	C00624	CC(=O)NC(CCC(=O)O
91	N-Acetyl-L-alanine	N-Acetyl-L-alanine	HMDB0000766	88064		C[C@@H](C(=O)O)NC
92	NAD	NAD	HMDB0000902	5893	C00003	C1=CC(=C[N+](=C1)[
93	NADH	NADH	HMDB0001487	928	C00004	C1C=CN(C=C1C(=O)N
94	NADP	NADP	HMDB0000217	5886	C00006	C1=CC(=C[N+](=C1)[
95	O-Acylcarnitine	O-Acylcarnitine		5355	C02301	
96	O-Butanoylcarnitine	Butyrylcarnitine	HMDB0002013	439829	C02862	CCCC(=O)OC(CC(=O
97	O-Propanoylcarnitine	Propionylcarnitine	HMDB0000824	107738	C03017	CCC(=O)OC(CC(=O)[
98	Pantothenate	Pantothenic acid	HMDB0000210	6613	C00864	CC(C)(CO)C(C(=O)NC
99	Proline	L-Proline	HMDB0000162	145742	C00148	C1C[C@H](NC1)C(=O)
100	Purine	Purine	HMDB0001366	1044	C15587	C1=C2C(=NC=N1)N=
101	Pyroglutamate	Pyroglutamic acid	HMDB0000267	7405	C01879	C1CC(=O)N[C@@H]1C
102	Pyrroline-5-carboxylic acid	NA	NA	NA	NA	NA
103	Pyruvate	Pyruvic acid	HMDB0000243	1060	C00022	CC(=O)C(=O)O
104	Ribitol	Ribitol	HMDB0000508		C00474	OC[C@H](O)[C@H](O)
105	Ribose phosphate	Ribose 1-phosphate	HMDB0001489	439236	C00620	C([C@@H]1[C@H]([C@
106	S-adenosyl-L-methionine	S-Adenosylmethionine	HMDB0001185	16757548	C00019	C[S+](CC[C@H](C(=O
107	Serine	Serine	HMDB0062263	5951	C00716	N[C@@H](CO)C(O)=O
108	Sorbitol	Sorbitol	HMDB0000247	5780	C00794	C([C@H]([C@H]([C@@H
109	Spermine	Spermine	HMDB0001256	1103	C00750	C(CCNCCCN)CNCCC
110	Stearic acid	Stearic acid	HMDB0000827	5281	C01530	CCCCCCCCCCCCCCC
111	Succinate	Succinic acid	HMDB0000254	1110	C00042	C(CC(=O)O)C(=O)O
112	Thiamine	Thiamine	HMDB0000235	1130	C00378	CC1=C(SC=[N+]1CC2
113	Threonic acid	Threonic acid	HMDB0000943	151152	C01620	C([C@H]([C@@H](C(=
114	Threonine	L-Threonine	HMDB0000167	6288	C00188	C[C@H]([C@@H](C(=O
115	Thymidine	Thymidine	HMDB0000273	5789	C00214	CC1=CN(C(=O)NC1=
116	Tridecanoic acid	Tridecanoic acid	HMDB0000910	656741	C17076	CCCCCCCCCCCCC(=
117	Trigonelline	Trigonelline	HMDB0000875	5570	C01004	C[N+]1=CC=CC(=C1)
118	Tryptamine	Tryptamine	HMDB0000303	1150	C00398	C1=CC=C2C(=C1)C(=
119	Tryptophan	L-Tryptophan	HMDB0000929	6305	C00078	C1=CC=C2C(=C1)C(=
120	Tyramine	Tyramine	HMDB0000306	5610	C00483	C1=CC(=CC=C1CCN
121	Tyrosine	L-Tyrosine	HMDB0000158	6057	C00082	C1=CC(=CC=C1C[C@
122	UDP-D-Glucose	Uridine diphosphate glucose	HMDB0000286	53477679	C00029	C1=CN(C(=O)NC1=O
123	Uracil	Uracil	HMDB0000300	1174	C00106	C1=CNC(=O)NC1=O
124	Uridine	Uridine	HMDB0000296	6029	C00299	C1=CN(C(=O)NC1=O
125	Xanthine	Xanthine	HMDB0000292	1188	C00385	C1=NC2=C(N1)C(=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.

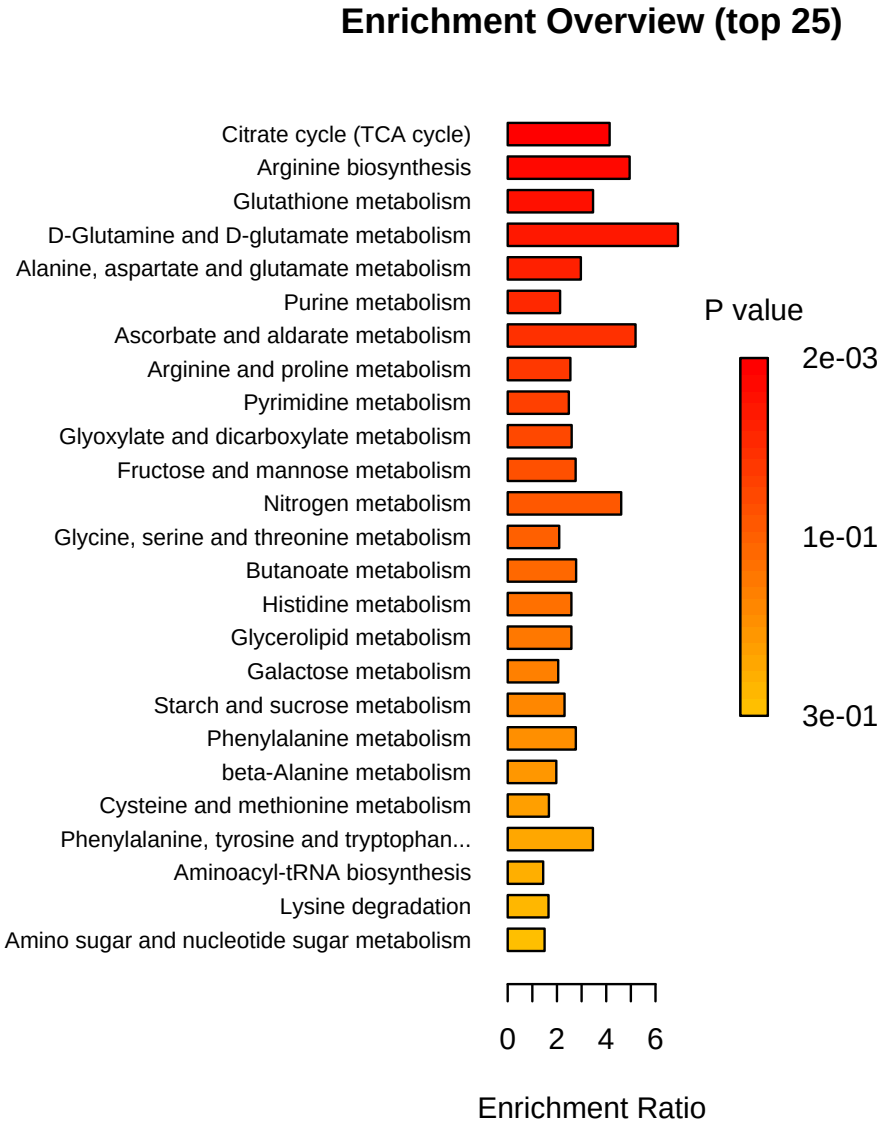

Figure 1: Summary Plot for Over Representation Analysis (ORA)

Table 2: Result from Over Representation Analysis

	total	expected	hits	Raw p	Holm p	FDR
Citrate cycle (TCA cycle)	20	1.45	6	2.09E-03	1.75E-01	7.91E-02
Arginine biosynthesis	14	1.01	5	2.13E-03	1.77E-01	7.91E-02
Glutathione metabolism	28	2.02	7	2.83E-03	2.32E-01	7.91E-02
D-Glutamine and D-glutamate metabolism	6	0.43	3	6.26E-03	5.07E-01	1.31E-01
Alanine, aspartate and glutamate metabolism	28	2.02	6	1.26E-02	1.00E+00	1.73E-01
Purine metabolism	65	4.70	10	1.56E-02	1.00E+00	1.73E-01
Ascorbate and aldarate metabolism	8	0.58	3	1.57E-02	1.00E+00	1.73E-01
Arginine and proline metabolism	38	2.75	7	1.65E-02	1.00E+00	1.73E-01
Pyrimidine metabolism	39	2.82	7	1.89E-02	1.00E+00	1.76E-01
Glyoxylate and dicarboxylate metabolism	32	2.31	6	2.39E-02	1.00E+00	2.01E-01
Fructose and mannose metabolism	20	1.45	4	5.08E-02	1.00E+00	3.88E-01
Nitrogen metabolism	6	0.43	2	6.41E-02	1.00E+00	4.49E-01
Glycine, serine and threonine metabolism	33	2.39	5	8.41E-02	1.00E+00	5.30E-01
Butanoate metabolism	15	1.08	3	8.84E-02	1.00E+00	5.30E-01
Histidine metabolism	16	1.16	3	1.03E-01	1.00E+00	5.42E-01
Glycerolipid metabolism	16	1.16	3	1.03E-01	1.00E+00	5.42E-01
Galactose metabolism	27	1.95	4	1.25E-01	1.00E+00	6.19E-01
Starch and sucrose metabolism	18	1.30	3	1.36E-01	1.00E+00	6.33E-01
Phenylalanine metabolism	10	0.72	2	1.59E-01	1.00E+00	7.05E-01
beta-Alanine metabolism	21	1.52	3	1.90E-01	1.00E+00	7.97E-01
Cysteine and methionine metabolism	33	2.39	4	2.12E-01	1.00E+00	8.46E-01
Phenylalanine, tyrosine and tryptophan biosynthesis	4	0.29	1	2.59E-01	1.00E+00	9.21E-01
Aminoacyl-tRNA biosynthesis	48	3.47	5	2.63E-01	1.00E+00	9.21E-01
Lysine degradation	25	1.81	3	2.68E-01	1.00E+00	9.21E-01
Amino sugar and nucleotide sugar metabolism	37	2.67	4	2.76E-01	1.00E+00	9.21E-01
Glycolysis / Gluconeogenesis	26	1.88	3	2.89E-01	1.00E+00	9.21E-01
Nicotinate and nicotinamide metabolism	15	1.08	2	2.96E-01	1.00E+00	9.21E-01
Tyrosine metabolism	42	3.04	4	3.61E-01	1.00E+00	1.00E+00
Inositol phosphate metabolism	30	2.17	3	3.71E-01	1.00E+00	1.00E+00
Pentose and glucuronate interconversions	18	1.30	2	3.78E-01	1.00E+00	1.00E+00
Pantothenate and CoA biosynthesis	19	1.37	2	4.04E-01	1.00E+00	1.00E+00
Thiamine metabolism	7	0.51	1	4.09E-01	1.00E+00	1.00E+00
Valine, leucine and isoleucine biosynthesis	8	0.58	1	4.52E-01	1.00E+00	1.00E+00
Taurine and hypotaurine metabolism	8	0.58	1	4.52E-01	1.00E+00	1.00E+00
Pentose phosphate pathway	22	1.59	2	4.80E-01	1.00E+00	1.00E+00
Pyruvate metabolism	22	1.59	2	4.80E-01	1.00E+00	1.00E+00
Ubiquinone and other terpenoid-quinone biosynthesis	9	0.65	1	4.92E-01	1.00E+00	1.00E+00
Tryptophan metabolism	41	2.96	3	5.80E-01	1.00E+00	1.00E+00
Glycerophospholipid metabolism	36	2.60	2	7.48E-01	1.00E+00	1.00E+00
Propanoate metabolism	23	1.66	1	8.24E-01	1.00E+00	1.00E+00
Phosphatidylinositol signaling system	28	2.02	1	8.80E-01	1.00E+00	1.00E+00
Porphyrin and chlorophyll metabolism	30	2.17	1	8.97E-01	1.00E+00	1.00E+00
Biosynthesis of unsaturated fatty acids	36	2.60	1	9.35E-01	1.00E+00	1.00E+00
Steroid hormone biosynthesis	85	6.14	2	9.89E-01	1.00E+00	1.00E+00

7 Appendix: R Command History

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 [1] "mSet<-InitDataObjects(\"conc\", \"msetora\", FALSE)"
 [2] "cmpd.vec<-c(\"1 3-Dimethyluric acid\",\"1-Methylhistidine\",\"11a-Hydroxyprogesterone\",\"3-Ph
 [3] "mSet<-Setup.MapData(mSet, cmpd.vec);"
 [4] "mSet<-CrossReferencing(mSet, \"name\");"
 [5] "mSet<-CreateMappingResultTable(mSet)"
 [6] "mSet<-PerformDetailMatch(mSet, \"1 3-Dimethyluric acid\");"
 [7] "mSet<-GetCandidateList(mSet);"
 [8] "mSet<-SetCandidate(mSet, \"1 3-Dimethyluric acid\", \"1,3-Dimethyluric acid\");"
 [9] "mSet<-PerformDetailMatch(mSet, \"Acetyl glycine\");"
[10] "mSet<-GetCandidateList(mSet);"
[11] "mSet<-SetCandidate(mSet, \"Acetyl glycine\", \"Phenylacetylglycine\");"
[12] "mSet<-PerformDetailMatch(mSet, \"Acetyl-arginine\");"
[13] "mSet<-GetCandidateList(mSet);"
[14] "mSet<-SetCandidate(mSet, \"Acetyl-arginine\", \"N-a-Acetyl-L-arginine\");"
[15] "mSet<-PerformDetailMatch(mSet, \"Arginine-Alanine\");"
[16] "mSet<-GetCandidateList(mSet);"
[17] "mSet<-SetCandidate(mSet, \"Arginine-Alanine\", \"Arginyl-Alanine\");"
[18] "mSet<-PerformDetailMatch(mSet, \"Arginine-Glutamine\");"
[19] "mSet<-GetCandidateList(mSet);"
[20] "mSet<-SetCandidate(mSet, \"Arginine-Glutamine\", \"Arginyl-Glutamine\");"
[21] "mSet<-PerformDetailMatch(mSet, \"Arginine-Valine\");"
[22] "mSet<-GetCandidateList(mSet);"
[23] "mSet<-SetCandidate(mSet, \"Arginine-Valine\", \"Arginyl-Valine\");"
[24] "mSet<-PerformDetailMatch(mSet, \"Dihydroxybenzeneacetic acid\");"
[25] "mSet<-GetCandidateList(mSet);"
[26] "mSet<-SetCandidate(mSet, \"Dihydroxybenzeneacetic acid\", \"3,4-Dihydroxybenzeneacetic acid\")
[27] "mSet<-PerformDetailMatch(mSet, \"gamma-amino butyrate\");"
[28] "mSet<-GetCandidateList(mSet);"
[29] "mSet<-SetCandidate(mSet, \"gamma-amino butyrate\", \"Gamma-Aminobutyric acid\");"
[30] "mSet<-PerformDetailMatch(mSet, \"Glutaryl-carnitine\");"
[31] "mSet<-GetCandidateList(mSet);"
[32] "mSet<-PerformDetailMatch(mSet, \"Hydroxyphenyl pyruvate\");"
[33] "mSet<-GetCandidateList(mSet);"
[34] "mSet<-SetCandidate(mSet, \"Hydroxyphenyl pyruvate\", \"3-(3,4-Dihydroxyphenyl)pyruvate\");"
[35] "mSet<-PerformDetailMatch(mSet, \"Lysine-Glutamine\");"
[36] "mSet<-GetCandidateList(mSet);"
[37] "mSet<-SetCandidate(mSet, \"Lysine-Glutamine\", \"Lysyl-Glutamine\");"
[38] "mSet<-PerformDetailMatch(mSet, \"Methyloxovaleric acid (Ketoleucine)\");"
[39] "mSet<-GetCandidateList(mSet);"
[40] "mSet<-PerformDetailMatch(mSet, \"Methylphenyllactate\");"
[41] "mSet<-GetCandidateList(mSet);"
[42] "mSet<-SetCandidate(mSet, \"Methylphenyllactate\", \"3-Methylphenylacetic acid\");"
[43] "mSet<-PerformDetailMatch(mSet, \"N N N-Trimethyllysine\");"
[44] "mSet<-GetCandidateList(mSet);"
[45] "mSet<-SetCandidate(mSet, \"N N N-Trimethyllysine\", \"N6,N6,N6-Trimethyl-L-lysine\");"
[46] "mSet<-PerformDetailMatch(mSet, \"Pyrroline-5-carboxylic acid\");"
[47] "mSet<-GetCandidateList(mSet);"
[48] "mSet<-SetCandidate(mSet, \"Pyrroline-5-carboxylic acid\", \"1-Pyrroline-5-carboxylic acid\");"
[49] "mSet<-PerformDetailMatch(mSet, \"Ribose phosphate\");"
[50] "mSet<-GetCandidateList(mSet);"
[51] "mSet<-SetCandidate(mSet, \"Ribose phosphate\", \"Ribose 1-phosphate\");"
[52] "mSet<-SetMetabolomeFilter(mSet, F);"
[53] "mSet<-SetCurrentMsetLib(mSet, \"kegg_pathway\", 2);"
[54] "mSet<-CalculateHyperScore(mSet)"
[55] "mSet<-PlotORA(mSet, \"ora_0_\", \"net\", \"png\", 72, width=NA)"
[56] "mSet<-PlotEnrichDotPlot(mSet, \"ora\", \"ora_dot_0_\", \"png\", 72, width=NA)"
```

```
[57] "mSet<-CalculateHyperScore(mSet)"
[58] "mSet<-PlotORA(mSet, \"ora_1_\", \"net\", \"png\", 72, width=NA)"
[59] "mSet<-PlotEnrichDotPlot(mSet, \"ora\", \"ora_dot_1_\", \"png\", 72, width=NA)"
[60] "mSet<-SaveTransformedData(mSet)"
[61] "mSet<-PreparePDFReport(mSet, \"guest30431135571130566 81\")\n"
```

The report was generated on Wed Nov 24 14:57:50 2021 with R version 4.1.1 (2021-08-10).