

Metabolome-Microbiome-Meta Data Correlation Analysis (3Mcor)

Manual

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1、Introduction

The Metabolite-Microbiome (16s rRNA)-Meta data correlation analysis method (3Mcor) is an cross-omics data analysis method based on WGCNA (weighted gene co-expression network analysis). It is designed for the correlation analysis among metabolites, microbial 16s rRNA and phenotypes, and for phenotype-relevant biomarkers screening. The main steps of 3Mcor include the dimension reduction of metabolome and microbiome data to dozens of modules, the identification of key modules which are highly correlated to each other and to the phenotype, and the identification of key metabolites or microbes within the key modules. Some strengths of 3Mcor are as follows. (1) The ideas of co-expression, co-regulation or interaction of related genes were incorporated and hence both data characteristics and biological links (pathways and inter-associations) were considered for module construction. (2) The top-down analysis strategy is effective to find out key biomarkers quickly. (3) The 3D linkages of phenotype, microbiome and metabolome contain more information and are conducive to a better understanding of biological and medical phenomena. (4) R code and demo data are available for academic use.

2、Steps for usage

1) Install R , R Studio ;

2) Install the required R package :

```
install.packages(WGCNA) #### -Clustering software. Previously reported work done  
####using v1.34
```

```
install.packages(flashClust) #### Clustering software
```

```
install.packages(ppcor) #### Partial Spearman correlations, for confounder analysis.  
####previously reported work done using v1.0
```

```
install.packages(gplots) #### Plotting
```

```
install.packages(cowplot) #### Plotting; to arrange several plots on the same page
```

```
install.packages(ggplot2) #### Plotting
```

```
install.packages(plyr) #### Data transformations
```

3) Operation procedure :

Firstly, store the input data in the specified location. Then, double-click to open the **protocol.Rproj** file. And then run the code of **protocol_all.R**. Finally, read the results in the specified output data path.

Note :

Input data is stored by default at D:\3Mcor-protocol\top\data

The output data is stored by default at D:\3Mcor-protocol\top\result

3、Details of input and output data

1) Input data

There are 3 files, stored in (default) D:\3Mcor-protocol\top\data.

(1) metabolites.csv.file Row name is sample name and column name is metabolite name.

	M_1	M_2	M_3	M_4	M_5	M_6	M_7	M_8	M_9	M_10	M_11	M_12	M_13	M_14	M_15	M_16	M_17
B3_3	34.01	13.11	3.67	8.54	10.54	10.53	4.53	2.72	7.43	5.83	2.45	1.42	1.48	11.46	5.54	29.58	1.4
B4_3	26.48	12.35	3.2	6.93	6.9	7.58	3.44	1.63	5.27	7.13	1.66	0.97	0.88	6.44	4.55	21.02	1.4
B5_2	30.71	10.16	2.16	7.56	5.11	7.77	3.56	1.96	4.99	3.35	1.77	1.08	1.14	7.52	4.43	25.63	0.0
B6_1	35.35	15.36	5.02	8.55	9.19	9.81	4.63	2.62	7.92	6.76	2.23	1.38	1.63	9.53	6.23	29.08	1.4
B7_1	25.85	11.99	3.67	6.84	4.73	7.47	3.03	1.69	7.8	3.82	1.53	0.91	0.98	6.45	4.96	18.77	0.0
B8_1	32.82	12.74	4.29	8.53	6.04	9.93	4.63	2.55	6.38	7.11	2.47	1.45	1.65	10.1	5.58	31.3	1.4
C1_1	13.22	5.84	3.17	5.98	6.56	10.05	3.58	1.88	5.75	7.53	3.57	2.21	1.38	7.15	7.48	9.53	1.4
C2_2	13.33	4.29	2.32	7.07	3.98	11.34	3.66	2.65	5.71	6.75	3.74	2.45	1.75	7.52	9.46	10.64	1.4
C3_2	12.35	5.33	3.16	7.34	3.76	13.16	3.67	2.58	6.75	6.3	4.21	2.21	1.49	8.18	9.87	10.02	1.4
C6_1	11.36	4.39	3.43	6.53	4.66	8.34	3.15	1.95	2.74	4.82	3.07	1.93	1.15	6.47	8.06	6.51	1.4
C7_1	10.83	8.38	2.36	7.31	7.42	10.08	3.9	3.01	4.58	5.11	3.89	2.93	1.72	6.26	9.61	10.03	2.4
C11_1	12.12	5.72	4.58	7.22	6.06	13.42	3.86	2.18	5.6	8.82	4.5	2.59	1.28	8	8.37	9.59	1.4
E1_2	4.88	5.81	5.17	7.2	4.18	7.32	7.28	6.9	6.01	5.36	6.72	7.78	4.28	8.52	7.57	4.34	4.4
E2_2	4.82	7.11	5.12	7.68	6.58	7.07	6.68	6.5	6.11	5.51	6.13	6.86	3.86	8.35	8.53	4.21	4.4
E3_2	3.92	5.9	4.1	6.98	4.93	8.1	6.18	6.74	6.59	5.18	6.04	5.73	4.07	7.14	7.39	4.3	4.4
E4_3	4.84	5.51	6.94	8.01	6.98	8.93	7.43	7.09	5.94	7.35	7.1	6.8	4.6	8.09	8.38	5.01	5.4
E6_1	3.43	2.45	6.49	6.02	4.47	6.77	5.39	5.5	4.37	4.22	5.11	5.01	4.5	4.94	6.78	4.78	3.4
E7_2	4.55	5.2	5.27	8.51	5.8	7.88	7.3	7.6	7.34	6.72	7.06	6.38	5.82	7.19	9.69	5.92	5.4
F5_2	6	8.43	6.14	7.75	6.6	10.88	6.92	6.76	9.44	7.73	6.93	6.48	4.34	7.35	8.73	6.9	4.4
F6_1	4.4	5.81	6.07	7.32	10.29	5.25	7.41	9.54	8.2	6.45	8.77	7.74	11.91	7.95	7.1	5.07	12.4
F9_1	4.56	6.35	3.26	7.76	6.81	6.95	6.97	7.11	6.69	6.35	6.41	6.2	5.69	7.57	8.2	5.32	5.4
F10_1	5.46	3.56	5.06	6.08	5.83	9.44	6.11	5.43	5.27	6.87	6.23	3.39	6.71	6.69	6.11	4.4	4.4
F11_1	6.4	8.91	8.58	8.12	4.67	11.58	6.73	5.54	6.51	7.99	6.86	6.34	3.52	7.83	9.86	6.45	4.4

(2) microbiome.csv.file: Row name is sample name and column name is microbiome name.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1		s. Coryneb.	s. Coryneb.	s. Rothia	s. Propioni	s. Bifidobac	s. Aureimo	s. Flavobac	s. Bacillus	s. Planocor	s. Lactobac	s. Streptoc	s. Clostridi	s. Clostridi	s. Clostr			
2	B3_3	0.001161	0.002968	0.00271	0.001807	0.000258	0.000387	0.00413	0.009679	0.000129	0.000258	0.003871	0.003226	0.00142	0.000387	0.000516	0.000516	0.0001
3	B4_3	0.001288	0.000429	0.000286	0.000715	0.000429	0.000286	0.004864	0.004578	0.000286	0.000286	0.001144	0.000858	0.000286	0	0	0.000286	0.0004
4	B5_2	0.001212	0.000121	0.000121	0.002302	0	0.000121	0.000121	0.000727	0.000121	0.000121	0.000242	0.001575	0.000121	0	0	0.000121	0.0001
5	B6_1	0.001074	0.000569	0.000126	0.003981	0	0.000442	0.001517	0.001264	0.00019	0.000506	0.000202	0.000822	0.000316	0.000316	0.000506	6.32E-05	6.32E-05
6	B7_1	0.005321	0.000124	0	0.00396	0.000124	0.000124	0.000619	0.003341	0.000371	0.000495	0.001361	0.000124	0.000619	0.000124	0.001609	0.000371	
7	B8_1	0.00173	0.002472	0.000741	0.002224	0.000371	0.000247	0.004202	0.009021	0.000371	0.001359	0.009392	0.000618	0.000741	0.001359	0.000741	0.000618	0.0001
8	C1_1	0.009901	0.0027	0.006301	0.024302	0.0018	0.005401	0.006301	0.007201	0.007201	0	0.017102	0.024302	0.009189	0.0009	0.021602	0.070207	0.00
9	C2_2	0.058708	0.003914	0	0.107632	0	0.009785	0.003914	0	0	0	0.003914	0.031311	0.101761	0	0.007828	0.050881	
10	C3_2	0.008089	0.002528	0.003033	0.017189	0	0.001011	0	0.00455	0	0	0.002528	0.005056	0.027806	0	0.132963	0.64459	
11	C6_1	0.004376	0.002188	0.009482	0.032093	0.000729	0.006565	0.025529	0.019694	0.001459	0.005835	0.025529	0.009482	0.06054	0.001459	0.032093	0.020423	0.0058
12	C7_1	0.008929	0.000638	0.003189	0.048469	0	0.005102	0.002551	0.004464	0.000638	0.001276	0.002551	0.012117	0.197066	0.003827	0.003189	0.01148	
13	C11_1	0.010912	0.003118	0.005456	0.041309	0.000779	0.017147	0.01403	0.01325	0.001559	0	0.004677	0.050663	0.367108	0.000779	0.011691	0.000779	
14	E1_2	0.006803	0.003401	0	0.071429	0	0.129252	0	0.003401	0.003401	0	0.006803	0.098639	0.098639	0	0.003401	0.003401	0.0034
15	E2_2	0.013357	0.001742	0	0.224739	0	0.016841	0	0.000581	0.002323	0.001742	0.004065	0.006388	0.079559	0	0.018583	0.000581	
16	E3_2	0.022857	0.011429	0	0.094286	0	0.168571	0	0	0.002857	0	0.017143	0.002857	0.077143	0	0.137143	0.008571	
17	E4_3	0	0.004717	0	0.028302	0	0.165094	0	0	0.009434	0	0.009434	0.004717	0.028302	0.09434	0.009434	0.042453	0.0047
18	E6_1	0.001496	0	0	0.014211	0	0.060583	0	0	0.000748	0	0.000748	0.005984	0.00374	0	0.668661	0.004488	
19	F2_2	0.039773	0.011364	0	0.028409	0.005682	0.159091	0.005682	0	0	0	0	0.079545	0.147727	0	0.0625	0.005682	
20	F5_2	0.030151	0.241206	0.015075	0.015075	0	0	0.180905	0.060302	0.01005	0.020101	0.005025	0.025126	0.005025	0.020101	0	0.0351	
21	F6_1	0.00307	0.004605	0	0.000767	0.000767	0.003837	0	0.04528	0.023024	0.007675	0.000767	0	0.00921	0.000767	0.00921	0.0168	
22	F9_1	0.005282	0.001761	0.002641	0.014965	0.00088	0.00088	0	0.02993	0.016725	0.002641	0.003521	0	0	0.002641	0.005282	0	
23	F10_1	0.003086	0	0.006173	0.009259	0.003086	0	0	0.135802	0.092593	0.012346	0.012346	0	0.012346	0	0.015432	0.0493	
24	F11_1	0.015798	0.060032	0.004739	0.015798	0.00316	0.00158	0	0.047393	0.041074	0.004739	0.012638	0.00158	0.023697	0.00158	0.014218	0	0.0063

(3) phenotypes.csv.file: Meta data (supporting only one phenotypic variable). The first column is sample name, and the second is the phenotypic data.

	A	B	C	D	E	F
1		age				
2	B3_3	1				
3	B4_3	1				
4	B5_2	1				
5	B6_1	1				
6	B7_1	1				
7	B8_1	1				
8	C1_1	3				
9	C2_2	3				
10	C3_2	3				
11	C6_1	3				
12	C7_1	3				
13	C11_1	3				

2) Output data:

There are 10 files and they are stored in D:\3Mcor-protocol\top\result.

(1) age_cluster_bacteria.txt. Correlations results between microbiome clusters and phenotypic variables (such as age). The first column is the microbiome clusters name. The age_estimate is correlation coefficient, age_p.value is p value, and age_p.adjust is corrected p value.

	age_estimate	age_p.value	age_p.adjust
L1	-0.40072399	0.008542508	0.020882
L2	-0.71010648	1.39E-07	1.53E-06
L3	-0.60501465	2.19E-05	0.000149
L4	0.269615668	0.084218705	0.143542
L5	0.183665162	0.244301662	0.314552
L6	-0.10026227	0.527543987	0.580298
L7	-0.37597832	0.014132997	0.031093
L8	-0.56376365	0.000101152	0.000445
L9	-0.79850148	2.37E-10	5.20E-09
L10	-0.53528082	0.000259617	0.000952
L11	-0.22102332	0.159536343	0.233987
L12	-0.26911366	0.084820461	0.143542
L13	-0.17875433	0.257360636	0.314552
L14	-0.31625766	0.041307237	0.082614
L15	0.178972627	0.25677043	0.314552
L16	0.599637031	2.71E-05	0.000149

(2) age_cluster_metabolites.txt. Correlations results between microbiome clusters and phenotypic variables (such as age).

	age_estimate	age_p.value	age_p.adjust
M1	0.051072666	0.7480515	0.897662
M2	-0.25143466	0.1082232	0.216446
M3	-0.200362	0.2032826	0.318704
M4	-0.56474582	9.78E-05	0.00044
M5	-0.84368115	2.30E-12	2.07E-11
M6	-0.75233965	9.20E-09	5.52E-08
M7	-0.12768166	0.4203548	0.540456
M8	0.502869322	0.0006886	0.002066
M9	0.0088395	0.9556934	1
M10	0.931093979	4.06E-19	7.31E-18
M11	0.483225989	0.0011886	0.002674
M12	-0.023572	0.8822052	0.992481
M13	0.205272829	0.1921957	0.318704
M14	0.545102488	0.0001894	0.000682
M15	0.490101155	0.0009855	0.002534
M16	0	1	1

(3) individual_bacteria.txt. The clustering result of each microbiome: the first column

is the microbiome name, the module represents clusters color, kME means the correlation strength between each microbiome and its corresponding microbial module variable, and kIN is connectivity and importance of each microbiome in the corresponding module, and cluster_name is the clustering ID. The correlation results with phenotypic data include age_estimate (correlation coefficient), age_p.value (p value), age_p.adjust (corrected p-value).

	A	B	C	D	E	F	G	H
1		module	kME	kIN	cluster_name	age_estimate	age_p.value	age_p.adjust
2	g_Adlercreutzia.spp	pink	0.861987	0.474325	L1	-0.44315262	0.003290915	0.01220381
3	g_Ruminococcus.spp	pink	0.830024	0.431219	L1	-0.37033685	0.015771578	0.03954001
4	g_Desulfovibrio.spp	pink	0.766013	0.388569	L1	-0.52646265	0.000341839	0.00190148
5	g_Dorea.spp	pink	0.755289	0.367259	L1	-0.36024657	0.019103686	0.04658159
6	g_Allobaculum.spp	pink	0.733815	0.331865	L1	-0.53186479	0.000289075	0.00165985
7	g_Turicibacter.spp	pink	0.652971	0.254775	L1	-0.22196966	0.157711569	0.2462514
8	s_Ruminococcus.gnavus	pink	0.683939	0.23508	L1	-0.06890819	0.664567958	0.7939134
9	g_Blautia.spp	pink	0.670612	0.14833	L1	-0.20537783	0.191963378	0.29456449
10	g_Planctomyces.spp	darkred	0.928378	1.867913	L10	-0.52054832	0.000409403	0.00208211
11	g_Pedobacter.spp	darkred	0.891745	1.591557	L10	-0.65586201	2.42E-06	2.69E-05
12	g_Dyadobacter.spp	darkred	0.826851	1.184075	L10	-0.71825488	8.54E-08	3.04E-06
13	g_Phenylobacterium.spp	darkred	0.813859	1.069361	L10	-0.26912456	0.084807356	0.14946247
14	g_Planococcus.spp	darkred	0.833389	1.024724	L10	-0.35854894	0.019718684	0.04743143
15	g_Candidatus.Rhabdochlamy	darkred	0.789746	0.873122	L10	-0.41571396	0.006182041	0.02076233
16	g_KSA1.spp	darkred	0.784632	0.589494	L10	-0.5217768	0.000394456	0.0020651
17	g_Lysobacter.spp	darkred	0.681295	0.552723	L10	-0.5148949	0.000484955	0.00239783
18	g_Acetobacter.spp	darkred	0.667667	0.482552	L10	-0.40571835	0.00768209	0.02398968
19	g_Micrococcus.spp	darkred	0.687949	0.473062	L10	-0.5366286	0.00024876	0.00147597
20	g_Actinomyces.spp	darkred	0.682941	0.45888	L10	-0.41449112	0.006350742	0.02093393
21	g_Haliscamenobacter.spp	darkred	0.663243	0.406622	L10	-0.41594436	0.006150694	0.02076233
22	g_Odoribacter.spp	darkred	0.610755	0.334687	L10	-0.27915433	0.073404239	0.13332607
23	g_Corynebacterium.spp	darkred	0.608757	0.311432	L10	-0.23964866	0.126362984	0.20630318
24	g_Veillonella.spp	darkred	0.478962	0.159758	L10	-0.30275275	0.051312371	0.09821077

(4) individual_metabolites.txt. The clustering result of each metabolite.

	A	B	C	D	E	F	G	H
1		module	kME	kIN	cluster_name	age_estimate	age_p.value	age_p.adjust
2	M_274	greenyellow	0.876906008	0.626214	M1	-0.11540926	0.466734162	0.539947364
3	M_304	greenyellow	0.850261747	0.626151	M1	-0.06679004	0.674298472	0.72555037
4	M_316	greenyellow	0.842319571	0.565107	M1	-0.03732384	0.814466386	0.843089847
5	M_282	greenyellow	0.86878305	0.560146	M1	0.073662498	0.642926189	0.698146843
6	M_224	greenyellow	0.800659878	0.490016	M1	-0.12571733	0.427598078	0.499570031
7	M_254	greenyellow	0.73060659	0.31542	M1	0.288756993	0.063651973	0.098828064
8	M_350	greenyellow	0.618056067	0.13902	M1	0.109020498	0.491916256	0.561736628
9	M_17	blue	0.967885302	16.41404	M10	0.89728194	8.68E-16	4.26E-14
10	M_92	blue	0.975796451	15.89259	M10	0.939103517	3.70E-20	1.31E-17
11	M_97	blue	0.975402293	15.7792	M10	0.903930539	2.42E-16	1.72E-14
12	M_18	blue	0.942505572	15.36916	M10	0.907521979	1.17E-16	1.04E-14
13	M_11	blue	0.972834309	14.81227	M10	0.877074813	2.60E-14	6.57E-13
14	M_62	blue	0.954263477	14.76023	M10	0.900683305	4.57E-16	2.70E-14
15	M_13	blue	0.942034062	14.5655	M10	0.881985647	1.20E-14	3.55E-13
16	M_91	blue	0.936489973	14.55826	M10	0.91152451	5.02E-17	5.92E-15
17	M_12	blue	0.958776019	14.16467	M10	0.857466222	4.15E-13	7.00E-12
18	M_96	blue	0.94120506	13.61095	M10	0.869287922	8.23E-14	1.71E-12
19	M_8	blue	0.951158492	13.20305	M10	0.838804299	4.06E-12	5.74E-11
20	M_93	blue	0.951894649	13.19087	M10	0.916584321	1.62E-17	2.87E-15
21	M_7	blue	0.925336518	12.22685	M10	0.822631226	2.34E-11	2.76E-10
22	M_24	blue	0.8807483	11.63987	M10	0.866832306	1.17E-13	2.17E-12
23	M_56	blue	0.915809815	11.52402	M10	0.804918177	1.32E-10	1.26E-09
24	M_69	blue	0.893633137	10.42202	M10	0.894335201	1.49E-15	5.84E-14

(5) MEs_bacteria_clusters.txt. New microbial module variables after microbiome

clustering. Row name is sample name, column name is microbial module number.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1		L1	L10	L11	L12	L13	L14	L15	L16	L17	L18	L19	L2	L20
2	B3_3	0.028124	0.214399	0.225793	0.144595	0.188915	0.174114	0.096925	-0.05312	0.118613	0.127861	0.009262	0.101781	0.159185
3	B4_3	-0.08868	0.218652	0.183179	0.143266	0.174673	0.161042	0.10965	-0.12277	0.087755	0.099547	-0.02385	0.076027	0.094274
4	B5_2	-0.074	0.119487	-0.11147	-0.11727	-0.02727	0.07942	-0.10695	-0.25593	-0.09383	-0.07681	-0.06287	0.064536	-0.19255
5	B6_1	-0.04225	0.224214	0.172416	0.174078	0.16267	0.161313	0.119955	-0.06323	-0.087	0.115673	-0.01662	0.049539	0.112439
6	B7_1	-0.01853	0.251004	0.181174	0.153611	0.161952	0.131976	0.136576	-0.05684	-0.0906	0.071814	-0.07298	0.102466	-0.04609
7	B8_1	0.081788	0.303315	0.265247	0.251423	0.290859	0.256357	-0.20916	-0.0001	0.116371	0.211689	0.0777	0.109041	0.227469
8	C1_1	0.1001	0.189323	0.153042	0.122578	0.151062	0.126948	0.156639	0.062159	0.136354	0.046291	0.033609	0.35554	0.129878
9	C2_2	-0.02733	0.019919	-0.20627	-0.10828	-0.21025	-0.04449	0.127141	-0.34379	-0.23947	-0.19953	-0.17367	0.28243	-0.1627
10	C3_2	0.238329	0.123601	0.074748	0.028105	0.059465	0.079343	-0.20916	-0.22801	-0.01629	0.027034	-0.12451	0.313676	-0.14104
11	C6_1	0.161912	0.237349	0.266382	0.262099	0.26837	0.236721	0.151601	0.052192	0.163493	0.193615	0.089806	0.253037	0.222774
12	C7_1	0.035472	0.050959	0.040376	-0.04439	-0.00355	0.065771	-0.20916	-0.10179	-0.02174	-0.02667	-0.10371	0.194366	-0.19389
13	C11_1	0.036699	0.049086	0.122127	-0.00171	0.086196	0.111491	-0.20916	0.034889	0.110642	0.045208	-0.10972	0.111628	0.06781
14	E1_2	-0.0411	-0.08935	-0.15915	-0.15363	-0.20812	-0.13384	0.114179	-0.18453	-0.23947	-0.19874	-0.14404	0.139819	0.044689
15	E2_2	0.120427	0.020294	0.022977	-0.06829	-0.04256	-0.02983	0.097246	-0.05532	-0.23947	-0.14475	-0.12181	0.129271	0.051341
16	E3_2	0.315437	-0.0068	-0.08588	-0.01071	-0.19469	-0.1139	-0.20916	-0.18827	-0.16865	-0.21767	-0.26767	0.151776	-0.29351
17	E4_3	0.053739	-0.09099	-0.21117	-0.11405	-0.2929	-0.2092	-0.20916	0.153867	-0.23947	-0.25381	-0.16776	0.213553	-0.14246

(6) MEs_metabolites_clusters.txt.New metabolite module variables after metabolite

clustering. The row name is the sample name, and the column name is the metabolite module number.

	A	B	C	D	E	F	G	H	I	J	K	L	M
1		M1	M10	M11	M12	M13	M14	M15	M16	M17	M18	M2	M3
2	B3_3	-0.21897	-0.22906	-0.22655	0.01521	-0.00747	-0.20683	0.095275	-0.28189	-0.04156	-0.03077	-0.0821	0.044522
3	B4_3	0.33542	-0.2911	-0.08953	-0.01544	-0.30458	-0.31026	-0.2683	-0.36144	-0.20693	0.083301	0.352455	0.019685
4	B5_2	-0.24715	-0.28333	-0.20155	0.10057	0.042781	-0.18853	-0.24915	-0.22167	-0.2592	0.018285	0.021547	0.359391
5	B6_1	-0.16567	-0.20442	-0.18889	-0.06427	0.057833	-0.24353	-0.25346	-0.32483	0.022634	0.029473	-0.06916	0.241651
6	B7_1	-0.12231	-0.31156	-0.15974	0.053076	0.035071	-0.32949	-0.30212	-0.2782	-0.27141	-0.0062	0.034558	-0.2906
7	B8_1	0.189387	-0.24875	-0.16777	-0.35223	-0.22824	-0.22662	-0.31279	-0.30908	-0.04483	-0.0092	0.291708	0.249051
8	C1_1	0.365519	-0.15683	-0.14502	-0.03555	-0.19595	0.132892	-0.00594	0.133436	0.060873	0.028945	0.272586	-0.09042
9	C2_2	-0.13541	-0.18347	-0.16447	0.066928	0.120861	0.046895	0.103427	0.111764	0.089536	-0.03413	-0.05027	-0.22207
10	C3_2	-0.02704	-0.19024	-0.18768	0.112136	0.013158	0.196779	0.07223	0.245691	0.210764	0.042317	0.082233	0.115997
11	C6_1	-0.01862	-0.26877	-0.19124	-0.01702	0.03391	0.161004	0.02446	0.146933	-0.06958	-0.01853	0.093175	0.006946
12	C7_1	0.025037	-0.20279	-0.17158	0.092323	0.065498	0.171338	0.004274	0.123778	0.113184	-0.04528	0.048434	0.241583
13	C11_1	0.155922	-0.17392	-0.167	-0.4277	-0.2095	0.180288	0.03854	0.177755	0.17615	0.05459	0.277489	0.071253
14	E1_2	-0.04475	0.025989	0.088142	0.08352	0.007845	-0.13655	-0.09787	-0.00095	0.00053	-0.009	-0.13681	0.058487
15	E2_2	0.227676	0.043915	0.207621	0.124883	-0.05446	-0.09466	-0.13888	0.23071	0.027903	0.021234	0.172163	-0.05269
16	E3_2	-0.19638	0.015642	0.183478	0.050746	0.037043	-0.09904	-0.10961	0.196954	-0.01316	-0.00176	-0.39518	-0.0854
17	E4_3	-0.02911	0.075679	0.181754	-0.03563	0.169386	-0.08758	-0.15837	-0.01762	0.143362	-0.01774	-0.11239	-0.02686

(7) bac_MEtlip_cor.csv. The correlation strength values of metabolites clusters and the microbiome clusters.

	A	B	C	D	E	F	G	H	I
1		M4	M5	M6	M8	M10	M11	M14	M15
2	L1	0.039462	0.187262	0.27834	-0.53569	-0.2986	0.02828	-0.22729	-0.2025
3	L2	0.452881	0.552224	0.550928	-0.50539	-0.64444	-0.35937	-0.12811	-0.2503
4	L3	0.152257	0.405883	0.538935	-0.44494	-0.54218	-0.16781	-0.19796	-0.13184
5	L7	0.402881	0.39914	0.227337	-0.25929	-0.39418	-0.35092	-0.14318	-0.1714
6	L8	0.455474	0.522891	0.360668	-0.17495	-0.5015	-0.45985	-0.09651	-0.23069
7	L9	0.507982	0.735354	0.623693	-0.28596	-0.77214	-0.56422	-0.24236	-0.30994
8	L10	0.534884	0.609594	0.38287	-0.25176	-0.53796	-0.44753	-0.21384	-0.27996
9	L14	0.295033	0.44656	0.212868	-0.11012	-0.28904	-0.2516	-0.15987	-0.3054
10	L16	-0.30939	-0.44236	-0.44715	0.2978	0.574126	0.327458	0.227057	0.126656
11	L19	-0.15047	-0.29649	-0.36618	0.245118	0.410745	0.135564	0.079491	0.08176
12	L22	-0.4075	-0.26424	-0.132	0.196986	0.399562	0.362288	0.188721	0.222753

(8) bac_MEtlip_p.csv. The correlation p values of metabolites clusters and the microbiome clusters.

	A	B	C	D	E	F	G	H	I
1		M4	M5	M6	M8	M10	M11	M14	M15
2	L1	0.803579	0.234172	0.074531	0.000317	0.05515	0.858668	0.147409	0.197755
3	L2	0.002853	0.000191	0.000199	0.000752	7.05E-06	0.019946	0.417458	0.109836
4	L3	0.334543	0.008072	0.000287	0.003434	0.00026	0.287025	0.208153	0.403944
5	L7	0.008161	0.008832	0.147649	0.097281	0.009794	0.02269	0.365676	0.277783
6	L8	0.002683	0.00046	0.01948	0.266806	0.000835	0.002416	0.54194	0.14132
7	L9	0.0007	1.97E-07	1.60E-05	0.066692	4.92E-08	0.000131	0.121865	0.046221
8	L10	0.000324	2.71E-05	0.012814	0.10773	0.000296	0.003234	0.173386	0.072805
9	L14	0.058229	0.003307	0.175385	0.48621	0.063717	0.107962	0.310696	0.049639
10	L16	0.046177	0.003353	0.002989	0.055438	7.02E-05	0.03427	0.148162	0.424128
11	L19	0.340286	0.056953	0.017599	0.117584	0.007293	0.390688	0.615685	0.605609
12	L22	0.007805	0.090953	0.403363	0.210431	0.009191	0.01891	0.230498	0.155827

(9) bac_METlip_p.adjust.csv. The correlation corrected p values of metabolites clusters and the microbiome clusters.

	A	B	C	D	E	F	G	H	I
1		M4	M5	M6	M8	M10	M11	M14	M15
2	L1	0.803579	0.234172	0.10248	0.003482	0.060665	0.858668	0.42258	0.310757
3	L2	0.007845	0.000701	0.001053	0.004134	3.88E-05	0.041597	0.510227	0.285683
4	L3	0.374314	0.012144	0.001053	0.01259	0.000651	0.350809	0.42258	0.46654
5	L7	0.014962	0.012144	0.18046	0.161677	0.011971	0.041597	0.502804	0.381951
6	L8	0.007845	0.001266	0.030611	0.293486	0.001531	0.011856	0.596134	0.285683
7	L9	0.00385	2.17E-06	0.000175	0.146723	5.41E-07	0.001436	0.42258	0.266951
8	L10	0.003567	0.000149	0.028192	0.161677	0.000651	0.011856	0.42258	0.266951
9	L14	0.080064	0.006148	0.192923	0.48621	0.063717	0.148448	0.488237	0.266951
10	L16	0.072564	0.006148	0.008221	0.146723	0.000258	0.053853	0.42258	0.46654
11	L19	0.374314	0.069609	0.030611	0.161677	0.011461	0.429757	0.615685	0.605609
12	L22	0.014962	0.100048	0.403363	0.257193	0.011971	0.041597	0.42258	0.285683

(10) heatmap_bacteria_vs_metabolite_clusters.pdf. The correlation heatmap of metabolites clusters and the microbiome clusters. The labels “+”, “*” and “**” represent $p < 0.1$, $p < 0.05$, $p < 0.01$ respectively.

