

1 **Supplementary Information**

2 **Suppl. Fig. S1: Growth of *C. cohnii* under various conditions. A) BHA supplementation.**

3 Different BHA concentrations were indicated by colors and shown inside the figure. C_{DMSO}
4 represents media supplemented with only 0.4% (v/v) DMSO. **B) PG supplementation.** Different
5 PG concentrations were indicated by colors and shown inside the figure.

6 **Suppl. Fig. S2: Lipid accumulation in *C. cohnii* supplemented with PG.** The lipid content in
7 the control without any PG supplement was set as 100%, and the % changes under various
8 concentrations of PG were indicated.

9 **Suppl. Fig. S3: WGCNA analysis of GC-MS metabolomic profiles. A) 24 h; B) 48 h; and C)**
10 72 h. The distinct modules identified at each time point were indicated by the clustering patterns
11 of the red color squares along the diagonal inside the plots. The modules highly associated with
12 BHA treatment ($r > 0.6$ and p -value < 0.05) were identified and indicated by the color bar shown
13 along the left side and at the top, where one color represents one distinct module. The
14 metabolites within each of the BHA-responsive modules were listed in **Table 2.**

15

16 **Suppl. Table S1. Compound-specific collisional mass spectrometric parameters used in**
17 **MRM.**

18

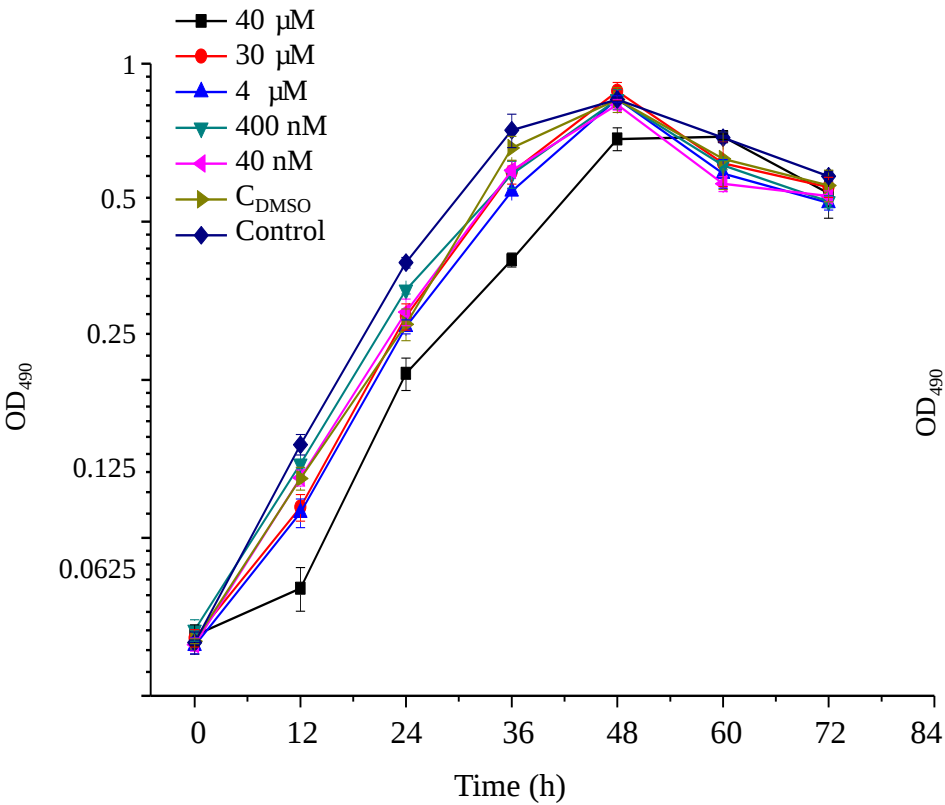
19 **Suppl. Table S2. LC-MS metabolomics data and reproducibility tests.**

20

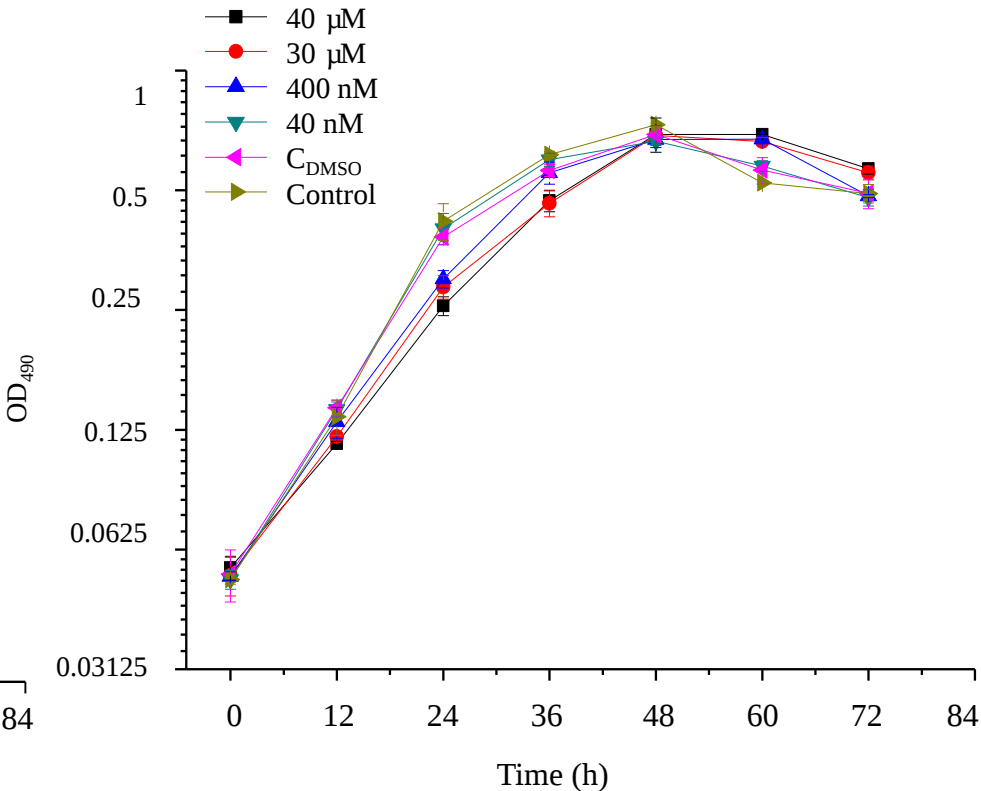
21 **Suppl. Table S3: GC-MS metabolomic data obtained in this study.**

Suppl. Fig. 1

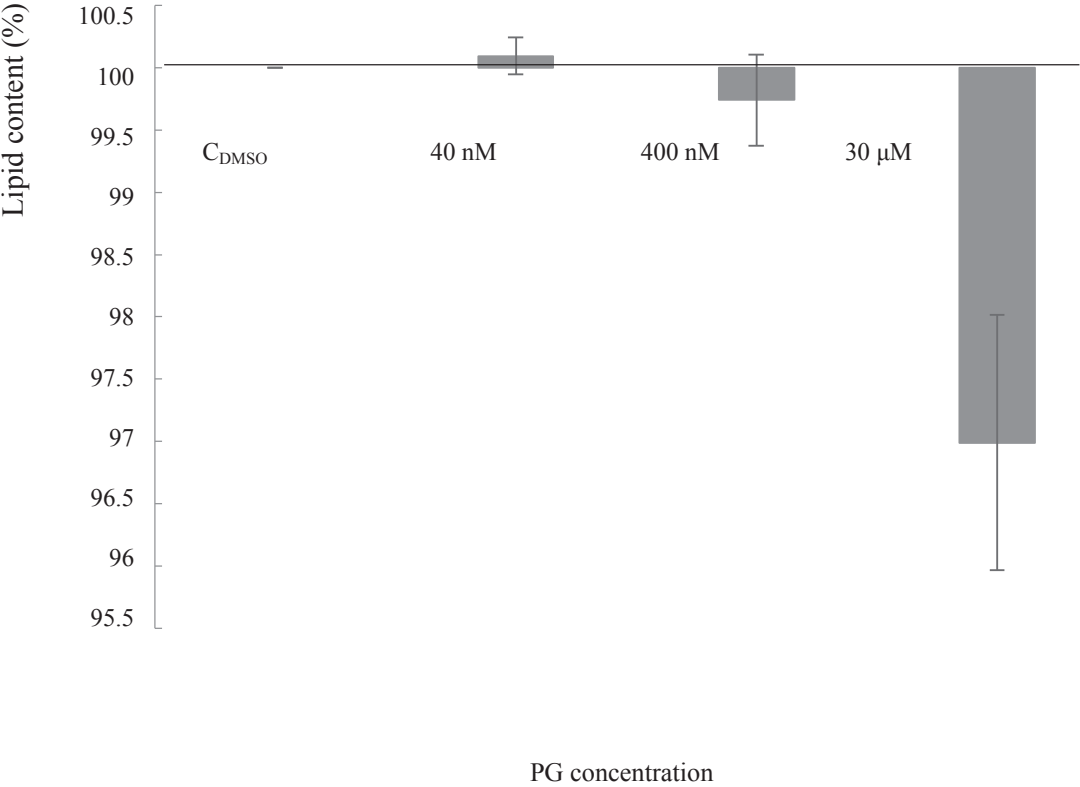
A) BHA



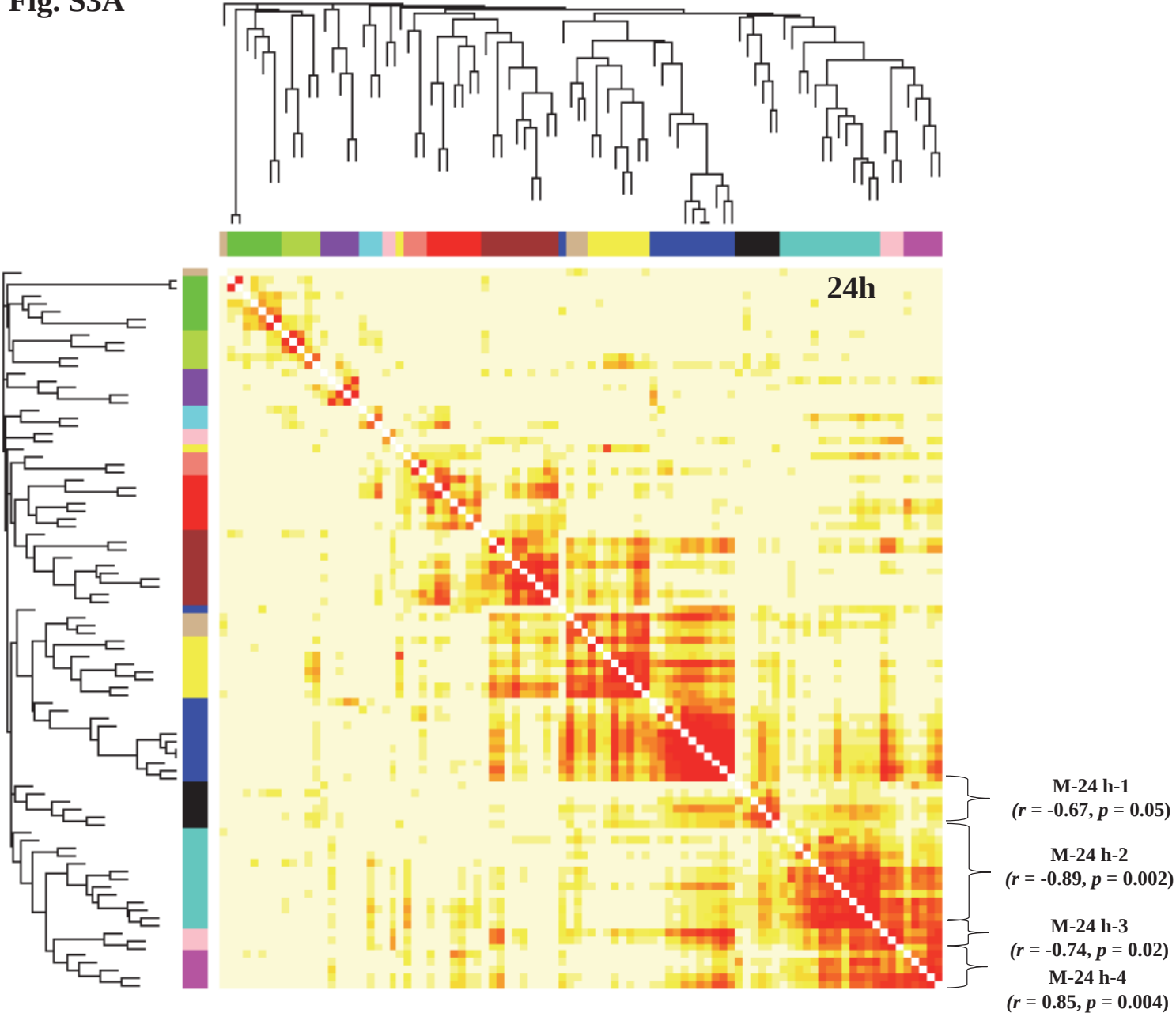
B) PG



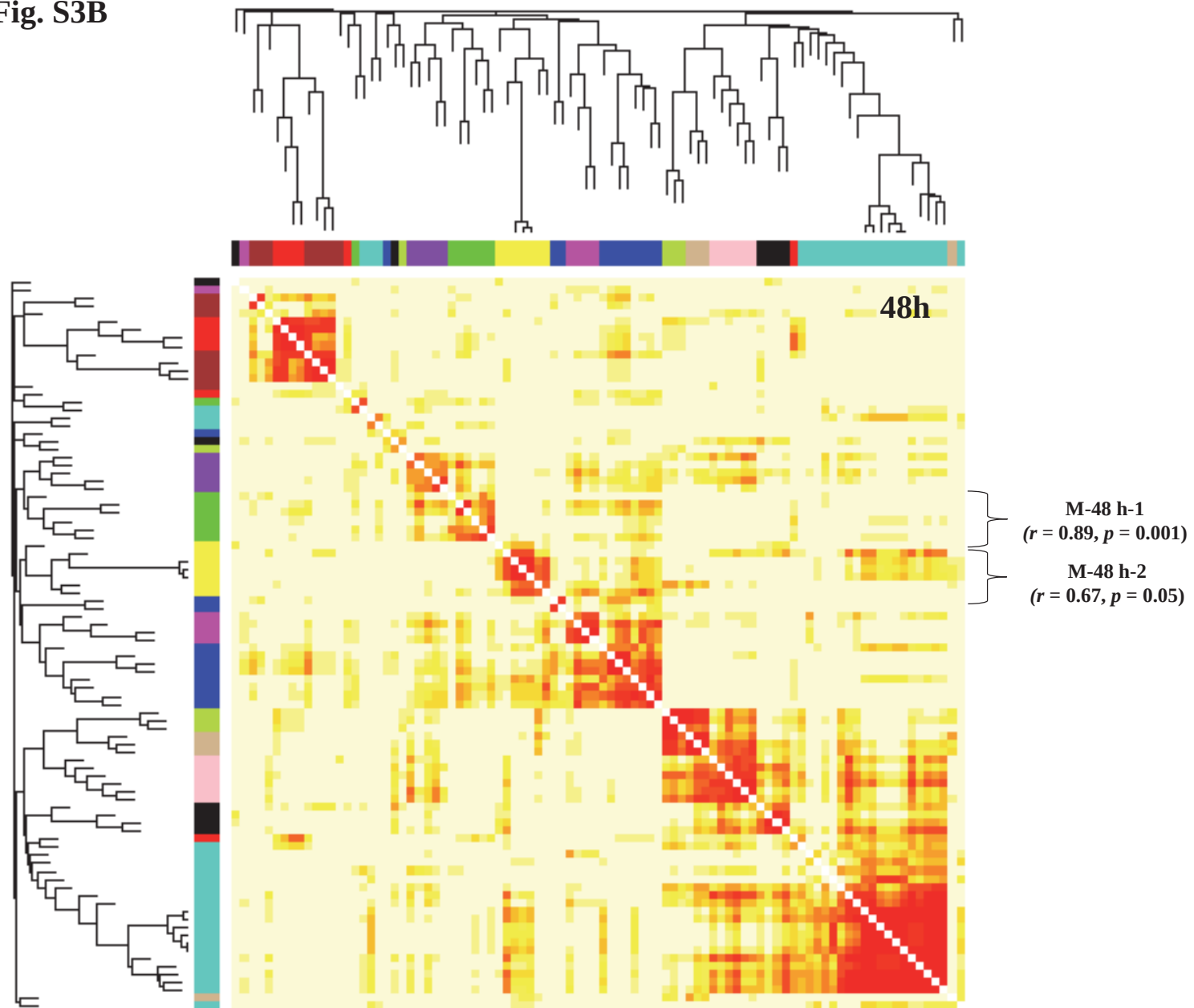
Suppl. Fig. S2



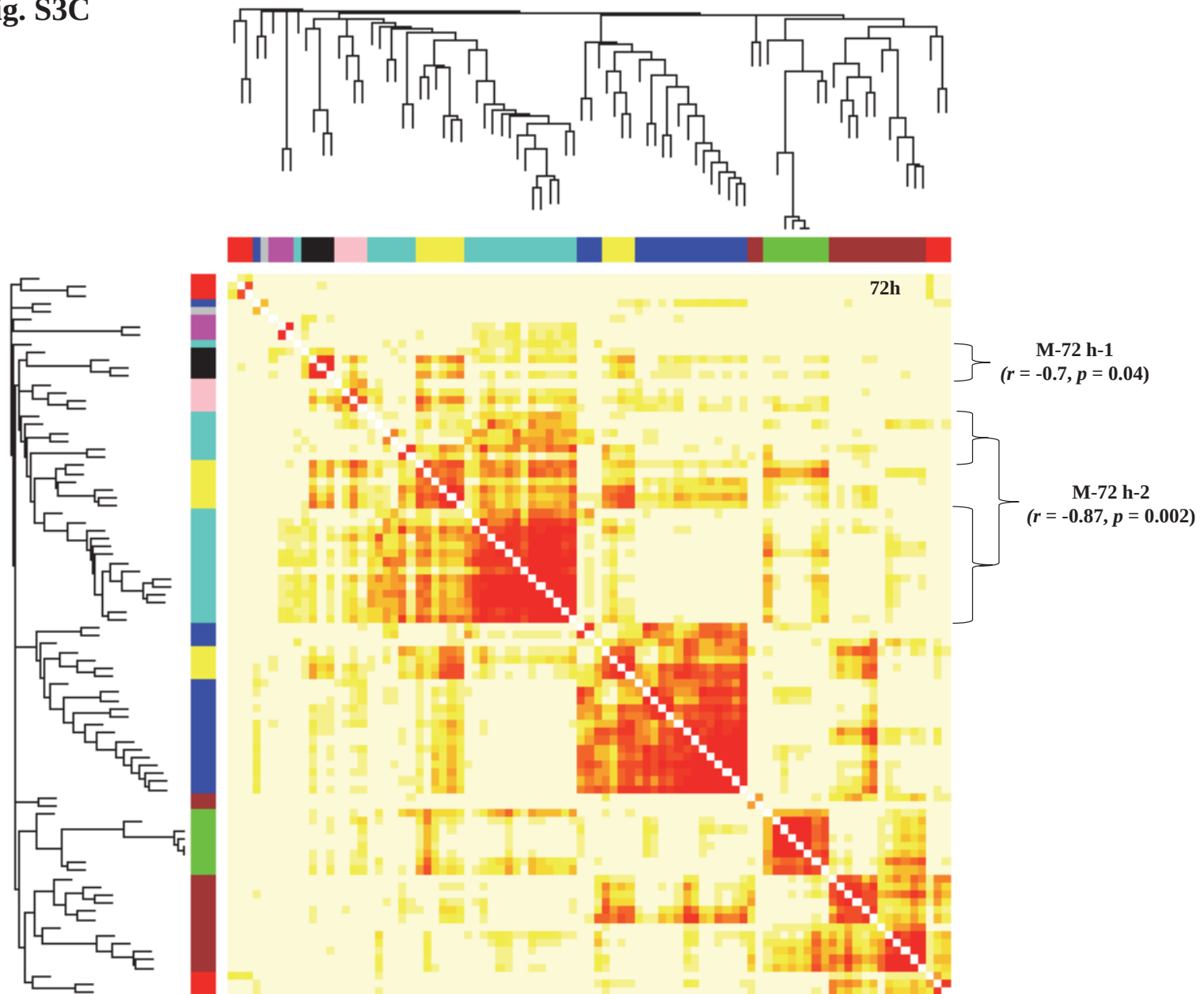
Suppl. Fig. S3A



Suppl. Fig. S3B



Suppl. Fig. S3C



Suppl. Table S1. Compound-specific collisional mass spectrometric parameters used in MRM

compound	Abbrev	(M-H) ⁻	FV1(V)	Product ion	CV2(V)	Retention Time (min)
Acetyl coenzyme A	AcCOA	808	260	79	130	28.25
NADPH	NADPH	744	200	79	112	27.55
NADP	NADP	742	140	620	8	21.19
NADH	NADH	664	190	79	108	20.78
α-Nicotinamide adenine dinucleotide	NAD	662	100	540	8	13.53
Adenosine-5'-diphosphoglucose	ADP-GCS	588	170	346	20	19.07
Uridine 5'-diphosphoglucose	UDP-GCS	565	160	323	10	17.82
Adenosine 5'-triphosphate	ATP	506	142	79	92	27.36
Adenosine 5'-diphosphate	ADP	426	150	79	60	21.10
Coenzyme A hydrate	COA	382.5	110	79	68	28.12
Adenosine 5'-monophosphate	AMP	346	140	79	45	16.14
D-Fructose 1,6-bisphosphate	FBP	339	110	97	18	21.50
D-Ribulose 1,5-bisphosphate	RiBP	309	104	97	14	22.70
D-Fructose 6-phosphate	F6P	259	86	97	4	11.04
D-Glucose 6-phosphate	G6P	259	100	97	4	11.63
D-Ribose 5-phosphate	R5P	229	78	97	12	11.52
D-(-)-3-Phosphoglyceric acid	3PG	185	84	97	4	19.34
Dihydroxyacetone phosphate	DHAP	169	84	97	4	14.26
DL-Glyceraldehyde 3-phosphate	GAP	169	66	97	8	12.14
Phospho(enol)pyruvic acid	PEP	167	82	79	4	21.08
L-Glutamic acid	GLU	145	80	127	8	2.19
α-Ketoglutaric acid	AKG	145	60	101	6	18.53
Oxaloacetic acid	OXA	131	110	87	0	17.74
Sodium fumarate dibasic	FUM	115	58	71	0	18.65

1 Fragmentation voltage at which maximal parent ion intensity is observed

2 Collision cell voltage at which maximal product ion intensity is observed

Suppl. Table S2. LC-MS metabolomics data and reproducibility tests.

Metabolite	BHA24h-1	BHA24h-2	BHA24h-3	Mean	Standard Deviation	Coefficient of Variation	C24h-1	C24h-2	C24h-3	Mean	Standard Deviation	Coefficient of Variation	C _{DMSO} 24h-1	C _{DMSO} 24h-2	C _{DMSO} 24h-3	Mean	Standard Deviation	Coefficient of Variation	BHA48h-1	BHA48h-2	BHA48h-3	Mean	Standard Deviation	Coefficient of Variation	C48h-1	C48h-2	C48h-3	Mean	Standard Deviation	Coefficient of Variation	C _{DMSO} 48h-1	C _{DMSO} 48h-2	C _{DMSO} 48h-3	Mean	Standard Deviation	Coefficient of Variation	BHA72h-1	BHA72h-2	BHA72h-3	Mean	Standard Deviation	Coefficient of Variation	C72h-1	C72h-2	C72h-3	Mean	Standard Deviation	Coefficient of Variation	C _{DMSO} 72h-1	C _{DMSO} 72h-2	C _{DMSO} 72h-3	Mean	Standard Deviation	Coefficient of Variation
Acetyl coenzyme A	344.047619	357.638889	286.5079365	329.39815	37.76053952	8.72334327	270.02688	246.10215	294.35484	270.16129	24.126625	11.19764126	317.5595238	238.9880952	223.7103175	260.0859788	50.3563194	5.164912409	240.8099526	272.33642	277.759628	263.63533	19.9524765	13.21316348	208.2784423	219.7726195	214.0255309	214.025531	5.7470886	37.24068755	265.0144535	237.5898711	255.8841564	252.8294937	13.96514065	18.10432849	103.9949458	104.4949215	86.46246459	98.317444	10.2697564	9.573493317	202.0393954	226.2894379	212.370578	213.56647	12.1691725	17.54979398	152.7434258	164.3873935	175.5629256	164.231248	11.4105512	14.39292856
NADPH	45.56878307	39.3187831	30.45634921	38.447972	7.593757207	5.06310259	22.34543	23.319892	25.403226	23.689516	1.5620483	15.16567459	40.31084656	24.17328042	24.00793651	29.4973545	9.36512374	3.149702591	32.50656665	39.13856	35.7082184	35.784448	3.31665359	10.78932342	28.09321811	45.05453971	30.3333666	34.4937081	9.21427908	3.743505906	32.07395878	30.22094645	41.87807853	34.72432792	6.264225772	5.543275288	22.83222369	24.53214107	22.59890169	23.3210888	1.05527033	22.09963481	26.6086083	31.8240284	27.9373778	28.7900048	2.71023641	10.62269134	23.65599169	28.67494325	34.32962868	28.8868545	5.33997298	5.409550692
NADP	205.0595238	242.92328	185.2843915	211.08907	29.28868221	7.2071889	220.2957	227.28495	192.37231	213.31765	18.47276	11.54768712	258.0357143	226.6203704	277.3809524	254.0123457	25.6183487	9.915250519	339.5057695	272.07506	320.328529	310.63645	34.7444572	8.940604592	276.518944	284.35738	280.438162	280.438162	3.919218	71.55462187	324.1760833	293.1128586	363.9316205	327.0735208	35.49817766	9.213811591	127.1938184	134.9934393	120.6941343	127.627131	7.15949373	17.8262787	327.8738626	309.9022557	334.351614	324.042577	12.6669585	25.58171942	289.8277228	272.0271746	303.7804082	288.545102	15.9154264	18.12990077
NADH	51.09126984	49.5039683	24.4047619	41.666667	14.97030055	2.78328859	22.916667	15.557796	29.53629	22.670251	6.9925045	3.242078865	40.34391534	18.61772487	21.32936508	26.76366843	11.8387321	2.260687057	28.22680763	30.644381	26.8873411	28.586177	1.90412649	15.01275093	18.08109817	27.43452601	22.75781209	22.7578121	4.67671392	4.86619718	28.67115433	27.79518486	21.73078089	26.06570669	3.779618621	6.896385405	41.56464662	36.93153846	36.63155304	38.3759127	2.76559502	13.87618668	33.45177098	24.68189259	23.4527809	27.1954815	5.45284767	4.987390648	52.66553171	27.16925778	42.82838665	40.8877254	12.8584455	3.179834248
α-Nicotinamide adenine dinucleotide	2858.862434	3027.21561	2514.517196	2800.1984	261.3350646	10.714974	2517.5067	2269.6237	2215.4906	2334.207	161.0332	14.4951912	2779.960317	2540.410053	2301.190476	2540.520282	239.38494	10.61269889	2910.203468	2917.6522	2772.00972	2866.6218	82.021063	34.94982503	2509.122886	2618.663382	2563.893134	2563.89313	54.770248	46.8117861	2649.201183	2495.805454	2692.292143	2612.432927	103.2747948	25.29593916	2021.068443	2022.468375	1922.073254	1988.53669	57.5632805	34.54522872	2894.956788	3070.62011	2947.90825	2971.16172	90.1107286	32.9723415	2988.317219	2764.271221	2973.159985	2908.58281	125.207073	23.23017973
Adenosine 5'-diphosphoglucose	1.091269841	0.95899471	0.892857143	0.9810406	0.101026801	9.71069614	0	0	0.4032258	0.1344086	0.2328025	0.577350269	0.330687831	0	0.595238095	0.308641975	0.2982308	1.03490978	0	0	0	0	0	0	0	0.823365126	0.499	0.44078838	0.41475773	1.062761076	0	0.505366998	0.606440397	0.370602465	0.324905522	1.140646864	0	0	0.599970841	0.19999028	0.34639333	0.577350269	0.498288545	0.664384727	0.63116549	0.59794625	0.08788984	6.803360509	0	0.468435479	0	0.15614516	0.27045135	0.577350269
Uridine 5'-diphosphoglucose	1305.588624	1380.42328	1154.06746	1280.0265	115.3226244	11.0995259	1063.7433	967.37231	1057.4597	1029.5251	53.9175	19.09445167	1395.10582	1165.707672	1086.772487	1215.861993	160.168514	7.591142353	1071.769272	1079.022	1034.78693	1061.8594	23.7242382	44.75841916	550.0408389	531.3998525	540.7203457	540.720346	9.3204932	58.01413446	635.3136981	620.9275843	628.2385602	628.1599475	7.193379076	87.32473861	62.93027492	67.26339767	82.36266384	70.8521121	10.2011562	6.94549819	186.3266966	178.9852453	141.115316	168.809086	24.2627884	6.957530321	125.6745471	99.70983768	178.2062401	134.530208	39.9904782	3.364056001
Adenosine 5'-triphosphate	1141.964286	1223.54497	1125.628307	1163.7125	52.45624612	22.1844415	948.75672	886.62634	857.52688	897.63665	46.600869	19.26222991	1197.453704	983.994709	1048.941799	1076.796737	109.421702	9.840796839	499.7517086	547.02508	486.063014	510.9466	31.9857389	15.97420027	301.8785899	331.0915845	316.4850872	316.485087	14.6064973	21.66741832	441.21908	403.0807172	395.6349768	413.3115913	24.45364401	16.90184053	48.6976333	34.23166967	22.03226257	34.9871885	13.3487305	2.621012429	131.8803682	138.2916808	126.532071	132.234707	5.88780701	22.45907629	107.7067005	81.440854	149.1297807	112.759112	34.1261314	3.304186766
Adenosine 5'-diphosphate	447.0238095	596.891534	444.3121693	496.07584	87.31948104	5.6811588	542.43952	579.7379	478.76344	533.64695	51.058225	10.45173328	656.9444444	541.7989418	667.7910053	622.1781305	69.821361	8.91099975	399.1610366	343.98155	395.894045	379.67888	30.9579191	12.26435392	339.3581704	415.9311272	380.025478	378.438259	38.3111456	9.878019896	425.6537764	411.2676626	416.3550237	417.7588209	7.295070425	57.26590651	126.7938378	102.5950139	117.9276021	115.772151	12.2425588	9.456532187	343.5533421	310.367325	294.754284	316.224984	24.921299	12.68894467	278.7860294	295.4824082	351.7615851	308.676674	38.2351203	8.073118949
Coenzyme A hydrate	22.8505291	18.8492064	20.86640212	20.855379	2.00068415	10.4241238	16.431452	20.295699	20.665323	19.130824	2.3450193	8.158067014	21.62698413	21.89153439	19.31216931	20.94356261	1.41900662	14.75931284	13.16597624	17.576415	17.151706	15.964699	2.43304983	6.5615997	16.82958318	13.79959952	15.31459135	15.3145914	1.51499183	10.10869567	12.97108627	15.96959712	16.03697939	14.99255426	1.750966795	8.562443502	13.63267079	12.49939253	11.29945085	12.4771714	1.16676868	10.69378326	17.87194915	14.35071009	18.7356493	16.9861028	2.32281418	7.31272566	15.15723371	15.15723371	14.88955563	15.0680079	0.15454362	97.5000291
Adenosine 5'-monophosphate	1144.212963	1272.8836	1053.306878	1156.8011	110.3282863	10.4850822	1103.1922	1305.4772	1280.1411	1229.6035	110.2059	11.1573296	1245.535714	1204.464286	1119.510582	1189.836861	64.273281	18.51215376	799.2695007	860.6236	1015.34833	891.74714	111.350891	8.008441944	1041.326342	1054.269642	1047.797992	1047.79799	6.47165	161.9058497	934.6594163	937.1188691	975.3583052	949.0455302	22.82068849	41.58706827	1731.415853	1744.215231	1709.816903	1728.48266	17.3857398	99.4195636	1511.209499	1466.928257	1453.93954	1477.3591	30.0260552	49.20257056	1528.003073	1702.997184	1618.779177	1616.59314	87.5175341	18.4716487
D-Fructose 1,6-bisphosphate	43.02248677	45.5026455	43.05555556	43.860229	1.422470272	30.833846	42.674731	37.063172	44.086022	41.274642	3.7148744	11.11064254	52.61243386	43.38624339	46.42857143	47.47574956	4.70139173	10.0982331	45.21516407	62.693569	36.6883159	48.199016	13.2569164	3.635763788	42.22216367	54.24329451	48.23272909	48.2327291	6.01056542	8.024657535	46.56114604	39.89030167	36.55487949	41.00210907	5.094941544	8.047611286	40.23137809	40.69802208	45.29779853	42.0757329	2.80012845	15.02635812	41.52404541	14.35071009	36.7404754	30.8717436	14.5061727	2.128179789	38.98052379	43.76525761	43.26336246	42.003048	2.62958436	15.97326503
D-Ribulose 1,5-bisphosphate	19.90740741	27.8769841	21.19708995	22.993827	4.277819156	5.37512838	24.193548	26.41129	19.018817	23.207885	3.7935226	6.1177665	21.79232804	21.19708995	19.11375661	20.7010582	1.40649275	14.71821183	32.04918783	26.822001	23.9143787	27.595189	4.12215293	6.694363293	22.92248511	24.50334616	23.71291563	23.7129156	0.79043053	29.99999985	23.75224888	23.71855775	16.74449318	21.40509994	4.036239002	5.303229053	20.49900375	19.29906207	17.83246668	19.2101775	1.3354888	14.38437933	26.30963517	23.88463092	19.8983226	23.3641962	3.23718575	7.217440718	15.42491113	16.46216112	20.1427256	17.343266	2.47925445	6.995355374
D-Fructose 6-phosphate	141.9973545	144.675926	171.1309524	152.60141	16.10284498	9.47667391	151.20968	156.85484	114.41532	140.82661	23.046348	6.11058261	133.8624339	140.7738095	152.3148148	142.3170194	9.32248426	15.26599728	105.7851888	105.94854	106.863296	106.19901	0.58105935	182.7679166	99.92359172	90.76777151	95.34568161	95.3456816	4.57791011	20.82733811	107.3736414	110.9449015	109.4288005	109.2491145	1.792397829	60.95137624	36.96487017	33.03172799	41.23132949	37.0759759	4.10092972	9.040870836	42.78637639	43.2514457	53.5161897	46.5180039	6.065066	7.669826497	47.311198338	36.80564478	61.09737034	48.4049995	12.1826925	3.973259574
D-Glucose 6-phosphate	44.1468254	43.9153439	43.45238095	43.83																																																		

Supplementary Table S3. GC-MS metabolomic dataset used in this study. A, B, and C represent biological triplicates for each treatment

[illegible]

Xylitol	0	0	0	0	0	0	0.009551	0.006156	0.005668	0.007125	0.002115	0.29683146	0.010082	0.004239	0.003539	0.005953	0.003593	0.60347108	0	0	0	0	0
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