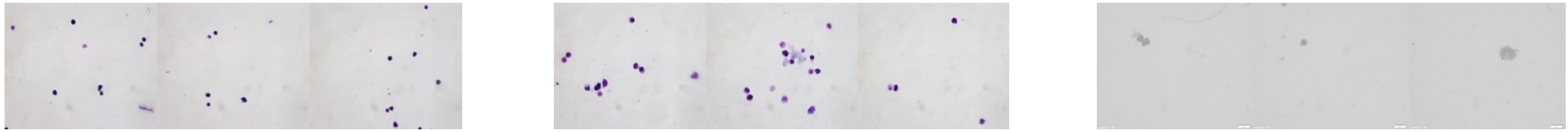
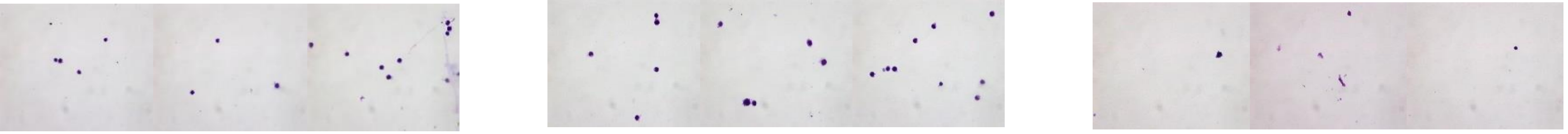
Supplementary Figure 1. Different morphological size of Leukemic cells.



Jurkat Control

HL-60 Control

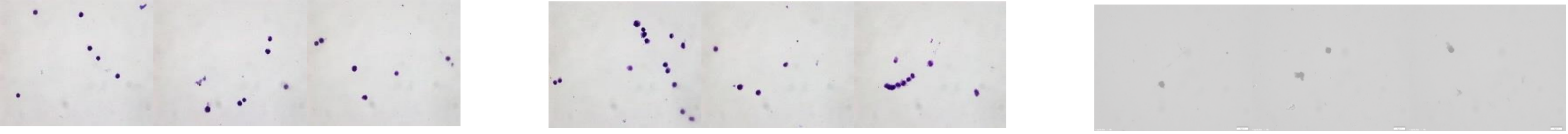
K-562 Control



Jurkat with TQ 5 μM

HL-60 with TQ 5 μM

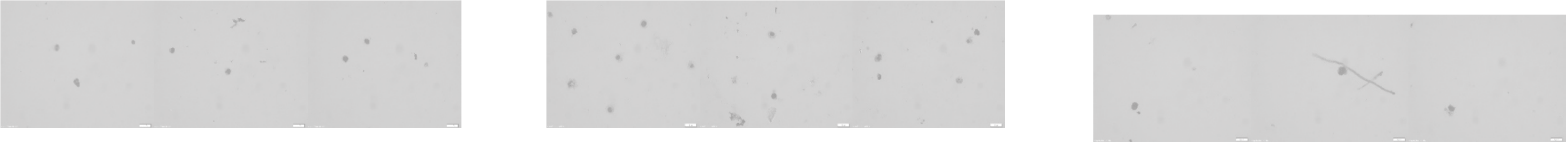
K-562 with TQ 5 μM



Jurkat with TQ 10 μM

HL-60 with TQ 10 μM

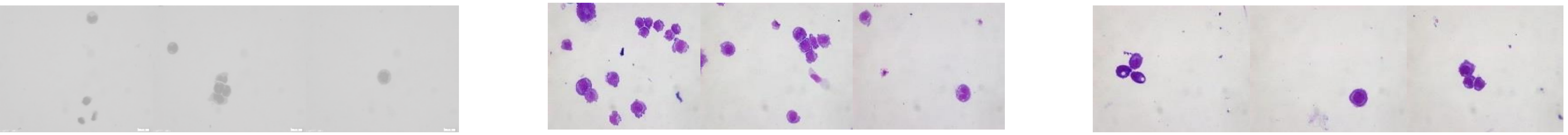
K-562 with TQ 10 μM



Jurkat with H_2O_2 5 μM

HL-60 with H_2O_2 5 μM

K-562 with H_2O_2 5 μM

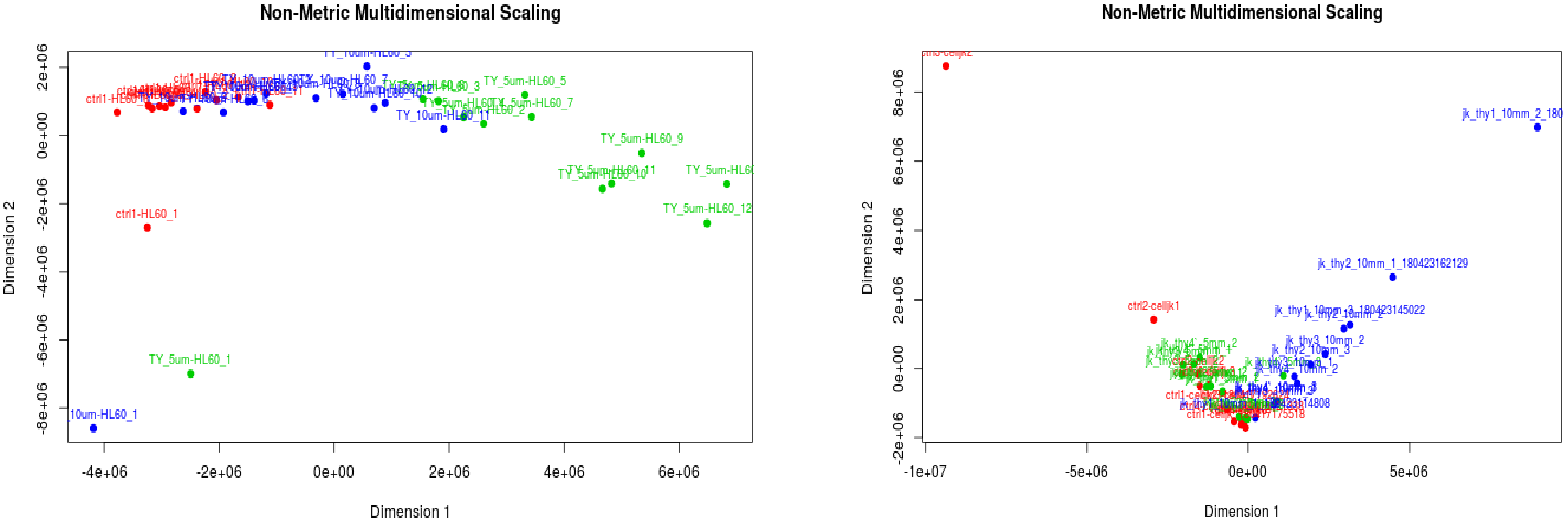


Jurkat with Ethanol 5 μM

HL-60 with Ethanol 5 μM

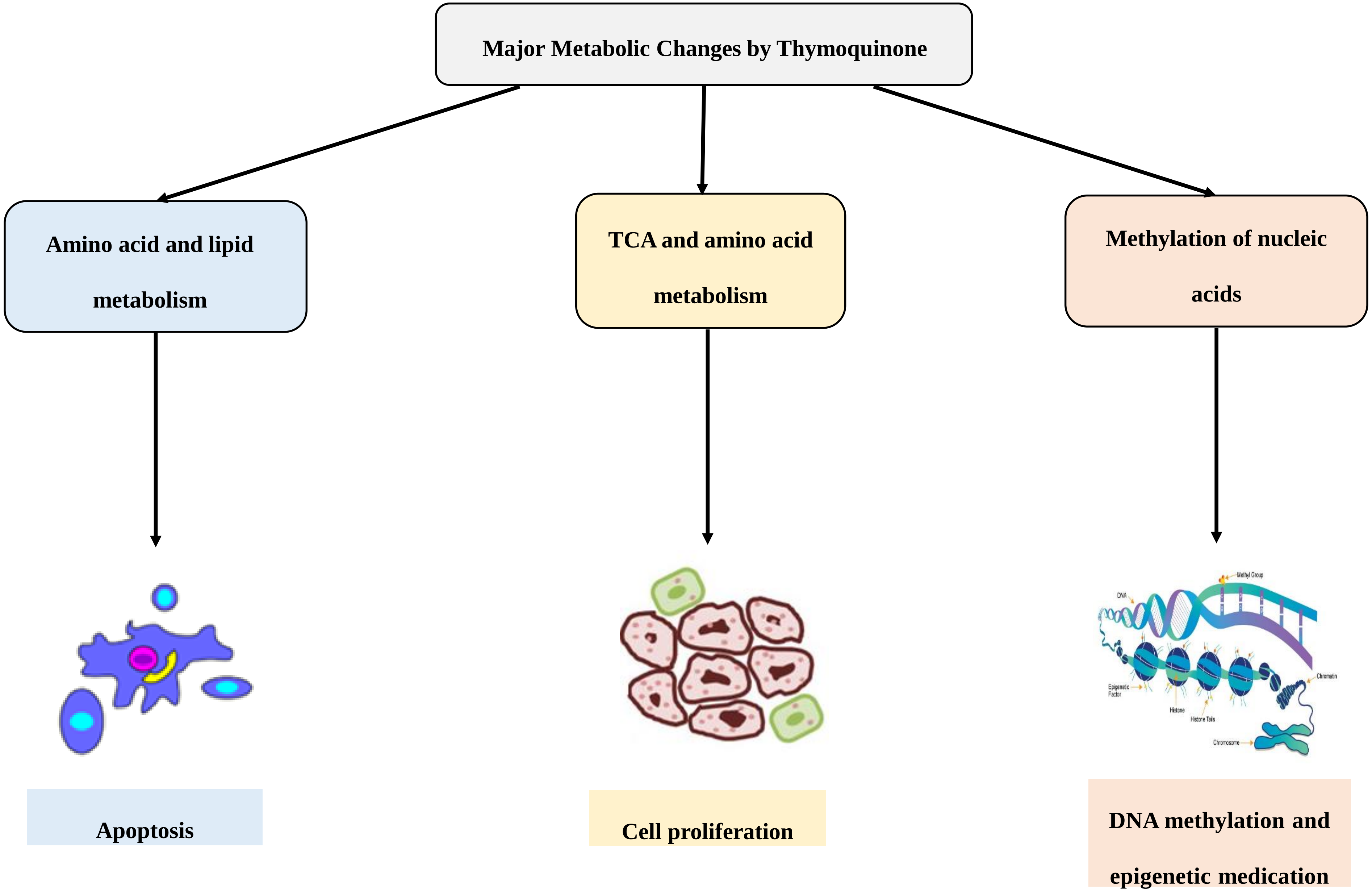
K-562 with Ethanol 5 μM

Supplementary Figure 2. 2D Variation of Difference between RAW files in HL-60 Cell and Jurkat Cell.


HL-60

Jurkat

Supplementary Figure 3. Major Metabolic Changes by Thymoquinone.



Major Metabolic Changes by Thymoquinone

Amino acid and lipid metabolism

TCA and amino acid metabolism

Methylation of nucleic acids

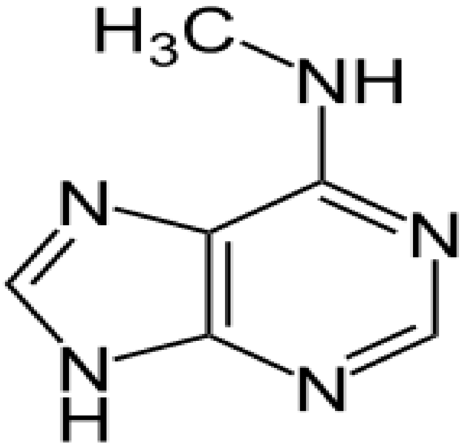
Apoptosis

Cell proliferation

DNA methylation and epigenetic medication

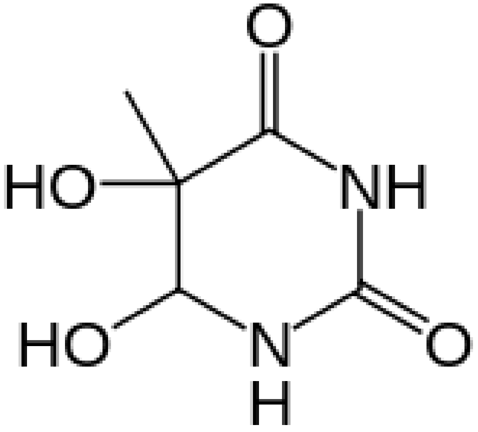
Supplementary Figure 4. Structure of the some compound founded in metabolism with the important.

A. 6-methyladenine



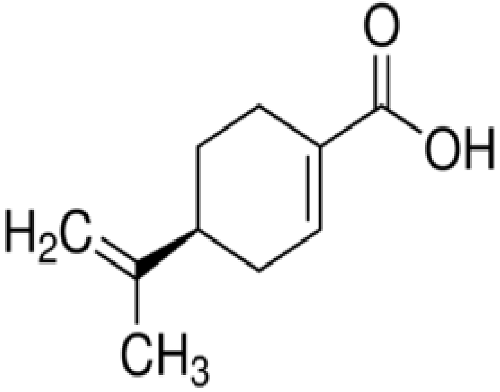
(A) Methylation of N6 adenosine (m6A) is the most abundant form of messenger RNA (mRNA) modification in eukaryotes. It is known to play crucial roles in the regulation of gene expression, protein translation, and splicing in normal biology.

B. Thymine glycol



(B) The presence of thymine glycol in DNA can have profound consequences on DNA replication. The presence of thymine glycol may also induce structural changes at the initiation and termination points leading to alterations in the relative amounts of the termination bands of DNA synthesis.

C. Perillic acid



(C) Perillic acid is currently on clinical trials as a multi-target anti-cancer agent. The prospective anticancer activity of perillic acid relates to the accepted mechanism for these monoterpenes as inhibitors of protein prenylation in cancer cells.

Supplementary Table 1. Percentages of live, early apoptotic, late apoptotic, and necrotic leukemia cells upon treatment with TQ treatment by flow cytometry.

Jurkat cell

Phases	Control	TQ Dose 5 μM	TQ Dose 10 μM
% Necrotic	75.1	90.2	89.3
% Late Apoptosis	0.8	3.3	0
% Live	24.1	6.5	10.7
% Early Apoptosis	0	0	0

HL-60

Phases	Control	TQ Dose 5 μM	TQ Dose 10 μM
% Necrotic	85.7	90.4	90.9
% Late Apoptosis	2.1	2.5	2.8
% Live	12.1	7	6.1
% Early Apoptosis	0	0.1	0.2

K-562 cell

Phases	Control	TQ Dose 5 μM	TQ Dose 10 μM
% Necrotic	33.4	50.3	51.4
% Late Apoptosis	30.4	42	39.3
% Live	29.6	6.1	6.2
% Early Apoptosis	6.6	1.6	2.5

Supplementary Table 2. The percentages of the cell cycle phases of leukemia cells line upon treatment with TQ treatment by flow cytometry.

Jurkat cell

Cell cycle phases	Control	TQ Dose 5 µM	TQ Dose 10 µM
Apoptotic	6.6	3.2	7.3
G1/G0	61.1	64	59.2
S	20.3	19.4	18.8
G2/M	11	12	13.9

HL-60 cell

Cell cycle phases	Control	TQ Dose 5 µM	TQ Dose 10 µM
Apoptotic	2.7	21.9	12.2
G1/G0	55.3	53.1	57.5
S	21.7	15.1	18.9
G2/M	17.7	9.4	10.6

K-562 cell

Cell cycle phases	Control	TQ Dose 5 µM	TQ Dose 10 µM
Apoptotic	4.8	9.8	13.4
G1/G0	31.1	47.5	45.4
S	27.3	25.8	25.2
G2/M	33.3	14.6	13.6

Supplementary Table 3. Raw metabolomic datasets extracted from XCMS database.

featureidx	name	mzmed	mzmin	mzmax	rtmed	rtmin	rtmax	npeaks
1	M86T5	86.03821	85.92044	86.05632	4.632783	3.464748	4.884887	19
2	M403T8	403.3552	403.337	403.3719	8.345605	8.087223	8.549472	10
3	M344T5	344.4143	344.3549	344.4491	5.165696	4.825887	5.835453	12
4	M388T5	388.4465	388.4392	388.5077	5.171168	4.817698	5.495433	12
5	M294T5	294.2631	294.2308	294.321	4.579524	4.534977	4.722842	10
6	M323T5	323.2353	323.1773	323.2531	4.910777	4.748247	5.22985	21
7	M404T8	404.3817	404.3616	404.4263	8.352753	8.089535	8.489643	10
8	M314T5	314.2733	314.2556	314.324	4.59147	4.563005	4.728507	15
9	M127T5	127.0584	126.9882	127.1454	4.635805	4.592405	5.175502	22
10	M174T5	174.0514	174.0011	174.1457	4.603803	3.766963	4.938027	32
11	M311T5	311.2684	311.2631	311.318	4.710884	4.615372	4.883565	10
12	M132T5	132.056	131.9632	132.1308	4.626476	4.404047	4.975167	30
13	M477T5	476.5485	476.4845	476.5636	5.170188	4.800562	5.644097	13
14	M133T5	133.0708	133.0053	133.1309	4.597893	4.52215	4.807623	22
15	M125T5	125.0504	125.0114	125.1242	4.689032	4.55158	5.354145	23
16	M297T5	297.1961	297.1628	297.2427	4.582013	4.534977	4.677878	17
17	M325T5	325.3278	325.2711	325.3775	4.839259	4.631947	5.094492	22
18	M331T6	331.3559	331.2392	331.432	5.61722	5.301902	6.717672	23
19	M359T5	359.3617	359.3464	359.5293	4.634463	4.565832	5.554575	14
20	M270T7	270.2839	270.267	270.3285	6.967975	6.459652	7.178153	8
21	M503T8	502.5382	502.5174	502.5491	7.872158	7.365097	8.207987	8
22	M223T5	223.1618	223.0626	223.256	4.576538	4.510578	4.690018	12
23	M120T5	120.0586	120.034	120.1237	4.683622	4.6082	4.95588	23
24	M273T5	273.2951	273.2486	273.3382	4.87758	4.512252	5.282557	40
25	M259T5	259.2548	259.2178	259.3301	4.833018	4.606828	5.226058	38
26	M331T5	331.366	331.3329	331.4465	4.730055	4.563005	5.142007	25
27	M130T5	130.0326	129.9596	130.1386	4.655774	3.583923	5.051045	32
28	M276T5	276.254	276.1973	276.2711	4.64802	4.623633	4.910857	17

29	M430T5	430.4428	430.3497	430.4803	4.705287	3.80082	5.594457	34
30	M439T14	438.5027	438.4712	438.5394	13.92583	13.71556	14.09794	10
31	M455T12	454.5221	454.4628	454.535	12.22604	12.05158	12.30137	10
32	M295T5	295.2795	295.2559	295.3263	4.656998	4.615372	4.892948	7
33	M88T5_1	88.05086	87.98825	88.15427	4.613634	4.024837	4.835405	28
34	M456T12	455.5417	455.5253	455.5523	12.21907	12.04494	12.3036	9
35	M173T5	172.9463	172.877	173.0582	4.600171	4.506617	5.058922	28
36	M239T7	239.2435	239.1675	239.2718	7.287099	6.771642	8.004913	20
37	M440T14	439.5411	439.4924	439.5525	13.92473	13.68874	14.07218	9
38	M166T5	166.0695	166.0523	166.1781	4.744203	4.586708	5.381615	32
39	M205T5	205.1406	205.0951	205.1868	4.768325	4.616197	5.08235	31
40	M327T5	327.3658	327.2272	327.4204	5.18684	4.840658	5.737203	12
41	M150T5	150.0651	150.0059	150.1196	4.584138	3.80082	4.763325	18
42	M481T13	480.5497	480.5258	480.5534	12.82689	12.60807	12.94736	8
43	M213T5	213.2154	213.1657	213.2302	5.209492	5.149608	5.598225	8
44	M638T11	637.5551	637.534	637.6099	11.49579	10.94977	11.97891	9
45	M115T5	114.9886	114.9373	115.15	4.681278	3.774872	6.00717	40
46	M267T7	267.1999	267.1409	267.3027	6.855823	6.587305	7.48176	8
47	M392T5	392.3849	392.3629	392.4408	4.68207	4.624823	4.82991	12
48	M358T5	358.4234	358.3398	358.5484	4.59596	4.498705	5.322833	29
49	M208T5_2	208.12	208.0613	208.1468	5.292748	5.122618	5.626582	20
50	M367T6	367.3733	367.3262	367.4326	6.202497	5.306638	7.222815	17
51	M312T5	312.2439	312.2324	312.2632	4.608397	4.553722	4.636218	9
52	M226T7	226.2322	226.1679	226.2522	6.710986	6.216225	7.424545	20
53	M426T8	426.4303	426.3808	426.4442	8.391491	8.077573	8.76924	10
54	M172T5	172.162	172.0851	172.2384	4.737507	4.563005	5.034417	24
55	M425T8	425.3743	425.3617	425.4302	8.385889	8.067898	8.771577	12
56	M74T4_1	73.90972	73.86966	73.93328	4.090846	4.00084	4.132953	8
57	M207T5	206.9649	206.9346	207.1138	4.710325	3.922137	5.026373	29
58	M167T5	167.1145	167.0687	167.145	4.741767	4.582013	5.051045	29
59	M135T5	135.071	135.0466	135.1469	4.844528	3.994998	5.335582	43

60	M146T5	146.0511	145.9879	146.1257	4.736136	3.879912	5.03403	24
61	M280T7	280.1657	280.0732	280.2176	6.609518	6.107202	7.337065	22
62	M187T6	187.1216	187.0467	187.1594	6.414293	5.835453	7.12864	23
63	M200T5	200.1455	200.0629	200.1948	4.8877	4.591883	5.523827	41
64	M179T5	179.0654	179.0532	179.1166	4.607565	4.487053	4.928165	18
65	M92T4	91.97455	91.94838	92.03751	4.053925	3.982608	4.13534	7
66	M278T6	278.3344	278.2616	278.3608	5.720584	5.433803	6.74317	18
67	M406T7	406.4423	406.3948	406.4724	7.041523	6.689432	7.225967	10
68	M188T5	188.1196	188.0529	188.158	4.677503	4.6082	5.007232	27
69	M208T5_1	208.0663	208.0463	208.1471	4.638455	3.958748	4.957938	24
70	M391T7	391.369	391.2347	391.4207	6.561392	6.304207	7.243367	14
71	M177T5	177.0648	177.0473	177.1254	4.733226	4.308623	5.051045	30
72	M220T5	220.1617	220.1399	220.2293	4.833999	4.57659	5.848925	32
73	M317T5	317.3443	317.2859	317.4146	4.813825	4.6082	5.074	29
74	M193T5	193.1525	193.1299	193.2315	4.759687	4.530382	5.093258	20
75	M221T5	221.174	221.1657	221.2199	4.979858	4.926942	5.101042	9
76	M316T5	316.3425	316.2198	316.3735	4.765487	4.584443	5.074	31
77	M266T7	266.0434	266.0318	266.1316	6.691898	6.207917	7.440292	19
78	M485T8	484.6534	484.6263	484.66	8.256312	8.025665	8.388897	8
79	M255T7_2	255.2686	255.2362	255.3363	6.569836	6.115373	6.803218	20
80	M225T6	225.2245	225.1354	225.268	6.071043	5.39591	7.424545	51
81	M182T5	182.0719	182.0434	182.1318	4.567497	3.464748	4.947872	20
82	M178T5	178.0756	177.9525	178.1363	4.755924	4.487053	5.084477	30
83	M397T8	396.5288	396.4841	396.5543	8.246338	8.071815	8.421867	7
84	M131T5	131.122	131.0508	131.1511	4.663193	4.4082	5.165063	17
85	M72T6	72.05058	71.95451	72.16005	6.124783	5.333265	6.813032	21
86	M263T5	263.2423	263.1701	263.2677	4.79075	4.613335	4.999563	16
87	M176T5	176.049	175.9523	176.1152	4.919953	4.549835	6.001552	49
88	M266T6	266.1447	266.0627	266.2094	5.510418	5.038627	5.659843	11
89	M353T5	353.2452	353.2239	353.3185	5.140983	4.888225	5.492832	32
90	M371T5	371.4163	371.3743	371.4595	5.171439	4.827015	5.389102	10

91	M369T7	369.3467	369.2537	369.3651	6.51023	6.08099	7.260225	17
92	M106T4	105.9382	105.8733	106.0417	4.063212	3.52749	4.550438	26
93	M357T5	357.4367	357.3631	357.455	4.977848	4.634423	5.787962	24
94	M521T5	520.5782	520.5648	520.6259	4.854988	4.800562	5.19786	9
95	M414T7	414.4479	414.335	414.4726	6.571032	6.041307	7.252895	14
96	M172T6	172.1432	172.1199	172.1579	6.133707	5.827775	6.821057	15
97	M202T5	202.17	202.1482	202.1797	4.990255	4.911543	5.126615	6
98	M158T7	158.1448	158.1343	158.1624	7.120552	6.685003	7.369298	7
99	M264T6	264.32	264.2702	264.3416	5.870879	5.476708	6.73376	12
100	M352T8	352.4778	352.4684	352.5288	8.259575	8.04997	8.424112	9
101	M244T5	244.2344	244.1522	244.292	4.867492	4.59545	5.43146	36
102	M74T4_2	74.0312	73.94011	74.16742	4.302002	3.774872	5.499508	34
103	M232T5	232.2348	232.1676	232.2619	4.807025	4.59147	4.993465	17
104	M123T5	123.0017	122.9495	123.052	5.020699	4.887887	5.104255	8
105	M335T5	335.2552	335.2374	335.2967	5.170685	4.860125	5.420178	17
106	M460T5	459.5425	459.5342	459.547	4.996394	4.842767	5.226058	6
107	M283T6	283.2785	283.2498	283.3304	5.859193	5.479027	6.525898	13
108	M392T7	392.371	392.3567	392.3791	6.517585	6.32531	7.243367	7
109	M213T6	213.1743	213.1318	213.2174	6.320772	5.855443	7.039818	8
110	M434T6	434.4426	434.3655	434.5135	6.145999	6.00387	6.528655	10
111	M387T6	387.3666	387.3378	387.4307	6.145427	5.941407	6.577873	11
112	M449T7	449.4712	449.3931	449.5229	6.732345	6.222043	7.422218	19
113	M365T5	365.2912	365.2337	365.3594	5.227072	4.63994	5.859082	25
114	M376T6	376.3663	376.2666	376.387	5.655085	5.474603	6.717672	14
115	M161T5	161.065	161.0378	161.1412	4.663825	4.614862	4.930335	20
116	M134T5	134.1382	134.0785	134.1754	4.573527	4.462005	4.623803	12
117	M324T6	324.2499	324.2319	324.315	5.674939	5.622702	6.153257	12
118	M138T5	138.0558	137.9487	138.1698	4.501787	4.363835	4.524893	6
119	M436T6	436.3484	436.254	436.4198	6.460165	5.870322	7.130917	21
120	M432T6	432.3698	432.3265	432.5332	5.986876	4.724375	7.762662	74
121	M329T8	329.2668	329.2553	329.3252	8.415417	8.089535	8.531017	8

122	M369T5	369.3536	369.3395	369.4205	5.393728	5.18054	5.521213	12
123	M129T5	129.0513	128.9414	129.1696	4.631085	4.41297	5.365183	27
124	M474T6	474.3243	474.2454	474.3546	6.172282	6.0024	6.239987	7
125	M152T5	152.1082	152.0513	152.1497	4.88552	4.553662	5.036688	13
126	M325T7	325.2715	325.2497	325.356	6.932663	6.523583	7.124052	6
127	M326T5	326.3631	326.3312	326.4391	4.97847	4.653417	5.36114	27
128	M126T6	125.9425	125.9265	125.9547	5.744497	5.24264	5.927697	17
129	M260T9	260.2368	260.2297	260.253	8.885537	8.485632	9.349463	9
130	M425T10	425.4083	425.3508	425.472	9.710659	8.891108	11.34222	40
131	M229T5	229.221	229.1537	229.2941	4.840658	3.966078	5.249317	35
132	M188T6	188.1492	188.1273	188.1645	6.295739	5.476708	6.914247	12
133	M251T5	251.2539	251.2334	251.3257	4.865088	4.523812	5.290598	21
134	M97T4	96.94113	96.88057	97.04735	3.980068	3.907642	4.189938	15
135	M135T6	135.0588	135.0454	135.1108	5.78221	5.435147	6.724618	19
136	M403T10	403.3655	403.3303	403.4249	9.630463	8.778365	10.50355	32
137	M451T7	450.544	450.487	450.5634	6.697973	6.122972	7.196178	17
138	M261T5	261.2362	261.1741	261.2645	4.654195	4.536012	5.039612	19
139	M443T6	442.544	442.4419	442.6069	5.536385	4.964287	6.675498	43
140	M386T6	386.4164	386.352	386.4801	6.468517	5.929533	7.269918	20
141	M171T5	171.086	170.9592	171.1742	5.277487	4.015132	7.362828	84
142	M265T5	265.2666	265.2534	265.3167	4.837291	4.636192	5.098895	16
143	M749T5	748.7727	748.7487	748.8327	5.254344	5.204077	5.350302	6
144	M433T6	433.3886	433.3475	433.5404	6.032262	4.724375	7.7479	52
145	M426T10	426.4281	426.3636	426.4612	9.75558	8.871817	11.34222	33
146	M435T6	435.3417	435.3231	435.3588	6.453475	6.215662	7.12864	15
147	M303T6	303.3614	303.347	303.4293	5.787962	5.44812	6.721435	13
148	M359T6	358.5296	358.4465	358.5658	6.128988	5.631097	7.187682	30
149	M88T6	87.94592	87.90848	87.97305	6.428488	6.192818	7.1216	14
150	M476T5	475.5246	475.4604	475.573	4.901722	4.723618	5.247163	15
151	M416T7	416.3863	416.3646	416.4525	6.858348	6.534482	7.754625	15
152	M147T5	147.0459	146.9527	147.1119	4.698943	4.48582	4.938027	27

153	M247T5	247.262	247.1802	247.297	4.948613	4.622613	5.816215	12
154	M124T5_2	124.0537	124.026	124.0745	4.617241	4.528235	4.910857	12
155	M335T6	335.2448	335.1874	335.4188	6.325805	5.920495	6.74287	14
156	M257T5	257.2631	257.2351	257.3283	5.491283	4.604822	7.534892	90
157	M431T5	431.4501	431.3795	431.529	4.697648	4.570842	5.134262	17
158	M191T5	191.1229	191.0613	191.1579	4.798454	3.978033	5.848925	24
159	M190T5	190.1178	189.9575	190.1404	4.865817	4.316508	5.03403	20
160	M246T5	246.2288	246.0699	246.2807	4.87291	4.584443	6.030728	41
161	M183T5	183.0446	182.9704	183.107	5.227072	4.616197	6.695352	65
162	M156T5	156.0667	156.0481	156.1227	4.83406	4.622755	5.19075	19
163	M450T6	449.5445	449.5118	449.5614	5.527583	5.377458	5.649298	7
164	M189T5	189.1187	189.0748	189.1515	4.797717	4.524647	4.950863	11
165	M163T5	163.1486	163.1231	163.1592	4.998885	4.553722	5.462115	13
166	M196T5	196.0309	195.939	196.0693	5.14004	4.626225	5.875975	45
167	M354T7	354.4442	354.3667	354.4621	6.746231	6.361625	8.034702	32
168	M227T5	227.1832	227.1194	227.2382	5.018687	4.536012	6.267598	63
169	M336T6	336.2591	336.2319	336.3717	6.400085	5.939828	6.759375	13
170	M416T6	416.4134	416.3559	416.5353	5.908087	4.704952	6.422442	31
171	M226T6	226.239	226.1662	226.2545	5.513625	4.91999	5.745368	12
172	M298T5	298.3064	298.2472	298.3295	4.872331	4.829462	4.95576	6
173	M240T7	240.2505	240.2396	240.2574	7.433231	6.949325	8.014493	8
174	M212T5	212.1564	212.0792	212.1993	4.81497	4.597067	5.06108	15
175	M195T5	195.1478	195.089	195.2011	4.820496	4.496517	5.076653	22
176	M151T5	151.0715	151.0217	151.1328	4.618872	4.563142	4.922527	13
177	M255T7_1	255.2946	255.227	255.3441	7.372452	6.828473	8.515738	47
178	M290T6	290.332	290.2582	290.3571	5.629055	5.320175	6.215797	17
179	M175T5	175.1521	175.0599	175.2679	4.582457	4.545042	4.744037	13
180	M118T4	118.0675	118.0337	118.1517	4.460391	3.975738	4.576777	12
181	M329T6	329.3526	329.2387	329.4026	5.651147	5.166517	6.499023	13
182	M452T7	451.5617	451.5021	451.6147	6.74734	6.475758	7.432922	9
183	M170T5	170.055	170.0454	170.1646	5.494567	5.312513	6.251442	9

184	M389T5	389.4323	389.3688	389.5051	5.119243	4.711592	5.64562	18
185	M194T5	194.1305	194.0773	194.1728	4.879769	3.985343	5.816215	46
186	M283T5	283.2747	283.2573	283.3279	4.855122	4.665015	5.206798	9
187	M573T8	572.7379	572.6327	572.7564	8.047988	7.765975	8.287967	7
188	M355T8	355.2292	355.1718	355.269	8.383578	8.217482	8.74599	18
189	M265T6	265.2619	265.2378	265.2919	5.824332	5.48591	6.421703	13
190	M420T8	420.3601	420.3222	420.4266	8.404088	8.077573	8.547208	11
191	M415T6	415.3757	415.3375	415.5386	6.029583	4.716932	7.754625	69
192	M210T6	210.2465	210.237	210.2644	5.602781	4.935188	5.966517	8
193	M460T6	460.4621	460.3478	460.5523	6.008383	4.687955	7.102285	53
194	M214T5	214.0388	214.0067	214.1741	4.736208	4.494853	4.922248	12
195	M187T5	187.1374	187.0812	187.196	4.882978	4.487053	5.575695	48
196	M209T5	209.188	209.098	209.304	4.998899	3.922137	6.897212	64
197	M513T5	512.7247	512.6563	512.7331	5.253167	5.199528	5.78439	9
198	M144T5	144.0477	143.9489	144.1152	4.59545	4.479872	5.097193	25
199	M461T6	461.4652	461.35	461.5522	6.035273	5.462098	7.102285	25
200	M404T10_2	404.4417	404.4364	404.4485	10.0536	9.561152	10.55363	10
201	M160T5	160.0448	160.031	160.1436	4.897813	3.994998	5.416375	16
202	M475T6	475.4706	475.362	475.5465	5.723953	5.426943	6.281918	11
203	M306T6	306.3803	306.2188	306.4324	5.626352	4.981788	5.966517	7
204	M385T9	385.3663	385.3549	385.4282	8.808473	8.30787	9.355553	11
205	M284T5	284.3389	284.2731	284.3662	4.902873	4.626133	5.826607	19
206	M372T5	372.384	372.3624	372.437	4.609092	4.571563	4.831875	14
207	M215T5	215.1748	215.1396	215.2688	4.842089	4.298997	5.051045	10
208	M328T5	328.3826	328.312	328.4441	4.822493	4.636192	5.848925	12
209	M379T8	379.3869	379.3447	379.4502	8.220313	7.565443	9.349463	41
210	M404T10_1	404.3776	404.312	404.4338	9.57431	8.780678	10.77525	28
211	M264T5	264.2671	264.2537	264.274	4.720235	4.607517	4.96505	7
212	M378T8	378.353	378.2687	378.4206	8.13723	7.379988	9.03398	43
213	M503T7	503.4308	503.3626	503.4839	6.638138	6.178658	7.316297	18
214	M114T5	114.031	113.9646	114.1785	5.046988	4.420903	6.55469	61

215	M362T8	362.3892	362.3476	362.4384	8.231772	7.781733	9.35787	28
216	M353T6	353.2644	353.1886	353.3731	6.393686	6.054	7.258687	12
217	M196T6	195.9413	195.887	196.0527	6.389887	5.979288	7.20758	12
218	M384T5	384.475	384.377	384.5555	5.478747	5.17621	5.597997	11
219	M156T6	156.1225	156.1128	156.1296	5.873973	5.571797	5.99175	6
220	M111T6	111.0549	111.0427	111.122	5.742358	5.476708	6.267598	10
221	M271T5	271.2721	271.2128	271.3206	5.01235	4.63171	5.656568	20
222	M308T5	308.2241	308.1857	308.2746	4.73855	4.473382	4.755047	7
223	M273T6	273.2275	273.121	273.3001	5.888452	5.57893	6.221482	11
224	M224T5	224.022	223.8501	224.0541	5.154075	4.565117	6.679877	55
225	M105T25	104.9667	104.8762	105.0455	24.63055	23.9696	24.93992	15
226	M228T5	228.221	228.1191	228.2914	5.041906	4.512252	7.234532	68
227	M399T8	399.3723	399.3594	399.4397	7.94449	7.76532	8.270852	10
228	M355T7	355.4677	355.4437	355.5117	6.785228	6.675187	7.028888	9
229	M354T6	354.2663	354.256	354.2781	6.300807	6.062613	6.940233	7
230	M280T6	280.2175	280.1614	280.2848	5.610857	5.07418	6.015855	36
231	M259T6	259.247	259.2185	259.2655	5.660023	5.524598	6.038915	13
232	M127T6	126.9988	126.9693	127.0289	6.456532	6.020247	7.19737	9
233	M387T7	387.3564	387.3427	387.3744	6.972148	6.799232	7.797917	8
234	M565T5	564.6398	564.5613	564.6608	5.162512	4.815985	5.280285	9
235	M332T6	332.438	332.353	332.5483	5.55463	4.760728	6.370675	25
236	M259T10	259.234	259.172	259.2532	9.868698	9.35787	10.45108	19
237	M435T5	435.3585	435.3199	435.4422	5.44581	5.04333	6.084603	33
238	M105T5	104.9733	104.9417	105.0609	4.79096	4.548325	5.293372	15
239	M199T5	199.1487	199.0631	199.2472	4.863142	4.604983	5.247163	15
240	M140T5	139.9433	139.897	139.9651	5.291086	4.650345	7.20758	64
241	M103T39	102.9748	102.8854	103.0464	38.84832	38.35487	39.58609	13
242	M383T8	383.3468	383.2778	383.4302	8.143432	7.379988	9.35787	41
243	M102T5	101.9594	101.9356	102.0502	4.615892	3.929412	4.910857	14
244	M279T7_2	279.1445	279.1126	279.3053	6.517197	6.3692	6.780035	11
245	M124T5_1	124.0433	124.0338	124.0528	5.475711	5.287843	6.017035	6

246	M100T5	100.0637	99.96779	100.1629	4.949728	4.404047	5.198827	10
247	M155T5	155.0329	154.9533	155.1133	4.945187	4.109242	6.257265	60
248	M219T6	219.2452	219.2335	219.2743	6.259818	5.848925	6.689968	17
249	M272T5	272.2957	272.2031	272.3859	5.000985	4.41297	6.769828	65
250	M330T5	330.4589	330.3412	330.5579	5.276552	4.610405	6.738723	61
251	M158T5	158.1258	158.0591	158.2498	4.61727	3.814522	5.039612	22
252	M281T6	281.2461	281.2213	281.284	6.016673	5.456118	6.636765	20
253	M665T9	664.6787	664.6647	664.753	8.671957	8.196032	9.263683	13
254	M437T6	437.3727	437.337	437.491	6.127657	5.162562	7.754625	57
255	M384T8	384.3849	384.3452	384.4479	8.141454	7.565443	9.18486	36
256	M361T8	361.3551	361.2737	361.4278	8.165892	7.55931	9.237092	41
257	M365T6	365.2426	365.2244	365.2775	6.25881	5.995317	7.005225	9
258	M256T6	256.2565	256.2409	256.3412	5.969001	5.667265	6.753462	12
259	M420T10	420.3508	420.2641	420.426	9.745262	8.871817	11.33042	35
260	M380T8	380.377	380.3492	380.4697	8.137378	7.557453	9.34716	17
261	M577T9	576.6428	576.5682	576.7236	8.584213	8.198282	9.137933	16
262	M744T8	743.5694	743.4783	743.65	7.935583	7.55931	8.485632	22
263	M271T6	271.1649	271.0728	271.1802	6.000832	5.293717	6.60859	14
264	M259T8	259.2351	259.1521	259.2582	7.930364	7.379988	8.544132	38
265	M533T9	532.571	532.5509	532.6481	8.693738	8.206562	9.149787	12
266	M181T5	180.9381	180.8342	181.0528	5.216848	4.121085	7.012478	62
267	M185T8	185.0788	185.0436	185.1361	8.137378	7.55931	9.208072	37
268	M146T6	146.0686	145.9677	146.1044	5.551391	5.320175	6.355525	12
269	M88T5_2	87.99527	87.95979	88.063	5.489118	5.318035	5.601543	8
270	M273T7	273.179	273.1183	273.307	6.641673	6.292673	7.490648	14
271	M119T5	118.969	118.9469	119.0419	4.836427	4.013382	5.561873	11
272	M504T7	504.4521	504.4322	504.4624	6.779329	6.45922	7.063242	6
273	M329T10	329.2594	329.1856	329.2782	9.68801	8.883788	11.34222	27
274	M278T5	278.2761	278.211	278.4009	4.808074	4.620492	5.340865	28
275	M383T7	383.3439	383.2842	383.3539	7.051996	6.632302	7.211247	12
276	M709T9	708.7437	708.673	708.7995	8.643965	8.195282	9.24475	14

277	M279T6	279.1926	279.0923	279.2609	5.62136	4.762678	6.248753	48
278	M448T6	447.5505	447.4427	447.6552	5.777576	5.408868	6.454222	8
279	M375T5	374.5352	374.4553	374.5653	5.225307	4.624082	6.758938	38
280	M243T5	243.2403	243.1851	243.3583	4.95588	4.571563	6.717672	61
281	M621T9	620.6581	620.5957	620.7746	8.648293	8.198282	9.277915	13
282	M105T26	104.9312	104.876	104.9769	25.51545	25.22015	26.02356	13
283	M753T9	752.7597	752.7352	752.8523	8.662337	8.17681	9.233933	11
284	M173T6	173.0707	172.9439	173.1295	5.51022	5.312513	5.886313	9
285	M279T7_1	279.2346	279.0966	279.3036	7.152774	6.871842	7.518357	18
286	M165T5	165.0503	164.9516	165.1328	4.74451	4.470387	5.306073	21
287	M297T6	297.3413	297.2508	297.3643	5.606466	5.389577	5.93751	12
288	M448T10	448.4616	448.3934	448.5434	10.07723	9.40822	10.7569	13
289	M407T8	407.4525	407.3832	407.5258	7.993823	6.874367	9.35787	41
290	M406T8	406.4522	406.3628	406.5378	8.128526	7.370527	9.365162	44
291	M304T5	304.4022	304.3281	304.4565	5.150543	3.94781	6.483412	50
292	M233T6	233.1717	233.1307	233.2431	5.655197	5.417558	5.979752	8
293	M159T5	159.0735	158.9445	159.1317	4.527725	3.057935	4.9321	25
294	M242T5	242.2263	242.1127	242.2703	4.959802	4.489308	6.030728	50
295	M384T7	384.3632	384.324	384.4114	7.149315	6.632302	7.467075	15
296	M143T5	142.9448	142.8177	143.0298	4.774122	4.47596	5.41015	31
297	M501T7	500.568	500.4794	500.6402	6.527504	5.997102	7.047365	14
298	M387T5	387.3671	387.3469	387.5116	5.281855	5.133592	5.703458	18
299	M309T5	309.2598	309.195	309.3687	4.994132	4.514453	6.407647	51
300	M150T6	150.0447	150.0072	150.0755	5.501943	5.364565	5.780388	10
301	M241T5	241.2309	241.1364	241.2566	4.991993	4.543827	6.225378	61
302	M249T5	249.2296	249.0976	249.3052	5.069749	4.618872	6.753462	60
303	M279T8	279.2579	279.1397	279.2859	8.151089	7.6323	9.414298	30
304	M269T6	269.2736	269.1457	269.2808	5.891531	5.763825	6.178635	6
305	M87T5	87.04444	86.94773	87.11876	4.937164	4.38929	5.9054	30
306	M166T6	166.0692	166.052	166.0835	5.578662	5.402183	5.946	10
307	M259T7	259.223	259.1248	259.2573	7.006599	6.28361	7.22236	18

308	M363T6	363.4557	363.4366	363.5776	5.667163	5.271137	6.759375	16
309	M385T7	385.3705	385.3585	385.4628	7.03265	6.625083	7.42183	11
310	M274T5	274.3445	274.2299	274.4143	4.886673	3.694202	6.759375	70
311	M269T5	269.257	269.1977	269.3185	4.837958	4.568637	5.470238	23
312	M745T7	744.5654	744.4746	744.6621	7.069075	6.632302	7.382305	11
313	M268T5	268.2406	268.1213	268.279	4.866782	4.534728	5.263162	27
314	M90T4	89.98106	89.93311	90.05494	3.672078	3.452963	3.84648	10
315	M744T7	743.5469	743.4645	743.6116	7.149315	6.632302	7.467075	15
316	M136T5	136.0728	136.0132	136.1309	4.833405	4.528235	5.69791	35
317	M391T5	391.3636	391.3539	391.448	5.466252	5.159352	5.680545	9
318	M230T5	230.2741	230.2202	230.337	4.878348	3.708623	6.181288	64
319	M70T5	70.26607	70.18392	70.37566	4.585253	3.637205	4.696098	30
320	M168T5	168.0326	167.9553	168.1103	5.302423	4.648085	6.677562	65
321	M346T5	346.4617	346.3345	346.5588	5.228157	4.548605	6.343247	42
322	M310T5	310.2738	310.2294	310.3458	4.918743	4.630575	5.76445	21
323	M300T5	300.3557	300.2833	300.4228	4.901567	4.536012	6.17901	50
324	M149T5	149.0866	149.0561	149.1404	4.752138	4.426958	5.08235	25
325	M261T3	261.1536	261.1129	261.2276	3.451061	3.381335	3.601138	16
326	M355T5	355.2696	355.2425	355.3793	5.139967	4.888225	5.463988	27
327	M245T5	245.2425	245.1004	245.258	4.887887	4.597067	5.373245	23
328	M406T6	406.4855	406.4605	406.5404	5.582498	5.35197	6.122972	9
329	M318T5	318.421	318.3172	318.503	4.879078	3.766963	6.142183	68
330	M362T5	362.4546	362.3381	362.5408	4.8569	3.808715	6.220325	59
331	M258T5	258.3242	258.2516	258.3995	4.943578	4.564758	7.032885	54
332	M275T5	275.3404	275.2624	275.407	4.879197	3.895902	6.00717	53
333	M319T5	319.4282	319.3143	319.459	4.861863	3.760945	6.144503	49
334	M157T5	157.0629	156.972	157.1355	4.644663	3.791175	5.024163	32
335	M340T5	340.4178	340.3283	340.4631	4.983783	4.05034	6.74317	61
336	M180T5	180.1089	180.0466	180.1586	4.801418	4.504365	5.772545	34
337	M286T5	286.3582	286.2198	286.4336	5.06582	4.600172	5.923632	36
338	M116T4	116.028	115.9661	116.0476	4.451567	3.781553	4.645288	11

339	M477T3	477.3555	477.284	477.4262	3.45844	3.422433	4.00606	19
340	M225T5	225.22	225.076	225.2736	4.967244	4.584443	5.385685	40
341	M361T7	361.3473	361.2736	361.3599	7.154875	6.641883	7.476693	16
342	M255T5	255.2469	255.2051	255.4091	5.330778	4.630575	6.017035	34
343	M378T7	378.3466	378.2763	378.3965	7.07633	6.644183	7.237908	13
344	M478T3	478.3972	478.3304	478.471	3.454278	3.421262	3.736215	20
345	M362T7	362.3718	362.306	362.4329	7.056781	6.634605	7.235597	12
346	M185T7	185.0724	185.0551	185.0954	7.159033	6.644183	7.474392	15
347	M379T7	379.366	379.329	379.4061	7.156033	6.644183	7.484	16
348	M184T5	184.0849	184.0628	184.1326	5.27846	4.635747	7.20758	64
349	M239T3	239.1385	239.0578	239.1741	3.481778	3.433178	4.014758	35
350	M354T5	354.2597	354.1945	354.4242	5.150358	4.829887	5.61681	36
351	M559T6	558.6428	558.5846	558.6655	5.519207	5.115992	5.606415	9
352	M501T5	500.5765	500.5425	500.6465	5.446273	4.95971	5.8206	23
353	M256T5	256.2599	256.2145	256.3263	4.855108	4.613167	5.566637	37
354	M302T5	302.4176	302.3474	302.4954	4.937109	4.528235	6.340997	58

Supplementary Table 4. Identification of metabolic pathways associated by Thymoquinone treatment in (A) HL-60 and (B) Jurkat.

A. HL-60

Pathway Name	Hits	FDR	Impact
Linoleic acid metabolism	8	1	0.88541
Phenylalanine metabolism	18	1	0.41824
D-Arginine and D-ornithine metabolism	4	1	0.5
Arachidonic acid metabolism	21	1	0.27959
Arginine and proline metabolism	24	1	0.51252
Glycine, serine and threonine metabolism	13	1	0.29809
Valine, leucine and isoleucine biosynthesis	7	1	0.26921
Tyrosine metabolism	20	1	0.24942
beta-Alanine metabolism	7	1	0.12579
Sulfur metabolism	4	1	0.26693
Phenylalanine, tyrosine and tryptophan biosynthesis	6	1	0.0818
Pantothenate and CoA biosynthesis	6	1	0.30985
Biotin metabolism	2	1	0.19512
Caffeine metabolism	4	1	0.18429
Nitrogen metabolism	8	1	0.00763
Vitamin B6 metabolism	6	1	0.31289
Alanine, aspartate and glutamate metabolism	4	1	0.05128
Citrate cycle (TCA cycle)	3	1	0.18952
D-Glutamine and D-glutamate metabolism	1	1	0
Cysteine and methionine metabolism	10	1	0.33174
Primary bile acid biosynthesis	8	1	0.2378
Tryptophan metabolism	15	1	0.33769
Pentose and glucuronate interconversions	9	1	0.31882
Glycerophospholipid metabolism	6	1	0.30632
Thiamine metabolism	3	1	0.12481

Nicotinate and nicotinamide metabolism	7	1	0.19348
Ubiquinone and other terpenoid-quinone biosynthesis	5	1	0.16161
Taurine and hypotaurine metabolism	2	1	0
Glycosylphosphatidylinositol (GPI)-anchor biosynthesis	1	1	0.0439
Lysine biosynthesis	4	1	0.10418
Histidine metabolism	6	1	0.2664
Glyoxylate and dicarboxylate metabolism	7	1	0.19124
Valine, leucine and isoleucine degradation	5	1	0.03378
Cyanoamino acid metabolism	1	1	0
Galactose metabolism	5	1	0.11505
Lysine degradation	6	1	0.17953
Fructose and mannose metabolism	6	1	0.13693
Pyruvate metabolism	3	1	0
Pentose phosphate pathway	3	1	0.04289
Pyrimidine metabolism	8	1	0.13121
Ascorbate and aldarate metabolism	5	1	0.13739
Butanoate metabolism	4	1	0.09111
Propanoate metabolism	3	1	0.00164
Riboflavin metabolism	1	1	0
alpha-Linolenic acid metabolism	2	1	0.20335
Aminoacyl-tRNA biosynthesis	10	1	0
Ether lipid metabolism	1	1	0.03523
Glycolysis or Gluconeogenesis	2	1	0
Glutathione metabolism	3	1	0.0019
Glycerolipid metabolism	2	1	0.00714
Inositol phosphate metabolism	3	1	0.01203
Limonene and pinene degradation	6	1	0.14323
Fatty acid elongation in mitochondria	1	1	0
Fatty acid biosynthesis	3	1	0
Starch and sucrose metabolism	3	1	0.01265

Fatty acid metabolism	3	1	0.04482
Drug metabolism - other enzymes	1	1	0.05863
Folate biosynthesis	1	1	0.03372
Purine metabolism	6	1	0.03726
Steroid hormone biosynthesis	7	1	0.04156
Amino sugar and nucleotide sugar metabolism	5	1	0.00272
Metabolism of xenobiotics by cytochrome P450	1	1	0
Drug metabolism - cytochrome P450	2	1	0.01613
Porphyrin and chlorophyll metabolism	4	1	0.021

B. Jurkat

Pathway Name	Hits	FDR	Impact
Arachidonic acid metabolism	14	0.1495	0.27078
Tyrosine metabolism	15	0.20894	0.14394
Vitamin B6 metabolism	5	1	0.23812
Alanine, aspartate and glutamate metabolism	3	1	0.08547
Synthesis and degradation of ketone bodies	1	1	0.7
Taurine and hypotaurine metabolism	2	1	0.07014
Caffeine metabolism	2	1	0
Riboflavin metabolism	2	1	0.10178
Histidine metabolism	4	1	0.19919
Steroid hormone biosynthesis	9	1	0.09715
Propanoate metabolism	3	1	0.09079
Primary bile acid biosynthesis	4	1	0.12731
Glyoxylate and dicarboxylate metabolism	4	1	0.17092
Phenylalanine, tyrosine and tryptophan biosynthesis	2	1	0.00062
Valine, leucine and isoleucine biosynthesis	2	1	0.11871
Butanoate metabolism	3	1	0.09938
beta-Alanine metabolism	2	1	0.01119
Cysteine and methionine metabolism	4	1	0.0673

Fatty acid biosynthesis	3	1	0
Citrate cycle (TCA cycle)	1	1	0.04361
Fatty acid metabolism	3	1	0.04482
Ubiquinone and other terpenoid-quinone biosynthesis	2	1	0.11172
Nitrogen metabolism	2	1	0
Ether lipid metabolism	1	1	0.03523
Valine, leucine and isoleucine degradation	2	1	0.03938
Sphingolipid metabolism	1	1	0.29423
Fatty acid elongation in mitochondria	1	1	0
Pantothenate and CoA biosynthesis	1	1	0.05124
Lysine degradation	2	1	0.03404
Glycine, serine and threonine metabolism	2	1	0.0037
Tryptophan metabolism	4	1	0.08393
Pentose phosphate pathway	1	1	0
Pyruvate metabolism	1	1	0
Lysine biosynthesis	1	1	0.0423
Aminoacyl-tRNA biosynthesis	3	1	0
Glycerophospholipid metabolism	1	1	0.04571
Arginine and proline metabolism	3	1	0.03701
Nicotinate and nicotinamide metabolism	1	1	0.10565
Ascorbate and aldarate metabolism	1	1	5.00E-04
Phenylalanine metabolism	1	1	0.11906
Pyrimidine metabolism	1	1	0
Purine metabolism	2	1	0.02202
Porphyrin and chlorophyll metabolism	1	1	0.00331