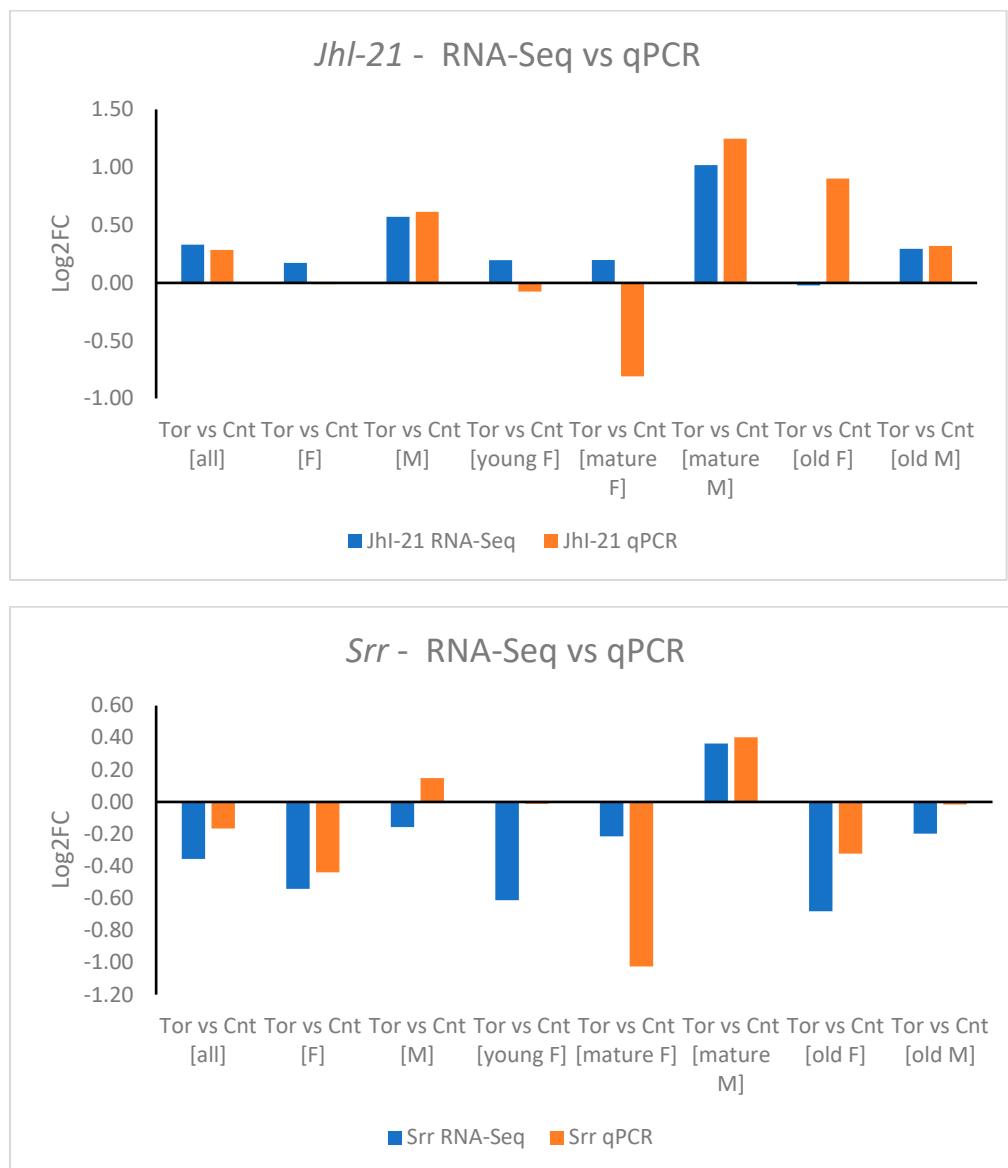
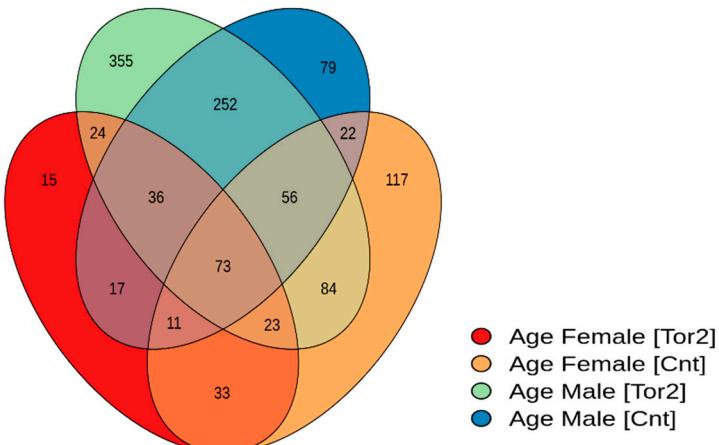


Supplementary Figure S1. qPCR evaluation of gene expression changes under the chronic administration of Torin-2. *eIF4A* is taken as the reference gene





Supplementary Figure S2. Venn diagram, which shows an overlap of the lists of genes whose expression changes significantly with age ($p < 0.05$) in control and Torin-treated flies of different genders.

Supplementary Table S1. Lifespan effects of Torin-2 treatment taken with various concentrations

	Media n (days)	delta- Medi an (%)	Fisher's exact test		90 th percen tile (days)	delta 90 th percen tile (%)	Fisher's exact test		Wang-Allison test		N, flies
			p	FDR			p	FDR	p	FDR	
Males											
Control	46		n/a	n/a	55		n/a	n/a	n/a	n/a	442
0.5 µM	48	4	p<0.00 01	p<0.00 01	57	3.6	p>0.05	p>0.05	p>0.05	p>0.05	490
1 µM	48	4	p<0.00 01	p<0.00 01	57	3.6	p<0.05	p>0.05	p>0.05	p>0.05	484
5 µM	46	0	p>0.05	p>0.05	55	0	p>0.05	p>0.05	p>0.05	p>0.05	460
10 µM	46	0	p>0.05	p>0.05	56	1.8	p>0.05	p>0.05	p>0.05	p>0.05	507
Females											
Control	55	n/a	n/a	n/a	63	n/a	n/a	n/a	n/a	n/a	470
0.5 µM	55	0	p>0.05	p>0.05	64	1.6	p>0.05	p>0.05	p<0.05	p>0.05	495
1 µM	55	0	p>0.05	p>0.05	63	0	p>0.05	p>0.05	p>0.05	p>0.05	480
5 µM	54	-2	p>0.05	p>0.05	61	-3	p<0.05	p<0.05	p>0.05	p>0.05	494
10 µM	54	-2	p>0.05	p>0.05	63	0	p>0.05	p>0.05	p>0.05	p>0.05	474

Supplementary Table S2. Differential gene expression data on pooled comparison of Torin-2-treated versus Control groups. p-values were not FDR-adjusted. LogFC is taken as “minimal” across 3 methods of 3'-bias adjustment, p-value is taken as “maximal”.

Symbol	Log ₂ FC	p (QLF test)	Symbol	Log ₂ FC	p (QLF test)
<i>cort</i>	2,03	0,0007	<i>Rassf</i>	0,2	0,02
<i>Or42b</i>	1,07	0,04	<i>Sirt2</i>	-0,16	0,05
<i>Or1a</i>	0,9	0,04	<i>Mondo</i>	-0,16	0,03
<i>CG11529</i>	0,67	0,007	<i>CG8858</i>	-0,17	0,03
<i>E23</i>	0,54	0,003	<i>CG8405</i>	-0,17	0,04
<i>bip1</i>	0,53	0,01	<i>hook</i>	-0,17	0,02
<i>Prat</i>	0,52	0,03	<i>CG11873</i>	-0,19	0,03
<i>CG5290</i>	0,5	0,01	<i>mRpS29</i>	-0,21	0,05
<i>CG10466</i>	0,44	0,01	<i>CG12531</i>	-0,22	0,03
<i>Stip1</i>	0,43	0,004	<i>Atx2</i>	-0,24	0,02
<i>CG17816</i>	0,4	0,01	<i>dbr</i>	-0,25	0,02
<i>CG5380</i>	0,38	0,02	<i>CG7997</i>	-0,26	0,04
<i>Bdp1</i>	0,38	0,006	<i>CG34354</i>	-0,26	0,04
<i>Rfc4</i>	0,38	0,02	<i>Golgin104</i>	-0,28	0,03
<i>SmD3</i>	0,37	0,03	<i>CG10731</i>	-0,28	0,04
<i>CG15270</i>	0,37	0,04	<i>tn</i>	-0,29	0,02
<i>BCL7-like</i>	0,35	0,03	<i>CG7470</i>	-0,32	0,008
<i>arx</i>	0,33	0,04	<i>HERC2</i>	-0,35	0,006
<i>GstE1</i>	0,33	0,02	<i>Srr</i>	-0,35	0,01
<i>CG16908</i>	0,32	0,03	<i>eya</i>	-0,36	0,02
<i>CG17378</i>	0,32	0,02	<i>AMPKalpha</i>	-0,36	0,01
<i>Sema2a</i>	0,31	0,01	<i>CG32085</i>	-0,38	0,008
<i>CG9667</i>	0,29	0,04	<i>Ugt36E1</i>	-0,41	0,02
<i>mbfl</i>	0,25	0,02	<i>CG13896</i>	-0,45	0,05
<i>Lsm10</i>	-0,5	0,02			

Supplementary Table S3. Differential gene expression data summary on various comparisons, only MAPK pathway (GO:0000165). m1, m2, m3 – various methods of 3'-bias adjustment, m4 – not adjusted.

Gene ID	Symbol	Name	LogFC:				LogFC:				LogFC:				LogFC:				LogFC:				LogFC:			
			Tor2 vs Cnt [Young, females]				Tor2 vs Cnt [Adult, females]				Tor2 vs Cnt [Old, females]				Tor2 vs Cnt [Young, males]				Tor2 vs Cnt [Adult, males]				Tor2 vs Cnt [Old, males]			
			m1:3 t-sl	m2:bi ns-sl	m3 :sl	m4:n one	m1:3 t-sl	m2:bi ns-sl	m3 :sl	m4:n one	m1:3 t-sl	m2:bi ns-sl	m3 :sl	m4:n one	m1:3 t-sl	m2:bi ns-sl	m3 :sl	m4:n one	m1:3 t-sl	m2:bi ns-sl	m3 :sl	m4:n one	m1:3 t-sl	m2:bi ns-sl	m3 :sl	m4:n one
FBgn0016756	Usp47	Ubiquitin specific protease 47	-0.50	-0.30	0.2 6	-0.16	-0.36	-0.49	0.5 3	-0.60	-0.44	-0.35	0	-0.20	0.48	0.34	5	0.40	-0.17	0.17	0.0 4	0.14	0.13	0.27	0.3 3	0.38
FBgn0001291	Jra	Jun-related antigen	-0.37	-0.10	4	-0.18	0.62	0.56	0.5 7	0.57	-0.51	-0.32	7	-0.39	0.30	0.38	6	0.36	0.65	0.54	0.7 0	0.68	0.18	0.09	8 8	0.05
FBgn0000711	flw	flapwing	0.94	0.34	2	0.34	-1.58	-0.28	0.2 5	-0.28	1.19	0.25	1	0.25	-0.42	-0.17	6	-0.14	-0.19	-0.51	0 0	-0.37	0.27	0.01	8 8	0.13
FBgn0064493	rdx	roadkill	0.20	0.43	0.4 4	0.49	0.80	0.57	0.5 4	0.50	0.63	0.47	1	0.56	0.23	0.02	4	0.06	-0.52	-0.65	2 -	-0.57	-0.02	-0.02	6 6	0.14
FBgn0014388	sty	sprouty	1.43	0.42	0.5 7	0.63	0.73	-0.27	0.2 2	-0.37	0.28	0.14	5	0.31	0.46	0.32	5	0.38	-0.58	-0.46	6 -	-0.49	0.94	0.23	5 5	0.35
FBgn0020767	Spred	Sprouty-related protein with EVH-1 domain	0.95	0.58	0.5 9	0.63	-0.57	-0.32	0.4 4	-0.38	0.53	0.16	8	0.23	-0.07	-0.02	1	0.03	-0.31	-0.50	5 -	-0.41	0.22	0.29	3 8	0.46
FBgn0024811	Crk	Crk oncogene	0.47	0.50	0.4 6	0.39	0.02	-0.33	0.2 3	-0.21	0.25	0.41	9	0.34	-0.20	-0.04	7	-0.09	-0.30	-0.39	9 -	-0.44	0.21	0.25	9 9	0.11
FBgn0003371	sgg	shaggy	0.54	0.53	0.5 6	0.61	-0.45	-0.29	0 0	-0.35	0.16	0.27	9	0.35	0.01	0.00	2	0.05	-0.47	-0.47	3 -	-0.38	-0.07	0.13	0 0	0.29
FBgn0015286	Rala	Ras-like protein A	0.04	0.37	0.3 7	0.38	0.41	0.34	0.3 7	0.34	0.08	0.08	7	0.09	-0.64	-0.30	9	-0.27	-0.56	-0.70	7 -	-0.55	-0.07	-0.19	9 9	-0.06
FBgn0003209	raw	raw	0.61	0.41	0.4 9	0.55	-0.23	-0.43	0.4 7	-0.52	0.07	-0.06	4	0.11	0.28	0.13	7	0.20	0.36	0.84	5 -	0.81	0.55	0.35	6 6	0.46
FBgn0032682	grnd	grindelwald	0.27	0.73	0.7 2	0.70	-0.22	-0.39	0.2 6	-0.27	0.26	0.45	0.3 6	0.36	0.33	0.19	8	0.19	-0.40	-0.51	1 -	-0.31	-0.03	-0.03	1 1	0.01
FBgn0003256	rl	rolled	1.61	0.89	0.8 8	0.90	0.13	-0.22	0.8 -	-0.21	0.53	0.36	2 2	0.35	-0.31	-0.48	7	-0.45	0.13	-0.30	7 -	-0.15	0.32	0.04	2 2	0.16
FBgn00086779	step	steppke	1.05	0.22	0.2 8	0.32	-1.28	-0.02	0.6 6	-0.10	0.81	0.31	4	0.39	-0.59	-0.20	8	-0.16	-0.24	-0.38	4 -	-0.30	0.40	-0.03	6 6	0.14
FBgn0036934	sNPFR	short neuropeptide F receptor	0.44	0.54	0.6 9	0.76	1.44	0.34	0.2 5	0.20	1.88	1.11	2	1.29	-0.27	1	0.34	-0.50	0.5	8	-0.52	-	0.47	0.4	8 8	0.59
FBgn0014006	Ask1	Apoptotic signal-regulating kinase 1	-0.29	-0.24	0 0	-0.11	0.65	0.40	0.5 5	0.28	-0.45	-0.41	6	-0.26	-0.18	-0.13	2	-0.08	-0.05	0.11	1 -	0.08	-0.17	-0.26	8 8	-0.14
FBgn0038331	Ccm3	Cerebral cavernous malformation 3	0.88	0.35	0.3 1	0.27	-0.42	-0.08	2 -	-0.02	0.44	0.26	0	0.19	-0.16	-0.24	7	-0.27	-0.31	-0.53	4 -	-0.36	0.29	0.11	0 0	0.08
FBgn0000173	ben	bendless	0.13	0.26	0.2 5	0.22	-0.07	-0.33	0.1 9	-0.19	-0.10	0.12	6	0.05	-0.25	-0.15	5	-0.15	-0.47	-0.79	9 -	-0.61	-0.11	-0.16	0 0	-0.12
FBgn0020224	Cbl	Cbl proto-oncogene	0.54	-0.10	1 1	0.06	-0.88	-0.28	0.4 4	-0.40	0.72	0.02	1	0.18	0.01	0.23	5	0.29	-0.20	-0.32	1 -	-0.34	0.38	0.15	7 7	0.27
FBgn0033153	Gadd45	Growth arrest and DNA damage-inducible 45	0.03	0.61	0.5 4	0.51	-1.62	1	-1.61	-	-0.27	-0.18	2	-0.24	0.62	0.51	6	0.46	0.64	0.52	9 -	0.66	0.27	0.28	8 8	0.25
FBgn0005672	spi	spitz	0.49	0.30	0.2 5	0.22	0.25	0.40	5 5	0.44	0.06	0.11	5	0.04	0.25	0.20	8	0.17	0.51	0.27	4 -	0.42	-0.01	0.01	0 0	-0.02

FBgn00	37655	Kcmf1	Potassium channel modulatory factor 1	-0.55	-0.44	0.49	-0.47	0.06	-0.04	0.06	-0.08	0.05	0.10	0.06	0.09	0.21	0.20	0.21	0.23	0.08	-0.08	0.02	0.05
FBgn00	30613	Rab3-GEF	Rab3 GDP-GTP exchange factor	-0.33	-0.29	0.32	-0.17	-0.43	-0.29	0.31	-0.41	-0.28	-0.16	0.14	0.00	0.06	0.13	0.14	0.20	-0.08	-0.11	0.26	-0.13
FBgn00	10303	hep	hemipterus	0.28	-0.05	0.1	0.10	-0.40	-0.55	0.61	-0.68	0.50	0.22	0.29	0.38	-0.49	-0.23	0.22	-0.18	0.42	0.31	0.20	0.29
FBgn00	34894	sigmar	salivary glands marred	1.01	0.06	0.3	0.02	-0.47	-0.27	0.4	-0.15	0.38	0.47	0.0	0.41	0.37	0.01	0.1	0.01	-0.27	-0.40	1	-0.22
FBgn00	40206	krz	kurtz	1.78	0.38	0.50	0.55	-0.93	0.03	0.4	-0.09	0.45	0.06	0.14	0.21	0.44	-0.04	0.02	0.00	-0.01	0.10	0.2	0.07
FBgn00	35538	DopEcR	Dopamine/Ecdysteroid receptor	0.16	0.25	0.4	0.30	-0.04	0.11	0	0.05	-0.05	0.08	0.0	0.16	-0.27	-0.13	0.1	-0.09	0.12	-0.01	0.2	0.07
FBgn02	64922	smt3	smt3	0.17	0.28	0.23	0.12	-0.08	-0.02	0.4	-0.10	0.06	0.14	0.16	0.07	0.02	0.06	0.05	0.01	-0.58	-0.32	0.3	-0.72
FBgn00	32840	sNPF	short neuropeptide F precursor	0.29	0.20	0.18	0.19	-0.62	-0.12	0.5	-0.18	0.98	0.29	0.26	0.28	0.27	0.01	0.2	0.03	-0.13	-0.06	0.6	0.09
FBgn00	40505	Alk	Anaplastic lymphoma kinase	-0.16	0.00	0	0.15	0.38	-0.15	0.8	-0.28	-0.01	0.12	0.3	0.28	0.07	0.02	0	0.07	-0.71	-0.63	0.9	-0.64
FBgn00	34199	Gbp1	Growth-blocking peptide 1	0.01	-0.17	0.4	-0.31	-0.20	0.06	0.2	-0.05	-0.02	-0.07	0.0	-0.14	-0.02	-0.06	0.5	-0.11	-0.41	-0.24	0.1	-0.65
FBgn00	26319	Traf4	TNF-receptor-associated factor 4	0.30	0	0.30	-	-	0.53	0.6	-0.59	0.84	0.48	0.5	0.48	-	0.86	0.7	0.88	0.84	0.02	0.9	0.12
FBgn00	11706	rpr	reaper	-0.40	0.04	0.6	-0.15	0.14	0.16	1	0.24	0.05	0.28	0	0.23	0.66	0.69	0.72	0.70	-0.57	-0.65	0.9	-0.87
FBgn02	59212	cno	canoe	0.53	0.14	0.17	0.31	-0.10	0.15	0	0.01	0.25	0.07	0.9	0.22	-0.46	-0.10	1	-0.05	0.00	-0.08	0.3	-0.10
FBgn00	24329	Mekk1	Mekk1	-0.64	-0.41	0.9	-0.28	0.34	0.04	1	-0.08	-0.02	-0.21	0.7	-0.06	0.00	-0.16	0.4	-0.10	0.27	0.70	0.8	0.67
FBgn00	00370	crc	cryptocephal	-	0.48	0.9	0.49	-	-0.18	0.4	-0.16	-	-0.19	0.2	-0.20	-	-0.30	0.8	-0.27	-	-0.45	1	-0.30
FBgn02	61524	lic	licorne	0.05	0.16	0.13	0.13	0.36	0.34	0.1	0.39	0.01	-0.09	0.4	-0.13	0.08	-0.05	0.6	-0.05	0.30	0.40	0.8	0.58
FBgn00	00229	bsk	basket	-0.08	0.04	0.1	-0.04	0.17	0.02	0	0.09	0.05	0.11	0.4	0.03	-0.30	-0.20	0.2	-0.23	-0.40	-0.62	0.4	-0.45
FBgn00	04569	aos	argos	0.65	0.17	1	0.24	-0.33	0.12	0.8	0.05	-0.21	-0.12	0	-0.05	0.41	0.34	0.4	0.36	-0.32	-0.03	1	0.05
FBgn02	86070	cnk	connector enhancer of ksr	-0.48	-0.39	0.5	-0.24	1.18	0.27	0.2	0.15	0.03	-0.14	0.9	0.02	0.18	0.19	0.1	0.25	-0.75	0.22	0.9	0.19
FBgn00	11573	Cdc37	Cdc37	-0.05	0.18	0.1	0.08	0.36	0.35	0.3	0.33	-0.31	-0.15	0.1	-0.22	0.10	0.11	0.9	0.09	1.11	0.93	1.0	0.08
FBgn00	10333	Rac1	Rac1	0.49	0.17	0.5	0.13	-0.38	-0.15	0.9	-0.10	-0.19	-0.03	0.8	-0.09	-0.19	0.07	0.7	0.07	-0.20	0.14	0.2	0.31
FBgn00	16641	PTP-ER	Protein tyrosine phosphatase-ERK/Enhancer of Ras1	-0.23	-0.32	0.7	-0.17	-0.16	-0.32	0.6	-0.43	-0.01	-0.13	0.7	0.03	-0.13	-0.05	0.4	0.00	-0.45	-0.17	0.8	-0.19
FBgn00	31030	Tao	Tao	-0.48	0.00	0	0.04	0.63	0.42	0.9	0.35	0.03	0.16	0.9	0.24	-0.14	-0.02	0.2	0.01	-0.24	-0.16	0.3	-0.08
FBgn00	34577	cpa	capping protein alpha	0.54	-0.03	0.6	-0.07	0.08	0.27	0.3	0.32	-0.08	0.06	0	0.00	-0.23	0.06	0.5	0.06	0.18	0.45	0.2	0.62
FBgn00	10341	Cdc42	Cdc42	-0.16	-0.05	0.7	-0.08	0.45	0.19	0.1	0.30	-0.20	-0.12	0.6	-0.16	-0.17	-0.06	0.6	-0.06	-0.03	-0.16	0.1	0.01

