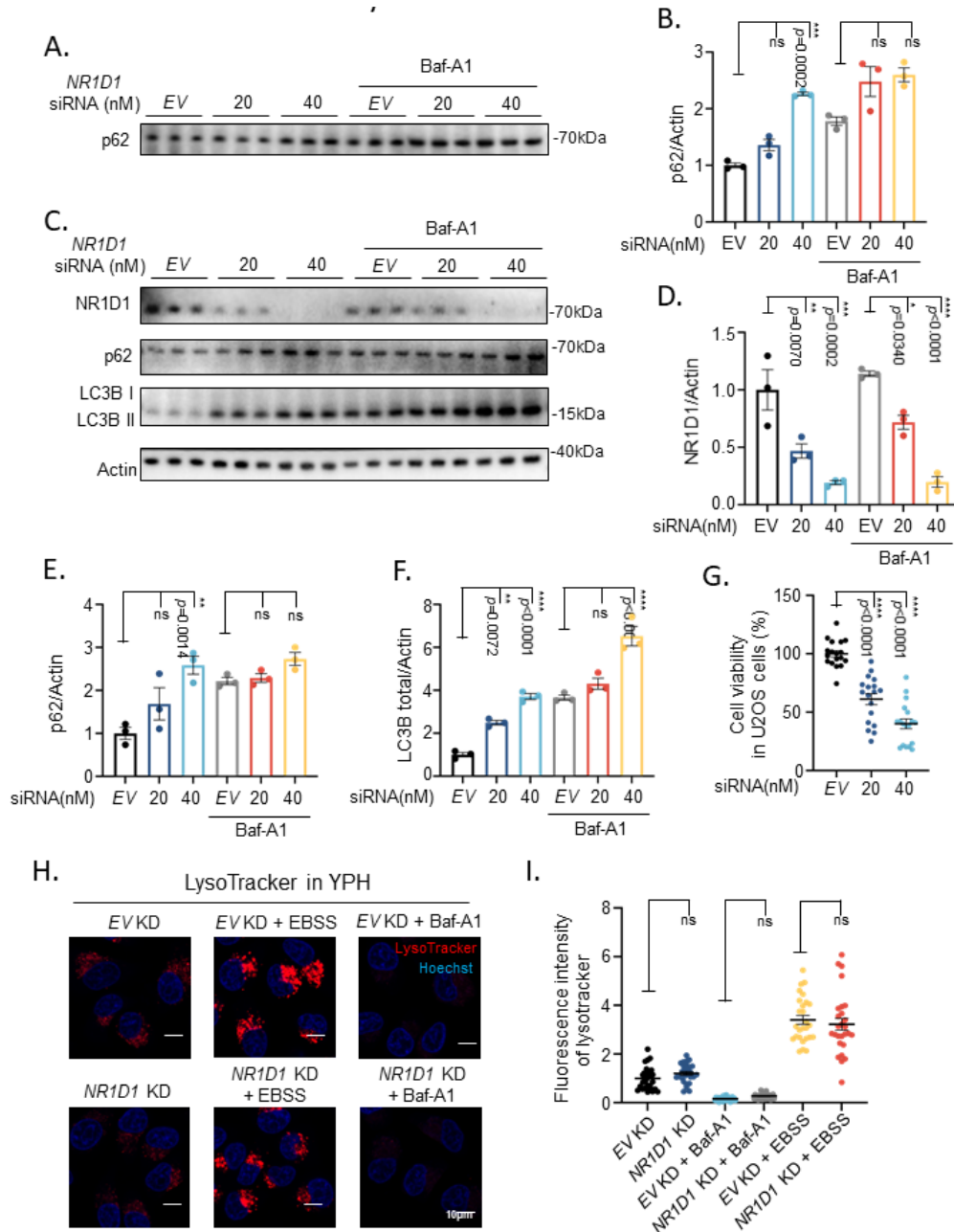


SUPPLEMENTARY DATA

NR1D1 Inhibition Enhances Autophagy and Mitophagy in Alzheimer's Disease Models

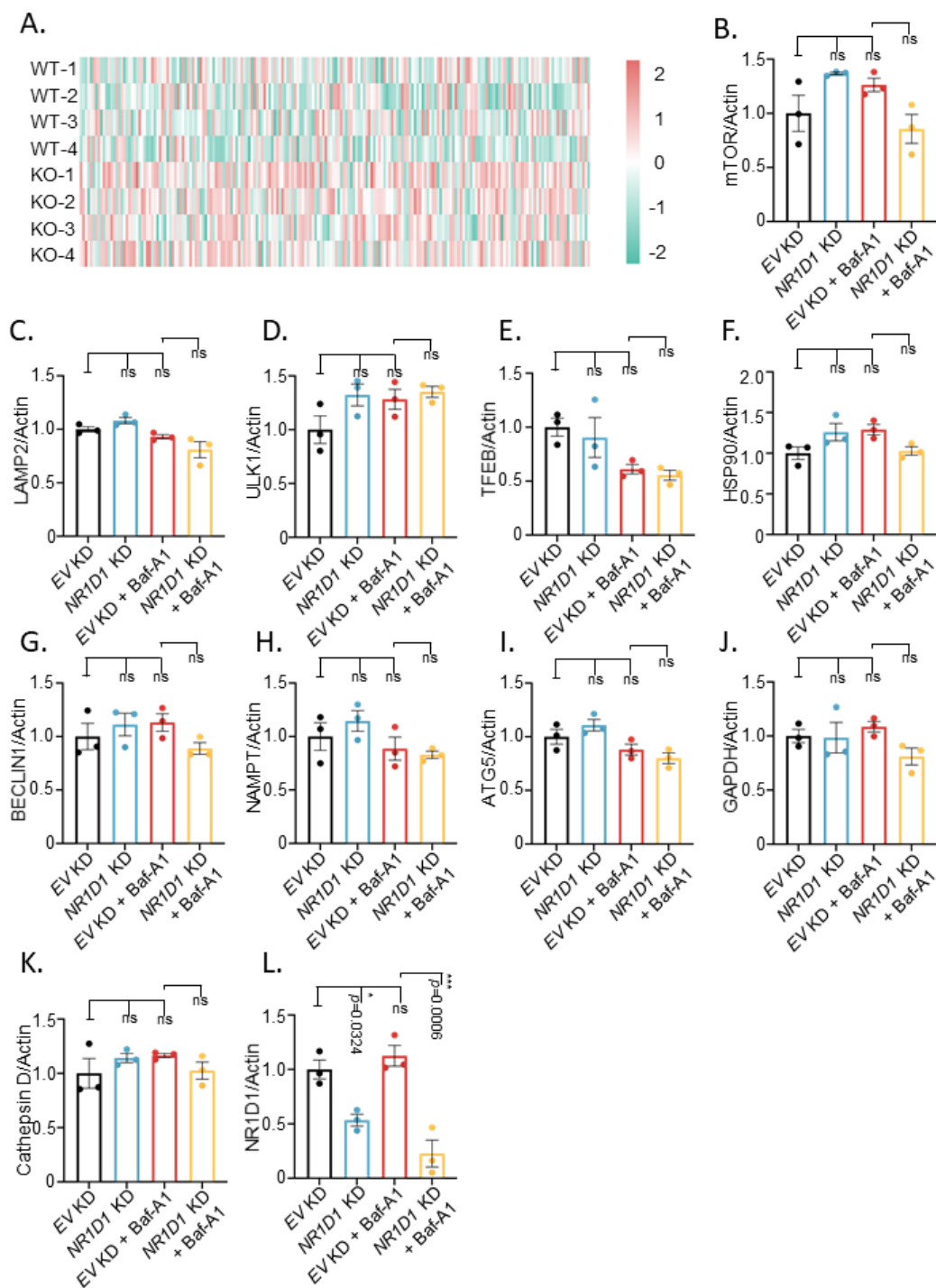
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SUPPLEMENTARY DATA



Supplementary Figure 1. Effects of NR1D1 Knockdown on Autophagic related Markers and Cell Viability. (A) Western blot detection was performed to detect p62 protein levels in HeLa cells treated with EV or NR1D1 siRNA (20 nM and 40 nM), with or without Baf-A1 treatment. Data represent results pooled from three biological replicates (n=3). (B) Quantification of p62 expression levels after NR1D1 knockdown. (C) Western blot detection of NR1D1, p62, LC3B, and Actin protein levels in U2OS cells treated with EV or NR1D1 siRNA (20nM and 40nM) with or without Baf-A1 treatment. Data are pooled from 3 biological replicates (n=3). (D-F) Quantification of NR1D1 (D), p62 (E) and LC3B (F) expression levels after NR1D1 knockdown, confirming the knockdown efficiency. (G) MTT assay in U2OS cells treated with EV or NR1D1 siRNA at different concentrations, demonstrating the effect of NR1D1 knockdown on cell viability. Data are pooled from 3 biological replicates and each repeat contains 6 technical repeats (n=18). (H) Representative confocal microscopy images of YPH cells stained with LysoTracker following treatment with EV KD, EV KD + EBSS, EV KD + Baf-A1, NR1D1 KD, NR1D1 KD + EBSS, or NR1D1 KD + Baf-A1, highlighting the lysosomal distribution under different conditions. Data are pooled from 3 biological replicates and each repeat contains 9 pictures (n=27). (I) Quantification of fluorescence intensity of LysoTracker staining across various conditions as an indicator of lysosomal activity. Two-way Tukey's multiple comparison test (B, D-G) and Kruskal-Wallis test with Dunn's multiple comparison test (I) with was performed were used for statistical analysis, with significance levels denoted as follows: ns = not significant, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$. All data are presented as mean \pm SEM.

SUPPLEMENTARY DATA



Supplementary Figure 2. Impact of *NR1D1* Knockdown on Key Autophagy -Related Proteins. (A) The heatmap of autophagy related genes transcription in RNA-seq database. Data has been normalized by row. (B-L) Quantification of protein expression levels for mTOR (B), LAMP2 (C), ULK1 (D), TFEB (E), HSP90 (F), Beclin1 (G), NAMPT (H), ATG5 (I), GAPDH (J), Cathepsin D (K) and NR1D1 (L) in cells treated with *EV* or *NR1D1* knockdown with or without Baf-A1 treatment. Data indicate the impact of *NR1D1* knockdown on these autophagy-related markers. Two-way with Tukey's multiple comparison test was performed were used for statistical analysis, with significance levels indicated as follows: ns = not significant, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$. Data are presented as mean \pm SEM.

SUPPLEMENTARY DATA

Supplementary Table 1. List of predicted protein-protein interactions between NR1D1 and autophagy-related proteins.

#node1	node2	node1_st ring_id	node2_st ring_id	neighborho od_on_chro mosome	gene _fus ion	phylogene tic_cooccu rrence	hom olog y	coex pres sion	experimentally _determined_i nteraction	databa se_ann otated	automat ed_text mining	comb ined_ score
HSP 90A B1	NR1 D1	9606.EN SP00000 360609	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.646	0.646
NR1 D1	SIR T1	9606.EN SP00000 246672	9606.EN SP00000 212015	0	0	0	0	0	0	0	0.57	0.57
AT G5	NR1 D1	9606.EN SP00000 358072	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.481	0.481
NA MP T	NR1 D1	9606.EN SP00000 222553	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.476	0.476
HD AC1	NR1 D1	9606.EN SP00000 362649	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.46	0.459
GA PD H	NR1 D1	9606.EN SP00000 380070	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.37	0.37
FO XO1	NR1 D1	9606.EN SP00000 368880	9606.EN SP00000 246672	0	0	0	0	0	0.071	0	0.34	0.361
KL HL2 4	NR1 D1	9606.EN SP00000 395012	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.349	0.349
AR NT	NR1 D1	9606.EN SP00000 351407	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.327	0.327
FOS	NR1 D1	9606.EN SP00000 306245	9606.EN SP00000 246672	0	0	0	0	0.04 2	0	0	0.325	0.325
MY C	NR1 D1	9606.EN SP00000 478887	9606.EN SP00000 246672	0	0	0	0	0.04 4	0	0	0.323	0.325
CC L2	NR1 D1	9606.EN SP00000 225831	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.314	0.313
NR1 D1	TP5 3	9606.EN SP00000 246672	9606.EN SP00000 269305	0	0	0	0	0	0	0	0.31	0.309
HIF 1A	NR1 D1	9606.EN SP00000 437955	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.27	0.27
FO XO3	NR1 D1	9606.EN SP00000 339527	9606.EN SP00000 246672	0	0	0	0	0.04 9	0.071	0	0.224	0.255
NF KB1	NR1 D1	9606.EN SP00000 226574	9606.EN SP00000 246672	0	0	0	0	0.04 2	0	0	0.243	0.244
NR1 D1	RPS 6KB 1	9606.EN SP00000 246672	9606.EN SP00000 225577	0	0	0	0	0.07 4	0	0	0.206	0.233
CD KN1 A	NR1 D1	9606.EN SP00000 384849	9606.EN SP00000 246672	0	0	0	0	0.06	0	0	0.212	0.227
ER BB2	NR1 D1	9606.EN SP00000 269571	9606.EN SP00000 246672	0	0	0	0	0.05 7	0.071	0	0.188	0.226
IFN G	NR1 D1	9606.EN SP00000 229135	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.221	0.221
MT OR	NR1 D1	9606.EN SP00000 354558	9606.EN SP00000 246672	0	0	0	0	0	0	0	0.221	0.221

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NFE 2L2	NR1 D1	9606.EN SP00000 380252	9606.EN SP00000 246672	0	0	0	0	0	0	0	0	0.207	0.207
BNI P3	NR1 D1	9606.EN SP00000 357625	9606.EN SP00000 246672	0	0	0	0	0	0	0	0	0.194	0.194
MA P1L C3A	NR1 D1	9606.EN SP00000 363970	9606.EN SP00000 246672	0	0	0	0	0.08 4	0	0	0	0.156	0.194
BC L2	NR1 D1	9606.EN SP00000 381185	9606.EN SP00000 246672	0	0	0	0	0	0	0	0	0.191	0.191
MA P1L C3B	NR1 D1	9606.EN SP00000 498476	9606.EN SP00000 246672	0	0	0	0	0.04 5	0	0	0	0.179	0.182
IKB KB	NR1 D1	9606.EN SP00000 430684	9606.EN SP00000 246672	0	0	0	0	0	0.045	0	0	0.174	0.178
GA BA RA PL1	NR1 D1	9606.EN SP00000 411256	9606.EN SP00000 246672	0	0	0	0	0.04 2	0	0	0	0.176	0.177
ATF 6	NR1 D1	9606.EN SP00000 356919	9606.EN SP00000 246672	0	0	0	0	0	0	0	0	0.17	0.17
NR1 D1	UL K1	9606.EN SP00000 246672	9606.EN SP00000 324560	0	0	0	0	0.07 4	0	0	0	0.14	0.169
AT G7	NR1 D1	9606.EN SP00000 346437	9606.EN SP00000 246672	0	0	0	0	0	0.063	0	0	0.147	0.166
CC R2	NR1 D1	9606.EN SP00000 292301	9606.EN SP00000 246672	0	0	0	0	0	0	0	0	0.165	0.165
CD KN2 A	NR1 D1	9606.EN SP00000 418915	9606.EN SP00000 246672	0	0	0	0	0	0	0	0	0.165	0.165
MA P2K 7	NR1 D1	9606.EN SP00000 381070	9606.EN SP00000 246672	0	0	0	0	0.07 2	0	0	0	0.137	0.164
MA PK3	NR1 D1	9606.EN SP00000 263025	9606.EN SP00000 246672	0	0	0	0	0.06 2	0	0	0	0.143	0.161
CAS P3	NR1 D1	9606.EN SP00000 311032	9606.EN SP00000 246672	0	0	0	0	0	0	0	0	0.153	0.153
AT G4C	NR1 D1	9606.EN SP00000 322159	9606.EN SP00000 246672	0	0	0	0	0	0	0	0	0.151	0.151
NR1 D1	REL A	9606.EN SP00000 246672	9606.EN SP00000 384273	0	0	0	0	0.06 2	0	0	0	0.131	0.15
NR1 D1	PAR P1	9606.EN SP00000 246672	9606.EN SP00000 355759	0	0	0	0	0	0	0	0	0.15	0.15

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Supplementary Table 2. List of the autophagy related genes transcription in NR1D1 knockout database (GSE248721).

ENSG0000003402.21	CFLAR	19.33	26.7	25.4	20.74	18.93	23.83	22.52	24.7
ENSG00000005884.18	ITGA3	289.11	269.26	268.87	288.26	272.95	255.59	250.22	264.65
ENSG00000005893.16	LAMP2	57.5	60.71	61.23	57.53	73.8	68.39	62.54	75.37
ENSG00000006210.7	CX3CL1	7.41	6.74	7.37	7.99	5.16	4.54	4.74	4.18
ENSG00000012174.12	MBTPS2	5.02	4.78	4.13	4.54	3.95	3.87	4.22	3.89
ENSG00000014216.16	CAPN1	114.07	119.84	126.55	114.67	126.1	131.82	129.53	131.35
ENSG00000015475.19	BID	30.6	27.62	30	23.81	24.9	30.16	25.73	24.15
ENSG00000023287.13	RB1CC1	21.8	20.96	22.11	19.54	25.81	23.1	22.06	23.28
ENSG00000026103.23	FAS	8.2	6.47	8.25	7.61	8.23	6.47	5.4	9.5
ENSG00000030110.14	BAK1	28.39	27.95	26.57	28.07	29.8	29.34	30.61	31.28
ENSG00000034693.15	PEX3	11.66	8.83	15.28	9.61	9.81	13.65	13.46	9.37
ENSG00000034713.8	GABARAPL2	97.5	90.33	97.09	105.59	133.58	131.53	129.55	125.99
ENSG00000035664.11	DAPK2	3.11	2.39	4.88	3.66	3.49	3.66	2.38	3.83
ENSG00000044574.9	HSPA5	234.12	209.47	226.61	228.99	260.4	250.85	247.65	242.2
ENSG00000047932.14	GOPC	14.31	13.84	16.24	14.76	18.99	20.04	20.32	20.13
ENSG00000049245.13	VAMP3	43.16	43.66	41.06	40.06	43.8	47.74	47.17	43.37
ENSG00000050748.18	MAPK9	29.9	26.84	30.09	27.34	29.56	29.24	27.91	27.55
ENSG00000055332.19	EIF2AK2	23.28	21.22	22.57	20.78	21.94	23.08	19.93	23.79
ENSG00000057663.16	ATG5	19.51	20.77	21.87	19.43	19.01	19.93	20.32	22.38
ENSG00000061676.15	NCKAP1	58.08	51.14	54.69	52.52	58.9	62.99	59.09	63.64
ENSG00000064012.23	CASP8	19.85	18.35	20.66	18.62	20.36	18.93	20.46	17.45
ENSG00000065135.12	GNAI3	25.87	24.09	26.4	23.92	29.51	28.98	28.52	27.11
ENSG00000065675.16	PRKCQ	5.05	4.66	5.49	5.45	3.97	3.99	3.53	3.15
ENSG00000066739.12	ATG2B	3.42	1.89	3.52	3.17	3.43	3.93	4.41	3.57
ENSG00000068903.21	SIRT2	15.19	16.54	17.26	14.91	21.13	18.54	22.16	22.74
ENSG00000070540.13	WIPI1	18.68	22.28	17.09	18.08	24	22.22	19.93	27.18
ENSG00000075785.14	RAB7A	137.29	125.37	132.77	130.49	169.32	165.91	156.17	158.4
ENSG00000076984.18	MAP2K7	24.33	26.74	23.92	25.32	26.17	24.71	26.61	25.68
ENSG00000078142.14	PIK3C3	19.64	15.64	21.83	12.99	21	21.69	16.6	24.26
ENSG00000078804.13	TP53INP2	29.64	32.52	29.48	31.89	32.29	27.66	28.46	29.05
ENSG00000078900.15	TP73	8.65	7.97	8.83	7.32	3.98	4.45	4.41	4.42
ENSG00000079332.15	SAR1A	52.34	64.49	59.04	55.83	58.37	56.19	59.33	57.2
ENSG00000083290.20	ULK2	1.53	2.72	1.2	1.98	3.01	2.69	2.49	2.66
ENSG00000083937.10	CHMP2B	25.79	20.89	22.17	22.05	24.77	26.65	25.84	23.95
ENSG00000085978.22	ATG16L1	15.76	16.52	14.7	14.58	15.57	15.44	11.86	16.65
ENSG00000087074.8	PPIR15A	29.99	29.6	30.23	32.96	38.67	37.07	37.11	34.92
ENSG00000087088.21	BAX	269.62	256.66	277.55	273.49	275.33	286.13	273.57	271
ENSG00000088832.18	FKBP1A	247.3	233.48	243.36	232.08	315.07	292.86	320.81	297.09
ENSG00000089685.15	BIRC5	251.55	231.63	240.04	238.32	272.71	263.87	263.41	268.03
ENSG00000091409.16	ITGA6	23.55	15.65	20.6	22.25	21.12	20.9	17.31	19.74
ENSG00000094631.21	HDAC6	65.65	90.69	75.77	77.02	91.74	80.83	80.17	72.18
ENSG00000096384.20	HSP90AB1	1163.51	1061.92	1117.01	1109.56	1552.43	1530.18	1517.73	1512.64
ENSG00000096717.12	SIRT1	15.09	14.65	15.3	14.47	17.05	15.76	16.35	17.92
ENSG00000097033.14	SH3GLB1	43.66	45.34	45.51	42.05	49.11	53.72	50.51	49.96
ENSG00000100030.15	MAPK1	97.82	99.64	100.45	93.22	99.61	97.79	92.6	97.76
ENSG00000100299.18	ARSA	26.83	28.2	28.43	30.44	26.75	24.89	22.56	26.14
ENSG00000100342.21	APOL1	5.98	5.47	6.88	7.46	1.76	2.69	1.82	2.62
ENSG00000100380.15	ST13	195.04	177.6	180.35	166.17	181.97	161.29	169.72	185.04
ENSG00000100644.17	HIF1A	110	102.58	107.16	90.42	82.95	78.89	80.24	86.96
ENSG00000100926.15	TM9SF1	45.98	45.54	50.23	51.36	51.98	47.12	48.45	45.03
ENSG00000101421.4	CHMP4B	119.87	115.36	113.63	117.04	129.78	135.31	133.86	129.16
ENSG00000101844.18	ATG4A	3.18	2.14	2.27	2.45	2.33	2.69	2.33	2.84
ENSG00000102882.12	MAPK3	93.87	112.43	94.47	91.61	83.05	77.87	84.82	95.58
ENSG00000103194.16	USP10	45.28	44.04	41.51	38.63	53.02	53.72	53.95	52.86
ENSG00000103197.18	TSC2	51.86	40.95	44.95	50.19	47.9	49.08	53.41	52.95
ENSG00000103319.12	EEF2K	4.28	6.47	5.89	3.85	4.25	5.01	4.23	4.64
ENSG00000103769.10	RAB11A	268.33	265.29	263.02	248.12	265.57	262.03	254.14	250.52
ENSG00000104365.16	IKBKB	17.19	20.25	14.5	16.46	19.92	18.59	17.36	20.27
ENSG00000104765.16	BNIP3L	97.49	82.02	86.98	90.6	79.69	72.07	79.7	86.88
ENSG00000105835.13	NAMPT	73.39	72.47	73.28	68.52	58.36	64.31	63.98	63.29
ENSG00000106615.10	RHEB	35.53	28.89	33.71	30.08	42.03	39.56	34.56	41.1
ENSG00000107262.26	BAG1	61.45	61.45	59.87	63.11	96.91	81.37	75.37	78.44
ENSG00000107643.17	MAPK8	76.1	75.26	79.39	76.54	88.22	81.05	90.98	85.36
ENSG00000108443.14	RPS6KB1	24.91	31.91	33.84	26.25	26.04	24.41	32.17	23.59
ENSG00000108691.9	CCL2	51.39	50.37	45.63	64.35	76.29	65.83	66.88	85.11

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ENSG00000108946.16	PRKARIA	164.52	144.54	177.59	154.73	164.58	161.62	160.52	166.99
ENSG00000109320.13	NFKB1	13.91	15.89	14.9	14.45	17.04	17.82	16.56	16.98
ENSG00000109971.14	HSPA8	1292.77	1172.76	1247.29	1174.38	1548.08	1579.64	1554.87	1534.83
ENSG00000110046.13	ATG2A	15.71	15.81	13.87	16.4	16.15	18.49	16.06	15.82
ENSG00000110497.15	AMBRA1	17.89	15.03	17.48	15.49	20.67	18.97	19.21	18.71
ENSG00000110931.19	CAMKK2	11.46	11.84	11.64	12.21	13.28	13.07	13.08	13
ENSG00000111276.12	CDKN1B	54.74	58.71	57.61	54.57	44.33	43.04	41.09	44.9
ENSG00000111640.15	GAPDH	7660.66	7733.39	7628.24	7514.18	6219.9	6469.1	6470.92	6558.07
ENSG00000111725.11	PRKAB1	28.7	33.75	23.89	24.1	30.48	26.8	27.83	26.05
ENSG00000112715.26	VEGFA	27.29	23.23	21.7	30.27	28.78	31.67	29.7	29.08
ENSG00000113273.17	ARSB	11.19	12.74	11.35	11.92	17.65	16.72	18.11	17
ENSG00000113734.18	BNIP1	20.07	18.48	21.27	18.78	23.61	19.57	23.2	20.18
ENSG00000114796.16	KLHL24	19.94	11.6	21.37	11.26	13.61	15.1	15.2	15.05
ENSG00000114867.22	EIF4G1	373.57	369.64	382.03	395.72	410.25	391.69	419.86	402.66
ENSG00000115760.15	BIRC6	33.25	27.33	35.97	33.6	34.09	34.85	40.44	40.24
ENSG00000116044.16	NFE2L2	47.6	39.07	44.5	40.59	40.67	44.4	46.01	43.09
ENSG00000116478.12	HDAC1	73.73	77.24	82.55	80.1	80.77	82.27	83.64	82.84
ENSG00000117335.20	CD46	62.07	72.69	66.34	78.53	72	75.25	80.92	55.74
ENSG00000117984.15	CTSD	203.47	246.28	220.92	237.04	240.61	245.76	236.61	262.43
ENSG00000118046.17	STK11	53.45	50.68	52.35	45.82	53.8	51.53	47.73	45.76
ENSG00000118217.7	ATF6	37.47	39.14	38.23	38.98	43.23	38.29	38.53	40.05
ENSG00000118689.15	FOXO3	9.75	10.49	11.21	9.31	10.42	10.21	10.13	10.44
ENSG00000119782.14	FKBP1B	10.94	11.99	12.33	13.44	9.83	11.63	11.99	10.59
ENSG00000119919.12	NKX2-3	0.18	0.07	0.11	0.12	0.17	0.12	0.27	0.06
ENSG00000121653.11	MAPK8IP1	44.32	54.46	48.81	43.2	56.72	66.23	67.6	64.54
ENSG00000124333.16	VAMP7	19.47	17.41	18.54	17	21.14	21.23	20.43	21.21
ENSG00000124762.14	CDKN1A	133.42	133.68	137.53	133.81	141.17	142.59	155.79	155.71
ENSG00000125703.15	ATG4C	6.81	7.42	6.56	5.08	7.46	5.73	7.53	7.5
ENSG00000126247.11	CAPNS1	1151.08	1095.98	1127.86	1106.02	1019.11	1057.35	1101.6	1102.03
ENSG00000126368.6	NR1D1	27.86	18.62	22.22	26.73	8.44	8.7	9.39	6.8
ENSG00000126581.13	BECN1	41.91	40.12	36.37	35.72	44.2	42.26	46.26	44.67
ENSG00000127022.16	CANX	188.37	184.08	188.88	179.51	213.11	208.78	212.38	218.99
ENSG00000128272.18	ATF4	458.88	446.8	463.94	420.06	395.82	421.18	411.97	400.06
ENSG00000128590.5	DNAJB9	7.39	10.87	9.32	9.04	8.45	5.88	8.1	6.87
ENSG00000130734.10	ATG4D	33.53	47.34	37.62	44.6	42.01	39.9	40.72	45.48
ENSG00000130766.5	SESN2	15	18.4	16.68	16.14	16.9	18.66	16.04	16.38
ENSG00000132002.9	DNAJB1	134.47	122.1	127.25	132.78	134.9	139.9	135.42	131.9
ENSG00000132155.14	RAF1	78.45	83.78	83.79	79.91	83.97	84.41	76.6	80.63
ENSG00000132470.14	ITGB4	24.02	28.24	25.67	36.25	18.81	27.39	19.24	26.12
ENSG00000134001.15	EIF2S1	265.1	246.65	275.77	258.83	232.92	253.24	231.56	237.58
ENSG00000134109.11	EDEM1	26.32	22.73	27.78	23.76	35.62	30.59	26.2	29.77
ENSG00000136048.14	DRAM1	9.91	9.37	11.48	11.95	7.48	6.5	8.8	6.39
ENSG00000136238.18	RAC1	377.05	363.2	383.7	377.53	376.12	362.45	358.08	372.39
ENSG00000136436.15	CALCOCO2	41.37	44.36	37.24	41.93	53.7	50.35	45.89	45.32
ENSG00000136997.21	MYC	42.8	39.58	34.81	34.04	62.51	57.98	59.31	48.32
ENSG00000137752.24	CASP1	1.87	2.29	1.16	1.18	0	0.56	0.85	0.83
ENSG00000138069.18	RAB1A	112.32	111.56	120.71	113.78	131.04	124.38	126.07	118.3
ENSG00000138363.15	ATIC	157.04	155.51	154.67	164.64	164.57	160.85	166.29	166.42
ENSG00000139112.11	GABARAPL1	38.21	33.13	32.61	35.38	46.53	41.74	43.8	43.48
ENSG00000139687.16	RB1	16.53	16.04	16.65	14.08	17.51	15.73	16.72	16.64
ENSG00000140474.14	ULK3	17.96	20.62	18.6	20.47	19.06	16.31	14.97	18.32
ENSG00000140941.14	MAP1LC3B	73.69	68.15	76.62	69.43	104.22	102.76	100.81	106.73
ENSG00000141456.16	PELP1	47.29	42.16	37.83	46.02	45.94	41.75	48.86	42.76
ENSG00000141458.13	NPC1	15.04	16.96	18.78	14.65	18.8	17.65	15.1	16.84
ENSG00000141510.18	TP53	40.93	36.33	38.14	37.48	48.15	45.94	47.67	47.88
ENSG00000141564.15	RPTOR	20.1	16.86	17.59	17.49	18.24	20.53	17.67	17.35
ENSG00000141736.14	ERBB2	41.05	45.1	46.49	42.91	41.99	39.24	39.34	37.14
ENSG00000142330.20	CAPN10	15.71	15.23	14.68	18.98	19.45	20.89	16.27	16.47
ENSG00000142655.13	PEX14	26.03	23.37	22.08	25.44	25.91	25.19	25.2	25.4
ENSG00000143437.21	ARNT	23.9	27.21	32.87	20.36	31.57	33.55	25.88	26.34
ENSG00000143799.14	PARP1	113.6	102.69	111.07	107.03	124.77	111.51	112.56	120.25
ENSG00000144566.11	RAB5A	39.45	35.61	38.42	33.52	38.94	41.13	32.54	32.24
ENSG00000144848.11	ATG3	60.39	64.69	53.78	50.5	54.22	48.72	51.34	53.48
ENSG00000145414.9	NAF1	10.53	9.67	8.27	10.24	9.61	8.27	10.14	7.25
ENSG00000145782.13	ATG12	36.34	36.03	33.72	36.32	39.66	38.34	36.89	41.66
ENSG00000146648.20	EGFR	4.68	6.19	5.45	4.9	3.17	3.54	2.31	2.74
ENSG00000150093.20	ITGB1	466.42	413.86	445.63	432.47	456.3	435.65	447.37	446.1
ENSG00000150907.10	FOXO1	2.15	2.85	2.73	2.47	2.53	2.33	2.5	2.56
ENSG00000150995.21	ITPR1	9.4	6.02	6.33	3.88	8.5	8.65	9.27	9.32
ENSG00000151929.10	BAG3	30.24	29.36	31.66	30.67	44.38	41.77	37.69	38.17

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ENSG00000152137.8	HSPB8	30.65	22.85	24.67	28.58	47.89	46.75	50.96	48.44
ENSG00000152208.13	GRID2	5.33	5.09	5.64	4.8	2.67	2.69	2.33	3.08
ENSG00000152348.16	ATG10	7.54	6.78	4.54	7.36	8.42	11.88	8.01	12.5
ENSG00000157168.20	NRG1	7.19	7.1	6.77	6.07	6.2	7.17	7.62	6.56
ENSG00000157954.15	WIPI2	108.95	105.4	112.92	114.82	121.73	115.22	121.81	115.83
ENSG00000158458.21	NRG2	0.71	0.67	0.43	0.92	0.42	0.3	0.83	0.94
ENSG00000158828.8	PINK1	50.8	53.42	53.14	52.21	76.09	71.33	70.87	76.04
ENSG00000161011.20	SQSTM1	202.7	186.34	184.39	212.19	308.22	301.35	292.28	286.18
ENSG00000162595.8	DIRAS3	0.71	0.44	0.25	0.18	0.21	0.36	0.48	0.65
ENSG00000162734.13	PEA15	296.86	289.21	288.57	267.19	343.87	335.71	350.65	346.96
ENSG00000162892.16	IL24	0.2	0.11	0.39	0.1	0.61	0.5	0.66	0.3
ENSG00000162909.18	CAPN2	181.22	159.13	169.67	155.4	204.24	188.78	182.18	192.99
ENSG00000163625.16	WDFY3	22.72	30.39	32.45	24.49	29.15	30.52	24.49	31.16
ENSG00000163719.20	MTMR14	43.51	41.54	39.19	38.45	42.68	47.79	46.71	47.31
ENSG00000163932.15	PRKCD	14.82	15.12	13.36	13.89	17.47	17.36	15.61	17.7
ENSG00000164305.19	CASP3	16.77	17.01	17.37	15.65	15.25	15.01	12.96	16.08
ENSG00000164733.22	CTSB	336.19	372.25	362.67	370.3	303.42	286.4	292.03	320.89
ENSG00000164741.15	DLC1	35.62	26.42	25.21	24.78	26.63	18.99	26.07	20.72
ENSG00000164841.5	TMEM74	0.68	1.07	0.91	0.76	0.89	1.08	1.07	1.08
ENSG00000165699.15	TSC1	22.25	17.02	19.43	19.34	25.02	24.46	25.39	26.02
ENSG00000165861.14	ZFYVE1	18.77	18.84	14.83	18.13	13.4	14.31	13.3	15.77
ENSG00000167658.16	EEF2	1727.15	1789.66	1736.16	1667.18	1804.45	1878.47	1988.74	2002.8
ENSG00000167965.18	MLST8	97.44	101.51	91.64	92.18	89.25	93.55	86.59	93.7
ENSG00000168010.11	ATG16L2	3.26	4.25	4.27	5.42	6.27	7.64	4.46	5.14
ENSG00000168040.5	FADD	42.1	39.21	39.33	42.93	38.22	36.9	38.59	37.89
ENSG00000168397.17	ATG4B	53.32	55.88	59.16	59.08	63.13	67.72	63.62	66.11
ENSG00000169228.14	RAB24	24.06	28.34	23.6	25.81	24	21.29	23.35	25.15
ENSG00000169682.18	SPNS1	32.01	31.21	33.23	38.66	36.64	35.78	36.22	34.52
ENSG00000170296.10	GABARAP	334.02	383.34	340.78	332.88	362.84	364.46	369.35	397.02
ENSG00000170345.10	FOS	7.28	9.61	10.17	9.96	8.31	6.61	6.62	4.96
ENSG00000170759.11	KIF5B	60.64	54.06	57.53	49.32	58.88	55.23	56.19	57.44
ENSG00000171298.13	GAA	55.19	58.69	48.77	55.66	52.78	58.6	46.53	59.28
ENSG00000171552.14	BCL2L1	154.13	215.73	196.09	162.71	122.04	119.43	120.96	134.92
ENSG00000171700.14	RGS19	13.55	13.73	14.67	16.87	13.16	16.13	14.43	12.14
ENSG00000171791.14	BCL2	2.87	2.49	2.68	2.68	3.13	2.74	2.21	3.18
ENSG00000171862.12	PTEN	38.49	30.51	28.98	29.66	38.87	35.4	34.19	38.45
ENSG00000172007.7	RAB33B	4.45	3.15	3.23	2.56	3.83	3.49	3.79	2.99
ENSG00000172071.15	EIF2AK3	15.09	14.34	13.86	12.95	15.62	17.57	16.13	19.88
ENSG00000173039.20	RELA	89.06	91.52	83.68	79.37	96.28	92.76	94.23	109.1
ENSG00000175197.13	DDIT3	9.62	12.74	13.84	11.14	16.86	18.42	17.24	14.87
ENSG00000176170.14	SPHK1	13.64	10.52	11.91	12.42	12.22	15.35	13.51	9.66
ENSG00000176171.12	BNIP3	30.61	29.71	34.88	28.29	25.55	29.05	24.35	25.36
ENSG00000177169.10	ULK1	15.67	16.08	16.71	15.42	26.11	19.57	17.55	18.11
ENSG00000178607.17	ERN1	3.96	4.97	4.31	5.42	6.09	4.42	4.72	6.22
ENSG00000182771.19	GRID1	8.8	9.57	6.5	7.63	11.18	10.88	10.22	12.4
ENSG00000183735.11	TBK1	21.61	18.21	23.66	15.17	16.01	25.03	21.51	25.46
ENSG00000185359.14	HGS	132.65	135.8	130.63	127.66	163.83	147.1	164.83	160.13
ENSG00000185624.16	P4HB	679.59	709.14	696.37	717.31	705.5	695.98	704.74	729.33
ENSG00000185737.13	NRG3	3.03	3.09	3.38	3.01	2.99	2.1	2.35	1.98
ENSG00000185896.11	LAMP1	193.87	189.42	190.31	215.4	225.43	218.41	217.39	223.61
ENSG00000187840.5	EIF4EBP1	202.62	213.93	193.95	206	145.8	141.66	158.14	142.85
ENSG00000188554.15	NBR1	30.68	29.76	31.62	29.05	33.05	34.78	33.94	35.66
ENSG00000188603.22	CLN3	22.06	21.33	21.76	20.71	28.66	26.44	31.63	25.05
ENSG00000196455.8	PIK3R4	18.36	15.58	18.66	18.02	20.13	16.59	18.51	16.44
ENSG00000196730.13	DAPK1	0.27	0.23	0.33	0.41	0.76	0.89	0.64	0.84
ENSG00000196954.14	CASP4	27.8	28.82	29.29	27.69	30.46	29.42	27.66	29.7
ENSG00000196998.19	WDR45	50.79	57.58	45.64	58.42	58.25	63.99	65.74	63.49
ENSG00000197249.14	SERPINA1	88.69	94.33	95.23	101.09	54.19	51.3	55.36	55.69
ENSG00000197548.13	ATG7	21.39	14.83	22.65	17.29	18.06	20.01	21.89	17.54
ENSG00000197769.6	MAP1LC3C	5.68	3.8	2.79	5.94	0.75	1.49	0.91	1.69
ENSG00000198382.9	UVRAG	7.44	8.93	8.96	8.03	10.7	9.62	10.28	10.11
ENSG00000198680.6	TUSC1	27.26	27.07	27.48	28.39	25.7	24.69	27.73	26.58
ENSG00000198793.13	MTOR	30.62	30.77	32.37	33.5	32.89	33.22	33.31	37.74
ENSG00000198925.12	ATG9A	42.85	44.33	42.1	44.52	45.29	49.7	51.83	48.38
ENSG00000263528.8	IKBKE	5.61	5.74	5.67	5.28	8.36	7.92	6.57	6.87

SUPPLEMENTARY DATA

Supplementary Table 3. List of the primary antibodies and secondary antibodies.

Strain	Genotype	Notes	Source
N2	WT		CGC Tavernarakis Lab
IR1864	<i>Ex[punc-119::TOMM-20::Rosella;pRF4]</i>	mtRosella reporter	CGC
CL2355	<i>dvIs50 [pCL45 (snb-1::Abeta 1-42::3' UTR(long) + mtl-2::GFP] I</i> <i>sid-1(pk3321) V;uIs69 [pCFJ90 (myo-2p::mCherry) + unc-119p::sid-</i> <i>1] V</i>		Rafal Lab
TU3401	<i>Is[aex-3::tau4R1N(P301L) + myo-2p::gfp]</i>		Zuryn Lab
CK12	<i>dvIs50 [pCL45 (snb-1::Abeta 1-42::3' UTR(long) + mtl-2::GFP];sid-</i> <i>1(pk3321) V;uIs69 [pCFJ90 (myo-2p::mCherry) + unc-119p::sid-1] V</i>	crossed between CL2355 x TU3401	Fang Lab
EFF060	<i>sid-1(pk3321) V;uIs69 [pCFJ90 (myo-2p::mCherry) + unc-119p::sid-1]</i> <i>V; N2; Ex[punc-119TOMM-20::Rosella; rol-6(su1006)]</i>	crossed between IR1864 x TU3401	Fang Lab
EFF066	<i>Is[p_{aex-3}::tau4R1N(P301L) + p_{myo-2}::gfp];sid-1(pk3321) V;uIs69</i> <i>[pCFJ90 (myo-2p::mCherry) + unc-119p::sid-1] V</i>	crossed between neuronal CK12 x TU3401	Fang Lab
EFF029			