

## **FBXL4 deficiency increases mitochondrial removal by autophagy**

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**Appendix Table S1.** qPCR probe list used in the study

<b>Probe</b>	<b>Species</b>	<b>Reporter</b>	<b>Reference number</b>
ACTB	Mus musculus	FAM	Mm01205647_g1
B2M	Mus musculus	FAM	Mm00437762_m1
FBXL4	Mus musculus	FAM	Mm01217476_m1
ND1	Mus musculus	FAM	Mm04225274_s1
ND3	Mus musculus	FAM	Mm04225292_g1
ND6	Mus musculus	FAM	AIHSNT9
CYTB	Mus musculus	FAM	Mm04225271_g1
COX2	Mus musculus	FAM	Mm03294838_g1
ATP8	Mus musculus	FAM	Mm04225236_g1
TFAM	Mus musculus	FAM	Mm00447485_m1
POLRMT	Mus musculus	FAM	Mm00553272_m1
TFB2M	Mus musculus	FAM	Mm01620397_s1
VDAC1	Mus musculus	FAM	Mm00834272_m1
ACTB	Homo Sapiens	FAM	Hs99999903_m1
18S	Homo Sapiens	FAM	Hs99999901_s1
FBXL4	Homo Sapiens	FAM	Hs01091896_m1
ND1	Homo Sapiens	FAM	Hs02596873_s1
COX2	Homo Sapiens	FAM	Hs02596865_g1
ATP6	Homo Sapiens	FAM	Hs02596862_g1
RNR2	Homo Sapiens	FAM	Hs02596860_s1
VDAC1	Homo Sapiens	FAM	Hs01631624_gH
HSP60	Homo Sapiens	FAM	Hs01036753_g1
TFAM	Homo Sapiens	FAM	Hs00273372_s1
POLRMT	Homo Sapiens	FAM	Hs04187596_g1
TFB2M	Homo Sapiens	FAM	Hs00915025_m1
GAPDH	Homo Sapiens	FAM	Hs03929097_g1
LAMP1	Homo Sapiens	FAM	Hs00931461_m1

**Appendix Table S2.** Primary antibody list used in the study

<b>Antigen</b>	<b>Source</b>	<b>Company</b>	<b>Catalog Number</b>	<b>Method</b>	<b>Dilution</b>
Hsp60	Mouse	Enzo Lifesciences	AB1-SPA-807-E	WB	1:1000
Total OXPHOS Rodent	Mouse	Abcam	MS604-300	WB	1:1000
Tfam	Rabbit	Abcam	ab-131607	WB	1:1000
ActB	mouse	Abcam	ab8226	WB	1:1000
Vdac1	mouse	abcam	ab128568	WB	1:1000
Uqcrc2	Mouse	Abcam	ab14745	WB	1:1000
Atp5a	Mouse	Abcam	ab14748	WB	1:1000
Sdha	Mouse	Abcam	ab14715	WB	1:1000
Gapdh	Mouse	Abcam	ab8245	WB	1:1000
Mtco2	Mouse	Abcam	ab110258	WB	1:1000
Lamp2	mouse	abcam	ab25631	IF	1:250
Tom20	Rabbit	Cell Signaling	13929S	WB	1:1000
Lamp1	rabbit	Cell Signalling	9091S	WB	1:1000
Rpl6	mouse	Abcam	ab126100	WB	1:1000
Mrpl28	Rabbit	Abcam	ab196842	WB	1:1000
Lc3II	rabbit	Novus Bio	100-2331	WB	1:1000
p62/Sqstm1	mouse	Abcam	ab56416	WB	1:1000
Ub	mouse	Cell Signalling	3936S	WB	1:500
Iba1	Rabbit	Wako	0919-19741	IHC	1:1000

Appendix Table S3. Statistics summary table

Figure panel	Statistical test	Comparison	n	p-value	Summary
1B	Chi2 test	Embryo vs Expected Mendelian distribution (%)	79	0,15	n.s
	Chi2 test	Mice vs Expected Mendelian distribution(%)	339	1,3408E-09	***
1D	Student's t-test	Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	5	0,0373	*
1F	Student's t-test	Male Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	5	2,96858E-06	***
	Student's t-test	Female Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	6 (wt), 11 (KO)	0,0024	**
1G	Student's t-test	Male Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	5	0,0678	n.s
	Student's t-test	Female Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	5 (wt), 11 (KO)	0,8276	n.s
1H	Student's t-test	Male Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4 (wt), 5 (KO)	0,0389	*
	Student's t-test	Female Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	5 (wt), 11 (KO)	0,3619	n.s
1I	Student's t-test	Male Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4 (wt), 5 (KO)	0,0412	*
	Student's t-test	Female Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	5 (wt), 11 (KO)	0,1842	n.s
2A	Student's t-test	Heart, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0.3242	n.s
	Student's t-test	Liver, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0.000002	***
	Student's t-test	Kidney, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0.00256	**
	Student's t-test	Brain, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0.001496	**
	Student's t-test	Quadrieps, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0.5574	n.s
2B	Student's t-test	Heart, ND3, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,00107	**
	Student's t-test	Heart, ND6, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,00663	**
	Student's t-test	Heart, CYTB, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,00082	***
	Student's t-test	Heart, COX2, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,03610	*
	Student's t-test	Heart, ATP8, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,00178	**
	Student's t-test	Heart, TFAM, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,68137	n.s
	Student's t-test	Heart, POLRMT, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,74295	n.s
	Student's t-test	Heart, TFB2M, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,07989	n.s
	Student's t-test	Heart, VDAC, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,53017	n.s
	Student's t-test	Heart, FBXL4, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (7)	0,01407	*
	Student's t-test	Liver, ND3, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,00650	**
	Student's t-test	Liver, ND6, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,00118	**
	Student's t-test	Liver, CYTB, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,00019	***
	Student's t-test	Liver, COX2, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,00542	**
	Student's t-test	Liver, ATP8, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,00008	***
	Student's t-test	Liver, TFAM, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,69154	n.s
	Student's t-test	Liver, POLRMT, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,47252	n.s
	Student's t-test	Liver, TFB2M, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,55530	n.s
	Student's t-test	Liver, VDAC, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,92194	n.s
	Student's t-test	Liver, FBXL4, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (5), KO (8)	0,00188	**
	Student's t-test	Kidney, ND3, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,06788	n.s
	Student's t-test	Kidney, ND6, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,12486	n.s
	Student's t-test	Kidney, CYTB, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,00891	**
	Student's t-test	Kidney, COX2, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,00072	***
	Student's t-test	Kidney, ATP8, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,00002	***
	Student's t-test	Kidney, TFAM, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,34896	n.s
	Student's t-test	Kidney, POLRMT, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,91836	n.s
	Student's t-test	Kidney, TFB2M, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,54576	n.s
	Student's t-test	Kidney, VDAC, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,50744	n.s
	Student's t-test	Kidney, FBXL4, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	1,47E-08	***
	Student's t-test	Brain, ND3, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,03641	*
	Student's t-test	Brain, ND6, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,00565	**
Student's t-test	Brain, CYTB, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,01696	*	
Student's t-test	Brain, COX2, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,09564	n.s	
Student's t-test	Brain, ATP8, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,02101	*	
Student's t-test	Brain, TFAM, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,57586	n.s	
Student's t-test	Brain, POLRMT, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,99567	n.s	
Student's t-test	Brain, TFB2M, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,66057	n.s	
Student's t-test	Brain, VDAC, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	0,86484	n.s	
Student's t-test	Brain, FBXL4, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	wt (6), KO (8)	8,18E-05	***	
2D	Student's t-test	HSP60, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4	0,00823	**
	Student's t-test	ATP5A, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4	0,00604	**
	Student's t-test	UQCRC2, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4	0,000001	***
	Student's t-test	MTCO1, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4	0,00207	**
	Student's t-test	SDHB, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4	0,00104	**
	Student's t-test	NDUFB8, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4	0,07435	n.s
	Student's t-test	TFAM, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4	0,07048	n.s
	Student's t-test	ACTB, Fbx14 <sup>+/+</sup> vs Fbx14 <sup>-/-</sup>	4	0,17800	n.s

Figure panel	Statistical test	Comparison	n	p-value	Summary
3B	Student's t-test	Controls vs Patients	3		n.s
3D	Student's t-test	VDAC1, Controls vs Patients	3	0,00068	***
	Student's t-test	HSP60, Controls vs Patients	3	0,03502	*
	Student's t-test	UQCRC2, Controls vs Patients	3	0,00519	**
	Student's t-test	MTCO2, Controls vs Patients	3	0,01441	*
	Student's t-test	SDHA, Controls vs Patients	3	0,03171	*
	Student's t-test	ATP5A, Controls vs Patients	3	0,01299	*
	Student's t-test	MRPL28, Controls vs Patients	3	0,05439	n.s
	Student's t-test	TFAM, Controls vs Patients	3	0,01586	*
	Student's t-test	TOM20, Controls vs Patients	3	0,02768	*
	Student's t-test	GAPDH, Controls vs Patients	3	0,34086	n.s
	Student's t-test	RPL6, Controls vs Patients	3	0,88309	n.s
	Student's t-test	ACTB, Controls vs Patients	3	0,98986	n.s
	Student's t-test	LAMP1, Controls vs Patients	3	0,09369	n.s
3E	Student's t-test	FBXL4, Controls vs Patients	3	0,14880	n.s
	Student's t-test	ND1, Controls vs Patients	3	0,10418	n.s
	Student's t-test	MTCO2, Controls vs Patients	3	0,06840	n.s
	Student's t-test	ATP6, Controls vs Patients	3	0,07822	n.s
	Student's t-test	RNR2, Controls vs Patients	3	0,10942	n.s
	Student's t-test	VDAC1, Controls vs Patients	3	0,72615	n.s
	Student's t-test	HSP60, Controls vs Patients	3	0,41906	n.s
	Student's t-test	TFAM, Controls vs Patients	3	0,90184	n.s
	Student's t-test	POLRMT, Controls vs Patients	3	0,79077	n.s
	Student's t-test	TFB2M, Controls vs Patients	3	0,50759	n.s
	Student's t-test	GAPDH, Controls vs Patients	3	0,80683	n.s
	Student's t-test	LAMP1, Controls vs Patients	3	0,81890	n.s
	4C	Student's t-test	Pulse, wt vs KO	4	0,263117
Student's t-test		24h Chase, wt vs KO	4	0,0016	*
4D	Student's t-test	24h Chase, wt vs KO	4	0,01297	*
	Student's t-test	24h Chase + Epoxo, wt vs KO	3	0,03528	*
	Student's t-test	24h Chase + NH <sub>4</sub> Cl, wt vs KO	4	0,51949	n.s
5B	Non parametric Mann-Whitney	Control vs Patients	Control (67), Patients (303)	0,0006	***
EV1A	Student's t-test	Male Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	Wt (4), KO (5)	0,000031	***
	Student's t-test	Female Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	5 (wt), 11 (KO)	0,000045	***
EV1B	Student's t-test	Male Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	Wt (5), KO (5)	0,0000016	***
	Student's t-test	Female Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	5 (wt), 11 (KO)	0,000213	***
EV1C	Student's t-test	Male Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	Wt (4), KO (5)	0,11906	n.s
	Student's t-test	Female Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	5 (wt), 11 (KO)	0,00360	**
EV2I	Student's t-test	CI, Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	5	0,82240	n.s
	Student's t-test	CI+III, Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	5	0,47383	n.s
	Student's t-test	CII, Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	5	0,51135	n.s
	Student's t-test	CII+III, Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	5	0,65070	n.s
	Student's t-test	CIV, Fbxl4 <sup>+/+</sup> vs Fbxl4 <sup>-/-</sup>	5	0,00906	**
EV3B	Student's t-test	Controls vs Patients	3	0,7305	n.s

