

Supplementary Data

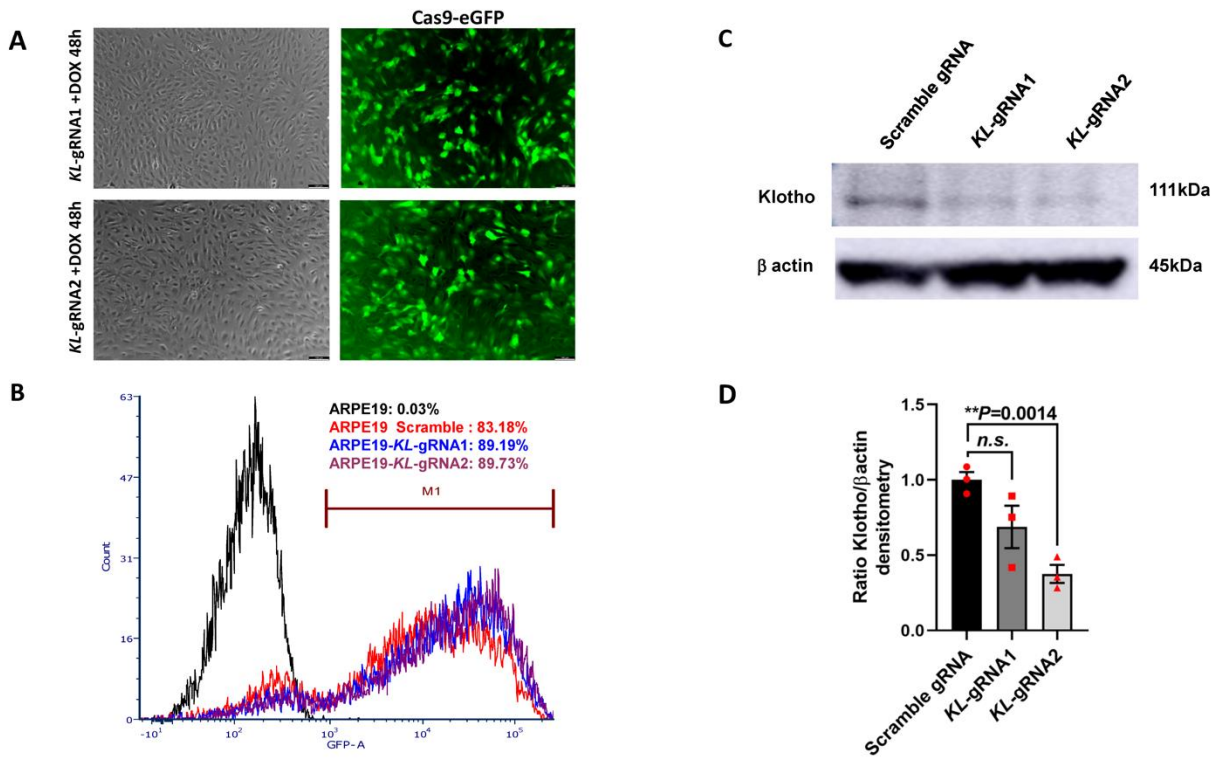


Figure S1. Identification of ARPE19 CRISPR/Cas9 *KL* KO cells and verification of the efficiency of *KL* inhibition with different sgRNAs

(A) ARPE19-*KL* KO cells were incubated with 2μM Doxycycline (DOX) for 48h to test the eGFP, which confirms the expression of Cas9. (B) ARPE19 cells were transfected with CRISPR/Cas9-*KL* sgRNAs vectors and selected by 2μg/ml puromycin for 2 weeks, followed by incubation with 2μM Doxycycline for 48h to induce the Cas9-eGFP expression. Flow cytometry was performed to analyze the ratio of Cas9-eGFP cells. (C,D) *KL* protein levels in Scramble control group and 2 different sgRNA groups were analyzed by Western Blots. Compared with control, *KL* protein was inhibited ~ 31% by sgRNA1 and 66% by sgRNA2. The relative densities of the bands were determined

using ImageJ software. The Unpaired *t*-test was performed using GraphPad Prism

8.3.0. Graph represents mean \pm SEM, n=3, ***P*≤0.01.

Table S1. Primers used for qPCR analyses.

Primers	Primer Sequence (5'-3')
human <i>PGC-1a</i> FOR	TCTGAGTCTGTATGGAGTGACAT
human <i>PGC-1a</i> REV	CCAAGTCGTTACATCTAGTTCA
human <i>DRP1</i> FOR	TTTGACACTTGTGGATTGCCA
human <i>DRP1</i> REV	AGTGACAGCGAGGATAATGGA
human <i>ACADM</i> FOR	ACAGGGGTTTCAGACTGCTATT
human <i>ACADM</i> REV	TCCTCCGTTGGTTATCCACAT
human <i>NDUFS2</i> FOR	GCTGTTATGTACCCAAGCAAAGA
human <i>NDUFS2</i> REV	TCCCCACTCAATTCCATCACT
human <i>NDUFS8</i> FOR	CCATCAACTACCCGTTTCGAGA
human <i>NDUFS8</i> REV	CCGCAGTAGATGCACTTGG
human <i>NDUFA8</i> FOR	CCCAACAAGGAGTTTATGCTCT
human <i>NDUFA8</i> REV	CACAGTGACGTTTTATCTGCCT
human <i>NDUFB10</i> FOR	AGCCCAATCCCATCGTCTACA
human <i>NDUFB10</i> REV	GCTGCCGCTCTATAAATTCTCT
human <i>OPA1</i> FOR	TGTGAGGTCTGCCAGTCTTTA
human <i>OPA1</i> REV	TGTCCTTAATTGGGGTCGTTG
human <i>ND1</i> FOR	CCTAGCCGTTTACTCAATCCT
human <i>ND1</i> REV	TGATGGCTAGGGTGACTTCAT
human <i>ACTB</i> FOR	CATCTCTTGCTCGAAGTCCA
human <i>ACTB</i> REV	ATCATGTTTGAGACCTTCAACA

human <i>GAPDH</i> FOR	GGAGCGAGATCCCTCCAAAAT
human <i>GAPDH</i> REV	GGCTGTTGTCATACTTCTCATGG
Mouse <i>Pgc1a</i> FOR	AGCCGTGACCACTGACAACGAG
Mouse <i>Pgc1a</i> REV	GCTGCATGGTTCTGAGTGCTAAA
Mouse <i>Gapdh</i> FOR	AGACAGCCGCATCTTCTTGT
Mouse <i>Gapdh</i> REV	AATCTCCACTTTGCCACTGC
Mouse <i>Acadm</i> FOR	AACACAACACTCGAAAGCGG
Mouse <i>Acadm</i> REV	TTCTGCTGTTCCGTCAACTCA
Mouse <i>Drp1</i> FOR	CAAGGTTTTCTCGCCCAACG
Mouse <i>Drp1</i> REV	CTGCCCTTACCATCTGGATCTA
Mouse <i>Ndufs2</i> FOR	CAGCCAGATATTGAATGGGCA
Mouse <i>Ndufs2</i> REV	TGTTGGTCACCGCTTTTTCT
Mouse <i>Ndufs8</i> FOR	AGTGGCGGCAACGTACAAG
Mouse <i>Ndufs8</i> REV	TCGAAAGAGGTAAGTTAGGGTCA
Mouse <i>Ndufa8</i> FOR	GGAGCTGCCAACTCTGGAAG
Mouse <i>Ndufa8</i> REV	CCAGCGGCACAGCATAAAC
Mouse <i>Ndufb10</i> FOR	CTCCCTAACCCCATCACCTAC
Mouse <i>Ndufb10</i> REV	TGGCACTCGACGGTACTGT
Mouse <i>Opa1</i> FOR	TGGAAAATGGTTCGAGAGTCAG
Mouse <i>Opa1</i> REV	CATTCCGTCTCTAGGTTAAAGCG
Mouse <i>Nd1</i> FOR	CTCTTATCCACGCTTCCGTTACG
Mouse <i>Nd1</i> REV	GATGGTGGTACTCCCGCTGTA
Mouse <i>H19</i> FOR	GTACCCACCTGTCGTCC
Mouse <i>H19</i> REV	GTCCACGAGACCAATGACTG

Table S2. Antibodies used for Western blot analyses

Antibody	Company	Catalog Number	Dilution
AMPK alpha Rabbit	Cell Signaling Technology	5832S	1:1000
p-AMPK alpha Rabbit	Cell Signaling Technology	2535S	1:1000
ATF2/ATF7 Rabbit	Cell Signaling Technology	82870S	1:1000
p- ATF2/ATF7 Rabbit	Cell Signaling Technology	24329S	1:1000
p38 MAPK Rabbit	Cell Signaling Technology	8690S	1:1000
p-p38 MAPK Rabbit	Cell Signaling Technology	9215S	1:1000
CREB Rabbit	Cell Signaling Technology	9197S	1:1000
p- CREB Rabbit	Cell Signaling Technology	9198S	1:1000
mTOR Rabbit	Cell Signaling Technology	2972S	1:1000
p-mTOR Rabbit	Cell Signaling Technology	2974S	1:1000
DRP1 Rabbit	Cell Signaling Technology	8570S	1:1000
GAPDH Rabbit	Cell Signaling Technology	5174S	1:8000
β actin Rabbit	Cell Signaling Technology	8457S	1:5000-1:30000
Goat anti-Rabbit IgG	Jackson ImmunoResearch	111-035-144	1:4000
Anti-PGC1a (Rabbit)	Millipore	AB3242	1:1000
Anti-KLOTHO (Rabbit)	Sigma Aldrich	SAB3500604	3 μ g/ml