

Supplementary Data

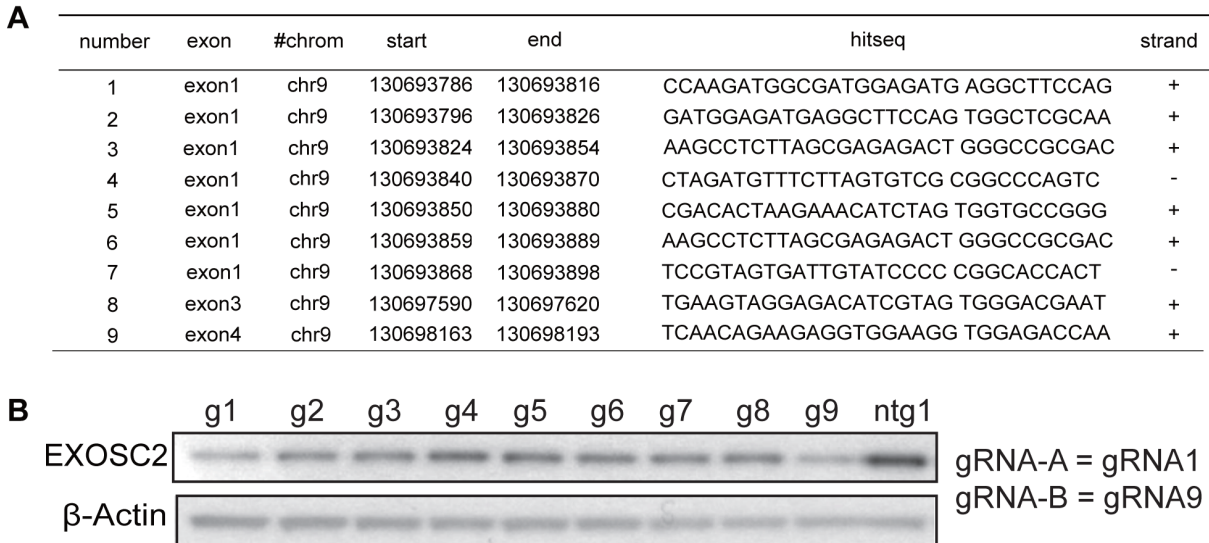


Figure S1. Nine gRNAs targeting *EXOSC2*. **(A)** Information on the top 9 gRNAs designed to target *EXOSC2*. **(B)** Western blot of *EXOSC2* CRISPR knock out keratinocytes targeted by the 9 gRNAs. Data is representative of at least two biological repeats.

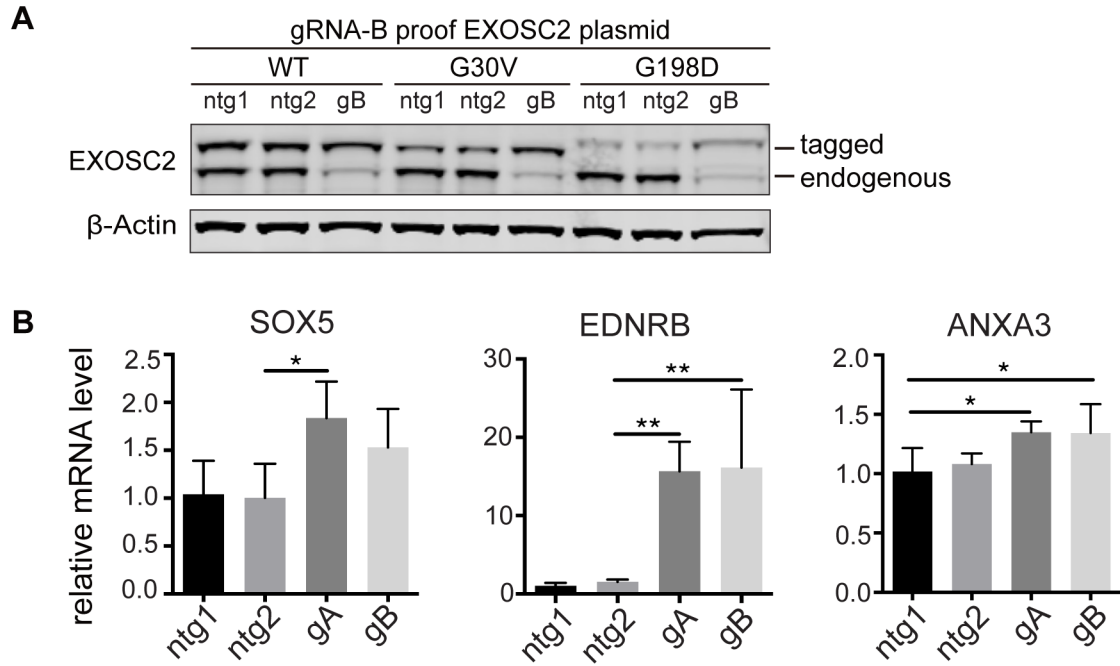


Figure S2. Knocking down EXOSC2 in keratinocytes decreases their cell proliferation rate. **(A)** Western blot of EXOSC2 KO keratinocytes transfected with WT, G30V or G198D forms of hEXOSC2. Data is representative of at least two biological repeats. **(B)** qPCR of *SOX5*, *EDNRB*, *ANXA3* mRNA level in EXOSC2 CRISPR KO keratinocytes. * and ** indicate $p < 0.05$ and $p < 0.01$, respectively, in one-way ANNOVA test ($n=3$).

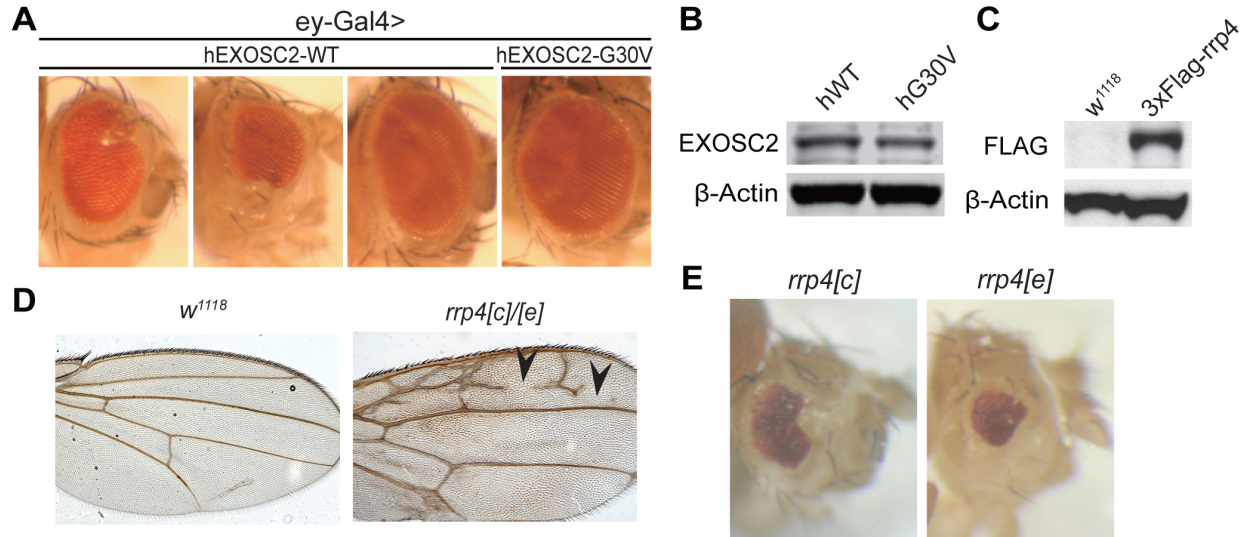


Figure S3. Characterization of *rrp4* PBac mutants and *rrp4* RNAi flies. **(A)** Microphotographs of representative fly eyes expressing human EXOSC2-WT and G30V transgenes driven by *ey-Gal4*. **(B)** Western blot of EXOSC2 level in *da-Gal4>UAS-hEXOSC2-WT/G30V* flies. **(C)** Western blot of Rrp4 level of *Actin-5C-Gal4>UAS-3xFLAG-rrp4* flies. **(D)** Microphotographs of wing vein morphology of homozygous *rrp4^{cl/e}* escaper flies, with the broken places of L2 wing vein marked with black arrows. **(E)** Microphotographs of fly eyes showing eyFLP-generated homozygous clones of the *rrp4[c]* and *rrp4[e]* mutant alleles. The genotypes are: *ey-Flp/+; FRT42D, rrp4[c]/FRT42D, w+, cl (rrp4[c] clone)* or *ey-Flp/+; FRT42D, rrp4[e]/FRT42D, w+, cl (rrp4[e] clone)*.

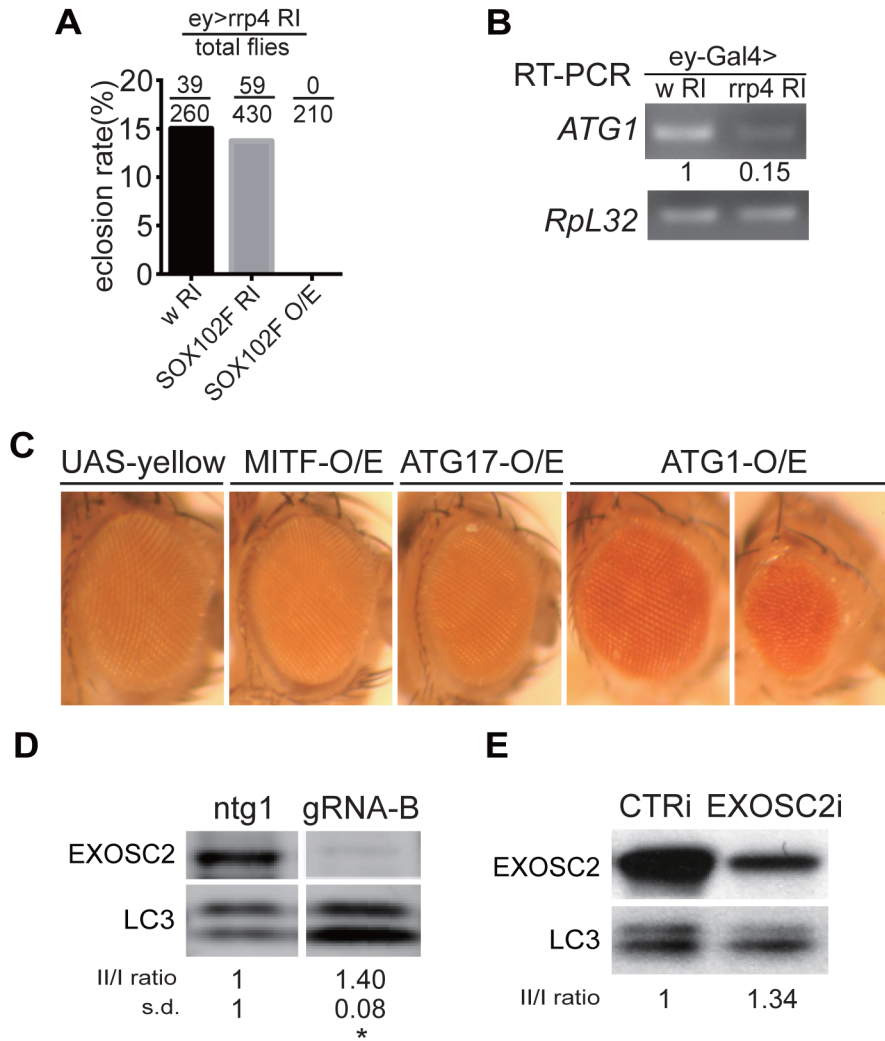


Figure S4. Characterization of *rrp4* genetic interaction flies and mammalian cells for autophagy defects. **(A)** Assessing the rescue of the eclosion rate of *ey-Gal4>rrp4 RNAi* flies by SOX102F RNAi or SOX102F overexpression; Mendelian rate is 50%. Data represents one-time experiment. **(B)** RT-PCR analysis of *ATG1* mRNA level in *ey-Gal4>UAS-rrp4 RNAi* fly eyes. Data represents one-time experiment. **(C)** Microphotographs of fly eyes overexpressing the indicated transgenes driven by *ey-Gal4* in wild type background. **(D)** Western blot of LC-3 and EXOSC2 level in EXOSC2 CRISPR knocking out keratinocytes. Values under the blot show relative LC3-

II/LC3-I ratio. * indicates $p < 0.05$ in Student's t -test ($n=3$). s.d, standard deviation. (E) Western blot of LC-3 and EXOSC2 level in HEK293T cells transfected with EXOSC2 siRNA. Values under the blot show relative LC3-II/LC3-I ratio. Data is representative of two biological repeats.