

Supplementary Information

REEP6 Deficiency Leads to Retinal Degeneration through Disruption of ER Homeostasis and Protein Trafficking

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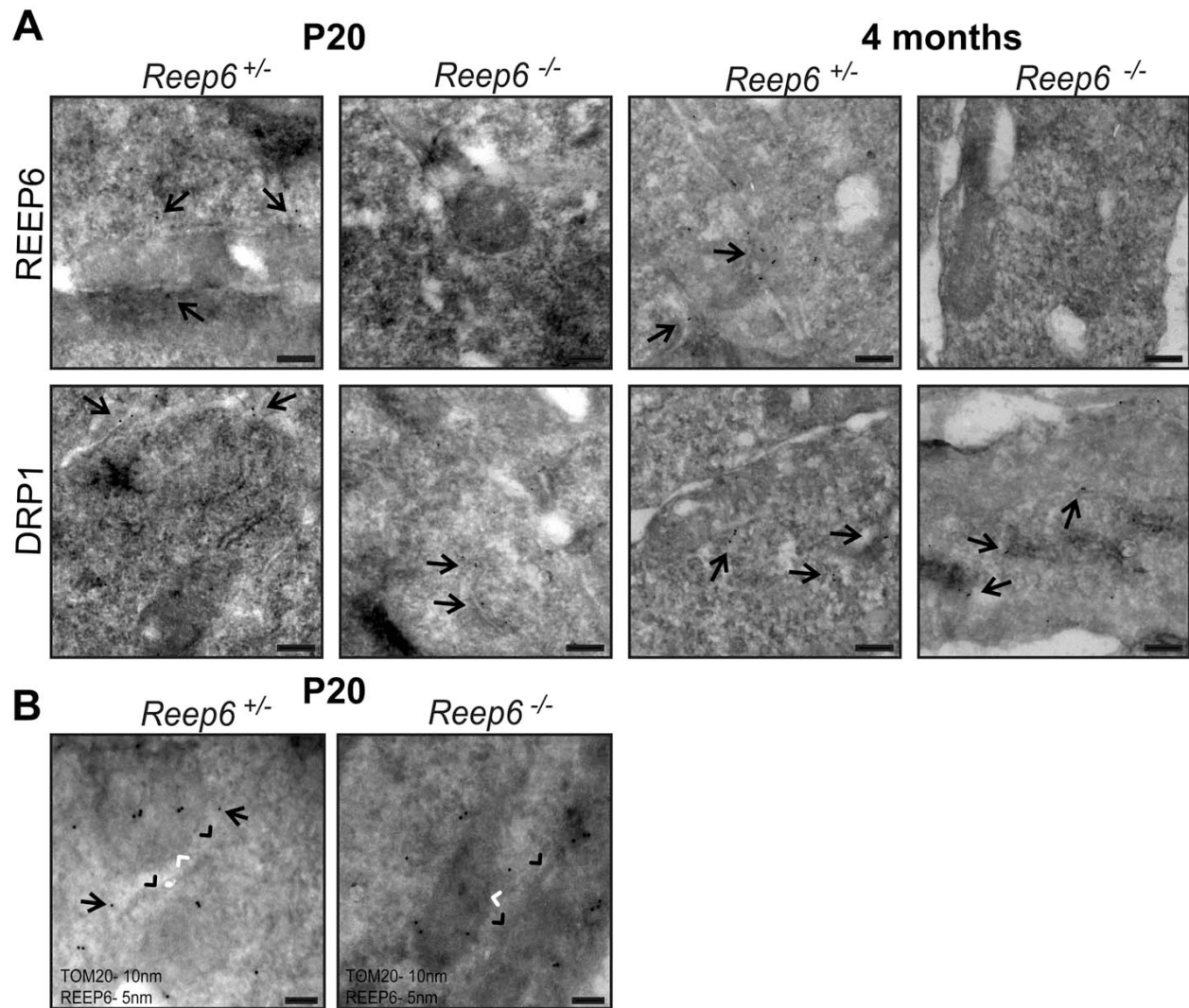
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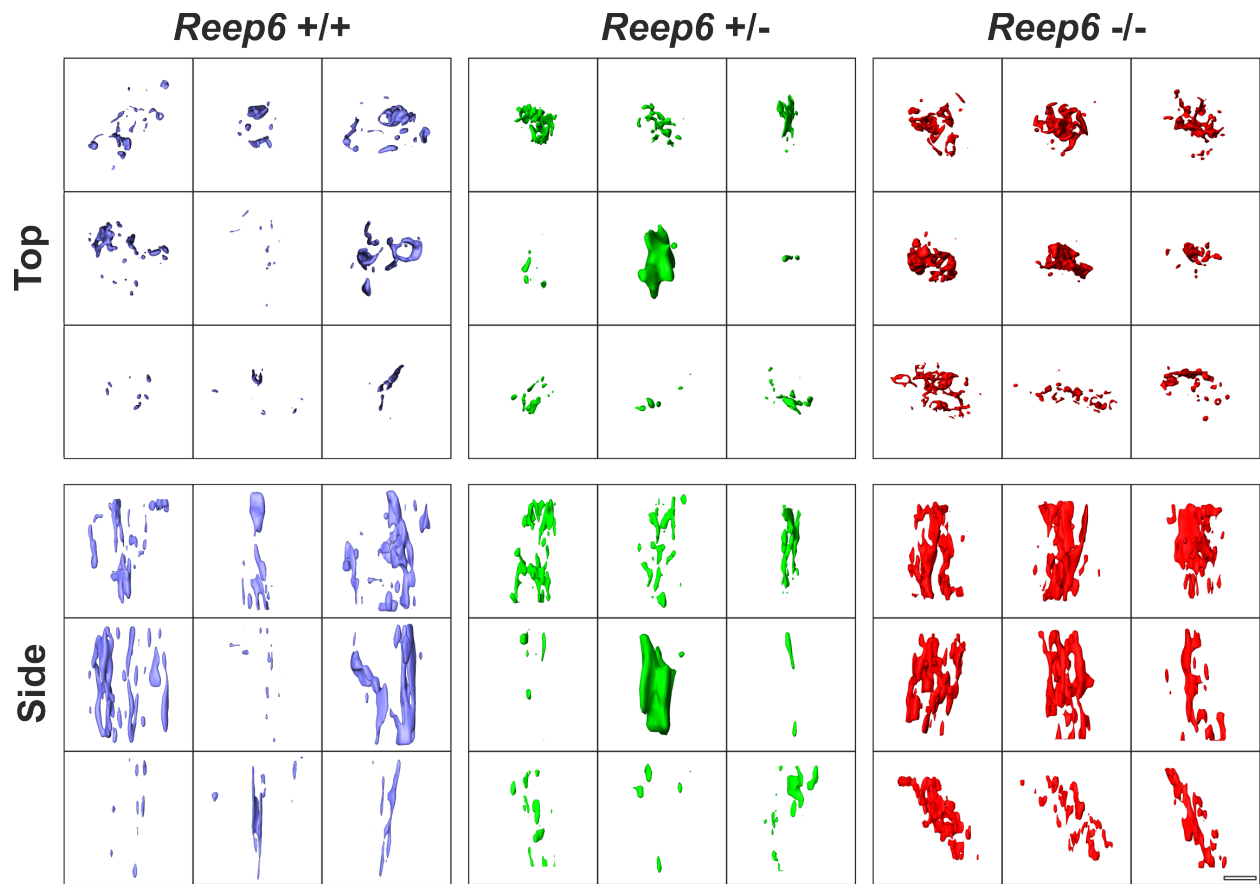
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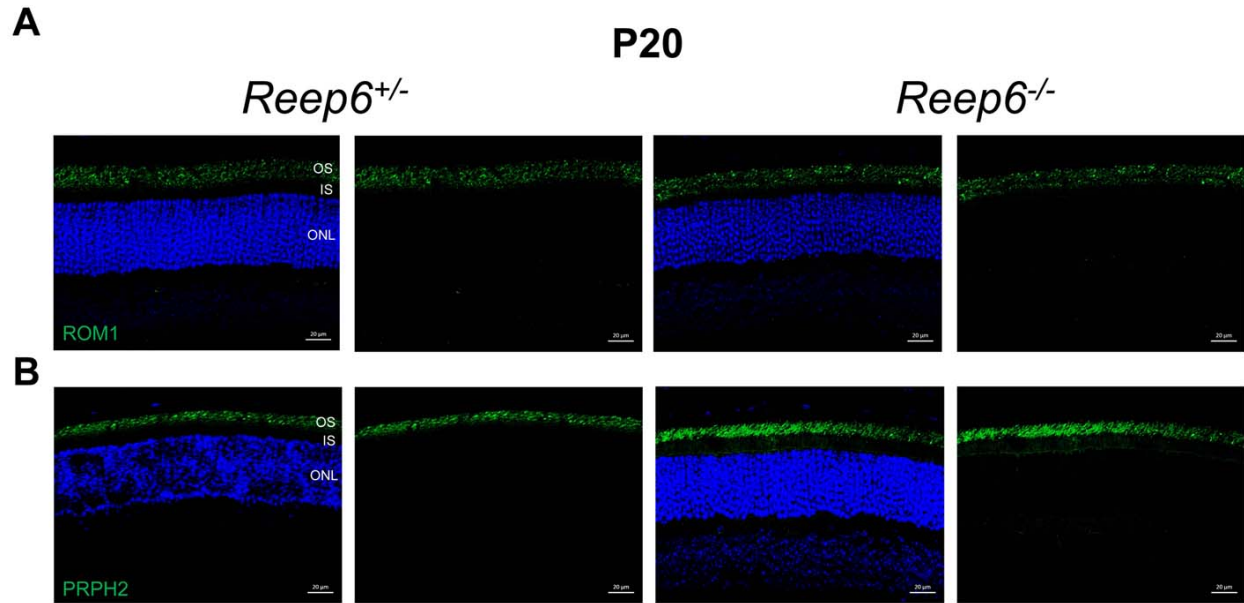
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Supplemental material Fig.1 Immuno-EM labelling of REEP6, Drp1 and Tom20. REEP6 immunoreactivity is detected close to potential ER-mitochondrial contact sites. Immuno-EM using TOM20, a mitochondrial marker and Drp1 (dynamin-related protein 1), a mitochondrial-ER interface marker, shows that REEP6 is expressed near the ER-mitochondrial contact sites. **(A)** Arrows indicate immuno-gold labelling of REEP6 and Drp1. **(B)** Dual immuno-EM labelling of Tom20 (10nm gold) and REEP6 (5nm gold). Arrows highlight REEP6 labelling, black arrow heads ER and white arrow mitochondria at sites of potential mitochondrial-ER interface. Scale bar= **(A)** 200nm, **(B)** 100nm.



Supplemental material Fig. 2 Models of distal inner segment (IS) ER generated from the serial block-face SEM data of nine *Reep6*^{+/+}, *Reep6*^{+/-} and *Reep6*^{-/-} photoreceptors at P20. Top view and corresponding side view of models used to calculate the volume of distal IS ER. Scale bar= 200nm



Supplemental material Fig. 3 Trafficking of ROM1 and PRPH2 is unaffected in *Reep6* KO mice at P20. **(A)** Localization of retinal outer segment membrane protein 1 (ROM1), shown in green, is not affected in *Reep6*^{-/-} retina at P20. **(B)** Localization of disk morphogenesis protein, peripherin 2 (also known as RDS), is not affected in *Reep6*^{-/-} retina at P20. Nuclei are counter-stained with DAPI (blue). Scale bar= **(A, B)** 20 μm.