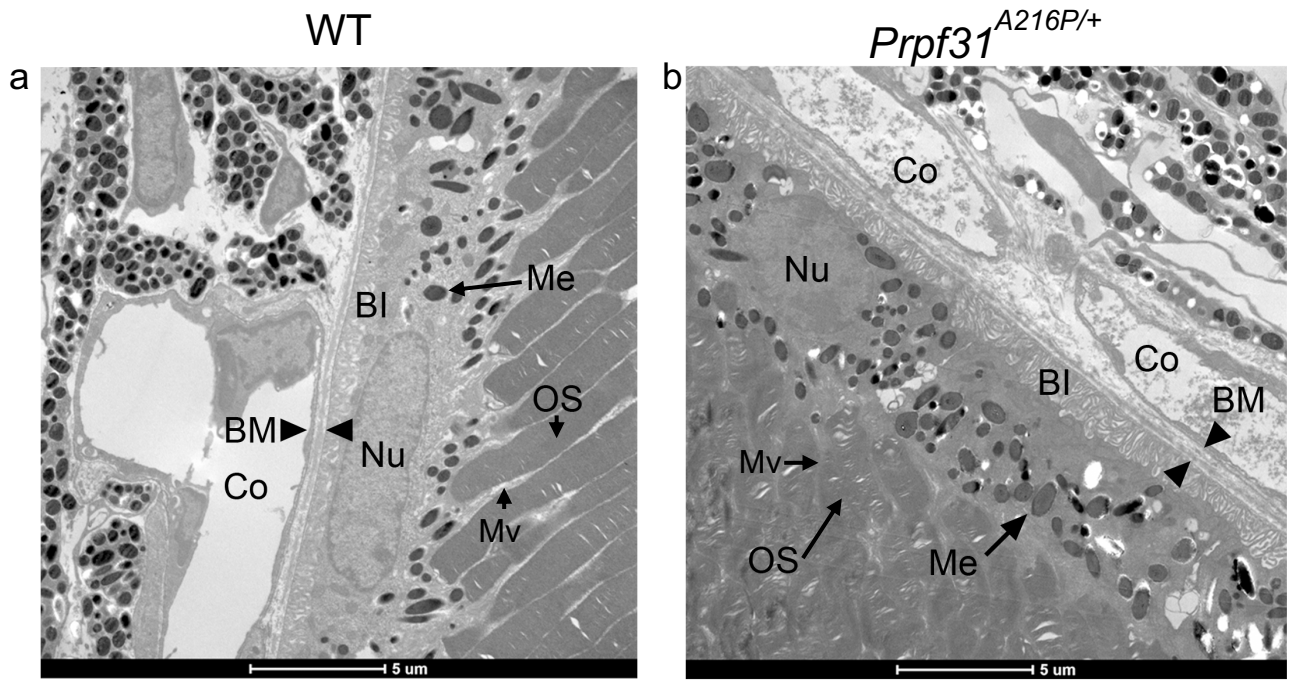
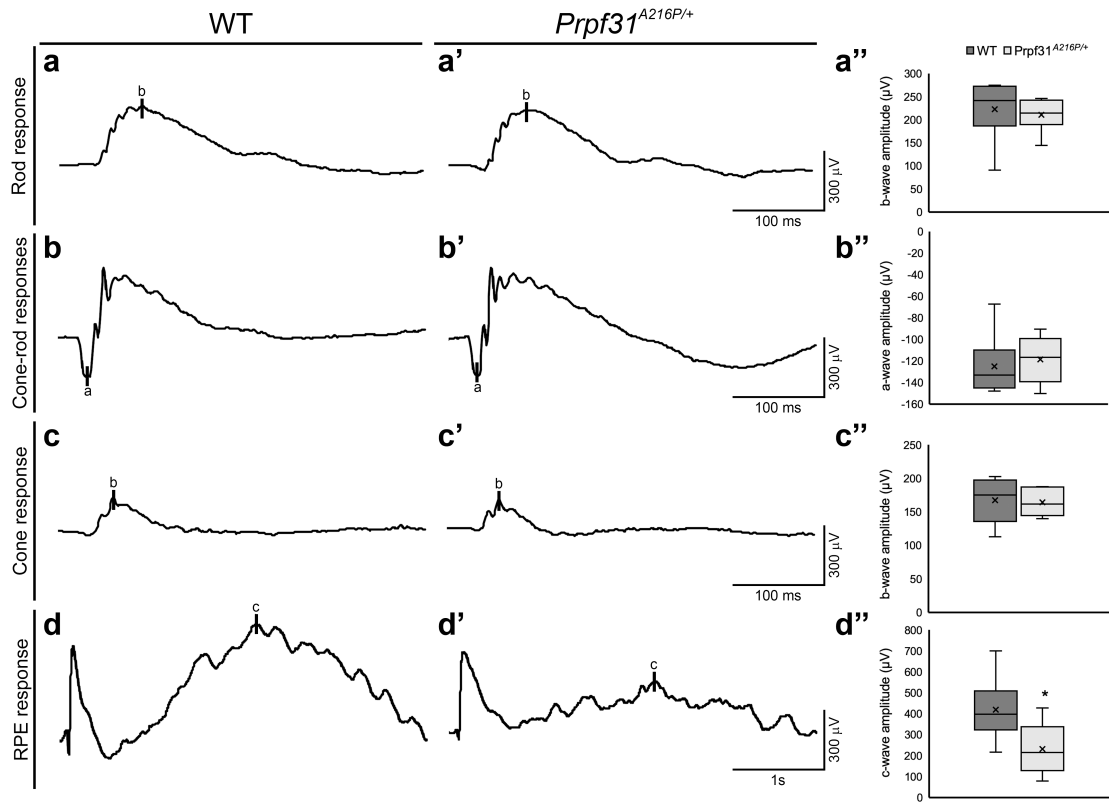


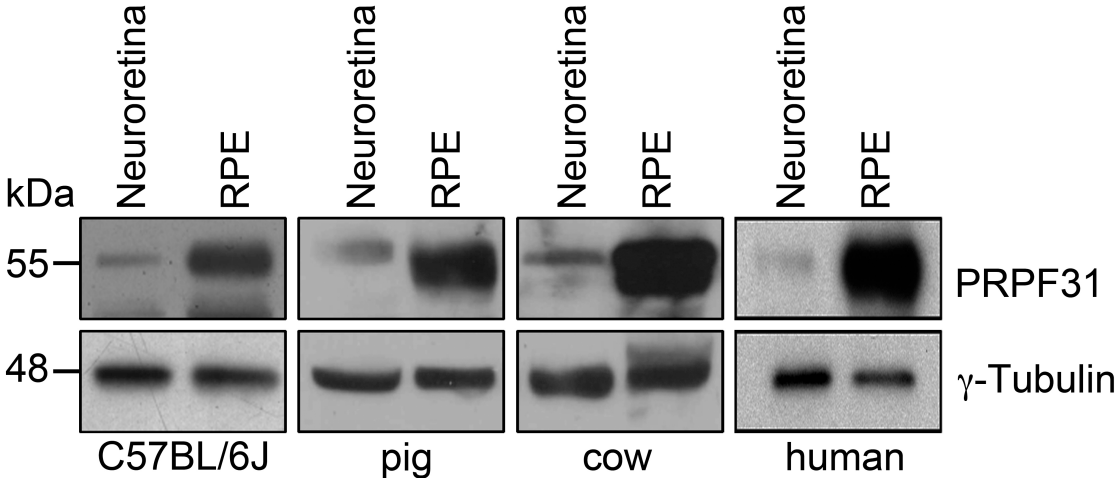
Supplementary Figure 1



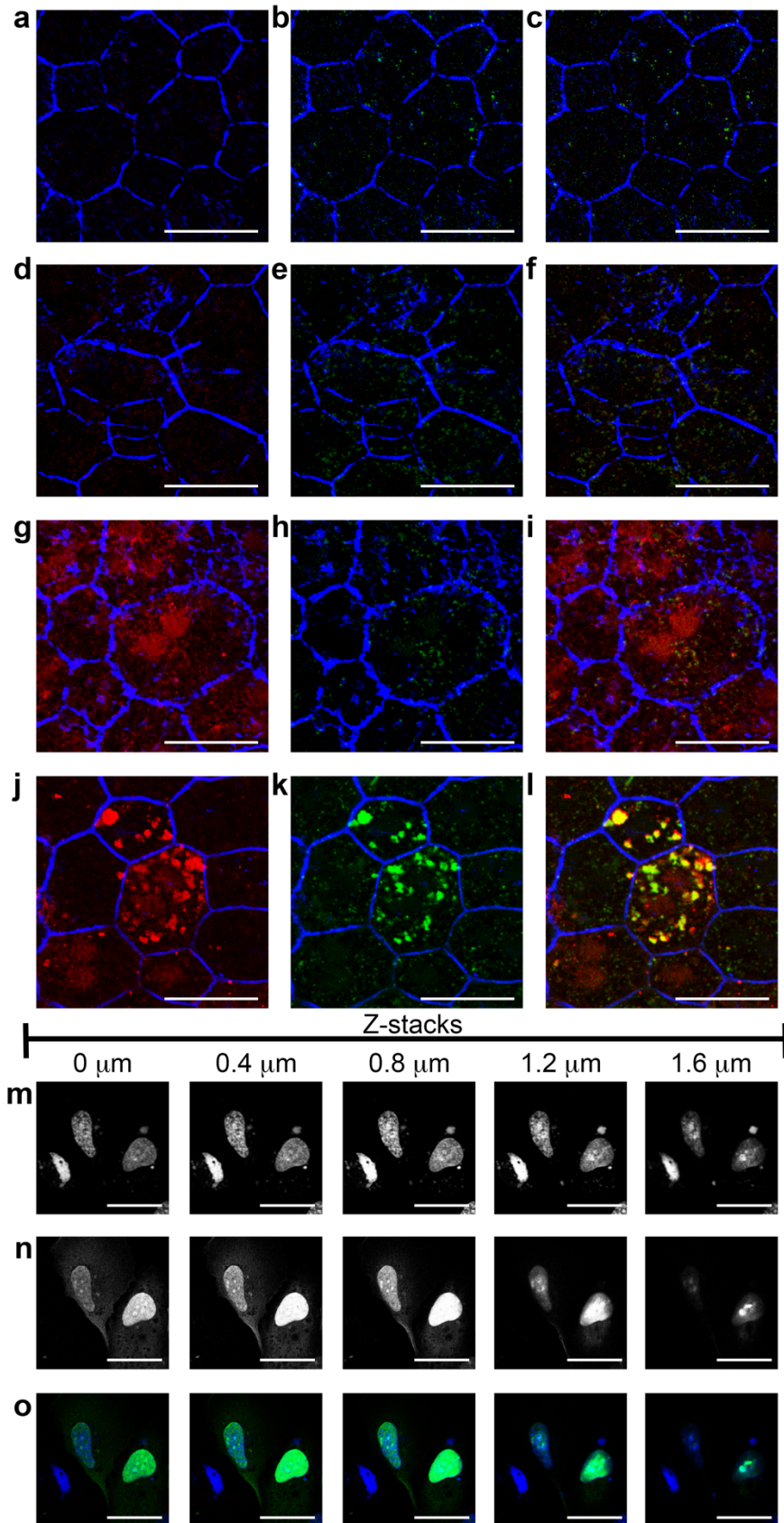
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



Supplementary Table 1: Gene ontology of differentially expressed genes in *Prpf31*^{A216P/+} mice. The top 20 terms of 84 are listed.

Term	Count (number of genes)	p-Value
Protein binding	123	<0.001
Nucleotide binding	51	0.089
Calcium ion binding	31	<0.001
Signal transducer activity	27	0.002
Protein domain specific binding	23	<0.001
Protein heterodimerization activity	22	0.004
Protein complex binding	20	<0.001
Ion channel activity	17	<0.001
Histone binding	14	<0.001
Voltage-gated ion channel activity	13	<0.001
Syntaxin binding	12	<0.001
Microtubule binding	12	0.004
Gtpase activity	12	0.005
Chloride channel activity	11	<0.001
Symporter activity	11	<0.001
Lyase activity	11	<0.001
Protein C-terminus binding	11	0.014
Extracellular ligand-gated ion channel activity	10	<0.001
Voltage-gated potassium channel activity	10	<0.001
Ion channelbinding	10	0.001

DAVID v6.8, GOTERM_MF_DIRECT category.

Supplementary Table 2: Candidate genes differentially expressed in the RPE of *Prpf31*^{A216P/+} vs WT mice. Default filter criteria, fold change < -2 or > 2 and *p*-value < 0.05.

Functional Categories	Signaling Pathways and Diseases	Up-regulated	Down-regulated
Cell adhesion and migration	PI3K-Akt-mTOR-signaling pathway	<i>Akt3, Vtn, Fgf11, Gnb1, Gngt1, Gng3, Ppp2r2b</i>	
	Focal adhesion	<i>Vtn, Shc3, Akt3</i>	
	Integrin-mediated cell adhesion	<i>Mapk10, Akt3, Shc3</i>	
	α 6- β 4 Integrin signaling pathway	<i>Prkca</i>	
Cell proliferation, differentiation and migration	MAPK signaling pathway	<i>Rasgrf2, Ppp3cc, Mapk10, Akt3</i>	<i>Il1a</i>
	Wnt signaling pathway	<i>Mapk10, Prkd1, Prkca, Akt3</i>	
Cellular apoptosis	Apoptosis modulation by HSP70	<i>Mapk10</i>	
	FAS pathway and stress induction of HSP regulation		<i>Il1a</i>
Cilium	Ciliogenesis	<i>Ahi1, Bbs4, Bbs7, Bbs9, Fam161a, Rp1, Rp111, Rpgrip1</i>	
Inflammation	Chemokine signaling pathway	<i>Shc3, Gnb1, Gnb3, Gnb5, Gngt, Grk1, Adcy1, Akt3</i>	
	Toll-like receptor signaling	<i>Mapk10, Akt3</i>	
	TNF- α NF- κ B signaling pathway	<i>Tnfaip3</i>	
	B cell receptor signaling pathway	<i>Prkd1</i>	
	T cell receptor signaling pathway	<i>Unc119</i>	
	IL-1 signaling pathway		<i>Il1a, Il1f8, Il1f9</i>
	IL-3 signaling pathway	<i>Dnm1, Prkca, Kcnip3</i>	
	IL-5 signaling pathway	<i>Unc119</i>	
	IL-6 signaling pathway	<i>Ppp2r2b</i>	
	Inflammatory response pathway	<i>Vnt</i>	
	mRNA Processing	mRNA processing	<i>Snrpn, Elavl3, Pcbp3, Pcbp4</i>
Oxidative stress	Oxidative stress	<i>Mapk10</i>	
	Keap1-Nrf2 pathway	<i>Prkca</i>	
Pluripotency	Wnt signaling pathway	<i>Prkca, Prkd1, Mapk10, Ppp2r2b</i>	
Protein metabolism	Proteasome degradation	<i>Uchl1</i>	
	Protein processing	<i>Hspa4l</i>	
Retinol metabolism	Retinol metabolism	<i>Rdh8, Rdh12</i>	
Voltage-gated channels	K ⁺ channel	<i>Kcnip3, Kcnma1, Kcnb1, Kcnab2</i>	<i>Kcnj13</i>
	Ca ²⁺ channel	<i>Cacna1f</i>	

Transcriptome Analysis Console Software and DAVID v6.8.

Supplementary Table 3: Functional categories of genes having alternative splicing in *Prpf31*^{A216P/+} mice. The top 40 terms of 174 are listed.

Term	Count (number of genes)	p-Value
Phosphoprotein	2676	<0.001
Membrane	2195	0.066
Alternative splicing	1929	<0.001
Cytoplasm	1499	<0.001
Nucleus	1394	<0.001
Glycoprotein	1117	<0.001
Coiledcoil	1113	<0.001
Metal-binding	1107	<0.001
Acetylation	908	<0.001
Disulfide bond	831	0.005
Transport	668	<0.001
Zinc	652	<0.001
Nucleotide-binding	647	<0.001
Transferase	558	<0.001
Transcription	553	<0.001
Transcription regulation	539	<0.001
Ubl conjugation	536	<0.001
ATP-binding	530	<0.001
Hydrolase	517	<0.001
Zinc-finger	482	<0.001
DNA-binding	451	<0.001
Cytoskeleton	406	<0.001
Calcium	375	<0.001
Methylation	371	<0.001
Isopeptide bond	346	<0.001
Cell projection	309	<0.001
Cell junction	308	<0.001
Developmental protein	303	<0.001
Ion transport	275	<0.001
Endoplasmic reticulum	268	0.068
Golgi apparatus	265	<0.001
Kinase	263	<0.001
Lipoprotein	253	<0.001
Differentiation	240	<0.001
Synapse	214	<0.001
Cell adhesion	211	<0.001
RNA-binding	205	<0.001
Cell cycle	198	<0.001
Activator	194	<0.001
Magnesium	191	<0.001

DAVID v6.8, UP_KEYWORDS category.

Supplementary Table 4: Number of candidate genes showing alternative splicing in the RPE of *Prpf31*^{A216P/+} vs WT mice. Default filter criteria, splicing index < -2 or > 2 and ANOVA *p* value < 0.05.

Functional Categories	Signaling Pathways and Diseases	High splicing index	Low splicing index	Total number of genes showing alternative splining
Angiogenesis	VEGF signaling pathway	1	0	1
Cell adhesion and migration	PI3K-Akt-mTOR-signaling pathway	47	69	116
	Focal adhesion	29	51	80
	Integrin-mediated cell adhesion	20	22	42
	α 6- β 4 Integrin signaling pathway	10	17	27
Cell proliferation, differentiation and migration	MAPK signaling pathway	29	21	50
	Wnt signaling pathway	18	13	31
Cellular apoptosis	Apoptosis modulation by HSP70	7	13	20
	FAS pathway and stress induction of HSP regulation	3	4	7
Cilium	Ciliogenesis	2	5	7
Inflammation	Chemokine signaling pathway	37	26	63
	Toll-like receptor signaling	10	17	27
	TNF- α NF- κ B signaling pathway	34	27	61
	B cell receptor signaling pathway	25	20	45
	T cell receptor signaling pathway	21	21	42
	IL-1 signaling pathway	2	7	9
	IL-3 signaling pathway	15	15	30
	IL-5 signaling pathway	9	13	22
	IL-6 signaling pathway	16	13	29
	Inflammatory response pathway	3	9	12
mRNA Processing	mRNA processing	72	30	102
Oxidative stress	Oxidative Stress	2	0	2
	Keap1-Nrf2 Pathway	2	0	2
Protein metabolism	Proteasome degradation	3	4	7
Pluripotency	Wnt signaling pathway	16	13	29
Retinol metabolism	Retinol metabolism	5	5	10

Transcriptome Analysis Console Software and DAVID v6.8