

Supplementary Tables

Supplementary Table S1. Primer sequences used for Sanger sequencing of *AIPL1* and *BBS2* coding exons.

Gene	Variant (amplicon, GRCh38)	Amplicon size (bp)	Primer	Sequence (5'→3')
<i>AIPL1</i>	p.R302L (chr17:6425523– 6425919)	397	AIPL1_F	TGCGGACAGCTCTGCAGATG
			AIPL1_R	GTCTTGGAGGCTGGTGAGTC
<i>BBS2</i>	p.P134R (chr16:56510995– 56511424)	430	BBS2_F	GAGAGGATTACACAAAACACG
			BBS2_R	AATGTGTGAGGCCACCCAC

Supplementary Table S2. Electrostatic Surface Potential and Charge Shift at Mutation Sites

Protein	Residue Change	APBS $\Delta\Phi$ (kT/e)	Surface Charge Shift	Functional Implication
<i>AIPL1</i>	R302 → L	−12.3	Positive → neutral	Loss of PDE6 γ interaction groove polarity
<i>BBS2</i>	P134 → R	+8.7	Neutral → positive	Charge repulsion near acidic residues

Supplementary Table S3. Electrostatic Potential Shift at Mutation Sites (APBS)

Protein	Residue Change	$\Delta\Phi$ (kT/e) @ Site	Surface Charge Shift	Functional Interpretation
<i>AIPL1</i>	R302 → L	−12.3	Positive → Neutral	Loss of positive groove for PDE6 γ
<i>BBS2</i>	P134 → R	+8.7	Neutral → Positive	Electrostatic clash at β - interface

Supplementary Table S4. Docking Score and Interface Metrics (HDOCK + SAMSON)

Complex Configuration	Docking Tool	Docking Score	Cluster Size	Interface Area (Å ²)	H-Bonds	Salt Bridges	ΔBSA (vs WT)
WT AIPL1 + WT BBS2	HDOCK	-176.4	42	1020	6	2	—
AIPL1 R302L + BBS2 P134R	HDOCK	-141.2	18	680	2	0	-33%
WT AIPL1 + BBS2 P134R	HDOCK	-163.1	29	860	4	1	-16%
AIPL1 R302L + WT BBS2	HDOCK	-150.2	21	740	3	1	-27%

Supplementary Table S5. AIPL1–BBS2 Complex Properties (SAMSON Analysis)

Complex Configuration	BSA (Å ²)	Interface RMSD (Å)	Interaction Hotspots	Visual Stability (Video)	Structural Outcome
WT	1020	—	Arg302 (AIPL1), Glu196 (BBS2)	Supplementary Video S2	Stable interface
Double mutant (R302L+P134R)	680	2.6	Leu302, Arg134 → clash	Supplementary Video S3	Interface deformation

Supplementary Table S6. Expression and Co-expression Profile of AIPL1 and BBS2 (EyeIntegration & GTEx)

Gene	Retina (TPM)	RPE (TPM)	Rods (log2FC)	Cones (log2FC)	Co-expression Partners (r > 0.8)
AIPL1	87.3	15.6	+3.8	+3.1	<i>PDE6A, RPGR, BBS9</i>
BBS2	42.1	10.3	+2.6	+2.0	<i>CEP290, BBS9, ARL6, IFT172</i>

Supplementary Table S7. Summary of Pathway Enrichment for AIPL1 and BBS2 Shared Interactors

Enriched GO Term	GO ID	Description	Genes Involved	FDR
Cilium morphogenesis	GO:0060271	Biogenesis and structure of primary cilium	<i>AIPL1, BBS2, CEP290, RPGR</i>	1.3×10^{-4}
Protein folding	GO:0006457	Assisted polypeptide folding	<i>AIPL1, HSP90AA1, DNAJB6</i>	4.6×10^{-3}
Photoreceptor outer segment organization	GO:0001750	Morphology of outer segment of rods/cones	<i>BBS2, BBS9, PDE6A, CNGB1</i>	6.1×10^{-4}

Supplementary Table S8. Co-Expression in Retinal Tissues (EyeIntegration v1.1)

Gene	Retina TPM	Rod-specific log2FC	Top Co-Expressed Genes	Shared Pathways
AIPL1	87.3	+3.8	<i>PDE6A, RPGR, BBS9</i>	Protein folding, phototransduction
BBS2	42.1	+2.6	<i>CEP290, IFT172, ARL6</i>	Ciliary trafficking

Supplementary Videos

Supplementary Video S1. Rotational animation of the wild-type AIPL1 protein structure highlighting the TPR domain surface topology.

Supplementary Video S2. Comparison of the wild-type and R302L mutant AIPL1, showing changes in electrostatic surface potential.

Supplementary Video S3. Dynamic visualization of BBS2 P134R variant highlighting distortion in the β -sheet core.