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Variant: NM_001034853.2:c.2506G>T

Version: 1.0

CA412730484

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: 9a4ea781-276b-4d23-9b77-0ba3841307c5
Approved on: 2025/9/5
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HGVS expressions

NM_001034853.2:c.2506G>T
NC_000023.11:g.38286493C>A
CM000685.2:g.38286493C>A
NC_000023.10:g.38145746C>A
CM000685.1:g.38145746C>A
NC_000023.9:g.38030690C>A
NG_009553.1:g.46043G>T
ENST00000494707.6:c.953+1372G>T
ENST00000642170.1:n.1826+4466G>T
ENST00000642395.2:c.1905+601G>T
ENST00000642739.1:c.1572+4466G>T
ENST00000644238.1:c.1386+4466G>T
ENST00000644337.1:c.1719+601G>T
ENST00000645032.1:c.2506G>T
ENST00000645124.1:c.*101+601G>T
ENST00000646020.1:c.*594+601G>T
ENST00000318842.11:c.1905+601G>T
ENST00000339363.7:c.2520+601G>T
ENST00000378505.6:c.2506G>T
ENST00000465127.1:c.172-379628C>A
ENST00000474584.5:c.*37+4466G>T
ENST00000482855.5:c.1905+601G>T
ENST00000494707.5:c.139+4466G>T
NM_000328.2:c.1905+601G>T
NM_001034853.1:c.2506G>T
NM_001367245.1:c.1902+601G>T
NM_001367246.1:c.1719+601G>T
NM_001367247.1:c.1572+4466G>T
NM_001367248.1:c.1602+4466G>T
NM_001367249.1:c.1569+4466G>T
NM_001367250.1:c.1569+4466G>T
NM_001367251.1:c.1386+4466G>T
NR_159803.1:n.2263+601G>T
NR_159804.1:n.1648+4466G>T
NR_159805.1:n.1714+4466G>T
NR_159806.1:n.1866+601G>T
NR_159807.1:n.1622+4466G>T

NR_159808.1:n.1826+4466G>T
NM_000328.3:c.1905+601G>T

Pathogenic

Met criteria codes 3

PM2_Supporting PP4 PVS1

Evidence Links 0

Expert Panel

X-linked Inherited Retinal Disease VCEP

Criteria Specification Information

Criteria Specification: *ClinGen X-linked Inherited Retinal Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RPGR Version 1.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

X-linked Inherited Retinal Disease VCEP

NM_001034853.2(RPGR):c.2506G>T (p.Glu836Ter) is a nonsense variant that introduces a premature stop in codon 836 within exon 15 of 15 that is predicted to disrupt a critical C-terminal region required for proper glutamylation of RPGR (PVS1, PMID: 36445968). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). At least one proband harboring this variant exhibits a phenotype including presentation with poor visual acuity (0.5 pts) with onset at age 3 years (1 pt), reduced rod electroretinogram responses, fundus appearance showing widespread retinal pigment epithelium degeneration with mid-periphery pigment deposits (0.5 pts), optic disc pallor (0.5 pts), cataract, severe macular degeneration, artery attenuation, and genotyping by next-generation sequencing with a panel of 483 genes identifying no alternative basis for retinal disease (2 pts), which together are specific for RPGR-related retinopathy (4.5 points, PMID: 36276946, PP4). In summary, this variant is classified as pathogenic for RPGR-related retinopathy based on the ClinGen X-linked Inherited Retinal Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RPGR Version 1.0.0; PVS1, PM2_Supporting, and PP4.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP4	✔	At least one proband harboring this variant exhibits a phenotype including Early onset at age 3 (1 pts), poor visual acuity (first symptom, 0.5 pts), reduced visual acuity- BCVA blind in both eyes, diminished responses on ERG (markedly reduced rod responses in all patients.), Fundus appearance shown with widespread retinal pigment epithelium degeneration, mid-periphery pigment deposits (0.5 pts), Optic disc pallor (0.5 pts), cataract, severe macular degeneration and artery attenuation, The NGS using IRD panel (HEDEP) of 483 IRD genes (2 pts), which together are specific for RPGR-related recessive retinopathy (4.5 points, PMID: 36276946, PP4).
PVS1	✔	This is a nonsense variant that introduces a premature stop codon between amino acids 1-1132 that is predicted to either trigger nonsense-mediated decay or to disrupt a critical C-terminal region required for proper glutamylation of RPGR (PVS1, PMID: 36445968).

Curation History

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