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Variant: NM_001034853.2:c.3001G>T

Version: 1.0

CA412729246

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: 9946c416-9919-4705-ae90-3520aade8508
Approved on: 2025/9/6
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HGVS expressions

NM_001034853.2:c.3001G>T
NC_000023.11:g.38285998C>A
CM000685.2:g.38285998C>A
NC_000023.10:g.38145251C>A
CM000685.1:g.38145251C>A
NC_000023.9:g.38030195C>A
NG_009553.1:g.46538G>T
ENST00000494707.6:c.953+1867G>T
ENST00000642170.1:n.1826+4961G>T
ENST00000642395.2:c.1905+1096G>T
ENST00000642739.1:c.1572+4961G>T
ENST00000644238.1:c.1386+4961G>T
ENST00000644337.1:c.1719+1096G>T
ENST00000645032.1:c.3001G>T
ENST00000645124.1:c.*101+1096G>T
ENST00000646020.1:c.*594+1096G>T
ENST00000318842.11:c.1905+1096G>T
ENST00000339363.7:c.2520+1096G>T
ENST00000378505.6:c.3001G>T
ENST00000465127.1:c.172-380123C>A
ENST00000474584.5:c.*37+4961G>T
ENST00000482855.5:c.1905+1096G>T
ENST00000494707.5:c.139+4961G>T
NM_000328.2:c.1905+1096G>T
NM_001034853.1:c.3001G>T
NM_001367245.1:c.1902+1096G>T
NM_001367246.1:c.1719+1096G>T
NM_001367247.1:c.1572+4961G>T
NM_001367248.1:c.1602+4961G>T
NM_001367249.1:c.1569+4961G>T
NM_001367250.1:c.1569+4961G>T
NM_001367251.1:c.1386+4961G>T
NR_159803.1:n.2263+1096G>T
NR_159804.1:n.1648+4961G>T
NR_159805.1:n.1714+4961G>T
NR_159806.1:n.1866+1096G>T
NR_159807.1:n.1622+4961G>T

NR_159808.1:n.1826+4961G>T
NM_000328.3:c.1905+1096G>T

Pathogenic

Met criteria codes 4

PP4 PVS1 PM2_Supporting PP1_Moderate

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.3001G>T (p.Glu1001Ter) is a nonsense variant that introduces a premature stop in codon 1001 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 night blindness (0.5 pts) with onset at age 5 years (1 pt), reduced visual acuity (0.5 pts), diminished electroretinogram responses from rods, fundus appearance showing pigment deposits (0.5 pts), visual field constriction (0.5 pts), optic disc pallor (0.5 pts), severe macular degeneration, artery attenuation, and genotyping by next-generation sequencing with a 483-gene panel showing no alternative basis for inherited retinal disease (2 pts), which together are specific for RPGR-related retinopathy (5.5 points, PMID: 36276946, PP4). The variant has been reported to segregate with retinal dystrophy through at least 5 affected meioses from 1 family (PP1_Moderate; PMID: 36276946). 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, PP1_Moderate, and PP4.

Met criteria codes

PP4	✔	At least one proband harboring this variant exhibits a phenotype including presentation with night blindness (0.5 pts) with onset at age 5 years (1 pt), reduced visual acuity (0.5 pts), diminished electroretinogram responses from rods, fundus appearance showing pigment deposits (0.5 pts), visual field constriction (0.5 pts), optic disc pallor (0.5 pts), severe macular degeneration, artery attenuation, and genotyping by next-generation sequencing with a 483-gene panel showing no alternative basis for inherited retinal disease (2 pts), which together are specific for RPGR-related retinopathy (5.5 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).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP1_Moderate	✔	The variant has been reported to segregate with retinal dystrophy through at least 5 affected meioses from 1 family (PP1_Moderate; PMID: 36276946)

Curation History

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