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Variant: NM_001034853.2(RPGR):c.2716G>T (p.Glu906Ter)

Version: 1.0

CA412729953

1802328 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: 26b9b762-0c19-4704-b79d-6a479456c88a
Approved on: 2025/9/5
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HGVS expressions

NM_001034853.2(RPGR):c.2716G>T (p.Glu906Ter)
NM_001034853.2:c.2716G>T
NC_000023.11:g.38286283C>A
CM000685.2:g.38286283C>A
NC_000023.10:g.38145536C>A
CM000685.1:g.38145536C>A
NC_000023.9:g.38030480C>A
NG_009553.1:g.46253G>T
ENST00000494707.6:c.953+1582G>T
ENST00000642170.1:n.1826+4676G>T
ENST00000642395.2:c.1905+811G>T
ENST00000642739.1:c.1572+4676G>T
ENST00000644238.1:c.1386+4676G>T
ENST00000644337.1:c.1719+811G>T
ENST00000645032.1:c.2716G>T
ENST00000645124.1:c.*101+811G>T
ENST00000646020.1:c.*594+811G>T
ENST00000318842.11:c.1905+811G>T
ENST00000339363.7:c.2520+811G>T
ENST00000378505.6:c.2716G>T
ENST00000465127.1:c.172-379838C>A
ENST00000474584.5:c.*37+4676G>T
ENST00000482855.5:c.1905+811G>T
ENST00000494707.5:c.139+4676G>T
NM_000328.2:c.1905+811G>T
NM_001034853.1:c.2716G>T
NM_001367245.1:c.1902+811G>T
NM_001367246.1:c.1719+811G>T
NM_001367247.1:c.1572+4676G>T
NM_001367248.1:c.1602+4676G>T
NM_001367249.1:c.1569+4676G>T
NM_001367250.1:c.1569+4676G>T
NM_001367251.1:c.1386+4676G>T
NR_159803.1:n.2263+811G>T
NR_159804.1:n.1648+4676G>T
NR_159805.1:n.1714+4676G>T
NR_159806.1:n.1866+811G>T

NR_159807.1:n.1622+4676G>T
NR_159808.1:n.1826+4676G>T
NM_000328.3:c.1905+811G>T

Pathogenic

Met criteria codes 5

PS4_Supporting | PP1_Moderate | PM2_Supporting | PVS1 | PP4

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.2716G>T (p.Glu906Ter) is a nonsense variant that introduces a premature stop in codon 906 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 hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). At least one proband harboring this variant exhibits a phenotype including family history consistent with X-linked inheritance (2 pts), first/second decade onset (1 pt), decreased visual acuity (0.5 pts), cone involvement greater than rod involvement consistent with the variant location after position c.2128 (1 pt), photophobia (1 pt), central scotoma / macular atrophy (1 pt), abnormal color vision (0.5 pts), and pigmentary retinopathy (0.5 pts), which together are specific for RPGR-related retinopathy (7.5 points, PMID: 29769798, PP4). This variant has been reported in at least 1 proband meeting one of the PS4 requirements of a male with some functional vision impairment by age 30 years and/or decreased or absent electroretinogram responses, in addition to the apparently unrelated proband previously used for the PP4 code (PMID: 17325176, PMID: 29769798, PMID: 22807293; PS4_Supporting). The variant has been reported to segregate with retinal dystrophy through at least 3 affected meioses from 1 family (PP1_Moderate; PMID: 22807293). 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, PS4_Supporting, PP4, and PP1_Moderate.

Met criteria codes

PS4_Supporting	✔	This variant has been reported in at least 1 proband meeting one of the PS4 requirements of a male with some functional vision impairment by age 30 and/or decreased or absent ERG responses, as well as a second apparently unrelated proband previously used for the PP4 code (PMIDs: 17325176,, 22807293; PS4_Supporting).
PP1_Moderate	✔	The variant has been reported to segregate with retinal dystrophy through at least 3 affected meioses from 1 family. (PP1_moderate; PMID: 22807293).
PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
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).

PP4		✔	At least one proband harboring this variant exhibits a phenotype including family history consistent with X-linked inheritance (2 pts), first/second decade onset (1 pt), cone>rod involvement after c.2128 (1 pt), photophobia (1 pt), central scotoma / macular atrophy, after c.2128 (1 pt), abnormal color vision (0.5 pt), abnormal BCVA / decreased vision acuity (0.5), and pigmentary retinopathy / "bull's eye maculopathy" (0.5 pt), which together are specific for RPGR-related retinopathy (7.5 points, PMID: 29769798, PP4_Supporting).

Curation History

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