Variant: NM_001034853.2(RPGR):c.2260G>T (p.Glu754Ter)

Version: 1.0

CA412731062

866844 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: dff94027-63b3-4acf-a68c-0e25e50e3cab
Approved on: 2025-08-28
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HGVS expressions

NM_001034853.2:c.2260G>T
NM_001034853.2(RPGR):c.2260G>T (p.Glu754Ter)
NC_000023.11:g.38286739C>A
CM000685.2:g.38286739C>A
NC_000023.10:g.38145992C>A
CM000685.1:g.38145992C>A
NC_000023.9:g.38030936C>A
NG_009553.1:g.45797G>T
ENST00000494707.6:c.953+1126G>T
ENST00000642170.1:n.1826+4220G>T
ENST00000642395.2:c.1905+355G>T
ENST00000642739.1:c.1572+4220G>T
ENST00000644238.1:c.1386+4220G>T
ENST00000644337.1:c.1719+355G>T
ENST00000645032.1:c.2260G>T
ENST00000645124.1:c.*101+355G>T
ENST00000646020.1:c.*594+355G>T
ENST00000318842.11:c.1905+355G>T
ENST00000339363.7:c.2520+355G>T
ENST00000378505.6:c.2260G>T
ENST00000465127.1:c.172-379382C>A
ENST00000474584.5:c.*37+4220G>T
ENST00000482855.5:c.1905+355G>T
ENST00000494707.5:c.139+4220G>T
NM_000328.2:c.1905+355G>T
NM_001034853.1:c.2260G>T
NM_001367245.1:c.1902+355G>T
NM_001367246.1:c.1719+355G>T
NM_001367247.1:c.1572+4220G>T
NM_001367248.1:c.1602+4220G>T
NM_001367249.1:c.1569+4220G>T
NM_001367250.1:c.1569+4220G>T
NM_001367251.1:c.1386+4220G>T
NR_159803.1:n.2263+355G>T
NR_159804.1:n.1648+4220G>T
NR_159805.1:n.1714+4220G>T
NR_159806.1:n.1866+355G>T

NR_159807.1:n.1622+4220G>T
NR_159808.1:n.1826+4220G>T
NM_000328.3:c.1905+355G>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.2260G>T (p.Glu754Ter) is a nonsense variant that introduces a premature stop codon 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) at age 7 (1 pt), pigment deposits (0.5 pts), optic disc pallor (0.5 pts), and genotyping by next-generation sequencing with a 483-gene panel finding 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 presentation with night blindness (0.5 pts) at age 7 (1 pt), pigment deposits (0.5 pts), optic disc pallor (0.5 pts), and genotyping by next-generation sequencing with a 483-gene panel finding no alternative basis for retinal disease (2 pts), which together are specific for RPGR-related retinopathy (4.5 points, PMID: 36276946, PP4).
PVS1	✓	This is a nonsense variant that introduces a premature stop codon within exon 15 of 15 that is predicted to disrupt a critical C-terminal region required for proper glutamylation of RPGR (PVS1, PMID: 36445968).

Curation History

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