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Variant: NM_001034853.2(RPGR):c.1541C>G (p.Ser514Ter)

Version: 1.0

CA412737625

1213922 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: c166ad14-610c-4ad8-99a3-c52476741955
Approved on: 2025/8/1
Published on: 2025/8/2

HGVS expressions

NM_001034853.2:c.1541C>G
NM_001034853.2(RPGR):c.1541C>G (p.Ser514Ter)
NC_000023.11:g.38290990G>C
CM000685.2:g.38290990G>C
NC_000023.10:g.38150243G>C
CM000685.1:g.38150243G>C
NC_000023.9:g.38035187G>C
NG_009553.1:g.41546C>G
ENST00000494707.6:c.745C>G
ENST00000642170.1:n.1795C>G
ENST00000642395.2:c.1541C>G
ENST00000642739.1:c.1541C>G
ENST00000644238.1:c.1355C>G
ENST00000644337.1:c.1355C>G
ENST00000645032.1:c.1541C>G
ENST00000645124.1:c.1541C>G
ENST00000646020.1:c.*234C>G
ENST00000318842.11:c.1541C>G
ENST00000339363.7:c.1541C>G
ENST00000378505.6:c.1541C>G
ENST00000465127.1:c.172-375131G>C
ENST00000474584.5:c.*6C>G
ENST00000482855.5:c.1541C>G
ENST00000494707.5:c.108C>G
NM_000328.2:c.1541C>G
NM_001034853.1:c.1541C>G
NM_001367245.1:c.1538C>G
NM_001367246.1:c.1355C>G
NM_001367247.1:c.1541C>G
NM_001367248.1:c.1571C>G
NM_001367249.1:c.1538C>G
NM_001367250.1:c.1538C>G
NM_001367251.1:c.1355C>G
NR_159803.1:n.1903C>G
NR_159804.1:n.1617C>G
NR_159805.1:n.1683C>G
NR_159806.1:n.1683C>G

NR_159807.1:n.1591C>G
NR_159808.1:n.1795C>G
NM_000328.3:c.1541C>G

Pathogenic

Met criteria codes 3

PP4 PM2_Supporting 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.1541C>G (p.Ser514Ter) is a nonsense variant that substitutes a premature stop codon for amino acid 514 within exon 13 of 15 and is predicted to trigger nonsense-mediated decay (PVS1). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). At least one proband harboring this variant exhibits a phenotype including early onset (1 pt), night blindness (0.5 pts), reduction in visual acuity (0.5 pts), pigment deposits (0.5 pts), and genotyping by next-generation sequencing panel of 483 genes finding no alternative explanation for retinal disease (2 pts), which together are specific for RPGR-related retinopathy (4.5 pts, 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. (date of approval 05/16/2025).

Met criteria codes

PP4	✔	At least one proband harboring this variant exhibits a phenotype including NGS with a panel of 483 genes (2 pts), early onset (1 pt), night blindness (0.5 pts), reduction in visual acuity (0.5 pts), pigment deposits (0.5 pts), which together are specific for RPGR-related retinopathy (4.5 pts, PMID: 36276946, PP4).
PM2_Supporting	✔	This variant is absent from 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).

Curation History

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