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Variant: NM_001034853.2:c.2080A>T

Version: 1.0

CA412731500

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: 0bfa08a9-98f4-446a-abe4-019f10c3c0c4
Approved on: 2025/9/7
Published on: 2025/9/7

HGVS expressions

NM_001034853.2:c.2080A>T
NC_000023.11:g.38286919T>A
CM000685.2:g.38286919T>A
NC_000023.10:g.38146172T>A
CM000685.1:g.38146172T>A
NC_000023.9:g.38031116T>A
NG_009553.1:g.45617A>T
ENST00000494707.6:c.953+946A>T
ENST00000642170.1:n.1826+4040A>T
ENST00000642395.2:c.1905+175A>T
ENST00000642739.1:c.1572+4040A>T
ENST00000644238.1:c.1386+4040A>T
ENST00000644337.1:c.1719+175A>T
ENST00000645032.1:c.2080A>T
ENST00000645124.1:c.*101+175A>T
ENST00000646020.1:c.*594+175A>T
ENST00000318842.11:c.1905+175A>T
ENST00000339363.7:c.2520+175A>T
ENST00000378505.6:c.2080A>T
ENST00000465127.1:c.172-379202T>A
ENST00000474584.5:c.*37+4040A>T
ENST00000482855.5:c.1905+175A>T
ENST00000494707.5:c.139+4040A>T
NM_000328.2:c.1905+175A>T
NM_001034853.1:c.2080A>T
NM_001367245.1:c.1902+175A>T
NM_001367246.1:c.1719+175A>T
NM_001367247.1:c.1572+4040A>T
NM_001367248.1:c.1602+4040A>T
NM_001367249.1:c.1569+4040A>T
NM_001367250.1:c.1569+4040A>T
NM_001367251.1:c.1386+4040A>T
NR_159803.1:n.2263+175A>T
NR_159804.1:n.1648+4040A>T
NR_159805.1:n.1714+4040A>T
NR_159806.1:n.1866+175A>T
NR_159807.1:n.1622+4040A>T

NR_159808.1:n.1826+4040A>T
NM_000328.3:c.1905+175A>T

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 1

PS4

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.2080A>T (p.Lys694Ter) is a nonsense variant introducing a premature stop in codon 694 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). This variant has been reported in at least 2 apparently unrelated probands (PMID: 31953110, PMID: 14564670), however, the number of individuals meeting one of the PS4 requirements of some functional vision impairment in affected males by age 30 years, and/or decreased or absent cone and/or rod electroretinogram responses was fewer than the requirement of at least 2 unrelated probands, so PS4_Supporting was not met. In summary, this variant is classified as likely 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 and PM2_Supporting.

Met criteria codes

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 v4.0.0 (PM2_Supporting).

Not Met criteria codes

PS4	✖	This variant has been reported in at least 2 apparently unrelated probands (PMID: 31953110 and PMID: 14564670). However, the number of individuals meeting the PS4 requirement of some functional vision impairment in affected males by age 30, with decreased or absent cone and/or rod ERG responses was fewer than the requirement of at least 2 unrelated probands, so PS4_Supporting was not met.

Curation History

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