

Variant: *NM_001034853.2:c.2176G>T*

Version: 1.0

CA412731265 [↗](#)

Gene: RPGR ([HGNC:6103](#))

Condition: RPGR-related retinopathy ([MONDO:0100437](#))

Inheritance Mode: X-linked inheritance

UUID: 78072885-ea95-440e-981a-a7296e774d0e

Approved on: 2025/8/3

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HGVS expressions

NM_001034853.2:c.2176G>T

NC_000023.11:g.38286823C>A

CM000685.2:g.38286823C>A

NC_000023.10:g.38146076C>A

CM000685.1:g.38146076C>A

NC_000023.9:g.38031020C>A

NG_009553.1:g.45713G>T

ENST00000494707.6:c.953+1042G>T

ENST00000642170.1:n.1826+4136G>T

ENST00000642395.2:c.1905+271G>T

ENST00000642739.1:c.1572+4136G>T

ENST00000644238.1:c.1386+4136G>T

ENST00000644337.1:c.1719+271G>T

ENST00000645032.1:c.2176G>T

ENST00000645124.1:c.*101+271G>T

ENST00000646020.1:c.*594+271G>T

ENST00000318842.11:c.1905+271G>T

ENST00000339363.7:c.2520+271G>T

ENST00000378505.6:c.2176G>T

ENST00000465127.1:c.172-379298C>A

ENST00000474584.5:c.*37+4136G>T

ENST00000482855.5:c.1905+271G>T

ENST00000494707.5:c.139+4136G>T

NM_000328.2:c.1905+271G>T

NM_001034853.1:c.2176G>T

NM_001367245.1:c.1902+271G>T

NM_001367246.1:c.1719+271G>T

NM_001367247.1:c.1572+4136G>T

NM_001367248.1:c.1602+4136G>T

NM_001367249.1:c.1569+4136G>T

NM_001367250.1:c.1569+4136G>T

NM_001367251.1:c.1386+4136G>T

NR_159803.1:n.2263+271G>T

NR_159804.1:n.1648+4136G>T

NR_159805.1:n.1714+4136G>T

NR_159806.1:n.1866+271G>T

NR_159807.1:n.1622+4136G>T

NR_159808.1:n.1826+4136G>T
NM_000328.3:c.1905+271G>T

Pathogenic

Met criteria codes 3

PS4_Supporting

PM2_Supporting

PVS1

Not Met criteria codes 7

BS1

BP3

BP7

PS1

BA1

PM5

PM4

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.2176G>T (p.Glu726Ter) is a nonsense variant that substitutes a premature stop codon for amino acid 726 within exon 15 of 15, which disrupts 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 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, or a female with functional visual abnormality and documentation of a male relative affected with retinitis pigmentosa (PMID: 21857984, PMID: 17325176, PS4_Supporting). 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, PS4_Supporting, and PM2_Supporting. (date of approval 05/16/2025).

Met criteria codes

PS4_Supporting



This variant has been reported in at least 2 apparently unrelated probands meeting one of the PS4 requirements of a male with some functional vision impairment by age 30 and/or decreased or absent ERG responses, or a female with functional visual abnormality and documentation of a male relative affected with retinitis pigmentosa (PMID: 21857984, PMID: 17325176, PS4_Supporting).

PM2_Supporting



This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

PVS1



This is a nonsense variant 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).

Not Met criteria codes

BS1



No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BP3			No indels
BP7			Causes amino acid change so not silent
PS1			Not previously curated
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			Not previously curated
PM4			No indels

Curation History 		
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