

Variant: *NM\_001034853.2:c.122C>G*

Version: 1.0

CA412745793 [↗](#)

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

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

**Inheritance Mode:** X-linked inheritance

**UUID:** 9825e969-0cc1-4750-a89a-659f26690b3b

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### *HGVS expressions*

**NM\_001034853.2:c.122C>G**

NC\_000023.11:g.38323431G>C

CM000685.2:g.38323431G>C

NC\_000023.10:g.38182684G>C

CM000685.1:g.38182684G>C

NC\_000023.9:g.38067628G>C

NG\_009553.1:g.9105C>G

ENST00000642170.1:n.532C>G

ENST00000642373.1:c.122C>G

ENST00000642395.2:c.122C>G

ENST00000642558.1:c.122C>G

ENST00000642739.1:c.122C>G

ENST00000644238.1:c.122C>G

ENST00000644337.1:c.122C>G

ENST00000645032.1:c.122C>G

ENST00000645124.1:c.122C>G

ENST00000646020.1:c.122C>G

ENST00000647261.1:c.122C>G

ENST00000318842.11:c.122C>G

ENST00000339363.7:c.122C>G

ENST00000378505.6:c.122C>G

ENST00000465127.1:c.172-342690G>C

ENST00000474584.5:c.122C>G

ENST00000482855.5:c.122C>G

NM\_000328.2:c.122C>G

NM\_001034853.1:c.122C>G

NM\_001367245.1:c.122C>G

NM\_001367246.1:c.122C>G

NM\_001367247.1:c.122C>G

NM\_001367248.1:c.152C>G

NM\_001367249.1:c.122C>G

NM\_001367250.1:c.122C>G

NM\_001367251.1:c.122C>G

NR\_159803.1:n.264C>G

NR\_159804.1:n.264C>G

NR\_159805.1:n.264C>G

NR\_159806.1:n.264C>G

NR\_159807.1:n.264C>G  
NR\_159808.1:n.532C>G  
NM\_000328.3:c.122C>G

Likely Pathogenic

Met criteria codes 2

PM2\_Supporting PVS1

Not Met criteria codes 2

PP1 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.122C>G (p.Ser41Ter) is a nonsense variant that substitutes a premature stop codon for amino acid 41 in exon 2 of 15 and is predicted to trigger nonsense-mediated decay (PVS1). This variant is absent from gnomAD v4.1.0 (PM2\_Supporting). The variant has been reported to segregate with retinal dystrophy through at least 1 affected meiosis from 1 family, but details are not sufficient to meet the PP1 code (PMID: 16969763). This variant has been reported in at least 2 apparently unrelated probands (PMIDs: 34745198, 16969763). 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 ERG 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. (date of approval 05/16/2025).

### Met criteria codes

PM2\_Supporting  

This variant is absent from gnomAD v2.1.1 (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).

### Not Met criteria codes

PP1  

The variant has been reported to segregate with retinal dystrophy through at least 1 affected meiosis from 1 family (PMID: 16969763).

PS4  

This variant has been reported in at least 2 apparently unrelated probands (PMIDs: 34745198, 16969763). 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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