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Variant: NM_001034853.2(RPGR):c.154G>A (p.Gly52Arg)

Version: 1.0

CA412745725

593841 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: df740ed6-94dd-4c52-bccb-3fcc306802e1
Approved on: 2025/9/7
Published on: 2025/9/7

HGVS expressions

NM_001034853.2:c.154G>A
NM_001034853.2(RPGR):c.154G>A (p.Gly52Arg)
NC_000023.11:g.38323399C>T
CM000685.2:g.38323399C>T
NC_000023.10:g.38182652C>T
CM000685.1:g.38182652C>T
NC_000023.9:g.38067596C>T
NG_009553.1:g.9137G>A
ENST00000642170.1:n.564G>A
ENST00000642373.1:c.154G>A
ENST00000642395.2:c.154G>A
ENST00000642558.1:c.154G>A
ENST00000642739.1:c.154G>A
ENST00000644238.1:c.154G>A
ENST00000644337.1:c.154G>A
ENST00000645032.1:c.154G>A
ENST00000645124.1:c.154G>A
ENST00000646020.1:c.154G>A
ENST00000647261.1:c.154G>A
ENST00000318842.11:c.154G>A
ENST00000339363.7:c.154G>A
ENST00000378505.6:c.154G>A
ENST00000465127.1:c.172-342722C>T
ENST00000474584.5:c.154G>A
ENST00000482855.5:c.154G>A
NM_000328.2:c.154G>A
NM_001034853.1:c.154G>A
NM_001367245.1:c.154G>A
NM_001367246.1:c.154G>A
NM_001367247.1:c.154G>A
NM_001367248.1:c.184G>A
NM_001367249.1:c.154G>A
NM_001367250.1:c.154G>A
NM_001367251.1:c.154G>A
NR_159803.1:n.296G>A
NR_159804.1:n.296G>A
NR_159805.1:n.296G>A

NR_159806.1:n.296G>A
NR_159807.1:n.296G>A
NR_159808.1:n.564G>A
NM_000328.3:c.154G>A

Pathogenic

Met criteria codes 5

PP1_Strong | PS4 | PP3 | PP4 | PM2_Supporting

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.154G>A (p.Gly52Arg) is an apparent missense variant encoding the substitution of glycine with arginine at amino acid 52, and is located in the final nucleotide of exon 2. The splicing impact predictor SpliceAI gives a score of 0.66 for splice donor loss, which is above the ClinGen X-linked IRD VCEP recommended threshold of ≥0.2 and predicts a damaging impact on splicing (PP3). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). At least one proband harboring this variant exhibits a phenotype including diagnosis of retinitis pigmentosa with electroretinogram responses characteristic of rod-cone dystrophy (1 pt), genotyping by exome sequencing identifying no alternative basis for inherited retinal disease (2 pts), visual field changes (0.5 pts), and fundus abnormalities (0.5 pts), which together are specific for RPGR-related retinopathy (4 points, PMID: 33372982, PP4). The variant has been reported to segregate with retinal dystrophy through at least 4 affected meioses from 2 families (PP1_Strong; PMID: 22888088, DOI 10.1055/s-0044-1779398). This variant has been reported in at least 6 apparently unrelated probands meeting one of the PS4 requirements of some functional vision impairment in affected males by age 30 years, and/or decreased or absent electroretinogram responses (PMID: 16969763, PMID: 22888088, PMID: 35432464, PMID: 36445968, PMID: 28559085, DOI 10.1055/s-0044-1779398, PS4_Strong). Other publications have reported probands carrying this variant but did not meet the requirements for inclusion in the PS4 code (PMID: 34985506, PMID: 31213501, PMID: 37798099, PMID: 33372982). 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; PM2_Supporting, PP3, PP4, PP1_Strong, and PS4.

Met criteria codes

PP1_Strong	✔	The variant has been reported to segregate with retinal dystrophy through at least 4 affected meioses from 2 families. (PP1_Strong; PMID: 22888088, DOI 10.1055/s-0044-1779398).
PS4	✔	This variant has been reported in at least 6 apparently unrelated probands 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 (PMIDs: 16969763, 22888088, 35432464, 36445968, 28559085, DOI 10.1055/s-0044-1779398, PS4_Strong). Other publications reported proband carrying this variant but failed to meet the requirements of the PS4 code (PMIDs: 34985506, 31213501, 37798099, 33372982).

PP3		✔	The splicing impact predictor SpliceAI gives a score of 0.66 (donor loss), which is above the ClinGen X-linked IRD VCEP recommended threshold of ≥0.2 and predicts a damaging impact on splicing (PP3).
PP4		✔	At least one proband harboring this variant exhibits a phenotype including diagnosis of retinitis pigmentosa with electroretinogram responses characteristic of rod-cone dystrophy (1 pt), genotyping by exome sequencing excluding an alternative basis for inherited retinal disease (2 pts), visual field changes (0.5 pts), and fundus abnormalities (0.5 pts), which together are specific for RPGR-related retinopathy (4 points, PMID: 33372982, PP4).
PM2_Supporting		✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History

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