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Variant: NM_001034853.2(RPGR):c.485_486del (p.Phe162fs)

Version: 1.0

CA226423

98787 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: 8cecca83-4d65-49fe-86ff-13a3e33c052d
Approved on: 2025/9/7
Published on: 2025/9/7

HGVS expressions

NM_001034853.2(RPGR):c.485_486del (p.Phe162fs)
NM_001034853.2:c.485_486del
NC_000023.11:g.38317452_38317453del
CM000685.2:g.38317452_38317453del
NC_000023.10:g.38176705_38176706del
CM000685.1:g.38176705_38176706del
NC_000023.9:g.38061649_38061650del
NG_009553.1:g.15086_15087del
ENST00000642170.1:n.895_896del
ENST00000642373.1:c.*64_*65del
ENST00000642395.2:c.485_486del
ENST00000642558.1:c.392_393del
ENST00000642739.1:c.485_486del
ENST00000644238.1:c.485_486del
ENST00000644337.1:c.485_486del
ENST00000645032.1:c.485_486del
ENST00000645124.1:c.485_486del
ENST00000646020.1:c.485_486del
ENST00000647261.1:c.485_486del
ENST00000318842.11:c.485_486del
ENST00000339363.7:c.485_486del
ENST00000378505.6:c.485_486del
ENST00000465127.1:c.172-348669_172-348668del
ENST00000470183.1:n.178_179del
ENST00000474584.5:c.485_486del
ENST00000482855.5:c.485_486del
NM_000328.2:c.485_486del
NM_001034853.1:c.485_486del
NM_001367245.1:c.485_486del
NM_001367246.1:c.485_486del
NM_001367247.1:c.485_486del
NM_001367248.1:c.515_516del
NM_001367249.1:c.482_483del
NM_001367250.1:c.485_486del
NM_001367251.1:c.485_486del
NR_159803.1:n.627_628del
NR_159804.1:n.627_628del

NR_159805.1:n.627_628del
NR_159806.1:n.627_628del
NR_159807.1:n.627_628del
NR_159808.1:n.895_896del
NM_000328.3:c.485_486del

Pathogenic

Met criteria codes 5

PM2_Supporting | PP4 | PVS1 | PS4_Supporting | PP1_Moderate

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.485_486del (p.Phe162TyrfsTer4) is a frameshift variant due to a 2-nucleotide deletion resulting in a premature stop codon after 4 amino acids within exon 6 of 15, which is predicted to trigger nonsense-mediated decay (PVS1). 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: 17325176, PMID: 32795431; PS4_Supporting). At least one proband harboring this variant exhibits a phenotype including onset in the first or second decade of life (1 pt), night blindness (0.5 pts), reduced visual acuity (0.5 pts), visual field constriction (0.5 pts), and myopia (0.5 pts), with a family history consistent with X-linked inheritance (2 pts), which together are specific for RPGR-related retinopathy (5 points, PMID: 26197217, PP4). The variant has been reported to segregate with retinal dystrophy through at least 6 affected meioses from 1 family (PP1_Moderate; PMID: 26197217). 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, PM2_Supporting, PP1_Moderate, and PP4.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PP4	✔	At least one proband harboring this variant exhibits a phenotype including X-linked inheritance (2 pts), female present phenotypes (1 pt), early onset (1 pt), night blindness (0.5 pts), reduce visual acuity (0.5 pts), visual filed constrictions (0.5 pts), myopia (0.5 pts), which together are specific for RPGR-related retinopathy (6 points, PP4).
PVS1	✔	This is a frameshift 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).
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 (PMIDs: 17325176, 32795431; PS4_Supporting).

PP1_Moderate ✔ The variant has been reported to segregate with retinal dystrophy through at least 3 affected meioses from 1 family. (PP1; PMID: 26197217).

Curation History

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