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Variant: NM_001034853.2(RPGR):c.1872_1873del (p.Glu624fs)

Version: 1.0

CA1139667436

872283 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance (dominant (HP:0001423))
UUID: 167bd9f4-65e2-4e0f-80d5-401e99ae19dd
Approved on: 2025/10/5
Published on: 2025/10/6

HGVS expressions

NM_001034853.2(RPGR):c.1872_1873del (p.Glu624fs)
NM_001034853.2:c.1872_1873del
NC_000023.11:g.38287129_38287130del
CM000685.2:g.38287129_38287130del
NC_000023.10:g.38146382_38146383del
CM000685.1:g.38146382_38146383del
NC_000023.9:g.38031326_38031327del
NG_009553.1:g.45409_45410del
ENST00000494707.6:c.953+738_953+739del
ENST00000642170.1:n.1826+3832_1826+3833del
ENST00000642395.2:c.1872_1873del
ENST00000642739.1:c.1572+3832_1572+3833del
ENST00000644238.1:c.1386+3832_1386+3833del
ENST00000644337.1:c.1686_1687del
ENST00000645032.1:c.1872_1873del
ENST00000645124.1:c.*68_*69del
ENST00000646020.1:c.*561_*562del
ENST00000318842.11:c.1872_1873del
ENST00000339363.7:c.2487_2488del
ENST00000378505.6:c.1872_1873del
ENST00000465127.1:c.172-378992_172-378991del
ENST00000474584.5:c.*37+3832_*37+3833del
ENST00000482855.5:c.1872_1873del
ENST00000494707.5:c.139+3832_139+3833del
NM_000328.2:c.1872_1873del
NM_001034853.1:c.1872_1873del
NM_001367245.1:c.1869_1870del
NM_001367246.1:c.1686_1687del
NM_001367247.1:c.1572+3832_1572+3833del
NM_001367248.1:c.1602+3832_1602+3833del
NM_001367249.1:c.1569+3832_1569+3833del
NM_001367250.1:c.1569+3832_1569+3833del
NM_001367251.1:c.1386+3832_1386+3833del
NR_159803.1:n.2230_2231del
NR_159804.1:n.1648+3832_1648+3833del

NR_159805.1:n.1714+3832_1714+3833del
NR_159806.1:n.1833_1834del
NR_159807.1:n.1622+3832_1622+3833del
NR_159808.1:n.1826+3832_1826+3833del
NM_000328.3:c.1872_1873del

Pathogenic

Met criteria codes 5

PP1 PP4 PVS1 PM2_Supporting PS4_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.1872_1873del (p.Glu624AspfsTer5) is a frameshift variant due to a two-nucleotide deletion that introduces a premature stop codon within exon 15 of 15 that is predicted to disrupt a critical C-terminal region required for proper function of RPGR (PVS1, PMID: 36445968). This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). At least one proband harboring this variant exhibits a phenotype including early onset (1 pt), night blindness (0.5 pts), electroretinogram responses consistent with retinitis pigmentosa, and reduced visual fields (0.5 pts), with genotyping by next-generation sequencing identifying no alternative basis for retinal disease (2 pts), which together are specific for RPGR-related retinopathy (4 points, ClinVar Accession: SCV001427266.1, PP4). This variant has been reported in at least 1 proband meeting one of the PS4 requirements of some functional vision impairment in affected males by age 30 years, and/pr decreased or absent electroretinogram responses (PMID: 34745198), in addition to the proband previously used to meet the PP4 code (ClinVar Accession: SCV001427266.1) (PS4_Supporting). This variant has been reported in at least 6 other apparently unrelated probands (PMID: 34985506, PMID: 37217489, PMID: 12657579, PMID: 12402343, PMID: 32531858, PMID: 30902645, ClinVar Accession: SCV001427266.1) who were not described in sufficient detail for inclusion in PS4. The variant has been reported to segregate with retinal dystrophy through an affected mother and son (PP1; PMID: 34745198). 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, PM2_Supporting, PP4, PS4_Supporting, and PP1.

Met criteria codes

PP1	✔	The variant has been reported to segregate with retinal dystrophy through an affected mother and son (PP1; PMID: 34745198).
PP4	✔	At least one proband harboring this variant exhibits a phenotype including early onset (1 pt), night blindness (0.5 pts), electroretinogram responses consistent with retinitis pigmentosa, and reduced visual fields (0.5 pts), with genotyping by next-generation sequencing identifying no alternative basis for retinal disease (2 pts), which together are specific for RPGR-related retinopathy (4 points, ClinVar Accession: SCV001427266.1, PP4).
PVS1	✔	

This is a frameshift variant due to a two-nucleotide deletion that introduces a premature stop codon within exon 15 of 15 that is predicted to disrupt a critical C-terminal region required for proper function of RPGR (PVS1, PMID: 36445968).

PM2_Supporting	✔	his variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PS4_Supporting	✔	This variant has been reported in at least 1 proband meeting one of the PS4 requirements of some functional vision impairment in affected males by age 30 years, and/pr decreased or absent electroretinogram responses (PMID: 34745198), in addition to the proband previously used to meet the PP4 code (ClinVar Accession: SCV001427266.1) (PS4_Supporting). This variant has been reported in at least 6 other apparently unrelated probands (PMID: 34985506, PMID: 37217489, PMID: 12657579, PMID: 12402343, PMID: 32531858, PMID: 30902645, ClinVar Accession: SCV001427266.1) who were not described in sufficient detail for inclusion in PS4.

Curation History

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