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Variant: NM_001034853.2(RPGR):c.1234C>T (p.Arg412Ter)

Version: 1.0

CA412739725

636102 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance (dominant (HP:0001423))
UUID: 115b1910-d7a5-4ec6-9078-0ce71bb7d8bb
Approved on: 2025/10/5
Published on: 2025/10/5

HGVS expressions

NM_001034853.2(RPGR):c.1234C>T (p.Arg412Ter)
NM_001034853.2:c.1234C>T
NC_000023.11:g.38298967G>A
CM000685.2:g.38298967G>A
NC_000023.10:g.38158220G>A
CM000685.1:g.38158220G>A
NC_000023.9:g.38043164G>A
NG_009553.1:g.33569C>T
ENST00000494707.6:c.438C>T
ENST00000642170.1:n.1488C>T
ENST00000642395.2:c.1234C>T
ENST00000642739.1:c.1234C>T
ENST00000644238.1:c.1060-1515C>T
ENST00000644337.1:c.1060-1515C>T
ENST00000645032.1:c.1234C>T
ENST00000645124.1:c.1234C>T
ENST00000646020.1:c.1294C>T
ENST00000318842.11:c.1234C>T
ENST00000339363.7:c.1234C>T
ENST00000378505.6:c.1234C>T
ENST00000464437.1:c.300C>T
ENST00000465127.1:c.172-367154G>A
ENST00000474584.5:c.1234C>T
ENST00000482855.5:c.1234C>T
ENST00000494841.1:n.497C>T
NM_000328.2:c.1234C>T
NM_001034853.1:c.1234C>T
NM_001367245.1:c.1231C>T
NM_001367246.1:c.1060-1515C>T
NM_001367247.1:c.1234C>T
NM_001367248.1:c.1264C>T
NM_001367249.1:c.1231C>T
NM_001367250.1:c.1231C>T
NM_001367251.1:c.1060-1515C>T
NR_159803.1:n.1436C>T
NR_159804.1:n.1285C>T
NR_159805.1:n.1376C>T

NR_159806.1:n.1376C>T
NR_159807.1:n.1376C>T
NR_159808.1:n.1488C>T
NM_000328.3:c.1234C>T

Pathogenic

Met criteria codes 5

PVS1 PP1 PP4 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.1234C>T (p.Arg412Ter) is a nonsense variant that introduces a premature stop codon in exon 10 of 15, which is predicted to trigger nonsense-mediated decay (PVS1). 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 a family history consistent with X-linked inheritance showing no male-to-male transmission (2 pts) and female carriers showing milder symptoms (1 pt), night blindness (0.5 pts), visual acuity reduction (0.5 pts), myopia (0.5 pts), and non-recordable electroretinogram responses, with genotyping by whole exome sequencing panel identifying no alternative basis for retinal disease (2 pts), which together are specific for RPGR-related retinopathy (6.5 points, PMID: 32702353, PP4). This variant has been reported in at least 1 proband 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, as well as a second apparently unrelated proband previously used for the PP4 code (PMID: 24938718, PMID: 34745198, PMID: 32702353, PS4_Supporting). The variant has been reported to segregate with retinal dystrophy through at least 2 affected meioses from at least 1 family (PP1; PMID: 24938718). 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, PP1, PP4, and PS4_Supporting.

Met criteria codes

PVS1	✔	This is a nonsense variant that introduces a premature stop codon in exon 10 of 15, which is predicted to trigger nonsense-mediated decay (PVS1).
PP1	✔	The variant has been reported to segregate with retinal dystrophy through at least 2 affected meioses from at least 1 family (PP1; PMID: 24938718).
PP4	✔	At least one proband harboring this variant exhibits a phenotype including a family history consistent with X-linked inheritance showing no male-to-male transmission (2 pts) and female carriers showing milder symptoms (1 pt), night blindness (0.5 pts), visual acuity reduction (0.5 pts), myopia (0.5 pts) , WES panel (2 pts), and non-recordable

electroretinogram results, which together are specific for RPGR-related retinopathy (6.5 points, PMID: 32702353, PP4).

PM2_Supporting ✔ This 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 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, as well as a second apparently unrelated proband previously used for the PP4 code (PMIDs: 24938718, 34745198, 32702353, PS4_Supporting).

Curation History

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