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Variant: NM_001034853.2(RPGR):c.1345C>T (p.Arg449Ter)

Version: 1.0

CA412739485

866558 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance (dominant (HP:0001423))
UUID: 164707a5-79bc-43a1-bbd4-4faa6acfc1cc
Approved on: 2025/10/5
Published on: 2025/10/6

HGVS expressions

NM_001034853.2(RPGR):c.1345C>T (p.Arg449Ter)
NM_001034853.2:c.1345C>T
NC_000023.11:g.38297353G>A
CM000685.2:g.38297353G>A
NC_000023.10:g.38156606G>A
CM000685.1:g.38156606G>A
NC_000023.9:g.38041550G>A
NG_009553.1:g.35183C>T
ENST00000494707.6:c.549C>T
ENST00000642170.1:n.1599C>T
ENST00000642395.2:c.1345C>T
ENST00000642739.1:c.1345C>T
ENST00000644238.1:c.1159C>T
ENST00000644337.1:c.1159C>T
ENST00000645032.1:c.1345C>T
ENST00000645124.1:c.1345C>T
ENST00000646020.1:c.1405C>T
ENST00000318842.11:c.1345C>T
ENST00000339363.7:c.1345C>T
ENST00000378505.6:c.1345C>T
ENST00000465127.1:c.172-368768G>A
ENST00000474584.5:c.1345C>T
ENST00000482855.5:c.1345C>T
ENST00000494841.1:n.608C>T
NM_000328.2:c.1345C>T
NM_001034853.1:c.1345C>T
NM_001367245.1:c.1342C>T
NM_001367246.1:c.1159C>T
NM_001367247.1:c.1345C>T
NM_001367248.1:c.1375C>T
NM_001367249.1:c.1342C>T
NM_001367250.1:c.1342C>T
NM_001367251.1:c.1159C>T
NR_159803.1:n.1547C>T
NR_159804.1:n.1421C>T
NR_159805.1:n.1487C>T
NR_159806.1:n.1487C>T

NR_159807.1:n.1487C>T
NR_159808.1:n.1599C>T
NM_000328.3:c.1345C>T

Pathogenic

Met criteria codes 5

PS4_Supporting PP1_Strong PM2_Supporting PVS1 PP4

Not Met criteria codes 1

PS2

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.1345C>T (p.Arg449Ter) is a nonsense variant that introduces a premature stop codon in exon 11 of 15 that is predicted to trigger nonsense-mediated decay (PVS1). This variant is absent from hemizygous individuals in 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 some functional vision impairment in affected males by age 30 years, and/or decreased or absent electroretinogram responses (PMID: 35432464, PMID: 29528978, PS4_Supporting). The variant has been reported in additional male probands that did not meet the phenotype requirement (PMID: 33090715, PMID: 32860923, PMID: 11992260, PMID: 23150612, PMID: 37217489). At least one proband harboring this variant exhibits a phenotype including a family history consistent with X-linked inheritance (2 pts), early nyctalopia (0.5 pts), decreased peripheral visual field (0.5 pts), macular dystrophy (0.5 pts), bone spicule pigmentation (0.5 pts), myopia (0.5 pts), and reduced visual acuity (0.5 pts), with genotyping by next-generation sequencing panel identifying no alternative basis for retinal disease (2 pts), which together are specific for RPGR-related retinopathy (7 points, PP4). The variant has been reported to segregate with retinal dystrophy through at least 4 affected meioses from at least 2 families (PP1_Strong; PMID: 30105367, PMID: 29528978, PMID: 35432464). This variant has been identified as a de novo occurrence with confirmed maternal relationships in 1 individual, however, the requirement of some functional vision impairment in affected males by age 30 years, and/or decreased or absent electroretinogram responses were not met, so PS2_Supporting was not applied (ARVO Abstract, Demirci et al., 2023, https://iovs.arvojournals.org/article.aspx?articleid=2414118). 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, PS4_Supporting, PP4, and PP1.

Met criteria codes

PS4_Supporting	✔	This variant has been reported in at least 2 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: 35432464, PMID: 29528978, PS4_Supporting). The variant has been reported in additional male probands that did not meet the phenotype requirement (PMID: 33090715, PMID: 32860923, PMID: 11992260, PMID: 23150612, PMID: 37217489).
PP1_Strong	✔	The variant has been reported to segregate with retinal dystrophy through at least 4 affected meioses from at least 2 families (PP1_Strong; PMID: [30105367, 29528978, 35432464 and a clinical report]).

PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PVS1	✔	This is a nonsense variant that introduces a premature stop codon in exon 11 of 15 that is predicted to trigger nonsense-mediated decay (PVS1).
PP4	✔	At least one proband harboring this variant exhibits a phenotype including a family history consistent with X-linked inheritance (2 pts), early nyctalopia (0.5 pts), decreased peripheral visual field (0.5 pts), macular dystrophy (0.5 pts), bone spicule pigmentation (0.5 pts), myopia (0.5 pts), and reduced visual acuity (0.5 pts), with genotyping by next-generation sequencing panel identifying no alternative basis for retinal disease (2 pts), which together are specific for RPGR-related retinopathy (7 points, PP4).

Not Met criteria codes

PS2	✖	This variant has been identified as a de novo occurrence with confirmed maternal relationships in 1 individual, however, the requirement of some functional vision impairment in affected males by age 30 years, and/or decreased or absent electroretinogram responses were not met, so PS2_Supporting was not applied (ARVO Abstract, Demirci et al., 2023, https://iovs.arvojournals.org/article.aspx?articleid=2414118).

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_001034853.2(RPGR):c.1345C>T (p...	Pathogenic	RPGR-Related Retinopathy	2025-10-06	1.0	ClinGen X-linked Inherited Retinal Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RPGR Version 1.0.0	RPGR

Showing 1 to 1 of 1 rows

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