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Variant: NM_001034853.2:c.1154T>A

Version: 1.0

CA412739890

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: 684c1552-de73-4aa0-8107-678b0d3c8597
Approved on: 2025/8/1
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HGVS expressions

NM_001034853.2:c.1154T>A
NC_000023.11:g.38299047A>T
CM000685.2:g.38299047A>T
NC_000023.10:g.38158300A>T
CM000685.1:g.38158300A>T
NC_000023.9:g.38043244A>T
NG_009553.1:g.33489T>A
ENST00000494707.6:c.358T>A
ENST00000642170.1:n.1408T>A
ENST00000642395.2:c.1154T>A
ENST00000642558.1:c.1061T>A
ENST00000642739.1:c.1154T>A
ENST00000644238.1:c.1060-1595T>A
ENST00000644337.1:c.1060-1595T>A
ENST00000645032.1:c.1154T>A
ENST00000645124.1:c.1154T>A
ENST00000646020.1:c.1214T>A
ENST00000318842.11:c.1154T>A
ENST00000339363.7:c.1154T>A
ENST00000378505.6:c.1154T>A
ENST00000464437.1:c.220T>A
ENST00000465127.1:c.172-367074A>T
ENST00000474584.5:c.1154T>A
ENST00000482855.5:c.1154T>A
ENST00000494841.1:n.417T>A
NM_000328.2:c.1154T>A
NM_001034853.1:c.1154T>A
NM_001367245.1:c.1151T>A
NM_001367246.1:c.1060-1595T>A
NM_001367247.1:c.1154T>A
NM_001367248.1:c.1184T>A
NM_001367249.1:c.1151T>A
NM_001367250.1:c.1151T>A
NM_001367251.1:c.1060-1595T>A
NR_159803.1:n.1356T>A
NR_159804.1:n.1205T>A
NR_159805.1:n.1296T>A

NR_159806.1:n.1296T>A
NR_159807.1:n.1296T>A
NR_159808.1:n.1408T>A
NM_000328.3:c.1154T>A

Pathogenic

Met criteria codes 3

PP1 PM2_Supporting PVS1

Not Met criteria codes 2

PS3 PS4

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.1154T>A (p.Leu385Ter) is a nonsense variant that substitutes a premature stop codon for amino acid 385 in exon 10 of 15 and is predicted to trigger nonsense-mediated decay (PVS1). Fibroblast cells expressing the variant exhibit loss of RPGR localization to the ciliary axoneme (PMID: 33182541). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The variant has been reported to segregate with retinal dystrophy through at least 2 affected meioses from 1 family (PP1; PMID: 37541846). 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, and PP1. (date of approval 05/16/2025).

Met criteria codes

PP1	✔	The variant has been reported to segregate with retinal dystrophy through at least 2 affected meioses from 1 family. (PP1; PMID: 37541846)
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PVS1	✔	This is a nonsense 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).

Not Met criteria codes

PS3	✖	Fibroblast cells expressing the variant exhibit loss of RPGR localization to the ciliary axoneme (PMID: 33182541, PS3_Supporting). This code is not met as PVS1 has already been used to reward the predicted null impact.
PS4	✖	

This variant has been reported in at least 1 proband 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 or a female with functional visual abnormality and documentation of a male relative affected with retinitis pigmentosa (PMID: 37541846). However, PS4_Supporting requires at least 2 unrelated probands, so this criterion was not met.

Curation History

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