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Variant: NM_001034853.2(RPGR):c.2650G>T (p.Glu884Ter)

Version: 1.0

CA254931

9908 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance
UUID: fbca8cdb-cf7e-443f-a261-96f37add5939
Approved on: 2025/9/5
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HGVS expressions

NM_001034853.2(RPGR):c.2650G>T (p.Glu884Ter)
NM_001034853.2:c.2650G>T
NC_000023.11:g.38286349C>A
CM000685.2:g.38286349C>A
NC_000023.10:g.38145602C>A
CM000685.1:g.38145602C>A
NC_000023.9:g.38030546C>A
NG_009553.1:g.46187G>T
ENST00000494707.6:c.953+1516G>T
ENST00000642170.1:n.1826+4610G>T
ENST00000642395.2:c.1905+745G>T
ENST00000642739.1:c.1572+4610G>T
ENST00000644238.1:c.1386+4610G>T
ENST00000644337.1:c.1719+745G>T
ENST00000645032.1:c.2650G>T
ENST00000645124.1:c.*101+745G>T
ENST00000646020.1:c.*594+745G>T
ENST00000318842.11:c.1905+745G>T
ENST00000339363.7:c.2520+745G>T
ENST00000378505.6:c.2650G>T
ENST00000465127.1:c.172-379772C>A
ENST00000474584.5:c.*37+4610G>T
ENST00000482855.5:c.1905+745G>T
ENST00000494707.5:c.139+4610G>T
NM_000328.2:c.1905+745G>T
NM_001034853.1:c.2650G>T
NM_001367245.1:c.1902+745G>T
NM_001367246.1:c.1719+745G>T
NM_001367247.1:c.1572+4610G>T
NM_001367248.1:c.1602+4610G>T
NM_001367249.1:c.1569+4610G>T
NM_001367250.1:c.1569+4610G>T
NM_001367251.1:c.1386+4610G>T
NR_159803.1:n.2263+745G>T
NR_159804.1:n.1648+4610G>T
NR_159805.1:n.1714+4610G>T
NR_159806.1:n.1866+745G>T

NR_159807.1:n.1622+4610G>T
NR_159808.1:n.1826+4610G>T
NM_000328.3:c.1905+745G>T

Pathogenic

Met criteria codes 4

PP4 PS4_Supporting PM2_Supporting PVS1

Not Met criteria codes 15

BP7 BP4 BP3 BS2 BS1 BS4 PP1 PP3 PM5 PM4 PM6 BA1 PS1 PS2 PS3

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.2650G>T (p.Glu884Ter) is a nonsense variant that introduces a premature stop codon within exon 15 of 15 that is predicted to disrupt a critical C-terminal region required for proper glutamylation of RPGR (PVS1, PMID: 36445968). 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: 30567410, PS4_Supporting). At least one proband harboring this variant exhibits a phenotype including onset of visual defects before the age of 30 years, fundus autofluorescence imaging showing radial pattern reflex, a family history consistent with X-linked inheritance with no male-to-male transmission (2 pts) and delayed/milder phenotype in females (1 pt), night blindness (0.5 pts), and pigmentary retinopathy (0.5 pts) which together are specific for RPGR-related retinopathy (4 points, PMID: 30567410, PP4). 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, and PP4.

Met criteria codes

PP4	✔	At least one proband harboring this variant exhibits a phenotype including onset of visual defects before the age of 30 years, fundus autofluorescence imaging showing radial pattern reflex, a family history with no male-to-male transmission (2 pts) and delayed/milder phenotype in females (1 pt), night blindness (0.5 pts), and pigmentary retinopathy (0.5 pts) which together are specific for RPGR-related retinopathy (4 points, PMID: 30567410, PP4).
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 (PMID: 17325176, PMID: 30567410, PS4_Supporting).
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 is predicted to disrupt a critical C-terminal region required for proper glutamylation of ORF15 of RPGR (PVS1, PMID: 36445968).

Not Met criteria codes

BP7	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3	✖	No insertions/deletions
BS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	✖	Not previously examined by VCEP
PM4	✖	stop-loss variant
PM6	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	✖	Not previously examined by VCEP
PS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS3	✖	Causing premature stop/shorter protein

Curation History

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