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Variant: NM_001034853.2(RPGR):c.730A>T (p.Lys244Ter)

Version: 1.0

CA226439

98796 (ClinVar)

Gene: RPGR (HGNC:6103)
Condition: RPGR-related retinopathy (MONDO:0100437)
Inheritance Mode: X-linked inheritance (dominant (HP:0001423))
UUID: dd0abccb-401d-44de-a528-3064d41dac6e
Approved on: 2025/5/20
Published on: 2025/5/20

HGVS expressions

NM_001034853.2(RPGR):c.730A>T (p.Lys244Ter)
NM_001034853.2:c.730A>T
NC_000023.11:g.38310663T>A
CM000685.2:g.38310663T>A
NC_000023.10:g.38169916T>A
CM000685.1:g.38169916T>A
NC_000023.9:g.38054860T>A
NG_009553.1:g.21873A>T
ENST00000642170.1:n.1140A>T
ENST00000642373.1:c.*309A>T
ENST00000642395.2:c.730A>T
ENST00000642558.1:c.637A>T
ENST00000642739.1:c.730A>T
ENST00000644238.1:c.730A>T
ENST00000644337.1:c.730A>T
ENST00000645032.1:c.730A>T
ENST00000645124.1:c.730A>T
ENST00000646020.1:c.730A>T
ENST00000647261.1:c.730A>T
ENST00000318842.11:c.730A>T
ENST00000339363.7:c.730A>T
ENST00000378505.6:c.730A>T
ENST00000465127.1:c.172-355458T>A
ENST00000474584.5:c.730A>T
ENST00000482855.5:c.730A>T
NM_000328.2:c.730A>T
NM_001034853.1:c.730A>T
NM_001367245.1:c.727A>T
NM_001367246.1:c.730A>T
NM_001367247.1:c.730A>T
NM_001367248.1:c.760A>T
NM_001367249.1:c.727A>T
NM_001367250.1:c.727A>T
NM_001367251.1:c.730A>T
NR_159803.1:n.872A>T
NR_159804.1:n.781A>T
NR_159805.1:n.872A>T

NR_159806.1:n.872A>T
NR_159807.1:n.872A>T
NR_159808.1:n.1140A>T
NM_000328.3:c.730A>T

Pathogenic

Met criteria codes 4

PM2_Supporting | PP4 | PVS1 | PP1_Moderate

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.730A>T (p.Lys244Ter) is a nonsense variant that introduces a premature stop codon into exon 7 of 15, and is predicted to lead to nonsense-mediated decay in the RPGR gene in which loss-of-function is an established disease mechanism (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 a family pedigree consistent with X-linked inheritance (2 points), night blindness (0.5 points), delayed or milder phenotype in females (1 point), rod involvement relatively greater than cone involvement (1 point), and peripheral visual field constriction (0.5 points), which together are specific for RPGR-related retinopathy (5 points, PMIDs: 11180598, 21857984, PP4). The variant has been reported to segregate with retinal dystrophy through at least 4 affected meioses from 1 family (PP1_Moderate). In summary, this variant meets the criteria to be 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_Moderate, and PP4. (date of approval 05/16/2025).

Met criteria codes

PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PP4	✔	At least one proband harboring this variant exhibits a phenotype including a family pedigree consistent with X-linked inheritance (2 points), night blindness (0.5 points), delayed or milder phenotype in females (1 point), rod involvement relatively greater than cone involvement (1 point), and peripheral visual field constriction (0.5 points), which together are specific for RPGR-related recessive retinopathy (5 points, PMID: 11180598, PP4).
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 function of RPGR (PVS1, PMID: 36445968).
PP1_Moderate	✔	The variant has been reported to segregate with retinal dystrophy through at least 4 affected meioses from 1 family (PP1_Moderate).

Curation History

Showing 1 to 1 of 1 rows

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