The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000330.4(RS1):c.149G>A (p.Trp50Ter)

Version: 1.0

CA412376221

1419115 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance (recessive (HP:0001419))
UUID: 6856d4d6-1f58-4710-9e27-dfec279d8d57
Approved on: 2025/5/19
Published on: 2025/5/20

HGVS expressions

NM_000330.4:c.149G>A
NM_000330.4(RS1):c.149G>A (p.Trp50Ter)
NC_000023.11:g.18656688C>T
CM000685.2:g.18656688C>T
NC_000023.10:g.18674808C>T
CM000685.1:g.18674808C>T
NC_000023.9:g.18584729C>T
NG_008659.3:g.25761G>A
ENST00000379984.4:c.149G>A
ENST00000379984.3:c.149G>A
NM_000330.3:c.149G>A

Pathogenic

Met criteria codes 3

PVS1 PP4 PM2_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 RS1 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

X-linked Inherited Retinal Disease VCEP

The NM_000330.4(RS1):c.149G>A variant is a nonsense variant in amino acid 50, which results in a premature stop codon and causes a truncated protein. This is a frameshift variant that introduces a premature stop codon between amino acids 1-223 that is predicted to either trigger nonsense-mediated decay or to disrupt a critical C-terminal region required for proper multimerization of RS1 (PVS1, PMID: 19849666). 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 appearance of schisis and reduced visual acuity before age 13 years, which together are specific for X-linked retinoschisis (PMID: 16272055, PP4). In summary, this variant is classified as pathogenic for X-linked retinoschisis based on the

ClinGen X-linked Inherited Retinal Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RS1 Version 1.0.0: PVS1, PP4, and PM2_supporting (date of approval 01/24/2025).

Met criteria codes

PVS1	✔	This is a frameshift variant that introduces a premature stop codon between amino acids 1-223 that is predicted to either trigger nonsense-mediated decay or to disrupt a critical C-terminal region required for proper multimerization of RS1 (PVS1, PMID: 19849666).
PP4	✔	At least one proband harboring this variant exhibits a phenotype including appearance of schisis and reduced visual acuity before age 13 years, which together are specific for X-linked retinoschisis (PMID: 16272055, PP4).
PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).

Curation History

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