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.304C>T (p.Arg102Trp)

Version: 1.0

CA226667

9887 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance (recessive (HP:0001419))
UUID: 85b41b42-e14f-46af-ae75-6c3e6bb93d67
Approved on: 2025/5/19
Published on: 2025/5/20

HGVS expressions

NM_000330.4(RS1):c.304C>T (p.Arg102Trp)
NM_000330.4:c.304C>T
NC_000023.11:g.18647213G>A
CM000685.2:g.18647213G>A
NC_000023.10:g.18665333G>A
CM000685.1:g.18665333G>A
NC_000023.9:g.18575254G>A
NG_008475.1:g.226609G>A
NG_008659.3:g.35236C>T
ENST00000379984.4:c.304C>T
ENST00000379984.3:c.304C>T
ENST00000379989.6:c.2797+1123G>A
ENST00000379996.7:c.2797+1123G>A
ENST00000476595.1:n.795C>T
NM_000330.3:c.304C>T
NM_001037343.1:c.2797+1123G>A
NM_003159.2:c.2797+1123G>A
NM_001037343.2:c.2797+1123G>A
NM_003159.3:c.2797+1123G>A

Pathogenic

Met criteria codes 4

PP1_Strong PS4 PP3_Strong PP4

Not Met criteria codes 2

BS1 PM2

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.304C>T variant is a missense variant encoding the substitution of Arginine with Tryptophan at amino acid 102. This variant is present in gnomAD v.4.1.0 at a frequency of 0.000008256 among hemizygous individuals, with 3 variant alleles / 363368 total hemizygous alleles, which is between the ClinGen X-linked IRD VCEP PM2_Supporting and BS1 thresholds of <0.000002 and >0.00002 and fails to meet these criteria. The computational predictor REVEL gives a score of 0.958, which is above the ClinGen X-linked IRD VCEP threshold of >0.932 and predicts a damaging effect on RS1 function (PP3_strong). The computational splicing predictor SpliceAI gives a delta score of 0.01 Acceptor Gain, which is below the ClinGen X-linked IRD VCEP threshold of >0.2 and does not predict that the variant disrupts RS1 splicing. The variant has been reported to segregate with retinal dystrophy through 3 meioses in a family including two affected brothers and 5 other affected members (PP1_strong; PMID: 36695495, 9326935, 16901436, 24634885). 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 (5 points, PMID: 24634885, PP4). This variant has been reported in at least 5 apparently unrelated probands meeting one of the PS4 requirements of a male diagnosed with X-linked retinoschisis (PMIDs: 33124204, 9326935, 22245991, 36695495, 28348004, 35456481, PS4). 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: PP3_strong, PP1_strong, PS4, and PP4 (date of approval 01/24/2025).

Met criteria codes

PP1_Strong	✔	The variant has been reported to segregate with retinal dystrophy through 3 meiosis in a family- One family included two affected brothers and the other 5 affected members. (PP1; PMID: 36695495, 9326935, 16901436, 24634885).
PS4	✔	This variant has been reported in at least 5 apparently unrelated probands meeting one of the PS4 requirements of a male diagnosed with XLRS (PMIDs: 33124204, 9326935, 22245991, 36695495, 28348004, 35456481, PS4).
PP3_Strong	✔	The computational predictor REVEL gives a score of 0.958, which is above the ClinGen X-linked IRD VCEP threshold of >0.932 and predicts a damaging effect on RS1 function (PP3_strong). The computational splicing predictor SpliceAI gives a delta score of 0.01 Acceptor Gain, which is below the ClinGen X-linked IRD VCEP threshold of >0.2 and does not predict that the variant disrupts RS1 splicing.
PP4	✔	At least one proband harboring this variant exhibits a phenotype including appearance of schisis and reduced visual acuity before age 13 years, and was diagnosed with XLRS, which together are specific for X-linked retinoschisis (5 points, PMID: 24634885, PP4).

Not Met criteria codes

BS1	✖	This variant is present in gnomAD v.4.1.0 at a frequency of 0.000008256 among hemizygous individuals, with 3 variant alleles / 363368 total hemizygous alleles, which is between the ClinGen X-linked IRD VCEP PM2_Supporting and BS1 threshold of 0.000002 to 0.00002 and fails to meet these criteria.
PM2	✖	This variant is present in gnomAD v.4.1.0 at a frequency of 0.000008256 among hemizygous individuals, with 3 variant alleles / 363368 total hemizygous alleles, which is between the ClinGen X-linked IRD VCEP PM2_Supporting and BS1 threshold of 0.000002 to 0.00002 and fails to meet these criteria.

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
⌑ Powered by BCM's Genboree.