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Variant: NM_000330.4(RS1):c.575C>T (p.Pro192Leu)

Version: 1.0

CA412370409

863203 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance
UUID: c8005218-d759-4cd2-8139-843f4c25fe0a
Approved on: Sat, 26 Sep 2026 00:00:00 +0000
Published on: Sat, 26 Sep 2026 00:00:00 +0000

HGVS expressions

NM_000330.4(RS1):c.575C>T (p.Pro192Leu)
NM_000330.4:c.575C>T
NC_000023.11:g.18642104G>A
CM000685.2:g.18642104G>A
NC_000023.10:g.18660224G>A
CM000685.1:g.18660224G>A
NC_000023.9:g.18570145G>A
NG_008475.1:g.221500G>A
NG_008659.3:g.40345C>T
ENST00000379984.4:c.575C>T
ENST00000379984.3:c.575C>T
ENST00000379989.6:c.2714-3903G>A
ENST00000379996.7:c.2714-3903G>A
ENST00000476595.1:n.1066C>T
NM_000330.3:c.575C>T
NM_001037343.1:c.2714-3903G>A
NM_003159.2:c.2714-3903G>A
NM_001037343.2:c.2714-3903G>A
NM_003159.3:c.2714-3903G>A

Pathogenic

Met criteria codes 4

PM2_Supporting PP3_Strong PP4_Moderate 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 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.575C>T (p.Pro192Leu) variant is a missense variant encoding the substitution of Proline and Leucine at amino acid 192. This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.963, 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 0.02 for donor gain, which is below the ClinGen X-linked IRD VCEP threshold of >0.2 and does not predict that the variant disrupts RS1 splicing. At least one proband harboring this variant exhibits a phenotype including the appearance of schisis and reduced visual acuity before age 13 years, and showing retinal detachment, which together are highly specific for X-linked retinoschisis (PMID: 32300273, PP4_Moderate). 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: 19093009, 19324861, 28348004, 33124204, 36460718, 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: PM2_Supporting, PP3_Strong, PP4_Moderate, and PS4.

Met criteria codes

PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PP3_Strong	✔	The computational predictor REVEL gives a score of 0.963, 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 0.02 for donor 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_Moderate	✔	At least one proband harboring this variant exhibits a phenotype including the appearance of schisis and reduced visual acuity before age 13 years, and showing retinal detachment, which together are highly specific for X-linked retinoschisis (PMID: 32300273, PP4_Moderate).
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: 19093009, 19324861, 28348004, 33124204, 36460718, PS4).

Curation History

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