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Variant: NM_000330.4(RS1):c.217T>C (p.Ser73Pro)

Version: 1.0

CA226628

98917 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance
UUID: 21d8a608-7ff9-4ad1-8827-d508eebbb204
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.217T>C (p.Ser73Pro)
NM_000330.4:c.217T>C
NC_000023.11:g.18647300A>G
CM000685.2:g.18647300A>G
NC_000023.10:g.18665420A>G
CM000685.1:g.18665420A>G
NC_000023.9:g.18575341A>G
NG_008475.1:g.226696A>G
NG_008659.3:g.35149T>C
ENST00000379984.4:c.217T>C
ENST00000379984.3:c.217T>C
ENST00000379989.6:c.2797+1210A>G
ENST00000379996.7:c.2797+1210A>G
ENST00000476595.1:n.708T>C
NM_000330.3:c.217T>C
NM_001037343.1:c.2797+1210A>G
NM_003159.2:c.2797+1210A>G
NM_001037343.2:c.2797+1210A>G
NM_003159.3:c.2797+1210A>G

Likely Pathogenic

Met criteria codes 5

PM2_Supporting PP4 PS4_Supporting PP1_Strong PP3_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 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.217T>C (p.Ser73Pro) variant is a missense variant encoding the substitution of Serine and Proline at amino acid 73. This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.925, which is within the ClinGen X-linked IRD VCEP range between 0.931 and 0.773 and predicts a damaging effect on RS1 function (PP3_moderate). The computational splicing predictor SpliceAI gives a delta score of 0.00 for all predictive splice changes, 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 the following phenotypes, including the appearance of schisis and reduced visual acuity before age 13 years, which together are specific for X-linked retinoschisis (PMID: 17615541, PP4). The variant has been reported to segregate with retinal dystrophy through >3 meioses in one family (PP1_Strong; PMID: 17615541). This variant has been reported in at least one proband meeting the PS4 requirements of a male diagnosed with XLRS (PMID: 15531314, PS4_Supporting). In summary, this variant is classified as likely 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_Moderate, PP4, PP1_Strong, and PS4_Supporting.

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 the following phenotypes, including the appearance of schisis and reduced visual acuity before age 13 years, which together are specific for X-linked retinoschisis (PMID: 17615541, PP4).
PS4_Supporting	✔	This variant has been reported in at least one proband meeting the PS4 requirements of a male diagnosed with XLRS (PMID: 15531314, PS4_Supporting).
PP1_Strong	✔	The variant has been reported to segregate with retinal dystrophy through >3 meioses in one family (PP1_Strong; PMID: 17615541).
PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.925, which is within the ClinGen X-linked IRD VCEP range between 0.931 and 0.773 and predicts a damaging effect on RS1 function (PP3_moderate). The computational splicing predictor SpliceAI gives a delta score of 0.00 for all predictive splice changes, which is below the ClinGen X-linked IRD VCEP threshold of >0.2 and does not predict that the variant disrupts RS1 splicing.

Curation History

Showing 1 to 1 of 1 rows

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