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Variant: NM_000330.4(RS1):c.170T>C (p.Leu57Ser)

Version: 1.0

CA16621289

423184 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance (recessive (HP:0001419))
UUID: d85e7d94-b88e-4dfc-940a-609d6c7be5e7
Approved on: 2025/5/19
Published on: 2025/5/20

HGVS expressions

NM_000330.4(RS1):c.170T>C (p.Leu57Ser)
NM_000330.4:c.170T>C
NC_000023.11:g.18656667A>G
CM000685.2:g.18656667A>G
NC_000023.10:g.18674787A>G
CM000685.1:g.18674787A>G
NC_000023.9:g.18584708A>G
NG_008659.3:g.25782T>C
ENST00000379984.4:c.170T>C
ENST00000379984.3:c.170T>C
NM_000330.3:c.170T>C

Uncertain Significance

Met criteria codes 2

PP3 PM2_Supporting

Not Met criteria codes 1

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.170T>C variant is a missense variant encoding the substitution of Leucine with Serine at amino acid 57. This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.653, which is within the ClinGen X-linked IRD VCEP range between 0.772 to 0.644 and predicts a damaging effect on RS1 function (PP3). The computational splicing predictor SpliceAI gives a delta score of 0.01 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. This variant has been reported in at least 1 individual (PMID: 30464253), however, the publication did not include any retinal test or diagnosis of retinoschisis. In summary, this variant is classified as a variant of uncertain significance 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 and PP3 (date of approval 01/24/2025).

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.653, which is within the ClinGen X-linked IRD VCEP range between 0.772 to 0.644 and predicts a damaging effect on RS1 function (PP3). The computational splicing predictor SpliceAI gives a delta score of 0.01 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.
PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

PS4	✖	This variant has been reported in at least 1 individual (PMID: 30464253). However, the individual was not reported to have any retinal test or diagnosis of retinoschisis.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000330.4(RS1):c.170T>C (p.Leu57...	Uncertain Significance	X-Linked Retinoschisis	2025-05-20	1.0	ClinGen X-linked Inherited Retinal Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RS1 Version 1.0.0	RS1

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