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Variant: NM_000330.4(RS1):c.214G>C (p.Glu72Gln)

Version: 1.0

CA226623

98916 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance
UUID: 06ab0d76-d400-4a95-a8e7-cb925dcb4091
Approved on: Sat, 26 Sep 2026 00:00:00 +0000
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HGVS expressions

NM_000330.4(RS1):c.214G>C (p.Glu72Gln)
NM_000330.4:c.214G>C
NC_000023.11:g.18647303C>G
CM000685.2:g.18647303C>G
NC_000023.10:g.18665423C>G
CM000685.1:g.18665423C>G
NC_000023.9:g.18575344C>G
NG_008475.1:g.226699C>G
NG_008659.3:g.35146G>C
ENST00000379984.4:c.214G>C
ENST00000379984.3:c.214G>C
ENST00000379989.6:c.2797+1213C>G
ENST00000379996.7:c.2797+1213C>G
ENST00000476595.1:n.705G>C
NM_000330.3:c.214G>C
NM_001037343.1:c.2797+1213C>G
NM_003159.2:c.2797+1213C>G
NM_001037343.2:c.2797+1213C>G
NM_003159.3:c.2797+1213C>G

Pathogenic

Met criteria codes 6

PP3_Moderate | PP1 | PP4 | PS4 | PM2_Supporting | PM1

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.214G>C (p.Glu72Gln) variant is a missense variant encoding the substitution of Glutamic acid and Glutamine at amino acid 72. This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.931, 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 0.05 for 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. This variant p.Glu72, of the RS1 gene, is a missense substitution affecting an established residue involved in cross-linking the adjacent RS1 subunit defined by the ClinGen X-linked IRD VCEP (PMID: 27114531, PM1). 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: 19390641, PP4). The variant has been reported to segregate with retinal dystrophy through two brothers (PP1; PMID: 11295123). This variant has been reported in at least 5 apparently unrelated probands meeting the PS4 requirement of a male diagnosed with XLRS (PMIDs: 11295123, 28348004, 36460718, 39462066, 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: PM2_Supporting, PP3_Moderate, PM1, PP4, PP1, and PS4.

Met criteria codes

PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.931, 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 0.05 for 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.
PP1	✔	The variant has been reported to segregate with retinal dystrophy through two brothers (PP1; PMID: 11295123).
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: 19390641, PP4).
PS4	✔	This variant has been reported in at least 5 apparently unrelated probands meeting the PS4 requirement of a male diagnosed with XLRS (PMIDs: 11295123, 28348004, 36460718, 39462066, 35456481, PS4).
PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PM1	✔	This variant p.Glu72, of the RS1 gene, is a missense substitution affecting an established residue involved in cross-linking the adjacent RS1 subunit defined by the ClinGen X-linked IRD VCEP (PMID: 27114531, PM1).

Curation History

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