

Variant: *NM_000330.4(RS1):c.533G>A (p.Gly178Asp)*

Version: 1.0

CA226772 [↗](#)

98983 (ClinVar) [↗](#)

Gene: RS1 ([HGNC:6247](#))

Condition: X-linked retinoschisis ([MONDO:0010725](#))

Inheritance Mode: X-linked inheritance (recessive (HP:0001419))

UUID: 7a3e35ed-ac35-436f-bad6-d460c05e43ea

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HGVS expressions

NM_000330.4:c.533G>A

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NC_000023.11:g.18642146C>T

CM000685.2:g.18642146C>T

NC_000023.10:g.18660266C>T

CM000685.1:g.18660266C>T

NC_000023.9:g.18570187C>T

NG_008475.1:g.221542C>T

NG_008659.3:g.40303G>A

ENST00000379984.4:c.533G>A

ENST00000379984.3:c.533G>A

ENST00000379989.6:c.2714-3861C>T

ENST00000379996.7:c.2714-3861C>T

ENST00000476595.1:n.1024G>A

NM_000330.3:c.533G>A

NM_001037343.1:c.2714-3861C>T

NM_003159.2:c.2714-3861C>T

NM_001037343.2:c.2714-3861C>T

NM_003159.3:c.2714-3861C>T

Pathogenic

Met criteria codes **4**

PP1_Strong

PP3_Strong

PS4_Moderate

PM2_Supporting

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

NM_000330.4(RS1):c.533G>A (p.Gly178Asp) is a missense variant encoding the substitution of glycine with aspartic acid at amino acid 178. This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). This variant has been reported in at least 3 apparently unrelated probands meeting the PS4 requirement of a male diagnosed with X-linked retinoschisis (PMID: 9618178, PMID: 11738458, PMID: 31149861, PMID: 12928282, PMID: 31087526, PS4_Moderate). The variant has been reported to segregate with retinal dystrophy through at least 3 meioses in two apparently unrelated families, one with affected 3 brothers and the other with two affected brothers (PP1_Strong; PMID: 12928282, PMID: 31087526). The computational predictor REVEL gives a score of 0.989, 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 0.00 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. 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, PP1_Strong, and PS4_Moderate.

Met criteria codes

PP1_Strong	 	The variant has been reported to segregate with retinal dystrophy through at least 3 meioses in two apparently unrelated families, one with affected 3 brothers and the other with two affected brothers (PP1_Strong; PMID: 12928282, PMID: 31087526).
PP3_Strong	 	The computational predictor REVEL gives a score of 0.989, 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 0.00 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.
PS4_Moderate	 	This variant has been reported in at least 3 apparently unrelated probands meeting the PS4 requirements of a male diagnosed with XLRS (PMIDs: 9618178, 11738458, 31149861, 12928282, 31087526, PS4_Moderate)
PM2_Supporting	 	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).

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.533G>A (p.Gly17...	Pathogenic	X-Linked Retinoschisis ↗	2025-09-19	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 ↗

Showing 1 to 1 of 1 rows

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