The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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
Approved on: 2025/9/18
Published on: 2025/9/19

HGVS expressions

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

PP3_Strong PP1_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

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.
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).
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

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.