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.52+2T>C

Version: 1.0

CA226766

98977 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance
UUID: 53f89741-e77f-41a4-878b-cfc4a85c60d2
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:c.52+2T>C
NM_000330.4(RS1):c.52+2T>C
NC_000023.11:g.18672015A>G
CM000685.2:g.18672015A>G
NC_000023.10:g.18690135A>G
CM000685.1:g.18690135A>G
NC_000023.9:g.18600056A>G
NG_008659.3:g.10434T>C
ENST00000379984.4:c.52+2T>C
ENST00000379984.3:c.52+2T>C
NM_000330.3:c.52+2T>C

Pathogenic

Met criteria codes 4

PS4_Moderate PVS1 PM2_Supporting PP4_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.52+2T>C variant is a canonical splice site variant in intron 1, located 2 nucleotides after exon 1. This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). This variant occurs at a canonical splice site in intron 1 and is predicted to disrupt splicing and induce skipping of exon 1, which is expected to disrupt a critical functional domain in RS1 (PVS1). At least one proband harboring this variant exhibits the following phenotypes: schisis, reduced visual acuity before age 13 years, and retinal detachment, which together are specific for X-linked retinoschisis (PMID: 17615541, PP4_Moderate). This variant has been reported in at least 3 apparently unrelated probands meeting one of the PS4 requirements of a male diagnosed with XLRS (PMIDs: 11217940, 11738458, 17296904, 28348004, 29739629, 30551202, 34822951, PS4_Moderate). 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, PVS1, PP4_Moderate, and PS4_Moderate.

Met criteria codes

PS4_Moderate	✔	This variant has been reported in at least 3 apparently unrelated probands meeting one of the PS4 requirements of a male diagnosed with XLRS (PMIDs: 11217940, 11738458, 17296904, 28348004, 29739629, 30551202, 34822951, PS4_Moderate).
PVS1	✔	This variant occurs at a canonical splice site in intron 1 and is predicted to disrupt splicing and induce skipping of exon 1, which is expected to disrupt a critical functional domain in RS1 (PVS1).
PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PP4_Moderate	✔	At least one proband harboring this variant exhibits the following phenotypes: schisis, reduced visual acuity before age 13 years, and retinal detachment, which together are specific for X-linked retinoschisis (PMID: 17615541, PP4_Moderate).

Curation History

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