

Variant: *NM_000330.4(RS1):c.98G>A (p.Trp33Ter)*

Version: 1.0

CA412376521 [↗](#)

1380589 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 3f716af9-1cca-4b65-908b-240f0d89e94c

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HGVS expressions

NM_000330.4:c.98G>A

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NC_000023.11:g.18656739C>T

CM000685.2:g.18656739C>T

NC_000023.10:g.18674859C>T

CM000685.1:g.18674859C>T

NC_000023.9:g.18584780C>T

NG_008659.3:g.25710G>A

ENST00000379984.4:c.98G>A

ENST00000379984.3:c.98G>A

NM_000330.3:c.98G>A

Pathogenic

Met criteria codes **5**

PVS1

PS4_Supporting

PP4

PM2_Supporting

PP1_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

NM_000330.4(RS1):c.98G>A (p.Trp33Ter) is a nonsense variant that introduces a premature stop codon in exon 3 of 6 and is predicted to trigger nonsense-mediated decay (PVS1). This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). At least one proband harboring this variant exhibits a phenotype that includes the appearance of schisis and reduced visual acuity before age 13 years, which together are specific for X-linked retinoschisis (PMID: 24505212, PP4). This variant has been reported in at least 2 apparently unrelated probands meeting one of the PS4 requirements of a male diagnosed with XLRS (PMID: 30652005, <https://doi.org/10.2174/1874364102115010201>, PS4_Supporting). The variant has been reported to segregate through at least 2 meioses in one family (PP1_Moderate; <https://doi.org/10.2174/1874364102115010201>). 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, PP1_Moderate, and PS4_Supporting.

Met criteria codes

PVS1			This is a nonsense variant that introduces a premature stop codon between amino acids 1 and 223 that is predicted to either trigger nonsense-mediated decay or to disrupt a critical C-terminal region required for the proper function of RS1 (PVS1, PMID: 19849666).
PS4_Supporting			This variant has been reported in at least 2 apparently unrelated probands meeting one of the PS4 requirements of a male diagnosed with XLRS (PMID: 30652005, https://doi.org/10.2174/1874364102115010201 , PS4_Supporting).
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: 24505212, PP4).
PM2_Supporting			This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PP1_Moderate			The variant has been reported to segregate through at least 2 meioses in one family (PP1_moderate; https://doi.org/10.2174/1874364102115010201).

Curation History

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