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# *Variant: NM_000330.4(RS1):c.177T>C (p.Cys59=)*

Version: 1.0

*CA515477887*

*1541778 (ClinVar)*

**Gene**: RS1 (HGNC:6247)
**Condition**: X-linked retinoschisis (MONDO:0010725)
**Inheritance Mode**: X-linked inheritance (recessive (HP:0001419))
**UUID:** f6ace292-1671-4377-b486-c8abc2aaf55b
**Approved on**: 2025/9/23
**Published on**: 2025/9/23

## *HGVS expressions*

**NM_000330.4:c.177T>C**
**NM_000330.4(RS1):c.177T>C (p.Cys59=)**
NC_000023.11:g.18656660A>G
CM000685.2:g.18656660A>G
NC_000023.10:g.18674780A>G
CM000685.1:g.18674780A>G
NC_000023.9:g.18584701A>G
NG_008659.3:g.25789T>C
ENST00000379984.4:c.177T>C
ENST00000379984.3:c.177T>C
NM_000330.3:c.177T>C

**Likely Benign**

**Met criteria codes** 2

BP7 BP4

**Not Met criteria codes** 2

BS1 PM2

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.177T>C (p.Cys59=) is a synonymous variant at amino acid 59, within exon 3, and does not have predicted splicing impact (BP7). The splicing impact predictor SpliceAI gives a delta score of 0.00, which is below the ClinGen X-linked IRD VCEP recommended threshold of <0.1 and does not strongly predict an impact on splicing (BP4). This variant is present in gnomAD v4.1.0 at a frequency of 0.000007745 among hemizygous individuals, with 3 variant alleles / 387,371 total alleles, which is between the ClinGen X-linked IRD VCEP PM2_Supporting threshold of <0.000002 and BS1 threshold of >0.00002 and fails to meet these criteria. In summary, this variant is classified as likely benign 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: BP4 and BP7.**

**Met criteria codes**

| | | |
|---|---|---|
| **BP7** | ✔ | This silent variant c.177T>C causing a synonymous variant at codon 59 does not have an impact at splicing sites according to Splice AI, which predicts a delta score of 0.00 for all predictive splice changes, which is below the ClinGen X-linked IRD VCEP recommended threshold of <0.1 and does not strongly predict an impact on splicing (BP7). |
| **BP4** | ✔ | The splicing impact predictor SpliceAI gives a delta score of 0.00, which is below the ClinGen X- linked IRD VCEP recommended threshold of <0.1 and does not strongly predict an impact on splicing (BP4). |

**Not Met criteria codes**

| | | |
|---|---|---|
| **BS1** | ✖ | This variant is present in gnomAD v4.1.0 at a frequency of 0.000007745 among hemizygous individuals, with 3 variant alleles / 387,371 total alleles, which is between the ClinGen X-linked IRD VCEP PM2_Supporting threshold of <0.000002 and BS1 threshold of >0.00002 and fails to meet these criteria. |
| **PM2** | ✖ | This variant is present in gnomAD v4.1.0 at a frequency of 0.000007745 among hemizygous individuals, with 3 variant alleles / 387,371 total alleles, which is between the ClinGen X-linked IRD VCEP PM2_Supporting threshold of <0.000002 and BS1 threshold of >0.00002 and fails to meet these criteria. |

## 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.177T>C (p.Cys59… | Likely Benign | X-Linked Retinoschisis | 2025-09-23 | 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 |

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