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Variant: NM_000330.4(RS1):c.69G>A (p.Ser23=)

Version: 1.0

CA10360821

1671968 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance
UUID: a52454c0-03be-4482-8d40-77990c7d9645
Approved on: 2025/5/19
Published on: 2025/5/20

HGVS expressions

NM_000330.4(RS1):c.69G>A (p.Ser23=)
NM_000330.4:c.69G>A
NC_000023.11:g.18657649C>T
CM000685.2:g.18657649C>T
NC_000023.10:g.18675769C>T
CM000685.1:g.18675769C>T
NC_000023.9:g.18585690C>T
NG_008659.3:g.24800G>A
ENST00000379984.4:c.69G>A
ENST00000379984.3:c.69G>A
NM_000330.3:c.69G>A

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

The NM_000330.4(RS1):c.69G>A variant is a synonymous variant at amino acid 23. The splicing impact predictor SpliceAI gives a delta score of 0.06, 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 silent variant c.69G>A causing a synonymous variant at codon 23 does not have an impact at splicing sites according to Splice AI, which predicts a delta score of 0.06 for donor loss which is below the ClinGen X-linked IRD VCEP recommended threshold of <0.2 and does not strongly predict an impact on splicing (BP7). This variant is present in gnomAD v.4.1.0 at a frequency of 0.000007727 among hemizygotes, with 3 variant alleles / 388269 total hemizygous alleles, which is between the ClinGen X-linked IRD VCEP thresholds of >0.00002 and <0.000002 and fails to meet either BS1 or PM2_supporting. 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: BP7 and BP4_supporting. (date of approval 01/24/2025).

Met criteria codes

BP7	✔	This silent variant c.69G>A causing a synonymous variant at codon 23 does not have an impact at splicing sites according to Splice AI, which predicts a delta score of 0.06 for donor loss which is below the ClinGen X-linked IRD VCEP recommended threshold of <0.2 and does not strongly predict an impact on splicing (BP7).
BP4	✔	The splicing impact predictor SpliceAI gives a delta score of 0.06, 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 v.4.0.0 at a frequency of 0.000007727 among XY individuals, with 3 variant alleles / 388269 total hemizygous alleles, which is lower than the ClinGen X-linked IRD VCEP BS1 threshold of >>0.00002 and fails to meet this criterion.
PM2	✖	This variant is present in gnomAD v.4.0.0 at a frequency of 0.000007727 among hemizygous individuals, with 3 variant alleles / 388269 total hemizygous alleles, which is higher than the ClinGen X-linked IRD VCEP PM2_Supporting threshold of <0.000002 and fails to meet this criterion.

Curation History

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