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_003159.3:c.2714-3985G>T

Version: 1.0

CA412370054

Gene: CDKL5 (HGNC:6792)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance (recessive (HP:0001419))
UUID: d86d609d-f4ec-4d18-8cd6-8fda631f9952
Approved on: Sat, 26 Sep 2026 00:00:00 +0000
Published on: Sat, 26 Sep 2026 00:00:00 +0000

HGVS expressions

NM_003159.3:c.2714-3985G>T
NC_000023.11:g.18642022G>T
CM000685.2:g.18642022G>T
NC_000023.10:g.18660142G>T
CM000685.1:g.18660142G>T
NC_000023.9:g.18570063G>T
NG_008475.1:g.221418G>T
NG_008659.3:g.40427C>A
ENST00000379984.4:c.657C>A
ENST00000379984.3:c.657C>A
ENST00000379989.6:c.2714-3985G>T
ENST00000379996.7:c.2714-3985G>T
ENST00000476595.1:n.1148C>A
NM_000330.3:c.657C>A
NM_001037343.1:c.2714-3985G>T
NM_003159.2:c.2714-3985G>T
NM_000330.4:c.657C>A
NM_001037343.2:c.2714-3985G>T

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PS4_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*
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.657C>A variant is a nonsense variant in amino acid 219, which results in a premature stop codon and causes a truncated protein. This is a nonsense variant that introduces a premature stop codon between amino acids 1-223 that is predicted to either trigger nonsense-mediated decay or to disrupt a critical C-terminal region required for proper multimerization of RS1 (PVS1, PMID: 19849666). This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). This variant has been reported in at least 2 apparently unrelated probands meeting the PS4 requirement of a male diagnosed with XLRS (PMID: 35309139, PS4_Supporting). 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, PS4_supporting, and PVS1.

Met criteria codes

PVS1	✔	This is a nonsense variant that introduces a premature stop codon between amino acids 1-223 that is predicted to either trigger nonsense-mediated decay or to disrupt a critical C-terminal region required for proper multimerization of RS1 (PVS1, PMID: 19849666).
PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PS4_Supporting	✔	This variant has been reported in at least 2 apparently unrelated probands meeting the PS4 requirement of a male diagnosed with XLRS (PMID: 35309139, PS4_Supporting).

Curation History

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