

Variant: *NM_003159.3:c.2714-1496C>T*

Version: 1.0

CA412371717 [↗](#)

Gene: CDKL5 ([HGNC:6792](#))

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

Inheritance Mode: X-linked inheritance (recessive (HP:0001419))

UUID: 11e7f8b8-7775-4eb2-9b82-1ef928d7dd89

Approved on: 2025/5/19

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HGVS expressions

NM_003159.3:c.2714-1496C>T

NC_000023.11:g.18644511C>T

CM000685.2:g.18644511C>T

NC_000023.10:g.18662631C>T

CM000685.1:g.18662631C>T

NC_000023.9:g.18572552C>T

NG_008475.1:g.223907C>T

NG_008659.3:g.37938G>A

ENST00000379984.4:c.441G>A

ENST00000379984.3:c.441G>A

ENST00000379989.6:c.2714-1496C>T

ENST00000379996.7:c.2714-1496C>T

ENST00000476595.1:n.932G>A

NM_000330.3:c.441G>A

NM_001037343.1:c.2714-1496C>T

NM_003159.2:c.2714-1496C>T

NM_000330.4:c.441G>A

NM_001037343.2:c.2714-1496C>T

Pathogenic

Met criteria codes **4**

PM2_Supporting

PP1

PVS1

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 1.0.0*

[↗](#) **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.441G>A variant is a nonsense variant in amino acid 147, which results in a premature stop codon and causes a truncated protein. This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). 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). The variant has been reported to segregate with retinal dystrophy through 1 meiosis in a family (PP1; PMID: 33851411). This variant has been reported in at least 2 apparently unrelated probands meeting the PS4 requirement of a male diagnosed with X-linked retinoschisis (PMIDs: 34645606, 33851411, 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, PVS1, PP1, and PS4_supporting (date of approval 01/24/2025).

Met criteria codes

PM2_Supporting			This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).
PP1			The variant has been reported to segregate with retinal dystrophy through 1 meiosis in a family. (PP1; PMID: 33851411).
PVS1			This is a frameshift 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).
PS4_Supporting			This variant has been reported in at least 2 apparently unrelated probands meeting the PS4 requirement of a male diagnosed with XLRS (PMIDs: 34645606, 33851411, PS4_Supporting).

Curation History

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