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Variant: NM_025114.4(CEP290):c.2695C>T (p.Gln899Ter)

Version: 1.0

CA385971165

2925499 (ClinVar)

Gene: CEP290 (HGNC:80184)
Condition: CEP290-related ciliopathy (MONDO:0100451)
Inheritance Mode: Autosomal recessive inheritance
UUID: 02c8435c-1a93-43e8-9b9e-0664e26d56b1
Approved on: 2026/7/20
Published on: 2026/7/21

HGVS expressions

NM_025114.4(CEP290):c.2695C>T (p.Gln899Ter)
NM_025114.4:c.2695C>T
NC_000012.12:g.88106797G>A
CM000674.2:g.88106797G>A
NC_000012.11:g.88500574G>A
CM000674.1:g.88500574G>A
NC_000012.10:g.87024705G>A
NG_008417.1:g.40420C>T
NG_008417.2:g.40420C>T
ENST00000309041.12:c.2695C>T
ENST00000552810.6:c.2695C>T
ENST00000672414.2:c.*866C>T
ENST00000673058.2:c.2695C>T
ENST00000674971.1:c.2695C>T
ENST00000675230.1:c.2674C>T
ENST00000675408.1:c.2695C>T
ENST00000675476.1:c.3556C>T
ENST00000675628.1:n.2922C>T
ENST00000675794.1:c.*866C>T
ENST00000675833.1:c.3463C>T
ENST00000676074.1:c.2695C>T
ENST00000676363.1:n.4758C>T
ENST00000676448.1:c.*608C>T
ENST00000309041.11:c.2701C>T
ENST00000552810.5:c.2695C>T
ENST00000604024.5:c.1954C>T
NM_025114.3:c.2695C>T

Pathogenic

Met criteria codes 3

PM3_Supporting PVS1 PM2_Supporting

Evidence Links 0

Expert Panel

Leber Congenital Amaurosis/early onset Retinal Dystrophy VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Leber Congenital Amaurosis/early onset Retinal Dystrophy Expert Panel*

Specifications to the ACMG/AMP Variant Interpretation Guidelines for CEP290 Version 1.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Leber Congenital Amaurosis/early onset Retinal Dystrophy VCEP

NM_025114.4(CEP290):c.2695C>T (p.Gln899Ter) is a nonsense variant that introduces a premature stop codon into exon 25 of 54 and is predicted to lead to nonsense-mediated decay in a gene in which loss-of-function is an established mechanism of disease (PVS1). This variant is present in gnomAD v4.1.1 at a total allele frequency of 0.0000006218, with 1 allele / 1,608,202 total alleles, which is lower than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0006 (PM2_Supporting). This variant has been reported in at least 1 proband with early-onset severe retinal dystrophy who was compound heterozygous with the NM_025114.4(CEP290):c.2991+1655A>G variant suspected in trans, which was previously classified pathogenic by the ClinGen LCA/eoRD VCEP (0.5 total points, PMID: 20683928, PM3_Supporting). In summary, this variant meets the criteria to be classified as Pathogenic for CEP290-related ciliopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen LCA/eoRD VCEP: PVS1, PM2_Supporting, and PM3_Supporting. (LCA/eoRD VCEP Specifications for CEP290 Version 1.0.0)

Met criteria codes

PM3_Supporting	✔	This variant has been reported in at least 1 proband with early-onset severe retinal dystrophy who was compound heterozygous with the NM_025114.4(CEP290):c.2991+1655A>G variant suspected in trans, which was previously classified pathogenic by the ClinGen LCA/eoRD VCEP (0.5 total points, PMID: 20683928, PM3_Supporting).
PVS1	✔	NM_025114.4(CEP290):c.2695C>T (p.Gln899Ter) is a nonsense variant that introduces a premature stop codon into exon 25 of 54 and is predicted to lead to nonsense-mediated decay in a gene in which loss-of-function is an established mechanism of disease (PVS1).
PM2_Supporting	✔	This variant is present in gnomAD v4.1.0 at a total allele frequency of 0.0000006218, with 1 allele / 1,608,202 total alleles, which is lower than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0006 (PM2_Supporting).

Curation History

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