

Variant: NM_025114.4(CEP290):c.1558T>C (p.Phe520Leu)

Version: 1.0

CA6712524 [↗](#)

261827 (ClinVar) [↗](#)

Gene: CEP290 ([HGNC:80184](#))

Condition: CEP290-related ciliopathy ([MONDO:0100451](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 829f6351-dde1-4445-aea1-3ac257c43a87

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HGVS expressions

NM_025114.4(CEP290):c.1558T>C (p.Phe520Leu)

NM_025114.4:c.1558T>C

NC_000012.12:g.88118708A>G

CM000674.2:g.88118708A>G

NC_000012.11:g.88512485A>G

CM000674.1:g.88512485A>G

NC_000012.10:g.87036616A>G

NG_008417.1:g.28509T>C

NG_008417.2:g.28509T>C

ENST00000309041.12:c.1558T>C

ENST00000397838.8:c.1504T>C

ENST00000547926.7:c.1558T>C

ENST00000552810.6:c.1558T>C

ENST00000671822.2:n.3155T>C

ENST00000672414.2:c.1558T>C

ENST00000673058.2:c.1558T>C

ENST00000674971.1:c.1558T>C

ENST00000675230.1:c.1537T>C

ENST00000675408.1:c.1558T>C

ENST00000675476.1:c.1558T>C

ENST00000675559.1:c.*104T>C

ENST00000675628.1:n.1785T>C

ENST00000675794.1:c.1558T>C

ENST00000675833.1:c.1558T>C

ENST00000676074.1:c.1558T>C

ENST00000676351.1:c.*2441T>C

ENST00000676363.1:n.3621T>C

ENST00000676418.1:c.*15T>C

ENST00000676448.1:c.1558T>C

ENST00000309041.11:c.1558T>C

ENST00000397838.7:c.1558T>C

ENST00000547926.6:c.1456T>C

ENST00000552810.5:c.1558T>C

ENST00000604024.5:c.724T>C

NM_025114.3:c.1558T>C

Benign

Met criteria codes 2

BA1 BS2

Not Met criteria codes 1

BP4

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.1558T>C (p.Phe520Leu) is a missense variant that replaces phenylalanine with leucine at amino acid 520. This variant is present in gnomAD v4.1.1 at a Grpmax allele frequency of 0.01772, with 1,655 alleles / 1,612,938 total alleles in the African/African-American population, which is higher than the ClinGen LCA/eoRD VCEP BA1 threshold of >0.016 (BA1). This variant has been found in the homozygous state in 30 adult individuals in gnomAD which exceeds the LCA/eoRD VCEP threshold of ≥ 6 (gnomAD version 4.1.1; BS2). The computational predictor CADD gives a PHRED score of 22.5, which is above the ClinGen LCA/eoRD VCEP threshold of <17.3 and does not predict a non-damaging effect on CEP290 protein function, so BP4 is not met. The splicing impact predictor SpliceAI gives a delta score of 0.09 for donor gain, which is below the ClinGen LCA/eoRD VCEP recommended threshold of <0.1 and does not predict an impact on splicing. In summary, this variant meets the criteria to be classified as Benign for CEP290-related ciliopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen LCA/eoRD VCEP: BA1 and BS2. (LCA/eoRD VCEP Specifications for CEP290 Version 1.0.0)

Met criteria codes

BA1			This variant is present in gnomAD v4.1.1 at a GrpMax allele frequency of 0.01772, with 1,655 alleles / 1,612,938 total alleles in the African/African-American population, which is higher than the ClinGen LCA/eoRD VCEP BA1 threshold of >0.016 (BA1).
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BS2			This variant has been found in the homozygous state in 30 adult individuals in gnomAD which exceeds the LCA/eoRD VCEP threshold of ≥ 6 (gnomAD version 4.1.1; BS2)
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Not Met criteria codes

BP4			The computational predictor CADD gives a PHRED score of 22.5, which is above the ClinGen LCA/eoRD VCEP threshold of <17.3 and does not predict a non-damaging effect on CEP290 protein function, so BP4 is not met. The splicing impact predictor SpliceAI gives a delta score of 0.09 for donor gain, which is below the ClinGen LCA/eoRD VCEP recommended threshold of <0.1 and does not predict an impact on splicing.
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