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Variant: NM_025114.4(CEP290):c.1666del (p.Ile556fs)

Version: 1.0

CA277812

217622 (ClinVar)

Gene: CEP290 (HGNC:80184)
Condition: CEP290-related ciliopathy (MONDO:0100451)
Inheritance Mode: Autosomal recessive inheritance
UUID: 622bb731-2ac2-45b4-943a-3c7db36340e7
Approved on: 2026/7/20
Published on: 2026/7/21

HGVS expressions

NM_025114.4:c.1666del
NM_025114.4(CEP290):c.1666del (p.Ile556fs)
NM_025114.4:c.1666delA
NC_000012.12:g.88118537del
CM000674.2:g.88118537del
NC_000012.11:g.88512314del
CM000674.1:g.88512314del
NC_000012.10:g.87036445del
NG_008417.1:g.28689del
NG_008417.2:g.28689del
ENST00000309041.12:c.1666del
ENST00000397838.8:c.1612del
ENST00000547926.7:c.1666del
ENST00000552810.6:c.1666del
ENST00000671822.2:n.3335del
ENST00000672414.2:c.1666del
ENST00000673058.2:c.1666del
ENST00000674971.1:c.1666del
ENST00000675230.1:c.1645del
ENST00000675408.1:c.1666del
ENST00000675476.1:c.1666del
ENST00000675559.1:c.*212del
ENST00000675628.1:n.1893del
ENST00000675794.1:c.1666del
ENST00000675833.1:c.1666del
ENST00000676074.1:c.1666del
ENST00000676351.1:c.*2621del
ENST00000676363.1:n.3729del
ENST00000676418.1:c.*123del
ENST00000676448.1:c.1666del
ENST00000309041.11:c.1672del
ENST00000397838.7:c.1672del
ENST00000547926.6:c.1564del
ENST00000552810.5:c.1666del
ENST00000604024.5:c.832del
NM_025114.3:c.1666del

Pathogenic

Met criteria codes 3

PP1 PM2_Supporting PVS1

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.1666del (p.Ile556PhefsTer17) is a frameshift variant that introduces a premature stop codon into exon 17 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 0.0001611, with 242 alleles / 1,502,300 total alleles, which is lower than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0006 (PM2_Supporting). The variant has been reported to segregate with childhood-onset severe retinal dystrophy through the proband plus 1 similarly affected relative, with the variant present in the compound heterozygous state (PMID: 34196655, PP1). 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 PP1. (LCA/eoRD VCEP Specifications for CEP290 Version 1.0.0)

Met criteria codes

PP1	✔	The variant has been reported to segregate with childhood-onset severe retinal dystrophy through the proband plus 1 similarly affected relative, with the variant present in the compound heterozygous state (PMID: 34196655, PP1).
PM2_Supporting	✔	This variant is present in gnomAD v4.1.0 at a total allele frequency of 0.0001611, with 242 alleles / 1,502,300 total alleles, which is lower than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0006 (PM2_Supporting).
PVS1	✔	This is a frameshift variant that introduces a premature stop codon into exon 17 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).

Curation History

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