

Variant: NM_014336.5(AIPL1):c.34dup (p.Val12fs)

Version: 1.0

CA8328680 [↗](#)

813151 (ClinVar) [↗](#)

Gene: AIPL1 ([HGNC:23746](#))
Condition: AIPL1-related retinopathy ([MONDO:0100438](#))
Inheritance Mode: Autosomal recessive inheritance
UUID: d883da51-7056-4ff2-b2fa-7e196697c22c
Approved on: 2025/9/29
Published on: 2025/9/29

HGVS expressions

NM_014336.5(AIPL1):c.34dup (p.Val12fs)
NM_014336.5:c.34dup
NC_000017.11:g.6435074dup
CM000679.2:g.6435074dup
NC_000017.10:g.6338394dup
CM000679.1:g.6338394dup
NC_000017.9:g.6279118dup
NG_008474.1:g.5129dup
ENST00000381129.8:c.34dup
ENST00000250087.9:c.34dup
ENST00000381128.2:c.34dup
ENST00000381129.7:c.34dup
ENST00000570466.5:c.34dup
ENST00000570584.5:c.9dup
ENST00000571740.5:c.34dup
ENST00000574506.5:c.34dup
ENST00000574913.1:c.34dup
ENST00000575265.5:c.34dup
ENST00000576307.5:c.34dup
ENST00000576776.5:c.34dup
ENST00000621374.4:c.34dup
NM_001033054.2:c.34dup
NM_001033055.2:c.34dup
NM_001285399.2:c.34dup
NM_001285400.2:c.34dup
NM_001285401.2:c.34dup
NM_001285402.1:c.-142dup
NM_001285403.2:c.34dup
NM_014336.4:c.34dup
NM_001033054.3:c.34dup
NM_001033055.3:c.34dup
NM_001285399.3:c.34dup
NM_001285400.3:c.34dup
NM_001285401.3:c.34dup
NM_001285402.2:c.-142dup
NM_001285403.3:c.34dup
NM_001285403.4:c.34dup

Likely Pathogenic

Met criteria codes 2

PM2_Supporting

PVS1

Not Met criteria codes 2

PP4

PM3

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 AIPL1 Version 1.0.0

[Criteria Specification Approval History](#)

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Leber Congenital Amaurosis/early onset Retinal Dystrophy VCEP

NM_014336.5(AIPL1):c.34dup (p.Val12GlyfsTer?) is a 1 bp duplication that changes amino acid p.12 from valine to glycine and alters the reading frame, with a new stop codon encountered after 32 amino acids. This premature stop codon in exon 1 of 6 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 v.4.1.0 at a total allele frequency of 0.000001859, with 3 /1614036 total alleles, which is lower than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0004 (PM2_Supporting). This variant has been reported in at least 1 proband with early-onset severe retinal dystrophy who harbored the variant in the compound heterozygous state (PMID: 32531858). However, the proband was not counted for PM3_Supporting because the other variant p.Arg80Trp is currently classified as a VUS and was not confirmed to be in trans. In summary, this variant meets the criteria to be classified as Likely Pathogenic for AIPL1-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen LCA/eoRD VCEP: PVS1 and PM2_supporting. (VCEP specifications version 1.0.0; date of approval 09/24/2025).

Met criteria codes

PM2_Supporting			This variant is present in gnomAD v.4.1.0 at a total allele frequency of 0.000001859, with 3 /1614036 total alleles, which is lower than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0004 (PM2_Supporting).
PVS1			This is a frameshift variant that introduces a premature stop codon into exon 1 of 6 and is predicted to lead to nonsense-mediated decay in a gene in which loss-of-function is an established mechanism of disease (PVS1).

Not Met criteria codes

PP4			Patient diagnosed with LCA (0.5 pts), no additional phenotype description.
PM3			This variant has been reported in at least 1 proband with early-onset severe retinal dystrophy who harbored the variant in the compound heterozygous state (PMID: 32531858). However, the proband was not counted for this criterion because the other variant p.Arg80Trp is currently classified as a VUS and was not confirmed to be in trans. PM3_Supporting requires at least 0.5 total points, so this criterion was not met.

Curation History



 

 

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