

Variant: *NM_014336.5(AIPL1):c.815G>C (p.Arg272Pro)*

Version: 1.2

CA397394869 [↗](#)

635995 (ClinVar) [↗](#)

Gene: AIPL1 ([HGNC:23746](#))

Condition: AIPL1-related retinopathy ([MONDO:0100438](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: fc5df0f6-7626-44cf-8f1a-67bf962858a6

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HGVS expressions

NM_014336.5(AIPL1):c.815G>C (p.Arg272Pro)

NM_014336.5:c.815G>C

NC_000017.11:g.6425800C>G

CM000679.2:g.6425800C>G

NC_000017.10:g.6329120C>G

CM000679.1:g.6329120C>G

NC_000017.9:g.6269844C>G

NG_008474.1:g.14400G>C

ENST00000381129.8:c.815G>C

ENST00000250087.9:c.626G>C

ENST00000381128.2:c.*687G>C

ENST00000381129.7:c.815G>C

ENST00000570466.5:c.749G>C

ENST00000570584.5:c.251+8119G>C

ENST00000574506.5:c.779G>C

ENST00000575265.5:c.*786G>C

ENST00000576307.5:c.635G>C

ENST00000576776.5:c.743G>C

ENST00000621374.4:c.815G>C

NM_001033054.2:c.626G>C

NM_001033055.2:c.635G>C

NM_001285399.2:c.779G>C

NM_001285400.2:c.749G>C

NM_001285401.2:c.743G>C

NM_001285402.1:c.698G>C

NM_014336.4:c.815G>C

NM_001033054.3:c.626G>C

NM_001033055.3:c.635G>C

NM_001285399.3:c.779G>C

NM_001285400.3:c.749G>C

NM_001285401.3:c.743G>C

NM_001285402.2:c.698G>C

NM_001285403.3:c.*786G>C

NM_001285403.4:c.*786G>C

Uncertain Significance

Met criteria codes 2

PP3PM2_Supporting

Not Met criteria codes 2

PP4PM3

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.815G>C (p.Arg272Pro) is a missense variant predicted to replace arginine with proline at amino acid p.272. This variant is absent from gnomAD v4.1.0 (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_014336.4:c.(? -1)_(276+1_277-1)del variant suspected in trans (0.25 points, PMID: 30718709), which was previously classified likely pathogenic by the ClinGen LCA/eoRD VCEP. The variant has also been reported in a second proband with early-onset severe retinal dystrophy who was heterozygous with no second AIPL1 variant identified in trans (PMID: 26626312). At least one proband harboring this variant exhibits a phenotype including diagnosis of Leber congenital amaurosis (0.5 pts) with genotyping by next-generation sequencing panel targeting more than 150 inherited retinal disease-associated genes (2 pts), which together are not sufficiently specific for AIPL1-related retinopathy to meet PP4 (total 2.5 points, PMID: 30718709). The computational predictor REVEL gives a score of 0.692, which is above the ClinGen LCA/eoRD VCEP threshold of ≥ 0.644 and predicts a damaging effect on AIPL1 protein function (PP3). The splicing impact predictor SpliceAI gives a score of 0.02 for acceptor gain, which is below the ClinGen LCA/eoRD VCEP recommended threshold of ≥ 0.2 and does not strongly predict an impact on splicing. In summary, this variant meets the criteria to be classified as a variant of uncertain significance for AIPL1-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen LCA/eoRD VCEP: PM2_Supporting and PP3. (VCEP specifications version 1.0.0; date of approval 09/24/2025).

Met criteria codes

- PP3

The computational predictor REVEL gives a score of 0.692, which is above the ClinGen LCA/eoRD VCEP threshold of ≥ 0.644 and predicts a damaging effect on AIPL1 protein function (PP3). The splicing impact predictor SpliceAI gives a score of 0.02 for acceptor gain, which is below the ClinGen LCA/eoRD VCEP recommended threshold of ≥ 0.2 and does not strongly predict an impact on splicing.
- PM2_Supporting

This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

- PP4

At least one proband harboring this variant exhibits a phenotype including diagnosis of Leber congenital amaurosis (0.5 pts) with genotyping by next-generation sequencing panel targeting more than 150 inherited retinal disease-associated genes (2 pts), which together are not sufficiently specific for AIPL1-related retinopathy to meet PP4 (total 2.5 points, PMID: 30718709).

PM3

This variant has been reported in at least 1 proband with early-onset severe retinal dystrophy who was compound heterozygous with the NM_014336.4:c.(?_1)_(276+1_277-1)del variant suspected in trans (0.25 points, PMID: 30718709), which was previously classified likely pathogenic by the ClinGen LCA/eoRD VCEP. The variant has also been reported in a second proband with early-onset severe retinal dystrophy who was heterozygous with no second AIPL1 variant identified in trans (PMID: 26626312).

Curation History

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