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Variant: NM_001285403.4:c.216G>A

Version: 1.0

CA397397285

Gene: AIPL1 (HGNC:23746)
Condition: AIPL1-related retinopathy (MONDO:0100438)
Inheritance Mode: Autosomal recessive inheritance
UUID: 36c3ba02-b4f3-4575-ae55-32e61c165527
Approved on: 2025/9/29
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HGVS expressions

NM_001285403.4:c.216G>A
NC_000017.11:g.6433979C>T
CM000679.2:g.6433979C>T
NC_000017.10:g.6337299C>T
CM000679.1:g.6337299C>T
NC_000017.9:g.6278023C>T
NG_008474.1:g.6221G>A
ENST00000381129.8:c.216G>A
ENST00000250087.9:c.216G>A
ENST00000381128.2:c.*88G>A
ENST00000381129.7:c.216G>A
ENST00000570466.5:c.150G>A
ENST00000570584.5:c.191G>A
ENST00000571740.5:c.216G>A
ENST00000574506.5:c.180G>A
ENST00000574913.1:c.216G>A
ENST00000575265.5:c.216G>A
ENST00000576307.5:c.96+1030G>A
ENST00000576776.5:c.216G>A
ENST00000621374.4:c.216G>A
NM_001033054.2:c.216G>A
NM_001033055.2:c.96+1030G>A
NM_001285399.2:c.180G>A
NM_001285400.2:c.150G>A
NM_001285401.2:c.216G>A
NM_001285402.1:c.99G>A
NM_001285403.2:c.216G>A
NM_014336.4:c.216G>A
NM_001033054.3:c.216G>A
NM_001033055.3:c.96+1030G>A
NM_001285399.3:c.180G>A
NM_001285400.3:c.150G>A
NM_001285401.3:c.216G>A
NM_001285402.2:c.99G>A
NM_001285403.3:c.216G>A
NM_014336.5:c.216G>A

Pathogenic

Met criteria codes 3

PM2_Supporting | PP4 | 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 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.216G>A (p.Trp72Ter) is a nonsense variant that introduces a premature stop codon into exon 2 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). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). At least one proband harboring this variant exhibits a phenotype including a diagnosis of Leber congenital amaurosis (0.5 pts), severely reduced central visual acuity (1 pt), kinetic visual field extent (V-4e) undetectable (1 pt), nystagmus (1 pt), and nondetectable electroretinogram responses from both rods (0.5 pts) and cones (1 pt), which together are specific for AIPL1-related retinopathy (total 5 points, PMID: 20702822, PP4). In summary, this variant meets the criteria to be classified as Pathogenic for AIPL1-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen LCA/eoRD VCEP: PVS1, PM2_Supporting, and PP4. (VCEP specifications version 1.0.0; date of approval 09/24/2025).

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP4	✔	At least one proband harboring this variant exhibits a phenotype including a diagnosis of Leber congenital amaurosis (0.5 pts), severely reduced central visual acuity (1 pt), kinetic visual field extent (V-4e) undetectable (1 pt), nystagmus (1 pt), and nondetectable electroretinogram responses from both rods (0.5 pts) and cones (1 pt), which together are specific for AIPL1-related retinopathy (total 5 points, PMID: 20702822, PP4).
PVS1	✔	This is a nonsense variant that introduces a premature stop codon into exon 2 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).

Curation History

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