

Variant: NM_014336.5(AIPL1):c.589G>C (p.Ala197Pro)

Version: 1.0

CA227886 [↗](#)

65709 (ClinVar) [↗](#)

Gene: AIPL1 ([HGNC:23746](#))
Condition: AIPL1-related retinopathy ([MONDO:0100438](#))
Inheritance Mode: Autosomal recessive inheritance
UUID: 15c4d185-4ea1-4183-9aba-b611fa2b36c5
Approved on: 2025/9/29
Published on: 2025/9/29

HGVS expressions

NM_014336.5:c.589G>C
NM_014336.5(AIPL1):c.589G>C (p.Ala197Pro)
NC_000017.11:g.6426934C>G
CM000679.2:g.6426934C>G
NC_000017.10:g.6330254C>G
CM000679.1:g.6330254C>G
NC_000017.9:g.6270978C>G
NG_008474.1:g.13266G>C
ENST00000381129.8:c.589G>C
ENST00000250087.9:c.400G>C
ENST00000381128.2:c.*461G>C
ENST00000381129.7:c.589G>C
ENST00000570466.5:c.523G>C
ENST00000570584.5:c.251+6985G>C
ENST00000571740.5:c.565G>C
ENST00000574506.5:c.553G>C
ENST00000574913.1:c.601G>C
ENST00000575265.5:c.589G>C
ENST00000576307.5:c.409G>C
ENST00000576776.5:c.589G>C
ENST00000621374.4:c.589G>C
NM_001033054.2:c.400G>C
NM_001033055.2:c.409G>C
NM_001285399.2:c.553G>C
NM_001285400.2:c.523G>C
NM_001285401.2:c.589G>C
NM_001285402.1:c.472G>C
NM_001285403.2:c.565G>C
NM_014336.4:c.589G>C
NM_001033054.3:c.400G>C
NM_001033055.3:c.409G>C
NM_001285399.3:c.553G>C
NM_001285400.3:c.523G>C
NM_001285401.3:c.589G>C
NM_001285402.2:c.472G>C
NM_001285403.3:c.565G>C
NM_001285403.4:c.565G>C

Pathogenic

Met criteria codes 5

- PM2_Supporting
- PP3_Strong
- PP1_Strong
- 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.589G>C (p.Ala197Pro) is a missense variant replacing the alanine at position p.197 with proline. This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.969, which is above the ClinGen LCA / eoRD VCEP threshold of ≥ 0.93 and predicts a damaging effect on AIPL1 function (PP3_Strong). This variant has been reported in 2 probands with early-onset severe retinal dystrophy who were homozygous for the variant (PMIDs 10873396, 15024725). (1 point, PM3). At least one proband harboring this variant exhibits a phenotype including a diagnosis of LCA (0.5 pts) with severe visual impairment from birth or during early infancy (1 pt) accompanied by nystagmus (1 pt), absent or very sluggish pupillary responses (0.5 pts), and absent or markedly reduced electroretinogram responses from both rods (0.5 pts) and cones (1 pt), which together are specific for AIPL1-related retinopathy (total 4.5 points, PMID: 10873396, PP4). The variant has been reported to segregate with childhood-onset severe retinal dystrophy through the proband plus at least 3 similarly affected relatives, with the variant present in the homozygous state (PP1_Strong; PMID: 10873396). 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: PM2_Supporting, PP3_Strong, PM3, PP4, and PP1_Strong. (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).
PP3_Strong			The computational predictor REVEL gives a score of 0.969, which is above the ClinGen LCA / eoRD VCEP threshold of ≥ 0.93 and predicts a damaging effect on AIPL1 function (PP3_Strong).
PP1_Strong			The variant has been reported to segregate with childhood-onset severe retinal dystrophy through the proband plus at least 3 similarly affected relatives, with the variant present in the homozygous state (PP1_Strong; PMID: 10873396).
PP4			At least one proband harboring this variant exhibits a phenotype including a diagnosis of LCA (0.5 pts) with severe visual impairment from birth or during early infancy (1 pt) accompanied by nystagmus (1 pt), absent or very sluggish pupillary responses (0.5 pts), and absent or markedly reduced electroretinogram responses from both rods (0.5 pts) and cones (1 pt), which together are specific for AIPL1-related retinopathy (total 4.5 points, PMID: 10873396, PP4).

PM3

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This variant has been reported in 2 probands with early-onset severe retinal dystrophy who were homozygous for the variant (PMIDs 10873396, 15024725). (1 point, PM3)

Curation History [↗](#)

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