

Variant: NM_014336.5(AIPL1):c.152A>G (p.Asp51Gly)

Version: 1.0

CA397397594 [↗](#)

2736407 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 65489f0a-652a-4c5b-b304-54564ba497d3

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HGVS expressions

NM_014336.5:c.152A>G

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NC_000017.11:g.6434043T>C

CM000679.2:g.6434043T>C

NC_000017.10:g.6337363T>C

CM000679.1:g.6337363T>C

NC_000017.9:g.6278087T>C

NG_008474.1:g.6157A>G

ENST00000381129.8:c.152A>G

ENST00000250087.9:c.152A>G

ENST00000381128.2:c.*24A>G

ENST00000381129.7:c.152A>G

ENST00000570466.5:c.97-11A>G

ENST00000570584.5:c.127A>G

ENST00000571740.5:c.152A>G

ENST00000574506.5:c.116A>G

ENST00000574913.1:c.152A>G

ENST00000575265.5:c.152A>G

ENST00000576307.5:c.96+966A>G

ENST00000576776.5:c.152A>G

ENST00000621374.4:c.152A>G

NM_001033054.2:c.152A>G

NM_001033055.2:c.96+966A>G

NM_001285399.2:c.116A>G

NM_001285400.2:c.97-11A>G

NM_001285401.2:c.152A>G

NM_001285402.1:c.35A>G

NM_001285403.2:c.152A>G

NM_014336.4:c.152A>G

NM_001033054.3:c.152A>G

NM_001033055.3:c.96+966A>G

NM_001285399.3:c.116A>G

NM_001285400.3:c.97-11A>G

NM_001285401.3:c.152A>G

NM_001285402.2:c.35A>G

NM_001285403.3:c.152A>G

NM_001285403.4:c.152A>G

Likely Pathogenic

Met criteria codes 4

PM2_Supporting

PP4_Moderate

PM3_Strong

PP3_Moderate

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.152A>G (p.Asp51Gly) is a missense variant predicted to replace the aspartic acid at position p.51 with glycine. This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.86, which is above the ClinGen LCA/eoRD VCEP threshold of ≥ 0.774 and predicts a damaging effect on AIPL1 protein function (PP3_Moderate). This variant has also been reported in 2 probands with early-onset severe retinal dystrophy who were compound heterozygous with the p.Gln141Ter variant confirmed in trans (2 points, PMID: 31630094), which was previously classified pathogenic by the ClinGen LCA/eoRD VCEP (2 total points, PM3_Strong). At least one proband harboring this variant exhibits a phenotype including diagnosis of LCA (0.5 pts) with onset at age 1 (1 pt) and has photophobia (1 pt), severely reduced electroretinogram responses from both rods (0.5 pts) and cones (1 pt), nystagmus (1 pt), decreased central visual acuity (1 pt), and has had gene panel testing with no additional likely cause found (2 pts). Together these are highly specific for AIPL1-related retinopathy (8 points, PMID: 31630094, PP4_Moderate). 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: PM3_Strong, PP3_Moderate, PP4_Moderate, PM2_Supporting, (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_Moderate



At least one proband harboring this variant exhibits a phenotype including diagnosis of LCA (0.5 pts) with onset at age 1 (1 pt) and has photophobia (1 pt), severely reduced ERGs (1.5 pts), nystagmus (1 pt), decreased central visual acuity (1 pt), and had gene panel testing with no additional likely cause found (2 pts). Together these are highly specific for AIPL1-related recessive retinopathy (8 points, PMID: 31630094, PP4_Moderate).

PM3_Strong



This variant has also been reported in at least 2 probands with early-onset severe retinal dystrophy who were compound heterozygous with the p.Gln141Ter variant confirmed in trans (2 points, PMID: 31630094), which was previously classified pathogenic by the ClinGen LCA/eoRD VCEP (2 total points, PM3_Strong).

PP3_Moderate



The computational predictor REVEL gives a score of 0.86, which is above the ClinGen LCA/eoRD VCEP threshold of ≥ 0.644 and predicts a damaging effect on AIPL1 protein function (PP3).

Curation History 

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