

Variant: NM_014336.5(AIPL1):c.724AAG[1] (p.Lys243del)

Version: 1.0

CA8328415 [↗](#)

1419404 (ClinVar) [↗](#)

Gene: [AIPL1](#)
Condition: AIPL1-related retinopathy ([MONDO:0100438](#))
Inheritance Mode: Autosomal recessive inheritance
UUID: 26888b4c-1df8-4b35-91f3-b7b87f6c1a8e
Approved on: 2025/9/29
Published on: 2025/9/29

HGVS expressions

NM_014336.5:c.724AAG[1]
NM_014336.5(AIPL1):c.724AAG[1] (p.Lys243del)
NC_000017.11:g.6426674_6426676del
CM000679.2:g.6426674_6426676del
NC_000017.10:g.6329994_6329996del
CM000679.1:g.6329994_6329996del
NC_000017.9:g.6270718_6270720del
NG_008474.1:g.13528_13530del
ENST00000381129.8:c.727_729del
ENST00000250087.9:c.538_540del
ENST00000381128.2:c.*599_*601del
ENST00000381129.7:c.727_729del
ENST00000570466.5:c.661_663del
ENST00000570584.5:c.251+7247_251+7249del
ENST00000571740.5:c.703_705del
ENST00000574506.5:c.691_693del
ENST00000575265.5:c.727_729del
ENST00000576307.5:c.547_549del
ENST00000576776.5:c.655_657del
ENST00000621374.4:c.727_729del
NM_001033054.2:c.538_540del
NM_001033055.2:c.547_549del
NM_001285399.2:c.691_693del
NM_001285400.2:c.661_663del
NM_001285401.2:c.655_657del
NM_001285402.1:c.610_612del
NM_001285403.2:c.703_705del
NM_014336.4:c.727_729del
NM_001033054.3:c.538_540del
NM_001033055.3:c.547_549del
NM_001285399.3:c.691_693del
NM_001285400.3:c.661_663del
NM_001285401.3:c.655_657del
NM_001285402.2:c.610_612del
NM_001285403.3:c.703_705del
NM_014336.5:c.727_729del
NM_001285403.4:c.703_705del

Likely Pathogenic

Met criteria codes 4

PM3_Strong

PM4_Supporting

PP4

PM2_Supporting

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.727_729del (p.Lys243del) is an in-frame deletion of three nucleotides predicted to cause a change in the length of the protein due to deletion of 1 amino acid in a non-repeat region, with at least one of the deleted base pairs highly conserved with a PhyloP conservation score of 2.5 (PM4_Supporting). This variant is present in gnomAD v.4.1.0 at a total allele frequency of 0.00001115, with 18 / 1,614,218 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 was homozygous for the variant (0.5 points, VCEP member-provided data). This variant has also been reported in at least 2 probands with early-onset severe retinal dystrophy who were compound heterozygous with either the NM_014336.5(AIPL1):c.834G>A (p.Trp278Ter) variant suspected in trans (0.5 points, PMID: 32865313), which was previously classified pathogenic by the ClinGen LCA/eoRD VCEP, or the NM_014336.5(AIPL1):c.190G>A (p.Gly64Arg) variant confirmed in trans (1 point, VCEP member-provided data, Blueprint Genetics), which was previously classified likely pathogenic by the ClinGen LCA/eoRD VCEP (2 total points, PM3_Strong). A fourth proband with retinal dystrophy has been reported harboring the variant in the compound heterozygous state with the NM_014336.5(AIPL1):c.364G>A (p.Gly122Arg) variant, however, additional information will be required for inclusion in PM3 (VCEP member-provided data). At least one proband harboring this variant exhibits a phenotype including a diagnosis of Leber congenital amaurosis (0.5 pts) with light-seeking behavior (1 pt) from birth (1 pt), nystagmus (1 pt), central visual acuity limited to light perception (1 pt), and relatively normal fundus appearance at age 1 year with very mild granular RPE pigmentation (0.5 pts), which together are specific for AIPL1-related retinopathy (total 4 points, PMID: 32865313, PP4). 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: PM4_Supporting, PM2_Supporting, PM3_Strong, and PP4. (VCEP specifications version 1.0.0; date of approval 09/24/2025).

Met criteria codes

PM3_Strong



This variant has been reported in at least 1 proband with early-onset severe retinal dystrophy who was homozygous for the variant (0.5 points, VCEP member-provided data). This variant has also been reported in at least 2 probands with early-onset severe retinal dystrophy who were compound heterozygous with either the NM_014336.5(AIPL1):c.834G>A (p.Trp278Ter) variant suspected in trans (0.5 points, PMID: 32865313), which was previously classified pathogenic by the ClinGen LCA/eoRD VCEP, or the NM_014336.5(AIPL1):c.190G>A (p.Gly64Arg) variant confirmed in trans (1 point, VCEP member-provided data, Blueprint Genetics), which was previously classified likely pathogenic by the ClinGen LCA/eoRD VCEP (2 total points, PM3_Strong). A fourth proband with retinal dystrophy has been reported harboring the variant in the compound heterozygous state with the NM_014336.5(AIPL1):c.364G>A (p.Gly122Arg) variant, however, additional information will be required for inclusion in PM3 (VCEP member-provided data).

PM4_Supporting			This variant is predicted to cause a change in the length of the protein due to an in-frame deletion encoding 1 amino acids in a non-repeat region, with at least one of the deleted base pairs highly conserved with a PhyloP conservation score of 2.5 (PM4_Supporting).
PP4			At least one proband harboring this variant exhibits a phenotype including a diagnosis of Leber congenital amaurosis (0.5 pts) with light-seeking behavior (1 pt) from birth (1 pt), nystagmus (1 pt), central visual acuity limited to light perception (1 pt), and relatively normal fundus appearance at age 1 year with very mild granular RPE pigmentation (0.5 pts), which together are specific for AIPL1-related retinopathy (total 4 points, PMID: 32865313, PP4).
PM2_Supporting			This variant is present in gnomAD v.4.1.0 at a total allele frequency of 0.00001115, with 18 / 1,614,218 total alleles, which is lower than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0004 (PM2_Supporting).

Curation History 		
    		
Showing 1 to 1 of 1 rows		

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.