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Variant: NM_000350.3:c.6449G>A

Version: 1.0

CA227408

99463 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: f17b618c-df7c-4a3d-bf86-04165e6bd0d8
Approved on: 2026/6/23
Published on: 2026/7/28

HGVS expressions

NM_000350.3:c.6449G>A
NC_000001.11:g.94000866C>T
CM000663.2:g.94000866C>T
NC_000001.10:g.94466422C>T
CM000663.1:g.94466422C>T
NC_000001.9:g.94239010C>T
NG_009073.1:g.125284G>A
ENST00000370225.4:c.6449G>A
ENST00000370225.3:c.6449G>A
ENST00000536513.5:c.2825G>A
NM_000350.2:c.6449G>A

Pathogenic

Met criteria codes 4

PP3_Moderate | PS4 | PM3_Strong | PM2_Supporting

Evidence Links 0

Expert Panel

ABCA4 VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen ABCA4 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ABCA4 Version 1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

ABCA4 VCEP

The NM_000350.3(ABCA4):c.6449G>A is a missense variant predicted to cause substitution of cysteine by tyrosine at amino acid 2150 (p.Cys2150Tyr). The total minor allele frequency in gnomAD v4.1.0 is 0.0000489 (79/1614100 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.923 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate). The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls with an OR of 103 and CI of 40.79 to 333.44, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629). This variant has been detected in six individuals with ABCA4-related retinopathy who were compound heterozygous for the variant and a pathogenic variant, phase unconfirmed

(PM3 = 2 pts, PM3_Strong; PMID: 27820952). In summary, this variant meets the criteria to be classified as pathogenic for ABCA4-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen ABCA4 VCEP (Specification Version 1.0): PS4, PM3_Strong, PP3_Moderate, PM2_Supporting.

Met criteria codes

PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.923 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).
PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 103 and the CI is 40.79 to 333.44, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PM3_Strong	✔	This variant has been detected in six individuals with ABCA4-related retinopathy who were compound heterozygous for the variant and a pathogenic variant, phase unconfirmed (PM3 = 2 pts, PM3_Strong; PMID: 27820952).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.0000489 (79/1614100 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).

Curation History

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