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Variant: NM_000350.3(ABCA4):c.6416G>A (p.Arg2139Gln)

Version: 1.0

CA956878

1477198 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 69df6ff5-b331-4571-a6a2-db95f5a08ae3
Approved on: 2026/5/26
Published on: 2026/5/26

HGVS expressions

NM_000350.3:c.6416G>A
NM_000350.3(ABCA4):c.6416G>A (p.Arg2139Gln)
NC_000001.11:g.94000899C>T
CM000663.2:g.94000899C>T
NC_000001.10:g.94466455C>T
CM000663.1:g.94466455C>T
NC_000001.9:g.94239043C>T
NG_009073.1:g.125251G>A
ENST00000370225.4:c.6416G>A
ENST00000370225.3:c.6416G>A
ENST00000536513.5:c.2792G>A
NM_000350.2:c.6416G>A

Likely Pathogenic

Met criteria codes 4

PP3_Moderate | PM3 | PM5 | 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 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

ABCA4 VCEP

The NM_000350.3(ABCA4):c.6416G>A variant in ABCA4 is a missense variant predicted to cause substitution of arginine by glutamine at amino acid 2139; p.Arg2139Gln. The total minor allele frequency in gnomAD v4.1.0 is 0.00008054 (130/1614074 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.964 which is above the threshold of >0.772 meeting PP3_Moderate. This variant has been detected in at least 1 individual with ABCA4-related retinopathy who was compound heterozygous for the variant confirmed in trans with a pathogenic variant (c.6445C>T, p.Arg2149Ter) (PM3; PMID: 37705246). Another missense variant, c.6416G>C; p.Arg2139Pro, in the same codon has been classified as pathogenic for

ABCA4-related retinopathy by the ClinGen ABCA4 VCEP, and Splice AI revealed no expected effects on splicing (PM5). In summary, this variant meets the criteria to be classified as likely pathogenic for ABCA4-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen ABCA4 VCEP (Specification Version 1.0.0): PM3, PP3_Moderate, PM5, PM2_Supporting.

Met criteria codes

PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.964 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).
PM3	✔	This variant has been detected in at least 1 individual with ABCA4-related retinopathy. This individual was compound heterozygous for the variant and a pathogenic variant (c.6445C>T, p.Arg2149Ter) which was confirmed in trans by parental/family testing (PM3= 1 point; PMID: 37705246; PM3).
PM5	✔	Another missense variant, c.6416G>C; p.Arg2139Pro, in the same codon has been classified as pathogenic for ABCA4-related retinopathy by the ClinGen ABCA4 VCEP, and Splice AI revealed no expected effects on splicing (PM5).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.00008054 (130/1614074 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting). 1 homozygote present in South Asian population

Curation History

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