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Variant: NM_000350.3(ABCA4):c.32T>C (p.Leu11Pro)

Version: 1.0

CA227106

99217 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: c9c216b9-97ce-43a8-834f-f6808ce70962
Approved on: 2025-12-05
Published on: 2025-12-22

HGVS expressions

NM_000350.3:c.32T>C
NM_000350.3(ABCA4):c.32T>C (p.Leu11Pro)
NC_000001.11:g.94121014A>G
CM000663.2:g.94121014A>G
NC_000001.10:g.94586570A>G
CM000663.1:g.94586570A>G
NC_000001.9:g.94359158A>G
NG_009073.1:g.5136T>C
ENST00000370225.4:c.32T>C
ENST00000649773.1:c.32T>C
ENST00000370225.3:c.32T>C
NM_000350.2:c.32T>C

Pathogenic

Met criteria codes 4

PM3_Strong | PS4 | PP3_Moderate | 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.32T>C variant in ABCA4 is a missense variant predicted to cause substitution of leucine by proline at amino acid 11 (p.Leu11Pro). The total minor allele frequency in gnomAD v4.1.0 is 0.000004337 (7/1613874 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.948 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 95.5 and the CI is 12.78-41149.08, 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 at least 2 individuals with ABCA4-related retinopathy who were compound heterozygotes for the variant and a pathogenic variant (c.1A>G; p.Met1Val, c.2888delG) and both of those were confirmed in trans by family testing (PM3_Strong; PMIDs: 19365591, 17325136). 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, PM2_Supporting, PP3_Moderate.

Met criteria codes

PM3_Strong	✔	This variant has been detected in at least 2 individuals with ABCA4-related retinopathy. Of those individuals, both were compound heterozygous for the variant and a pathogenic variant (c.1A>G p.(Met1Val); c.2888delG) and both of those were confirmed in trans by family testing (PM3= 2 points; PM3_Strong; PMIDs: 19365591, 17325136).
PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 95.5 and the CI is 12.78-41149.08, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.948 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.000004337 (7/1613874 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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