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Variant: NM_000350.3:c.5318C>T

Version: 1.0

CA957302

236129 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 742224c5-1470-4506-8296-718398450204
Approved on: 2026/3/24
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HGVS expressions

NM_000350.3:c.5318C>T
NC_000001.11:g.94014685G>A
CM000663.2:g.94014685G>A
NC_000001.10:g.94480241G>A
CM000663.1:g.94480241G>A
NC_000001.9:g.94252829G>A
NG_009073.1:g.111465C>T
ENST00000370225.4:c.5318C>T
ENST00000370225.3:c.5318C>T
ENST00000536513.5:c.1694C>T
NM_000350.2:c.5318C>T

Pathogenic

Met criteria codes 5

PM2_Supporting | PP1 | PS4 | PM3_Strong | PP3_Moderate

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.5318C>T is a missense variant predicted to cause substitution of alanine by valine at amino acid 1773 (p.Ala1773Val). Minor allele frequency in gnomAD v4.1.0 is 0.0000254 (41/1613990 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.79 which is above the threshold of >0.772 meeting PP3_Moderate. The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls with an OR of 138.9 and CI of 56.18 to 447.50, which is above the ABCA4 VCEP threshold of >3, where the CI does not contain 1 (PS4; PMID: 35120629). This variant has been detected in at least ten individuals with ABCA4-related retinopathy. Of those individuals, one was compound heterozygous for the variant and a pathogenic variant, confirmed in trans by family testing. In addition, this variant has

been detected in at least nine individuals with ABCA4-related retinopathy and who were homozygous for the variant, which may represent a founder variant in Mexico (PM3_Strong, PMID: 29422768, 37774808). The variant has been reported to segregate with ABCA4-related retinopathy in one proband and 1 similarly affected relative (PP1; PMID: 29422768). 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 1.0.0: PS4, PM3_Strong, PP3_Moderate, PP1, PM2_supporting.

Met criteria codes

PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.0000254 (41/1613990 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).
PP1	✔	The variant has been reported to segregate with ABCA4-related retinopathy in one proband and 1 similarly affected relative. Of note, the variant was identified as recurrent among unrelated families from a central region of Mexico (PP1_Supporting; PMID: 29422768)
PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 138.9 and the CI is 56.18 to 447.50, which is above the ABCA4 VCEP threshold of >3, where the CI does not contain 1 (PS4; PMID: 35120629).
PM3_Strong	✔	This variant has been detected in at least ten individuals with ABCA4-related retinopathy. Of those individuals, one was compound heterozygous for the variant and a pathogenic variant, confirmed in trans by family testing. In addition, this variant has been detected in at least nine individuals with ABCA4-related retinopathy and who were homozygous for the variant (PM3 = 2 pts; PM3_Strong, PMIDs: 29422768, 37774808).
PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.79 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).

Curation History

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