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Variant: NM_000350.3(ABCA4):c.5753A>T (p.Asp1918Val)

Version: 1.0

CA341280422

871507 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 3c480a36-8e82-4522-82fa-43eb89509b26
Approved on: 2025/12/5
Published on: 2025/12/19

HGVS expressions

NM_000350.3:c.5753A>T
NM_000350.3(ABCA4):c.5753A>T (p.Asp1918Val)
NC_000001.11:g.94008833T>A
CM000663.2:g.94008833T>A
NC_000001.10:g.94474389T>A
CM000663.1:g.94474389T>A
NC_000001.9:g.94246977T>A
NG_009073.1:g.117317A>T
ENST00000370225.4:c.5753A>T
ENST00000370225.3:c.5753A>T
ENST00000465352.1:n.169A>T
ENST00000536513.5:c.2129A>T
NM_000350.2:c.5753A>T

Pathogenic

Met criteria codes 5

PP4 PM3 PP3_Moderate PS4 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 c.5732A>T (NM_000350.3) variant in ABCA4 is a missense variant predicted to cause substitution of aspartic acid by valine at amino acid 1918 (p.Asp1918Val). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.836 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. The OR is infinity and the CI is 2.24 to infinity, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629). At least

one patient met ABCA4-related retinopathy phenotype criteria (PP4, PMID: 27939946). This variant has been detected in at least four individuals with ABCA4-related retinopathy (PMID: 27939946, 32531858, 38003421). Of those individuals, two were compound heterozygous for the variant and a pathogenic or likely pathogenic variant and one of those were confirmed in trans by parental testing (PMID: 27939946, 32531858; PM3). 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 v.1.0): PS4, PM3, PP3, PP4_Supporting, PM2_Supporting.

Met criteria codes

PP4	✔	Patient reported with macular flecks and decreased central visual acuity with onset at age 9 and compound heterozygous variants ABCA4:c.5743A>T, c.2537A>T as detected using a 325 gene NGS panel. (PP4_Supporting met).
PM3	✔	This variant has been detected in at least two individuals with ABCA4-related retinopathy. Of those individuals, two were compound heterozygous for the variant and a pathogenic or likely pathogenic variant and one of those were confirmed in trans by parental testing (PMID: 27939946, 32531858; PM3 met).
PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.836 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 infinity and the CI is 2.24 to infinity, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History

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