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Variant: NM_000350.3(ABCA4):c.3322C>T (p.Arg1108Cys)

Version: 1.0

CA220683

92867 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: c7812dec-8607-4b00-b3b7-bfe968667049
Approved on: 2026/6/23
Published on: 2026/7/28

HGVS expressions

NM_000350.3(ABCA4):c.3322C>T (p.Arg1108Cys)
NM_000350.3:c.3322C>T
NC_000001.11:g.94042767G>A
CM000663.2:g.94042767G>A
NC_000001.10:g.94508323G>A
CM000663.1:g.94508323G>A
NC_000001.9:g.94280911G>A
NG_009073.1:g.83383C>T
ENST00000370225.4:c.3322C>T
ENST00000370225.3:c.3322C>T
ENST00000536513.5:c.-64-2678C>T
NM_000350.2:c.3322C>T

Pathogenic

Met criteria codes 4

PS4 PP3_Moderate PP1 PM3_Strong

Not Met criteria codes 1

PM2

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:c.3322C>T variant in ABCA4 is a missense variant predicted to cause substitution of arginine by cysteine at amino acid 1108; p.Arg1108Cys. The computational predictor REVEL gives a score of 0.887 which is above the threshold of >0.772 (PP3_Moderate). The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls with an OR of 79.8 and CI of 50.21-133.45, 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 many individuals with ABCA4-related retinopathy. Of those individuals, at least six were compound heterozygous for the variant, and a pathogenic or likely pathogenic variant (c.5882G>A/p.G1961E; c.5714+5G>A;

c.4139C>T/p.Pro1380Leu; c.3056C>T/p.Thr1019Met; c.4577C>T/p.Thr1526Met), and one of those was confirmed in trans by family testing (3.5 PM3 Points; PM3_Strong; PMID: 32531858, 37705246). The variant has been reported to segregate with ABCA4-related retinopathy in the proband and 1 similarly affected relative (PP1; PMID: 32531858). 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): PP3_Moderate, PS4, PM3_Strong, PP1.

Met criteria codes

PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 79.8 and the CI is 50.21-133.45, 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 0.887 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).
PP1	✔	The variant has been reported to segregate with ABCA4-related retinopathy in the proband and 1 similarly affected relative (PP1; PMID:32531858).
PM3_Strong	✔	This variant has been detected in many individuals with ABCA4-related retinopathy. Of those individuals, at least six were compound heterozygous for the variant, and a pathogenic or likely pathogenic variant (c.5882G>A/p.G1961E; c.5714+5G>A; c.4139C>T/p.Pro1380Leu; c.3056C>T/p.Thr1019Met; c.4577C>T/p.Thr1526Met), and one of those was confirmed in trans by family testing (3.5 PM3 Points; PM3_Strong; PMID:32531858,37705246).

Not Met criteria codes

PM2	✖	The total minor allele frequency in gnomAD v4.1.0 is 0.00019 (313/1614208 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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