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Variant: NM_000350.3(ABCA4):c.6319C>T (p.Arg2107Cys)

Version: 1.0

CA956906

635988 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: e1a115a1-a0e0-43b7-bf7d-8abd218fe741
Approved on: 2026/4/28
Published on: 2026/4/30

HGVS expressions

NM_000350.3:c.6319C>T
NM_000350.3(ABCA4):c.6319C>T (p.Arg2107Cys)
NC_000001.11:g.94001069G>A
CM000663.2:g.94001069G>A
NC_000001.10:g.94466625G>A
CM000663.1:g.94466625G>A
NC_000001.9:g.94239213G>A
NG_009073.1:g.125081C>T
ENST00000370225.4:c.6319C>T
ENST00000370225.3:c.6319C>T
ENST00000536513.5:c.2695C>T
NM_000350.2:c.6319C>T

Pathogenic

Met criteria codes 4

PP3_Moderate | PS4 | PM3_Strong | PM2_Supporting

Not Met criteria codes 2

PM5 | PP4

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.6319C>T (NM_000350.3) variant in ABCA4 is a missense variant predicted to cause substitution of arginine by cysteine at amino acid 2107; p.Arg2107Cys. The total minor allele frequency in gnomAD v4.1.0 is 0.00003656 (59/1613986 alleles), meeting PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.966 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 35.7 and the CI is 8.92 - 205.21, 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 5 individuals with ABCA4-related retinopathy. Of those individuals, 4 were compound heterozygous

for the variant and another pathogenic variant but they were not confirmed in trans (PMID: 31812472, PMID: 31812472, PMID: 29310964, PMID: 11527935), and 1 individual was compound heterozygous for the variant and another likely pathogenic variant that were confirmed in trans (PMID: 26377081) meeting PM3_strong. 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): PM2_Supporting, PP3_Moderate, PS4, PM3_Strong.

Met criteria codes

PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.966 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 35.7 and the CI is 8.92 - 205.21, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PM3_Strong	✔	This variant has been detected in at least 5 individuals with ABCA4-related retinopathy. Of those individuals, 4 were compound heterozygous for the variant and another pathogenic variant but they were not confirmed in trans (participant 8 with c.6319C>T and c.5461-10T>C phase unconfirmed (+0.5 pts; PMID: 31812472), participant 41 with c.6319C>T and c.5461-10T>C phase unconfirmed (+0.5 pts; PMID: 31812472), participant 42215152 with c.6319C>T and c.5461-10T>C phase unconfirmed (+0.5 pts; PMID: 29310964); participant 032-018 with c.6319C>T and p.Arg152Ter phase unconfirmed (+0.5 pt; PMID: 11527935). 1 individual was compound heterozygous for the variant and another likely pathogenic variant that were confirmed in trans (participant 90 with c.6319C>T and c.6213C>G (+1 pt; PMID: 26377081). Total points 3, PM3_Strong.
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.00003656 (59/1613986 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).

Not Met criteria codes

PM5	✖	This variant is used to help curate another missense variant, NM_000350.3(ABCA4):c.6320G>A; p.Arg2107His. .
PP4	✖	One patient with this variant displayed presence of at least two ABCA4 variants, onset under 18 years of age, decreased central visual acuity and decreased cone ERG response, but fundoscopy does not indicate "macular flecks." PP4 not met (PMID:29310964).

Curation History

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