The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000350.3:c.3476T>C

Version: 1.0

CA341290608

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: f8c64bce-e2f2-4fec-8241-219236862265
Approved on: 2026/5/5
Published on: 2026/5/17

HGVS expressions

NM_000350.3:c.3476T>C
NC_000001.11:g.94041255A>G
CM000663.2:g.94041255A>G
NC_000001.10:g.94506811A>G
CM000663.1:g.94506811A>G
NC_000001.9:g.94279399A>G
NG_009073.1:g.84895T>C
ENST00000370225.4:c.3476T>C
ENST00000370225.3:c.3476T>C
ENST00000536513.5:c.-64-1166T>C
NM_000350.2:c.3476T>C

Likely Pathogenic

Met criteria codes 3
PM2_Supporting PM3 PS4

Not Met criteria codes 3
PP3 PP4 BP4

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.3476T>C variant in ABCA4 is a missense variant predicted to cause substitution of arginine by leucine at amino acid 1159 (p.Leu1159Ser) is absent from gnomAD v4.1.0 (PM2_Supporting). 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 14.02 to infinity, 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 two individuals with ABCA4-related retinopathy. Of those individuals, one was compound heterozygous for the variant and a pathogenic or likely pathogenic variant, confirmed in trans by family testing, and one individual was homozygous for the variant (PM3; PMID: 37774808). In

summary, this variant meets the criteria to be classified as likely 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, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PM3	✔	Two probands were scored. One proband with Stargardt disease with variant in trans with pathogenic variant c.1222C>T; p.Arg408* (PMID: 37774808). A second individual is homozygous for the variant (PMID: 26780318) PM3 = 1.5 points
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 14.02 to infinity, which is above the ABCA4 VCEP threshold of >5, where the CI does not contain 1 (PS4; PMID: 35120629).

Not Met criteria codes

PP3	✖	The computational predictor REVEL gives a score of 0.642 which is neither above nor below the thresholds predicting a damaging (>0.644) or benign (<0.29) impact on ABCA4 function, and SpliceAI gives a score <0.2. PP3 not met.
PP4	✖	Study reporting proband homozygous for variant included patients in study based on a definition of Stargardt disease, but there was limited specific information for this proband (PMID: 26780318). Therefore, PP4 is not met due to a lack of PP4 points.
BP4	✖	The computational predictor REVEL gives a score of 0.642 which is neither above nor below the thresholds predicting a damaging (>0.644) or benign (<0.29) impact on ABCA4 function, and SpliceAI gives a score <0.2. BP4 not met.

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.