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(ABCA4):c.4532C>A (p.Pro1511His)

Version: 1.0

CA16617202

417992 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 1024d13e-fd28-4a37-802c-f9d88e733b7a
Approved on: 2026/1/27
Published on: 2026/1/28

HGVS expressions

NM_000350.3:c.4532C>A
NM_000350.3(ABCA4):c.4532C>A (p.Pro1511His)
NC_000001.11:g.94029452G>T
CM000663.2:g.94029452G>T
NC_000001.10:g.94495008G>T
CM000663.1:g.94495008G>T
NC_000001.9:g.94267596G>T
NG_009073.1:g.96698C>A
ENST00000370225.4:c.4532C>A
ENST00000370225.3:c.4532C>A
ENST00000536513.5:c.908C>A
NM_000350.2:c.4532C>A

Likely Pathogenic

Met criteria codes 4

PS4 PP3_Moderate PM3_Supporting PM2_Supporting

Not Met criteria codes 1

PM5

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:c.4532C>A variant in ABCA4 is a missense variant predicted to cause substitution of proline by histidine at amino acid 1511; p.Pro1511His. The total minor allele frequency in gnomAD v4.1.0 is 0.000002578 (4/1551676 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.918 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 with an OR of 6.0 and the CI is 1.31 - 22.34, 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 3

individuals with ABCA4-related retinopathy; however, only one individual was scoreable (0.50 PM3 points; PM3_Supporting; PMID:22427542, 29925512, 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, PP3_Moderate, PM3_Supporting, PM2_Supporting.

Met criteria codes

PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 6.0 and the CI is 1.31 - 22.34, 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 0.918 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).
PM3_Supporting	✔	This variant has been detected in 3 individuals with ABCA4-related retinopathy. Of those individuals, 1 was compound heterozygous for the variant and a pathogenic variant in an unknown phase (0.5). Another eligible proband was used as evidence for the in trans variant, so could not be used as evidence for this variant. The 3rd individual has another VUS with phase unknown. (Total 0.5 PM3 points; PM3_Supporting; PMID:22427542, 29925512, 37774808).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.000002578 (4/1551676 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001).

Not Met criteria codes

PM5	✖	This variant will be used to score PM5 for other changes at this residue.

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.