

Variant: *NM_000350.3(ABCA4):c.2023G>A (p.Val675Ile)*

Version: 1.0

CA958364 [↗](#)

288341 (ClinVar) [↗](#)

Gene: ABCA4 ([HGNC:24](#))

Condition: ABCA4-related retinopathy ([MONDO:0800406](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 53fd82a5-110e-4f8b-9a64-eef1f3e036b6

Approved on: 2026/8/25

Published on: 2026/8/25

HGVS expressions

NM_000350.3(ABCA4):c.2023G>A (p.Val675Ile)

NM_000350.3:c.2023G>A

NC_000001.11:g.94060674C>T

CM000663.2:g.94060674C>T

NC_000001.10:g.94526230C>T

CM000663.1:g.94526230C>T

NC_000001.9:g.94298818C>T

NG_009073.1:g.65476G>A

ENST00000370225.4:c.2023G>A

ENST00000649773.1:c.2023G>A

ENST00000370225.3:c.2023G>A

ENST00000472033.1:n.143G>A

ENST00000536513.5:c.-65+2500G>A

NM_000350.2:c.2023G>A

Pathogenic

Met criteria codes **4**

PM3_Strong

PS4

PP3

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

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

ABCA4 VCEP

The NM_000350.3(ABCA4):c.2023G>A is a missense variant predicted to cause substitution of valine by isoleucine at amino acid 675; p.Val675Ile. The total minor allele frequency in gnomAD v4.1.0 is 0.00003098 (50/1614116 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold (<0.0001) for PM2_Supporting. The computational predictor REVEL gives a score of 0.705 which is in the range of 0.644-0.772 meeting PP3. The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in

controls with an OR of 29.8 and CI of 10.93 to 93.94, 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 well over five individuals with ABCA4-related retinopathy who were homozygous or compound heterozygous for the variant and a pathogenic or likely pathogenic variant (PM3_Strong, 2.25 pts; PMIDs: 23499370, 28041643, 41642025, 39643591). 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): PS4, PM3_Strong, PP3, PM2_Supporting.

Met criteria codes

PM3_Strong			This variant has been detected in at least four individuals with ABCA4-related retinopathy who were compound heterozygous for the variant and a pathogenic or likely pathogenic variant and one of those were confirmed in trans by whole gene sequencing (PMIDs: 23499370, 28041643, 39643591). There is also at least one proband with Stargardt disease who is homozygous for the variant (PMID: 41642025). PM3: 2 pts.
PS4			The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 29.8 and the CI is 10.93 to 93.94, which is above the ABCA4 VCEP threshold of ≥ 5 , where the CI does not contain 1 (PS4; PMID: 35120629).
PP3			The computational predictor REVEL gives a score of 0.705 which is in the range of 0.644-0.772, evidence that predicts a damaging effect on ABCA4 function (PP3).
PM2_Supporting			The total minor allele frequency in gnomAD v4.1.0 is 0.00003098 (50/1614116 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).

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.