

Variant: NM_000350.3:c.4469G>A

Version: 1.0

CA227198 [↗](#)

99288 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 7f82fd40-05b6-4059-a6df-5007bb8b3725

Approved on: 2026/6/23

Published on: 2026/7/28

HGVS expressions

NM_000350.3:c.4469G>A

NC_000001.11:g.94029515C>T

CM000663.2:g.94029515C>T

NC_000001.10:g.94495071C>T

CM000663.1:g.94495071C>T

NC_000001.9:g.94267659C>T

NG_009073.1:g.96635G>A

ENST00000370225.4:c.4469G>A

ENST00000370225.3:c.4469G>A

ENST00000536513.5:c.845G>A

NM_000350.2:c.4469G>A

Pathogenic

Met criteria codes **4**

PS3_Supporting

PM3_Very Strong

PP3_Moderate

PS4

Not Met criteria codes **2**

BS1

PM2

Evidence Links **1**

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.4469G>A is a missense variant predicted to cause substitution of cysteine by tyrosine at amino acid 1490, p.Cys1490Tyr. The computational predictor REVEL gives a score of 0.95 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 167.2 and CI of 93.20 to 327.21, 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 15 individuals with ABCA4-related retinopathy. Of those individuals, six were compound heterozygous for the variant and a pathogenic variant. Nine individuals were homozygous for the variant (PM3 = 4 points, PM3_Very Strong, PMID: 23695285). ATPase activity in COS7 cells showed a 21.4% decrease from wildtype indicating that this variant impacts protein function

(PS3_Supporting; PMID: 16103129). 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): PM3_Very Strong, PS4, PP3_Moderate, PS3_Supporting.			
Met criteria codes			
PS3_Supporting			ATPase activity in COS7 cells showed a 21.4% decrease from wildtype indicating that this variant impacts protein function (PS3_Supporting; PMID: 16103129).
Figure 3: ATP hydrolytic activity assay in which C1490Y ABCA4 were expressed in COS7 cells showed a 21.4% decrease from wildtype. PubMed:16103129 			
PM3_Very Strong			This variant has been detected in at least 15 individuals with ABCA4-related retinopathy. Of those individuals, six were compound heterozygous for the variant and a pathogenic variant. Nine individuals were homozygous for the variant (PM3 = 4 points, PM3_Very Strong, PMID: 23695285).
PP3_Moderate			The computational predictor REVEL gives a score of 0.95 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 167.2 and the CI is 93.20 to 327.21, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
Not Met criteria codes			
BS1			The total minor allele frequency in gnomAD v4.1.0 is 0.0001556 (250/1606364 alleles), and the GroupMax filtering allele frequency is 0.00018099. This is higher than the ClinGen ABCA4 VCEP’s threshold for PM2_Supporting (<0.0001), and lower than the threshold for BS1_Supporting (>0.00163). Therefore, none of the population data codes are met.
PM2			The total minor allele frequency in gnomAD v4.1.0 is 0.0001556 (250/1606364 alleles), and the GroupMax filtering allele frequency is 0.00018099. This is higher than the ClinGen ABCA4 VCEP’s threshold for PM2_Supporting (<0.0001), and lower than the threshold for BS1_Supporting (>0.00163). Therefore, none of the population data codes are 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.