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Variant: NM_000350.3(ABCA4):c.1819G>A (p.Gly607Arg)

Version: 1.0

CA226936

99087 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4e46c0f0-40ae-41cf-86dd-a271c50dceba
Approved on: 2025/12/16
Published on: 2025/12/19

HGVS expressions

NM_000350.3(ABCA4):c.1819G>A (p.Gly607Arg)
NM_000350.3:c.1819G>A
NC_000001.11:g.94062695C>T
CM000663.2:g.94062695C>T
NC_000001.10:g.94528251C>T
CM000663.1:g.94528251C>T
NC_000001.9:g.94300839C>T
NG_009073.1:g.63455G>A
ENST00000370225.4:c.1819G>A
ENST00000649773.1:c.1819G>A
ENST00000370225.3:c.1819G>A
ENST00000536513.5:c.-65+479G>A
NM_000350.2:c.1819G>A

Pathogenic

Met criteria codes 6

PM3_Supporting | PP3_Moderate | PS4 | PM2_Supporting | PP1 | 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 NM_000350.3:c.1819G>A variant in ABCA4 is a missense variant predicted to cause substitution of glycine by arginine at amino acid 607 (p.Gly607Arg). The total minor allele frequency in gnomAD v4.1.0 is 0.00001735 (28/1614146 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.951 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. The OR is 131.4 and the CI is 41.15 - 670.77, which

is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629). At least one patient with this variant meets criteria for ABCA4-related retinopathy (PP4, PMID:24632595). The variant has been reported to segregate with ABCA4-related retinopathy in the proband and 1 similarly affected relative (PP1; PMID:24632595). This variant has been detected in at least two individuals with ABCA4-related retinopathy. One of those individuals was compound heterozygous for the variant and a pathogenic variant in an unconfirmed phase (ABCA4 c.3386G>T; p.Arg1129Leu) meeting PM3_Supporting (PMID:23755871). 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): PS4, PP3_Moderate, PP1, PP4, PM2_Supporting, PM3_Supporting.

Met criteria codes

PM3_Supporting	✔	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 variant in an unconfirmed phase (c.3386G>T (p.Arg1129Leu)) (0.5 PM3 points; PM3_Supporting; PMID:23755871).
PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.951 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate). No significant splice impact predicted by SpliceAI.
PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 131.4 and the CI is 41.15 - 670.77, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.00001735 (28/1614146 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001).
PP1	✔	The variant has been reported to segregate with ABCA4-related retinopathy in the proband and 1 similarly affected relative (PP1; PMID:24632595).
PP4	✔	At least one patient with this variant displayed presence of at least two ABCA4 variants, onset under 18 years of age, macular flecks and yellow dots on fundus with decreased central visual acuity, which is highly specific for ABCA4-related retinopathy (PP4, PMID:24632595).

Curation History

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