

Variant: NM_000350.3(ABCA4):c.1804C>T (p.Arg602Trp)

Version: 1.0

CA226932 [↗](#)

99084 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 58bce46d-3cda-44fe-95c1-1934c357c89d

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HGVS expressions

NM_000350.3(ABCA4):c.1804C>T (p.Arg602Trp)

NM_000350.3:c.1804C>T

NC_000001.11:g.94062710G>A

CM000663.2:g.94062710G>A

NC_000001.10:g.94528266G>A

CM000663.1:g.94528266G>A

NC_000001.9:g.94300854G>A

NG_009073.1:g.63440C>T

ENST00000370225.4:c.1804C>T

ENST00000649773.1:c.1804C>T

ENST00000370225.3:c.1804C>T

ENST00000536513.5:c.-65+464C>T

NM_000350.2:c.1804C>T

Pathogenic

Met criteria codes **5**

PS4

PP4

PP3_Moderate

PM3

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 1.0.0

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

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

Evidence submitted by expert panel

ABCA4 VCEP

The NM_000350.3:c.1804C>T variant in ABCA4 is a missense variant predicted to cause substitution of arginine by tryptophan at amino acid 602 (p.Arg602Trp). The total minor allele frequency in gnomAD v4.1.0 is 0.00002292 (37/1613984 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.934 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 odds ratio is 276.1 and the confidence interval

is 131.28 to 703.91, 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. At least one patient with this variant met criteria for the ABCA4-related retinopathy phenotype (PP4, PMID: 24444108). Of those individuals, one was compound heterozygous for the variant and a pathogenic, confirmed in trans by Sanger sequencing or familial testing (PMID: 26161775). The other individual was homozygous for the variant (PM3, PMID: 24444108). 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 (v.1.0.0): PS4, PM3, PP3_Moderate, PP4, 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 276.1 and the CI is 131.28 to 703.91, which is above the ABCA4 VCEP threshold of >5, where the CI does not contain 1 (PS4; PMID: 35120629).
PP4			At least one patient with this variant displayed presence of at least two ABCA4 variants, onset under 18 years of age, macular flecks on fundus autofluorescence, progressive vision loss, and macular atrophy, which is highly specific for ABCA4-related retinopathy (PP4, PMID: 24444108).
PP3_Moderate			The computational predictor REVEL gives a score of 0.934 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).
PM3			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, confirmed in trans by Sanger sequencing or familial testing (PMID: 26161775). One individual was homozygous for the variant (PMID: 24444108, PM3).
PM2_Supporting			The total minor allele frequency in gnomAD v4.1.0 is 0.00002292 (37/1613984 alleles), which is lower than the ClinGen ABCA4 VCEP’s threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).

Curation History



 

 

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