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Variant: NM_000350.3(ABCA4):c.634C>T (p.Arg212Cys)

Version: 1.0

CA203216

7898 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7ee03012-22a4-42d2-869e-71c2164977ec
Approved on: 2025/12/5
Published on: 2025/12/19

HGVS expressions

NM_000350.3:c.634C>T
NM_000350.3(ABCA4):c.634C>T (p.Arg212Cys)
NC_000001.11:g.94098928G>A
CM000663.2:g.94098928G>A
NC_000001.10:g.94564484G>A
CM000663.1:g.94564484G>A
NC_000001.9:g.94337072G>A
NG_009073.1:g.27222C>T
ENST00000370225.4:c.634C>T
ENST00000649773.1:c.634C>T
ENST00000370225.3:c.634C>T
NM_000350.2:c.634C>T

Pathogenic

Met criteria codes 3

PP3_Moderate PS4 PM3_Strong

Not Met criteria codes 2

PM2 BS1

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(ABCA4):c.634C>T variant in ABCA4 is a missense variant predicted to cause substitution of arginine by cysteine at amino acid 212 (p.Arg212Cys). The total minor allele frequency in gnomAD v4.1.0 is 0.0001134 (183/1613308 alleles), and the GroupMax filtering allele frequency is 0.00022087. This is higher than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), and lower than the threshold for BS1 (>0.0163). Therefore, none of the population data codes are met. The computational predictor REVEL gives a score of 0.847 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 100.1 and

the CI is 55.99 to 192.76, 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 five individuals with ABCA4-related retinopathy, who were compound heterozygous for the variant and a pathogenic, phase unconfirmed (PMID: 19265867, 34073554, PM3_Strong). 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): PM3_Strong, PS4, PP3_Moderate.

Met criteria codes

PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.847 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 100.1 and the CI is 55.99 to 192.76, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PM3_Strong	✔	This variant has been detected in at least five individuals with ABCA4-related retinopathy, who were compound heterozygous for the variant and a pathogenic, phase unconfirmed (PMID: 19265867, 34073554, PM3_Strong, PM3 = 2.5 points)

Not Met criteria codes

PM2	✖	The total minor allele frequency in gnomAD v4.1.0 is 0.0001134 (183/1613308 alleles), and the GroupMax filtering allele frequency is 0.00022087. This is higher than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), and lower than the threshold for BS1 (>0.0163). Therefore, none of the population data codes are met.
BS1	✖	The total minor allele frequency in gnomAD v4.1.0 is 0.0001134 (183/1613308 alleles), and the GroupMax filtering allele frequency is 0.00022087. This is higher than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), and lower than the threshold for BS1 (>0.0163). Therefore, none of the population data codes are met.

Curation History

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