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Variant: NM_000350.3:c.2041C>T

Version: 1.0

CA226973

99114 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 5b6283c8-1219-4c2b-a290-1c9fb07caf52
Approved on: 2026/7/28
Published on: 2026/7/28

HGVS expressions

NM_000350.3:c.2041C>T
NC_000001.11:g.94060656G>A
CM000663.2:g.94060656G>A
NC_000001.10:g.94526212G>A
CM000663.1:g.94526212G>A
NC_000001.9:g.94298800G>A
NG_009073.1:g.65494C>T
ENST00000370225.4:c.2041C>T
ENST00000649773.1:c.2041C>T
ENST00000370225.3:c.2041C>T
ENST00000472033.1:n.161C>T
ENST00000536513.5:c.-65+2518C>T
NM_000350.2:c.2041C>T

Pathogenic

Met criteria codes 3

PM2_Supporting PVS1 PS4

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.2041C>T, p.Arg681Ter variant in ABCA4 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 14 of 50 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). The total minor allele frequency in gnomAD v4.1.1 is 0.00001921 (31/1613940 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls with an OR of 667.8 and CI of 115.11 to 16384.00, which is above the ABCA4 VCEP threshold of

≥5, where the CI does not contain 1 (PS4; PMID: 35120629). 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): PVS1, PS4, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.1 is 0.00001921 (31/1613940 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).
PVS1	✔	This is a nonsense variant located in exon 14 out of 50, and introduces a premature stop codon between codons 1-2255 (PVS1).
PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 667.8 and the CI is 115.11 to 16384.00, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).

Curation History

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