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Variant: NM_000350.3(ABCA4):c.3994C>T (p.Gln1332Ter)

Version: 1.0

CA227152

99249 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 75572ca3-cdc5-4077-b0fa-ebc6458f9199
Approved on: 2025/12/5
Published on: 2025/12/19

HGVS expressions

NM_000350.3(ABCA4):c.3994C>T (p.Gln1332Ter)
NM_000350.3:c.3994C>T
NC_000001.11:g.94031912G>A
CM000663.2:g.94031912G>A
NC_000001.10:g.94497468G>A
CM000663.1:g.94497468G>A
NC_000001.9:g.94270056G>A
NG_009073.1:g.94238C>T
ENST00000370225.4:c.3994C>T
ENST00000370225.3:c.3994C>T
ENST00000536513.5:c.370C>T
NM_000350.2:c.3994C>T

Pathogenic

Met criteria codes 3

PS4 PVS1 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(ABCA4):c.3994C>T; p.Gln1332Ter variant in ABCA4 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 27/50 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 v4.1.0 is 0.000001239 (2/1614046 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 infinity and the CI is 2.24-infinity, 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

PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is infinity and the CI is 2.24-infinity, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PVS1	✔	This is a nonsense variant located in exon 27 out of 50, and introduces a premature stop codon between codons 1-2255 (PVS1).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.000001239 (2/1614046 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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