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Variant: NM_000350.3:c.3007C>T

Version: 1.0

CA341275107

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 87f34277-cda0-439b-bfda-e569e012ef1e
Approved on: 2025/12/5
Published on: 2025/12/22

HGVS expressions

NM_000350.3:c.3007C>T
NC_000001.11:g.94044656G>A
CM000663.2:g.94044656G>A
NC_000001.10:g.94510212G>A
CM000663.1:g.94510212G>A
NC_000001.9:g.94282800G>A
NG_009073.1:g.81494C>T
ENST00000370225.4:c.3007C>T
ENST00000370225.3:c.3007C>T
ENST00000536513.5:c.-64-4567C>T
NM_000350.2:c.3007C>T

Pathogenic

Met criteria codes 3

PM3_Supporting PVS1 PM2_Supporting

Not Met criteria codes 2

PP4 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 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

ABCA4 VCEP

The NM_000350.3:c.3007C>T (p.Gln1003Ter) variant in ABCA4 is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 20/50 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). This variant has been detected in at least two individuals with ABCA4-related retinopathy, of which, at least one was compound heterozygous for the variant and a pathogenic variant (PM3_Supporting; PMID: 28446513, 33909047). 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 (v1.0.0): PSV1, PM3_Supporting, PM2_Supporting.

Met criteria codes

PM3_Supporting	✔	Patient 3792 (part of a large familial ABCA4 disease cohort) found to be compound heterozygous for c.3007C>T (p.Gln1003*) and pathogenic variant c.5882G>A (p.G1961E). Phase not confirmed. 0.5pts applied towards PM3_Supporting.
PVS1	✔	This is a nonsense variant located in exon 20 out of 50, and introduces a premature stop codon between codons 1-2255 (PVS1).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

PP4	✖	Onset at age 6 years (+0.5pts), compound heterozygous for two variants in ABCA4 gene c.3007C>T and c.768G>T (+0.5pts), WES testing (+2 pts), bull's eye lesions (+1pt), decreased central visual acuity (+1pt). Inquiry to author regarding presence of macular flecks were not received in timely manner. Upon review of macular images, the ABCA4 VCEP determined the patient did not show macular flecks, thereby, PP4 is not met.
PS4	✖	The OR is infinity and the CI is 0.31 to infinity, which is above the ABCA4 VCEP threshold of ≥5, but the CI contains 1 which does not meet the criterion for PS4 set by the ABCA4 VCEP (PS4_not met; PMID: 35120629).

Curation History

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