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Variant: NM_000350.3(ABCA4):c.2879del (p.Ala960fs)

Version: 1.0

CA2573132716

1372740 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 3cdd7b12-a832-4d7d-81c0-d8859a606ef7
Approved on: 2025/12/5
Published on: 2025/12/19

HGVS expressions

NM_000350.3:c.2879del
NM_000350.3(ABCA4):c.2879del (p.Ala960fs)
NC_000001.11:g.94046958del
CM000663.2:g.94046958del
NC_000001.10:g.94512514del
CM000663.1:g.94512514del
NC_000001.9:g.94285102del
NG_009073.1:g.79192del
ENST00000370225.4:c.2879del
ENST00000649773.1:c.2657del
ENST00000370225.3:c.2879del
ENST00000536513.5:c.-64-6869del
NM_000350.2:c.2879del

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.2879del (p.Ala960AspfsTer17) variant in ABCA4 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 19/50 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 0.0000006195 (1/1614136 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). This variant has been detected in at least 1 individual with ABCA4-related retinopathy who was compound heterozygous for the variant and a pathogenic variant (c.6119G>A; p.Arg2040Gln) which was not

confirmed in trans (PM3_Supporting; PMID: 29343940). In summary, this variant meets the criteria to be classified as likely pathogenic for ABCA4-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen ABCA4 VCEP (Specification Version 1): PVS1, PM3_Supporting, PM2_Supporting.

Met criteria codes

PM3_Supporting	✔	This variant has been detected in at least 1 individual with ABCA4-related retinopathy. This individual was compound heterozygous for the variant and a pathogenic variant (c.6119G>A (p.Arg2040Gln)) which was not confirmed in trans (PM3= 0.5 points; PM3_Supporting; PMID: 29343940).
PVS1	✔	This is a frameshift variant located in exon 19 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 0.0000006195 (1/1614136 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).

Not Met criteria codes

PP4	✖	At least 1 individual with a diagnosis of Stargardt disease was reported to have this variant, but the phenotype does not meet the phenotype criteria to apply PP4 as specified by the ABCA4 VCEP.
PS4	✖	The prevalence of the variant in affected individuals is not significantly increased compared with the prevalence in controls. The OR is infinity and the CI is 0.31-infinity, which is above the ABCA4 VCEP threshold of ≥5, but the CI does contain 1 (PMID: 35120629).

Curation History

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