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Variant: NM_000350.3(ABCA4):c.5554C>T (p.Gln1852Ter)

Version: 1.0

CA341281026

1454986 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 8ca85ee0-e408-4bb7-8c78-08436d090d26
Approved on: 2025/12/5
Published on: 2025/12/19

HGVS expressions

NM_000350.3(ABCA4):c.5554C>T (p.Gln1852Ter)
NM_000350.3:c.5554C>T
NC_000001.11:g.94011292G>A
CM000663.2:g.94011292G>A
NC_000001.10:g.94476848G>A
CM000663.1:g.94476848G>A
NC_000001.9:g.94249436G>A
NG_009073.1:g.114858C>T
ENST00000370225.4:c.5554C>T
ENST00000370225.3:c.5554C>T
ENST00000536513.5:c.1930C>T
NM_000350.2:c.5554C>T

Pathogenic

Met criteria codes 4

PM3_Supporting PP1 PVS1 PM2_Supporting

Not Met criteria codes 1

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.5554C>T (p.Gln1852Ter) variant in ABCA4 is a nonsense variant located in exon 39 out of 50 and introduces a premature stop codon between codons 1-2255 (PVS1). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). This variant has been detected in at least 1 individual with ABCA4-related retinopathy who was compound heterozygous for the variant and a likely pathogenic variant confirmed in trans by family testing (ABCA4 c.3113C>T; p.Ala1038Val) (PM3_Supporting; PMID: 28559085). The variant has been reported to segregate with ABCA4-related retinopathy in the proband and 1 similarly affected relative (PP1; PMID: 28559085). In summary,

this variant meets the criteria to be classified as pathogenic for autosomal recessive ABCA4-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen ABCA4 VCEP (Specification Version 1.0): PVS1, PM2_Supporting, PM3_Supporting, PP1.

Met criteria codes

PM3_Supporting	✔	ABCA4 c.3113C>T; p.Ala1038Val found in trans (segregation of variants reported) in two individuals with clinically diagnosed Stargardt Disease (versus Pattern Dystrophy).
PP1	✔	The variant has been reported to segregate with ABCA4-related retinopathy in the proband and 1 similarly affected relative (PP1; PMID: 28559085).
PVS1	✔	This is a nonsense variant located in exon 39 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

PS4	✖	The prevalence of the variant in affected individuals is increased compared with the prevalence in controls, however, the prevalence is not statistically significant. The OR is infinity and the CI is [0.31-infinity] (PS4; PMID: 35120629). Thus, PS4 is not met.

Curation History

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