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Variant: NM_000350.3(ABCA4):c.6601_6602del (p.Arg2201fs)

Version: 1.0

CA227421

99472 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 9999a507-2664-439d-b776-c994e5d920cb
Approved on: 2026/2/24
Published on: 2026/2/27

HGVS expressions

NM_000350.3(ABCA4):c.6601_6602del (p.Arg2201fs)
NM_000350.3:c.6601_6602del
NC_000001.11:g.93997991_93997992del
CM000663.2:g.93997991_93997992del
NC_000001.10:g.94463547_94463548del
CM000663.1:g.94463547_94463548del
NC_000001.9:g.94236135_94236136del
NG_009073.1:g.128161_128162del
ENST00000370225.4:c.6601_6602del
ENST00000370225.3:c.6601_6602del
ENST00000536513.5:c.2977_2978del
NM_000350.2:c.6601_6602del

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PS4

Not Met criteria codes 2

PP1 PP4

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.6601_6602del (p.Arg2201AlafsTer) variant in ABCA4 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 48/50 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 0.0000006196 (1/1614010 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. 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). 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 1.0.0): PVS1, PS4, PM2_Supporting.

Met criteria codes

PVS1	✔	This is a frameshift variant located in exon 48 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 0.0000006196 (1/1614010 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).
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).

Not Met criteria codes

PP1	✖	This variant segregates in 2 family members (siblings), but they do not appear to be affected based on the pedigree.
PP4	✖	This variant has been reported in the literature in several individuals with ABCA4-related retinopathy, but none with phenotypes that meet the requirements of the PP4 code as specified by the ClinGen ABCA4 VCEP (PMIDs: 34440443, 32307445, 20647261, 10958761, 12037008).

Curation History

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