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Variant: NM_000350.3(ABCA4):c.1531C>T (p.Arg511Cys)

Version: 1.0

CA958502

377402 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 93e2382f-4088-4642-98a1-abb54b0fe297
Approved on: 2026/5/26
Published on: 2026/5/26

HGVS expressions

NM_000350.3(ABCA4):c.1531C>T (p.Arg511Cys)
NM_000350.3:c.1531C>T
NC_000001.11:g.94077713G>A
CM000663.2:g.94077713G>A
NC_000001.10:g.94543269G>A
CM000663.1:g.94543269G>A
NC_000001.9:g.94315857G>A
NG_009073.1:g.48437C>T
ENST00000370225.4:c.1531C>T
ENST00000649773.1:c.1531C>T
ENST00000370225.3:c.1531C>T
NM_000350.2:c.1531C>T

Pathogenic

Met criteria codes 5

PS4 PP3 PP4 PM3_Strong PM2_Supporting

Not Met criteria codes 1

BS1

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.1531C>T variant in ABCA4 is a missense variant predicted to cause substitution of arginine by cysteine at amino acid 511; p.Arg511Cys. The total minor allele frequency in gnomAD v4.1.0 is 0.000078 (126/1613382 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.699 which is in the range of 0.644-0.772 meeting PP3. The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls with an OR of 5.3 and CI of 2.44-10.82 (PS4; PMID: 35120629). At least one patient with this variant displayed presence of at least two ABCA4 variants identified by a gene panel of over 100 genes, onset under 18 years of age, macular flecks, which is

highly specific for ABCA4-related retinopathy (PP4, PMID:33301772). This variant has been detected in at least four more individuals with ABCA4-related retinopathy. Of those individuals, all four were compound heterozygous for the variant and a pathogenic or likely pathogenic variant not confirmed in trans (p.Arg602Trp; p.Thr1537Met; p.Gly1961Glu; p.Arg2107His) (PM3_Strong; PMID:32307445, 26780318, 29925512, 33261146). 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): PS4, PM3_Strong, PP4, PP3, 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 5.3 and the CI is 2.44-10.82, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PP3	✔	The computational predictor REVEL gives a score of 0.699 which is in the range of 0.644-0.772, evidence that predicts a damaging effect on ABCA4 function (PP3).
PP4	✔	At least one patient with this variant displayed presence of at least two ABCA4 variants identified by a gene panel of over 100 genes, onset under 18 years of age, macular flecks, which is highly specific for ABCA4-related retinopathy (PP4, PMID:33301772).
PM3_Strong	✔	This variant has been detected in at least four more individuals with ABCA4-related retinopathy. Of those individuals, all four were compound heterozygous for the variant and a pathogenic or likely pathogenic variant not confirmed in trans (p.Arg602Trp; p.Thr1537Met; p.Gly1961Glu; p.Arg2107His)(2.25 PM3 points; PM3_Strong; PMID:32307445, 26780318, 29925512, 33261146).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.000078 (126/1613382 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001).

Not Met criteria codes

BS1	✖	GrpMax = 0.0010066 < 0.00163

Curation History

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