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Variant: NM_000350.3(ABCA4):c.6397T>C (p.Cys2133Arg)

Version: 1.0

CA341277387

2021273 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 2b56ef69-e38a-4ffd-ae31-1d7f1d0918ec
Approved on: 2026/3/24
Published on: 2026/4/17

HGVS expressions

NM_000350.3:c.6397T>C
NM_000350.3(ABCA4):c.6397T>C (p.Cys2133Arg)
NC_000001.11:g.94000918A>G
CM000663.2:g.94000918A>G
NC_000001.10:g.94466474A>G
CM000663.1:g.94466474A>G
NC_000001.9:g.94239062A>G
NG_009073.1:g.125232T>C
ENST00000370225.4:c.6397T>C
ENST00000370225.3:c.6397T>C
ENST00000536513.5:c.2773T>C
NM_000350.2:c.6397T>C

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PS4 PP3_Moderate PM3_Supporting

Not Met criteria codes 1

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(ABCA4):c.6397T>C;p.Cys2133Arg variant in ABCA4 is a missense variant predicted to cause substitution of cysteine by arginine at amino acid 2133. This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.978, which is above the threshold of >0.772 meeting PP3_Moderate. The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls with an OR of infinity and CI 2.24-infinity meeting PS4 (PMID: 35120629). This variant has been detected in at least 3 individuals with ABCA4-related retinopathy. Of those individuals, two were compound heterozygous for a pathogenic or likely pathogenic variant (c.4555delA p.(T1519Rfs*5); c.3113C>T p.(Ala1038Val)) and none were

confirmed in trans (PM3_Supporting; PMIDs: 33846575, 32893963). 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 1.0.0): PS4, PM2_Supporting, PP3_Moderate, PM3_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (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).
PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.978 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).
PM3_Supporting	✔	This variant has been detected in at least 3 individuals with ABCA4-related retinopathy. Of those individuals, 2 were compound heterozygous for the variant and a pathogenic or likely pathogenic variant (c.4555delA p.(T1519Rfs*5); c.3113C>T p.(Ala1038Val)) and none were confirmed in trans (PM3=0.50 points; PM3_Supporting; PMIDs: 33846575, 32893963).

Not Met criteria codes

PP4	✖	This variant was found in 3 individuals in the literature; however, none of them meet the PP4 criteria as specified by the ABCA4 VCEP (PMIDs: 32893963, 33846575, 32307445).

Curation History

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