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Variant: NM_000350.3(ABCA4):c.3413T>C (p.Leu1138Pro)

Version: 1.0

CA341290944

866229 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 47bd17b1-722c-4cbf-abcf-eb23400e7f70
Approved on: 2026/3/24
Published on: 2026/3/28

HGVS expressions

NM_000350.3(ABCA4):c.3413T>C (p.Leu1138Pro)
NM_000350.3:c.3413T>C
NC_000001.11:g.94041318A>G
CM000663.2:g.94041318A>G
NC_000001.10:g.94506874A>G
CM000663.1:g.94506874A>G
NC_000001.9:g.94279462A>G
NG_009073.1:g.84832T>C
ENST00000370225.4:c.3413T>C
ENST00000370225.3:c.3413T>C
ENST00000536513.5:c.-64-1229T>C
NM_000350.2:c.3413T>C

Pathogenic

Met criteria codes 6

PS4 PP3_Moderate PM3_Supporting PP1 PP4 PM2_Supporting

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.3413T>C variant in ABCA4 is a missense variant predicted to cause substitution of leucine by proline at amino acid 1138; p.Leu1138Pro. The total minor allele frequency in gnomAD v4.1.0 is 0.000001859 (3/1613950 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.97 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function meeting PP3_Moderate. The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 35.7 and the CI is 2.87 - 1852.51, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629). At least one patient with this

variant displayed presence of at least two ABCA4 variants, onset under 18 years of age, macular flecks on fundus autofluorescence, and genomic testing that has ruled out alternative causes for the disease, which is highly specific for ABCA4-related retinopathy (PP4, PMID:39264853). Additionally, VCEP member reported siblings with diagnosis of Stargardt disease homozygous for this variant (PM3_Supporting, PP1). 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, PP3_Moderate, PM3_Supporting, PP1, PP4, 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 35.7 and the CI is 2.87 - 1852.51, 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 0.97 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate). No splice impact predicted by Splice AI.
PM3_Supporting	✔	Proband and sibling with diagnosis of Stargardt disease both homozygous for p.Leu1138Pro variant (0.5 PM3 points).
PP1	✔	Proband and sibling with diagnosis of Stargardt disease both homozygous for p.Leu1138Pro variant.
PP4	✔	At least one patient with this variant displayed presence of at least two ABCA4 variants, onset under 18 years of age, macular flecks on fundus autofluorescence, and genomic testing that has ruled out alternative causes for the disease, which is highly specific for ABCA4-related retinopathy (PP4, PMID:39264853).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.000001859 (3/1613950 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001).

Curation History

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