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Variant: NM_000350.3(ABCA4):c.3G>T (p.Met1Ile)

Version: 1.0

CA10602781

280328 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: db310fc0-57b0-4838-b622-cd792402c696
Approved on: 2025/12/5
Published on: 2025/12/22

HGVS expressions

NM_000350.3(ABCA4):c.3G>T (p.Met1Ile)
NM_000350.3:c.3G>T
NC_000001.11:g.94121043C>A
CM000663.2:g.94121043C>A
NC_000001.10:g.94586599C>A
CM000663.1:g.94586599C>A
NC_000001.9:g.94359187C>A
NG_009073.1:g.5107G>T
ENST00000370225.4:c.3G>T
ENST00000649773.1:c.3G>T
ENST00000370225.3:c.3G>T
NM_000350.2:c.3G>T

Pathogenic

Met criteria codes 3
PM2_Supporting PVS1 PM5

Not Met criteria codes 3
PM3 PS4 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.3G>T; p.Met1Ile variant in ABCA4 may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein (PVS1). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). Another missense variant, c.1A>G; p.Met1Val, in the same codon has been classified as pathogenic for ABCA4-related retinopathy by the ClinGen ABCA4 VCEP (PM5). 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): PVS1, PM2_Supporting, PM5.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PVS1	✔	The NM_000350.3:c.3G>T (p.Met1Ile) variant in ABCA4 may cause a truncated or absent protein by altering the start codon of the coding sequence and is predicted to lead to the omission of a critical region of the protein (PVS1).
PM5	✔	Another missense variant, c.1A>G (p.Met1Val), ClinVar Variation ID: 99110, in the same codon has been classified as pathogenic for ABCA4-related retinopathy by the ClinGen ABCA4 VCEP, and Splice AI revealed no expected effects on splicing (PM5).

Not Met criteria codes

PM3	✖	This variant was seen in compound heterozygosity with c.6383A>G (p.His2128Arg), but the other variant will not be scored as PM3 for the current variant in order to avoid circular logic.
PS4	✖	The prevalence of the variant in affected individuals is not significantly increased compared with the prevalence in controls. The OR is infinity and the CI is 0.31-infinity, however the CI does contain 1 so this code is not applicable.
PP4	✖	This variant has been reported in the literature in an individual with ABCA4-related retinopathy, but they do not meet the PP4 criteria specified by the ABCA4 VCEP (PMID: 37648803).

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000350.3(ABCA4):c.3G>T (p.Met1I...	Pathogenic	ABCA4-Related Retinopathy	2025-12-22	1.0	ClinGen ABCA4 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for ABCA4 Version 1.0.0	ABCA4

Showing 1 to 1 of 1 rows

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