

Variant: *NM_000350.3(ABCA4):c.1654G>A (p.Val552Ile)*

Version: 1.0

CA239745 [↗](#)

193990 (ClinVar) [↗](#)

Gene: ABCA4 ([HGNC:24](#))

Condition: ABCA4-related retinopathy ([MONDO:0800406](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: f9b1aeda-8970-4d1c-a8ec-657fbc4663e3

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HGVS expressions

NM_000350.3(ABCA4):c.1654G>A (p.Val552Ile)

NM_000350.3:c.1654G>A

NC_000001.11:g.94063218C>T

CM000663.2:g.94063218C>T

NC_000001.10:g.94528774C>T

CM000663.1:g.94528774C>T

NC_000001.9:g.94301362C>T

NG_009073.1:g.62932G>A

ENST00000370225.4:c.1654G>A

ENST00000649773.1:c.1654G>A

ENST00000370225.3:c.1654G>A

ENST00000536513.5:c.-109G>A

NM_000350.2:c.1654G>A

Likely Benign

Met criteria codes **3**

BS3_Supporting

PP3

BS1_Supporting

Not Met criteria codes **4**

PP4

PS4

PM2

PM3

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.1654G>A variant in ABCA4 is a missense variant predicted to cause substitution of valine by isoleucine at amino acid 552; p.Val552Ile. The GroupMax filtering allele frequency in gnomAD v4.1.0 is 0.004481, which is greater than the ClinGen ABCA4 VCEP's threshold for BS1_Supporting (>0.00163). The computational predictor REVEL gives a score of 0.685 which is in the range of 0.644-0.772 meeting PP3. ABCA4 expression and ATPase activity in HEK293 cells showed expression close to WT levels and only a modest reduction in ATPase activity, indicating that this variant does not impact protein function (BS3_Supporting; PMID: 29847635). In summary,

this variant meets the criteria to be classified as likely benign for ABCA4-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen ABCA4 VCEP (Specification Version 1.0.0): **BS1_Supporting, BS3_Supporting, PP3**.

Met criteria codes

BS3_Supporting			ABCA4 expression and ATPase activity in HEK293 cells showed expression close to WT levels and only a modest reduction in ATPase activity, indicating that this variant does not impact protein function (BS3_Supporting; PMID: 29847635).
PP3			The computational predictor REVEL gives a score of 0.685 which is in the range of 0.644-0.772, evidence that predicts a damaging effect on ABCA4 function (PP3).
BS1_Supporting			The GroupMax filtering allele frequency in gnomAD v4.1.0 is 0.004481, which is greater than the ClinGen ABCA4 VCEP's threshold for BS1_Supporting (>0.00163), and therefore meets this criterion (BS1_Supporting). 16 homozygotes

Not Met criteria codes

PP4			This rule is not applicable for variants meeting BS1 or BA1 criteria.
PS4			The prevalence of the variant in affected individuals is not significantly increased compared with the prevalence in controls. The OR is 0.2 and the CI is 0.06-0.35 (PMID: 35120629).
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3			This rule is not applicable for variants meeting BS1 or BA1 criteria.

Curation History



 

 

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