

Variant: NM_000350.3(ABCA4):c.4924_4927del
(p.Ser1642fs)

Version: 1.0

CA957427 [↗](#)

3381789 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 95b7c9f0-e2a6-4a34-b997-76310e19e4fa

Approved on: 2025/12/5

Published on: 2025/12/19

HGVS expressions

NM_000350.3:c.4924_4927del

NM_000350.3(ABCA4):c.4924_4927del (p.Ser1642fs)

NC_000001.11:g.94021334_94021337del

CM000663.2:g.94021334_94021337del

NC_000001.10:g.94486890_94486893del

CM000663.1:g.94486890_94486893del

NC_000001.9:g.94259478_94259481del

NG_009073.1:g.104816_104819del

ENST00000370225.4:c.4924_4927del

ENST00000370225.3:c.4924_4927del

ENST00000460514.1:n.418_421del

ENST00000470771.1:n.34_37del

ENST00000536513.5:c.1300_1303del

NM_000350.2:c.4924_4927del

Pathogenic

Met criteria codes **4**

PP1_Moderate

PVS1

PM2_Supporting

PM3_Supporting

Not Met criteria codes **1**

PS4

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.4924_4927del (p.Ser1642fs) variant in ABCA4 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 35/50 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). The total minor allele frequency in gnomAD v4.1.0 is 0.000001239 (2/1614206 alleles), which is lower than the ClinGen

ABCA4 VCEP’s threshold for PM2_Supporting (<0.0001). The prevalence of the variant in affected individuals is not significantly increased compared with the prevalence in controls with an OR of infinity and the CI is 0.31-infinity, which is above the ABCA4 VCEP threshold of ≥ 5 , but the CI does contain 1 (PMID: 35120629). This variant has been detected in at least 1 individual with ABCA4-related retinopathy who was homozygous for the variant (PM3_Supporting; ClinVar SCV: SCV005415477.1). The variant has been reported to segregate with ABCA4-related retinopathy in the proband and 2 similarly affected relatives (PP1_Moderate; ClinVar SCV: SCV005415477.1). 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, PM3_Supporting, PM2_Supporting, PP1_Moderate.

Met criteria codes

PP1_Moderate			The variant has been reported to segregate with ABCA4-related retinopathy in the proband and 2 similarly affected relatives (PP1_Moderate; ClinVar SCV: SCV005415477.1).
PVS1			This is a frameshift variant located in exon 35 out of 50, and introduces a premature stop codon between codons 1-2255 (PVS1).
PM2_Supporting			The total minor allele frequency in gnomAD v4.1.0 is 0.000001239 (2/1614206 alleles), which is lower than the ClinGen ABCA4 VCEP’s threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).
PM3_Supporting			This variant has been detected in at least 1 individual with ABCA4-related retinopathy. This individual was homozygous for the variant (0.5 points; PM3_Supporting; ClinVar SCV: SCV005415477.1).

Not Met criteria codes

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, which is above the ABCA4 VCEP threshold of ≥ 5 , but the CI does contain 1 (PMID: 35120629).
-----	---	---	--

Curation History



 

 

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

[ClinGen Terms of Use.](#)

[⌕ Powered by BCM's Genboree.](#)