

Variant: *NM\_000350.3(ABCA4):c.1988G>A (p.Trp663Ter)*

Version: 1.0

CA16042332 [↗](#)

372289 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal recessive inheritance

**UUID:** 876ff52c-1dd4-4bf0-aa5f-c405e8984d50

**Approved on:** 2026/7/28

**Published on:** 2026/8/4

### *HGVS expressions*

**NM\_000350.3(ABCA4):c.1988G>A (p.Trp663Ter)**

**NM\_000350.3:c.1988G>A**

NC\_000001.11:g.94060709C>T

CM000663.2:g.94060709C>T

NC\_000001.10:g.94526265C>T

CM000663.1:g.94526265C>T

NC\_000001.9:g.94298853C>T

NG\_009073.1:g.65441G>A

ENST00000370225.4:c.1988G>A

ENST00000649773.1:c.1988G>A

ENST00000370225.3:c.1988G>A

ENST00000472033.1:n.108G>A

ENST00000536513.5:c.-65+2465G>A

NM\_000350.2:c.1988G>A

**Pathogenic**

**Met criteria codes** **3**

PM2\_Supporting

PS4

PVS1

**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

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

#### **ABCA4 VCEP**

The NM\_000350.3:c.1988G>A (p.Trp663Ter) variant in ABCA4 is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 14/50 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 v4.1.1 is 0.000001239 (2/1614018 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2\_Supporting (<0.0001). This variant has been observed in individuals with Stargardt disease and retinal

dystrophy (PMID: 25640233, 27353947, 29848554). The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls with an OR of Infinity and CI of 42.77 to Infinity, which is above the ABCA4 VCEP threshold of  $\geq 5$ , where the CI does not contain 1 (PS4; PMID: 35120629). 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 (v.1.0.0): PVS1, PS4, PM2\_Supporting.

Met criteria codes

|                |                                                                                   |                                                                                   |                                                                                                                                                                                                                                                                                             |
|----------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PM2_Supporting |  |  | This variant is present in gnomAD v4.1.1 at a total MAF = 0.000001239 (cutoff $<0.0001$ ) meeting 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 42.77 to infinity, which is above the ABCA4 VCEP threshold of $\geq 5$ , where the CI does not contain 1 (PS4; PMID: 35120629). |
| PVS1           |  |  | This is a nonsense variant located in exon 14 out of 50, and introduces a premature stop codon between codons 1-2255 (PVS1).                                                                                                                                                                |

Curation History 



 

 

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