

Variant: *NM_000350.3(ABCA4):c.5371dup (p.Ala1791fs)*

Version: 1.0

CA2573335086 [↗](#)

2585325 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 5d7bb5c5-8f11-4c04-a160-187990cf16ea

Approved on: 2025/12/5

Published on: 2025/12/19

HGVS expressions

NM_000350.3:c.5371dup

NM_000350.3(ABCA4):c.5371dup (p.Ala1791fs)

NC_000001.11:g.94014632dup

CM000663.2:g.94014632dup

NC_000001.10:g.94480188dup

CM000663.1:g.94480188dup

NC_000001.9:g.94252776dup

NG_009073.1:g.111518dup

ENST00000370225.4:c.5371dup

ENST00000370225.3:c.5371dup

ENST00000536513.5:c.1747dup

NM_000350.2:c.5371dup

Pathogenic

Met criteria codes **3**

PM3_Supporting

PM2_Supporting

PVS1

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.5371dup (p.Ala1791GlyfsTer9) variant in ABCA4 is a frameshift variant predicted to cause a premature stop codon in biologically-relevant exon 38/50 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). This variant has been detected in at least one individual with ABCA4-related retinopathy. This individual was compound heterozygous for the variant and a pathogenic variant (c.5882G>A; p.Gly1961Glu) presumed to be in trans by NGS targeted gene panel testing (PM3_Supporting; PMID: 31816670). 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): PVS1, PM3_Supporting, PM2_Supporting.			
Met criteria codes			
PM3_Supporting			Variant detected in proband with cone dystrophy who also harbors pathogenic variant ABCA4:c.5882G>A, p.G1961E. Testing involved NGS gene panel (200-7000 genes) associated with retinal phenotypes. Authors noted limitations on phase determination. Awarded 0.5 points towards criteria PM3_Supporting consideration.
PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PVS1			This is a frameshift variant located in exon 38 out of 50, and introduces a premature stop codon between codons 1-2255 (PVS1).
Not Met criteria codes			
PS4			While odds ratio for this variant is above 5, the confidence interval contains 1 (PMID:35120629). Therefore, PS4 is not met.

Curation History



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