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Variant: NM_000350.3(ABCA4):c.6820T>A (p.Ter2274Arg)

Version: 1.0

CA341275647

916723 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: c7e908f7-83da-40fe-90fb-9bd2bf8add31
Approved on: 2026/4/28
Published on: 2026/5/1

HGVS expressions

NM_000350.3:c.6820T>A
NM_000350.3(ABCA4):c.6820T>A (p.Ter2274Arg)
NC_000001.11:g.93993239A>T
CM000663.2:g.93993239A>T
NC_000001.10:g.94458795A>T
CM000663.1:g.94458795A>T
NC_000001.9:g.94231383A>T
NG_009073.1:g.132911T>A
ENST00000370225.4:c.6820T>A
ENST00000370225.3:c.6820T>A
ENST00000536513.5:c.3196T>A
NM_000350.2:c.6820T>A

Uncertain Significance

Met criteria codes 1

PM2_Supporting

Not Met criteria codes 5

PS4 PP1 PP4 PM4 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 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

ABCA4 VCEP

The NM_000350.3(ABCA4):c.6820T>A, p.(Ter2274ArgextTer34) variant in ABCA4 is a stop loss variant predicted to substitute a normal termination codon at codon 2274 with an arginine, leading to a C-terminal extended missense sequence and introduction of a stop codon at the 34th codon of the new reading frame. This variant is absent from gnomAD v4.1.0 (PM2_Supporting). At least one patient with this variant displayed homozygosity of a complex allele [c.1610G>A;c.6820T>A] with onset under 18 years of age, macular flecks on imaging and fundus autofluorescence, decreased central visual acuity, and/or macular atrophy, which is highly specific for ABCA4-related retinopathy (PMID: 32783370). However, the case is not counted as evidence due to the complex allele, where the ABCA4 c.1610G>A

variant is classified as likely pathogenic by the ABCA4 VCEP. In summary, this variant meets the criteria to be classified as variant of uncertain significance for ABCA4-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen ABCA4 VCEP (Specification Version 1.0.0): PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

PS4	✖	This variant has confidence interval that includes 1 and does not meet the ABCA4 VCEP threshold for PS4 (PS4 not met; PMID: 35120629).
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4	✖	At least one patient with this variant displayed presence of a complex ABCA4 allele [1610G>A;6820T>A], onset under 18 years of age, macular flecks on imaging and fundus autofluorescence, decreased central visual acuity, and/or macular atrophy, which is highly specific for ABCA4-related retinopathy (PMID: 32783370). Case is not counted due to ABCA4 c.1610G>A being classified as likely pathogenic using ABCA4 VCEP rules, and the uncertainty of the impact of this variant.
PM4	✖	The NM_000350.3:c.6820T>A variant is predicted to cause a change in the length of the protein (p.Ter2274Arg) due to an in-frame stop loss variant of 1 amino acid in a non-repeat region. However, the PhyloP score is 1.011, which is less than the ABCA4 VCEP threshold of ≥7.367. Therefore, PM4 is not met.
PVS1	✖	Variant is located in the last exon and leads to an extended C-terminal missense sequence. It is unlikely to lead to NMD. PVS1 not met.

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.6820T>A (p.Te...	Uncertain Significance	ABCA4-Related Retinopathy	2026-05-01	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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