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Variant: NM_000350.3(ABCA4):c.5584G>A (p.Gly1862Ser)

Version: 1.0

CA341280970

867094 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: 9f6b17c8-6b19-44f9-9a13-e1a6d26da6bd
Approved on: 2026/6/15
Published on: 2026/6/15

HGVS expressions

NM_000350.3:c.5584G>A
NM_000350.3(ABCA4):c.5584G>A (p.Gly1862Ser)
NC_000001.11:g.94011262C>T
CM000663.2:g.94011262C>T
NC_000001.10:g.94476818C>T
CM000663.1:g.94476818C>T
NC_000001.9:g.94249406C>T
NG_009073.1:g.114888G>A
ENST00000370225.4:c.5584G>A
ENST00000370225.3:c.5584G>A
ENST00000536513.5:c.1960G>A
NM_000350.2:c.5584G>A

Likely Pathogenic

Met criteria codes 4

PS1 PP3 PM3_Supporting PM2_Supporting

Not Met criteria codes 3

PM5 PS4 PP4

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.5584G>A variant in ABCA4 is a missense variant predicted to cause substitution of glycine by serine at amino acid 1862 (p.Gly1862Ser). The total minor allele frequency in gnomAD v4.1.0 is 0.0000006196 (1/1614060 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.661 which is in the range of 0.644-0.772, and SpliceAI gives a score of 0.69 which is above the threshold of >0.2, evidence that predicts a damaging effect on ABCA4 function (PP3). Another variant, c.5584G>C; p.Gly1862Arg, at the same nucleotide position has been classified as pathogenic by the ABCA4 VCEP. Splicing prediction using SpliceAI revealed similar predicted impacts on splicing for both variants (c.5584G>A donor loss

score=0.69; c.5584G>C donor loss score=0.78) meeting PS1. At least one proband has been reported with a second pathogenic variant (c.6320G>A; p.Arg2107His) phase unknown meeting PM3_Supporting (0.5 points; LOVD database). In summary, this variant meets the criteria to be classified as likely pathogenic for ABCA4-related retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen ABCA4 VCEP specification version 1.0.0: PS1, PM3_Supporting, PM2_Supporting, PP3.

Met criteria codes

PS1	✔	Another variant, c.5584G>C (p.Gly1862Arg), at the same nucleotide position has been classified as pathogenic by the ABCA4 VCEP. Splicing prediction using SpliceAI revealed similar predicted impacts on splicing for both variants (c.5584G>A donor loss score=0.69; c.5584G>C donor loss score=0.78) (PS1).
PP3	✔	The computational predictor REVEL gives a score of 0.661 which is in the range of 0.644-0.772, and SpliceAI gives a donor loss score of 0.69 which is above the threshold of >0.2, evidence that predicts a damaging effect on ABCA4 function (PP3).
PM3_Supporting	✔	At least one proband reported with a second pathogenic variant (c.6320G>A; p.Arg2107His) phase unknown. PM3 = 0.5.
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.0000006196 (1/1614060 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001), meeting this criterion (PM2_Supporting).

Not Met criteria codes

PM5	✖	Another missense variant, c.5584G>C (p.Gly1862Arg), in the same codon has been classified as pathogenic by ClinVar, but Splice AI revealed expected effects on splicing (donor loss score=0.78). Since both variants have high SpliceAI scores, evaluating for PS1 given Walker et al. splicing guidance.
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, however the CI does contain 1 (PMID: 35120629).
PP4	✖	Four individuals from databases (ClinVar and LOVD) have been reported to have this variant, but none with a phenotypic description sufficient to meet PP4 criteria as specified by the ClinGen ABCA4 VCEP.

Curation History

Showing 1 to 1 of 1 rows

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