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Variant: NM_000350.3(ABCA4):c.6121G>A (p.Gly2041Ser)

Version: 1.0

CA341278913

1410089 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: e2fee552-1b60-4d0a-891c-9c095a087c26
Approved on: 2026/5/26
Published on: 2026/5/26

HGVS expressions

NM_000350.3(ABCA4):c.6121G>A (p.Gly2041Ser)
NM_000350.3:c.6121G>A
NC_000001.11:g.94005467C>T
CM000663.2:g.94005467C>T
NC_000001.10:g.94471023C>T
CM000663.1:g.94471023C>T
NC_000001.9:g.94243611C>T
NG_009073.1:g.120683G>A
ENST00000370225.4:c.6121G>A
ENST00000370225.3:c.6121G>A
ENST00000465352.1:n.537G>A
ENST00000484388.1:n.235G>A
ENST00000536513.5:c.2497G>A
NM_000350.2:c.6121G>A

Likely Pathogenic

Met criteria codes 4

PP3_Moderate PP4 PM5 PM2_Supporting

Not Met criteria codes 2

PS4 PM3

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.6121G>A variant in ABCA4 is a missense variant predicted to cause substitution of glycine by serine at amino acid 2041; p.Gly2041Ser. The total minor allele frequency in gnomAD v4.1.0 is 0.0000006195 (1/1614140 alleles), which is lower than the ClinGen ABCA4 VCEP's threshold for PM2_Supporting (<0.0001). The computational predictor REVEL gives a score of 0.935 which is above the threshold of >0.772 meeting PP3_Moderate. Another missense variant, c.6122G>A; p.Gly2041Asp (ClinVar Variation ID 1048145), in the

same codon has been classified as pathogenic for ABCA4-related retinopathy by the ClinGen ABCA4 VCEP meeting PM5. At least one patient with this variant displayed presence of at least two ABCA4 variants, onset under 18 years of age, macular flecks on imaging, macular atrophy, and decreased vision acuity, which is highly specific for ABCA4-related retinopathy (PP4, ClinVar SCV002182102.4, Invitae). 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): PM5, PP3_Moderate, PP4, PM2_Supporting.

Met criteria codes

PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.935 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).
PP4	✔	At least one patient with this variant displayed presence of at least two ABCA4 variants, onset under 18 years of age, macular flecks on imaging, macular atrophy, and decreased vision acuity, which is highly specific for ABCA4-related retinopathy (PP4_Supporting, ClinVar SCV002182102.4, Invitae).
PM5	✔	Another missense variant, c.6122G>A (p.Gly2041Asp) (PMID: 2735394, 33546218, 38540785; ClinVar Variation ID 1048145), in the same codon has been classified as pathogenic for ABCA4-related retinopathy by the ClinGen ABCA4 VCEP, and Splice AI (score of 0) revealed no expected effects on splicing (PM5).
PM2_Supporting	✔	The total minor allele frequency in gnomAD v4.1.0 is 0.0000006195 (1/1614140 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

PS4	✖	This variant is not found in Cornelis et al. (PMID: 35120629).
PM3	✖	Clinvar Accession: SCV002182102.4. Adult female with ABCA4, c.6721C>G (p.Leu2241Val), c.6121G>A (p.Gly2041Ser) phase undetermined and a clinical diagnosis of Stargardt disease. Variant in trans with likely pathogenic variant, phase unconfirmed, giving only 0.25 points in PM3 for this proband which is less than the criteria to meet PM3 using ABCA4 VCEP specifications for this criterion.

Curation History

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