The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000350.3(ABCA4):c.6320G>A (p.Arg2107His)

Version: 1.0

CA227389

99448 (ClinVar)

Gene: ABCA4 (HGNC:24)
Condition: ABCA4-related retinopathy (MONDO:0800406)
Inheritance Mode: Autosomal recessive inheritance
UUID: bc46646f-490f-4e50-b862-3382f122b60c
Approved on: 2026/5/26
Published on: 2026/5/26

HGVS expressions

NM_000350.3:c.6320G>A
NM_000350.3(ABCA4):c.6320G>A (p.Arg2107His)
NC_000001.11:g.94001068C>T
CM000663.2:g.94001068C>T
NC_000001.10:g.94466624C>T
CM000663.1:g.94466624C>T
NC_000001.9:g.94239212C>T
NG_009073.1:g.125082G>A
ENST00000370225.4:c.6320G>A
ENST00000370225.3:c.6320G>A
ENST00000536513.5:c.2696G>A
NM_000350.2:c.6320G>A

Pathogenic

Met criteria codes 5

PS3_Supporting PM3 PM5 PS4 PP3_Moderate

Not Met criteria codes 4

BA1 PM2 BS1 BS3

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 c.6320G>A (NM_000350.3) variant in ABCA4 is a missense variant predicted to cause substitution of arginine by histidine at amino acid 2107; p.Arg2107His. The GroupMax filtering allele frequency in gnomAD v4.1.0 is 0.01986, which is greater than the ClinGen ABCA4 VCEP's threshold for BS1 (>0.0163); however, this variant is listed on the BS1 exclusion list. The computational predictor REVEL gives a score of 0.88 which is above the threshold of >0.772, meeting PP3_Moderate. The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls with an OR of 6.1 and CI of 4.76-7.68, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629). This variant has been detected in at least 2 individuals with ABCA4-related

retinopathy. Of those individuals, 1 was compound heterozygous for the variant and a pathogenic or likely pathogenic variant but was not confirmed in trans (c.3523-1G>A; PMID: 9781034), and 1 individual was homozygous for the variant (PMID: 9781034) (PM3). Another missense variant, c.6319C>T; p.Arg2107Cys (ClinVar:635988), in the same codon has been classified as pathogenic for ABCA4-related retinopathy by the ClinGen ABCA4 VCEP, and Splice AI revealed no expected effects on splicing (PM5). ABCA4 expression in HEK293 cells showed relative protein expression of 0.90 +/- 0.17. However, ABCA4 ATPase activity in HEK293 cells showed decreased basal ATPase activity (0.66 +/- 0.13) indicating that this variant impacts protein function (PS3_Supporting; PMID 32845050). 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 1.0.0): PS4, PM3, PP3_Moderate, PM5 and PS3_Supporting.

Met criteria codes

PS3_Supporting	✔	ABCA4 expression in HEK293 cells showed relative protein expression of 0.90 +/- 0.17. However, ABCA4 ATPase activity in HEK293 cells showed decreased basal ATPase activity (0.66 +/- 0.13) indicating that this variant impacts protein function (PS3_Supporting; PMID 32845050).
PM3	✔	This variant has been detected in at least 2 individuals with ABCA4-related retinopathy. Of those individuals, 1 was compound heterozygous for the variant and a pathogenic or likely pathogenic variant but was not confirmed in trans (Patient #11 with STGD1 and variants c.3523-1G>A and p.(R2107H) phase unknown (+0.5) PMID: 9781034). 1 individual was homozygous for the variant (Patient #40 was homozygous for the p.R2107H (+0.5) PMID: 9781034).
PM5	✔	Another missense variant, c.6319C>T; p.Arg2107Cys (ClinVar:635988), in the same codon has been classified as pathogenic for ABCA4-related retinopathy by the ClinGen ABCA4 VCEP, and Splice AI revealed no expected effects on splicing (PM5).
PS4	✔	The prevalence of the variant in affected individuals is significantly increased compared with the prevalence in controls. The OR is 6.1 and the CI is 4.76 - 7.68, which is above the ABCA4 VCEP threshold of ≥5, where the CI does not contain 1 (PS4; PMID: 35120629).
PP3_Moderate	✔	The computational predictor REVEL gives a score of 0.88 which is above the threshold of >0.772, evidence that predicts a damaging effect on ABCA4 function (PP3_Moderate).

Not Met criteria codes

BA1	✖	The GroupMax filtering allele frequency in gnomAD v4.1.0 is 0.01986, which is greater than the ClinGen ABCA4 VCEP's threshold for BS1 (>0.0163). The total minor allele frequency in gnomAD v4.1.0 is 0.001149 (1854/1614112alleles, 17 homozygotes). However, this variant is excluded from population codes.
PM2	✖	The GroupMax filtering allele frequency in gnomAD v4.1.0 is 0.01986, which is greater than the ClinGen ABCA4 VCEP's threshold for BS1 (>0.0163). The total minor allele frequency in gnomAD v4.1.0 is 0.001149 (1854/1614112alleles, 17 homozygotes). However, this variant is excluded from population codes.
BS1	✖	The GroupMax filtering allele frequency in gnomAD v4.1.0 is 0.01986, which is greater than the ClinGen ABCA4 VCEP's threshold for BS1 (>0.0163). The total minor allele frequency in gnomAD v4.1.0 is 0.001149 (1854/1614112alleles, 17 homozygotes). However, this variant is excluded from population codes.
BS3	✖	

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.

¤ Powered by BCM's Genboree.