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Variant: NM_000261.2(MYOC):c.1099G>A (p.Gly367Arg)

Version: 2.0

CA119176

7952 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: 75e7b7fd-1db7-4c60-8dd5-07f1be2fa1f2
Approved on: 2026/1/19
Published on: 2026/1/21

HGVS expressions

NM_000261.2(MYOC):c.1099G>A (p.Gly367Arg)
NM_000261.2:c.1099G>A
NC_000001.11:g.171636341C>T
CM000663.2:g.171636341C>T
NC_000001.10:g.171605481C>T
CM000663.1:g.171605481C>T
NC_000001.9:g.169872104C>T
NG_008859.1:g.21293G>A
ENST00000037502.11:c.1099G>A
ENST00000637303.1:c.235-2289C>T
ENST00000638471.1:c.*437G>A
ENST00000037502.10:c.1099G>A
ENST00000614688.1:c.*63G>A
NM_000261.1:c.1099G>A

Pathogenic

Met criteria codes 5

PP3_Moderate PP1_Strong PS3_Moderate PS4 PM2_Supporting

Not Met criteria codes 9

PM5 PM4 BA1 BS1 BS3 BP7 BP4 PS1 PS2

Evidence Links 5

Expert Panel

Glaucoma VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Glaucoma Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MYOC Version 2.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Glaucoma VCEP

The c.1099G>A variant in MYOC is a missense variant predicted to cause substitution of Glycine by Arginine at amino acid 367 (p.Gly367Arg). This variant was not found in any genetic ancestry group of gnomAD (v4.1.0), meeting the ≤ 0.0001 threshold set for PM2_Supporting in a genetic ancestry group of at least 10,000 alleles. The REVEL score = 0.787, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function. The Gly367Arg protein had increased insolubility and instability and

reduced secretion levels compared to wild type myocilin protein in these studies (PMIDs: 35196929, 16466712, 36267417, 21612213, 23129764). The assays met the OddsPath threshold for PS3_Moderate (> 4.3), indicating that this variant did impact protein function. This protein has also been assessed in this other study (PMID: 17679945), however, the same level of evidence was not met. 35 segregations in 7 families, with juvenile or primary open angle glaucoma (JOAG or POAG), have been reported (PMIDs: 17304254, 32300215, 12189160, 11815346), which fulfilled PP1_Strong (≥7 meioses in >1 family). There were many more families published than presented here. 16 probands with JOAG or POAG have been reported carrying this variant (PMIDs: 32300215, 12189160, 11774072, 9345106, 23453510, 12872267, 14627955, 12442283, 17304254), which met PS4 (≥ 15 probands). There were many more probands published than presented here. In summary, this variant met the criteria to receive a score of 13 and to be classified as pathogenic (pathogenic classification ≥ 10, adapted from PMID: 32720330) for juvenile open angle glaucoma based on the ACMG/AMP criteria met, as specified by the ClinGen Glaucoma VCEP (v2.0.0, 5 Dec 2024): PS4, PP1_Strong, PS3_Moderate, PP3_Moderate, PM2_Supporting

Met criteria codes

PP3_Moderate	✔	The REVEL score = 0.787, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function.
PP1_Strong	✔	35 segregations in 7 families, with juvenile or primary open angle glaucoma (JOAG or POAG), have been reported (PMIDs: 17304254, 32300215, 12189160, 11815346), which fulfilled PP1_Strong (≥7 meioses in >1 family). There were many more families published than presented here.
PS3_Moderate	✔	The Gly367Arg protein had increased insolubility and instability and reduced secretion levels compared to wild type myocilin protein in these studies (PMIDs: 35196929, 16466712, 36267417, 21612213, 23129764). The assays met the OddsPath threshold for PS3_Moderate (> 4.3), indicating that this variant did impact protein function. This protein has also been assessed in this other study (PMID: 17679945), however, the same level of evidence was not met. The G367R protein is unstable. The assay in this study meets the OddsPath threshold for PS3_Moderate (> 4.3) (when combined with PMIDs: 20334347, 21612213, 25524706, 36579626) PubMed:23129764 The G367R protein is insoluble and has reduced secretion. The assay in this study meets the OddsPath threshold for PS3_Moderate (> 4.3). PubMed:36267417 The G367R protein is insoluble and has reduced secretion. The assay in this study meets the OddsPath threshold for PS3_Moderate (> 4.3). PubMed:35196929 The G367R protein is unstable. The assay in this study meets the OddsPath threshold for PS3_Moderate (> 4.3) (when combined with PMIDs: 20334347, 23129764, 25524706, 36579626). PubMed:21612213 The G367R protein is unstable. Note: this is a duplicated result from PMID: 23129764 PubMed:25524706
PS4	✔	16 probands with JOAG or POAG have been reported carrying this variant (PMIDs: 32300215, 12189160, 11774072, 9345106, 23453510, 12872267, 14627955, 12442283, 17304254), which met PS4 (≥ 15 probands). There were many more probands published than presented here.
PM2_Supporting	✔	This variant was not found in any genetic ancestry group of gnomAD (v4.1.0), meeting the ≤ 0.0001 threshold set for PM2_Supporting in a genetic ancestry group of at least 10,000 alleles.

Not Met criteria codes

PM5	✖	No other LP or P missense variants at this amino acid residue have been identified.

PM4		✖	This variant does not cause a protein length change.
BA1		✖	This criterion was not met as PM2_Supporting has been met.
BS1		✖	This criterion was not met as PM2_Supporting has been met.
BS3		✖	This criterion was not met as PS3_Moderate has been met.
BP7		✖	This is not an intronic, synonymous or non-coding variant.
BP4		✖	This criterion was not met as PP3 has been met.
PS1		✖	An established LP or P variant causing this same amino acid change has not been identified.
PS2		✖	This variant has not been identified de novo.

Curation History

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