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_000261.2:c.1151A>G

Version: 2.0

CA343724521

2570632 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: 1be3ddb6-b1f9-42ee-8822-851cfc5bec0b
Approved on: 2026/2/19
Published on: 2026/2/18

HGVS expressions

NM_000261.2:c.1151A>G
NC_000001.11:g.171636289T>C
CM000663.2:g.171636289T>C
NC_000001.10:g.171605429T>C
CM000663.1:g.171605429T>C
NC_000001.9:g.169872052T>C
NG_008859.1:g.21345A>G
ENST00000037502.11:c.1151A>G
ENST00000637303.1:c.235-2341T>C
ENST00000638471.1:c.*489A>G
ENST00000037502.10:c.1151A>G
ENST00000614688.1:c.*115A>G
NM_000261.1:c.1151A>G

Likely Pathogenic

Met criteria codes 4

PP3_Strong PP1_Moderate PM5_Supporting PM2_Supporting

Not Met criteria codes 10

PM4 BA1 BS1 BS3 BP7 BP4 PS1 PS2 PS3 PS4

Evidence Links 1

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.1151A>G variant in MYOC is a missense variant predicted to cause substitution of Aspartate by Glycine at amino acid 384 (p.Asp384Gly). 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 = 0.975, which met the ≥ 0.932 threshold for PP3_Strong, predicting a damaging effect on MYOC function. The assay in this study (PMID: 40081751), measuring solubility and secretion of the Asp384Gly protein, did not meet the OddsPath threshold for PS3_Supporting (> 2.1). 8 segregations in 1 family, with juvenile or

primary open angle glaucoma (JOAG or POAG), have been reported (PMID: 22876119), which fulfilled PP1_Moderate (5-6 meioses). Only 1 proband with JOAG had been reported (PMID: 22876119), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting. Another missense variant (c.1150G>A, p.Asp384Asn, Grantham score = 23, ClinVar ID: 1342205) at the same codon has been classified as likely pathogenic independently of PM5 for juvenile open angle glaucoma by the ClinGen Glaucoma VCEP. The c.1151A>G, p.Asp384Gly variant has a higher Grantham score (= 94) than the previously classified amino acid change, was not predicted to affect splicing as assessed with SpliceAI (≤ 0.2), and met PP3, meeting the conditions for PM5_Supporting to apply. In summary, this variant met the criteria to receive a score of 8 and to be classified as likely pathogenic (likely pathogenic classification range 6 to 9, 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): PP3_Strong, PP1_Moderate, PM2_Supporting, PM5_Supporting.

Met criteria codes

PP3_Strong	✔	The REVEL score = 0.975, which met the ≥ 0.932 threshold for PP3_Strong, predicting a damaging effect on MYOC function.
PP1_Moderate	✔	8 segregations in 1 family, with juvenile or primary open angle glaucoma (JOAG or POAG), have been reported (PMID: 22876119), which fulfilled PP1_Moderate (5-6 meioses).
PM5_Supporting	✔	Another missense variant (c.1150G>A, p.Asp384Asn, Grantham score = 23, ClinVar ID: 1342205) at the same codon has been classified as likely pathogenic independently of PM5 for juvenile open angle glaucoma by the ClinGen Glaucoma VCEP. The c.1151A>G, p.Asp384Gly variant has a higher Grantham score (= 94) than the previously classified amino acid change, was not predicted to affect splicing as assessed with SpliceAI (≤ 0.2), and met PP3, meeting the conditions for PM5_Supporting to apply.
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

PM4	✖	This criterion did not apply to this variant.
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	✖	Although the OddsPath threshold for PS3_Supporting was not met, this variant may impact protein function (see PS3 comment). The Asp384Gly protein is insoluble in 1 assay and demonstrates reduced secretion and an indeterminate level of solubility in other assays in this study. None of the assays in this study meet the OddsPath threshold for PS3_Supporting (> 2.1). PubMed:40081751
BP7	✖	This criterion did not apply to this variant.
BP4	✖	This criterion was not met as PP3_Strong 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.
PS3		✖	The assay in this study (PMID: 40081751), measuring solubility and secretion of the Asp384Gly protein, did not meet the OddsPath threshold for PS3_Supporting (> 2.1). The Asp384Gly protein is insoluble in 1 assay and demonstrates reduced secretion and an indeterminate level of solubility in other assays in this study. None of the assays in this study meet the OddsPath threshold for PS3_Supporting (> 2.1). PubMed:40081751
PS4		✖	Only 1 proband with JOAG had been reported (PMID: 22876119), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting.

Curation History

Showing 1 to 2 of 2 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.