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.1139A>G

Version: 2.0

CA343724569

1342964 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: b02e5129-d33a-4445-ab99-aa3dd8fc3d6d
Approved on: 2026/1/21
Published on: 2026/1/20

HGVS expressions

NM_000261.2:c.1139A>G
NC_000001.11:g.171636301T>C
CM000663.2:g.171636301T>C
NC_000001.10:g.171605441T>C
CM000663.1:g.171605441T>C
NC_000001.9:g.169872064T>C
NG_008859.1:g.21333A>G
ENST00000037502.11:c.1139A>G
ENST00000637303.1:c.235-2329T>C
ENST00000638471.1:c.*477A>G
ENST00000037502.10:c.1139A>G
ENST00000614688.1:c.*103A>G
NM_000261.1:c.1139A>G

Likely Pathogenic

Met criteria codes 4

PS3_Moderate PM5_Supporting PP3_Strong PM2_Supporting

Not Met criteria codes 10

PM4 BA1 BS1 BS3 BP7 BP4 PS1 PS2 PS4 PP1

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.1139A>G variant in MYOC is a missense variant predicted to cause substitution of Aspartic Acid by Glycine at amino acid 380 (p.Asp380Gly). 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 = 0.964, which met the ≥ 0.932 threshold for PP3_Strong, predicting a damaging effect on MYOC function. The Asp380Gly protein had increased insolubility and reduced secretion levels compared to wild type myocilin protein in this study (J Hulleman pers. comm.). The assays met the OddsPath threshold for PS3_Moderate

(> 4.3) (when combined with PMID: 35196929), indicating that this variant did impact protein function. Only 1 proband with juvenile open angle glaucoma had been reported (PMID: 9535666), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting. Another missense variant (c.1138G>C, p.Asp380His, Grantham score = 81, ClinVar ID: 7961) in the same codon has been classified as likely pathogenic for juvenile open angle glaucoma by the ClinGen Glaucoma VCEP. The c.1139A>G, p.Asp380Gly 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, PS3_Moderate, PM2_Supporting, PM5_Supporting

Met criteria codes

PS3_Moderate	✔	The Asp380Gly protein had increased insolubility and reduced secretion levels compared to wild type myocilin protein in this study (J Hulleman pers. comm.). The assays met the OddsPath threshold for PS3_Moderate (> 4.3) (when combined with PMID: 35196929), indicating that this variant did impact protein function. The D380G protein is insoluble and has reduced secretion (J Hulleman pers. comm. unpublished data as part of the PMID:35196929 study). The assay in this study meets the OddsPath threshold for PS3_Moderate (> 4.3). PubMed:35196929
PM5_Supporting	✔	Another missense variant (c.1138G>C, p.Asp380His, Grantham score = 81, ClinVar ID: 7961) in the same codon has been classified as likely pathogenic for juvenile open angle glaucoma by the ClinGen Glaucoma VCEP. The c.1139A>G, p.Asp380Gly 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. This variant was used to apply PM5 to variant MYOC c.1139A>C, p.Asp380Ala which is located at the same amino acid residue.
PP3_Strong	✔	The REVEL score = 0.964, which met the ≥ 0.932 threshold for PP3_Strong, predicting a damaging effect on MYOC function.
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 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.
PS4		✖	Only 1 proband with juvenile open angle glaucoma had been reported (PMID: 9535666), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting.
PP1		✖	No segregations have been reported for this variant.

Curation History

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