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.1111T>G

Version: 2.0

CA343724686

2500835 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: 26ec0e40-daee-4c45-9d87-22e7bcbd14e5
Approved on: 2026/2/19
Published on: 2026/2/18

HGVS expressions

NM_000261.2:c.1111T>G
NC_000001.11:g.171636329A>C
CM000663.2:g.171636329A>C
NC_000001.10:g.171605469A>C
CM000663.1:g.171605469A>C
NC_000001.9:g.169872092A>C
NG_008859.1:g.21305T>G
ENST00000037502.11:c.1111T>G
ENST00000637303.1:c.235-2301A>C
ENST00000638471.1:c.*449T>G
ENST00000037502.10:c.1111T>G
ENST00000614688.1:c.*75T>G
NM_000261.1:c.1111T>G

Likely Pathogenic

Met criteria codes 4

PS3_Moderate PP3_Moderate PM2_Supporting PP1

Not Met criteria codes 10

PM5 PM4 BA1 BS1 BS3 BP7 BP4 PS1 PS2 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.1111T>G variant in MYOC is a missense variant predicted to cause substitution of Tyrosine by Aspartic Acid at amino acid 371 (p.Tyr371Asp). 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 = 0.892, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function. The Tyr371Asp protein had increased insolubility and reduced secretion levels compared to wild type myocilin protein in this study (PMID: 36267417). The assays met the OddsPath threshold for PS3_Moderate (>

4.3), indicating that this variant did impact protein function. 3 segregations in 1 family, with juvenile open angle glaucoma (JOAG), have been reported (PMID: 19784393), which fulfilled PP1 (3-4 meioses). Only 1 proband with JOAG had been reported (PMID: 19784393), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting. In summary, this variant met the criteria to receive a score of 6 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): PS3_Moderate, PP3_Moderate, PP1, PM2_Supporting

Met criteria codes

PS3_Moderate	✔	The Tyr371Asp protein had increased insolubility and reduced secretion levels compared to wild type myocilin protein in this study (PMID: 36267417). The assays met the OddsPath threshold for PS3_Moderate (> 4.3), indicating that this variant did impact protein function. The Y371D protein is insoluble and has reduced secretion. The assay in this study meets the OddsPath threshold for PS3_Moderate (> 4.3). PubMed:36267417
PP3_Moderate	✔	The REVEL score = 0.892, which was within the 0.773-0.931 range for PP3_Moderate, 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.
PP1	✔	3 segregations in 1 family, with juvenile open angle glaucoma (JOAG), have been reported (PMID: 19784393), which fulfilled PP1 (3-4 meioses).

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	✖	No functional evidence has been found for this variant.
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 JOAG had been reported (PMID: 19784393), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting.

Curation History

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