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.1456C>T

Version: 2.0

CA343723062

1810378 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4db440da-dcdc-4712-9b98-81ce3dafa573
Approved on: 2026/2/19
Published on: 2026/2/18

HGVS expressions

NM_000261.2:c.1456C>T
NC_000001.11:g.171635984G>A
CM000663.2:g.171635984G>A
NC_000001.10:g.171605124G>A
CM000663.1:g.171605124G>A
NC_000001.9:g.169871747G>A
NG_008859.1:g.21650C>T
ENST00000037502.11:c.1456C>T
ENST00000637303.1:c.235-2646G>A
ENST00000638471.1:c.*794C>T
ENST00000037502.10:c.1456C>T
ENST00000614688.1:c.*420C>T
NM_000261.1:c.1456C>T

Likely Pathogenic

Met criteria codes 4

PP1_Moderate PS4_Supporting PP3_Moderate PM2_Supporting

Not Met criteria codes 10

PM5 PM4 BA1 BS1 BS3 BP7 BP4 PS1 PS2 PS3

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.1456C>T variant in MYOC is a missense variant predicted to cause substitution of Leucine by Phenylalanine at amino acid 486 (p.Leu486Phe). 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 = 0.891, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function. The assay in this study (PMID: 40081751), measuring secretion of the Leu486Phe protein, did not meet the OddsPath threshold for PS3_Supporting (> 2.1). 5 segregations in 1 family, with juvenile open angle

glaucoma (JOAG), have been reported (PMID: 27900994), which fulfilled PP1_Moderate (5-6 meioses). 3 probands with JOAG or POAG (primary open angle glaucoma) have been reported carrying this variant (PMIDs: 24825108, 37032519, 27900994), which met PS4_Supporting (≥ 2 probands). 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): PP1_Moderate, PP3_Moderate, PS4_Supporting, PM2_Supporting

Met criteria codes

PP1_Moderate	✔	5 segregations in 1 family, with juvenile open angle glaucoma (JOAG), have been reported (PMID: 27900994), which fulfilled PP1_Moderate (5-6 meioses).
PS4_Supporting	✔	3 probands with JOAG or POAG (primary open angle glaucoma) have been reported carrying this variant (PMIDs: 24825108, 37032519, 27900994), which met PS4_Supporting (≥ 2 probands).
PP3_Moderate	✔	The REVEL score = 0.891, 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.

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	✖	Although the OddsPath threshold for PS3_Supporting was not met, this variant may impact protein function (see PS3 comment). The L486F protein is partially 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 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.
PS3		✖	The assays in this study (PMID: 40081751), measuring secretion and solubility of the Leu486Phe protein, did not meet the OddsPath threshold for PS3_Supporting (> 2.1). The L486F protein is partially 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

Curation History

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