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.1364C>A

Version: 2.0

CA343723562

2575101 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: f6b6b529-db5d-4217-9fb4-dc6e8209689f
Approved on: 2026/2/19
Published on: 2026/2/18

HGVS expressions

NM_000261.2:c.1364C>A
NC_000001.11:g.171636076G>T
CM000663.2:g.171636076G>T
NC_000001.10:g.171605216G>T
CM000663.1:g.171605216G>T
NC_000001.9:g.169871839G>T
NG_008859.1:g.21558C>A
ENST00000037502.11:c.1364C>A
ENST00000637303.1:c.235-2554G>T
ENST00000638471.1:c.*702C>A
ENST00000037502.10:c.1364C>A
ENST00000614688.1:c.*328C>A
NM_000261.1:c.1364C>A

Likely Pathogenic

Met criteria codes 3

PP3_Strong PP1_Moderate PM2_Supporting

Not Met criteria codes 11

BA1 PM5 PM4 BS1 BS3 PS1 PS2 PS3 PS4 BP4 BP7

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.1364C>A variant in MYOC is a missense variant predicted to cause substitution of Threonine by Lysine at amino acid 455 (p.Thr455Lys). 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 = 0.938, which met the ≥ 0.932 threshold for PP3_Strong, predicting a damaging effect on MYOC function. The assays in this study (PMID: 40081751), measuring solubility and secretion of the Thr455Lys protein, did not meet the OddsPath threshold for PS3_Supporting (> 2.1). 10 segregations in 1 family, with juvenile or

primary open angle glaucoma (JOAG or POAG), have been reported (PMID: 18067072), which fulfilled PP1_Moderate (≥5 meioses in ≥1 family, but not the ≥7 meioses in >1 family for the strong criterion). Only 1 proband with JOAG had been reported (PMID: 18067072), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting. In summary, this variant met the criteria to receive a score of 7 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

Met criteria codes

PP3_Strong	✔	The REVEL score = 0.938, which met the ≥ 0.932 threshold for PP3_Strong, predicting a damaging effect on MYOC function.
PP1_Moderate	✔	10 segregations in 1 family, with juvenile or primary open angle glaucoma (JOAG or POAG), have been reported (PMID: 18067072), which fulfilled PP1_Moderate (≥5 meioses in ≥1 family, but not the ≥7 meioses in >1 family for the strong criterion).
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

BA1	✖	This criterion was not met as PM2_Supporting has been met.
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.
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 T455K 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
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 solubility and secretion of the Thr455Lys protein, did not meet the OddsPath threshold for PS3_Supporting (> 2.1). The T455K 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: 18067072), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting.
BP4	✖	This criterion was not met as PP3 has been met.
BP7	✖	This is not an intronic, synonymous or non-coding variant.

Curation History

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