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.1504T>C

Version: 2.0

CA343722794

1686794 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: c1e74a9b-b014-42e8-a917-476e4337fb7a
Approved on: 2026/2/19
Published on: 2026/2/18

HGVS expressions

NM_000261.2:c.1504T>C
NC_000001.11:g.171635936A>G
CM000663.2:g.171635936A>G
NC_000001.10:g.171605076A>G
CM000663.1:g.171605076A>G
NC_000001.9:g.169871699A>G
NG_008859.1:g.21698T>C
ENST00000037502.11:c.1504T>C
ENST00000637303.1:c.235-2694A>G
ENST00000638471.1:c.*842T>C
ENST00000037502.10:c.1504T>C
ENST00000614688.1:c.*468T>C
NM_000261.1:c.1504T>C

Likely Pathogenic

Met criteria codes 4

PP3 PS3_Moderate PP1_Moderate PM2_Supporting

Not Met criteria codes 10

BA1 PM5 PM4 BS1 BS3 PS1 PS2 PS4 BP4 BP7

Evidence Links 3

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.1504T>C variant in MYOC is a missense variant predicted to cause substitution of Serine by Proline at amino acid 502 (p.Ser502Pro). 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 = 0.657, which was within the 0.644-0.772 range for PP3, predicting a damaging effect on MYOC function. The Ser502Pro protein had increased instability and reduced secretion levels compared to wild type myocilin protein in these studies (PMIDs: 16466712, 21612213, 23129764). The assays met the OddsPath threshold for PS3_Moderate (>

4.3), indicating that this variant did impact protein function. 6 segregations in 1 family, with juvenile open angle glaucoma (JOAG), have been reported (PMID: 9863594), which fulfilled PP1_Moderate (5-6 meioses). Only 1 proband with JOAG had been reported (PMID: 9863594), 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, PP1_Moderate, PP3, PM2_Supporting.

Met criteria codes

PP3	✔	The REVEL score = 0.657, which was within the 0.644-0.772 range for PP3, predicting a damaging effect on MYOC function.
PS3_Moderate	✔	The Ser502Pro protein had increased instability and reduced secretion levels compared to wild type myocilin protein in these studies (PMIDs: 16466712, 21612213, 23129764). The assays met the OddsPath threshold for PS3_Moderate (> 4.3), indicating that this variant did impact protein function. Note: this is a duplicated result from PMID: 23129764 PubMed:25524706 The Ser502Pro protein is unstable. The assay in this study meets the OddsPath threshold for PS3_Moderate (> 4.3) (when combined with PMIDs: 20334347, 23129764, 25524706, 36579626). PubMed:21612213 The Ser502Pro protein is unstable. The assay in this study meets the OddsPath threshold for PS3_Moderate (> 4.3) (when combined with PMIDs: 20334347, 21612213, 25524706, 36579626). PubMed:23129764
PP1_Moderate	✔	6 segregations in 1 family, with JOAG, have been reported (PMID: 9863594), which fulfilled PP1_Moderate (5-6 meioses).
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 criterion did not apply to this variant.
BS1	✖	This criterion was not met as PM2_Supporting has been met.
BS3	✖	This criterion was not met as PS3_Moderate 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: 9863594), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting.
BP4		✖	This criterion was not met as PP3 has been met.
BP7		✖	This criterion did not apply to this variant.

Curation History

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