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Variant: NM_000261.2:c.1452G>A

Version: 2.0

CA421938581

2429763 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: ca98206c-190d-4706-87c3-4473c409e130
Approved on: 2026/2/19
Published on: 2026/2/18

HGVS expressions

NM_000261.2:c.1452G>A
NC_000001.11:g.171635988C>T
CM000663.2:g.171635988C>T
NC_000001.10:g.171605128C>T
CM000663.1:g.171605128C>T
NC_000001.9:g.169871751C>T
NG_008859.1:g.21646G>A
ENST00000037502.11:c.1452G>A
ENST00000637303.1:c.235-2642C>T
ENST00000638471.1:c.*790G>A
ENST00000037502.10:c.1452G>A
ENST00000614688.1:c.*416G>A
NM_000261.1:c.1452G>A

Likely Benign

Met criteria codes 2

BP7 BP4

Not Met criteria codes 12

PS1 PS2 PS3 PS4 BA1 PP1 PP3 PM5 PM4 PM2 BS1 BS3

Evidence Links 0

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.1452G>A variant in MYOC is a synonymous variant (p.Lys484=). This variant was identified in controls in a North Indian study (PMID: 39998747). The gnomAD (v4.1.0) database did not well represent the genetic ancestry group from which the variant has been reported (South Asian). Thus PM2_Supporting was not applied to this variant. The SpliceAI score = 0.01, which met the ≤ 0.1 threshold for BP4, suggesting that the variant does not impact MYOC function. This synonymous variant meets BP4, so BP7 is met. There was no functional evidence predicting a damaging or benign impact of this variant on MYOC function. Although probands with juvenile open angle glaucoma

have been reported carrying this variant, PM2_Supporting was not met, therefore PS4 did not apply. In summary, this variant met the criteria to receive a score of -2 and to be classified as likely benign (likely benign classification range -2 to -6, 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): BP4, BP7

Met criteria codes

BP7	✔	This synonymous variant meets BP4, so BP7 is met.
BP4	✔	The SpliceAI score = 0.01, which met the ≤ 0.1 threshold for BP4, suggesting that the variant does not impact MYOC function.

Not Met criteria codes

PS1	✖	This variant does not involve an amino acid change.
PS2	✖	This variant has not been identified de novo.
PS3	✖	No functional evidence has been found for this variant.
PS4	✖	Although probands with juvenile open angle glaucoma have been reported carrying this variant, PM2_Supporting was not met, therefore PS4 did not apply.
BA1	✖	This variant did not meet the ≥ 0.01 minor allele frequency threshold in gnomAD (v4.1.0).
PP1	✖	No segregations have been reported for this variant.
PP3	✖	This criterion did not apply to this variant.
PM5	✖	This is not a missense variant.
PM4	✖	This variant does not cause a protein length change.
PM2	✖	This variant was identified in controls in a North Indian study (PMID: 39998747). The gnomAD (v4.1.0) database did not well represent the genetic ancestry group from which the variant has been reported (South Asian). Thus PM2_Supporting was not applied to this variant.
BS1	✖	The highest minor allele frequency of this variant was in the African/African American genetic ancestry group of gnomAD (v4.1.0) = 0.00002669 (2 alleles out of 74,934), which did not meet the ≥ 0.001 threshold set for BS1.
BS3	✖	No functional evidence has been found for this variant.

Curation History

Showing 1 to 2 of 2 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000261.2:c.1452G>A	Likely Benign	Open-Angle Glaucoma	2026-02-18	2.0	ClinGen Glaucoma Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MYOC Version 2.0.0	MYOC
View	NM_000261.2:c.1452G>A	Uncertain Significance	Juvenile Open Angle Glaucoma	2023-02-15	1.0	-	MYOC

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