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Variant: NM_000261.2:c.991T>A

Version: 2.0

CA32685841

2442271 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4dc08f6a-487b-4619-9c21-e26bd6338a43
Approved on: 2026/1/19
Published on: 2026/1/21

HGVS expressions

NM_000261.2:c.991T>A
NC_000001.11:g.171636449A>T
CM000663.2:g.171636449A>T
NC_000001.10:g.171605589A>T
CM000663.1:g.171605589A>T
NC_000001.9:g.169872212A>T
NG_008859.1:g.21185T>A
ENST00000037502.11:c.991T>A
ENST00000637303.1:c.235-2181A>T
ENST00000638471.1:c.*329T>A
ENST00000037502.10:c.991T>A
ENST00000614688.1:c.991T>A
NM_000261.1:c.991T>A

Uncertain Significance

Met criteria codes 1

PM2_Supporting

Not Met criteria codes 13

PS1 **PS2** **PS3** **PS4** **BA1** **PP1** **PP3** **PM5** **PM4** **BS1** **BS3** **BP7** **BP4**

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.991T>A variant in MYOC is a missense variant predicted to cause substitution of Serine by Threonine at amino acid 331 (p.Ser331Thr). 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 = 0.543, which was neither above nor below the thresholds for PP3 (≥ 0.644) or BP4 (≤ 0.290), predicting a damaging or benign impact on MYOC function. There was no functional evidence predicting a damaging or benign impact of this variant on MYOC function. Only 1 proband with primary open angle glaucoma had

been reported (PMID: 17417611), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting. In summary, this variant met the criteria to receive a score of 1 and to be classified as a variant of uncertain significance (uncertain significance classification range -1 to 5, adapted from PMID: 32720330) for primary open angle glaucoma based on the ACMG/AMP criteria met, as specified by the ClinGen Glaucoma VCEP (v2.0.0, 5 Dec 2024): PM2_Supporting

Met criteria codes

PM2_Supporting	✔	This variant was not found in any population of gnomAD (v4.1.0), meeting the ≤ 0.0001 threshold set for PM2_Supporting in a population of at least 10,000 alleles.

Not Met criteria codes

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	✖	No functional evidence has been found for this variant.
PS4	✖	Only 1 proband with primary open angle glaucoma had been reported (PMID: 17417611), not meeting the ≥ 2 probands threshold required to meet PS4_Supporting.
BA1	✖	This criterion was not met as PM2_Supporting has been met.
PP1	✖	No segregations have been reported for this variant.
PP3	✖	This missense variant had a REVEL score = 0.543, which did not meet the ≥ 0.644 threshold required for PP3.
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	✖	No functional evidence has been found for this variant.
BP7	✖	This is not an intronic, synonymous or non-coding variant.
BP4	✖	This missense variant had a REVEL score = 0.543, which did not meet the ≤ 0.290 threshold required for BP4.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000261.2:c.991T>A	Uncertain Significance	Open-Angle Glaucoma	2026-01-21	2.0	ClinGen Glaucoma Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for MYOC Version 2.0.0	MYOC
View		Uncertain Significance	Primary Open Angle Glaucoma	2023-02-15	1.0	-	MYOC

Showing 1 to 2 of 2 rows

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