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Variant: NM_000261.2:c.816A>T

Version: 2.0

CA1244148

2570629 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: dc4619f5-2785-45f7-8c0d-02455cf12ed5
Approved on: 2026/1/21
Published on: 2026/1/20

HGVS expressions

NM_000261.2:c.816A>T
NC_000001.11:g.171636624T>A
CM000663.2:g.171636624T>A
NC_000001.10:g.171605764T>A
CM000663.1:g.171605764T>A
NC_000001.9:g.169872387T>A
NG_008859.1:g.21010A>T
ENST00000037502.11:c.816A>T
ENST00000637303.1:c.235-2006T>A
ENST00000638471.1:c.*154A>T
ENST00000037502.10:c.816A>T
ENST00000614688.1:c.816A>T
NM_000261.1:c.816A>T

Likely Benign

Met criteria codes 2

BP4 BP7

Not Met criteria codes 12

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

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.816A>T variant in MYOC is a synonymous variant (p.Arg272=). The highest minor allele frequency of this variant was in the South Asian genetic ancestry group of gnomAD (v4.1.0) = 0.0002087 (19 alleles out of 91,040), which did not meet the PM2_Supporting allele frequency threshold (≤ 0.0001) or the BS1 allele frequency threshold (≥ 0.001). 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 a proband with primary open angle

glaucoma had 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 primary 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

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

Not Met criteria codes

PM5	✖	This is not a missense variant.
PM4	✖	This variant does not cause a protein length change.
PM2	✖	The highest minor allele frequency of this variant was in the South Asian genetic ancestry group of gnomAD (v4.1.0) = 0.0002087 (19 alleles out of 91,040), which did not meet the ≤ 0.0001 threshold set for PM2_Supporting.
BS1	✖	The highest minor allele frequency of this variant was in the South Asian genetic ancestry group of gnomAD (v4.1.0) = 0.0002087 (19 alleles out of 91,040), which did not meet the ≥ 0.001 threshold set for BS1.
BS3	✖	No functional evidence has been found for this variant.
BA1	✖	This variant did not meet the ≥ 0.01 minor allele frequency threshold in gnomAD (v4.1.0).
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 a proband with POAG had been reported carrying this variant, PM2_Supporting was not met, therefore PS4 did not apply.
PP1	✖	No segregations have been reported for this variant.
PP3	✖	This is not a missense variant.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000261.2:c.816A>T	Likely Benign	Open-Angle Glaucoma	2026-01-20	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	2023-07-05	1.0	ClinGen Glaucoma Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 1.1	MYOC

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