

Variant: *NM_000261.2:c.897T>C*

Version: 2.0

CA32686006 [↗](#)

1723172 (ClinVar) [↗](#)

Gene: MYOC ([HGNC:4653](#))

Condition: open-angle glaucoma ([MONDO:0005338](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: fe811573-724a-4189-8adb-40f341fdbaa5

Approved on: 2025/12/4

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HGVS expressions

NM_000261.2:c.897T>C

NC_000001.11:g.171636543A>G

CM000663.2:g.171636543A>G

NC_000001.10:g.171605683A>G

CM000663.1:g.171605683A>G

NC_000001.9:g.169872306A>G

NG_008859.1:g.21091T>C

ENST00000037502.11:c.897T>C

ENST00000637303.1:c.235-2087A>G

ENST00000638471.1:c.*235T>C

ENST00000037502.10:c.897T>C

ENST00000614688.1:c.897T>C

NM_000261.1:c.897T>C

Uncertain Significance

Met criteria codes **3**

BP4

BP7

PM2_Supporting

Not Met criteria codes **12**

PM6

PM5

PM4

BS1

BS3

PS1

PS2

PS3

PS4

BA1

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.897T>C variant in MYOC is a synonymous variant (p.Phe299=). The highest minor allele frequency of this variant was in the Admixed American genetic ancestry group of gnomAD (v4.1.0) = 0.00001676 (1 allele out of 59,660), which met the ≤ 0.0001 threshold set for PM2_Supporting in a genetic ancestry group of at least 10,000 alleles. 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. Only 1 proband with primary open angle glaucoma had

been reported (ANZRAG [E. Souzeau pers. comm.]), 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, 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.
PM2_Supporting			The highest minor allele frequency of this variant was in the Admixed American genetic ancestry group of gnomAD (v4.1.0) = 0.00001676 (1 allele out of 59,660), which met the ≤ 0.0001 threshold set for PM2_Supporting in a genetic ancestry group of at least 10,000 alleles.

Not Met criteria codes

PM6			This variant has not been identified de novo.
PM5			This is not a missense variant.
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.
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			Only 1 proband with primary open angle glaucoma had been reported (ANZRAG [E. Souzeau pers. comm.]), 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 is not a missense variant.

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Curation History 		
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