

Variant: NM\_000261.2:c.960G>A

Version: 2.0

CA421938611 [↗](#)

1810369 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** 2709da4c-a4b9-4478-ab77-9cebba095708

**Approved on:** 2025/11/13

**Published on:** 2025/11/13

### HGVS expressions

**NM\_000261.2:c.960G>A**

NC\_000001.11:g.171636480C>T

CM000663.2:g.171636480C>T

NC\_000001.10:g.171605620C>T

CM000663.1:g.171605620C>T

NC\_000001.9:g.169872243C>T

NG\_008859.1:g.21154G>A

ENST00000037502.11:c.960G>A

ENST00000637303.1:c.235-2150C>T

ENST00000638471.1:c.\*298G>A

ENST00000037502.10:c.960G>A

ENST00000614688.1:c.960G>A

NM\_000261.1:c.960G>A

Uncertain Significance

Met criteria codes **3**

PM2\_Supporting BP7 BP4

Not Met criteria codes **11**

BS1 BS3 PS1 PS2 PS3 PS4  
BA1 PP1 PP3 PM5 PM4

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.960G>A variant in MYOC is a synonymous variant (p.Arg320=). This variant was not found in any genetic ancestry group of gnomAD (v4.1.0), meeting the  $\leq 0.0001$  threshold set for PM2\_Supporting in a genetic ancestry group of at least 10,000 alleles. The SpliceAI score = 0, which met the  $\leq 0.1$  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  $\geq 2$  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

|                |                                                                                   |                                                                                   |                                                                                                                                                                                                 |
|----------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PM2_Supporting |  |  | This variant was not found in any genetic ancestry group of gnomAD (v4.1.0), meeting the $\leq 0.0001$ threshold set for PM2_Supporting in a genetic ancestry group of at least 10,000 alleles. |
| BP7            |  |  | This synonymous variant meets BP4, so BP7 is met.                                                                                                                                               |
| BP4            |  |  | The SpliceAI score = 0, which met the $\leq 0.1$ threshold for BP4, suggesting that the variant does not impact MYOC function.                                                                  |

Not Met criteria codes

|     |                                                                                     |                                                                                     |                                                                                                                                                                                  |
|-----|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 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 $\geq 2$ 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 criterion did not apply to this variant.                                                                                                                                    |
| PM5 |  |  | This is not a missense variant.                                                                                                                                                  |
| PM4 |  |  | This variant does not cause a protein length change.                                                                                                                             |

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