

Variant: *NM_000261.2:c.1150G>A*

Version: 2.0

CA343724529 [↗](#)

1342205 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 1d496dac-748e-4a00-954f-e320d270d7fa

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HGVS expressions

NM_000261.2:c.1150G>A

NC_000001.11:g.171636290C>T

CM000663.2:g.171636290C>T

NC_000001.10:g.171605430C>T

CM000663.1:g.171605430C>T

NC_000001.9:g.169872053C>T

NG_008859.1:g.21344G>A

ENST00000037502.11:c.1150G>A

ENST00000637303.1:c.235-2340C>T

ENST00000638471.1:c.*488G>A

ENST00000037502.10:c.1150G>A

ENST00000614688.1:c.*114G>A

NM_000261.1:c.1150G>A

Likely Pathogenic

Met criteria codes 4

PP1_Strong

PP3_Moderate

PS4_Supporting

PM2_Supporting

Not Met criteria codes 10

PS1

PS2

PS3

BA1

BS1

BS3

PM5

PM4

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.1150G>A variant in MYOC is a missense variant predicted to cause substitution of Aspartic acid by Asparagine at amino acid 384 (p.Asp384Asn). The highest minor allele frequency of this variant was in the Admixed American genetic ancestry group of gnomAD (v4.1.0) = 0.00001667 (1 allele out of 59,992), which met the ≤ 0.0001 threshold set for PM2_Supporting in a genetic ancestry group of at least 10,000 alleles. The REVEL score = 0.914, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function. The assay in this study (PMID: 19234343), measuring solubility of the Asp384Asn protein, did not meet the OddsPath threshold

for PS3_Supporting (> 2.1). 20 segregations in 3 families, with JOAG or POAG, have been reported (PMIDs: 23826516, 19234343, 34273563), which fulfilled PP1_Strong (≥ 7 meioses in > 1 family). 5 probands with JOAG or POAG have been reported carrying this variant (PMIDs: 23826516, 11853639, 19234343, 32476818, 34273563), which met PS4_Supporting (≥ 2 probands). In summary, this variant met the criteria to receive a score of 8 and to be classified as likely pathogenic (likely pathogenic classification range 6 to 9, 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): PP1_Strong, PP3_Moderate, PS4_Supporting, PM2_Supporting.

Met criteria codes

PP1_Strong			20 segregations in 3 families, with JOAG or POAG, have been reported (PMIDs: 23826516, 19234343, 34273563), which fulfilled PP1_Strong (≥ 7 meioses in > 1 family).
PP3_Moderate			The REVEL score = 0.914, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function.
PS4_Supporting			5 probands with JOAG or POAG have been reported carrying this variant (PMIDs: 23826516, 11853639, 19234343, 32476818, 34273563), which met PS4_Supporting (≥ 2 probands).
PM2_Supporting			The highest minor allele frequency of this variant was in the Admixed American genetic ancestry group of gnomAD (v4.1.0) = 0.00001667 (1 allele out of 59,992), 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

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			The assay in this study (PMID: 19234343), measuring solubility of the Asp384Asn protein, did not meet the OddsPath threshold for PS3_Supporting (> 2.1).
BA1			This criterion was not met as PM2_Supporting has been met.
BS1			This criterion was not met as PM2_Supporting has been met.
BS3			Although the OddsPath threshold for PS3_Supporting was not met, this variant may impact protein function (see PS3 comment).
PM5			PM5 could not be applied to this novel missense variant as although it did meet PP3, the Grantham score was lower (= 23) than the score for the two different missense changes at the same amino acid residue determined to be likely pathogenic by the ClinGen Glaucoma VCEP (c.1150G>C, p.Asp384His, Grantham score = 81 and c.1151A>G, p.Asp384Gly, Grantham score = 94).
PM4			This criterion did not apply to this variant.

BP7			This criterion did not apply to this variant.
BP4			This criterion was not met as PP3 has been met.

Curation History 

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