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Variant: NM_000261.2:c.752T>C

Version: 2.0

CA343726262

1342196 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4c28aa89-61ff-4446-8824-3254caef54d3
Approved on: 2026/1/21
Published on: 2026/1/20

HGVS expressions

NM_000261.2:c.752T>C
NC_000001.11:g.171636688A>G
CM000663.2:g.171636688A>G
NC_000001.10:g.171605828A>G
CM000663.1:g.171605828A>G
NC_000001.9:g.169872451A>G
NG_008859.1:g.20946T>C
ENST00000037502.11:c.752T>C
ENST00000637303.1:c.235-1942A>G
ENST00000638471.1:c.*90T>C
ENST00000037502.10:c.752T>C
ENST00000614688.1:c.752T>C
NM_000261.1:c.752T>C

Pathogenic

Met criteria codes 5

PS2_Moderate PP3_Moderate PP1_Strong PS4_Supporting PM2_Supporting

Not Met criteria codes 9

BP7 BP4 BS1 BS3 PS1 PS3 BA1 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.752T>C variant in MYOC is a missense variant predicted to cause substitution of Valine by Alanine at amino acid 251 (p.Val251Ala). 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 = 0.839, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function. There was no functional evidence predicting a damaging or benign impact of this variant on MYOC function. 17 segregations in 3 families, with juvenile or primary open angle glaucoma (JOAG or POAG), have been reported

(PMIDs: 32937162, 23517641 and Pasutto pers. comm.), which fulfilled PP1_Strong (≥7 meioses in >1 family). 3 probands with JOAG or POAG have been reported (PMIDs: 32937162, 23517641 and Pasutto pers. comm.) carrying this variant, which met PS4_Supporting (≥ 2 probands). One of these was a confirmed de novo proband with juvenile open angle glaucoma (PMID: 23517641) (PS2_Moderate). In summary, this variant met the criteria to receive a score of 10 and to be classified as pathogenic (pathogenic classification ≥ 10, 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, PS2_Moderate, PP3_Moderate, PM2_Supporting, PS4_Supporting

Met criteria codes

PS2_Moderate	✔	1 confirmed de novo proband with JOAG has been identified.
PP3_Moderate	✔	The REVEL score = 0.839, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function.
PP1_Strong	✔	17 segregations in 3 families, with juvenile or primary open angle glaucoma (JOAG or POAG), have been reported (PMIDs: 32937162, 23517641 and Pasutto pers. comm.), which fulfilled PP1_Strong (≥7 meioses in >1 family).
PS4_Supporting	✔	3 probands with JOAG or POAG have been reported (PMIDs: 32937162, 23517641 and Pasutto pers. comm.) carrying this variant, which met PS4_Supporting (≥ 2 probands).
PM2_Supporting	✔	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.

Not Met criteria codes

BP7	✖	This is not an intronic, synonymous or non-coding variant.
BP4	✖	This criterion was not met as PP3 has been met.
BS1	✖	This criterion was not met as PM2_Supporting has been met.
BS3	✖	No functional evidence has been found for this variant.
PS1	✖	An established LP or P variant causing this same amino acid change has not been identified.
PS3	✖	No functional evidence has been found for this variant.
BA1	✖	This criterion was not met as PM2_Supporting has been met.
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.

Curation History

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