The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000261.2:c.760C>A

Version: 2.0

CA343726248

2429764 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: 34a2100b-b9f7-4a83-b98b-20471a046610
Approved on: 2026/1/21
Published on: 2026/1/20

HGVS expressions

NM_000261.2:c.760C>A
NC_000001.11:g.171636680G>T
CM000663.2:g.171636680G>T
NC_000001.10:g.171605820G>T
CM000663.1:g.171605820G>T
NC_000001.9:g.169872443G>T
NG_008859.1:g.20954C>A
ENST00000037502.11:c.760C>A
ENST00000637303.1:c.235-1950G>T
ENST00000638471.1:c.*98C>A
ENST00000037502.10:c.760C>A
ENST00000614688.1:c.760C>A
NM_000261.1:c.760C>A

Likely Pathogenic

Met criteria codes 3

PP3_Strong PM2_Supporting PS4_Supporting

Not Met criteria codes 11

PS1 PS2 PS3 PP1 PM5 PM4 BA1 BS1 BS3 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.760C>A variant in MYOC is a missense variant predicted to cause substitution of Proline by Threonine at amino acid 254 (p.Pro254Thr). 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 = 0.933, which met the ≥ 0.932 threshold for PP3_Strong, predicting a damaging effect on MYOC function. There was no functional evidence predicting a damaging or benign impact of this variant on MYOC function. 2 probands with juvenile or primary open angle glaucoma have been reported carrying this variant (PMIDs:

32830442, 33793440), which met PS4_Supporting (≥ 2 probands). In summary, this variant met the criteria to receive a score of 6 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): PP3_Strong, PS4_Supporting, PM2_Supporting.

Met criteria codes

PP3_Strong	✔	The REVEL score = 0.933, which met the ≥ 0.932 threshold for PP3_Strong, predicting a damaging effect on MYOC function.
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.
PS4_Supporting	✔	2 probands with JOAG or POAG have been reported carrying this variant (PMIDs: 32830442, 33793440), which met PS4_Supporting (≥ 2 probands).

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	✖	No functional evidence has been found for this variant.
PP1	✖	No segregations have been reported for this variant.
PM5	✖	PM5 could not be applied to this variant as the other missense variants at this amino acid residue have higher Grantham scores.
PM4	✖	This variant does not cause a protein length change.
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	✖	No functional evidence has been found for 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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