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Variant: NM_000261.2:c.608C>T

Version: 2.0

CA343727142

1342208 (ClinVar)

Gene: MYOC (HGNC:4653)
Condition: open-angle glaucoma (MONDO:0005338)
Inheritance Mode: Autosomal dominant inheritance
UUID: 27008272-946b-44b3-8a05-45be2c558549
Approved on: 2025/12/4
Published on: 2025/12/4

HGVS expressions

NM_000261.2:c.608C>T
NC_000001.11:g.171638719G>A
CM000663.2:g.171638719G>A
NC_000001.10:g.171607859G>A
CM000663.1:g.171607859G>A
NC_000001.9:g.169874482G>A
NG_008859.1:g.18915C>T
ENST00000037502.11:c.608C>T
ENST00000637303.1:c.324G>A
ENST00000638471.1:c.138C>T
ENST00000037502.10:c.608C>T
ENST00000614688.1:c.608C>T
NM_000261.1:c.608C>T

Uncertain Significance

Met criteria codes 2

PM2_Supporting BS3_Supporting

Not Met criteria codes 12

BS1 BP7 BP4 PS1 PS2 PS3 PS4 PP1 PP3 BA1 PM5 PM4

Evidence Links 1

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.608C>T variant in MYOC is a missense variant predicted to cause substitution of Serine by Phenylalanine at amino acid 203 (p.Ser203Phe). The highest minor allele frequency of this variant was in the European (non-Finnish) genetic ancestry group of gnomAD (v4.1.0) = 0.00000085 (1 allele out of 1,179,946), which met the ≤ 0.0001 threshold set for PM2_Supporting in a genetic ancestry group of at least 10,000 alleles. The REVEL score = 0.344, which was neither above nor below the thresholds for PP3 (≥ 0.644) or BP4 (≤ 0.290), predicting a damaging or benign impact on MYOC function.The Ser203Phe protein had similar secretion levels to wild type myocilin protein

in this study (PMID: 16466712). The assay met the OddsPath threshold for BS3_Moderate (< 0.23), indicating that this variant did not impact protein function. This variant has not yet been identified in a proband with juvenile or primary open angle glaucoma, only in participants of the control cohorts. 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): BS3_Moderate, PM2_Supporting

Met criteria codes

PM2_Supporting	✔	The highest minor allele frequency of this variant was in the European (non-Finnish) genetic ancestry group of gnomAD (v4.1.0) = 0.00000085 (1 allele out of 1,179,946), which met the ≤ 0.0001 threshold set for PM2_Supporting in a genetic ancestry group of at least 10,000 alleles.
BS3_Supporting	✔	Applied at the BS3_Moderate level. The Ser203Phe protein had similar secretion levels to wild type myocilin protein in this study (PMID: 16466712). The assay met the OddsPath threshold for BS3_Moderate (< 0.23), indicating that this variant did not impact protein function. The S203F protein is secreted. The assay in this study meets the OddsPath threshold for BS3_Moderate (< 0.23) PubMed:16466712

Not Met criteria codes

BS1	✖	This criterion was not met as PM2_Supporting has been met.
BP7	✖	This is not an intronic, synonymous or non-coding variant.
BP4	✖	The REVEL score = 0.344, which did not meet the ≤ 0.290 threshold required for BP4.
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	✖	This criterion was not met as BS3_Moderate has been met.
PS4	✖	This variant has not yet been identified in a proband with juvenile or primary open angle glaucoma, only in participants of the control cohorts.
PP1	✖	No segregations have been reported for this variant.
PP3	✖	The REVEL score = 0.344, which did not meet the ≥ 0.644 threshold required for PP3.
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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