

Variant: *NM_000261.2:c.1021T>C*

Version: 2.0

CA343725060 [↗](#)

1439558 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 133402f4-70d2-411b-a4db-71d90bdfdcc0

Approved on: 2026/1/21

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HGVS expressions

NM_000261.2:c.1021T>C

NC_000001.11:g.171636419A>G

CM000663.2:g.171636419A>G

NC_000001.10:g.171605559A>G

CM000663.1:g.171605559A>G

NC_000001.9:g.169872182A>G

NG_008859.1:g.21215T>C

ENST00000037502.11:c.1021T>C

ENST00000637303.1:c.235-2211A>G

ENST00000638471.1:c.*359T>C

ENST00000037502.10:c.1021T>C

ENST00000614688.1:c.1020T>C

NM_000261.1:c.1021T>C

Pathogenic

Met criteria codes 5

PS4_Moderate PS3 PP1_Strong

PM2_Supporting PP3_Moderate

Not Met criteria codes 9

BA1 BS1 BS3 BP4 BP7 PS1

PS2 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.1021T>C variant in MYOC is a missense variant predicted to cause substitution of Serine by Proline at amino acid 341 (p.Ser341Pro). 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 = 0.821, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function. A transgenic mouse model carrying human MYOC Ser341Pro (PMID: 38212635), and displaying reduced secretion of the Ser341Pro protein in vivo, exhibited a glaucoma phenotype (including IOP elevation and retina

ganglion cell loss), meeting PS3. 12 segregations in 4 families, with juvenile or primary open angle glaucoma (JOAG or POAG), have been reported (PMIDs: 17867509, 24825108, 33214997, 25777973), which fulfilled PP1_Strong (≥ 7 meioses in >1 family). There were more family studies published than presented here. 8 probands with JOAG or POAG have been reported carrying this variant (PMIDs: 9510647, 24825108, 25777973, 33214997, 17867509, ClinVar: Invitae), which met PS4_Moderate (≥ 6 probands). In summary, this variant met the criteria to receive a score of 13 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): PS3, PP1_Strong, PS4_Moderate, PP3_Moderate, PM2_Supporting

Met criteria codes

PS4_Moderate			8 probands with JOAG or POAG have been reported carrying this variant (PMIDs: 9510647, 24825108, 25777973, 33214997, 17867509, ClinVar: Invitae), which met PS4_Moderate (≥ 6 probands).
PS3			A transgenic mouse model carrying human MYOC Ser341Pro (PMID: 38212635), and displaying reduced secretion of the Ser341Pro protein in vivo, exhibited a glaucoma phenotype (including IOP elevation and retina ganglion cell loss), meeting PS3.
			A transgenic mouse model carrying human MYOC S341P and displaying non secretion of S341P protein in vivo exhibited a glaucoma phenotype (including IOP elevation, retina ganglion cell loss) PubMed:38212635 
PP1_Strong			12 segregations in 4 families, with juvenile or primary open angle glaucoma (JOAG or POAG), have been reported (PMIDs: 17867509, 24825108, 33214997, 25777973), which fulfilled PP1_Strong (≥ 7 meioses in >1 family). There were more family studies published than presented here.
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.
PP3_Moderate			The REVEL score = 0.821, which was within the 0.773-0.931 range for PP3_Moderate, predicting a damaging effect on MYOC function.

Not Met criteria codes

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			This criterion was not met as PS3 has been met.
BP4			This criterion was not met as PP3 has been met.
BP7			This is not an intronic, synonymous or non-coding variant.
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.
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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