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Variant: NM_000104.4(CYP1B1):c.352C>T (p.Pro118Ser)

Version: 1.0

CA1620050

3251563 (ClinVar)

Gene: CYP1B1 (HGNC:1545)
Condition: CYP1B1-related glaucoma with or without anterior segment dysgenesis (MONDO:0800472)
Inheritance Mode: Autosomal recessive inheritance
UUID: 4652fcd8-3f65-4c92-971b-5594de654597
Approved on: Tue, 13 Oct 2026 00:00:00 +0000
Published on: Tue, 13 Oct 2026 00:00:00 +0000

HGVS expressions

NM_000104.4(CYP1B1):c.352C>T (p.Pro118Ser)
NM_000104.4:c.352C>T
NC_000002.12:g.38075037G>A
CM000664.2:g.38075037G>A
NC_000002.11:g.38302180G>A
CM000664.1:g.38302180G>A
NC_000002.10:g.38155684G>A
NG_008386.2:g.6065C>T
ENST00000490576.2:c.352C>T
ENST00000610745.5:c.352C>T
ENST00000490576.1:c.352C>T
ENST00000494864.1:c.-70-3727C>T
ENST00000610745.4:c.352C>T
ENST00000613082.1:n.376-629C>T
ENST00000614273.1:c.352C>T
NM_000104.3:c.352C>T

Uncertain Significance

Met criteria codes 3

PM2_Supporting PP3 PM3

Not Met criteria codes 13

BS1 BS4 PVS1 PS1 PS2 PS3 BP7 BP4 PP1 BA1 PM1 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 CYP1B1 Version 2.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Glaucoma VCEP

The c.352C>T variant in CYP1B1 is a missense variant predicted to cause substitution of Proline by Serine at amino acid 118 (p.Pro118Ser). The highest minor allele frequency of this variant was in the European (non-Finnish) genetic ancestry group of gnomAD (v4.1) =

0.00000085 (1 allele out of 1,175,530), which met the ≤ 0.0005 threshold set for PM2_Supporting in a genetic ancestry group of at least 2,000 alleles. The REVEL score = 0.729, which was within the 0.644-0.772 range for PP3, predicting a damaging effect on CYP1B1 function. There was no functional evidence predicting a damaging or benign impact of this variant on CYP1B1 function. This variant has been identified in 2 individuals with a CYP1B1-related phenotype. 1 individual is compound heterozygous for the variant and a pathogenic variant (phase unknown) and 1 is homozygous (non-consanguineous) (PMIDs: 38459225, 18852424). Total proband points = 1, meeting PM3. In summary, this variant met the criteria to receive a score of 4 and to be classified as a variant of uncertain significance (uncertain significance classification range -1 to 5, adapted from PMID: 32720330) for CYP1B1-related glaucoma with or without anterior segment dysgenesis (ASD) based on the ACMG/AMP criteria met, as specified by the ClinGen Glaucoma VCEP (v2.0, 16.07.2026): PM3, PP3, 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) = 0.0000008507 (1 allele out of 1,175,530), which met the ≤ 0.0005 threshold set for PM2_Supporting in a genetic ancestry group of at least 2,000 alleles.
PP3	✔	The REVEL score = 0.729, which was within the 0.644-0.772 range for PP3, predicting a damaging effect on CYP1B1 function.
PM3	✔	This variant has been identified in 2 individuals with a CYP1B1-related phenotype. 1 individual is compound heterozygous for the variant and a pathogenic variant (phase unknown) and 1 is homozygous (non-consanguineous) (PMIDs: 38459225, 18852424). Total proband points = 1, meeting PM3.

Not Met criteria codes

BS1	✖	This criterion was not met as PM2_Supporting has been met.
BS4	✖	Non-segregation involving this variant has not been reported.
PVS1	✖	This criterion did not apply to this variant.
PS1	✖	An established likely pathogenic or pathogenic variant causing the 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.
BP7	✖	This criterion did not apply to this variant.
BP4	✖	This criterion was not met as PP3 has been met.
PP1	✖	No segregations have been reported for this variant.

BA1	✖	This criterion was not met as PM2_Supporting has been met.
PM1	✖	This missense variant is located outside well-established functional domains.
PM5	✖	No other likely pathogenic or pathogenic missense variant at this amino acid residue has been identified.
PM4	✖	This criterion did not apply to this variant.

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000104.4(CYP1B1):c.352C>T (p.Pr...	Uncertain Significance	CYP1B1-Related Glaucoma With Or Without Anterior Segment Dysgenesis	2026-10-13	1.0	ClinGen Glaucoma Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for CYP1B1 Version 2.0	CYP1B1

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