

Variant: *NM_000104.4(CYP1B1):c.710C>A (p.Ala237Glu)*

Version: 1.0

CA346328674 [↗](#)

1338800 (ClinVar) [↗](#)

Gene: CYP1B1 ([HGNC:1545](#))

Condition: CYP1B1-related glaucoma with or without anterior segment dysgenesis ([MONDO:0800472](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 66c76f6b-187a-45ef-8513-3682f7e6973e

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Published on: 2025/11/18

HGVS expressions

NM_000104.4(CYP1B1):c.710C>A (p.Ala237Glu)

NM_000104.4:c.710C>A

NC_000002.12:g.38074679G>T

CM000664.2:g.38074679G>T

NC_000002.11:g.38301822G>T

CM000664.1:g.38301822G>T

NC_000002.10:g.38155326G>T

NG_008386.2:g.6423C>A

ENST00000490576.2:c.710C>A

ENST00000610745.5:c.710C>A

ENST00000494864.1:c.-70-3369C>A

ENST00000610745.4:c.710C>A

ENST00000613082.1:n.376-271C>A

ENST00000614273.1:c.710C>A

NM_000104.3:c.710C>A

Likely Pathogenic

Met criteria codes **3**

PM2_Supporting

PP3

PM3_Strong

Not Met criteria codes **13**

PVS1

BS1

BS4

BP7

BP4

PS1

PS2

PS3

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 1.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Glaucoma VCEP

The c.710C>A variant in CYP1B1 is a missense variant predicted to cause substitution of Alanine by Glutamic acid at amino acid 237 (p.Ala237Glu). The highest minor allele frequency of this variant was in the European (non-Finnish) genetic ancestry group of gnomAD (v4.1.0) = 0.000008475 (1 allele out of 1,179,982), which met the ≤ 0.0005 threshold set for PM2_Supporting in a genetic ancestry group

of at least 2,000 alleles. The REVEL score = 0.717, which was within the 0.644-0.772 range for PP3, predicting a damaging effect on CYP1B1 function. PS3_Supporting was not applied, as although the OddsPath threshold was met (> 2.1), the threshold for abnormal impact on protein function in the assays could not be determined (PMID: 27060699). This variant has been identified in four individuals with a CYP1B1-related phenotype. Two of these individuals are compound heterozygous for the variant and a pathogenic or likely pathogenic variant (1 phase unknown and 1 confirmed in trans) and two individuals are homozygous (non-consanguineous) (PMIDs: 21815720, 23218183, 25950505, ClinVar). Total proband points = 2.5, meeting PM3_Strong. 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 CYP1B1-related glaucoma with or without anterior segment dysgenesis (ASD) based on the ACMG/AMP criteria met, as specified by the ClinGen Glaucoma VCEP (v1.0, 06.11.2025): PM3_Strong, 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) = 0.0000008475 (1 allele out of 1,179,982), 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 = 0.717, which was within the 0.644-0.772 range for PP3, predicting a damaging effect on CYP1B1 function.
PM3_Strong			This variant has been identified in four individuals with a CYP1B1-related phenotype. Two of these individuals are compound heterozygous for the variant and a pathogenic or likely pathogenic variant (1 phase unknown and 1 confirmed in trans) and two individuals are homozygous (non-consanguineous) (PMIDs: 21815720, 23218183, 25950505, ClinVar). Total proband points = 2.5, meeting PM3_Strong.

Not Met criteria codes

PVS1			This criterion did not apply to this variant.
BS1			This criterion was not met as PM2_Supporting has been met.
BS4			Non-segregation involving this variant has not been reported.
BP7			This criterion did not apply to this variant.
BP4			This criterion was not met as PP3 has been met.
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			PS3_Supporting was not applied, as although the OddsPath threshold was met (> 2.1), the threshold for abnormal impact on protein function in the assays could not be determined (PMID: 27060699).
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 

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