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_001386306.1:c.1090G>C

Version: 1.0

CA343772421

Gene: SERPINC1 (HGNC:462)
Condition: antithrombin III deficiency (MONDO:0013144)
Inheritance Mode: Autosomal dominant inheritance
UUID: cbdef16f-29d5-4a00-a7e9-1b233ad00e0a
Approved on: 2025-02-21
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HGVS expressions

NM_001386306.1:c.1090G>C
NC_000001.11:g.173903978C>G
CM000663.2:g.173903978C>G
NC_000001.10:g.173873116C>G
CM000663.1:g.173873116C>G
NC_000001.9:g.172139739C>G
NG_012462.1:g.18401G>C
ENST00000367698.4:c.1306G>C
ENST00000367698.3:c.1306G>C
ENST00000617423.4:c.691G>C
NM_000488.3:c.1306G>C
NM_001365052.1:c.1162G>C
NM_000488.4:c.1306G>C
NM_001365052.2:c.1162G>C
NM_001386302.1:c.1429G>C
NM_001386303.1:c.1387G>C
NM_001386304.1:c.1285G>C
NM_001386305.1:c.1249G>C

Uncertain Significance

Met criteria codes 4

PP3 PP4 PM2_Supporting PM5_Supporting

Evidence Links 0

Expert Panel

Thrombosis VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Thrombosis Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SERPINC1 Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Thrombosis VCEP

The c.1306G> variant in SERPINC1 is a missense variant predicted to cause substitution of alanine by proline at amino acid 436 (p.Ala436Pro). At least one patient with this variant displayed an antithrombin activity level of <0.8 IU/mL with repeated independent samples over time, which is highly specific for hereditary antithrombin deficiency (PP4, PMID:24684277). This variant is absent from gnomAD v2.1.1, 3.1.2 and 4.1.0 (PM2_Supporting). Another missense variant c.1306G>A (p.Ala436Thr) (ClinVarID:18003) in the same codon has been classified as likely pathogenic for hereditary antithrombin deficiency by the ClinGen Thrombosis VCEP (PM5_Supporting). The computational predictor REVEL gives a score of 0.843, which is above the threshold of 0.6, evidence that correlates with impact to SERPINC1 function (PP3). In summary, this variant meets the criteria to be classified as uncertain significance due to insufficient evidence for autosomal dominant hereditary antithrombin deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen Thrombosis VCEP: PP3, PP4, PM2_Supporting, PM5_Supporting.

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.843, which is above the threshold of 0.6, evidence that correlates with impact to SERPINC1 function (PP3).
PP4	✔	At least one patient with this variant displayed an antithrombin activity level of < 0.8 IU/mL with repeated independent samples over time, which is highly specific for hereditary antithrombin deficiency (PP4, PMID:24684277).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1, 3.1.2 and 4.1.0 (PM2_Supporting).
PM5_Supporting	✔	Another missense variant c.1306G>A (p.Ala436Thr) (ClinVarID:18003) in the same codon has been classified as likely pathogenic for hereditary antithrombin deficiency by the ClinGen Thrombosis VCEP (PM5_Supporting).

Curation History

Showing 1 to 1 of 1 rows