

Variant: NM_000488.4(SERPINC1):c.1141T>C (p.Ser381Pro)

Version: 1.0

CA210783 [↗](#)

18032 (ClinVar) [↗](#)

Gene: SERPINC1 (HGNC:462)

Condition: antithrombin III deficiency (MONDO:0013144)

Inheritance Mode: Autosomal dominant inheritance

UID: 44c9f3ad-2029-492d-903a-3987d3bd9d6b

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HGVS expressions

NM_000488.4:c.1141T>C

NM_000488.4(SERPINC1):c.1141T>C (p.Ser381Pro)

NC_000001.11:g.173909564A>G

CM000663.2:g.173909564A>G

NC_000001.10:g.173878702A>G

CM000663.1:g.173878702A>G

NC_000001.9:g.172145325A>G

NG_012462.1:g.12815T>C

ENST00000367698.4:c.1141T>C

ENST00000367698.3:c.1141T>C

ENST00000617423.4:c.560-2071T>C

NM_000488.3:c.1141T>C

NM_001365052.1:c.997T>C

NM_001365052.2:c.997T>C

NM_001386302.1:c.1264T>C

NM_001386303.1:c.1222T>C

NM_001386304.1:c.1120T>C

NM_001386305.1:c.1084T>C

NM_001386306.1:c.925T>C

Uncertain Significance

Met criteria codes **4**

PS4_Supporting

PM2_Supporting

PP1

PP3

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.1141T>C variant in SERPINC1 is a missense variant predicted to cause substitution of serine by proline at amino acid 381 (p.Ser381Pro). This variant has been reported in 2 probands meeting an antithrombin activity level of < 0.8 IU/mL. Only one had a family history of disease supported with reported antithrombin activity levels (PS4_Supporting; PMIDs: 1551681, 30975910). The variant has been reported to segregate with hereditary antithrombin deficiency in two affected meioses from one family (PP1; PMID:1551681). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.616, 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: PP1, PP3, PM2_Supporting, PS4_Supporting. (ClinGen Thrombosis Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SERPINC1 Version 1.0.0; date of approval)

Met criteria codes

PS4_Supporting			This variant has been reported in 2 probands meeting an antithrombin activity level of < 0.8 IU/mL. Only one had a family history of disease supported with reported antithrombin activity levels (PS4_Supporting; PMIDs: 1551681, 30975910).
PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP1			The variant has been reported to segregate with hereditary antithrombin deficiency in two affected meioses from one family (PP1; PMID:1551681).
PP3			The computational predictor REVEL gives a score of 0.616, which is above the threshold of 0.6, evidence that correlates with impact to SERPINC1 function (PP3).

Curation History

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