

Variant: NM_000488.3(SERPINC1):c.1315C>T (p.Pro439Ser)

Version: 1.0

CA343772365 [↗](#)

529741 (ClinVar) [↗](#)

Gene: SERPINC1 (HGNC:462)

Condition: antithrombin III deficiency (MONDO:0013144)

Inheritance Mode: Autosomal dominant inheritance

UID: 32ac3600-08e8-4f5c-9752-6c1e4ae4e9da

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HGVS expressions

NM_000488.3:c.1315C>T

NM_000488.3(SERPINC1):c.1315C>T (p.Pro439Ser)

NC_000001.11:g.173903969G>A

CM000663.2:g.173903969G>A

NC_000001.10:g.173873107G>A

CM000663.1:g.173873107G>A

NC_000001.9:g.172139730G>A

NG_012462.1:g.18410C>T

ENST00000367698.4:c.1315C>T

ENST00000367698.3:c.1315C>T

ENST00000617423.4:c.700C>T

NM_001365052.1:c.1171C>T

NM_000488.4:c.1315C>T

NM_001365052.2:c.1171C>T

NM_001386302.1:c.1438C>T

NM_001386303.1:c.1396C>T

NM_001386304.1:c.1294C>T

NM_001386305.1:c.1258C>T

NM_001386306.1:c.1099C>T

NM_000488.4(SERPINC1):c.1315C>T (p.Pro439Ser)

Uncertain Significance

Met criteria codes **3**

PM2_Supporting PM5 PP3

Not Met criteria codes **1**

PS4

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**

Thrombosis VCEP

The c.1315C>T (NM_000488.3) variant in SERPINC1 is a missense variant predicted to cause substitution of proline by serine at amino acid 439 (p.Pro439Ser). This variant is completely absent from gnomAD v2.1.1, v3.1.2 and v4.0.0 (PM2_Supporting). One proband with this variant is reported in the literature but cannot be counted towards PS4 as the AT levels of this patient are not published. The computational predictor REVEL gives a score of 0.901, which is above the threshold of 0.6, evidence that correlates with impact to SERPINC1 function (PP3). Another missense variant c.1315C>A (p.Pro439Thr) (ClinVarID:627228) in the same codon has been classified as pathogenic for autosomal dominant antithrombin III deficiency by the ClinGen Thrombosis VCEP (PM5). 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: PM5, PP3, PM2_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

- | | | | |
|-----------------------|---|---|--|
| PM2_Supporting |  |  | This variant is completely absent from gnomAD v2.1.1, v3.1.2 and v4.0.0 (PM2). |
| PM5 |  |  | Another missense variant c.1315C>A (p.Pro439Thr) (ClinVarID:627228) in the same codon has been classified as pathogenic for autosomal dominant antithrombin III deficiency by the ClinGen Thrombosis VCEP (PM5). |
| PP3 |  |  | The computational predictor REVEL gives a score of 0.901, which is above the threshold of 0.6, evidence that correlates with impact to SERPINC1 function (PP3). |

Not Met criteria codes

- | | | | |
|------------|---|---|--|
| PS4 |  |  | 1 proband without AT levels is reported in PMID: 31064749, but does not meet PS4 |
|------------|---|---|--|

Curation History

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