Variant: NM_001386306.1:c.391C>G

Version: 1.0

CA343777244

Gene: SERPINC1 (HGNC:462)
Condition: antithrombin III deficiency (MONDO:0013144)
Inheritance Mode: Autosomal dominant inheritance
UUID: bf29d89c-2a5c-456b-ac84-147ac3439b9b
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HGVS expressions

NM_001386306.1:c.391C>G
NC_000001.11:g.173914570G>C
CM000663.2:g.173914570G>C
NC_000001.10:g.173883708G>C
CM000663.1:g.173883708G>C
NC_000001.9:g.172150331G>C
NG_012462.1:g.7809C>G
ENST00000367698.4:c.391C>G
ENST00000367698.3:c.391C>G
ENST00000487183.1:n.96C>G
ENST00000494024.1:n.617C>G
ENST00000617423.4:c.391C>G
NM_000488.3:c.391C>G
NM_001365052.1:c.247C>G
NM_000488.4:c.391C>G
NM_001365052.2:c.247C>G
NM_001386302.1:c.391C>G
NM_001386303.1:c.472C>G
NM_001386304.1:c.391C>G
NM_001386305.1:c.391C>G

Uncertain Significance

Met criteria codes 4

PM2_Supporting PP3 PP4 PM5

Evidence Links 0

Expert Panel

Thrombosis VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Thrombosis VCEP

The NM_000488.4:c.391C>G variant in SERPINC1 is a missense variant predicted to cause substitution of Leucine by Valine at amino acid 131 (p.Leu131Val). This variant is also known as antithrombin Southport (Legacy nomenclature: Leu99Val) in the literature. One proband

from PMID: 7734360 with AT deficiency (type II-HBS) meets criteria for PP4. At least one patient with this variant displayed AT deficiency (type II- HBS) which is highly specific for SERPINC1 (PP4, PMID: 7734360). Another missense variant, c.391C>T (p.Leu131Phe), in the same codon has been classified as pathogenic for antithrombin deficiency by the ClinGen Thrombosis VCEP (PM5). The computational predictor REVEL gives a score of 0.764, which is above the threshold of 0.6, evidence that correlates with impact to SERPINC1 gene function (PP3). This variant is absent from gnomAD v2.1.1-v4. In summary, this variant meets the criteria to be classified as a variant of uncertain significance for antithrombin deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen Thrombosis VCEP. (Specifications version 1.0.0; date of approval: 7/17/2023)

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1-v4
PP3	✔	The computational predictor REVEL gives a score of 0.764, which is above the threshold of 0.6, evidence that correlates with impact to SERPINC1 gene function.
PP4	✔	At least one patient with this variant displayed AT deficiency (type II- HBS) which is highly specific for SERPINC1 (PP4, PMID: 7734360)
PM5	✔	Another missense variant, c.391C>T (p.Leu131Phe), in the same codon has been classified as pathogenic for antithrombin deficiency by the ClinGen Thrombosis VCEP and meets criteria for PM5.

Curation History

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