Variant: NM_000488.4(SERPINC1):c.1247dup (p.Ser417fs)

Version: 1.0

CA2580061383

1687103 (ClinVar)

Gene: SERPINC1 (HGNC:462)
Condition: antithrombin III deficiency (MONDO:0013144)
Inheritance Mode: Autosomal dominant inheritance
UUID: a03cb4d3-50d8-442c-943f-c2eb6bff0f84
Approved on: 2024-12-20
Published on: 2024-12-20

HGVS expressions

NM_000488.4:c.1247dup
NM_000488.4(SERPINC1):c.1247dup (p.Ser417fs)
NC_000001.11:g.173904037dup
CM000663.2:g.173904037dup
NC_000001.10:g.173873175dup
CM000663.1:g.173873175dup
NC_000001.9:g.172139798dup
NG_012462.1:g.18342dup
ENST00000367698.4:c.1247dup
ENST00000367698.3:c.1247dup
ENST00000617423.4:c.632dup
NM_000488.3:c.1247dup
NM_001365052.1:c.1103dup
NM_001365052.2:c.1103dup
NM_001386302.1:c.1370dup
NM_001386303.1:c.1328dup
NM_001386304.1:c.1226dup
NM_001386305.1:c.1190dup
NM_001386306.1:c.1031dup

Uncertain Significance

Met criteria codes 4

PVS1_Moderate | PM2_Supporting | PS3_Supporting | PS4_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.1247dup (p.Ser417LysfsTer?) variant in SERPINC1 is a frameshift variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove <10% of the protein (PVS1_Moderate). This variant has been reported in at least one family meeting an antithrombin activity level of < 0.8 IU/mL and a family history of the disease with reported antithrombin levels (PS4_Supporting; PMID: 38347553). More affected individuals without the details required for scoring were reported in ClinVar (SCV002520629.1). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). 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: PVS1_moderate, PM2_supporting, PS4_supporting.

Met criteria codes

PVS1_Moderate	✔	The c.1247dup (p.Ser417LysfsTer?) variant in SERPINC1 is a frameshift variant that may cause loss of function of the protein, however it is predicted to escape nonsense mediated decay and remove <10% of the protein (PVS1_Moderate).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PS3_Supporting	✔	Secretion defect demonstrated in PMIDs 36214221, 38347553. Variant activity cannot be measured because the protein is not secreted.
PS4_Supporting	✔	This variant has been reported in at least one family meeting an antithrombin activity level of < 0.8 IU/mL and a family history of the disease with reported antithrombin levels (PS4_Supporting; PMID: 38347553). More affected individuals without the details required for scoring were reported in ClinVar (SCV002520629.1).

Curation History

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