Functional, biochemical, molecular and clinical characterization of antithrombin c.1157T>C (p.Ile386Thr), a recurrent Polish variant with a founder effect

Anna Weronska,[1][*] Belen de la Morena-Barrio,[2][*] Sarah Goldman-Mazur,[3] Maria Eugenia de la Morena-Barrio,[2] José Padilla,[2] Antonia Miñano,[2] Pedro Garrido-Rodriguez,[2] Jacek Treliński,[4] Daniel Piotr Potaczek,[5,6,7] Anita Szczepanek,[8,9] Anetta Undas,[10,11] Javier Corral[2][#] and Ewa Wypasek[1,11][#]

[1]Faculty of Medicine and Health Sciences, Andrzej Frycz Modrzewski Krakow University, Kraków, Poland; [2]Servicio de Hematología, Hospital Universitario Morales Meseguer, Centro Regional de Hemodonación, IMIB, CIBERER-ISCIII, Universidad de Murcia, Murcia, Spain; [3]Department of Hematology, Cellular Therapy and Hemostaseology, Leipzig University Hospital, Leipzig, Germany; [4]Department of Hemostasis Disorders, Medical University of Lodz, Łódź, Poland; [5]Translational Inflammation Research Division and Core Facility for Single Cell Multiomics, Medical Faculty, Philipps University of Marburg, Marburg, Germany; [6]Center for Infection and Genomics of the Lung (CIGL), Universities of Gießen and Marburg Lung Center (UGMLC), Gießen, Germany; [7]Bioscientia MVZ Labor Mittelhessen GmbH, Gießen, Germany; [8]Institute of Archaeology and Ethnology, Polish Academy of Sciencies, Kraków, Poland; [9]Department of Anatomy, Jagiellonian University Medical College, Kraków, Poland; [10]Institute of Cardiology, Jagiellonian University Medical College, Kraków, Poland and [11]John Paul II Hospital, Kraków, Poland

[*]*AW and BdlM-B contributed equally as first authors.*
[#]*JC and EW contributed equally as senior authors.*

Correspondence:
E. WYPASEK - ewa.wypasek@wp.pl

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Supplementary Table 1. Pathogenicity scores of the SERPINC1 c.1157T>C; p.Ile386Thr variant obtained from Varsome using the dbNSFP version 4.2.

Pathogenicity Scores *SERPINC1* c.1157T>C; p.Ile386Thr variant

Meta scores

Engine	Calibrated Prediction	Score	Indicative Prediction	Rankscore
BayesDel addAF	Pathogenic	0.2497	Damaging	0.7857
BayesDel noAF	Uncertain	0.1209	Damaging	0.7829
MetaLR	Uncertain	0.8265	Damaging	0.9417
MetaRNN	Pathogenic	0.9481	Damaging	0.9414
MetaSVM	Pathogenic	0.9079	Damaging	0.9578
REVEL	Pathogenic	0.7519		0.9161

Individual Predictions

Engine	Calibrated Prediction	Score	Indicative Prediction	Rankscore
BLOSUM	Uncertain	3		
DANN	Uncertain	0.9973		0.8241
DEOGEN2	Pathogenic	0.8817	Damaging	0.9753
EIGEN	Pathogenic	0.912		0.9233
EIGEN PC	Pathogenic	0.8168		0.9093
EVE	Uncertain	0.5856		
FATHMM	Uncertain	2.07	Damaging	0.8594
FATHMM-MKL	Pathogenic	0.9964	Damaging	0.9824
FATHMM-XF	Pathogenic	0.9594	Damaging	0.9797
LIST-S2	Benign	0.7022	Tolerated	0.3121
LRT	Benign	-0.0375	Neutral	0.2439
M-CAP	Uncertain	0.1329	Damaging	0.8153
Mutation assessor	Pathogenic	3.41	Medium	0.9179
MutationTaster	Benign	0.9998	Disease causing	0.4939
MutPred	Pathogenic	0.808		0.9251
MVP	Uncertain	0.8433		0.8418
PrimateAI	Uncertain	0.5681	Tolerated	0.4841
PROVEAN	Uncertain	2.75	Damaging	0.5841
SIFT	Uncertain	-0.003	Damaging	0.6824
SIFT4G	Uncertain	-0.008	Damaging	0.6789

Supplementary Figure 1. Plasma antithrombin in heterozygous carriers of the p.Ile386Thr variant (+/-). *A) Western blot under native and denaturing (SDS) conditions. Native antithrombin is marked by a black arrow, while a red arrow points the aberrant antithrombin detected under native conditions in carriers of the mutation. B) Crossed immunoelectrophoresis (CIE). Results of three carriers of the mutation, one control and one carrier of a type II heparin-binding site deficiency-causing variant (p.Arg79Cys) are shown. Arrows point the forms with high and low heparin affinity.*
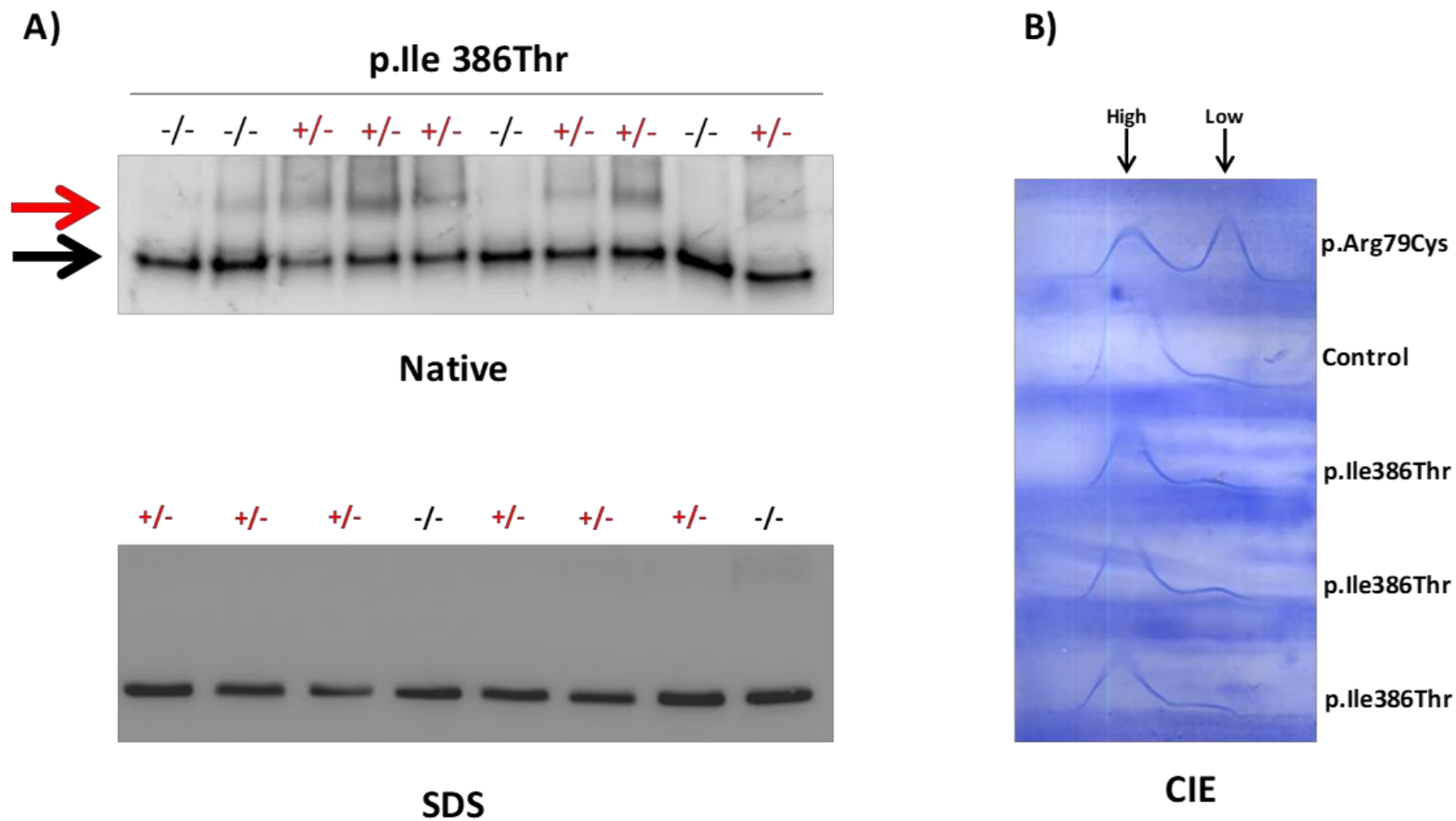
Supplementary Figure 2. Localization of the Ile386 (blue sphere) in the structure of native (green) and latent (red) antithrombin.