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Incidental findings of inherited thrombosis and hemostasis disorders in clinical exomes with unrelated indications

Running title: Incidental findings in hemostasis genes

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Author Contributions

M.D'A., G.D'A., M.G.P., C.C., and R.S.: Conceptualization; software; investigation; validation. **G.C., A.L., I.A., and P.S.:** methodology; data interpretation**. M.M.:** clinical responsibility**. M.D'A., M.M., and R.S.:** visualization; supervision; writing original draft**.**

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Clinical exome sequencing (CES) is widely used for diagnosing rare genetic diseases and frequently identifies pathogenic variants unrelated to the primary testing indication.1,2 ACMG guidelines recommend reporting pathogenic variants in clinically actionable genes as secondary findings. Inherited bleeding, thrombotic, and platelet disorders are rare but clinically important because early molecular diagnosis can improve management and counselling.3 The ISTH defined a Tier1 list of 99 genes with strong evidence of disease association, but the prevalence of pathogenic variants in these genes during routine CES remains unknown.4,5 We evaluated the prevalence and spectrum of pathogenic or likely pathogenic (P/LP) variants involving ISTH Tier1 genes in a large consecutive cohort of individuals referred for CES because of suspected genetic disorders unrelated to bleeding, thrombosis, or platelet disease.

We retrospectively reviewed 1,135 consecutive individuals referred to the Medical Genetics Unit of the University Hospital of Foggia between April 2021 and May 2026. CES had been requested for the diagnostic evaluation of suspected genetic disorders unrelated to inherited disorders of hemostasis. The cohort included pediatric and adult patients with predominantly neurological, cardiovascular, developmental, immunological, and multisystem disorders. The study was approved by the Local Ethical Committee.

Sequencing libraries were generated using Illumina DNA Prep with Enrichment and sequenced on the Illumina NextSeq 550 platform. Sequence alignment and variant calling were performed using the DRAGEN Bio-IT Platform against the GRCh37/hg19 reference genome. Variants in the 99 ISTH Tier1 genes were interpreted according to ACMG/AMP recommendations. Initial classification using Franklin (Genoox) and eVai was independently reviewed by experienced molecular geneticists. Discordant or borderline variants underwent manual review incorporating ClinVar, HGMD, disease-specific databases (ISTH Protein S Mutation Database, the Imperial College London Antithrombin Mutation Database, EAHAD coagulation factor databases), population frequencies, literature, and gene-specific evidence. Only pathogenic or likely pathogenic variants after expert review were retained.

Genes were interpreted according to their established inheritance pattern. For autosomal dominant disorders, only heterozygous variants with a minor allele frequency ≤0.005 were considered. For autosomal recessive disorders, only genotypes compatible with disease (i.e., two pathogenic or likely pathogenic variants in trans or presumed biallelic) were considered, whereas heterozygous carriers were not classified as incidental findings (IFs). For X-linked disorders, only hemizygous pathogenic variants were included. Accordingly, IFs were defined as genotypes predicted to be

biologically associated with a potentially pathogenic phenotype in ISTH Tier1 genes, unrelated to the clinical indication for testing and considered potentially relevant for future clinical management. The objective of the present study was not to establish genotype-phenotype correlations or estimate disease penetrance, but rather to determine the frequency with which potentially reportable variants in inherited disorders of hemostasis are encountered during routine CES.

The overall rate of germline pathogenic/likely pathogenic variants was 9.1%. Overall, 85 unique variants in 39 genes were identified (Suppl. Tab. 1), including 10 small deletions, 7 insertions, 14 nonsense, 6 splice-site, and 47 missense variants, plus one pathogenic non-coding *RNU4ATAC* variant located in the conserved 5' stem-loop region of the U4atac snRNA. Twenty-two variants were novel, although four affected codons harboring previously reported pathogenic variants, whereas 63 had already been described in public databases. Overall, 103 individuals carried pathogenic or likely pathogenic variants in ISTH Tier 1 genes. One individual was a compound heterozygote, and three carried likely pathogenic variants in two different genes (double heterozygotes). Fourteen variants occurred in ≥2 participants, yielding 107 pathogenic/likely pathogenic variant occurrences across 39 genes: 41 pathogenic (38.3%) and 66 likely pathogenic (61.7%).

The distribution by disease category is shown in Figure 1. Most involved bleeding/coagulation genes (n=51; 60.0%), followed by platelet genes (n=27; 31.8%) and thrombosis genes (n=7; 8.2%), reflecting the composition of the ISTH Tier 1 gene list.

Notably, a previously unreported homozygous likely pathogenic *KNG1* stop variant (p.Tyr96*) and two novel *KLKB1* variants in compound heterozygosity were identified. As current evidence links these genes only to prolonged partial thromboplastin time, neither finding was considered clinically actionable. A novel pathogenic *DIAPH1* nonsense variant (p.Arg932*), located within the FH2 domain and predicted to cause loss of function through premature truncation and/or nonsense-mediated decay, was likewise not associated with autosomal dominant macrothrombocytopenia.

Based on the ISTH Tier 1 gene list, 47 incidental findings (IFs) associated with potentially clinically actionable phenotypes unrelated to the testing indication were identified (4.1%; Suppl. Tab. 2). Most involved autosomal dominant disorders (44/47; 93.6%), followed by X-linked (2/47; 4.3%) and autosomal recessive (1/47; 2.1%) conditions. Hemorrhagic disorders accounted for 30 IFs (63.8%), thrombosis for 10 (21.3%), and inherited platelet disorders for 7 (14.9%) (Figure 2).

Overall, 30 individuals (2.6%) carried variants predisposing to bleeding. Sixteen harbored nine different heterozygous pathogenic/likely pathogenic *VWF* variants: six previously reported (one

associated with recessive type 2N von Willebrand disease, two with type 1 disease, two with type 2B disease, and one with low VWF levels) and three novel variants predicted to cause low VWF levels/type 1 (n=2) or type 2N disease (n=1). Heterozygous pathogenic/likely pathogenic variants were also identified in *F11* (10 individuals), *F7* (7), *F10* (1), and *F8* (2 men).

Among thrombosis-related findings, five individuals carried two different heterozygous *SERPINC1* variants (p.V30E and p.R79H), previously associated with mild type I and type IIb antithrombin deficiency, respectively.6 Four individuals carried three different *PROS1* variants (p.R41H, p.Y234C, and p.S501P), associated with protein S type II deficiency or the Heerlen variant, which confers mildly increased venous thrombosis risk.7-9 One additional participant carried a known pathogenic *PROC* variant associated with protein C deficiency. Overall, 10 individuals (0.9%) harbored thrombosis-predisposing variants.

In the platelet category, two individuals carried the same pathogenic *ITGA2B* variant, while four others harbored pathogenic/likely pathogenic variants in *GP1BA*, *ITGB3*, *MYH9*, or *TUBB1*. One individual was homozygous for the likely pathogenic *TBXAS1* p.G473W variant associated with Ghosal syndrome. Overall, inherited platelet disorders-predisposing variants were identified in 7 individuals (0.6%).

Overall, 7.5% of individuals carried a pathogenic or likely pathogenic variant in an ISTH Tier 1 gene. However, not all pathogenic variants were considered IFs. Variants were interpreted according to the established inheritance pattern of each gene, and only genotypes predicted to be associated with a potentially disease-associated phenotype were classified as IFs. Accordingly, heterozygous carriers of recessive disorders were not considered IFs unless their genotype was expected to confer disease risk. Approximately half of individuals carrying pathogenic or likely pathogenic variants fulfilled these criteria and were considered potentially clinically actionable IFs. This prevalence reflects pathogenic genotypes rather than disease prevalence, as incomplete penetrance means not all carriers of disease-associated genotype develop clinical manifestations. Pathogenic variants in the natural anticoagulant genes *SERPINC1*, *PROS1*, and *PROC* were identified in ten individuals, corresponding to prevalences of 0.4%, 0.4%, and 0.1%, respectively, consistent with population estimates.10 Three *SERPINC1* variants were associated with type IIb antithrombin deficiency, a qualitative defect generally considered less thrombogenic than type I deficiency, whereas two corresponded to variants previously associated with transient antithrombin. Two of the four *PROS1* variants corresponded to the Heerlen variant, a mild form of protein S deficiency.

Variants predisposing to bleeding were identified in 30 individuals (2.6%). Among these, 16 carried pathogenic or likely pathogenic *VWF* variants, including variants associated with type 1, type 2B, type 2N von Willebrand disease, or low VWF levels, corresponding to an overall prevalence of approximately 0.9%, in agreement with population estimates.11 Pathogenic or likely pathogenic variants were identified in *F11*, *F7*, *F10*, and *F8*. Although FVII and FXI deficiencies are typically recessive disorders, some heterozygous carriers, particularly of F11 variants, may experience clinically relevant bleeding after trauma or surgery.12

Variants associated with inherited platelet disorders were identified in seven individuals (0.6%), a prevalence comparable to previous population-based genomic estimates.13 Pathogenic variants involved *GP1BA, ITGA2B, ITGB3, MYH9, TUBB1,* and *TBXAS1*. Their recognition may have important clinical implications because some disorders are syndromic.14 For example, MYH9-related disease is associated with nephropathy, cataracts, and sensorineural hearing loss, supporting long-term clinical surveillance.

This study provides the first systematic estimate of clinically actionable IFs related to inherited hemostatic disorders in a large CES cohort. As genomic testing becomes integrated into clinical practice, patients should be informed about the possibility and implications of identifying such findings.

The return of IFs requires careful consideration because penetrance, expressivity, age at onset, disease severity, and clinical actionability vary substantially across disorders. Nevertheless, identifying inherited bleeding or thrombotic predisposition may inform perioperative management, pregnancy, invasive procedures, individualized thrombotic risk assessment, family counselling, and cascade testing.15

Several limitations should be acknowledged. Referral indications were based on the primary reported phenotype, and mild or unrecognized bleeding or thrombotic manifestations may have been overlooked, particularly in children. Exome sequencing does not reliably detect copy number variants, deep intronic variants, structural rearrangements, or large insertions/deletions, likely underestimating the true burden of pathogenic variants. Finally, variant classification will continue to evolve as additional functional and clinical evidence becomes available.

Overall, our findings provide the first empirical estimate of the frequency of pathogenic variants across the complete ISTH Tier 1 gene set in routine clinical exome sequencing. They establish an evidence-based framework for interpreting and reporting incidental findings in inherited disorders of hemostasis and support future studies evaluating their penetrance, clinical validity, and utility.

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Legend to Figure 1

Gene variants identified in the ISTH Tier 1 gene list according to disease domain and variant characteristics. (A) Distribution of gene variants by disease domain. (B) Distribution within each disease domain according to variant type (left), novelty (center), and level of pathogenicity (right). B/C: bleeding/coagulation; LP: likely pathogenic; P: pathogenic; PLT: platelets; THR: thrombosis.

Legend to Figure 2

Clinically actionable incidental findings (IFs) identified across disease domains. Distribution of clinically actionable IFs by disease domain. Insets show the genes identified in each disease domain and the number of individuals carrying clinically actionable IFs. B/C: bleeding/coagulation; PLT: platelets; THR: thrombosis.

Fig. 1

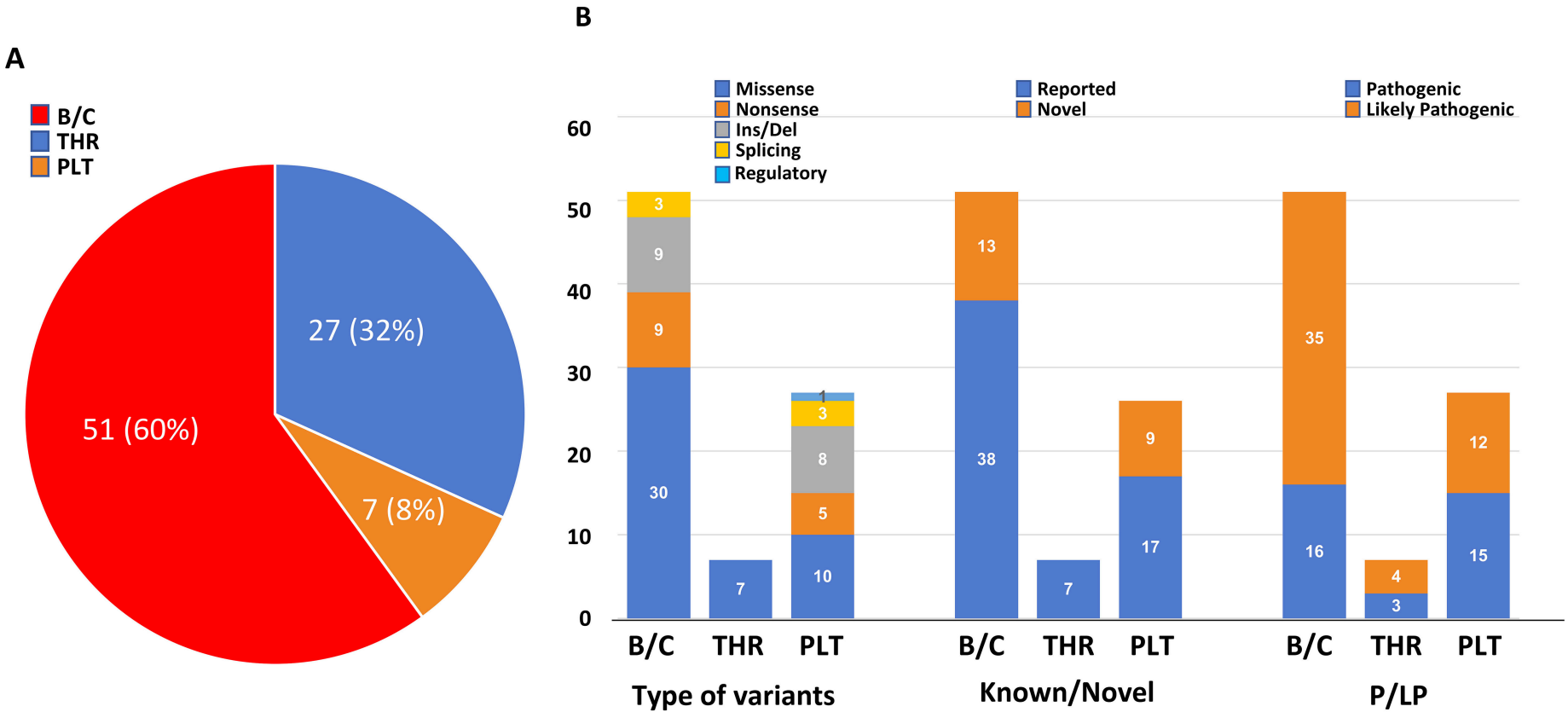
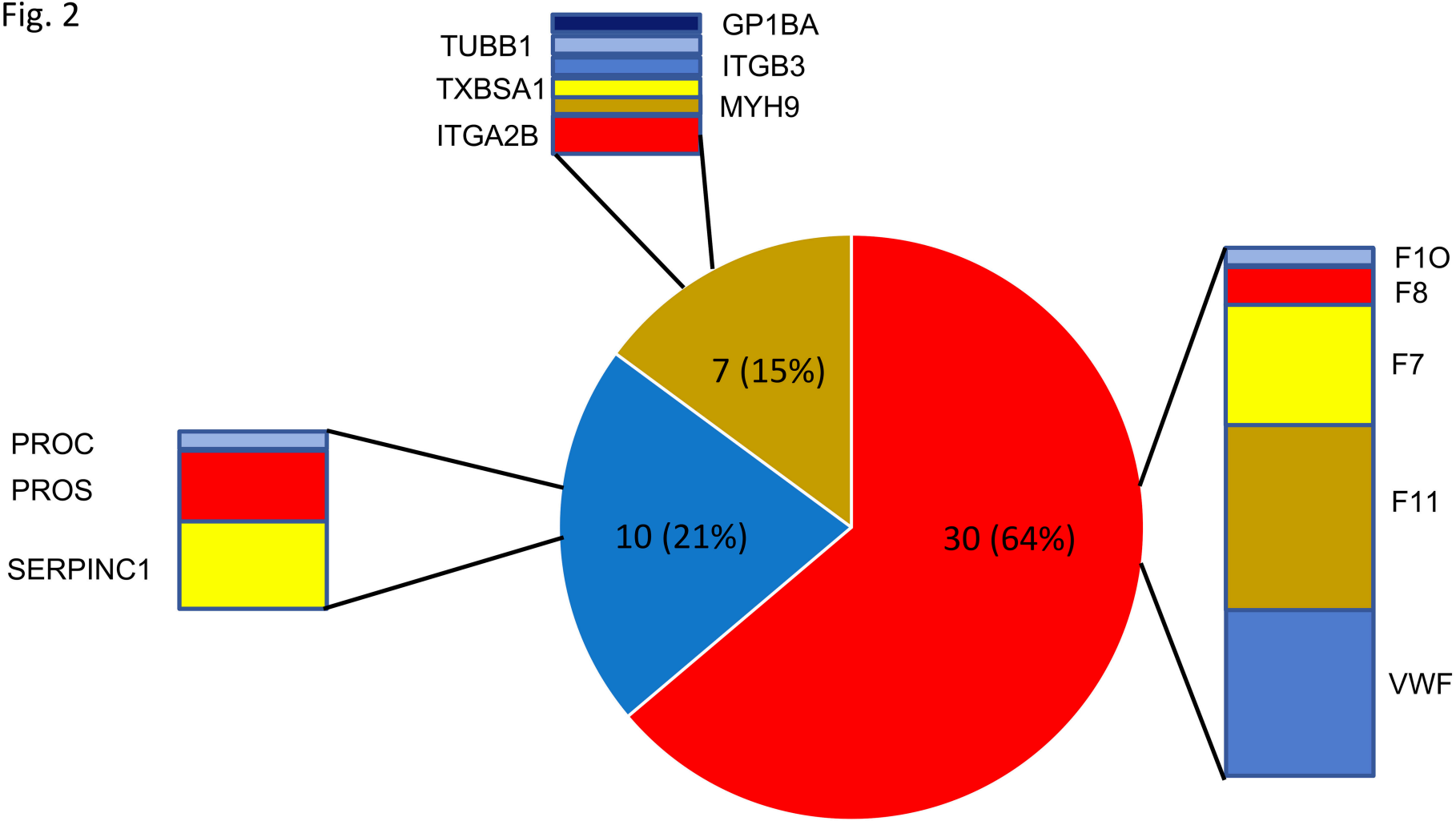

A
B/C
THR
PLT
27 (32%)
51 (60%)
7 (8%)
B
Missense
Nonsense
Ins/Del
Splicing
Regulatory
Reported
Novel
Pathogenic
Likely Pathogenic
60
50
40
30
20
10
0
3
9
9
30
7
1
3
8
5
10
13
38
7
9
17
35
16
4
3
12
15
B/C
THR
PLT
B/C
THR
PLT
B/C
THR
PLT
Type of variants
Known/Novel
P/LP

Fig. 2


TUBB1
GP1BA
ITGB3
TXBSA1
MYH9
ITGA2B
7 (15%)
PROC
PROS
SERPINC1
10 (21%)
30 (64%)
F10
F8
F7
F11
VWF

Suppl. Table 1

Unique gene variants identified in ISTH TIER1 gene list

TIER1	Gene	Protein position	cDNA position	Type	Reported/Novel	Pathogenicity	Note
Bleeding/Coagulation	F10	p.Gly421Ser	c.1261G>A	Missense	Novel [a]	Likely Pathogenic	
Bleeding/Coagulation	F11	p.Gln6*	c.16C>T	Nonsense	Reported	Pathogenic	
Bleeding/Coagulation	F11	p.Gly135*	c.403G>T	Nonsense	Reported	Pathogenic	
Bleeding/Coagulation	F11		c.486-2A>G	Splicing	Reported	Pathogenic	
Bleeding/Coagulation	F11	p.Arg268Cys	c.802C>T	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F11	p.Gly303Glufs*46	c.908del	Ins/Del	Reported	Pathogenic	
Bleeding/Coagulation	F11	p.Glu315Lys	c.943G>A	Missense	Reported	Likely Pathogenic	2 individuals
Bleeding/Coagulation	F11	p.Arg326His	c.977G>A	Missense	Reported	Pathogenic	
Bleeding/Coagulation	F11	p.Glu565Lys	c.1693G>A	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F11	p.Asp574Gly	c.1721A>G	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F12	p.Cys413*	c.1239C>A	Nonsense	Novel	Likely Pathogenic	
Bleeding/Coagulation	F12	p.Gly506fs	c.1517delG	Ins/Del	Reported	Pathogenic	
Bleeding/Coagulation	F5		c.158+1G>A	Splicing	Reported	Pathogenic	3 individuals
Bleeding/Coagulation	F5	p.Arg334Thr	c.1001G>C	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F5	p.Lys2176Asn	c.6528G>C	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F5	p.Arg2202His	c.6605G>A	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F7	p.Gly135Ser	c.403G>A	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F7	p.His143fs	c.428dupA	Ins/Del	Novel	Likely Pathogenic	
Bleeding/Coagulation	F7	p.Pro172Leu	c.515C>T	Missense	Novel [a]	Likely Pathogenic	
Bleeding/Coagulation	F7	p.Arg342Gln	c.1025G>A	Missense	Reported	Pathogenic	
Bleeding/Coagulation	F7	p.Arg353Trp	c.1057C>T	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F7	p.Gly369Ser	c.1105G>A	Missense	Reported	Pathogenic	2 individuals
Bleeding/Coagulation	F8	p.His118Arg	c.353A>G	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F8	p.Glu132Asp	c.396A>C	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F8	p.Arg1768Ser	c.5302C>A	Missense	Novel [a]	Likely Pathogenic	
Bleeding/Coagulation	F8	p.Gly2102Ser	c.6304G>A	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F8	p.Ser2125Thr	c.6374G>C	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	F9	p.Ala37Thr	c.109G>A	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	FGA	p.Arg178*	c.535C>T	Nonsense	Reported	Likely Pathogenic	
Bleeding/Coagulation	FGA	p.Trp373*	c.1118G>A	Nonsense	Reported	Pathogenic	
Bleeding/Coagulation	FGA	p.Gly552Fs*16	c.1653delT	Ins/Del	Reported	Pathogenic	
Bleeding/Coagulation	FGG	p.Ala108Gly	c.323C>G	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	FGG	p.Ser142*	c.425C>A	Nonsense	Novel	Likely Pathogenic	
Bleeding/Coagulation	FGG	p.Tyr237His	c.709T>C	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	GGCX	p.Pro313Argfs*33	c.938_939del	Ins/Del	Reported	Pathogenic	
Bleeding/Coagulation	KLKB1	p.Val36fs	c.107delT	Ins/Del	Novel	Likely Pathogenic	Compound Heterozygote with p.Ser38Profs*12
Bleeding/Coagulation	KLKB1	p.Ser38Profs*12	c.111-113delTTC	Ins/Del	Novel	Likely Pathogenic	Compound Heterozygote with p.Val36fs

Bleeding/Coagulation	KLKB1	p.Lys248*	c.742A>T	Splicing	Novel	Likely Pathogenic	
Bleeding/Coagulation	KLKB1	p.Trp402*	c.1205G>A	Nonsense	Reported	Pathogenic	
Bleeding/Coagulation	KNG1	p.Tyr96*	c.288C>G	Nonsense	Novel	Likely Pathogenic	Homozygote
Bleeding/Coagulation	LMAN1	p.Met1?	c.2T>C	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	LMAN1	p.Asn404fs	c.1208dupT	Ins/Del	Reported	Likely Pathogenic	
Bleeding/Coagulation	VWF	p.306Phefs*152	c.916_917ins	Ins/Del	Novel	Likely Pathogenic	
Bleeding/Coagulation	VWF	p.Ala542Gly	c.1625C>G	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	VWF	p.Arg854Gln	c.2561G>A	Missense	Reported	Pathogenic	4 individuals
Bleeding/Coagulation	VWF	p.Glu1078Gln	c.3232G>C	Missense	Novel	Likely Pathogenic	
Bleeding/Coagulation	VWF	p.Tyr1146*	c.3438T>G	Nonsense	Novel	Likely Pathogenic	
Bleeding/Coagulation	VWF	p.Pro1266Gln	c.3797C>A	Missense	Reported	Likely Pathogenic	
Bleeding/Coagulation	VWF	p.Arg1341Trp	c.4021C>T	Missense	Reported	Pathogenic	
Bleeding/Coagulation	VWF	p.Tyr1584Cys	c.4751A>G	Missense	Reported	Pathogenic	2 individuals
Bleeding/Coagulation	VWF	p.Arg2663Pro	c.7988G>C	Missense	Reported	Likely Pathogenic	4 individuals
Thrombosis	PLG	p.Lys38Glu	c.112A>G	Missense	Reported	Likely Pathogenic	4 individuals
Thrombosis	PROC	p.Arg220Trp	c.658C>T	Missense	Reported	Pathogenic	
Thrombosis	PROS1	p.Arg41His	c.122G>A	Missense	Reported	Likely Pathogenic	
Thrombosis	PROS1	p.Tyr234Cys	c.701A>G	Missense	Reported	Likely Pathogenic	
Thrombosis	PROS1	p.Ser501Pro	c.1501T>C	Missense	Reported	Pathogenic	2 individuals
Thrombosis	SERPINC1	p.Val30Glu	c.89T>A	Missense	Reported	Pathogenic	2 individuals
Thrombosis	SERPINC1	p.Arg79Hys	c.236G>A	Missense	Reported	Pathogenic	3 individuals
Platelet	ABCG8		c.965-1G>C	Splicing	Reported	Pathogenic	
Platelet	ABCG8	p.Trp361*	c.1083G>A	Nonsense	Reported	Pathogenic	
Platelet	ABCG8	p.Arg405Cys	c.1213C>T	Missense	Novel [a]	Likely Pathogenic	
Platelet	ADAMTS13	p.Asp187His	c.559G>C	Missense	Reported	Likely Pathogenic	
Platelet	ADAMTS13	p.Asp1051Thrfs*70	c.3151del	Ins/Del	Novel	Likely Pathogenic	
Platelet	ANO6		c.1386+1G>A	Splicing	Reported	Likely Pathogenic	2 individuals
Platelet	BLOC1S6	p.Gln78*	c.232C>T	Nonsense	Reported	Pathogenic	
Platelet	DIAPH1	p.Arg932*	c.2794C>T	Nonsense	Novel	Pathogenic	
Platelet	DTNBP1	p.Glu340fs	c.1019-1020delAG	Ins/Del	Reported	Likely Pathogenic	
Platelet	GNE	p.Val696Leu	c.2086G>T	Missense	Reported	Likely Pathogenic	
Platelet	GP1BA	p.Ala172Val	c.515C>T	Missense	Reported	Likely Pathogenic	
Platelet	HPS1	p.Pro373fs	c.1109-1116dupACTGCCTG	Ins/Del	Novel	Pathogenic	
Platelet	HPS5	p.Lys654*	c.1960A>T	Nonsense	Reported	Pathogenic	
Platelet	HPS6	p.Phe159Cysfs*20	c.466_475dup	Ins/Del	Reported	Pathogenic	
Platelet	HPS6	p.Tyr711fs	c.3232dupA	Ins/Del	Reported	Likely Pathogenic	
Platelet	ITGA2B	p.Cys705Arg	c.2113T>C	Missense	Reported	Pathogenic	2 individuals
Platelet	ITGB3	p.Asn329Asp	c.985A>G	Missense	Reported	Likely Pathogenic	
Platelet	LYST	p.Ser1351*	c.4052C>G	Nonsense	Reported	Likely Pathogenic	2 individuals
Platelet	LYST	pTyr2708fs	c.8122dupT	Ins/Del	Reported	Pathogenic	
Platelet	MPL	p.Arg257Cys	c.769C>T	Missense	Reported	Pathogenic	
Platelet	MYH9	p.Pro836Leu	c.2507C>T	Missense	Novel	Likely Pathogenic	
Platelet	RASGRP2		c.372-2A>C	Splicing	Novel	Likely Pathogenic	

Platelet	RNU4ATAC		c.196-609C>T	Regulatory	Reported	Likely Pathogenic	2 individuals
Platelet	STIM1	p.Asn443Profs*31	c.1327_1331del	Ins/Del	Novel	Likely Pathogenic	
Platelet	TBXAS1	p.Arg412Gln	c.1235G>A	Missense	Reported	Pathogenic	Homozygote
Platelet	TBXAS1	p.Gly473Trp	c.1417G>T	Missense	Novel	Likely Pathogenic	
Platelet	TUBB1	p.Gly235Alafs*2	c.704del	Ins/Del	Novel	Pathogenic	

[a]: a different variant in the same codon has been reported.

Suppl. Table 2

Clinically actionable IFs

TIER1	Inheritance	Gene	Protein position	cDNA position	OMIM phenotype(s)
Bleeding/Coagulation	AD	F10	p.Gly421Ser	c.1261G>A	Factor X deficiency (#227600)
Bleeding/Coagulation	AD	F11	p.Gln6*	c.16C>T	Factor XI deficiency (#612416)
Bleeding/Coagulation	AD	F11	p.Glu135*	c.403G>T	"
Bleeding/Coagulation	AD	F11		c.486-2A>G	"
Bleeding/Coagulation	AD	F11	p.Arg268Cys	c.802C>T	"
Bleeding/Coagulation	AD	F11	p.Gly303Glufs*46	c.908del	"
Bleeding/Coagulation	AD	F11	p.Glu315Lys	c.943G>A	"
Bleeding/Coagulation	AD	F11	p.Glu315Lys	c.943G>A	"
Bleeding/Coagulation	AD	F11	p.Arg326His	c.977G>A	"
Bleeding/Coagulation	AD	F11	p.Glu565Lys	c.1693G>A	"
Bleeding/Coagulation	AD	F11	p.Asp574Gly	c.1721A>G	"
Bleeding/Coagulation	AD	F7	p.Gly135Ser	c.403G>A	Factor VII deficiency (#227500)
Bleeding/Coagulation	AD	F7	p.His143fs	c.428dupA	"
Bleeding/Coagulation	AD	F7	p.Pro172Leu	c.515C>T	"
Bleeding/Coagulation	AD	F7	p.Arg342Gln	c.1025G>A	"
Bleeding/Coagulation	AD	F7	p.Arg353Trp	c.1057C>T	"
Bleeding/Coagulation	AD	F7	p.Gly369Ser	c.1105G>A	"
Bleeding/Coagulation	AD	F7	p.Gly369Ser	c.1105G>A	"
Bleeding/Coagulation	XLR	F8	p.His118Arg	c.353A>G	Hemophilia A (#306700)
Bleeding/Coagulation	XLR	F8	p.Arg1768Ser	c.5302C>A	"
Bleeding/Coagulation	AD	VWF	p.Pro1266Gln	c.3797C>A	von Willebrand disease, type 2B (#613554)
Bleeding/Coagulation	AD	VWF	p.Arg1341Trp	c.4021C>T	"
Bleeding/Coagulation	AD	VWF	p.306Phefs*152	c.916_917ins	von Willebrand disease, type 1 (#193400)
Bleeding/Coagulation	AD	VWF	p.Tyr1146*	c.3438T>G	"
Bleeding/Coagulation	AD	VWF	p.Tyr1584Cys	c.4751A>G	"
Bleeding/Coagulation	AD	VWF	p.Tyr1584Cys	c.4751A>G	"
Bleeding/Coagulation	AD	VWF	p.Arg2663Pro	c.7988G>C	"
Bleeding/Coagulation	AD	VWF	p.Arg2663Pro	c.7988G>C	"
Bleeding/Coagulation	AD	VWF	p.Arg2663Pro	c.7988G>C	"
Bleeding/Coagulation	AD	VWF	p.Arg2663Pro	c.7988G>C	"
Thrombosis	AD	PROC	p.Arg220Trp	c.658C>T	Thrombophilia due to protein C deficiency (#176860)
Thrombosis	AD	PROS1	p.Arg41His	c.122G>A	Thrombophilia due to protein S deficiency (#612336)
Thrombosis	AD	PROS1	p.Tyr234Cys	c.701A>G	"
Thrombosis	AD	PROS1	p.Ser501Pro	c.1501T>C	"
Thrombosis	AD	PROS1	p.Ser501Pro	c.1501T>C	"
Thrombosis	AD	SERPINC1	p.Val30Glu	c.89T>A	Thrombophilia due to antithrombin deficiency (#613118)
Thrombosis	AD	SERPINC1	p.Val30Glu	c.89T>A	"
Thrombosis	AD	SERPINC1	p.Arg79Hys	c.236G>A	"
Thrombosis	AD	SERPINC1	p.Arg79Hys	c.236G>A	"

Thrombosis	AD	SERPINC1	p.Arg79Hys	c.236G>A	"
Platelet	AD	DIAPH1	p.Arg932*	c.2794C>T	Deafness, with or without thrombocytopenia (#124900)
Platelet	AD	GP1BA	p.Ala172Val	c.515C>T	Bernard-Soulier syndrome, type A2 (#153670)
Platelet	AD	ITGA2B	p.Cys705Arg	c.2113T>C	Bleeding disorder, platelet-type, 16 (#187800)
Platelet	AD	ITGA2B	p.Cys705Arg	c.2113T>C	"
Platelet	AD	ITGB3	p.Asn329Asp	c.985A>G	Bleeding disorder, platelet-type, 24 (#619271)
Platelet	AD	MYH9	p.Pro836Leu	c.2507C>T	Deafness, autosomal dominant 17 (#603622) Macrothrombocytopenia and granulocyte inclusions with or without nephritis or sensorineural hearing loss (#155100)
Platelet	AR	TBXAS1	p.Arg412Gln	c.1235G>A	Ghosal hematodiaphyseal syndrome (#231095)
Platelet	AD	TUBB1	p.Gly235Alafs*2	c.704del	Macrothrombocytopenia, TUBB1-related (#613112)

AD: autosomal dominant; AR: autosomal recessive; XLR: X-linked recessive.