



## Data Article

# Dataset of GWAS-identified variants underlying venous thromboembolism susceptibility and linkage to cancer aggressiveness



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## ABSTRACT

Venous thromboembolism (VTE) is a common cardiovascular disease, for which several single nucleotide polymorphisms (SNPs) underlying susceptibility were identified. Apart from candidate gene approach, genome-wide association studies (GWAS) have contributed to the identification of novel VTE-associated SNPs, including some with no clear role in the haemostatic system. These genetic variants constitute potential cancer-related biomarkers, particularly predictive and prognostic biomarkers, as a two-way association between VTE and cancer is well established. The present dataset comprises the data obtained from GWAS performed to identify genetic variants associated with VTE risk. Furthermore, this dataset also comprises data regarding previously reported candidate gene and validation reports performed in adults of European ancestry that also analysed the VTE GWAS-identified variants. Lastly, to evaluate the impact of these

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genetic variants in carcinogenesis, a broad search was made, which has let us to establish putative links between several VTE-associated genes and cancer hallmarks in a review article entitled “Venous thromboembolism GWAS reported genetic makeup and the hallmarks of cancer: linkage to ovarian tumour behaviour”.

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## Specifications table

<b>Subject</b>	Biochemistry, Genetics and Molecular Biology
<b>Specific subject area</b>	Genetics; Molecular biology; Molecular medicine; Cancer Research
<b>Type of data</b>	Tables
<b>How data were acquired</b>	<i>NHGRI-EBI GWAS catalogue</i> NCBI database <i>GeneCards</i> database <i>Ensembl</i> database
<b>Data format</b>	Raw Filtered
<b>Parameters for data collection</b>	The collection of VTE GWAS data (VTE variants' characterization, study population description and overall risk conferred by each variant in VTE GWAS) was made by screening the <i>NHGRI-EBI GWAS catalogue</i> . Regarding candidate gene and validation reports, data collection was performed by searching the NCBI database. As for the impact of VTE-associated genes in carcinogenesis, putative links with cancer hallmarks were established by searching the <i>NCBI</i> , <i>GeneCards</i> and <i>Ensembl</i> databases.
<b>Description of data collection</b>	For VTE GWAS data collection, no restriction was made regarding the origin and age of the population. We gathered only the genetic variants statistically associated with VTE susceptibility in the GWAS discovery phase ( $P < 0.05$ ). For candidate gene and validation reports, we only gathered the reports that analysed incident VTE among adults of European ancestry with no strong risk factors and performed before and after GWAS findings, respectively. In terms of the links between VTE-associated genes and cancer hallmarks, we gathered the information from reports that addressed this topic.
<b>Data source location</b>	<i>NHGRI-EBI GWAS catalogue</i> NCBI database <i>GeneCards</i> database <i>Ensembl</i> database
<b>Data accessibility</b>	Data is provided in the article
<b>Related review article</b>	Tavares V., Pinto R., Assis J., Pereira D., Medeiros R. (2019). Venous thromboembolism GWAS reported genetic makeup and the hallmarks of cancer: Linkage to ovarian tumour behaviour. <i>Biochimica et Biophysica Acta (BBA)-Reviews on Cancer</i> , <a href="https://doi.org/10.1016/j.bbcan.2019.188331">https://doi.org/10.1016/j.bbcan.2019.188331</a>

## Value of the data

- Given the existence of a tight and bilateral relationship between VTE and cancer, VTE-associated single nucleotide polymorphisms (SNPs) constitute potential cancer-related predictive and prognostic biomarkers that are currently in need.
- Considering the growing incidence of VTE among cancer patients, with its underlying negative impact on patient prognosis, this dataset can benefit researchers and clinicians that work in the oncology field, who are interested in the genetic susceptibility for VTE, and how VTE-associated SNPs can be linked to cancer progression.
- This database can be used for the development of several experiments as the majority of VTE genetic variants with a putative role in cancer progression have not been studied among

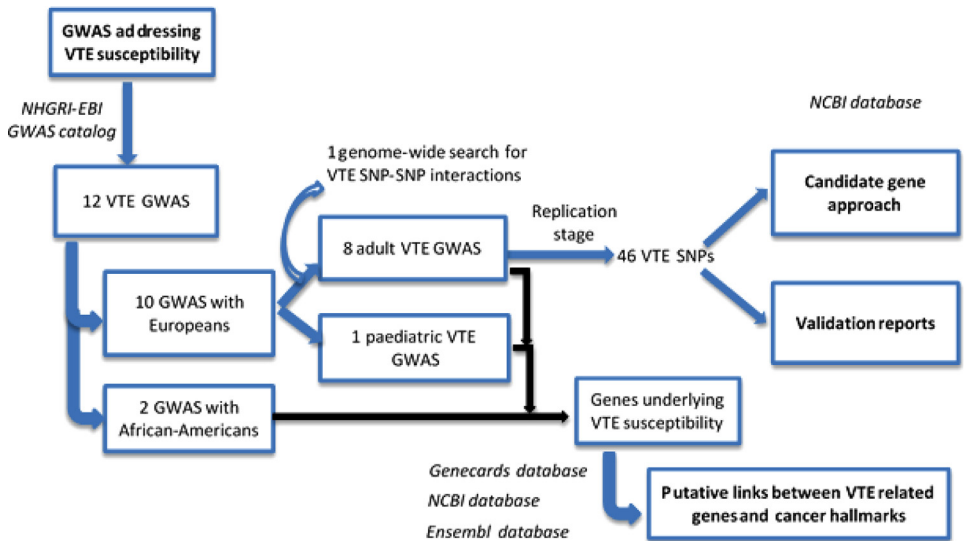


Fig. 1. Schematic diagram of data collection.

cancer patients, particularly ovarian cancer patients who are frequently diagnosed with VTE and/or present a blood hypercoagulability state in the blood coagulation tests.

## 1. Data

Table 1 comprises the data obtained from GWAS performed to identify genetic variants that are associated with VTE susceptibility. Table 2 includes the data of a genome-wide search of pairwise SNP interactions associated with VTE risk. Table 3 encompasses data regarding previously reported candidate gene and validation reports of GWAS-identified SNPs that are associated with VTE risk. Table 4 includes putative links between VTE-associated genes and several cancer hallmarks.

## 2. Experimental design, materials and methods

### (1) GWAS addressing VTE susceptibility:

All SNPs statistically associated ( $P < 0.05$ ) with susceptibility to VTE (deep vein thrombosis, pulmonary embolism or both) were gathered by screening *NHGRI-EBI GWAS catalogue* and respective articles. No restriction was made regarding the origin and age of the population. In total, 12 VTE GWAS were collected, including ten in populations of European ancestry (one searching for pairwise SNP interactions associated with disease risk and one performed to determine the genetic factors of paediatric VTE) and two in Afro-American populations (Fig. 1).

### (2) Other reports reporting VTE-associated SNPs:

After gathering all GWAS-identified SNPs associated with VTE risk, data regarding validation and candidate gene reports that stated the same associations were also collected, using the NCBI database, in order to confirm the GWAS findings (Fig. 1). Only SNPs reported by VTE GWAS among adults of European ancestry were considered. Hence, only validation and candidate gene reports with adults of European ancestry with incident VTE and with no strong risk factors were

**Table 1**  
SNPs identified by VTE susceptibility GWAS.

Report accession on NHGRI-EBI GWAS catalogue	Associated SNPs	Population	No. cases/controls (combined)	MAF	Locus	Gene/Variant	Overall risk		
							Allelic OR (95% CI)	P-value	
<b>GCST000354</b>	rs2420371	European ancestry	419/1228 (Discovery phase)	0.15 <sup>a</sup>	1q24.2	<i>F5</i> /intr	2.27 (1.62; 3.18) <sup>c</sup>	8.08 × 10 <sup>-10</sup>	
	rs1208134			0.12 <sup>a</sup>	1q24.2	<i>CCDC181</i> / intr	2.29 (1.58; 3.32) <sup>c</sup>	3.47 × 10 <sup>-7</sup>	
	rs657152			0.54 <sup>a</sup>	chr9: 133,263,862 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.89 (1.51; 2.36) <sup>c</sup>	2.22 × 10 <sup>-13</sup>	
	rs505922			0.52 <sup>a</sup>	chr9: 133,273,813 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.91 (1.53; 2.39) <sup>c</sup>	1.48 × 10 <sup>-14</sup>	
	rs630014			0.37 <sup>a</sup>	9q34.2	<i>ABO</i> /intr	0.64 (0.51; 0.80) <sup>c</sup>	2.00 × 10 <sup>-7</sup>	
	rs2420371 <sup>Y</sup>	European ancestry	1150/801 (Replication phase I)	0.21 <sup>a</sup>	1q24.2	<i>F5</i> /intr	1.39 (1.17; 1.64) <sup>c</sup>	3.00 × 10 <sup>-5</sup>	
	rs1208134 <sup>Y</sup>			0.19 <sup>a</sup>	1q24.2	<i>CCDC181</i> / intr	1.57 (1.31; 1.88) <sup>c</sup>	2.89 × 10 <sup>-7</sup>	
	rs6025			0.01	1q24.2	<i>F5</i> /mis	2.01 (1.63; 2.48) <sup>c</sup>	9.91 × 10 <sup>-11</sup>	
	rs657152 <sup>§</sup>			0.51 <sup>a</sup>	chr9: 133,263,862 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.75 (1.51; 2.03) <sup>c</sup>	1.20 × 10 <sup>-13</sup>	
	rs505922 <sup>§</sup>			0.49 <sup>a</sup>	chr9: 133,273,813 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.81 (1.56; 2.11) <sup>c</sup>	3.72 × 10 <sup>-15</sup>	
	rs630014 <sup>§</sup>			0.38 <sup>a</sup>	9q34.2	<i>ABO</i> /intr	0.66 (0.57; 0.76) <sup>c</sup>	1.21 × 10 <sup>-8</sup>	
	rs8176719			0.34	9q34.2	<i>ABO</i> /fra	0.33 (0.26; 0.42) <sup>c</sup>	1.70 × 10 <sup>-18</sup>	
	rs8176750			0.05	9q34.2	<i>ABO</i> /fra	0.53 (0.38; 0.74) <sup>c</sup>	2.46 × 10 <sup>-4</sup>	
	rs2420371 <sup>Y</sup>	European ancestry	607/607 (Replication phase II)	0.10 <sup>a</sup>	1q24.2	<i>F5</i> /intr	1.44 (1.07; 1.93) <sup>c</sup>	1.80 × 10 <sup>-3</sup>	
	rs6025			0.01	1q24.2	<i>F5</i> /mis	2.46 (1.55; 3.93) <sup>c</sup>	1.50 × 10 <sup>-4</sup>	
	rs657152 <sup>§</sup>			0.47 <sup>a</sup>	chr9: 133,263,862 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.58 (1.34; 1.87) <sup>c</sup>	5.19 × 10 <sup>-8</sup>	
	rs505922 <sup>§</sup>			0.46 <sup>a</sup>	chr9: 133,273,813 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.65 (1.39; 1.95) <sup>c</sup>	7.25 × 10 <sup>-9</sup>	
	rs630014 <sup>§</sup>			0.38 <sup>a</sup>	9q34.2	<i>ABO</i> /intr	0.63 (0.53; 0.74) <sup>c</sup>	5.01 × 10 <sup>-8</sup>	
	rs8176719	0.34	9q34.2	<i>ABO</i> /fra	0.53 (0.41; 0.69) <sup>c</sup>	2.21 × 10 <sup>-6</sup>			
	<b>GCST000621</b>	rs3813948	European ancestry	419/1228 ( <i>in silico</i> GWAS)	0.09 <sup>a</sup>	1q32.1	<i>C4BPB</i> /nc	-	0.011
		rs3813948		1706/1379 (Replication phase)	0.09 <sup>a</sup>	1q32.1	<i>C4BPB</i> /nc	1.24 (1.00; 1.53)	0.046
<b>GCST001253</b>	rs16861990	European ancestry	1542/1110 (Discovery phase)	0.13 <sup>a</sup>	1q24.2	<i>NME7</i> /intr	2.49 <sup>-</sup>	2.75 × 10 <sup>-15</sup>	
	rs1208134			0.13 <sup>a</sup>	1q24.2	<i>CCDC181</i> / intr	2.53 <sup>-</sup>	3.29 × 10 <sup>-16</sup>	
	rs2420371			0.15 <sup>a</sup>	1q24.2	<i>F5</i> /intr	2.62 <sup>-</sup>	8.44 × 10 <sup>-19</sup>	
	rs2066865			0.28 <sup>a</sup>	4q32.1	<i>FGG</i> /inter	1.55 <sup>-</sup>	1.17 × 10 <sup>-10</sup>	
	rs6825454			0.30 <sup>a</sup>	4q31.3	<i>FGA</i> /inter	1.50 <sup>-</sup>	1.32 × 10 <sup>-9</sup>	
	rs10029715			0.12 <sup>a</sup>	4q35.2	<i>F11-AS1</i> /intr	-	3.20 × 10 <sup>-9</sup>	
	rs2073828			0.32 <sup>a</sup>	chr9: 133,261,737 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	-	3.57 × 10 <sup>-9</sup>	
	rs657152	0.49 <sup>a</sup>	chr9: 133,263,862 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.70 <sup>c</sup>	1.10 × 10 <sup>-18</sup>			
	rs500498	0.33 <sup>a</sup>	chr9: 133,273,232 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	-	1.03 × 10 <sup>-12</sup>			
	rs505922	0.49 <sup>a</sup>	chr9: 133,273,813 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.85 <sup>c</sup>	1.06 × 10 <sup>-23</sup>			
	rs630014	0.38 <sup>a</sup>	9q34.2	<i>ABO</i> /intr	0.63 <sup>c</sup>	4.40 × 10 <sup>-14</sup>			
	rs495828	0.36 <sup>a</sup>	9q34.2	<i>ABO</i> /rr	1.64 <sup>c</sup>	1.78 × 10 <sup>-14</sup>			
	rs1018827	European ancestry	1961/2338 (meta-analysis) <sup>d</sup>	0.07	1q24.2	<i>F5</i> /intr	2.52	2.41 × 10 <sup>-26</sup>	
	rs7659024			0.30	4q31.3	<i>FGG</i> /inter	1.53	1.93 × 10 <sup>-13</sup>	
	rs505922			0.35	chr9: 133,273,813 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.92	1.39 × 10 <sup>-34</sup>	
	rs3756008			0.32	4q35.2	<i>F11</i> /inter	1.40	6.46 × 10 <sup>-11</sup>	

(continued on next page)

**Table 1** (continued)

Report accession on NHGRI-EBI GWAS catalogue	Associated SNPs	Population	No. cases/controls (combined)	MAF	Locus	Gene/Variant	Overall risk		
							Allelic OR (95% CI)	P-value	
<b>GCST001557</b>	rs6025	98.64% European ancestry (USA)	1503/1459 (Discovery phase)	0.01	1q24.2	F5/mis	3.75 (2.76; 4.60)	$1.68 \times 10^{-22}$	
	rs8176719			0.34	9q34.2	ABO/fra	1.47 (1.32; 1.64)	$5.68 \times 10^{-12}$	
	rs2519093			0.14	chr9: 133,266,456 <sup>b</sup>	ABO/intr <sup>b</sup>	1.69 (1.48; 1.91)	$8.08 \times 10^{-16}$	
	rs495828			0.16	9q34.2	ABO/tr	1.65 (1.46; 1.86)	$2.96 \times 10^{-16}$	
	rs7538157 <sup>W</sup>			<0.01	1q24.2	BLZF1/intr	2.69 (2.09; 3.45)	$1.04 \times 10^{-14}$	
	rs16861990 <sup>W</sup>			0.06	1q24.2	NME7/intr	2.02 (1.66; 2.45)	$1.69 \times 10^{-12}$	
	rs2038024			0.13	1q24.2	SLC19A2/nc	1.53 (1.32; 1.78)	$1.12 \times 10^{-8}$	
	rs1799963			<0.01	11p11.2	F2/utr	2.46 (1.70; 3.55)	$1.69 \times 10^{-6}$	
	rs6025			98.64% European ancestry (USA)	1407/1418 (Replication phase)	0.01	1q24.2	F5/mis	2.56 (1.97; 3.32)
	rs8176719	0.34	9q34.2			ABO/fra	1.58 (1.40; 1.78) <sup>e</sup>	$9.75 \times 10^{-14e}$	
	rs2519093	0.14	chr9: 133,266,456 <sup>b</sup>			ABO/intr <sup>b</sup>	1.85 (1.61; 2.13) <sup>e</sup>	$1.37 \times 10^{-17e}$	
	rs495828	0.16	9q34.2			ABO/tr	1.76 (1.54; 2.01) <sup>e</sup>	$3.60 \times 10^{-17e}$	
	rs1799963	<0.01	11p11.2			F2/utr	1.71 (1.12; 2.63) <sup>e</sup>	0.01 <sup>e</sup>	
	rs16861990	0.06	1q24.2			NME7/intr	1.79 (1.47; 2.18)	$4.89 \times 10^{-9}$	
						1.17 (0.89; 1.54) <sup>e</sup>	0.25 <sup>e</sup>		
	rs2038024	0.13	1q24.2			SLC19A2/nc	0.77 (0.65; 0.92) <sup>e</sup>	$4.00 \times 10^{-3e}$	
	<b>GCST002012</b>	rs6427196	European ancestry			1618/44,499 (Discovery phase)	0.09	1q24.2	F5/utr
		rs687621		0.38	chr9: 133,261,662 <sup>b</sup>		ABO/intr <sup>b</sup>	1.37 (1.26; 1.49) <sup>f</sup>	$3.42 \times 10^{-14}$
rs4253399		0.26		4q35.2	F11/intr		1.15 (1.06; 1.24) <sup>f</sup>	$7.59 \times 10^{-4}$	
rs6536024		0.46		4q32.1	FGG/interg		0.79 (0.73; 0.87) <sup>f</sup>	$4.04 \times 10^{-7}$	
rs6764623		0.35		3p26.3	CNTN6/interg		1.23 (1.11; 1.38) <sup>f</sup>	$9.56 \times 10^{-5}$	
rs4979078		0.33		9q31.3	SUSD1/intr		1.31 (1.17; 1.47) <sup>f</sup>	$2.46 \times 10^{-6}$	
rs7164569		0.33		15q13.3	OTUD7A/syn		0.84 (0.76; 0.92) <sup>f</sup>	$3.54 \times 10^{-4}$	
rs3733860		0.17		5q13.3	SV2C/utr		1.22 (1.09; 1.37) <sup>f</sup>	$6.27 \times 10^{-4}$	
rs6427196		European ancestry		3231/3536 (Replication phase)	0.09		1q24.2	F5/utr	2.31 (2.04; 2.62) <sup>f</sup>
rs687621			0.38		chr9: 133,261,662 <sup>b</sup>	ABO/intr <sup>b</sup>	1.75 (1.62; 1.89) <sup>f</sup>	$1.20 \times 10^{-44}$	
rs4253399			0.26		4q35.2	F11/intr	1.32 (1.23; 1.43) <sup>f</sup>	$2.07 \times 10^{-13}$	
rs6536024			0.46		4q32.1	FGG/interg	0.81 (0.75; 0.87) <sup>f</sup>	$5.59 \times 10^{-8}$	
rs6764623			0.35		3p26.3	CNTN6/interg	1.14 (1.05; 1.24) <sup>f</sup>	$2.00 \times 10^{-3}$	
rs4979078			0.33		9q31.3	SUSD1/intr	1.11 (1.00; 1.24) <sup>f</sup>	$4.70 \times 10^{-2}$	
rs7164569			0.33		15q13.3	OTUD7A/syn	0.88 (0.82; 0.95) <sup>f</sup>	$2.00 \times 10^{-3}$	
rs3733860			0.17		5q13.3	SV2C/utr	1.17 (1.05; 1.30) <sup>f</sup>	$3.00 \times 10^{-3}$	
rs6427196			European ancestry		4849/48,035 (Combined data of all nine studies)	0.09	1q24.2	F5/utr	2.07 (1.89; 2.28) <sup>f</sup>
rs687621		0.38		chr9: 133,261,662 <sup>b</sup>		ABO/intr <sup>b</sup>	1.55 (1.47; 1.64) <sup>f</sup>	$1.55 \times 10^{-52}$	
rs4253399		0.26		4q35.2		F11/intr	1.24 (1.17; 1.31) <sup>f</sup>	$2.78 \times 10^{-14}$	
rs6536024		0.46		4q32.1		FGG/interg	0.80 (0.76; 0.85) <sup>f</sup>	$1.75 \times 10^{-13}$	
rs6764623		0.35		3p26.3		CNTN6/interg	1.18 (1.10; 1.26) <sup>f</sup>	$1.57 \times 10^{-6}$	
rs4979078	0.33	9q31.3		SUSD1/intr		1.21 (1.11; 1.30) <sup>f</sup>	$3.06 \times 10^{-6}$		
rs7164569	0.33	15q13.3		OTUD7A/syn		0.87 (0.81; 0.92) <sup>f</sup>	$3.27 \times 10^{-6}$		
rs3733860	0.17	5q13.3		SV2C/utr		1.19 (1.10; 1.29) <sup>f</sup>	$8.06 \times 10^{-6}$		

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Table 1 (continued)

Report accession on NHGRI-EBI GWAS catalogue	Associated SNPs	Population	No. cases/controls (combined)	MAF	Locus	Gene/Variant	Overall risk			
							Allelic OR (95% CI)	P-value		
<b>GCST002808</b>	rs6025	European ancestry	7507/52,632 (Discovery phase)	0.01	1q24.2	<i>F5/mis</i>	3.25 (2.91; 3.64)			
	rs4524			0.27	1q24.2	<i>F5/mis</i>	1.20 (1.14; 1.26)			
	rs2066865			0.30	4q32.1	<i>FGG/inter</i>	1.24 (1.18; 1.31)			
	rs4253417			0.30	4q35.2	<i>F11/intr</i>	1.27 (1.22; 1.34)			
	rs529565			0.37	chr9: 133,274,084 <sup>b</sup>	<i>ABO/intr<sup>b</sup></i>	1.55 (1.48; 1.63)			
	rs1799963			<0.01	11p11.2	<i>F2/utr</i>	2.29 (1.75; 2.99)			
	rs6087685			0.39	20q11.22	<i>PROCR/intr</i>	1.15 (1.10; 1.21)			
	rs4602861			0.39	8q23.1	<i>ZFPM2/intr</i>	1.20 (1.13; 1.27)			
	rs78707713			0.05	10q22.1	<i>TSPAN15/intr</i>	1.28 (1.19; 1.39)			
	rs2288904			0.18	19p13.2	<i>SLC44A2/mis</i>	1.19 (1.12; 1.26)			
	rs78707713	European ancestry	3009/2586 (Replication phase)	0.05	10q22.1	<i>TSPAN15/intr</i>	1.42 (1.24; 1.62)			
	rs2288904			0.18	19p13.2	<i>SLC44A2/mis</i>	1.28 (1.16; 1.40)			
	rs4602861	European ancestry	10,516/55,218 (combined data)	0.39	8q23.1	<i>ZFPM2/intr</i>	-			
	rs78707713			0.05	10q22.1	<i>TSPAN15/intr</i>	-			
	rs2288904			0.18	19p13.2	<i>SLC44A2/mis</i>	-			
	<b>GCST003377</b>	rs62322307 <sup>#</sup>	West African Ancestry <sup>f</sup> (80%)	146/432 (Discovery phase)	0.15 <sup>a</sup>	4q22.2	<i>ATOH1/inter</i>	2.79 (1.80; 4.30)		
rs73692310		0.15 <sup>a</sup>			7p12.3	<i>IGFBP3/inter</i>	3.04 (2.00; 4.70)			
rs58952918 <sup>#</sup>		European and Asian ancestry	94/65 (Replication phase)	0.17 <sup>a</sup>	18p11.32	<i>AP005230.1/ intr</i>	2.48 (1.70; 3.70)			
rs28496996				0.17 <sup>a</sup>	18p11.32	<i>AP005230.1/ intr</i>	2.44 (1.60; 3.60)			
rs2144940				0.31 <sup>a</sup>	20p11.21	<i>THBD, CD93/inter</i>	2.18 (1.60; 2.90)			
rs2567617 <sup>#</sup>				0.31 <sup>a</sup>	20p11.21	<i>THBD, CD93/inter</i>	2.17 (1.60; 2.90)			
rs1998081				0.27 <sup>a</sup>	20p11.21	<i>THBD, CD93/inter</i>	2.28 (1.60; 3.10)			
rs687621				0.38	chr9: 133,261,662 <sup>b</sup>	<i>ABO/intr<sup>b</sup></i>	1.55 (1.20; 2.00)			
rs505922				0.35	chr9: 133,273,813 <sup>b</sup>	<i>ABO/intr<sup>b</sup></i>	1.52 (1.20; 2.00)			
rs657152				0.39	chr9: 133,263,862 <sup>b</sup>	<i>ABO/intr<sup>b</sup></i>	1.39 (1.10; 1.80)			
rs73692310				West African Ancestry <sup>f</sup> (77%)	94/65 (Replication phase)	0.09 <sup>a</sup>	7p12.3	<i>IGFBP3/inter</i>	1.27 (0.04; 2.70)	
rs28496996						0.13 <sup>a</sup>	18p11.32	<i>AP005230.1/ intr</i>	1.34 (0.60; 2.60)	
rs2144940		European and Asian ancestry	94/65 (Replication phase)	0.35 <sup>a</sup>	20p11.21	<i>THBD, CD93/inter</i>	1.89 (1.10; 3.30)			
rs1998081				0.30 <sup>a</sup>	20p11.21	<i>THBD, CD93/inter</i>	1.94 (1.10; 3.50)			
rs73692310		West African Ancestry <sup>f</sup> (79%)	240/497 (Combined data)	0.02	7p12.3	<i>IGFBP3/inter</i>	-			
rs28496996				0.03	18p11.32	<i>AP005230.1/ intr</i>	-			
rs2144940	0.12			20p11.21	<i>THBD, CD93/inter</i>	-				
rs1998081	0.11			20p11.21	<i>THBD, CD93/inter</i>	-				

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Table 1 (continued)

Report accession on NHGRI-EBI GWAS catalogue	Associated SNPs	Population	No. cases/controls (combined)	MAF	Locus	Gene/Variant	Overall risk			
							Allelic OR (95% CI)	P-value		
<b>GCST003390</b>	rs6025	European ancestry	6135/252,827 (Discovery phase)	0.01	1q24.2	<i>F5</i> /mis	2.93 (2.72; 3.15)	$3.60 \times 10^{-137}$		
	rs7654093			0.31	4q32.1	<i>FGG</i> /inter	1.22 (1.17; 1.27)	$2.00 \times 10^{-19}$		
	rs4444878			0.32	4q35.2	<i>F11-AS1</i> /intr	0.81 (0.78; 0.84)	$7.00 \times 10^{-28}$		
	rs1799963			<0.01	11p11.2	<i>F2</i> /utr	0.51 (0.46; 0.58)	$1.30 \times 10^{-24}$		
	rs34234989			0.39	20q11.22	<i>PROCR</i> /intr	0.89 (0.85; 0.92)	$6.70 \times 10^{-9}$		
	rs529565			0.37	chr9: 133,274,084 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	0.72 (0.70; 0.75)	$7.10 \times 10^{-63}$		
	rs9797861			0.21	19p13.2	<i>SLC44A2</i> /intr	1.15 (1.09; 1.20)	$6.10 \times 10^{-9}$		
	rs114209171			0.24	Xq28	<i>FUNDC2</i> /nc	1.15 (1.11; 1.20)	$7.00 \times 10^{-13}$		
	rs72798544			0.01	2p21	<i>COX7A2L</i> /intr	0.73 (0.65; 0.82)	$1.90 \times 10^{-7}$		
	rs17490626			0.04	10q22.1	<i>TSPAN15</i> /intr	1.17 (1.10; 1.24)	$2.90 \times 10^{-7}$		
	rs113092656			0.01	6p24.1		0.73 (0.65; 0.82)	$4.40 \times 10^{-7}$		
	rs60942712					0.06	3p11.1	<i>TMEM170B</i> / <i>ADTRP</i> /inter <i>EPHA3</i> /inter	1.21 (1.12; 1.31)	$8.00 \times 10^{-7}$
	rs114209171			European ancestry	26,112 participants (Replication phase)	0.24	Xq28	<i>FUNDC2</i> /nc	1.08 (1.02; 1.14)	0.01
	<b>GCST004012</b>	rs1304029	European ancestry	212 children with VTE / 424 parents and siblings (Discovery phase)	0.48	6q13	<i>B3GAT2</i> /intr	0.48 (0.36; 0.65)	$2.00 \times 10^{-6h}$	
rs9293858		0.26			6q13	<i>RIMS1</i> /intr	0.48 (0.34; 0.67)	$8.00 \times 10^{-6h}$		
rs2748331		0.41			6q13	<i>B3GAT2</i> /rr	0.49 (0.36; 0.67)	$1.80 \times 10^{-5h}$		
rs10498910		0.12			6q14.1	<i>LOC105377862</i> /intr <sup>b</sup>	2.21 (1.47; 3.31)	$6.89 \times 10^{-5h}$		
rs914958		0.23			1p22.1	<i>ABCA4</i> /intr	0.50 (0.36; 0.70)	$1.80 \times 10^{-5h}$		
rs4529013		0.28			4q21.3	<i>MAPK10</i> /intr	0.53 (0.39; 0.72)	$2.00 \times 10^{-5h}$		
rs9957519		0.27			18q23	-/inter	0.46 (0.32; 0.68)	$2.10 \times 10^{-5h}$		
rs1865590		0.31			2q22.1	<i>THSD7B</i> /intr	1.97 (1.44; 2.68)	$2.40 \times 10^{-5h}$		

(continued on next page)

Table 1 (continued)

Report accession on NHGRI-EBI GWAS catalogue	Associated SNPs	Population	No. cases/controls (combined)	MAF	Locus	Gene/Variant	Overall risk	
							Allelic OR (95% CI)	P-value
rs9606534				0.17	chr22: 16,916,985 <sup>b</sup>	IGKV2OR22-4/rr	0.43 (0.29; 0.63)	3.30 × 10 <sup>-5h</sup>
rs495828				0.16	9q34.2	ABO/rr	-	6.44 × 10 <sup>-4</sup>
rs505922				0.35	chr9: 133,273,813 <sup>b</sup>	ABO/intr <sup>b</sup>	-	4.03 × 10 <sup>-4</sup>
rs657152				0.39	chr9: 133,263,862 <sup>b</sup>	ABO/intr <sup>b</sup>	1.77 (1.34; 2.32)	3.44 × 10 <sup>-5</sup>
rs13146272				0.44	4q35.1	CYP4V2/miss	-	9.58 × 10 <sup>-4</sup>
rs925451				0.29	4q35.2	F11/intr	-	2.76 × 10 <sup>-3</sup>
rs11128790				0.06	3p24.3	RFTN1/intr	2.95 (1.78; 4.90)	3.40 × 10 <sup>-5h</sup>
rs4792119				0.21	17p12	SHISA6/Intr	0.51 (0.37; 0.71)	3.50 × 10 <sup>-5h</sup>
rs9399770				0.48	6q16.3	-/inter	0.55 (0.42; 0.74)	4.00 × 10 <sup>-5h</sup>
rs17576372				0.27	1p22.1	TGFBFR3/intr	1.84 (1.37; 2.47)	4.57 × 10 <sup>-5h</sup>
rs10247053				0.25	7p15.2	-/inter	0.53 (0.39; 0.72)	5.35 × 10 <sup>-5h</sup>
rs636434				0.34	6q12	EYS/intr	1.79 (1.34; 2.39)	5.35 × 10 <sup>-5h</sup>
rs10190178				0.31	2q22.1	THSD7B/intr	1.91 (1.40; 2.62)	6.15 × 10 <sup>-5h</sup>
rs5014872				0.12	2p16.3	LOC730100/ Intr <sup>b</sup>	0.46 (0.32; 0.68)	6.21 × 10 <sup>-5h</sup>
rs3823606				0.04	7q11.21	TPST1/intr	-	6.27 × 10 <sup>-5h</sup>
rs1565242				0.11	15q26.1	LOC105370982/intr <sup>b</sup>	0.44 (0.29; 0.67)	7.23 × 10 <sup>-5h</sup>
rs1958059				0.31	14q13.1	NPAS3/intr	0.45 (0.31; 0.67)	7.28 × 10 <sup>-5h</sup>
rs1521882				0.23	2q33.1	KIAA2012/intr	2.13 (1.46; 3.11)	7.48 × 10 <sup>-5h</sup>
rs17781793				0.05	12q15	MRPL40P1/ inter	0.38 (0.23; 0.63)	7.81 × 10 <sup>-5h</sup>
rs4775384				0.31	15q22.2	AC104574.2/ intr	0.41 (0.26; 0.65)	8.16 × 10 <sup>-5h</sup>
rs1948650				0.33	15q14	DPH6-DT/intr	1.84 (1.34; 2.51)	8.71 × 10 <sup>-5h</sup>
rs436985				0.34	5q12.1	C5orf64/intr	0.58 (0.44; 0.76)	9.13 × 10 <sup>-5h</sup>
rs4926448				0.47	1q44	SCCPDH/intr	0.57 (0.43; 0.76)	9.38 × 10 <sup>-5h</sup>
rs11153626				0.22	6q22.1	FAM162B/ inter	1.85 (1.34; 2.54)	9.49 × 10 <sup>-5h</sup>
rs2214810				0.26	7p15.2	-/inter	0.54 (0.40; 0.74)	9.62 × 10 <sup>-5h</sup>
rs2748331		European ancestry	413 children/ 826 parents and siblings (combined data of discovery phase and replication phase I)	0.41	6q13	B3GAT2/rr	-	7.88 × 10 <sup>-7</sup>
rs9446340				0.23	6q13	B3GAT2/ Inter	-	1.48 × 10 <sup>-3</sup>
rs10498910				0.12	6q14.1	LOC105377862/intr <sup>b</sup>	-	5.74 × 10 <sup>-5</sup>
rs2748331		European ancestry	651 adults with VTE/ 1356 controls (Replication phase II)	0.41	6q13	B3GAT2/rr	1.20 (1.02; 1.40)	0.02 <sup>g</sup>
rs1304029				0.48	6q13	B3GAT2/intr	1.18 (1.02; 1.36)	0.03 <sup>g</sup>

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Table 1 (continued)

Report accession on NHGRI-EBI GWAS catalogue	Associated SNPs	Population	No. cases/controls (combined)	MAF	Locus	Gene/Variant	Overall risk	
							Allelic OR (95% CI)	P-value
<b>GCST004068</b>	rs138916004 <sup>Ⓜ</sup>	African ancestry (African-Americans)	393/4941 (Discovery phase)	< 0.01	12q14.3	<i>LEMD3</i> /intr	3.17 (2.13; 4.72) <sup>j</sup>	1.27 × 10 <sup>-8j</sup>
	rs3804476 <sup>Ⓜ</sup>			0.28	6p25.1	<i>LY86</i> /intr	1.83 (1.48; 2.26) <sup>j</sup>	1.97 × 10 <sup>-8j</sup>
	rs142143628 <sup>Ⓜ</sup>			< 0.01	8q12.2	<i>LOC100130298</i> /intr <sup>b</sup>	4.97 (2.80; 8.83) <sup>j</sup>	4.35 × 10 <sup>-8j</sup>
	rs6025			0.01	1q24.2	<i>F5</i> /mis	5.00 (2.02; 11.03) <sup>j</sup>	2.00 × 10 <sup>-4j</sup>
	rs8176746			0.15	9q34.2	<i>ABO</i> /mis	1.33 (1.09; 1.62) <sup>j</sup>	5.00 × 10 <sup>-3j</sup>
	rs8176719			0.34	9q34.2	<i>ABO</i> /fra	1.30 (1.11; 1.53) <sup>j</sup>	2.00 × 10 <sup>-3j</sup>
	rs77121243 <sup>β</sup>			0.03	11p15.4	<i>HBB</i> /miss	1.51 (1.11; 2.06)	9.00 × 10 <sup>-3</sup>
	<b>GCST004256</b>			rs6025	European ancestry	3290/116,868 (Discovery phase)	0.01	1q24.2
rs2066865	0.30	4q32.1	<i>FGG</i> /inter	1.21 (1.15; 1.29)			3.10 × 10 <sup>-11</sup>	
rs4253416	0.41	4q35.2	<i>F11</i> /intr	1.18 (1.12; 1.24)			2.00 × 10 <sup>-10</sup>	
rs2519093	0.14	chr9: 133,266,456 <sup>b</sup>	<i>ABO</i> /intr <sup>b</sup>	1.41 (1.32; 1.50)			6.00 × 10 <sup>-26</sup>	
rs8176645	0.38	9q34.2	<i>ABO</i> /intr	1.28 (1.22; 1.35)			4.40 × 10 <sup>-21</sup>	
rs1799963	<0.01	11p11.2	<i>F2</i> /utr	2.63 (2.03; 3.40)			4.90 × 10 <sup>-13</sup>	
rs3136516	0.28	11p11.2	<i>F2</i> /intr	1.10 (1.04; 1.15) <sup>k</sup>			3.30 × 10 <sup>-4k</sup>	
rs4602861	0.39	8q23.1	<i>ZFPM2</i> /intr	1.08 (1.03; 1.15)			4.50 × 10 <sup>-3</sup>	
rs4602861	0.39	8q23.1	<i>ZFPM2</i> /intr	1.13 (1.08; 1.19)	5.04 × 10 <sup>-7</sup>			
rs3136516	0.28	11p11.2	<i>F2</i> /intr	1.10 (1.06; 1.15) <sup>k</sup>	5.65 × 10 <sup>-6k</sup>			
rs4602861	0.39	8q23.1	<i>ZFPM2</i> /intr	1.11 (1.07; 1.15)	4.88 × 10 <sup>-10</sup>			
rs3136516	0.28	11p11.2	<i>F2</i> /intr	1.10 (1.06; 1.13) <sup>k</sup>	7.60 × 10 <sup>-9k</sup>			

The data shown in Table 1 concerning locus, type of genetic variant, as well as MAF values for all populations were obtained on the "Ensembl" database. For intergenic variants, the nearest gene was indicated.

**MAF**: minor allele frequency; **OR**: odds ratio; **Inter**: Intergenic variant, **Intr**: Intronic variant, **Mis**: missense variant, **Fra**: frameshift variant, **Nc**: non coding transcript exon variant, **Syn**: synonymous variant, **UTR**: 3 prime UTR variant, **RR**: regulatory region variant.

<sup>a</sup> MAF values for cases in the Report

<sup>b</sup> Data obtained from "NCBI" database

<sup>c</sup> OR/RR associated with the minor allele

<sup>d</sup> 99 SNPs reached genome-wide significant ( $p < 2 \times 10^{-8}$ ), but only the hit SNPs of each locus (*F5*, *FGG*, *F11* and *ABO*) were included in the table

<sup>e</sup> Data after adjusting for rs6025

<sup>f</sup> SNPs predominantly found in populations of African descent

<sup>g</sup> After Bonferroni correction, the P-values became insignificant

<sup>h</sup> P-values of permutation testing

<sup>j</sup> After adjusting for sickle cell risk variant (*HBB* rs77121243-T allele) and other cofactors

<sup>k</sup> After adjusting for rs1799963.

<sup>∇</sup> SNPs not significantly associated with VTE risk after adjusting for rs6025

<sup>§</sup> SNPs not significantly associated with VTE risk after adjusting for ABO blood group (rs8176719 and rs8176750)

<sup>#</sup> SNPs not tested in replication cohort due to high LD or due to failed assay

<sup>\*</sup> SNPs further replicated using parametric bootstrap, internal cross-validation and meta-analysis methods

<sup>β</sup> SNP merged into rs334 according to "NCBI" database

**Table 2**  
Genome-wide search for VTE-associated pairwise SNP interactions.

Report	Pairwise SNP interactions <sup>++</sup>	Population	No. cases/controls (combined)	MAF	Locus	Gene/Variant	Overall risk	
							OR	P-value
<b>GCST001913</b>	rs493014	European ancestry	1953/2338 (Meta analysis of two previous GWAS)	0.30	9q34.2	<i>SURF6</i> /inter	1.64	$6.00 \times 10^{-11}$
	rs886090			0.32	9q34.2	<i>SURF6</i> /mis		
	rs1336472			0.40	1p31.3	<i>AK4</i> /utr	1.54	$4.24 \times 10^{-10}$
	rs4715555			0.38	6p12.1	<i>HMGCLL1</i> /inter	1.67	$4.51 \times 10^{-10}$
	rs380904			0.29	8q24.3	<i>ZC3H3</i> /intr		
	rs8086028			0.30	18p11.22	<i>PIEZO2</i> /utr	2.10	$6.84 \times 10^{-10}$
	rs6815916			0.09	4q34.3	<i>TENM3-AS1</i> /inter		
	rs6092326			0.47	20q13.31	<i>FAM209B</i> /inter	1.50	$8.36 \times 10^{-10}$
	rs2282015			0.41	10q26.13	<i>AL160290.2</i> /intr		
	rs13050454			0.42	21q21.3	<i>AP001595.1</i> /inter	1.56	$9.89 \times 10^{-10}$
	rs7648704			0.33	3p22.3	<i>TRIM71</i> /tr		
	rs4868644			0.49	5q35.2	<i>RNF44</i> /inter	0.66	$1.32 \times 10^{-9}$
	rs1985317			0.41	9q33.1	<i>AL445644.1</i> /inter		
	rs827637			0.46	10p14	<i>AC044784.1</i> /inter	0.49	$1.38 \times 10^{-9}$
	rs2321744			0.10	13q13.2	<i>RFC3</i> /inter		
	rs6497540			0.42	16p13.2	<i>GRIN2A</i> /intr	2.05	$1.42 \times 10^{-9}$
	rs315122			0.30	12q15	<i>YEATS4</i> /intr		
	rs884483			0.12	15q23	<i>TLE3</i> /inter	1.73	$1.63 \times 10^{-9}$
	rs1423386			0.20	5q12.1	<i>LRRC70</i> /inter		
	rs6491679			0.29	13q33.1	<i>FGF14</i> /intr	1.52	$1.75 \times 10^{-9}$
	rs7714670			0.44	5q13.2	<i>ARHGEF28</i> /miss		
	rs12880735			0.35	14q12	<i>AL390334.1</i> /intr	1.74	$1.83 \times 10^{-9}$
	rs9392653			0.28	6p25.1	<i>PPP1R3G</i> /inter		
	rs7780976			0.19	7p21.2	<i>DGKB</i> /inter	1.71	$1.90 \times 10^{-9}$
	rs9804128			0.26	1p36.13	<i>IGSF21</i> /inter		
	rs4784379			0.24	16q12.2	<i>IRX3</i> /inter	1.80	$2.10 \times 10^{-9}$
	rs1364505			0.32	7q32.3	<i>PLXNA4</i> /intr		
	rs1204660			0.16	20q11.22	<i>UQCC1</i> /intr	1.60	$2.11 \times 10^{-9}$
	rs2288073			0.29	2q23.3	<i>FAM228A</i> /miss		
	rs10771022			0.34	12p12.1	<i>SOX5</i> /intr	1.49	$2.20 \times 10^{-9}$
	rs1367228			0.44	2p16.1	<i>EFEMP1</i> /intr		
	rs3905075			0.40	13q33.3	<i>FAM155A1T1</i> /intr	0.63	$2.93 \times 10^{-9}$
	rs536477			0.43	1q43	<i>CHRM3</i> /inter		
rs1937920	0.27	10p15.1	<i>AKR1C2</i> /inter	0.40	$3.30 \times 10^{-9}$			
rs2710201	0.06	7q36.2	<i>ACTR3B</i> /inter					
rs3780293	0.35	9q21.2	<i>GNA14</i> /intr	1.65	$3.33 \times 10^{-9}$			
rs12541254	0.34	8p22	<i>DLC1</i> /intr					
rs305009	0.23	15q23	<i>TLE3</i> /inter					

(continued on next page)

Table 2 (continued)

Report	Pairwise SNP interactions <sup>++</sup>	Population	No. cases/controls (combined)	MAF	Locus	Gene/Variant	Overall risk	
							OR	P-value
	rs4507975			0.29	1q25.2	PAPPA2/intr	0.65	3.58 × 10 <sup>-9</sup>
	rs9914518			0.47	17p13.1	GSG1L2/intr		
	rs2771051			0.37	9q33.1	-/inter	0.67	3.82 × 10 <sup>-9</sup>
	rs827637			0.46	10p14	-/inter		
	rs10516089			0.31	5q35.1	SMIM23/intr	0.63	3.86 × 10 <sup>-9</sup>
	rs11072930			0.29	15q25.1	ARNT2/intr		
	rs10504130			0.14	8q11.22	PCMTD1/intr	1.88	4.46 × 10 <sup>-9</sup>
	rs2847351			0.31	18p11.22	APCDD1/intr		
	rs318497			0.49	6p25.2	AL133351.3/nc	0.43	4.54 × 10 <sup>-9</sup>
	rs7019259			0.07	9q21.2	PSAT1/intr		
	rs6695223			0.13	1p22.3	WDR63/intr	1.86	4.70 × 10 <sup>-9</sup>
	rs1763510			0.39	6q23.2	SGK1/intr		
	rs1336708			0.25	13q33.1	FGF14-IT1/intr	0.58	4.85 × 10 <sup>-9</sup>
	rs1423386			0.20	5q12.1	CKS1BP3/intr		
	rs6771316			0.13	3p13	LINC00877/intr	2.13	5.26 × 10 <sup>-9</sup>
	rs10986432			0.17	9q33.3	OLFML2A/intr		
	rs664910			0.30	3q21.3	MGLL/intr	1.50	6.63 × 10 <sup>-9</sup>
	rs877228			0.46	15q22.2	RORA/intr		
	rs9945428			0.30	18q22.3	FBXO15/intr	0.62	6.88 × 10 <sup>-9</sup>
	rs4823535			0.27	22q13.32	FAM19A5/intr		
	rs1910358			0.23	5q14.2	C5orf17/intr	2.03	7.14 × 10 <sup>-9</sup>
	rs9981595			0.11	21q22.2	BRWD1/intr		
	rs6771725			0.27	3q26.31	NAALADL2/intr	2.22	8.60 × 10 <sup>-9</sup>
	rs10507246			0.09	12q24.21	TBX5/intr		
	rs16865717			0.28	2p25.2	RSAD2/intr	1.56	8.82 × 10 <sup>-9</sup>
	rs2009579			0.36	20q12	-/inter		
	rs2028385			0.16	12q23.1	ACO07513.1/intr	1.69	8.82 × 10 <sup>-9</sup>
	rs2038227			0.38	16p13.3	RAB11FIP3/intr		
	rs10476160			0.20	5q35.2	SFXN1/intr	0.62	9.09 × 10 <sup>-9</sup>
	rs1707420			0.48	8p23.2	-/inter		
	rs971572			0.32	1q25.3	TSEN15/intr	0.42	9.30 × 10 <sup>-9</sup>
	rs10828151			0.07	10p12.31	NEBL/intr		
	rs6858430			0.21	4q34.1	ADAM29/intr	1.62	9.67 × 10 <sup>-9</sup>
	rs4800250			0.40	18q11.2	TAF4B/intr		
	rs467650			0.37	5q15	RGMB/intr	0.67	9.91 × 10 <sup>-9</sup>
	rs7153749			0.44	14q23.1	LINC01500/intr		

<sup>++</sup> The interactions did not reach the Bonferroni correction for the number of investigated interactions; **MAF** – minor allele frequency; **OR** – odds ratio

**Table 3**

SNPs reported by VTE GWAS in European populations and their analysis in previously reported candidate gene studies or validation studies also in European populations.

Gene	SNP	Type of Report	No. cases/controls (combined)	MAF (cases)	OR (95% CI)	P-value	References
F5	rs6025	Candidate gene approach	471/474	0.01*	6.50 (1.80–23.00) (GG vs. AG)	<0.05	[1]
	rs4524	Candidate gene approach	1488/1439	0.25**	0.77 (0.68–0.87)	$2.51 \times 10^{-5}$	[2]
	rs1018827	Validation	1040/16,936	0.07*	1.53 (1.29–1.79) (AA vs. AG)	$6.53 \times 10^{-6}$	[3]
	rs6427196	Validation	1040/16,936	0.09*	1.51 (1.28–1.78) (CC vs. CG)	$9.21 \times 10^{-6}$	[3]
	rs2420371 <sup>z</sup>	–	–	–	–	–	–
F2	rs1799963	Candidate gene approach	471/474	<0.01*	2.80 (1.40–5.60)	<0.05	[4]
	rs3136516	Candidate gene approach	428/795	0.28*	1.50 (1.00–2.20)	<0.05	[5]
	rs2066865	Candidate gene approach	471/471	0.30*	2.40 (1.50–3.90)	0.002	[6]
FGB/FGA/FGG	rs6825454	Candidate gene approach	419/1228	0.31	–	$2.80 \times 10^{-4}$	[7]
	rs7659024	Validation	1040/16,936	0.30*	1.40 (1.09–1.78) (AA vs. GG)	$3.03 \times 10^{-2}$	[3]
	rs6536024	Validation	1040/16,936	0.46*	–	<b>0.23</b>	[3]
	rs7654093 <sup>h</sup>	–	–	–	–	–	–
	rs3756008	Candidate gene approach	1837/2204	–	1.27 (1.16–1.38)	<0.05	[8]
F11	rs4253399	Candidate gene approach	1488/1439	0.41**	1.28 (1.15–1.43)	$6.33 \times 10^{-6}$	[2]
	rs4253417	–	–	–	–	–	–
	rs4444878	–	–	–	–	–	–
	rs4253416	–	–	–	–	–	–
	rs2519093	Candidate gene approach	1488/1439	0.24**	1.68 (1.48–1.91)	$8.08 \times 10^{-16}$	[2]
ABO	rs505922	Validation	1040/16,936	0.35*	1.78 (1.46–2.15) (CC vs. TT)	$5.17 \times 10^{-11}$	[3]
	rs630014	Validation	1040/16,936	0.42**	0.75 (0.67–0.84)	$2.67 \times 10^{-7}$	[2]
	rs8176719	Validation	1040/16,936	0.42**	1.47 (1.32–1.64)	$5.68 \times 10^{-12}$	[2]
ABO	rs8176719	Validation	96/148	0.48	1.62 (1.09–2.38)	0.015	[9]
	rs687621	Validation	1040/16,936	0.38*	1.74 (1.43–2.10) (AA vs. GG)	$5.45 \times 10^{-10}$	[3]
	rs495828	Validation	1040/16,936	0.16*	2.09 (1.64–2.63) (GG vs. TT)	$1.72 \times 10^{-10}$	[3]
	rs8176750	–	–	–	–	–	–
	rs657152	–	–	–	–	–	–
	rs529565	–	–	–	–	–	–
	rs8176645 <sup>o</sup>	–	–	–	–	–	–
	rs3813948	Validation	1433/1402	0.07	–	<b>0.25</b>	[10]
	rs16861990	Validation	1040/16,936	0.06*	4.11 (2.14–7.33) (CC vs. AA)	$2.90 \times 10^{-7}$	[3]
	rs6087685	Validation	1040/16,936	0.39*	–	<b>0.92</b>	[3]
rs34234989 <sup>i</sup>	–	–	–	–	–	–	

(continued on next page)

**Table 3** (continued)

Gene	SNP	Type of Report	No. cases/controls (combined)	MAF (cases)	OR (95% CI)	P-value	References
TSPAN15	rs78707713	Validation	1040/16,936	0.05*	0.77 (0.66–0.91) (TT vs. TC)	$6.22 \times 10^{-3}$	[3]
	rs17490626 <sup>‡</sup>	–	–	–	–	–	
ZFPM2	rs4602861	–	–	–	–	–	[3]
SLC44A2	rs2288904	Validation	1040/16,936	0.18*	0.63 (0.44–0.89) (AA vs. GG)	$2.42 \times 10^{-2}$	
	rs9797861 <sup>¥</sup>	–	–	–	–	–	
SLC19A2	rs2038024	–	–	–	–	–	
CCDC181	rs1208134	–	–	–	–	–	
CNTN6	rs6764623	–	–	–	–	–	
SUSD1	rs4979078	–	–	–	–	–	
OTUD7A	rs7164569	–	–	–	–	–	
SV2C	rs3733860	–	–	–	–	–	
FUNDC2	rs114209171	–	–	–	–	–	
COX7A2L	rs72798544	–	–	–	–	–	
–	rs113092656	–	–	–	–	–	
EPHA3	rs60942712	–	–	–	–	–	

**MAF:** minor allele frequency; **OR:** odds ratio.

\* MAF values obtained from “Ensembl” database

\*\* Total MAF in the report (cases and controls)

<sup>‡</sup> SNP in high LD with rs6427196, particularly for European ancestry populations ( $r^2 > 0.81$ ), according to “Ensembl” database

<sup>‡</sup> SNP in high LD with rs2066865 for all populations according to “Ensembl” database ( $r^2 > 0.81$ )

<sup>‡</sup> SNP in high LD with rs8176719, particularly for European ancestry populations ( $r^2 > 0.90$ ), according to “Ensembl” database

<sup>‡</sup> SNP in high LD with rs6087685 for all populations according to “Ensembl” database ( $r^2 > 0.86$ , except in Kenya population)

<sup>‡</sup> SNP in high LD with rs78707713 for most populations, particularly the European ancestry populations ( $r^2 = 1$ ), according to “Ensembl” database

<sup>¥</sup> SNP in high LD with rs2288904 for most populations, particularly the European ancestry populations ( $r^2 > 0.90$ ), according to “Ensembl” database.

**Table 4**

VTE related-genes reported by GWAS and their putative links with cancer hallmarks.

Genes	HUGO nomenclature	Molecular processes that promote carcinogenesis	Potential cancer hallmarks
F5	<i>Coagulation Factor V</i>	Generation of thrombin	Metastasis, angiogenesis, immune evasion and apoptosis [11]
CCDC181 ( <i>C1orf114</i> )	<i>Coiled-Coil Domain Containing 181</i>	Despite the unknown role in carcinogenesis, this gene is frequently methylated in patients with prostate cancer [12]	Genome instability and mutation
ABO	<i>ABO Blood Group</i>	Activation of adhesion molecules [13]	Inflammation, immune evasion and metastasis [13, 14]
C4BPB	<i>Complement Component 4 Binding Protein Beta</i>	Regulation of plasmatic levels of von Willebrand factor (vWF) [11]	Angiogenesis and apoptosis [15]
NME7 FGB/FGG/FGA	<i>NME/NM23 Family Member 7 Fibrinogen Beta Chain/ Fibrinogen Gamma Chain/ Fibrinogen Alpha Chain</i>	Inactivation of protein S, which is an important cofactor to activated protein C and constitutes a ligand for the Axl family of receptor tyrosine kinases [16, 17]	Inflammation and apoptosis [16] Proliferation signalling, invasion and apoptosis through Axl receptor tyrosine kinase signalling [18]
F11	<i>Coagulation Factor XI</i>	Embryonic Stem Cell Renewal [19]	Metastasis
SLC19A2 F2	<i>Solute Carrier Family 19 Member 2 Coagulation Factor II, thrombin</i>	Formation of fibrin clot	Angiogenesis [11]
CNTN6	<i>Contactin 6</i>	Immune response [20]	Immune evasion and inflammation
OTUD7A	<i>OTU Deubiquitinase 7A</i>	Augmentation of the proliferative effect of fibroblast growth factor-2 (FGF-2) [21]	Proliferative signalling and angiogenesis [21]
SV2C	<i>Synaptic Vesicle Glycoprotein 2C</i>	Generation of Factor Xa	Apoptosis [22]
		Generation of thrombin	Metastasis, angiogenesis, immune evasion and apoptosis [11]
		Metabolism	Cancer metabolism
		Generation of thrombin	Metastasis, angiogenesis, immune evasion and apoptosis [11]
		Activating of Notch signalling pathway [23]	Proliferative signalling and metastasis [11]
		Mediation of cell surface interactions	
		Modulation of nuclear factor kappa B (NF- $\kappa$ B) expression through interaction with TNF receptor associated factor 6 (TRAF6)	Metastasis [24]
		Modulation of dopamine release [25]	Apoptosis and inflammation [26]

(continued on next page)

**Table 4** (continued)

Genes	HUGO nomenclature	Molecular processes that promote carcinogenesis	Potential cancer hallmarks
<i>SUSD1</i> <i>PROCR</i>	<i>Sushi Domain Containing 1</i> <i>Protein C Receptor</i>	Unknown role in carcinogenesis Protein C pathway	unknown Proliferative signalling, invasion, metastasis, apoptosis and immune evasion [27] Angiogenesis [28]
<i>ZFPM2 (FOG2)</i>	<i>Zinc Finger Protein, FOG Family Member 2</i>	GATA transcriptional network	Apoptosis, invasion and inflammation [29] Angiogenesis [30]
<i>TSPAN15</i>	<i>Tetraspanin 15</i>	Mediates signal transduction events that play a role in the regulation of cell activation, growth, development and motility.	Metastasis [31]
<i>SLC44A2</i> <i>FUNDC2</i>	<i>Solute Carrier Family 44 Member 2</i> <i>FUN14 Domain Containing 2</i>	Metabolism Modulation of platelet survival [32]	Cancer metabolism Metastasis, angiogenesis and immune evasion [33]
<i>COX7A2L</i> <i>EPHA3</i>	<i>Cytochrome C Oxidase Subunit 7A2 Like</i> <i>EPH Receptor A3</i>	Regulation of oxidative phosphorylation Regulation of developmental events Regulation of cytoskeletal organization, cell-cell adhesion and cell migration	Cancer metabolism Invasion and metastasis [34] Angiogenesis [35]
<i>B3GAT2</i> <i>THBD</i>	<i>Beta-1,3-Glucuronyltransferase 2</i> <i>Thrombomodulin</i>	Mismatch repair deficiency [36] Protein C pathway Regulation of adhesion molecules [37]	Genome instability and mutation Angiogenesis [28] Invasion and metastasis [37]
<i>LEMD3 (MAN1)</i>	<i>LEM Domain Containing 3</i>	Regulation of transforming growth factor-beta (TGF-beta) signalling at the inner nuclear membrane	Proliferative signalling, invasion and apoptosis [38] Immune evasion [39]
<i>LY86 (MD-1)</i> <i>LOC100130298</i>	<i>Lymphocyte Antigen 86</i> <i>HCG1816373-Like</i>	Innate Immune System Unknown role in carcinogenesis	Inflammation Unknown

The data shown in Table 4 concerning the HUGO nomenclature and the molecular process involved in carcinogenesis were obtained from "Genecards" database (exceptions are referenced).

taken into account. To our best knowledge, the majority of VTE GWAS-reported SNPs are currently lacking validation.

### (3) Putative links between VTE-associated genes and cancer hallmarks:

A vast search using *NCBI*, *GeneCards* and *Ensembl* databases (Fig. 1) was made to collect data concerning VTE-associated genes and how they may be implicated in many cancer-related processes that contribute to cancer growth and progression.

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## Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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