Data Article

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

Valéria Tavares\textsuperscript{a,b}, Ricardo Pinto\textsuperscript{a}, Joana Assis\textsuperscript{a,c}, Deolinda Pereira\textsuperscript{a,d}, Rui Medeiros\textsuperscript{a,b,c,e,}\textsuperscript{*}

\textsuperscript{a} Molecular Oncology and Viral Pathology Group-Research Center, Portuguese Institute of Oncology, Edificio Laboratórios, 1\textsuperscript{st} piso, Rua Dr. António Bernardino de Almeida, 4200-072 Porto, Portugal
\textsuperscript{b} ICBAS, Abel Salazar Institute for the Biomedical Sciences, Rua de Jorge Viterbo Ferreira, 228, 4050-313 Porto, Portugal
\textsuperscript{c} FMUP, Faculty of Medicine, Porto University, Porto, Portugal
\textsuperscript{d} Oncology Department, Portuguese Institute of Oncology, 4200-072 Porto, Portugal
\textsuperscript{e} CEBIMED, Faculty of Health Sciences, Fernando Pessoa University, 4200-150 Porto, Portugal

\textbf{Article history:}
Received 31 January 2020
Revised 24 February 2020
Accepted 3 March 2020
Available online 9 March 2020

\textbf{Keywords:}
Venous thromboembolism
GWAS
SNPs
Validation reports
Cancer hallmarks

\textbf{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

\textsuperscript{*} Corresponding author at: Molecular Oncology and Viral Pathology Group-Research Center, Portuguese Institute of Oncology, Edificio Laboratórios, 1\textsuperscript{st} piso, Rua Dr. António Bernardino de Almeida, 4200-072 Porto, Portugal.

\textit{E-mail address:} ruimedei@ipoporto.min-saude.pt (R. Medeiros).

https://doi.org/10.1016/j.dib.2020.105399
2352-3409/© 2020 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license. (http://creativecommons.org/licenses/by-nc-nd/4.0/)
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”.

© 2020 Published by Elsevier Inc.
This is an open access article under the CC BY-NC-ND license. (http://creativecommons.org/licenses/by-nc-nd/4.0/)

| Specifications table |
|----------------------|
| **Subject**          | Biochemistry, Genetics and Molecular Biology |
| **Specific subject area** | Genetics; Molecular biology; Molecular medicine; Cancer Research |
| **Type of data**     | Tables |
| **How data were acquired** | NHGRI-EBI GWAS catalogue |
|                      | NCBI database |
|                      | GeneCards database |
|                      | Ensembl database |
| **Data format**     | Raw |
|                      | Filtered |
| **Parameters for data collection** | 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 NHGRI-EBI GWAS catalogue. 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 NCBI, GeneCards and Ensembl databases. |
| **Description of data collection** | 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. |
| **Data source location** | NHGRI-EBI GWAS catalogue |
|                      | NCBI database |
|                      | GeneCards database |
|                      | Ensembl database |
| **Data accessibility** | Data is provided in the article |
| **Related review article** | 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. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer, https://doi.org/10.1016/j.bbcan.2019.188331 |

### 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
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 \textit{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...
| 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 |
|---------------------------------------------|----------------|------------|-----------------------------|-----|-------|-------------|-------------|---------------------|---------|
| GCST000354                                  | rs2420371      | European   | 419/1228 (Discovery phase)  | 0.15^a | 1q24.2 | F5/intr     | 2.27 (1.62; 3.18)^c | 8.08 × 10^{-10} |
|                                             | rs1208134      | ancestry   |                             | 0.12^a | 1q24.2 | CCDC181/ intr | 2.29 (1.58; 3.32)^c | 3.47 × 10^{-7} |
|                                             | rs657152       |            |                             | 0.54^b | chr9: 133,263,862^b | ABO/intr^a | 1.89 (1.51; 2.36)^c | 2.22 × 10^{-11} |
|                                             | rs505922       |            |                             | 0.52^a | chr9: 133,273,813^b | ABO/intr^a | 1.91 (1.53; 2.39)^c | 1.48 × 10^{-14} |
|                                             | rs630014       |            |                             | 0.37^a | 9q34.2 | ABO/intr    | 0.64 (0.51; 0.80)^c | 2.00 × 10^{-7} |
|                                              | rs2420371^v    | European   | 1150/801 (Replication phase I) | 0.21^a | 1q24.2 | F5/intr     | 1.39 (1.17; 1.64)^c | 3.00 × 10^{-5} |
|                                              | rs1208134^v    | ancestry   |                             | 0.19^a | 1q24.2 | CCDC181/ intr | 1.57 (1.31; 1.88)^c | 2.89 × 10^{-7} |
|                                              | rs6025         |            |                             | 0.01  | 1q24.2 | F5/mis      | 2.01 (1.63; 2.48)^c | 9.91 × 10^{-11} |
|                                              | rs657152^g     |            |                             | 0.51^a | chr9: 133,263,862^b | ABO/intr^a | 1.75 (1.51; 2.03)^c | 1.20 × 10^{-13} |
|                                              | rs505922^g     |            |                             | 0.49^a | chr9: 133,273,813^b | ABO/intr^a | 1.81 (1.56; 2.11)^c | 3.72 × 10^{-15} |
|                                              | rs630014^g     |            |                             | 0.38^a | 9q34.2 | ABO/intr    | 0.66 (0.57; 0.76)^c | 1.21 × 10^{-8} |
|                                              | rs8176719      |            |                             | 0.34  | 9q34.2 | ABO/fra     | 0.33 (0.26; 0.42)^c | 1.70 × 10^{-18} |
|                                              | rs8176750      |            |                             | 0.05  | 9q34.2 | ABO/fra     | 0.53 (0.38; 0.74)^c | 2.46 × 10^{-4} |
|                                              | rs2420371^v    | European   | 607/607 (Replication phase II) | 0.10^a | 1q24.2 | F5/intr     | 1.44 (1.07; 1.93)^c | 1.80 × 10^{-3} |
|                                              | rs6025         |            |                             | 0.01  | 1q24.2 | F5/mis      | 2.46 (1.55; 3.93)^c | 1.50 × 10^{-4} |
|                                              | rs657152^g     |            |                             | 0.47^a | chr9: 133,263,862^b | ABO/intr^a | 1.58 (1.34; 1.87)^c | 5.19 × 10^{-8} |
|                                              | rs505922^g     |            |                             | 0.46^a | chr9: 133,273,813^b | ABO/intr^a | 1.65 (1.39; 1.95)^c | 7.25 × 10^{-9} |
|                                              | rs630014^g     |            |                             | 0.38^a | 9q34.2 | ABO/intr    | 0.63 (0.53; 0.74)^c | 5.01 × 10^{-8} |
|                                              | rs8176719      |            |                             | 0.34  | 9q34.2 | ABO/fra     | 0.53 (0.41; 0.69)^c | 2.21 × 10^{-6} |
| GCST000621                                   | rs3813948      | European   | 419/1228 (in silico GWAS)    | 0.09^a | 1q23.1 | C4BPB/nc     | –             | 0.011               |
|                                              | rs3813948      | ancestry   | 1706/1379 (Replication phase) | 0.09^a | 1q23.1 | C4BPB/nc     | 1.24 (1.00; 1.53) | 0.046               |
| GCST001253                                   | rs16861990     | European   | 1542/1110 (Discovery phase)  | 0.13^a | 1q24.2 | NM7/intr     | 2.49^ -  | 2.75 × 10^{-15} |
|                                              | rs1208134      | ancestry   |                             | 0.13^a | 1q24.2 | CCDC181/ intr | 2.53^c  | 3.29 × 10^{-16} |
|                                              | rs2420371      |            |                             | 0.15^a | 1q24.2 | F5/intr     | 2.62^ -  | 8.44 × 10^{-10} |
|                                              | rs2066865      |            |                             | 0.28^a | 4q32.1 | FGC/inter    | 1.55^ -  | 1.17 × 10^{-10} |
|                                              | rs6825454      |            |                             | 0.30^a | 4q31.3 | FG/A/inter   | 1.50^ -  | 1.32 × 10^{-9} |
|                                              | rs10029715     |            |                             | 0.12^a | 4q35.2 | FIT1-ASFlintr | –            | 3.20 × 10^{-9} |
|                                              | rs2073828      |            |                             | 0.32^a | chr9: 133,261,737^c | ABO/intr^a | –            | 3.57 × 10^{-9} |
|                                              | rs657152       |            |                             | 0.49^a | chr9: 133,263,862^b | ABO/intr^a | 1.70^ -  | 1.10 × 10^{-8} |
|                                              | rs500498       |            |                             | 0.33^a | chr9: 133,273,232^b | ABO/intr^a | –            | 1.03 × 10^{-12} |
|                                              | rs505922       |            |                             | 0.49^a | chr9: 133,273,813^b | ABO/intr^a | 1.85^ -  | 1.06 × 10^{-23} |
|                                              | rs630014       |            |                             | 0.38^a | 9q34.2 | ABO/intr    | 0.63^c  | 4.40 × 10^{-14} |
|                                              | rs495828       |            |                             | 0.36^a | 9q34.2 | ABO/rr      | 1.64^ -  | 1.78 × 10^{-14} |
|                                              | rs1018827      | European   | 1961/2338 (meta-analysis)^d | 0.07  | 1q24.2 | F5/intr     | 2.52^ -  | 2.41 × 10^{-26} |
|                                              | rs7659024      |            |                             | 0.30  | 4q31.3 | FGC/inter    | 1.53^ -  | 1.93 × 10^{-11} |
|                                              | rs505922       |            |                             | 0.35  | chr9: 133,273,813^b | ABO/intr^a | 1.92^ -  | 1.39 × 10^{-34} |
|                                              | rs3756008      |            |                             | 0.32  | 4q35.2 | FIT1/inter   | 1.40^ -  | 6.46 × 10^{-11} |

(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 |
|---------------------------------------------|----------------|------------|--------------------------------|-----|-------|--------------|-------------|---------------------|---------|
| GCST001557                                  | rs6025         | 98.64% European ancestry (USA) | 1503/1459 (Discovery phase) | 0.01 | 1q24.2 | F5/mis | 3.75 (2.76; 4.60) | 1.68 × 10−22 |
|                                            | rs8176719      |            |                                | 0.34 | 9q34.2 | ABO/fra  | 1.47 (1.32; 1.64) | 5.68 × 10−12 |
|                                            | rs2519093      |            |                                | 0.14 | chr9: 133,266,646b | ABO/intrb | 1.69 (1.48; 1.91) | 8.08 × 10−16 |
|                                            | rs495828       |            |                                | 0.16 | 9q34.2 | ABO/ir   | 1.65 (1.46; 1.86) | 2.96 × 10−16 |
|                                            | rs7538157V     |            |                                | <0.01 | 1q24.2 | BLZF1/intr | 2.69 (2.09; 3.45) | 1.04 × 10−16 |
|                                            | rs16861990V    |            |                                | 0.06 | 1q24.2 | NME7/intr | 2.02 (1.66; 2.45) | 1.69 × 10−12 |
|                                            | rs2038024      |            |                                | 0.13 | 1q24.2 | SLC19A2/nc | 1.53 (1.32; 1.78) | 1.12 × 10−8  |
|                                            | rs1799963      |            |                                | <0.01 | 11p11.2 | F2/utr  | 2.46 (1.70; 3.55) | 1.69 × 10−6  |
|                                            | rs6025         | 98.64% European ancestry (USA) | 1407/1418 (Replication phase) | 0.01 | 1q24.2 | F5/mis | 2.56 (1.97; 3.32) | 1.40 × 10−12 |
|                                            | rs8176719      |            |                                | 0.34 | 9q34.2 | ABO/fra  | 1.58 (1.40; 1.78) | 9.75 × 10−14e |
|                                            | rs2519093      |            |                                | 0.14 | chr9: 133,266,646b | ABO/intrb | 1.85 (1.61; 2.13) | 1.37 × 10−17 |
|                                            | rs495828       |            |                                | 0.16 | 9q34.2 | ABO/ir   | 1.76 (1.54; 2.01) | 3.60 × 10−17 |
|                                            | rs16861990     |            |                                | 0.06 | 1q24.2 | NME7/intr | 1.79 (1.47; 2.18) | 4.89 × 10−9  |
|                                            | rs2038024      |            |                                | 0.13 | 1q24.2 | SLC19A2/nc | 1.17 (0.89; 1.54) | 0.25 |
|                                            | rs6427196      | European ancestry | 1618/44,499 (Discovery phase) | 0.09 | 1q24.2 | F5/utr  | 1.82 (1.58; 2.10) | 1.97 × 10−16 |
|                                            | rs687621       |            |                                | 0.38 | chr9: 133,261,662b | ABO/utr  | 1.37 (1.26; 1.49) | 3.42 × 10−14 |
|                                            | rs4253399      |            |                                | 0.26 | 4q35.2 | F11/utr  | 1.15 (1.06; 1.24) | 7.59 × 10−4  |
|                                            | rs6536024      |            |                                | 0.46 | 4q32.1 | FGG/interg | 0.79 (0.73; 0.87) | 4.04 × 10−7  |
|                                            | rs6764623      |            |                                | 0.35 | 3p26.3 | CNTN6/interg | 1.23 (1.11; 1.38) | 9.56 × 10−5  |
|                                            | rs4979078      |            |                                | 0.33 | 9q31.3 | SUSDI/utr | 1.31 (1.17; 1.47) | 2.46 × 10−6  |
|                                            | rs7164569      |            |                                | 0.33 | 15q13.3 | OTUD7A/syn | 0.84 (0.76; 0.92) | 3.54 × 10−4  |
|                                            | rs3733860      |            |                                | 0.17 | 5q13.3 | SV2C/utr | 1.22 (1.09; 1.37) | 6.27 × 10−4  |
|                                            | rs6427196      | European ancestry | 3231/3536 (Replication phase) | 0.09 | 1q24.2 | F5/utr  | 2.31 (2.04; 2.62) | 2.56 × 10−38 |
|                                            | rs687621       |            |                                | 0.38 | chr9: 133,261,662b | ABO/utr  | 1.75 (1.62; 1.89) | 1.20 × 10−44 |
|                                            | rs4253399      |            |                                | 0.26 | 4q35.2 | F11/utr  | 1.32 (1.23; 1.43) | 2.07 × 10−13 |
|                                            | rs6536024      |            |                                | 0.46 | 4q32.1 | FGG/interg | 0.81 (0.75; 0.87) | 5.59 × 10−8  |
|                                            | rs6764623      |            |                                | 0.35 | 3p26.3 | CNTN6/interg | 1.14 (1.05; 1.24) | 2.00 × 10−3  |
|                                            | rs4979078      |            |                                | 0.33 | 9q31.3 | SUSDI/utr | 1.11 (1.00; 1.24) | 4.70 × 10−2  |
|                                            | rs7164569      |            |                                | 0.33 | 15q13.3 | OTUD7A/syn | 0.88 (0.82; 0.95) | 2.00 × 10−3  |
|                                            | rs3733860      |            |                                | 0.17 | 5q13.3 | SV2C/utr | 1.17 (1.05; 1.30) | 3.00 × 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) | 4.47 × 10−51 |
|                                            | rs687621       |            |                                | 0.38 | chr9: 133,261,662b | ABO/utr  | 1.55 (1.47; 1.64) | 1.55 × 10−52 |
|                                            | rs4253399      |            |                                | 0.26 | 4q35.2 | F11/utr  | 1.24 (1.17; 1.31) | 2.78 × 10−14 |
|                                            | rs6536024      |            |                                | 0.46 | 4q32.1 | FGG/interg | 0.80 (0.76; 0.85) | 1.75 × 10−11 |
|                                            | rs6764623      |            |                                | 0.35 | 3p26.3 | CNTN6/interg | 1.18 (1.10; 1.26) | 1.57 × 10−6  |
|                                            | rs4979078      |            |                                | 0.33 | 9q31.3 | SUSDI/utr | 1.21 (1.11; 1.30) | 3.06 × 10−6  |
|                                            | rs7164569      |            |                                | 0.33 | 15q13.3 | OTUD7A/syn | 0.87 (0.81; 0.92) | 3.27 × 10−6  |
|                                            | rs3733860      |            |                                | 0.17 | 5q13.3 | SV2C/utr | 1.19 (1.10; 1.29) | 8.06 × 10−6  |

(continued on next page)
| 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 |
|---------------------------------------------|----------------|------------|-------------------------------|-----|-------|--------------|-------------|---------------------|---------|
| GCST002808                                  | rs6025         | European ancestry | 7507/52,632 (Discovery phase) | 0.01 | 1q24.2 | F5/mis       | 3.25 (2.91; 3.64) | 1.10 × 10^{-6}  |
|                                             | rs4524         |             |                               | 0.27 | 1q24.2 | F5/mis       | 1.20 (1.14; 1.26) | 2.65 × 10^{-11} |
|                                             | rs2066865      |             |                               | 0.30 | 4q32.1 | FGG/ inter   | 1.24 (1.18; 1.31) | 1.03 × 10^{-16} |
|                                             | rs4253417      |             |                               | 0.30 | 4q35.2 | F11/intr     | 1.27 (1.22; 1.34) | 1.21 × 10^{-21} |
|                                             | rs520965       |             |                               | 0.37 | chr9: 133,274,084 | ABO/intr⁵ | 1.55 (1.48; 1.63) | 4.23 × 10^{-75} |
|                                             | rs179963       |             |                               | 0.01 | 11p11.2 | F2/intr     | 2.29 (1.75; 2.99) | 1.73 × 10^{-9}  |
|                                             | rs6087685      |             |                               | 0.39 | 20q11.22 | PROCR/intr | 1.15 (1.10; 1.21) | 1.65 × 10^{-8}  |
|                                             | rs4602861      |             |                               | 0.39 | 8q23.1  | ZFPM2/intr   | 1.20 (1.13; 1.27) | 3.48 × 10^{-9}  |
|                                             | rs78707713     |             |                               | 0.05 | 10q22.1 | TSPAN15/intr | 1.28 (1.19; 1.39) | 5.74 × 10^{-11} |
|                                             | rs2288904      |             |                               | 0.18 | 19p13.2 | SLC4A2/mis  | 1.19 (1.12; 1.26) | 1.07 × 10^{-9}  |
|                                             | rs78707713     | European ancestry | 3009/2586 (Replication phase) | 0.05 | 10q22.1 | TSPAN15/intr | 1.42 (1.24; 1.62) | 2.21 × 10^{-7}  |
|                                             | rs2288904      |             |                               | 0.18 | 19p13.2 | SLC4A2/mis  | 1.28 (1.16; 1.40) | 2.64 × 10^{-7}  |
|                                             | rs4602861      | European ancestry | 10,516/55,218 (combined data) | 0.39 | 8q23.1  | ZFPM2/intr   | –                | 5.04 × 10^{-7}  |
|                                             | rs78707713     |             |                               | 0.05 | 10q22.1 | TSPAN15/intr | –                | 1.67 × 10^{-16} |
|                                             | rs2288904      |             |                               | 0.18 | 19p13.2 | SLC4A2/mis  | –                | 2.75 × 10^{-15} |
| GCST003377                                  | rs2323307⁶     | West African ancestry | 146/432 (Discovery phase) | 0.15 | 4q22.2  | ATOH1/inter  | 2.79 (1.80; 4.30) | 2.25 × 10^{-7}  |
|                                             | rs73692310     | Ancestry (80%) |                               | 0.15 | 7p12.3  | IGFBP3/inter | 3.04 (2.00; 4.70) | 1.73 × 10^{-9}  |
|                                             | rs58952918⁶    | European and Asian ancestry |                               | 0.17 | 18p11.32 | AP005230.1/intr | 2.48 (1.70; 3.70) | 1.07 × 10^{-8}  |
|                                             | rs28496996     | Asian ancestry |                               | 0.17 | 18p11.32 | AP005230.1/intr | 2.44 (1.60; 3.60) | 1.13 × 10^{-8}  |
|                                             | rs2144940      |             |                               | 0.31 | 20p11.21 | THBD, CD93/inter | 2.18 (1.60; 2.90) | 3.52 × 10^{-7}  |
|                                             | rs2567617⁷     |             |                               | 0.31 | 20p11.21 | THBD, CD93/inter | 2.17 (1.60; 2.90) | 4.01 × 10^{-7}  |
|                                             | rs1998081      |             |                               | 0.27 | 20p11.21 | THBD, CD93/inter | 2.28 (1.60; 3.10) | 5.17 × 10^{-7}  |
|                                             | rs687621       |             |                               | 0.38 | chr9: 133,261,662 | ABO/intr⁶ | 1.55 (1.20; 2.00) | 2.00 × 10^{-3}  |
|                                             | rs505922       |             |                               | 0.35 | chr9: 133,273,813 | ABO/intr⁶ | 1.52 (1.20; 2.00) | 2.00 × 10^{-3}  |
|                                             | rs657152       |             |                               | 0.39 | chr9: 133,263,862 | ABO/intr⁶ | 1.39 (1.10; 1.80) | 0.03       |
|                                             | rs73692310     | West African ancestry | 94/65 (Replication phase) | 0.09 | 7p12.3  | IGFBP3/inter | 1.27 (0.04; 2.70) | 0.60       |
|                                             | rs28496996     | Ancestry (77%) |                               | 0.13 | 18p11.32 | AP005230.1/intr | 1.34 (0.60; 2.60) | 0.45       |
|                                             | rs2144940      | European and Asian ancestry |                               | 0.35 | 20p11.21 | THBD, CD93/inter | 1.89 (1.10; 3.30) | 0.02       |
|                                             | rs1998081      | Asian ancestry |                               | 0.30 | 20p11.21 | THBD, CD93/inter | 1.94 (1.10; 3.50) | 0.02       |
|                                             | rs73692310     | West African ancestry | 240/497 (Combined data) | 0.02 | 7p12.3  | IGFBP3/inter | –                | 2.48 × 10^{-8} |
|                                             | rs28496996     | Ancestry (79%) |                               | 0.03 | 18p11.32 | AP005230.1/intr | –                | 6.37 × 10^{-8} |
|                                             | rs2144940      | European and Asian ancestry |                               | 0.12 | 20p11.21 | THBD, CD93/inter | –                | 1.88 × 10^{-8} |
|                                             | rs1998081      | Asian ancestry |                               | 0.11 | 20p11.21 | THBD, CD93/inter | –                | 4.62 × 10^{-8} |

(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 |
|---------------------------------------------|----------------|------------|-------------------------------|-----|-------|-------------|--------------|-------------------|---------|
| GCST003390                                  | rs6025         | European ancestry | 6135/252,827 (Discovery phase) | 0.01| 1q24.2 | F5/mis | 2.93 (2.72; 3.15) | 3.60 × 10^{-17} |
|                                             | rs7654093      |             |                               | 0.31| 4q32.1 | FGG/inter | 1.22 (1.17; 1.27) | 2.00 × 10^{-10} |
|                                             | rs4444878      |             |                               | 0.32| 4q35.2 | F11-ASI/inter | 0.81 (0.78; 0.84) | 7.00 × 10^{-28} |
|                                             | rs1799963      |             |                               | <0.01| 11p11.2 | F2/utr | 0.51 (0.46; 0.58) | 1.30 × 10^{-24} |
|                                             | rs34234989     |             |                               | 0.39| 20q11.22 | PROCRA/inter | 0.89 (0.85; 0.92) | 6.70 × 10^{-9} |
|                                             | rs529565       |             |                               | 0.37| chr9: 133,274,084 | ABO/intr | 0.72 (0.70; 0.75) | 7.10 × 10^{-6} |
|                                             | rs9797861      |             |                               | 0.21| 19p13.2 | SLCA42/inter | 1.15 (1.09; 1.20) | 6.10 × 10^{-9} |
|                                             | rs114209171    |             |                               | 0.24| Xq28   | FUND2/nc | 1.15 (1.11; 1.20) | 7.00 × 10^{-13} |
|                                             | rs72798544     |             |                               | 0.01| 2p21   | TSPAN15/inter | 1.17 (1.10; 1.24) | 2.90 × 10^{-7} |
|                                             | rs17490626     |             |                               | 0.04| 10q22.1 | TSPAN15/inter | 0.73 (0.65; 0.82) | 4.40 × 10^{-7} |
|                                             | rs113092656    |             |                               | 0.01| 6p24.1 | TSPAN15/inter | 0.73 (0.65; 0.82) | 4.40 × 10^{-7} |
|                                             | rs60942712     | European ancestry | 26,112 participants (Replication phase) | 0.06| 3p11.1 | TMEM170B/ADTRP/inter | 1.21 (1.12; 1.31) | 8.00 × 10^{-7} |
|                                             | rs114209171    | European ancestry | 26,112 participants (Replication phase) | 0.24| Xq28   | FUND2/nc | 1.08 (1.02; 1.14) | 0.01 |
| GCST004012                                  | rs1304029      | European ancestry | 212 children with VTE / 424 parents and siblings (Discovery phase) | 0.48| 6q13   | B3GAT2/inter | 0.48 (0.36; 0.65) | 2.00 × 10^{-6} |
|                                             | rs9293858      |             |                               | 0.26| 6q13   | RIMS1/inter | 0.48 (0.34; 0.67) | 8.00 × 10^{-6} |
|                                             | rs2748331      |             |                               | 0.41| 6q13   | B3GAT2/rr | 0.49 (0.36; 0.67) | 1.80 × 10^{-5} |
|                                             | rs10498910     |             |                               | 0.12| 6q14.1 | LOC105377862/inter | 2.21 (1.47; 3.31) | 6.89 × 10^{-5} |
|                                             | rs914958       |             |                               | 0.23| 1p22.1 | ABC4/inter | 0.50 (0.36; 0.70) | 1.80 × 10^{-5} |
|                                             | rs4529013      |             |                               | 0.28| 4q21.3 | MAPK10/inter | 0.53 (0.39; 0.72) | 2.00 × 10^{-5} |
|                                             | rs9957519      |             |                               | 0.27| 18q23 | -/inter | 0.46 (0.32; 0.68) | 2.10 × 10^{-5} |
|                                             | rs1865590      |             |                               | 0.31| 2q22.1 | THSD7B/inter | 1.97 (1.44; 2.68) | 2.40 × 10^{-5} |

(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>h</sup> | IGKV20R22-4/rr               | 0.43| (0.29; 0.63)| 3.30 × 10<sup>−5</sup> |             |                   |         |
| rs495828                                     | 0.16           | 9q34.2     | ABO/rr                        |     | −     | –           | 6.44 × 10<sup>−4</sup> |                   |         |
| rs505922                                     | 0.35           | chr9:133,273,813<sup>h</sup> | ABO/intr<sup>b</sup>         |     | −     | –           | 4.03 × 10<sup>−4</sup> |                   |         |
| rs657152                                     | 0.39           | chr9:133,263,862<sup>h</sup> | ABO/intr<sup>b</sup>         | 1.77| (1.34; 2.32)| 3.44 × 10<sup>−5</sup> |             |                   |         |
| rs13146272                                   | 0.44           | 4q35.1     | CVP4V2/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>−5</sup> |             |                   |         |
| rs4792119                                    | 0.21           | 17p12      | SHISA6/intr                   | 0.51| (0.37; 0.71)| 3.50 × 10<sup>−5</sup> |             |                   |         |
| rs9399770                                    | 0.48           | 6q16.3     | -/inter                       | 0.55| (0.42; 0.74)| 4.00 × 10<sup>−5</sup> |             |                   |         |
| rs17576372                                   | 0.27           | 1p22.1     | TGFBR3/intr                   | 1.84| (1.37; 2.47)| 4.57 × 10<sup>−5</sup> |             |                   |         |
| rs10247053                                   | 0.25           | 7p15.2     | -/inter                       | 0.53| (0.39; 0.72)| 5.35 × 10<sup>−5</sup> |             |                   |         |
| rs636434                                     | 0.34           | 6q12       | EYS/intr                      | 1.79| (1.34; 2.39)| 5.35 × 10<sup>−5</sup> |             |                   |         |
| rs10190178                                   | 0.31           | 2q22.1     | THSD7B/intr                   | 1.91| (1.40; 2.62)| 6.15 × 10<sup>−5</sup> |             |                   |         |
| rs5014872                                    | 0.12           | 2p16.3     | LOC73100/Interb               | 0.46| (0.32; 0.68)| 6.21 × 10<sup>−5</sup> |             |                   |         |
| rs3823606                                    | 0.04           | 7q11.21    | TPST1/intr                    |     | −     | –           | 6.27 × 10<sup>−5</sup> |             |         |
| rs1565242                                    | 0.11           | 15q26.1    | LOC10537082/Intrb            | 0.44| (0.29; 0.67)| 7.23 × 10<sup>−5</sup> |             |                   |         |
| rs1958059                                    | 0.31           | 14q13.1    | NPS53/intr                   | 0.45| (0.31; 0.67)| 7.28 × 10<sup>−5</sup> |             |                   |         |
| rs1521882                                    | 0.23           | 2q33.1     | KIAA0212/intr                | 2.13| (1.46; 3.11)| 7.48 × 10<sup>−5</sup> |             |                   |         |
| rs17781793                                   | 0.05           | 12q15      | MRPL40P1/inter               | 0.38| (0.23; 0.63)| 7.81 × 10<sup>−5</sup> |             |                   |         |
| rs4775384                                    | 0.31           | 15q22.2    | AC104574.2/intr              | 0.41| (0.26; 0.65)| 8.36 × 10<sup>−5</sup> |             |                   |         |
| rs1948650                                    | 0.33           | 15q14      | DPH6-DT/intr                 | 1.84| (1.34; 2.51)| 8.71 × 10<sup>−5</sup> |             |                   |         |
| rs436985                                     | 0.34           | 5q12.1     | Csof64/intr                  | 0.58| (0.44; 0.76)| 9.13 × 10<sup>−5</sup> |             |                   |         |
| rs4926448                                    | 0.47           | 1q44       | SCCPDH/intr                  | 0.57| (0.43; 0.76)| 9.38 × 10<sup>−5</sup> |             |                   |         |
| rs11153626                                   | 0.22           | 6q22.1     | FAM162B/inter                | 1.85| (1.34; 2.54)| 9.49 × 10<sup>−5</sup> |             |                   |         |
| rs2214810                                    | 0.26           | 7p15.2     | -/inter                      | 0.54| (0.40; 0.74)| 9.62 × 10<sup>−5</sup> |             |                   |         |
| rs2748331 European ancestry                  | 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/Intrb           |     | −     | –           | 5.74 × 10<sup>−5</sup> |             |         |
| rs2748331 European ancestry                  | 0.41           | 6q13       | B3GAT2/rr                     | 1.20| (1.02; 1.40)| 0.02<sup>b</sup>       |             |                   |         |
| rs1304029 European ancestry                  | 0.48           | 6q13       | B3GAT2/intr                   | 1.18| (1.02; 1.36)| 0.03<sup>b</sup>       |             |                   |         |

(continued on next page)
| 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 |
|---------------------------------------------|----------------|------------|-------------------------------|-----|-------|-------------|--------------|-------------------|---------|
| GCST004068                                   | rs138916004<sup>a</sup> | African ancestry (Discovery phase) | 393/4941 (Continued) | < 0.01 | 12q14.3 | LEMD3/intr | 3.17 (2.13; 4.72)<sup>b</sup> | 1.27 × 10<sup>−8</sup> |
|                                             | rs3804476<sup>c</sup> | African ancestry (African-Americans) | 0.28 | 6p25.1 | LY6/intr | 1.83 (1.48; 2.26)<sup>b</sup> | 1.97 × 10<sup>−8</sup> |
|                                             | rs142143628<sup>a</sup> | European ancestry | < 0.01 | 22q12.2 | LOC10030298/intr<sup>d</sup> | 4.97 (2.80; 8.83)<sup>b</sup> | 4.35 × 10<sup>−8</sup> |
|                                             | rs6025           | European ancestry (Phase) | 0.01 | 1q24.2 | F5/mis | 5.00 (2.02; 11.03)<sup>b</sup> | 2.00 × 10<sup>−4</sup> |
|                                             | rs8176746        | European ancestry | 0.15 | 8q34.2 | ABO/mis | 1.33 (1.09; 1.62)<sup>b</sup> | 5.00 × 10<sup>−3</sup> |
|                                             | rs8176719        | European ancestry | 0.34 | 8q34.2 | ABO/fra | 1.30 (1.11; 1.53)<sup>b</sup> | 2.00 × 10<sup>−3</sup> |
|                                             | rs77121243<sup>e</sup> | European ancestry | 0.03 | 11p15.4 | HBB/miss | 1.51 (1.11; 2.06) | 9.00 × 10<sup>−3</sup> |
| GCST004256                                   | rs6025           | European ancestry (Discovery phase) | 3290/116,868 (Replication) | 0.01 | 1q24.2 | F5/mis | 3.49 (2.96; 4.11) | 7.10 × 10<sup>−5</sup> |
|                                             | rs2606865        | European ancestry (Phase) | 0.30 | 4q32.1 | FGG/inter | 1.21 (1.15; 1.29) | 3.10 × 10<sup>−1</sup> |
|                                             | rs4253416        | European ancestry (Phase) | 0.41 | 4q35.2 | F11/intr | 1.18 (1.12; 1.24) | 2.00 × 10<sup>−3</sup> |
|                                             | rs2519093        | European ancestry (Phase) | 0.14 | chr9:133,266,456<sup>f</sup> | ABO/intr<sup>a</sup> | 1.41 (1.32; 1.50) | 6.00 × 10<sup>−6</sup> |
|                                             | rs8176645        | European ancestry (Phase) | 0.38 | 9q34.2 | ABO/intr<sup>a</sup> | 1.28 (1.22; 1.35) | 4.40 × 10<sup>−2</sup> |
|                                             | rs1799963        | European ancestry (Phase) | < 0.01 | 11p11.2 | F2/inter | 2.63 (2.03; 3.40) | 4.90 × 10<sup>−1</sup> |
|                                             | rs3136516        | European ancestry (Phase) | 0.28 | 11p11.2 | F2/inter | 1.10 (1.04; 1.15)<sup>b</sup> | 3.30 × 10<sup>−4</sup> |
|                                             | rs4602861        | European ancestry (Phase) | 0.39 | 8q23.1 | ZFM2/inter | 1.08 (1.03; 1.15) | 4.50 × 10<sup>−3</sup> |
|                                             | rs4602861        | European ancestry (Phase) | 0.39 | 8q23.1 | ZFM2/inter | 1.13 (1.08; 1.19) | 5.04 × 10<sup>−7</sup> |
|                                             | rs3316516        | European ancestry (Phase) | 0.28 | 11p11.2 | F2/inter | 1.10 (1.06; 1.15)<sup>b</sup> | 5.65 × 10<sup>−6</sup> |
|                                             | rs4602861        | European ancestry (Phase) | 0.39 | 8q23.1 | ZFM2/inter | 1.11 (1.07; 1.15) | 4.88 × 10<sup>−10</sup> |
|                                             | rs3136516        | European ancestry (Phase) | 0.28 | 11p11.2 | F2/inter | 1.10 (1.06; 1.15)<sup>b</sup> | 7.60 × 10<sup>−9</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 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 × 10<sup>−8</sup>), but only the hit SNPs of each locus (F5, FGC, 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>§</sup> After Bonferroni correction, the P-values became insignificant
<sup>§</sup> P-values of permutation testing
<sup>a</sup> After adjusting for sickle cell risk variant (HBB rs77121243-T allele) and other cofactors
<sup>a</sup> After adjusting for rs1799963.
<sup>a</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>a</sup> SNPs not tested in replication cohort due to high LD or due to failed assay
<sup>x</sup> SNPs further replicated using parametric bootstrap, internal cross-validation and meta-analysis methods
<sup>b</sup> SNP merged into rs334 according to “NCBI” database
| Locus | Gene/Variant | Population | No. cases/controls (combined) | MAF | Locus | Gene/Variant | OR | P-value |
|-------|--------------|------------|-----------------------------|-----|-------|--------------|----|---------|
| rs493014 | GCST001913 | European ancestry | 1953/2338 (Meta analysis of two previous GWAS) | 0.30 | 9q34.2 | SURF6/inter | 1.64 | 6.00 x 10^{-11} |
| rs886090 |     |             |                             | 0.32 | 9q34.2 | SURF6/mis |   |         |
| rs1336472 |     |             |                             | 0.40 | 1p31.3 | AK4/utr | 1.54 | 4.24 x 10^{-10} |
| rs4715555 |     |             |                             | 0.38 | 6p12.1 | HMGCLL1/inter |   |         |
| rs380904 |     |             |                             | 0.29 | 8q24.3 | ZC3H3/intr | 1.67 | 4.51 x 10^{-10} |
| rs8086028 |     |             |                             | 0.30 | 18p11.22 | PIEZO2/utr |   |         |
| rs6815916 |     |             |                             | 0.09 | 4q34.3 | TNEM3-AS1/inter | 2.10 | 6.84 x 10^{-10} |
| rs6092326 |     |             |                             | 0.47 | 20q13.31 | FAM209B/inter |   |         |
| rs2282015 |     |             |                             | 0.41 | 10q26.13 | AL160290.2/intr | 1.50 | 8.36 x 10^{-10} |
| rs13050454 |     |             |                             | 0.42 | 21q21.3 | AP001595.1/inter |   |         |
| rs7648704 |     |             |                             | 0.33 | 3p22.3 | TRIM71/rr | 1.56 | 9.89 x 10^{-10} |
| rs4868644 |     |             |                             | 0.49 | 5q35.2 | RNF44/inter |   |         |
| rs1985317 |     |             |                             | 0.41 | 9q33.1 | ALA45644.1/inter | 0.66 | 1.32 x 10^{-9} |
| rs827637 |     |             |                             | 0.46 | 10p14 | ACO44784.1/inter |   |         |
| rs2321744 |     |             |                             | 0.10 | 13q13.2 | RFC3/inter | 0.49 | 1.38 x 10^{-9} |
| rs6497540 |     |             |                             | 0.42 | 16p13.2 | GRIN2A/intr |   |         |
| rs315122 |     |             |                             | 0.30 | 12q15 | YEATS4/intr | 2.05 | 1.42 x 10^{-9} |
| rs884483 |     |             |                             | 0.12 | 15q23 | TLE3/inter |   |         |
| rs1423386 |     |             |                             | 0.20 | 5q12.1 | LBRCT70/inter | 1.73 | 1.63 x 10^{-9} |
| rs6491679 |     |             |                             | 0.29 | 13q33.1 | FGF14/intr |   |         |
| rs7714670 |     |             |                             | 0.44 | 5q13.2 | ARHGEF28/miss | 1.52 | 1.75 x 10^{-9} |
| rs12880735 |    |             |                             | 0.35 | 14q12 | AL390334.1/intr |   |         |
| rs9392653 |     |             |                             | 0.28 | 6p25.1 | PPPIR3G/inter | 1.74 | 1.83 x 10^{-9} |
| rs7780976 |     |             |                             | 0.19 | 7p21.2 | DGX8/inter |   |         |
| rs9804128 |     |             |                             | 0.26 | 1p36.13 | IGSF21/intr | 1.71 | 1.90 x 10^{-9} |
| rs4784379 |     |             |                             | 0.24 | 16q12.2 | IRX3/inter |   |         |
| rs1364505 |     |             |                             | 0.32 | 7q32.3 | PLXNA4/intr | 1.80 | 2.10 x 10^{-9} |
| rs1204660 |     |             |                             | 0.16 | 20q11.22 | UQCC1/intr |   |         |
| rs2288073 |     |             |                             | 0.29 | 2q23.3 | FAM228A/miss | 1.60 | 2.11 x 10^{-9} |
| rs10771022 |    |             |                             | 0.34 | 12p12.1 | SOX5/intr |   |         |
| rs1367228 |     |             |                             | 0.44 | 2p16.1 | EFEMP1/intr | 1.49 | 2.20 x 10^{-9} |
| rs3905075 |     |             |                             | 0.40 | 13q33.3 | FAM155AT1/intr |   |         |
| rs536477 |     |             |                             | 0.43 | 1q43 | CHR3/intr | 0.63 | 2.93 x 10^{-9} |
| rs1937920 |     |             |                             | 0.27 | 10p15.1 | AKR1C2/inter |   |         |
| rs2710201 |     |             |                             | 0.06 | 7q36.2 | ACTR3B/inter | 0.40 | 3.30 x 10^{-9} |
| rs3780293 |     |             |                             | 0.35 | 9q21.2 | GNAH4/intr |   |         |
| rs12541254 |    |             |                             | 0.34 | 8p22 | DLC1/intr | 1.65 | 3.33 x 10^{-9} |
| rs305009 |     |             |                             | 0.23 | 15q23 | TLE3/inter |   |         |

(continued on next page)
| Report | Pairwise SNP interactions** | Population | No. cases/controls (combined) | MAF | Locus | Gene/Variant | OR | P-value |
|--------|-----------------------------|------------|-------------------------------|-----|-------|-------------|----|---------|
| rs4507975 |                            |            |                               | 0.29 | 1q25.2 | PAPPA2/intr  | 0.65 | 3.58 × 10⁻⁹ |
| rs9914518 |                            |            |                               | 0.47 | 1p13.1 | GSG112/intr  | 0.67 | 3.82 × 10⁻⁹ |
| rs2771051 |                            |            |                               | 0.37 | 9q33.1 | -/inter     | 0.63 | 3.86 × 10⁻⁹ |
| rs827637  |                            |            |                               | 0.46 | 10p14  | -/inter     | 0.63 | 3.86 × 10⁻⁹ |
| rs1056089 |                            |            |                               | 0.31 | 5q35.1 | SMIM23/intr  | 0.63 | 3.86 × 10⁻⁹ |
| rs11072930 |                           |            |                               | 0.29 | 15q25.1 | ARNT2/intr  | 1.88 | 4.46 × 10⁻⁹ |
| rs10504130 |                          |            |                               | 0.14 | 18q11.22 | PCMTD1/intr | 0.43 | 4.54 × 10⁻⁹ |
| rs2847351  |                            |            |                               | 0.31 | 18p11.22 | APCDD1/intr | 1.86 | 4.70 × 10⁻⁹ |
| rs318497   |                            |            |                               | 0.49 | 6p25.22 | AL133351.3/nc | 0.43 | 4.54 × 10⁻⁹ |
| rs7019259  |                            |            |                               | 0.07 | 9q21.2 | PSAT1/intr  | 0.43 | 4.54 × 10⁻⁹ |
| rs6695223  |                            |            |                               | 0.13 | 1p22.3  | WDR63/intr  | 0.58 | 4.85 × 10⁻⁹ |
| rs1763510  |                            |            |                               | 0.39 | 6q23.2  | SK1/intr    | 2.13 | 5.26 × 10⁻⁹ |
| rs1336708  |                            |            |                               | 0.25 | 1q33.1  | FGF14-IT1/intr | 2.03 | 7.14 × 10⁻⁹ |
| rs1423386  |                            |            |                               | 0.20 | 5q12.1  | CKS1BP3/intr | 2.13 | 5.26 × 10⁻⁹ |
| rs6771316  |                            |            |                               | 0.13 | 3p13    | LINCO0877/intr | 2.13 | 5.26 × 10⁻⁹ |
| rs10986432 |                            |            |                               | 0.17 | 9q33.3  | OLFML2A/intr | 2.13 | 5.26 × 10⁻⁹ |
| rs664910   |                            |            |                               | 0.30 | 3p21.3  | MGCL1/intr  | 1.50 | 6.63 × 10⁻⁹ |
| rs877228   |                            |            |                               | 0.46 | 15q22.2 | ROR2/intr   | 1.50 | 6.63 × 10⁻⁹ |
| rs9945428  |                            |            |                               | 0.30 | 18q11.22 | FBX015/intr | 0.62 | 6.88 × 10⁻⁹ |
| rs4823535  |                            |            |                               | 0.27 | 2q13.33 | FAM19A5/intr | 2.03 | 7.14 × 10⁻⁹ |
| rs1910358  |                            |            |                               | 0.23 | 5q14.2  | C5orf17/intr | 2.03 | 7.14 × 10⁻⁹ |
| rs9981595  |                            |            |                               | 0.11 | 21q22.2 | BRWD1/intr  | 2.03 | 7.14 × 10⁻⁹ |
| rs6771725  |                            |            |                               | 0.27 | 3q26.31 | NAAAL1D2/intr | 2.22 | 8.60 × 10⁻⁹ |
| rs10507246 |                            |            |                               | 0.09 | 12q24.21 | TBX5/intr  | 2.22 | 8.60 × 10⁻⁹ |
| rs16865717 |                            |            |                               | 0.28 | 2p25.2  | RSD2/intr   | 1.56 | 8.82 × 10⁻⁹ |
| rs2009559  |                            |            |                               | 0.36 | 20q12   | -/inter     | 1.56 | 8.82 × 10⁻⁹ |
| rs3023845  |                            |            |                               | 0.16 | 12q23.1 | ACO07513/intr | 1.69 | 8.82 × 10⁻⁹ |
| rs20382277 |                            |            |                               | 0.38 | 16p13.3 | RAB11FIP3/intr | 1.69 | 8.82 × 10⁻⁹ |
| rs10476160 |                            |            |                               | 0.20 | 5q35.2  | SNX11/intr  | 0.62 | 9.09 × 10⁻⁹ |
| rs1707420  |                            |            |                               | 0.48 | 8p23.2  | -/inter     | 0.62 | 9.09 × 10⁻⁹ |
| rs971572   |                            |            |                               | 0.32 | 1q25.3  | TSEN15/intr | 0.42 | 9.30 × 10⁻⁹ |
| rs10828151 |                            |            |                               | 0.07 | 10p12.31 | NEBL/intr  | 0.42 | 9.30 × 10⁻⁹ |
| rs6858430  |                            |            |                               | 0.21 | 4q34.1  | ADAM29/intr | 1.62 | 9.67 × 10⁻⁹ |
| rs4800250  |                            |            |                               | 0.40 | 1p11.22 | TAF4B/intr  | 0.67 | 9.91 × 10⁻⁹ |
| rs467650   |                            |            |                               | 0.37 | 5q15    | RGMB/intr   | 0.67 | 9.91 × 10⁻⁹ |
| rs7153749  |                            |            |                               | 0.44 | 1q23.1  | LINCO1500/intr | 0.67 | 9.91 × 10⁻⁹ |

++ 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 x 10^-5 | [2]        |
|      | rs1018827 | Validation              | 1040/16,936                  | 0.07*       | 1.53 (1.29–1.79) (AA vs. AG) | 6.53 x 10^-6 | [3]        |
|      | rs6427196 | Validation             | 1040/16,936                  | 0.09*       | 1.51 (1.28–1.78) (CC vs. CG) | 9.21 x 10^-6 | [3]        |
|      | rs2420371 | –                      | –                            | –           | –                          | –       | –          |
| 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 x 10^-4 | [7]        |
|      | rs7659024 | Validation             | 1040/16,936                  | 0.30*       | 1.40 (1.09–1.78) (AA vs. GG) | 3.03 x 10^-2 | [3]        |
|      | rs6536024 | Validation             | 1040/16,936                  | 0.46*       | –                          | **0.23  | [3]        |
|      | rs7654093 | –                      | –                            | –           | –                          | –       | –          |
| F11  | rs3756008 | Candidate gene approach | 1837/2204                    | 0.41**      | 1.28 (1.15–1.43)           | 6.33 x 10^-6 | [2]        |
|      | rs4253399 | Candidate gene approach | 1488/1439                    | 0.24**      | 1.68 (1.48–1.91)           | 8.08 x 10^-16 | [2]        |
|      | rs4253417 | –                      | –                            | –           | –                          | –       | –          |
|      | rs4444878 | –                      | –                            | –           | –                          | –       | –          |
|      | rs4253418 | –                      | –                            | –           | –                          | –       | –          |
| ABO  | rs2519093 | Candidate gene approach | 1488/1439                    | 0.24**      | 1.47 (1.32–1.64)           | 5.68 x 10^-12 | [2]        |
|      | rs505922  | Validation             | 1040/16,936                  | 0.35*       | 1.78 (1.46–2.15) (CC vs. TT) | 5.17 x 10^-11 | [3]        |
|      | rs630014  | Validation             | 1040/16,936                  | 0.42**      | 0.75 (0.67–0.84)           | 2.67 x 10^-7 | [2]        |
| ABO  | rs8176719 | Validation             | 1040/16,936                  | 0.42**      | 1.62 (1.09–2.38)           | 0.015   | [9]        |
|      | rs8176721 | Validation             | 96/148                       | 0.48       | 1.74 (1.43–2.10) (AA vs. GG) | 5.45 x 10^-10 | [3]        |
|      | rs495828  | Validation             | 1040/16,936                  | 0.16*       | 2.09 (1.64–2.63) (GG vs. TT) | 1.72 x 10^-10 | [3]        |
|      | rs8176750 | –                      | –                            | –           | –                          | –       | –          |
|      | rs657152  | –                      | –                            | –           | –                          | –       | –          |
|      | rs529565  | –                      | –                            | –           | –                          | –       | –          |
|      | rs8176645 | –                      | –                            | –           | –                          | –       | –          |
| C4BPB| rs3813948 | Validation             | 1433/1402                    | 0.07       | –                          | 0.25    | [10]       |
| NME7 | rs16861990 | Validation            | 1040/16,936                  | 0.06*       | 4.11 (2.14–7.33) (CC vs. AA) | 2.90 x 10^-7 | [3]        |
| PROCR| rs6087685 | Validation             | 1040/16,936                  | 0.39*       | –                          | **0.92  | [3]        |
|      | rs34234989 | –                      | –                            | –           | –                          | –       | –          |

(continued on next page)
| 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 × 10⁻³   | [3]        |
|       | rs17490626 |                |                               |             |                             |               |            |
| ZFPM2  | rs4602861  |                |                               |             |                             |               |            |
| SLC44A2 | rs2288904  | Validation     | 1040/16,936                   | 0.18∗       | 0.63 (0.44–0.89) (AA vs. GG) | 2.42 × 10⁻²   | [3]        |
|       | rs9797861† |                |                               |             |                             |               |            |
| SLC19A2 | rs2038924  |                |                               |             |                             |               |            |
| CCDC181 | rs1208134  |                |                               |             |                             |               |            |
| CNTN5  | 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)

† SNP in high LD with rs6427196, particularly for European ancestry populations \(r^2>0.81\), according to “Ensembl” database

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

§ SNP in high LD with rs8176719, particularly for European ancestry populations \(r^2>0.90\), according to “Ensembl” database

∥ SNP in high LD with rs6087685 for all populations according to “Ensembl” database \(r^2>0.86\) except in Kenya population

¶ SNP in high LD with rs78707713 for most populations, particularly the European ancestry populations \(r^2=1\), according to “Ensembl” database

†† 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            | Coagulation Factor V                     | Generation of thrombin                                             | Metastasis, angiogenesis, immune evasion and apoptosis [11]      |
| CCDC181 (C1orf14) | Coiled-Coil Domain Containing 181        | Despite the unknown role in carcinogenesis, this gene is frequently methylated in patients with prostate cancer [12] | Genome instability and mutation                                   |
| ABO           | ABO Blood Group                          | Activation of adhesion molecules [13]                             | Inflammation, immune evasion and metastasis [13, 14]             |
| C4BPB         | Complement Component 4 Binding Protein Beta | 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] |
| NME7/FGB/FGG  | NME/NM23 Family Member 7                | Embryonic Stem Cell Renewal [19]                                  | Metastasis                                                      |
|               | Fibrinogen Beta Chain/ Fibrinogen Gamma Chain/ Fibrinogen Alpha Chain | Formation of fibrin clot                                           | Angiogenesis [11]                                               |
|               |                                          | Immune response [20]                                              | Immune evasion and inflammation                                  |
|               |                                          | Augmentation of the proliferative effect of fibroblast growth factor-2 (FGF-2) [21] | Proliferative signalling and angiogenesis [21]                  |
| F11           | Coagulation Factor XI                    | Generation of Factor Xa                                            | Apoptosis [22]                                                  |
|               |                                          | Generation of thrombin                                             | Metastasis, angiogenesis, immune evasion and apoptosis [11]     |
|               |                                          |                                                                    | Cancer metabolism                                               |
| SLC19A2       | Solute Carrier Family 19 Member 2        | Metabolism                                                        | Metastasis, angiogenesis, immune evasion and apoptosis [11]     |
| F2            | Coagulation Factor II, thrombin          | Generation of thrombin                                             | Proliferative signalling and metastasis [11]                   |
| CNTN6         | Contactin 6                              | Activating of Notch signalling pathway [23]                        | Metastasis [24]                                                 |
| OTUD7A        | OTU Deubiquitinase 7A                    | Modulation of nuclear factor kappa B (NF-κB) expression through interaction with TNF receptor associated factor 6 (TRAF6) | Apoptosis and inflammation [26]                                |
| SV2C          | Synaptic Vesicle Glycoprotein 2C         | Modulation of dopamine release [25]                               |                                                                  |

(continued on next page)
Table 4 (continued)

| Genes          | HUGO nomenclature          | Molecular processes that promote carcinogenesis                                                                 | Potential cancer hallmarks                                                                 |
|----------------|----------------------------|---------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| SUSD1          | Sushi Domain Containing 1  | Unknown role in carcinogenesis                                                                                 | unknown                                                                                 |
| PROCR          | Protein C Receptor         | Protein C pathway                                                                                              | Proliferative signalling, invasion, metastasis, apoptosis and immune evasion [27]          |
| ZFPM2 (FOG2)   | Zinc Finger Protein, FOG Family Member 2 | GATA transcriptional network                                                                                   | Angiogenesis [28]                                                                         |
| TSPAN15        | Tetraspanin 1S             | Mediates signal transduction events that play a role in the regulation of cell activation, growth, development and motility. | Apoptosis, invasion and inflammation [29]                                                |
| SLC44A2        | Solute Carrier Family 44 Member 2 | Metabolism                                                                                                     | Metastasis, angiogenesis and immune evasion [33]                                         |
| FUND2C         | FUN14 Domain Containing 2  | Modulation of platelet survival [32]                                                                           | Cancer metabolism                                                                         |
| COX7A2L        | Cytochrome C Oxidase Subunit 7A2 Like | Regulation of oxidative phosphorylation                                                                          | Metastasis, angiogenesis and immune evasion [33]                                         |
| EPHA3          | EPH Receptor A3            | Regulation of developmental events                                                                             | Cancer metabolism                                                                         |
|                |                            | Regulation of cytoskeletal organization, cell-cell adhesion and cell migration                                   | Invasion and metastasis [34]                                                              |
|                |                            |                                                                                                                | Angiogenesis [35]                                                                         |
| B3GAT2         | Beta-1,3-Glucuronyltransferase 2 | Mismatch repair deficiency [36]                                                                               | Genome instability and mutation                                                            |
| THBD           | Thrombomodulin             | Protein C pathway                                                                                              | Angiogenesis [28]                                                                         |
| LEMD3 (MAN1)   | LEM Domain Containing 3    | Regulation of transforming growth factor-beta (TGF-beta) signalling at the inner nuclear membrane                | Invasion and metastasis [37]                                                             |
|                |                            |                                                                                                                | Proliferative signalling, invasion and apoptosis [38]                                    |
| LY86 (MD-1)    | Lymphocyte Antigen 86      | Innate Immune System                                                                                           | Immune evasion [39]                                                                       |
| LOC100130298   | HCG1816373-Like            | Unknown role in carcinogenesis                                                                                 | Inflammation                                                                             |

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.

Acknowledgements

We would like to thank the Liga Portuguesa Contra o Câncer-Centro Regional do Norte, Ministério da Saúde de Portugal (CFICS-45/2007), I.P.O.-Porto Projects CI-IPOP-91-2015 and CI-IPOP-22-2015, and Fundação para a Ciência e Tecnologia (FCT).

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.

References

[1] F. Rosendaal, T. Koster, J. Vandenbroucke, P. Reitsma, High risk of thrombosis in patients homozygous for factor V Leiden (activated protein C resistance)[see comments], Blood 85 (1995) 1504–1508.
[2] J.A. Heit, J.M. Cunningham, T.M. Petterson, S.M. Armasu, D.N. Rider, M. de Andrade, Genetic variation within the anticoagulant, procoagulant, fibrinolytic and innate immunity pathways as risk factors for venous thromboembolism, J. Thromb. Haemost. 9 (2011) 1133–1142.
[3] M. Crous-Bou, I. De Vivo, C.A. Camargo Jr, R. Varraso, F. Grodstein, M.K. Jensen, P. Kraft, S.Z. Goldhaber, S. Lindström, C. Kabrhel, Interactions of established risk factors and a GWAS-based genetic risk score on the risk of venous thromboembolism, Thromb. Haemost. 116 (2016) 705–713.
[4] S.R. Poort, F.R. Rosendaal, P.H. Reitsma, R.M. Bertina, A common genetic variation in the 3′-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis, Blood 88 (1996) 3698–3703.
[5] I. Martinelli, T. Battaglioli, A. Tosetto, C. Legnani, L. Sottile, R. Ghiotto, P. Mannucci, Prothrombin A1991G polymorphism and the risk of venous thromboembolism, J. Thromb. Haemost. 4 (2006) 2582–2586.
[6] S.U. de Willige, M.C. de Visser, J.J. Houwing-Duistermaat, F.R. Rosendaal, H.L. Vos, R.M. Bertina, Genetic variation in the fibrinogen gamma gene increases the risk for deep venous thrombosis by reducing plasma fibrinogen γ’ levels, Blood 106 (2005) 4176–4183.
[7] D.-A. Tréguoët, S. Heath, N. Saut, C. Biron-Andreani, J.-F. Schved, G. Pernod, P. Galan, L. Drouet, D. Zelenika, I. Juhan-Vague, Common susceptibility alleles are unlikely to contribute as strongly as the FV and ABO loci to VTE risk: results from a GWAS approach, Blood 113 (2009) 5298–5303.
[8] I.D. Bezemer, L.A. Bare, C.J. Doggen, A.R. Arellano, C. Tong, C.M. Rowland, J. Catanese, B.A. Young, P.H. Reitsma, J.J. Devlin, Gene variants associated with deep vein thrombosis, JAMA 299 (2008) 1306–1314.
[9] L. Manco, C. Silva, T. Fidalgo, P. Martinho, A.B. Sarmento, M.L. Ribeiro, Venous thromboembolism risk associated with ABO, F11 and FGG loci, Blood Coagul. Fibrinolysis 29 (2018) 528–532.
[10] M. Bruzelli, M. Bottai, M. Sabater-Lleal, R. Strawbridge, A. Bergendal, A. Silveira, A. Sundström, H. Kieler, A. Hamsten, J. Odeberg, Predicting venous thrombosis in women using a combination of genetic markers and clinical risk factors, J. Thromb. Haemost. 13 (2015) 219–227.
[11] V. Tavares, R. Pinto, J. Assis, D. Pereira, R. Medeiros, Venous thromboembolism GWAS reported genetic makeup and the hallmarks of cancer: linkage to ovarian tumour behaviour, Biochim. Biophys. Acta Rev. Cancer 1873 (2020) 188331.
[12] S. Strand, T. Orntoft, K. Sørensøen, Prognostic DNA methylation markers for prostate cancer, Int. J. Mol. Sci. 15 (2014) 16544–16576.
[13] S. Kiechl, G. Paré, M. Barbalic, L. Qi, J. Dupuis, A. Delghani, J.C. Bis, R.C. Laxton, Q. Xiao, E. Bonora, Association of variation at the ABO locus with circulating levels of soluble intercellular adhesion molecule-1, soluble P-selectin, and soluble E-selectin: a meta-analysis, Circ. Cardiovasc. Genet. 4 (2011) 681–686.
[14] M. Franchini, G.M. Liumbruno, G. Lippi, The prognostic value of ABO blood group in cancer patients, Blood Transfus. 14 (2016) 434.
[15] M. Franchini, F. Frattini, S. Crestani, C. Bonfanti, G. Lippi, von Willebrand factor and cancer: a renewed interest, Thromb. Res. 131 (2013) 290–292.
[16] S.M. Rezende, R.E. Simmonds, D.A. Lane, Coagulation, inflammation, and apoptosis: different roles for protein S and the protein S–C4b binding protein complex, Blood 103 (2004) 1192–1201.
[17] T.N. Stitt, G. Conn, M. Goret, C. Lai, J. Bruno, C. Radzlejewski, K. Mattsson, J. Fisher, D.R. Gies, P.F. Jones, The anticoagulation factor protein S and its relative, Gas6, are ligands for the Tyro 3/Axl family of receptor tyrosine kinases, Cell 80 (1995) 661–670.

[18] J.D. Paccez, M. Vogelsang, M.I. Parker, L.F. Zerbini, The receptor tyrosine kinase Axl in cancer: biological functions and therapeutic implications, Int. J. Cancer 134 (2014) 1024–1033.

[19] C.H. Wang, N. Ma, Y.T. Lin, C.C. Wu, M. Hsiao, F.L. Lu, C.C. Yu, S.Y. Chen, J. Lu, A shRNA functional screen reveals Nme6 and Nme7 are crucial for embryonic stem cell renewal, Stem Cells 30 (2012) 2199–2211.

[20] G. Girmann, H. Pees, G. Schwarze, P. Scheurle, Immunosuppression by micromolecular fibrinogen degradation products in cancer, Nature 259 (1976) 399.

[21] A. Sahni, P. Simpson-Haidaris, S. Sahni, G. Vaday, C. Francis, Fibrinogen synthesized by cancer cells augments the proliferative effect of fibroblast growth factor-2 (FGF-2), J. Thromb. Haemost. 6 (2008) 176–183.

[22] S.H. Versteeg, C.A. Spek, D.J. Richel, M.P. Peppelenbosch, Coagulation factors Vila and Xa inhibit apoptosis and anoikis, Oncogene 23 (2004) 410.

[23] X.-Y. Cui, Q.-D. Hu, M. Tekaya, Y. Shimoda, B.-T. Ang, D.-Y. Nie, L. Sun, W.-P. Hu, M. Karsak, T. Duka, NB-3/Notch1 pathway via Deltex1 promotes neural progenitor cell differentiation into oligodendrocytes, J. Biol. Chem. 279 (2004) 25858–25865.

[24] Z. Xu, L. Lei, L. Wang, F. Zhang, X. Hu, Y. Gui, Snail1-dependent transcriptional repression of Cezanne2 in hepatocellular carcinoma, Oncogene 33 (2014) 2836.

[25] A.R. Dunn, K.A. Stout, M. Oza, K.M. Lohr, C.A. Hoffman, A.I. Bernstein, Y. Li, M. Wang, C. Sgobio, N. Sastry, Synaptic vesicle glycoprotein 2C (SV2C) modulates dopamine release and is disrupted in Parkinson disease, Proc. Natl. Acad. Sci. 114 (2017) E2253–E2262.

[26] Y.-L. Lan, X. Wang, J.-S. Xing, Z.-L. Yu, J.-C. Lou, X.-C. Ma, B. Zhang, Anti-cancer effects of dopamine in human glialoma: involvement of mitochondrial apoptotic and anti-inflammatory pathways, Oncotarget 8 (2017) 88488.

[27] E. Ducros, S. Mirshahi, D. Azzazene, S. Camilleri-Broët, E. Mery, H. Al Farsi, H. Althawadi, S. Besbess, J. Chidiac, E. Pujade-Lauraine, Endothelial protein C receptor expressed by ovarian cancer cells as a possible biomarker of cancer onset, Int. J. Oncol. 41 (2012) 433–440.

[28] M. Uchiba, K. Okajima, Y. Oike, Y. Ito, K. Fukudome, H. Isobe, T. Suda, Activated protein C induces endothelial cell proliferation by mitogen-activated protein kinase activation in vitro and angiogenesis in vivo, Circ. Res. 95 (2004) 34–41.

[29] M.S. Kumar, D.C. Hancock, M. Molina-Arcas, M. Steckel, P. East, M. Diefenbacher, E. Armerentos-Monterroso, F. Lasailly, N. Matthews, E. Nye, The GATA2 transcriptional network is requisite for RAS oncogene-driven non-small cell lung cancer, Cell 149 (2012) 642–655.

[30] S.H. Choi, D. Ruggiero, R. Sorice, C. Song, T. Nuttle, A.V. Smith, M.P. Concas, M. Traglia, C. Barbieri, N.C. Ndiaye, Six novel loci associated with circulating VEGF levels identified by a meta-analysis of genome-wide association studies, PLoS Genet. 12 (2016) e1005874.

[31] B. Zhang, Z. Zhang, L. Li, Y.-R. Qin, H. Liu, C. Jiang, T.-T. Zeng, M.-Q. Li, D. Xie, Y. Li, TSPAN15 interacts with BTRC to promote oesophageal squamous cell carcinoma metastasis via activating NF-κB signaling, Nat. Commun. 9 (2018) 1423.

[32] Q. Ma, C. Zhu, W. Zhang, N. Ta, R. Zhang, L. Liu, D. Feng, H. Cheng, J. Liu, Q. Chen, Mitochondrial PIP3-binding protein FUNDC2 supports platelet survival via Akt signaling pathway, Cell Death Differ. 26 (2019) 321.

[33] S. Jain, J. Harris, J. Ware, Platelets: linking hemostasis and cancer, Arterioscler. Thromb. Vasc. Biol. 30 (2010) 2362–2367.

[34] X. Chen, B. Lu, Q. Ma, C.D. Ji, J.Z. Li, EphA3 inhibits migration and invasion of esophageal cancer cells by activating the mesenchymal-epithelial transition process, Int. J. Oncol. 54 (2019) 722–732.

[35] X.Y. Lv, J. Wang, F. Huang, P. Wang, J.G. Zhou, B. Wei, S.H. Li, EphA3 contributes to tumor growth and angiogenesis in human gastric cancer cells, Oncol. Rep. 40 (2018) 2408–2416.

[36] M. Noda, H. Okayama, K. Tachibana, W. Sakamoto, K. Saito, A.K.T. Min, M. Ashizawa, T. Nakajima, K. Aoto, T. Momma, Glycosyltransferase gene expression identifies a poor prognostic colorectal cancer subtype associated with mismatch repair deficiency and incomplete glycan synthesis, Clin. Cancer Res. 24 (2018) 4468–4481.

[37] N. Zheng, Z. Huo, B. Zhang, M. Meng, Z. Cao, Z. Wang, Q. Zhou, Thrombomodulin reduces tumorigenic and metastatic potential of lung cancer cells by up-regulation of E-cadherin and down-regulation of N-cadherin expression, Biochem. Biophys. Res. Commun. 476 (2016) 252–259.

[38] B. Kaminska, A. Wesolowska, M. Danilikiewicz, TGF beta signalling and its role in tumour pathogenesis, Acta Biochim. Pol. Engl. Ed. 52 (2005) 329.

[39] L. Corelik, R.A. Flavell, Transforming growth factor-β in T-cell biology, Nat. Rev. Immunol. 2 (2002) 46.