SUPPLEMENTAL MATERIAL

MULTILOCUS GENETIC RISK SCORES FOR VENOUS THROMBOEMBOLISM RISK ASSESSMENT

Soria et al

Table 1. Genetic variants included in the different genetic risk scores (GRS) assessed: coefficients (weights) assigned to each genetic risk factor, and allele frequency and Hardy-Weinberg equilibrium (H-W) data obtained in the two studies, Sant Pau and MARTHA.

					GRS				SANT PAU		MARTHA	
SNP	**Gene**	**Mutation**	**Genetic risk group***	**Risk coefficient assigned**	**1**	**2**	**3**	**4**	**Rare allele Frequency**	**H-W**	**Rare allele frequency**	**H-W**
rs6025	*F5 Leiden*	R506	A carriers	1.589					0.01	0.873	0.11	0.008
rs118203905	*F5 Hong Kong*	F5 Hong Kong	A carriers	1.589							0.00	0.982
rs118203906	*F5 Cambridge*	F5 Cambridge	C carriers	1.589							0.00	---
rs1799963	*F2*	G20210A	A carriers	0.293					0.01	0.822	0.10	0.020
ABO**	*ABO*		A1 carriers	0.956								
rs8176719	*ABO*			--							0.36	0.262
rs1801020	*F12*	C46T	TT homoz.	1.633					0.21	0.033	0.23	0.223
rs5985	*F13*	V34L	GG homoz.	0.198					0.25	0.832	0.27	0.929
rs2232698	*SERPINE10*	R67X	T carriers	1.358					0.01	0.898	0.01	0.854
rs121909548	*SERPINC1*	A384S	T carriers	2.277					0.00	0.975	0.00	0.945
rs2036914	*FXI*		CT heter. TT homoz.	0.293 0.519					0.46	0.293	0.50	0.890
rs2066865	*FGG*		TT homoz.	0.344					0.21	0.739	0.23	0.028
rs710446	*KNG1*		CC homoz.	0.182					0.44	0.831	0.42	0.131
rs2289252	*FXI*		CT heter. TT homoz.	0.315 0.577					0.40	0.788	0.40	0.655

*Homoz.=Homozygous; Heter.=Heterozygous. ** ABO: A1 carriers (rs8176719, rs7853989, rs8176743, rs8176750)

Table 2: Data sources and results of the meta-analyses undertaken by the authors to assign a risk coefficient to each variant included in the genetic risk score.

	Gen	Reference	Number of cases	Number of controls	OR	Lower confidence interval	Upper confidence interval	Risk Coefficient assigned
rs6025-FVL	F5	1						1.589
rs118203905-F5 Hong-Kong	F5							1.589
rs118203906-F5 Cambridge	F5							1.589
rs1799963	F2	2						0.293
AB0	AB0	3						0.956
rs8176719	AB0	3,4						
rs1801020	F12							
		5	250	250	4.82	1.50	15.60	
		6	--	--	4.57	1.55	13.40	
		7	32463	32463	5.99	2.10	17.30	
Meta-analysis					5.12			1.633
rs5985	F13							
		8	221	254	0.63	0.38	0.82	
		9	3165	4909	0.85	0.77	0.95	
		10	475	475	0.80	0.60	1.00	
Meta-analysis					0.82			-0.198 (0.198)*
rs2232698	SERPINE10							
		11	1018	1018	3.35	1.30	8.60	
		12	250	250	5.70	1.25	26.0	
Meta-analysis					3.89			1.358
rs121909548	SERPINC1	13						
rs2036914	F11							
Bezemer (2008) : Heteroz. Homoz.		14	1314	2877	1.38 1.71	1.17 1.43	1.64 2.05	
Austin (2011) : Heteroz. Homoz.		15	1076	1239	1.20 1.60	0.92 1.20	1.70 2.30	
Meta-analysis: Heteroz. Homoz.					1.34 1.68			0.293 0.519
rs2066865	FGG	16, 17, 18						0.344
rs710446	KNG1	19						0.182
rs2289252	F11							0.315

								0.577
Arellano (2010) : Heteroz. Homoz.		20	3921	4634	1.37 1.78	1.24 1.57	1.51 2.01	
Austin (2011): Heteroz. Homoz.		21	1076	1239	1.40 1.80	1.10 1.30	1.80 2.50	
Meta-analysis: Heteroz. Homoz.					1.37 1.78			0.315 0.577

*In the case of the variant rs5985, the rare variant wasassociatedwithlowerprobabilitye of presenting a VTE. To build the GRS the common variant wasconsidered to beassociatedwith a higherprobability of presenting of VTE.

Table 3. Observed and expected strengths of associations between selected clinical or genetic factors and venous thromboembolic events and p-values for the differences between observed and expected values.

		SANT PAU			**MARTHA**		
	Expected coefficients	**Observed**			**Observed**		
		Coefficients	**Standard Error**	**p-value ***	**Coefficients**	**Standard Error**	**p-value***
Family History	1.185	0.711	0.240	0.323	NA	NA	NA
*F5*** †	1.589	2.803	0.755	0.421	0.805	0.178	0.028
F2- rs1799963 †	0.293	0.773	0.489	0.624	0.378	0.199	0.831
ABO (A1)†	0.956	0.997	0.224	0.927	0.428	0.280	0.346
F12- rs1801020 †	1.633	0.859	0.621	0.533	0.305	0.345	0.054
F13- rs5985 †	0.198	-0.078	0.224	0.538	0.171	0.152	0.929
SERPINE10- rs2232698 †	1.358	0.937	0.753	0.780	0.572	0.502	0.434
SERPINC1- rs121909548 †	2.277	1.476	1.174	0.733	-0.983	1.264	0.197
F11- rs2036914 Hetero	0.293	-0.039	0.273	0.543	0.228	0.207	0.875
Homo	0.519	0.028	0.395	0.534	0.206	0.258	0.544

FGG- rs2066865 †	0.344	-0.095	0.227	0.334	0.328	0.151	0.958
KNG1- rs710446b ‡	0.182	-0.206	0.278	0.485	-0.086	0.190	0.481
F11- rs2289252 Hetero	0.315	0.186	0.299	0.829	0.191	0.190	0.744
Homo	0.577	-0.017	0.403	0.461	0.965	0.262	0.459

*for the difference between observed and expected coefficients.

** Carrier of any risk allele (Leiden, Hong-Kong or Cambridge).

NA indicates not applicable.

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