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Supplemental Data

A Follow-Up Study of a Genome-wide Association Scan Identifies a Susceptibility Locus for Venous Thrombosis on Chromosome 6p24.1

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Table S1. Genotype Distribution of rs169713 According to Age of VT Status in Four Independent Case-Control Status

rs169713	GWAS		MARTHA		FARIVE		MEGA	
	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases
TT	757 (62%)	215 (51%)	472 (59%)	575 (51%)	353 (62%)	332 (59%)	2897 (64%)	2299 (61%)
TC	427 (35%)	170 (41%)	297 (37%)	466 (41%)	186 (33%)	189 (34%)	1414 (31%)	1270 (34%)
CC	44 (3%)	34 (9%)	32 (4%)	88 (8%)	25 (5%)	40 (7%)	208 (5%)	184 (5%)
MAF	0.210	0.284	0.225	0.284	0.209	0.240	0.202	0.218
P*	$p = 7.24 \times 10^{-6}$		$p = 2.49 \times 10^{-5}$		$p = 0.089$		$p = 0.014$	
OR [95%CI]+	1.495 [1.250 – 1.788]		1.370 [1.181 – 1.589]		1.192 [0.977 – 1.454]		1.099 [1.020 – 1.180]	

* Cochran-Armitage trend test's p-value

+ Allelic Odds Ratio with its 95% confidence interval

In the GWAS analysis, individuals were typed with the Illumina Sentrix HumanHap300 Beadchip. In all replication studies (MARTHA, FARIVE and MEGA), genotyping was performed using TaqMan technology (Applied Biosystems). Genotyping success rate for the rs169713 was 98.9%, 93,1%, 99.9%, in the MARTHA, FARIVE, MEGA, respectively

Table S2. Risk Factors Prevalence in VT Cases

	GWAS	MARTHA	FARIVE	MEGA
FV Leiden	18%	35%	11%	16%
FII Leiden	7%	15%	8%	5%
Non O blood group	NA	75%	70%	78%
Age of onset ≤ 50	100%	81%	43%	55%

Table S3. Genotype Distribution of rs169713 According to Age of VT Onset in Cases

rs169713	MARTHA		FARIVE		MEGA	
	≤ 50 years old	> 50 years old	≤ 50 years old	> 50 years old	≤ 50 years old	> 50 years old
TT	468 (51%)	107 (49%)	139 (58%)	186 (59%)	1274 (61%)	1025 (61%)
TC	378 (41%)	88 (41%)	79 (34%)	109 (35%)	699 (34%)	571 (34%)
CC	68 (8%)	20 (10%)	20 (8%)	19 (6%)	111 (5%)	73 (4%)
MAF	0.281	0.304	0.249	0.233	0.221	0.215

Table S4. Genotype Distribution of rs169713 According to FV Leiden Mutation in Cases

rs169713	MARTHA		FARIVE		MEGA	
	FV Leiden carriers	Non carriers	FV Leiden carriers	Non carriers	FV Leiden carriers	Non carriers
TT	205 (52%)	370 (50%)	35 (61%)	290 (59%)	384 (62%)	1913 (61%)
TC	152 (39%)	314 (43%)	17 (30%)	171 (35%)	211 (34%)	1059 (34%)
CC	34 (8%)	54 (7%)	5 (9%)	33 (6%)	25 (4%)	159 (5%)
MAF	0.281	0.286	0.237	0.240	0.211	0.220

Table S5. Genotype Distribution of rs169713 According to VT Status Separately in Males and Females

rs169713	MARTHA				FARIVE			
	Males		Females		Males		Females	
	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases
TT	218 (57%)	183 (54%)	254 (61%)	392 (50%)	143 (60%)	136 (62%)	210 (64%)	196 (58%)
TC	147 (38%)	131 (39%)	150 (36%)	335 (42%)	84 (36%)	69 (31%)	102 (31%)	120 (35%)
CC	18 (5%)	23 (7%)	14 (3%)	65 (8%)	10 (4%)	15 (7%)	15 (5%)	25 (7%)
MAF	0.239	0.263	0.213	0.294	0.219	0.225	0.202	0.249

rs169713	MEGA			
	Males		Females	
	Controls	Cases	Controls	Cases
TT	1389 (65%)	1031 (61%)	1508 (63%)	1268 (61%)
TC	646 (30%)	572 (34%)	768 (32%)	698 (34%)
CC	96 (5%)	77 (5%)	112 (5%)	107 (5%)
MAF	0.197	0.216	0.208	0.220

Table S6. Genotype Distribution of rs169713 According to VT Status Separately in Idiopathic and Non Idiopathic Patients

rs169713	MARTHA			FARIVE			MEGA		
	Controls	Idiopathic Cases	Non Idiopathic Cases	Controls	Idiopathic Cases	Non Idiopathic Cases	Controls	Idiopathic Cases	Non Idiopathic Cases
TT	472 (59%)	168 (53%)	406 (50%)	353 (63%)	93 (60%)	239 (59%)	2897 (64%)	638 (61%)	1574 (62%)
TC	297 (37%)	123 (39%)	342 (42)	186 (33%)	52 (34%)	137 (34%)	1414 (31%)	376 (36%)	837 (33%)
CC	32 (4%)	27 (8%)	60 (8%)	25 (4%)	9 (6%)	31 (7%)	208 (5%)	38 (3%)	136 (5%)
MAF	0.225	0.278	0.286	0.209	0.227	0.244	0.202	0.215	0.217

Table S7. Genotype Distribution of rs169713 According to VT Events in Cases

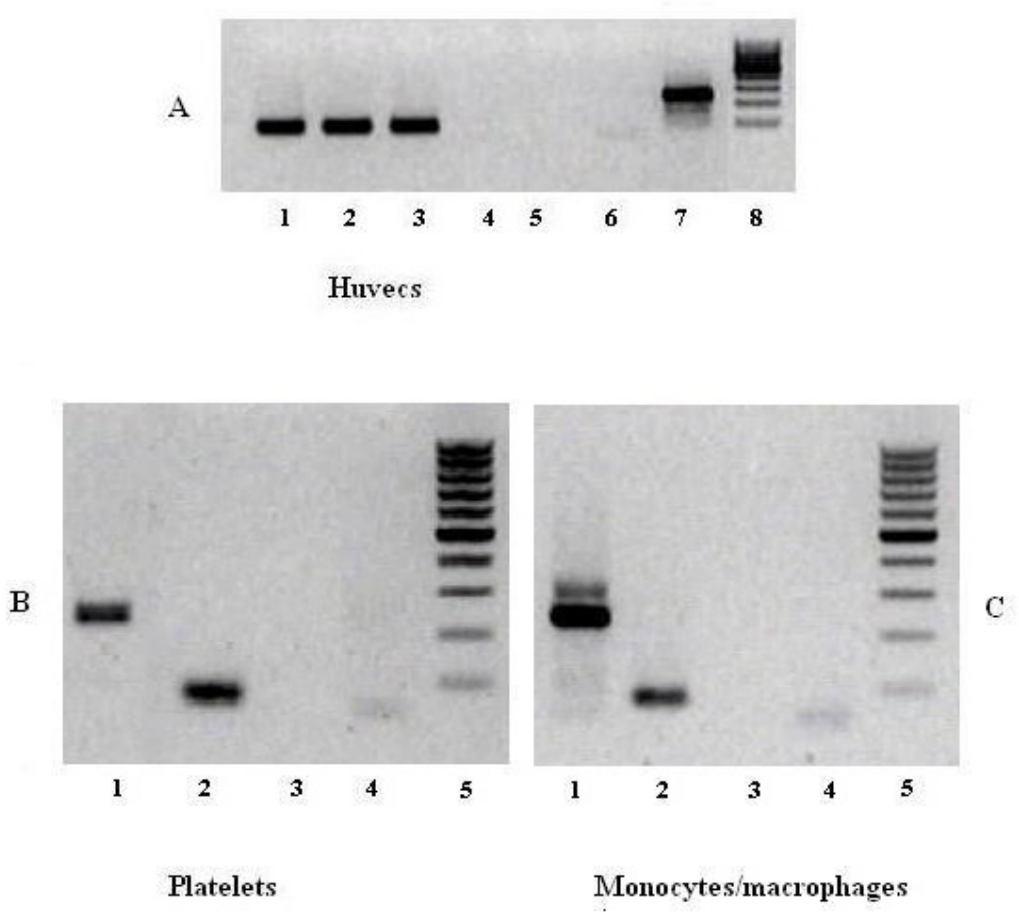
rs169713	MARTHA			FARIVE			MEGA		
	DVT	PE	DVT+PE	DVT	PE	DVT+PE	DVT	PE	DVT+PE
TT	440 (51%)	53 (49%)	82 (54%)	94 (59%)	129 (58%)	109 (61%)	1385(62%)	709 (60%)	205 (61%)
TC	364 (42%)	45 (42%)	57 (38%)	53 (33%)	77 (34%)	58 (33%)	747 (33%)	409(35%)	113 (34%)
CC	66 (7%)	10 (9%)	12 (8%)	13 (8%)	17 (8%)	10 (6%)	108 (5%)	58 (5%)	18 (5%)
MAF	0.285	0.301	0.268	0.247	0.249	0.220	0.215	0.223	0.222

Table S8. Association of SNPs at the *HIVEP1* Locus (Chromosome 6 : 12,120,710 – 12,273,217) with VT in the GWAS Scan

rsID	Position	MAF[1] Controls N = 1228	MAF[1] Cases N = 419	P value[2]
rs9368918	11952670	0.261	0.271	0.5570
rs6457906	11963601	0.087	0.094	0.4917
rs9366903	11966356	0.177	0.167	0.5144
rs932441	11968256	0.264	0.272	0.6318
rs4526189	11977931	0.360	0.370	0.5923
rs6457927	11978994	0.064	0.069	0.5637
rs2206928	11985018	0.096	0.107	0.3491
rs12211229	11994993	0.363	0.355	0.6881
rs6937349	12010577	0.072	0.087	0.1669
rs17406952	12016152	0.493	0.495	0.9157
rs876829	12026568	0.065	0.092	0.0082
rs6938400	12027400	0.251	0.235	0.3649
rs169713	**12028503**	**0.210**	**0.284**	**7.24×10^{-6}**
rs17533974	12029983	0.059	0.084	0.0133
rs209779	**12031151**	**0.146**	**0.211**	**1.04×10^{-5}**
rs9380643	**12038473**	**0.222**	**0.303**	**2.44×10^{-6}**
rs169715	12046783	0.050	0.050	0.9774
rs16872095	12053764	0.064	0.071	0.4993
rs1205887	12056122	0.136	0.183	**8.62×10^{-4}**
rs6927024	12068692	0.200	0.240	0.0139
rs6921943	**12069956**	**0.254**	**0.319**	**2.66×10^{-4}**
rs186017	12071208	0.122	0.124	0.8487
rs7775818	12073684	0.053	0.078	0.0099
rs9296224	**12080695**	**0.080**	**0.121**	**4.62×10^{-4}**
rs1409288	12082826	0.265	0.283	0.3109
rs4711507	12090447	0.213	0.206	0.6490
rs9380700	12099225	0.229	0.216	0.4434
rs6925772	12128227	0.192	0.206	0.3599
rs2327506	**12137410**	**0.418**	**0.499**	**5.48×10^{-5}**
rs9296237	12141237	0.049	0.074	0.0058
rs12234132	12150191	0.136	0.179	0.0020
rs1570989	12156813	0.217	0.226	0.6117
rs7749026	12172004	0.407	0.408	0.9609
rs4714170	12177683	0.249	0.269	0.2428
rs6916070	12179270	0.291	0.255	0.0411
rs2327508	12186698	0.399	0.420	0.3023
rs2327509	12186758	0.231	0.222	0.5644
rs9380764	12190200	0.060	0.081	0.0290
rs9380781	12207264	0.361	0.358	0.8717
rs7768491	12210601	0.107	0.138	0.0187
rs12213481	12219855	0.066	0.064	0.8802
rs4377779	12225330	0.355	0.356	0.9671
rs2228210	12230160	0.360	0.358	0.9045
rs2228220	12231235	0.111	0.142	0.0174
rs2228213	12232841	0.353	0.356	0.9103
rs1126472	12233758	0.123	0.160	0.0063
rs3777772	12243420	0.176	0.162	0.3601
rs2157494	12263635	0.248	0.252	0.8082

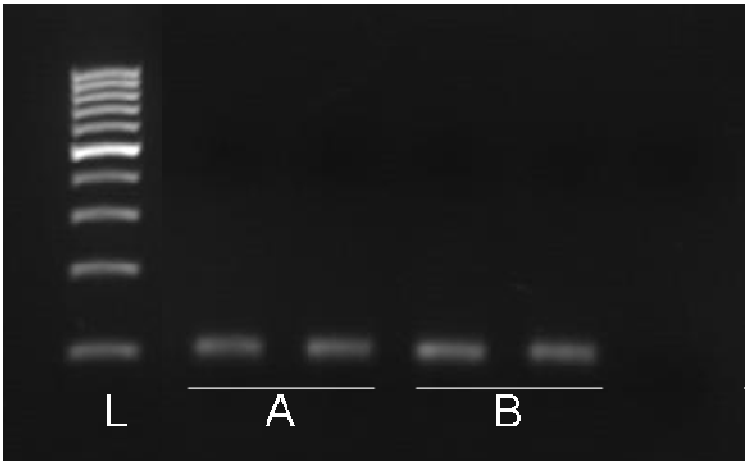
SNP associated with VT at $p < 10^{-3}$ are shown in bold.
[1] Minor Allele Frequency
[2] P values of the Cochran-Armitage trend test

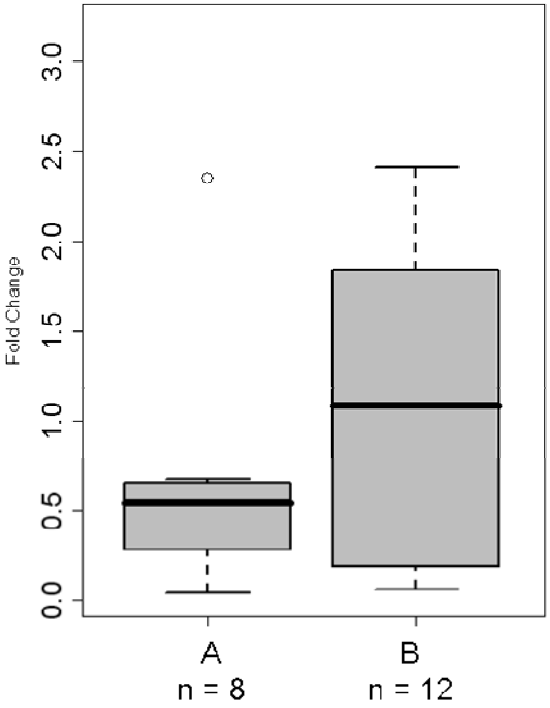
Figure S1. RT-PCR Amplification of *HIVEP1* in Huvecs (A), Platelets (B) and Monocytes/Macrophages (C)



A: Huvecs and leucocytes: lines 1-3: Huvec RT+; lines 4- 6: Huvecs RT-; line 7: genomic DNA, line 8: 100 bp DNA ladder
B: Platelets: line 1: genomic DNA, 2: RT+, 3: RT-, 4: H2O, 5: 100pb DNA ladder
C: monocytes/macrophages: line 1: genomic DNA, 2: RT+, 3: RT-, 4: H2O, 5: 100pb DNA ladder
Detailed experimental conditions for platelets and monocytes isolation, RNA extraction and RT-PCR can be obtained upon request.

Figure S2. RT-PCR Amplification (Left) and mRNA Expression (Right) of *HIVEP1* in Human Atherosclerotic Lesions





L: 100pb DNA ladder
A: fatty streaks
B: plaques

Fragments of human atherosclerotic lesions from full-thickness resections of carotids were obtained from the Department of Vascular Surgery (Pitié-Salpêtrière Hospital, Paris). Twenty fresh samples were dissected less than 3 hours after excision and divided into fatty streaks and plaques, and immediately extracted with Trizol (Invitrogen SARL, Cergy, France) for total RNA. RNA was purified with the RNeasy Kit (Qiagen GmbH, Hilden, Germany) and RNA preparations were subjected to Agilent Bioanalyser (Agilent, Massy, France). Only RNA with RIN >8 were amplified and used for RT-PCR.