Supplemental Table 1. SNP probe sequences for KASP™ genotyping assays.

SNP id	Gene	Minor allele	Probe sequence (forward strand)
rs10761741	*JMJD1C*	T	TTAGATTAATTTTTG[G/T]ATCCTATGGTCTCAT
rs11144351	*PIP5K1B*	G	CTAATTTCATTATGT[A/G]TCTTTGCAAGATTTT
rs12359150	*CUBN*	A	CAAATTCAACTCACC[A/G]AAAGGCCATCAAAAA
rs12566888	*PEAR1*	T	AGCTTTGTACTCCAG[G/T]ATAGGAAGTGATGAG
rs16876805	*ATP6VOD2*	C	TGAGGTTTCGGGATA[C/T]GGCCCTCTGGAGATT
rs2363910	*SHH*	T	TTTCCTATACCTGTT[G/T]ACCATGTGTATGTAT
rs2479008	*GMDS*	T	AAAAGATTCATTGAC[C/T]AGAGCTAATGAGCAA
rs342286	*PIK3CG*	G	ATCAACTGTGTTTca[A/G]taataatgggagagt
rs4128880	*RGS18*	T	ATACTTACTTAAAAG[C/T]ATTACTAAAATCACT
rs467053	*ADAMTS2*	C	GAGGACGGAGAGCTC[C/T]TGCTKTGAGCCGAGA
rs7940646	*MRVI1*	T	GGATGCTGCACTGTC[C/T]GGGTGAGTCAGCTTC
rs9996294	*RAPGEF2*	G	GTCATATTTTTAGCC[A/G]CTAAAGCAGATATGG

Supplemental Table 2: Sample size for each phenotype examined.

	Phase 2	Phase 3
Platelet Aggregation Measures		
1° ADP PRP aggregation 0.725 uM/L	1197 (990)	--
2° ADP PRP aggregation 0.725 uM/L[a]	1196 (990)	--
ADP Thrombin aggregation 0.056 units/mL	1196 (990)	--
Shear Stress (absolute PLT retention)	--	1136 (986)
Shear Stress (relative PLT retention)	--	1136 (986)
ADP WB impedance dose 1.5 Ω[b]		1187 (1025)
ADP WB impedance dose 21.5 Ω[b]		1168 (1005)
Platelet Cell Count Measures		
PLT	1250	1243
MPV	1251	1236
Cell Count and Hemostatic Factor Measures		
Red Blood Cell Count	1239	1241
Hemoglobin	1239	1241
Hematocrit	1238	1241
MCH	1239	1241
MCV	1239	1240
White Blood Cell Count	1239	1238
Neutrophil count	1238	1240
Lymphocyte count	1239	1227
Monocyte count	1178	1239
Eosinophil count[a]	1194	1235
Basophil count[a]	1178	1239
Leukocyte count	1194	1230
D-dimer (ELISA)	1185	--
D-dimer (Gold)	1153	--
Fibrinogen (Clauss)	896	--
PAI-1	993	--
tPA	1184	--
von Willebrand Factor	1183	--

[a]Log transformation; [b]Square root transformation; Numbers in parentheses indicate sample size following exclusions

Abbreviations: PLT, platelet count; MPV, mean platelet volume; WB, whole blood; PRP, platelet rich plasma; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular; PAI-1, plasminogen activator inhibitor-1; tPA, tissue plasminogen activator

Supplemental Table 3: Genetic association results under additive models for Primary ADP, Secondary ADP, and Thrombin for all 11 SNPs without sample exclusions.

Marker	Gene	Allele	1° ADP PRP		2° ADP PRP		Thrombin PRP	
			Effect	p-value	Effect	p-value	Effect	p-value
rs10761741	*JMJD1C*	G	-0.21	0.521	-0.023	0.0710	-0.13	0.586
rs11144351	*PIP5K1B*	G	-0.43	0.353	-0.0088	0.641	-0.63	0.0651
rs12359150	*CUBN*	A	1.10	0.0415	0.044	0.0450	0.47	0.239
rs12566888	*PEAR1*	T	-2.29	9.98×10^{-5}	-0.13	1.51×10^{-7}	-2.07	1.91×10^{-6}
rs2363910	*SHH*	T	-1.27	0.0161	-0.058	6.65×10^{-3}	-0.044	0.910
rs2479008	*GMDS*	T	-0.70	0.118	-0.013	0.471	0.012	0.972
rs342286	*PIK3CG*	G	0.37	0.248	0.00024	0.985	-0.32	0.180
rs4128880	*RGS18*	C	-0.64	0.0410	-0.036	4.35×10^{-3}	-0.31	0.179
rs467053	*ADAMTS2*	C	0.27	0.388	0.0069	0.593	0.18	0.440
rs7940646	*MRVI1*	C	-0.58	0.0937	-0.019	0.171	-0.37	0.145
rs9996294	*RAPGEF2*	G	0.38	0.423	0.027	0.166	0.42	0.226

Abbreviations: PRP, platelet-rich plasma

Supplemental Table 4: Genetic association results under additive models for Primary ADP, Secondary ADP, and Thrombin for all 11 SNPs with sample exclusions.

Marker	Gene	Allele	1° ADP PRP		2° ADP PRP		Thrombin PRP	
			Effect	p-value	Effect	p-value	Effect	p-value
rs10761741	*JMJD1C*	G	-0.16	0.6378	-0.022	0.1158	0.039	0.8817
rs11144351	*PIP5K1B*	G	-0.36	0.482	-0.0069	0.7418	-0.69	0.06999
rs12359150	*CUBN*	A	1.58	6.79×10^{-3}	0.046	0.05426	0.37	0.3938
rs12566888	*PEAR1*	T	-1.83	4.71×10^{-3}	-0.11	2.56×10^{-5}	-2.17	8.07×10^{-6}
rs2363910	*SHH*	T	-0.50	0.3765	-0.038	0.1107	0.22	0.6042
rs2479008	*GMDS*	T	-0.86	0.07935	-0.013	0.5306	-0.16	0.6678
rs342286	*PIK3CG*	G	0.22	0.5319	-0.014	0.3177	-0.25	0.3381
rs4128880	*RGS18*	C	-0.57	0.09606	-0.037	8.08×10^{-3}	-0.27	0.2991
rs467053	*ADAMTS2*	C	0.21	0.5366	0.0008	0.9569	0.072	0.7828
rs7940646	*MRVI1*	C	-0.73	0.04895	-0.026	0.09116	-0.50	0.1569
rs9996294	*RAPGEF2*	G	0.25	0.6356	0.028	0.1945	0.42	0.2792

Abbreviations: PRP, platelet-rich plasma

Supplemental Table 5: Genetic association results under additive models for Absolute and Relative Shear Stress for all 11 SNPs without sample exclusions.

Marker	Gene	Allele	Absolute Shear Stress		Relative Shear Stress	
			Effect	p-value	Effect	p-value
rs10761741	*JMJD1C*	G	-3.28	0.0420	0.0071	0.286
rs11144351	*PIP5K1B*	G	0.00056	0.999	-0.0029	0.764
rs12359150	*CUBN*	A	0.15	0.956	0.021	0.0515
rs12566888	*PEAR1*	T	0.80	0.785	-0.022	0.0688
rs2363910	*SHH*	T	0.20	0.939	-0.010	0.347
rs2479008	*GMDS*	T	-3.20	0.152	-0.011	0.236
rs342286	*PIK3CG*	G	-3.02	0.0609	-0.0077	0.252
rs4128880	*RGS18*	C	-0.98	0.535	0.0017	0.799
rs467053	*ADAMTS2*	C	-1.34	0.401	-0.0041	0.535
rs7940646	*MRVI1*	C	3.21	0.0622	0.0076	0.284
rs9996294	*RAPGEF2*	G	-1.69	0.469	-0.0068	0.489

Supplemental Table 6: Genetic association results under additive models for Absolute and Relative Shear Stress for all 11 SNPs with sample exclusions.

Marker	Gene	Allele	Absolute Shear Stress		Relative Shear Stress	
			Effect	p-value	Effect	p-value
rs10761741	*JMJD1C*	G	-2.86	0.1047	-0.010	0.1575
rs11144351	*PIP5K1B*	G	0.61	0.8064	0.002	0.8809
rs12359150	*CUBN*	A	0.42	0.8845	0.017	0.1545
rs12566888	*PEAR1*	T	0.18	0.9548	-0.031	0.0166
rs2363910	*SHH*	T	1.62	0.5784	-0.002	0.8702
rs2479008	*GMDS*	T	-2.65	0.2728	-0.009	0.3774
rs342286	*PIK3CG*	G	-1.96	0.2641	-0.002	0.7663
rs4128880	*RGS18*	C	-1.12	0.5119	-0.0003	0.9663
rs467053	*ADAMTS2*	C	-1.13	0.5058	-0.005	0.486
rs7940646	*MRVI1*	C	3.36	0.0711	0.004	0.6092
rs9996294	*RAPGEF2*	G	-0.50	0.8464	-0.003	0.7712

Supplemental Table 7: Genetic association results under additive models for ADP dose require for 1.5 Ω and 21.5 Ω impedance change for all 11 SNPs without sample exclusions.

Marker	Gene	Allele	ADP impedance 1.5 Ω		ADP impedance 21.5 Ω	
			Effect	p-value	Effect	p-value
rs10761741	*JMJD1C*	G	0.44	1.35×10^{-3}	0.42	8.52×10^{-3}
rs11144351	*PIP5K1B*	G	0.24	0.219	0.43	0.0612
rs12359150	*CUBN*	A	-0.34	0.144	-0.33	0.224
rs12566888	*PEAR1*	T	0.76	2.36×10^{-3}	0.60	0.0380
rs2363910	*SHH*	T	-0.047	0.834	-0.29	0.260
rs2479008	*GMDS*	T	0.069	0.720	0.14	0.543
rs342286	*PIK3CG*	G	-0.31	0.0223	-0.31	0.0545
rs4128880	*RGS18*	C	0.17	0.200	0.27	0.0928
rs467053	*ADAMTS2*	C	0.033	0.808	0.047	0.773
rs7940646	*MRVI1*	C	0.26	0.0777	0.34	0.0442
rs9996294	*RAPGEF2*	G	-0.15	0.459	-0.35	0.141

Supplemental Table 8: Genetic association results under additive models for ADP dose require for 1.5 Ω and 21.5 Ω impedance change for all 11 SNPs with sample exclusions.

Marker	Gene	Allele	ADP impedance 1.5 Ω		ADP impedance 21.5 Ω	
			Effect	p-value	Effect	p-value
rs10761741	*JMJD1C*	G	0.46	2.76×10^{-3}	0.42	0.01765
rs11144351	*PIP5K1B*	G	0.38	0.07185	0.47	0.06007
rs12359150	*CUBN*	A	-0.34	0.1745	-0.26	0.3725
rs12566888	*PEAR1*	T	0.81	3.86×10^{-3}	0.78	0.0162
rs2363910	*SHH*	T	-0.13	0.5914	-0.27	0.3468
rs2479008	*GMDS*	T	0.084	0.6907	0.11	0.6432
rs342286	*PIK3CG*	G	-0.28	0.06351	-0.28	0.1146
rs4128880	*RGS18*	C	0.16	0.2708	0.28	0.0995
rs467053	*ADAMTS2*	C	0.032	0.8298	0.024	0.8911
rs7940646	*MRVI1*	C	0.24	0.132	0.32	0.08638
rs9996294	*RAPGEF2*	G	-0.24	0.2952	-0.56	0.03336

Supplemental Table 9: Demographics of CaPs subjects.

Phenotype	Unit	Phase 2 Mean	Phase 2 SD	Phase 3 Mean	Phase 3 SD
Age	years	56.68	4.44	61.89	5.07
Smoking (current/former/never)	%	41.9/38.7/19.4		34.9/47.4/17.7	
Platelet Aggregation Measures					
1° ADP PRP aggregation 0.725 uM/L	%	24.89	7.61	-	-
2° ADP PRP aggregation 0.725 uM/L*	%	22.91	18.54	-	-
ADP Thrombin aggregation 0.056 units/mL	%	10.54	5.73	-	-
Shear Stress (absolute PLT retention)	10^9/L	-	-	125.69	37.37
Shear Stress (relative PLT retention)	%	-	-	64.66	15.50
ADP WB impedance dose 1.5 Ω†	μM/L	-	-	1.15	0.82
ADP WB impedance dose 21.5 Ω†	μM/L	-	-	1.53	1.02
Platelet Cell Count Measures					
PLT	10^9/L	263.17	57.80	235.39	54.37
MPV	fL x 10	88.54	10.26	78.18	9.175
Cell Count and Hemostatic Factor Measures					
Red Blood Cell Count	10^{12}/L	5.12	0.38	4.95	0.39
Hemoglobin	g/L	157.15	11.73	150.62	11.07
Hematocrit	%	46.42	3.43	45.71	3.31
MCH	pG	30.75	1.85	30.50	1.85
MCV	fL	90.75	4.28	92.53	5.05
White Blood Cell Count	10^9/L	7.56	1.98	6.49	1.68
Neutrophil count	10^9/L	5.59	0.73	5.57	0.82
Lymphocyte count	10^9/L	3.33	0.66	3.06	0.71
Monocyte count	10^9/L	0.59	0.16	0.74	0.18
Eosinophil count*	10^9/L	0.32	0.17	0.32	0.20
Basophil count*	10^9/L	0.08	0.04	0.09	0.06
Leukocyte count	10^9/L	0.10	0.06	0.21	0.10
D-dimer (ELISA)	ng/mL	82.86	69.46	-	-
D-dimer (Gold)	ng/mL	19.24	41.68	-	-
Fibrinogen (Clauss)	g/L	3.04	0.79	-	-
PAI-1 (% pool)	%	13.85	5.68	-	-
tPA	ng/mL	11.59	4.08	-	-
von Willebrand Factor	IU/dL	118.31	41.59	-	-

*Log transformation; †Square root transformation

Abbreviations: PLT, platelet count; MPV, mean platelet volume; WB, whole blood; PRP, platelet rich plasma; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular; PAI-1, plasminogen activator inhibitor-1; tPA, tissue plasminogen activator

Supplemental Table 10: Strongest genetic association result for each marker examined.

Marker	Gene	Allele	Phenotype	Model	Effect	p-value
rs10761741	*JMJD1C*	G	ADP impedance 1.5 Ω	Recessive	0.66	6.54×10^{-4}
rs11144351	*PIP5K1B*	G	Absolute Shear Stress	Recessive	20.12	0.0279
rs12359150	*CUBN*	A	2° ADP PRP aggregation	Dominant	0.048	0.0399
rs12566888	*PEAR1*	T	2° ADP PRP aggregation	Additive	-0.13	1.51×10^{-7}
rs2363910	*SHH*	T	2° ADP PRP aggregation	Additive	-0.058	6.65×10^{-3}
rs2479008	*GMDS*	T	Relative Shear Stress	Recessive	-0.064	0.0330
rs342286	*PIK3CG*	G	ADP impedance 1.5 Ω	Additive	-0.31	0.0223
rs4128880	*RGS18*	C	2° ADP PRP aggregation	Recessive	-0.060	2.90×10^{-3}
rs467053	*ADAMTS2*	C	Absolute Shear Stress	Dominant	-1.95	0.405
rs7940646	*MRVI1*	C	Absolute Shear Stress	Dominant	11.01	5.04×10^{-3}
rs9996294	*RAPGEF2*	G	ADP impedance 21.5 Ω	Dominant	-0.43	0.100