

Supplementary data to Koch et al. “4G/5G polymorphism and haplotypes of *SERPINE1* in atherosclerotic diseases of coronary arteries” (Thromb Haemost 2010; 103.6)

The supplementary data have the following sections in order:

1. Supplementary Table 1: Main characteristics of published studies included in the meta-analysis of the *SERPINE1* 4G/5G polymorphism.
2. Supplementary Table 2: Oligonucleotide primers and TaqMan probes used for genotyping.
3. Supplementary Table 3: Genotype distributions of *SERPINE1* polymorphisms in the women of the MI and control groups.
4. Supplementary Table 4: Genotype distributions of *SERPINE1* polymorphisms in the men of the MI and control groups.

Supplementary Table 1: Main characteristics of published studies included in the meta-analysis of the *SERPINE1* 4G/5G polymorphism.

Study	Origin(s) of sample	Cases/ controls	Phenotype of cases ^a	Age (years) of cases ^b	Women (%) among cases	P_{HWE} ^c of controls
Dawson et al. 1993 (18)	Sweden	107/73	MI	<45 (39.9 ± 0.4)	14.0	0.004
Ye et al. 1995 (19)	France/UK	476/601	MI	25 to 64	0	0.02
Eriksson et al. 1995 (20)	Sweden	93/100	MI	<45	0	0.40
Mansfield et al. 1995 (21)	UK	38/122	CAD	65 (61 to 70)	47.4	0.17
Ridker et al. 1997 (22)	USA ^d	374/495	MI	62.9 ± 8.8	0	0.99
Ossei-Gerning et al. 1997 (23)	UK	166/120 ^e	MI	ND	ND	0.22
Burzotta et al. 1997 (24)	Italy	108/175	MI	>45 (59 ± 7)	25.0	0.90
Junker et al. 1998 (25)	Germany	241/179	MI	≤45 (38.6 ± 4.4)	0	0.51
Iwai et al. 1998 (26)	Japan	204/148	MI	59.3 ± 10.3	22.5	0.31
Pastinen et al. 1998 (27)	Finland	151/150	MI	<65 (58.1 ± 4.9)	19.2	0.38
Sugano et al. 1998 (28)	Japan	66/62	MI	63.1 ± 9.2	12.1	0.94

Continued on next page

Supplementary Table 1 *Continued*

Study	Origin(s) of sample	Cases/ controls	Phenotype of cases ^a	Age (years) of cases ^b	Women (%) among cases	$P_{\text{HWE}}^{\text{c}}$ of controls
Gardemann et al. 1999 (29)	Germany	1,214/594 ^f	MI	62.2 ± 9.5	0	0.42
Anderson et al. 1999 (30)	USA	375/329	MI	63.7 ± 11.6	20.6	0.33
Doggen et al. 1999 (31)	The Netherlands	331/302	MI	<70 (56.1 ± 9.0)	0	0.95
Ardissino et al. 1999 (32)	Italy	200/200	MI	<45 (40.7 ± 4.1)	7.5	0.48
Beneš et al. 2000 (33)	Czech Republic	175/222	CAD	<56 (49.5 ± 4.5)	0	0.47
Song et al. 2000 (34)	Korea	158/139	CAD	60.7 ± 9.2	37.3	0.25
Mikkelsen et al. 2000 (35)	Finland	68/164	MI	ND	0	0.80
Viitanen et al. 2001 (36)	Finland	118/110	CHD ^g	56 ± 1	40.7	0.45
Fu et al. 2001 (37)	China	87/92	MI	51.3 ± 6.7	42.5	0.84
Yamada et al. 2002 (38)	Japan	589/704	MI	62.5 ± 10.8	100	0.63
Hindorff et al. 2002 (39)	USA	78/385	MI	39.7 (23 to 44)	100	0.67
ATVB Italy 2003 ^h (40)	Italy	1,210/1,210	MI	<45	12.3	0.37

Continued on next page

Supplementary Table 1 *Continued*

Study	Origin(s) of sample	Cases/ controls	Phenotype of cases ^a	Age (years) of cases ^b	Women (%) among cases	$P_{\text{HWE}}^{\text{c}}$ of controls
Leander et al. 2003 (41)	Sweden	1,168/1,517	MI	61.5 ± 6.8 (women) 58.3 ± 7.1 (men)	29.5	0.45
Juhan-Vague et al. 2003 (42)	Sweden, UK, France, Italy	483/507	MI	<60	0	0.15
Crainich et al. 2003 (43)	USA	264/753	MI	73.5 ± 5.5	40.2	0.41
Petrovič et al. 2003 (44)	Slovenia	154/194	MI	58.3 ± 11.3	33.8	0.42
Zhan et al. 2003 (45)	China	56/83	MI	67.1 ± 10.4	21.4	0.003
Tobin et al. 2004 (46)	UK	547/505	MI	<75 (61.9 ± 9.2)	32.0	0.26
ter Bogt et al. 2004 (47)	The Netherlands	285/293	CAD	56.5 ± 9.3	18	0.54
McCarthy et al. 2004 (48)	USA	159/389	MI	ND	ND	0.70
Whiting et al. 2005 (49)	USA	881/261	CAD	ND	ND	0.26
Pegoraro and Ranjith 2005 (50)	South Africa	195/300	MI	<45	ND	0.07

Continued on next page

Supplementary Table 1 *Continued*

Study	Origin(s) of samples	Cases/ controls	Phenotype of cases ^a	Age (years) of cases ^b	Women (%) among cases	$P_{\text{HWE}}^{\text{c}}$ of controls
Su et al. 2006 (51)	China	812/931	CHD ⁱ	54.5 ± 8.9	21.6	0.26
Ding et al. 2006 (52)	USA	101/1,640 (white)	MI	74 ± 3	28	0.36
		74/1,149 (black)	MI	73 ± 3	39	0.17
Agirbasli et al. 2006 (53)	Turkey	100/100	CAD	<55 (women) <45 (men)	20.0	0.04
Morgan et al. 2007 (54)	USA	806/656	ACS ^j	63.1 ± 13.2 (women) 60.7 ± 12.5 (men)	32.2	0.39
Sampaio et al. 2007 (55)	Brazil	115/104	MI	<40 (34.4 ± 4.9)	38.1	0.46
Taymaz et al. 2007 (56)	Turkey	54/21	CAD	ND	ND	0.06
Saely et al. 2008 (57)	Austria	406/266	CAD	ND	ND	1
Sarecka et al. 2008 (58)	Poland	178/202	CAD	43.8 ± 6.1	32.6	0.40
Onalan et al. 2008 (59)	Turkey	156/281	MI	59 ± 11	19.9	0.0009

Footnotes on next page

Footnotes to Supplementary Table 1

Please, note that references cited in this table refer to the reference list in the main paper.

ND—no data shown.

^a MI—myocardial infarction, CAD—coronary artery disease, CHD—coronary heart disease, ACS—acute coronary syndrome.

^b Age at onset or diagnosis; maximum (mean \pm standard deviation) (18, 25, 27, 31–33, 46, 55), range (19), maximum (20, 36, 40, 42, 50, 53), median (25th to 75th centile) (21), mean \pm standard deviation (22, 26, 28–30, 34, 37, 38, 41, 43–45, 47, 51, 52, 54, 58, 59), minimum (mean \pm standard deviation) (24), mean (range) (39).

^c Deviation from Hardy-Weinberg equilibrium (HWE) was assessed by the χ^2 square test, and *P* values for controls are shown.

^d Most study participants were whites; blacks, Asian Americans, and Hispanic Americans made up 1.0%, 1.3%, and 2.1% of the cohort, respectively, and were equally distributed between the case and control groups.

^e Controls: group with "normal vessels" (<50% stenosis), as established by coronary angiography.

^f Controls: group with "no vessel disease" (<50% stenosis), as established by coronary angiography.

^g CHD defined as: angiographic stenosis (>50%) in at least two coronary arteries.

^h Atherosclerosis, thrombosis, and vascular biology Italian study group 2003.

ⁱ CHD defined as: acute MI or severe angiographic stenosis (\geq 70%) in a major epicardial artery.

^j ACS defined as: MI (73%) or unstable angina pectoris (27%).

Supplementary Table 2: Oligonucleotide primers and TaqMan probes used for genotyping.

Polymorphism ^a	Alleles	Primers (5'→3')	TaqMan probes (5'→3') ^b
rs4727479	G>C	AGCGGGAGGCTCAGAGAGAG GATTTTCCATGACTGTCCCTCTGT	FAM-TGCTCTTC <u>C</u> TCTTTG VIC-TGCTCTTC <u>G</u> TCTTTG
rs6950982	A>G	CACATCTTCCCTATGCCTACAAGTTT GGGGAGCAGCTCTAGTCCTGAT	FAM-TAGTAAGTC <u>A</u> GCCACTTC VIC-TAAGTC <u>G</u> GCCACTTC
rs2227631	A>G	GTCTGTGTCTGGAGGAAGAGGATAAA GACCAGGGGTTACCATGGTAAAA	FAM-AAGTTTCACTT <u>C</u> TTCGAGC VIC-TTTCACTT <u>C</u> TTCGAGCTG
rs1799889	4G>5G	CAGACAAGGTTGTTGACACAAGAGA TCCCTCATCCCTGCCATGT	FAM-CACGGCTGACT <u>C</u> CCCCACGTG VIC-CGGCTGACT <u>C</u> CCCCACGTGT
rs2227667	A>G	AGGAACTAGACGGGTTTCATTTAACC CCCGGCTGAAGTTAGACAAAGTT	FAM-CATACATCCA <u>A</u> TTGAGGAC VIC-TACATCCAG <u>T</u> TGAGGACT
rs2227672	G>T	CACCTGACTCCAGGGTCTCATC CTCCCAAAGTGCTGGGATTACA	FAM-TCCCCCAG <u>C</u> AGGAT VIC-CCCAG <u>A</u> AGGATTTC
rs2227684	G>A	GAGAGCCTGGCTTCCAGAAATAG AACTCAGCTGTGAAGACGACAAGAT	FAM-AGCTCT <u>C</u> GCTGATGG VIC-CAGCTCT <u>T</u> GCTGATGG
rs1050813	G>A	AACTCGCTCCTAGTGTCTTTGTG CTCCGTCACGCTGGATGTC	FAM-TGTCAC <u>C</u> GTATCTCA VIC-TGTCAC <u>C</u> ATATCTCA
rs757717	C>T	GGCCGGAGGATCACTTGAG TCTTTTTCAAGACAGGGTCTCACTTT	FAM-ATTCAAG <u>C</u> GGGGCA VIC-ATTCAAG <u>C</u> TGGGGCAA

^a Identification number according to the National Center for Biotechnology Information SNP database

(<http://www.ncbi.nlm.nih.gov/projects/SNP>).

^b Fluorescent markers, FAM (6-carboxy-fluorescein) and VIC (proprietary dye of Applied Biosystems), were allele-specifically attached to the 5' ends of probe oligonucleotides. Allele-specific nucleotides are underlined. Conventional probes with TAMRA (6-carboxytetramethylrhodamine) as a quencher (rs1799889) and probes with conjugated minor groove binder groups and a dark quencher (rs4727479, rs6950982, rs2227631, rs2227667, rs2227672, rs2227684, rs1050813, rs757717) were used.

Supplementary Table 3: Genotype distributions of *SERPINE1* polymorphisms in the women of the group with myocardial infarction (MI) and the control group.

Poly- morphism ^a	Position ^b	Alleles	Women in MI group (<i>n</i> = 885)			Women in control group (<i>n</i> = 598)			<i>P</i> value
			Maj	Het	Min	Maj	Het	Min	
rs4727479	100552387	G>C	541 (61.1)	304 (34.4)	40 (4.5)	380 (63.5)	187 (31.3)	31 (5.2)	0.43
rs2227631	100556258	A>G	306 (34.6)	428 (48.4)	151 (17.1)	228 (38.1)	273 (45.7)	97 (16.2)	0.38
rs1799889	100556430/1	4G>5G	253 (28.6)	439 (49.6)	193 (21.8)	191 (31.9)	285 (47.7)	122 (20.4)	0.38
rs2227667	100561469	A>G	544 (61.5)	294 (33.2)	47 (5.3)	377 (63.0)	191 (31.9)	30 (5.0)	0.83
rs2227672	100562406	G>T	638 (72.1)	227 (25.6)	20 (2.3)	452 (75.6)	132 (22.1)	14 (2.3)	0.29
rs2227684	100563651	G>A	287 (32.4)	419 (47.3)	179 (20.2)	185 (30.9)	282 (47.2)	131 (21.9)	0.69
rs1050813	100568335	G>A	551 (62.3)	303 (34.2)	31 (3.5)	398 (66.6)	176 (29.4)	24 (4.0)	0.15
rs757717	100574669	C>T	704 (79.5)	165 (18.6)	16 (1.8)	460 (76.9)	133 (22.2)	5 (0.8)	0.08

Variables are presented as number (%) of individuals in the MI and control groups.

Maj (Min)–frequency of subjects homozygous for the major (minor) allele; Het–frequency of heterozygous subjects.

^a Identification number according to the National Center for Biotechnology Information SNP database (<http://www.ncbi.nlm.nih.gov/projects/SNP>).

^b Position of polymorphism on chromosome 7 (genome build 36.3).

Supplementary Table 4: Genotype distributions of *SERPINE1* polymorphisms in the men of the group with myocardial infarction (MI) and the control group.

Poly- morphism ^a	Position ^b	Alleles	Men in MI group (<i>n</i> = 2772)			Men in control group (<i>n</i> = 613)			<i>P</i> value
			Maj	Het	Min	Maj	Het	Min	
rs4727479	100552387	G>C	1737 (62.7)	923 (33.3)	112 (4.0)	384 (62.6)	205 (33.4)	24 (3.9)	0.99
rs2227631	100556258	A>G	962 (34.7)	1329 (47.9)	481 (17.4)	202 (33.0)	303 (49.4)	108 (17.6)	0.71
rs1799889	100556430/1	4G>5G	838 (30.2)	1348 (48.6)	586 (21.1)	169 (27.6)	305 (49.8)	139 (22.7)	0.39
rs2227667	100561469	A>G	1656 (59.7)	970 (35.0)	146 (5.3)	346 (56.4)	231 (37.7)	36 (5.9)	0.32
rs2227672	100562406	G>T	2021 (72.9)	697 (25.1)	54 (1.9)	429 (70.0)	170 (27.7)	14 (2.3)	0.33
rs2227684	100563651	G>A	856 (30.9)	1374 (49.6)	542 (19.6)	201 (32.8)	301 (49.1)	111 (18.1)	0.56
rs1050813	100568335	G>A	1838 (66.3)	825 (29.8)	109 (3.9)	387 (63.1)	207 (33.8)	19 (3.1)	0.11
rs757717	100574669	C>T	2168 (78.2)	576 (20.8)	28 (1.0)	505 (82.4)	104 (17.0)	4 (0.7)	0.07

Variables are presented as number (%) of individuals in the MI and control groups.

Maj (Min)–frequency of subjects homozygous for the major (minor) allele; Het–frequency of heterozygous subjects.

^a Identification number according to the National Center for Biotechnology Information SNP database (<http://www.ncbi.nlm.nih.gov/projects/SNP>).

^b Position of polymorphism on chromosome 7 (genome build 36.3).