Supplementary material

Świderska MK, Mostowska A, Skrypnik D, et al. Associations of ANGPTL6, DOCK6, FABP1, and PCSK9 single-nucleotide variants with hypercholesterolemia in the Polish population: a cross-sectional study. Pol Arch Intern Med. 2023; 133: 16393. doi:10.20452/pamw.16393

Table S1. Characteristics of the analyzed polymorphisms.

Gene symbol	rs no.	Location[a]	SNV function[b]	Alleles[c]	MAF[d]	MAF[e]
FABP1	rs2241883	chr2:88124547	Missense	C/T	0.348	0.325
FABP1	rs2919872	chr2:88129052	2KB Upstream	C/T	0.466	0.448
PCSK9	rs562556	chr1:55058564	Missense	A/G	0.179	0.172
PCSK9	rs11206510	chr1:55030366	-	C/T	0.172	0.184
ANGPTL6	rs8112063	chr19:10099035	Intron	C/T	0.434	0.424
DOCK6	rs737337	chr19:11236817	Synonymous	C/T	0.073	0.080
DOCK6	rs17699089	chr19:11233119	Intron	A/G	0.089	0.108

[a] NCBI build 38 / hg38.

[b] According to the Single Nucleotide Polymorphism database (dbSNP).

[c] Underline denotes the minor allele.

[d] Based on 1000 Genomes project, EUR samples

[e] Based on ALFA Allele Frequency, EUR samples

Abbreviations: ANGPTL6, Angiopoietin Like 6; DOCK6, Dedicator of Cytokinesis 6, FABP, Fatty Acid-Binding Protein; MAF, minor allele frequency; PCSK9, Proprotein Convertase Subtilisin/Kexin type 9; SNV, single nucleotide variant.

Table S2. Primer sequences and HRM conditions of the analyzed SNVs.

Gene	rs no.	Alleles[a]	Primers for PCR Amplification (5′–3′)	PCR product length (bp)	Annealing Temp. (°C)	Melt Temp. Range (°C)
FABP1	rs2241883	C/T	F: GTGATTATGTCGCCGTTGAG R: TGCAGACAGTGGTTCAGTTG	94	58	76 - 91
FABP1	rs2919872	C/T	F: GTGCACGTCCCAGTTCCT R: AAGGTTGACGCCAAAGTCC	98	58	80 - 95
PCSK9	rs562556	A/G	F: TCAGCACACTCGGGGCCTAC R: GCTCAGCAGCTCCTCATCTGG	142	58	80 – 95
PCSK9	rs11206510	C/T	F: GCTTCCCCAAGGATATAGGG R: GGAAGAGGAGCCAAAGACG	68	58	75 – 90
ANGPTL6	rs8112063	C/T	F: GATCCAACCCATCTCAGCAG R: AGTGGGGAGTAGCGGAGAC	96	58	80 – 95
DOCK6	rs737337	C/T	F: GGGTGCACAGAGGACACG R: TGGGTGGACGGTCACAAG	62	58	80 – 95
DOCK6	rs17699089	A/G	F: TCATTCACGTTGTCGTCTCT R: GTGGTTGCCACGTGTGTG	73	58	75 - 90

[a] Underline denotes the minor allele

Abbreviations: ANGPTL6, Angiopoietin Like 6; bp, base pairs; DOCK6, Dedicator of Cytokinesis 6, FABP, Fatty Acid-Binding Protein 1; HRM, High resolution melt; PCR,

polymerase chain reaction; PCSK9, Proprotein Convertase Subtilisin/Kexin type 9; SNV, single nucleotide variant.

Table S3. The expected power for 1.00 – 1.75 ORs in associations analyses between dyslipidemia in the Polish population

			The expected power		
	Allele	**Genotype**		**Genetic model**	
rs number	**frequency[a]**	**relative risk**	**Additive**	**Dominant**	**Recessive**
rs2241883	0.348	1.00	0.050	0.050	0.050
		1.25	0.938	0.639	0.275
		1.50	1.000	0.987	0.763
		1.75	1.000	1.000	0.977
rs2919872	0.466	1.00	0.050	0.050	0.050
		1.25	0.930	0.478	0.460
		1.50	1.000	0.915	0.946
		1.75	1.000	0.994	0.999
rs562556	0.179	1.00	0.050	0.050	0.050
		1.25	0.874	0.720	0.089
		1.50	1.000	0.999	0.211
		1.75	1.000	1.000	0.416

rs11206510	0.172	1.00	0.050	0.050	0.050
		1.25	0.867	0.717	0.085
		1.50	1.000	0.999	0.194
		1.75	1.000	1.000	0.377
rs8112063	0.434	1.00	0.050	0.050	0.050
		1.25	0.935	0.527	0.411
		1.50	1.000	0.947	0.918
		1.75	1.000	0.998	0.998
rs737337	0.073	1.00	0.050	0.050	0.050
		1.25	0.614	0.546	0.053
		1.50	1.000	0.991	0.062
		1.75	1.000	1.000	0.077
rs17699089	0.089	1.00	0.050	0.050	0.050
		1.25	0.683	0.599	0.055
		1.50	1.000	0.995	0.071
		1.75	1.000	1.000	0.099

Table S4. *FABP1* rs2919872 polymorphic variants and lipid levels in the study participants.

	All participants				Participants without hypercholesterolemia				Participants with hypercholesterolemia				
Parameter	TT n = 99	CT n = 184	CC n = 76	P value[a]	TT n = 68	CT n = 119	CC n = 63	P-value[a]	TT n = 31	CT n = 65	CC n = 13	P-value[a]	
Total cholesterol, mg/dL	202.0 (178.0 – 231.0)	201.0 (175.8 – 227.0)	202.0 (179.5 – 228.0)	0.82	200.5 (174.5 – 211.0)	201.0 (173.0 – 215.0)	200.0 (174.5 – 219.0)	0.95	210.0 (177.0 – 248.0)	208.0 (187.0 – 237.0)	203.0 (182.0 – 244.0)	0.57	Dominant
				0.62				0.41				0.74	Recessive
				0.82				0.31				0.59	Additive
HDL-cholesterol, mg/dL	61.0 (50.0 – 75.5)	60.0 (52.0 – 74.0)	63.0 (55.0 – 70.0)	0.72	60.5 (50.0 – 71.3)	59.0 (50.0 – 70.8)	63.0 (54.0 – 70.0)	0.87	61.0 (49.0 – 81.0)	64.0 (57.0 – 77.0)	60.0 (56.8 – 72.3)	0.41	Dominant
				0.47				0.25				0.93	Recessive
				0.96				0.91				0.91	Additive
LDL-cholesterol, mg/dL	105.0 (82.0 – 134.8)	106.0 (84.8 – 129.0)	114.0 (86.0 – 131.5)	0.66	106.0 (75.0 – 109.0)	103.0 (82.0 – 105.0)	110.0 (79.3 – 100.3)	0.70	117.3 (77.0 – 159.0)	111.5 (78.8 – 136.8)	134.0 (85.0 – 152.2)	0.96	Dominant
				0.38				0.43				0.41	Recessive
				0.71				0.54				0.88	Additive
Triglicerides, mg/dL	139.0 (91.5 – 219.5)	136.0 (94.0 – 186.0)	141.0 (92.0 – 185.0)	0.78	124.0 (86.5 – 195.0)	134.5 (92.0 – 188.5)	146.0 (89.5 – 187.0)	0.60	157.0 (107.0 – 228.0)	140.0 (99.0 – 182.0)	137.5 (109.2 – 148.0)	0.17	Dominant
				0.99				0.65				0.49	Recessive
				0.63				0.24				0.06	Additive

Values are shown as median (Q1–Q3) for nonparametric variables.

[a] Mann-Whitney U test

Abbreviations: FABP, Fatty Acid-Binding Protein; HDL, high density lipoprotein, LDL, low density lipoprotein.

Conversion to SI units: to change cholesterol to mmol/L, divide by 38.6; triglycerides to mmol/L, by 88.5.

Table S5. *FABP1* rs2241883 polymorphic variants and lipid levels in the study participants.

	All participants				Participants without hypercholesterolemia				Participants with hypercholesterolemia				
Parameter	TT n = 133	CT n = 159	CC n = 68	P value[a]	TT n = 95	CT n = 111	CC n = 45	P-value[a]	TT n = 38	CT n = 48	CC n = 23	P-value[a]	
Total cholesterol, mg/dL	202.0 (176.0 – 232.0)	201.0 (174.0 – 227.0)	209.0 (186.5 – 233.0)	0.79	200.0 (173.5 – 212.2)	197.0 (172.0 – 212.0)	204.0 (183.2 – 217.2)	0.41	202.5 (176.8 – 237.0)	207.0 (181.5 – 244.2)	219.0 (191.0 – 243.5)	0.48	Dominant
				0.21				0.39				0.37	Recessive
				0.76				0.50				0.27	Additive
HDL-cholesterol, mg/dL	61.0 (52.0 – 71.5)	60.0 (53.0 – 69.5)	64.0 (52.8 – 79.0)	0.78	60.5 (50.3 – 70.8)	60.0 (51.0 – 68.5)	63.0 (52.0 – 77.0)	0.76	64.0 (54.0 – 77.0)	61.0 (56.3 – 77.0)	64.0 (55.5 – 81.5)	0.95	Dominant
				0.19				0.27				0.55	Recessive
				0.33				0.35				0.83	Additive
LDL-cholesterol, mg/dL	107.0 (84.0 – 130.0)	104.0 (83.0 – 130.0)	109.0 (91.0 – 134.2)	0.96	106.0 (81.5 – 111.0)	103.0 (71.0 – 106.0)	108.0 (87.3 – 110.0)	0.85	112.8 (81.0 – 142.0)	111.0 (76.0 – 141.0)	112.0 (83.0 – 154.5)	0.74	Dominant
				0.25				0.26				0.55	Recessive
				0.57				0.94				0.43	Additive
Triglicerides, mg/dL	140.0 (93.5 – 210.5)	138.0 (94.5 – 196.0)	119.0 (90.5 – 189.5)	0.44	143.0 (89.0 – 189.0)	133.0 (94.0 – 192.0)	108.0 (78.0 – 181.0)	0.20	134.0 (100.0 – 165.0)	140.5 (96.5 – 204.0)	161.0 (110.5 – 201.0)	0.52	Dominant
				0.30				0.07				0.39	Recessive
				0.03				0.007				0.54	Additive

Values are shown as median (Q1–Q3) for nonparametric variables.

[a] Mann-Whitney U test

Abbreviations: FABP, Fatty Acid-Binding Protein; HDL, high density lipoprotein; LDL, low density lipoprotein.

Conversion to SI units: to change cholesterol to mmol/L, divide by 38.6; triglycerides to mmol/L, by 88.5.

Table S6. *ANGPTL6* rs8112063 polymorphic variants and lipid levels in the study participants.

	All participants				Participants without hypercholesterolemia				Participants with hypercholesterolemia				
Parameter	TT n = 97	CT n = 192	CC n = 71	P value[a]	TT n = 76	CT n = 129	CC n = 46	P-value[a]	TT n = 21	CT n = 63	CC n = 25	P-value[a]	
Total cholesterol, mg/dL	197.0 (173.0 – 220.0)	204.0 (181.8 – 230.2)	203.0 (175.0 – 231.5)	0.06	195.0 (170.0 – 204.8)	204.0 (177.5 – 221.5)	193.5 (170.0 – 217.0)	0.08	203.0 (177.0 – 231.0)	208.0 (180.0 – 238.5)	219.0 (187.0 – 244.0)	0.67	Dominant
				0.76				0.76				0.56	Recessive
				0.24				0.42				0.69	Additive
HDL-cholesterol, mg/dL	58.0 (50.0 – 68.0)	61.0 (53.0 – 76.0)	64.0 (54.0 – 76.5)	0.009	58.0 (49.8 – 69.0)	60.5 (52.0 – 72.3)	64.0 (50.0 – 70.8)	0.11	59.0 (51.0 – 64.8)	64.0 (54.5 – 79.0)	64.0 (60.0 – 79.0)	0.04	Dominant
				0.16				0.42				0.31	Recessive
				0.03				0.10				0.23	Additive
LDL-cholesterol, mg/dL	100.0 (82.8 – 129.3)	110.0 (85.0 – 134.0)	102.0 (84.0 – 131.5)	0.21	99.5 (82.0 – 104.5)	110.0 (79.0 – 112.0)	99.0 (73.0 – 106.0)	0.20	105.0 (75.0 – 152.0)	111.0 (78.0 – 146.0)	122.5 (83.5 – 137.5)	0.66	Dominant
				0.46				0.12				0.68	Recessive
				0.73				0.96				0.78	Additive
Triglicerides, mg/dL	142.0 (88.8 – 217.5)	126.0 (91.0 – 188.0)	153.0 (103.5 – 212.0)	0.68	132.0 (86.0 – 193.0)	120.5 (86.5 – 181.8)	157.5 (103.2 – 221.8)	0.73	144.5 (109.2 – 225.5)	133.0 (98.0 – 201.0)	144.0 (108.0 – 176.0)	0.62	Dominant
				0.10				0.08				0.76	Recessive
				0.21				0.39				0.27	Additive

Values are shown as median (Q1–Q3) for nonparametric variables.

[a] Mann-Whitney U test

Abbreviations: ANGPTL6, Angiopoietin Like 6; HDL, high density lipoprotein; LDL, low density lipoprotein.

Conversion to SI units: to change cholesterol to mmol/L, divide by 38.6; triglycerides to mmol/L, by 88.5.

Table S7. Multivariable regression analysis of selected demographic and genetic correlates of the circulating HDL-cholesterol in the study population

	All participants, n = 360			Without hypercholesterolemia, n = 251			With hypercholesterolemia, n = 109		
Parameter	β [a]	SE[b] β	P-value	β	SE β	P-value	β	SE β	P-value
ANGPLT6 rs8112063 CC vs CT + TT	3.40	1.84	0.07	2.27	2.06	0.27	7.17	4.05	0.08
Male gender	-14.05	1.73	<0.001	-14.28	2.06	<0.001	-13.87	3.41	<0.001
Age, years	-0.02	0.07	0.76	-0.04	0.08	0.60	0.06	0.15	0.71

[a] β coefficient values can be interpreted as follows: for a unitary change in an analysed parameter, the circulating HDL-cholesterol concentration would change by $\beta \pm$ SE (mg/dL).

[b] Standard error

Table S8. Associations between *PCSK9* rs562556 SNV and selected phenotypes.

Parameter	AA	AG	GG	Mode of inheritance	Odds ratio (95% CI)	P-value[a]
	n = 251	n = 96	n = 13			
Male gender, n (%)	133 (72.7)	44 (24.0)	6 (3.3)	Dominant	0.752 (0.478 – 1.179)	0.22
				Recessive	0.823 (0.260 – 2.527)	0.73
				Additive	0.760 (0.239 – 2.351)	0.63
Hypercholesterolemia, n (%)	78 (71.6)	27 (24.8)	4 (3.7)	Dominant	0.881 (0.538 – 1.445)	0.62
				Recessive[b]	1.023 (0.309 – 3.400)	0.97
				Additive	0.912 (0.594 - 1.401)	0.68
Hypertension, n (%)	87 (69.0)	33 (26.2)	6 (4.8)	Dominant	1.050 (0.656 – 1.680)	0.84
				Recessive[b]	1.621 (0.532 – 4.933)	0.39
				Additive	1.104 (0.737 – 1.654)	0.63
Obesity, n (%)	76 (70.4)	30 (27.8)	2 (1.9)	Dominant	0.957 (0.585 – 1.566)	0.86
				Recessive[b]	0.413 (0.090 – 1.897)	0.24
				Additive	0.883 (0.573 – 1.361)	0.57

[a] Pearson's chi-squared test;

[b] Fisher’s exact test.

Abbreviations: CI, confidence intervals, PCSK9, Proprotein Convertase Subtilisin/Kexin type 9; SNV, single nucleotide variant.

Table S9. Associations between *PCSK9* rs11206510 SNV and selected phenotypes.

Parameter	TT	CT	CC	Mode of inheritance	Odds ratio (95% CI)	P-value[a]
	n = 255	n = 89	n = 16			
Male gender, n (%)	134 (73.2)	40 (21.9)	9 (4.5)	Dominant	0.790 (0.500 – 1.245)	0.31
				Recessive	1.256 (0.420 – 3.338)	0.66
				Additive	1.161 (0.380 – 5.446)	0.77
Hypercholesterolemia, n (%)	82 (75.2)	23 (21.1)	4 (3.7)	Dominant	0.730 (0.438 – 1-217)	0.23
				Recessive[b]	0.759 (0.239 – 2.407)	0.64
				Additive	0.759 (0.487 – 1.182)	0.22
Hypertension, n (%)	88 (69.8)	35 (27.8)	3 (2.4)	Dominant	1.076 (0.670 – 1.730)	0.76
				Recessive[b]	0.415 (0.116 – 1.483)	0.16
				Additive	0.942 (0.624 – 1.423)	0.78
Obesity, n (%)	81 (75.0)	23 (21.3)	4 (3.7)	Dominant	0.744 (0.446 – 1.239)	0.26
				Recessive[b]	0.769 (0.242 – 2.441)	0.66
				Additive	0.771 (0.495 – 1.201)	0.25

[a] Pearson's chi-squared test;

[b] Fisher’s exact test.

Abbreviations: CI, confidence intervals, PCSK9, Proprotein Convertase Subtilisin/Kexin type 9; SNV, single nucleotide variant.

Table S10. *PCSK9* rs562556 polymorphic variants and lipid levels in the study participants.

Parameter	All participants				Participants without hypercholesterolemia				Participants with hypercholesterolemia				
	AA n = 251	AG n = 96	GG n = 13	P value[a]	AA n = 173	AG n = 69	GG n = 9	P-value[a]	AA n = 78	AG n = 27	GG n = 4	P-value[a]	
Total cholesterol, mg/dL	202.0 (177.0 – 229.0)	194.0 (175.8 – 224.5)	209.0 (203.0 – 248.0)	0.49	202.0 (172.0 – 215.2)	193.0 (175.2 – 213.0)	208.0 (196.5 – 209.0)	0.31	204.0 (178.2 – 242.2)	210.0 (179.5 – 235.0)	239.5 (224.0 – 254.8)	0.80	Dominant
				0.03				0.14				0.15	Recessive
				0.04				0.90				0.76	Additive
HDL-cholesterol, mg/dL	60.0 (51.0 – 74.5)	62.0 (56.5 – 71.0)	59.0 (54.3 – 68.3)	0.45	59.0 (50.0 – 70.0)	62.5 (56.8 – 70.3)	56.0 (49.0 – 69.0)	0.20	64.5 (54.0 – 79.0)	61.0 (55.5 – 73.5)	60.0 (58.5 – 60.5)	0.56	Dominant
				0.44				0.61				0.51	Recessive
				0.44				0.81				0.44	Additive
LDL-cholesterol, mg/dL	106.0 (85.0 – 128.0)	101.0 (82.0 – 124.5)	134.0 (121.0 – 163.5)	0.64	106.0 (78.0 – 109.0)	101.0 (81.8 – 103.0)	106.0 (101.0 – 109.0)	0.48	110.0 (81.5 – 146.0)	112.0 (75.5 – 132.5)	168.0 (160.5 – 180.0)	0.98	Dominant
				0.002				0.02				0.03	Recessive
				0.003				0.63				0.46	Additive
Triglicerides, mg/dL	140.0 (92.0 – 196.5)	126.0 (90.5 – 197.0)	147.0 (98.3 – 220.8)	0.57	139.0 (89.0 – 189.0)	119.5 (82.0 – 184.0)	180.0 (98.3 – 220.8)	0.32	140.0 (97.5 – 190.5)	165.0 (107.0 – 223.5)	108.0 (98.5 – 112.0)	0.47	Dominant
				0.69				0.26				0.17	Recessive
				0.71				0.57				0.87	Additive

Values are shown as median (Q1–Q3) for nonparametric variables.

[a] Mann-Whitney U test

Abbreviations: HDL, high density lipoprotein; LDL, low density lipoprotein; PCSK9, Proprotein Convertase Subtilisin/Kexin type 9.

Conversion to SI units: to change cholesterol to mmol/L, divide by 38.6; triglycerides to mmol/L, by 88.5.

Table S11. *PCSK9* rs11206510 polymorphic variants and lipid levels in the study participants.

	All participants				Participants without hypercholesterolemia				Participants with hypercholesterolemia				
Parameter	TT n = 255	CT n = 89	CC n = 16	P-value[a]	TT n = 173	CT n = 66	CC n = 12	P-value[a]	TT n = 82	CT n = 23	CC n = 4	P-value[a]	
Total cholesterol, mg/dL	202.0 (178.0 – 231.0)	198.0 (175.0 – 220.0)	217.0 (181.2 – 231.5)	0.26	200.0 (173.0 – 210.5)	201.0 (174.5 – 218.5)	217.0 (176.5 – 228.0)	0.50	219.0 (188.5 – 250.2)	194.0 (172.5 – 209.5)	213.5 (178.5 – 235.2)	0.006	Dominant
				0.66				0.42				0.78	Recessive
				0.35				0.62				0.02	Additive
HDL-cholesterol, mg/dL	60.0 (51.0 – 71.0)	63.0 (53.0 – 77.0)	59.0 (55.3 – 65.5)	0.31	60.0 (50.0 – 70.0)	60.0 (52.3 – 71.5)	59.0 (55.3 – 71.0)	0.73	61.0 (54.0 – 77.0)	72.0 (61.5 – 79.5)	59.0 (55.5 – 61.8)	0.13	Dominant
				0.81				0.73				0.33	Recessive
				0.49				0.72				0.54	Additive
LDL-cholesterol, mg/dL	109.0 (84.5 – 134.5)	101.0 (81.0 – 120.2)	108.0 (100.2 – 129.5)	0.07	105.0 (81.0 – 109.0)	104.0 (80.0 – 107.0)	108.0 (94.3 – 108.0)	0.97	121.5 (82.0 – 151.8)	85.0 (75.0 – 105.0)	128.0 (92.0 – 156.0)	0.01	Dominant
				0.50				0.55				0.79	Recessive
				0.07				0.95				0.06	Additive
Triglicerides, mg/dL	133.0 (92.0 – 200.0)	149.0 (98.0 – 202.0)	130.0 (81.8 – 181.5)	0.82	126.0 (89.0 – 183.0)	163.0 (84.8 – 205.8)	140.5 (81.8 – 186.3)	0.32	114.0 (97.0 – 216.0)	134.0 (103.0 – 170.0)	128.0 (99.0 – 140.2)	0.22	Dominant
				0.49				0.85				0.28	Recessive
				0.70				0.44				0.06	Additive

Values are shown as median (Q1–Q3) for nonparametric variables.

[a] Mann-Whitney U test

Abbreviations: HDL, high density lipoprotein; LDL, low density lipoprotein; PCSK9, Proprotein Convertase Subtilisin/Kexin type 9.

Conversion to SI units: to change cholesterol to mmol/L, divide by 38.6; triglycerides to mmol/L, by 88.5.