

APPENDIX: Tables A – E and Figures A, B

**Association of Extreme Blood Lipid Profile Phenotypic Variation
with 11 Reverse Cholesterol Transport Genes and
10 Nongenetic Cardiovascular Disease Risk Factors**

Alfredo Morabia¹, Eftihia Cayanis², Michael C. Costanza¹, Barbara M Ross²,
Maria Sol Flaherty², Gabriela B. Alvin², Kamna Das², and T. Conrad Gilliam²

¹ Division of Clinical Epidemiology, Geneva University Hospitals, 25 rue Micheli-du-Crest,
1211 Geneva 14, Switzerland

² Columbia Genome Center and Departments of Genetics & Development, and Psychiatry,
Columbia University, 1150 St. Nicholas Avenue, New York NY 10032, USA

Corresponding author : Prof. Alfredo Morabia (mailing address¹)

Telephone : (41-22) 37 29 577

Fax : (41-22) 37 29 565

Email : Alfredo.Morabia@hcuge.ch,

Website: www.epidemiology.ch

Appendix Table A. Type of sequence variants identified and frequency of the rare allele in 11 reverse cholesterol transport (RCT) genes of 95 subjects. (**Bold** : rare allele frequency $\geq 3\%$.)

GENE	<i>Exon</i>	<i>Base position</i> [§]	<i>Variant</i> [‡]	<i>Rare allele frequency (%)</i>
ABCA1				
Promotor		-1426	C-T	35
		-1283	G-A	9
		-1263	T-C	2
		-1248	C-T	8
		-1126	G-T	13
		-964	T-G	46
		-654	G-A	15
			del-ins	36
		-588	C-T	47
		-431	G-C	33
		-326	C-T	5
		-302	G-C	32
		-256	ins ACCCC	5
		-123	G-C	37
	-107	G-C	1	
	-38	C-T 5' f	38	
1		11	C-G 5' UTR	1
		+92	T-C 3' f	37
2		16	G ins 5' UTR	14
		76	G-C 5' UTR	13
		+68	G-A 3' f	7
3		-50	T-C 5' f	13
		+26	G-A 3' f	2
4			No variant	
5		-83	A-G 5' f	1
		+76	T-G 3' f	3
6		53	G-A nc	30
7		113	G-A nc	29
8			No variant	
9		-14	A ins 5' f	5
		123	C-T nc	14
		135	G-A nc	9
10			No variant	
11		-105	A-G 5' f	9
		-62	G ins 5' f	34
		-39-(-37)	TCC del 5' f	9
		-13	C-T 5' f	4
12-13			No variant	
14		+24	T-A 3' f	32
15		-59	C-T 5' f	3
		148	C-A nc	14
		+32	G-T 3' f	2
16		120	G-T nc	1
		196	G-A Val-Met	7
		210	C-G nc	1
		+55	G-C 3' f	1
		+95	T-A 3' f	17
17		136	G-A nc	3
18		107	A-G Ile-Met	11
		+75	G-A 3' f	1
19		-75	G-A 3' f	3
		-68	G-C 5' f	4
20			No variant	
21		-104	C-T 5' f	1

22	+118	T-G 3' f	32
23	+102	A-G 3' f	6
24	-65	G-A 5' f	1
	54	G-C nc	5
25	b.7	C-T Ser-Phe	1
	b.98	A-G nc	1
	+23	G-A 3' f	6
26		No variant	
27	+74	C-A 3' f	1
28	98	G-A nc	1
29	-34	C-T 5' f	1
30		No variant	
31	7	G-A nc	13
32	72	G-T nc	1
	+30	T-G 3' f	7
34	-144	C-T 5' f	1
	-132	CT ins 5' f	22
	-26	G-C 5' f	10
35	62	G-A Arg-Lys	23
36-37		No variant	
38	-61	T-C 5' f	1
	-47	T-C 5' f	1
39	139	C-T nc	1
40		No variant	
41	-25	C-T 5' f	1
42	-119	C-T 5' f	2
43		No variant	
44	+18	T-C 3' f	15
45	+68	T-C 3' f	15
46	-62	ins-del 5' f	1
	114	C-T nc	1
47	-39	T del 5' f	1
	-34	C-T 5' f	1
48	+13	A-G 3' f	5
49	+55	G-C 3' f	13
50	483	G-T 3' UTR	1
	834	C-T 3' UTR	28
	863	T-C 3' UTR	1
	1014-1015	CG del 3' UTR	1
	2037	A-G 3' UTR	14
	2064	A-C 3' UTR	2
	2452	A-G 3' UTR	21
	2658	T-G 3' UTR	6
	2691	T-G 3' UTR	1
	3038	G-A 3' UTR	5
APOA1			
1	+41	C-T 3' f	36
2	-14	C-T 5' f	1
	+33	C-T 3' f	14
3	75	C-T Thr-Ile	1
APOE			
1	+69	G-C 3' f	32
2	+64	C-T 3' f	1
	+78	G-A 3' f	5
3	-106	G-T 5' f	3
4	152	T-C Cys-Arg	8
	290	C-T Arg-Cys	15
	415	C-T n.c.	1
CETP			
1	-11	G-C 5' f	36

	66	G-A 5' UTR	1
	174	C-G Ala-Gly	1
	+95	C-A 3' f	4
2		No variant	
3	-48	C-A 5' f	1
4		No variant	
5	+64	C-T 3' f	1
6	-56	G-A 5' f	45
	7	G-A n.c.	1
7	-70	C-T 5' f	1
	+8	C-T 3' f	45
8	+77	G-A 3' f	3
9	-203	C-T 5' f	1
	-51	T-C 5' f	5
	54	G-T n.c.	1
	111	C-T n.c.	6
	+24	T-G 3' f	15
	+29	A-G 3' f	17
	+65	C-T 3' f	1
10-11		No variant	
12	7	G-A Val-Met	1
	22	G-C Ala-Pro	2
	+198	12bp INS 3' fl. (CTGCCAGGAAGA)	13
13	-14	C-T 5' f	31
14	16	A-G Ile-Val	31
15	82	G-A Arg-Gln	5
16	-30	A-G 5' f	36
	159	G-A 3' UTR	22

EL

1	229	T-G Trp-Gly (5' UTR)	40
	315	C-T n.c.	1
	+51	C-T 3' f	40
	+55	C-G 3' f	40
2	-44	C-T 5' f	2
3	-22	T-C 5' f	17
	7	G-A Gly-Ser	1
	53 (T111I)	C-T Thr-Ile	37
4	+98	G-A 3' f	34
5	-85	C-T 5' f	2
	+42	C-T 3' f	40
6	142	G-A Arg-His	1
7	-76	T-G 5' f	3
8	-101	T-C 5' f	1
	+120	A-T 3' f	2
9	-108	T-C 5' f	43
10	304	T-C 3' UTR	3
	337	A-G 3' UTR	9
	470	C-T 3' UTR	1
	504	A-G 3' UTR	28
	506	C-T 3' UTR	2
	769	G-A 3' UTR	1
	1004	C-T 3' UTR	1
	1026	T-C 3' UTR	1
	1109	T-A 3' UTR	3
	1349	T-C 3' UTR	3
	1525	T-G 3' UTR	1
	1528	T-C 3' UTR	2
	1572	G-A 3' UTR	1
	2053	T-G 3' UTR	5

	2055	T-G 3' UTR	1
HL			
Promotor	-544	C-T	30
	-510	C-T	2
	-280	G-A	32
1	+52	C-T 3' f	10
	+64	A-G 3' f	2
	+111	G-A 3' f	1
2		No variant	
3	-279	G-A 5' f	39
	-242	T-C 5' f	19
	-46	G-A 5' f	20
	10	G-A Val-Met	4
	42	C-T n.c.	1
	67-70	CCAG del	1
	156	G-A n.c.	1
	159	C-T n.c.	1
4	9	T-G n.c.	42
5	-95	T-G 5' f	1
	-31	C-T 5' f	1
	-8	C-A 5' f	5
	17	A-G n.c.	9
	70	A-G Asp-Ser	33
	98	C-G n.c.	44
6	58	C-T Ser-Phe	1
	173	C-T n.c.	1
	216	G-A Val-Ile	1
7	17	A-C Leu-Phe	1
	47	G-A n.c.	1
	+31	T-C 3' f	8
	+36	CA ins 3' f	1
	+110	G-A 3' f	1
	+111	A-T 3' f	1
	+125	G-C 3' f	1
8	45	C-T Thr-Met	1
	57	A-C Asp-Ala	1
	+28	C-T 3' f	1
	+111	T-C 3' f	36
9	49	C-A n.c.	7
	+124	A-G 3' f	1
LCAT			
1	+123	C-T 3' f	2
2-3		No variant	
4	-23	C-A 5' f	1
5	171	T-A n.c.	3
6	429	C-T n.c.	7
LPL			
1		No variant	
2	-91	G-A 5' flank	1
	18 (D9N)	G-A Asp-Asn	2
3	3	A-C n.c.	1
	156	G-A n.c.	3
	+134	T-C 3' f	1
4	b.6	G-A n.c.	6
5	-108	A-C 5' f	1
	+33	C-G 3' f	17
	+37	T-C 3' f	17
	+103	C-T 3' f	17
6	-83	C-G 5' f	1
	-34	C-T 5' f	1
	178 (N291S)	A-G Asn-Ser	1

	+16	T-C 3' f	1
	+73	T-G 3' f	22
	+82	C-A 3' f	17
	+108	G-A 3' f	16
7		No variant	
8	-102	C-G 5' f	1
	25	C-A n.c.	12
9	-90	T-G 5' f	34
	99 (S447X)	C-G Ser-STP	15
10	-11	C-T 5' f	15
	10	G-A 3' UTR	16
	15	T-A 3' UTR	1
PLTP			
Promotor	-405	C-T	1
	-180	G-GG	11
	-54-(-51)	GGA del. 5' f.	1
1	+26	G-C 3' f	11
2	-76	C-T 5' f	45
3	+56	G-A 3' f	1
4	106	G-T n.c.	1
	+97	A-C 3' f	24
5-7		No variant	
8	-145	G-A 5' f	1
9	140	G-A Arg-Gln	1
10	+70	G-T 3' f	6
11	-34	G-T 5' f	1
12	8	G-A Arg-His	1
	31	C-T Arg-Trp	1
	+68	A-C 3' f	34
13	+19	G-A 3' f	1
14	-64	G-T 5' f	1
SR-BI			
1	72	G-A Gly-Ser	6
2	-88	G-A 5' f	1
	+68	G-A 3' f	1
3	119	G-A Val-Ile	1
4	73	G-A Gly-Ser	1
	75	C-T n.c.	1
	+60	C-T 3' f	1
5	+54	C-T 3' f	10
6		No variant	
7	-202	A-G 5' f	1
	61	C-T n.c.	1
8	41	C-T n.c.	48
	+73	C-A 3' f	1
9-10		No variant	
11	-41	C-G 5' f	4
12		No variant	
13	49	C-T 3' UTR	1
	72	G-A 3' UTR	2
	+37	C-T poly A	1
	+72	T-C poly A	24

[§] Distance from the first/last exonic base on the 5' / 3' flanking regions.

[£] del : deletion ; f : flank ; ins : insertion ; n.c. : no amino acid change; UTR : untranslated region.

Appendix Table B. Tier 1 selected *Atherogenic*[‡], *Atheroprotective*[‡], and Gender-Dependent[‡] reverse cholesterol transport (RCT) gene SNPs assayed in all cases[§] and controls[§], with internal cross-validations in five 80%:20% subsamples. (➔ : 37 SNPs retained for Tier 2, 3, 4 modeling in the total sample; **1b** : 14 Tier 1b SNPs excluded due to high correlation or rare variant ≤ 5%.)

Gene		Internal Cross-Validations					➔ Total Sample Results	
		Individual SNP Odds Ratio (OR (95% CI)) [‡] (<i>Atherogenic</i> [‡] or <i>Atheroprotective</i> [‡]), or SNP x Gender interaction p [‡]					Individual SNP OR (95% CI) [‡] <i>Atherogenic</i> [‡] or <i>Atheroprotective</i> [‡]	SNP x Gender interaction p (OR _m , OR _w) [‡]
		Subsample						
Exon	Position [#]	A	B	C	D	E		
ABCA1								
1	➔ -1126		0.059	0.035	0.030	0.093		0.057 (0.42, 1.39)
	➔ -654	1.79 (0.91-3.52)	1.63 (0.84-3.16)	1.61 (0.80-3.24)	1.67 (0.87-3.22)	1.61 (0.84-3.09)	1.66 (0.91-3.00)	
	-326 (1b)	NA		0.052	NA	0.047		0.044 (7.25, 0.34)
	-38					0.097		
	+92					0.096		
2	➔ +68	0.43 (0.18-1.04)		0.60 (0.25-1.42)	0.56 (0.24-1.30)	0.59 (0.25-1.39)	0.58 (0.27-1.25)	
3	-50		1.74 (0.90-3.36)			1.52 (0.80-2.88)		
5	+76 (1b)	1.83 (0.44-7.69)	2.44 (0.52-11.4)	2.61 (0.66-10.4)	2.69 (0.65-11.0)	2.49 (0.62-10.0)	2.42 (0.69-8.52)	
6	53				0.064	0.087		
7	113				0.096			
9	123		1.92 (0.91-4.04)		1.55 (0.75-3.22)			
	135	0.64 (0.32-1.31)						
11	-13					0.65 (0.28-1.52)		
16	➔ 196	0.41 (0.12-1.36)	0.65 (0.19-2.24)			0.38 (0.11-1.33)	0.59 (0.21-1.68)	
17	136			0.64 (0.24-1.74)				
19	-68	1.61 (0.64-4.06)						
	-75 (1b)	0.014	NA	0.39 (0.06-2.32)	0.078	0.030		0.031 (2.88, 0.092)
22	+118			0.58 (0.32-1.05)	0.084			
23	➔ +102	0.053	1.63 (0.60-4.38)	0.058		1.57 (0.62-3.96)	1.51 (0.65-3.53)	
24	54	0.54 (0.18-1.63)		0.028				
32	➔ +30	2.10 (0.97-4.54)	1.98 (0.89-4.42)	3.53 (1.62-7.72)	0.057	2.69 (1.21-5.59)	2.28 (1.16-4.52)	
35	➔ 62	0.069	1.74 (0.97-3.10)	1.89 (1.05-3.44)	1.80 (1.00-3.22)		1.59 (0.95-2.66)	
45	+68		1.81 (0.98-3.34)					
48	+13			1.62 (0.68-3.85)				
49	+55				0.65 (0.33-1.28)	0.60 (0.32-1.13)		
50	➔ 834			0.60 (0.33-1.09)	0.61 (0.34-1.10)	0.52 (0.29-0.91)	0.63 (0.38-1.06)	
	➔ 2037			0.072	0.062	0.046		0.065 (0.73, 2.12)
	➔ 2452	0.059	0.079			0.063		0.067 (1.25, 0.44)
	➔ 3038	0.25 (0.09-0.70)	0.31 (0.11-0.84)	0.30 (0.12-0.73)	0.21 (0.08-0.55)	0.21 (0.08-0.54)	0.26 (0.11-0.61)	
APOA1								

2 → +33 | 2.05 (0.94-4.45) | 2.48 (1.09-5.64) | 1.97 (0.90-4.30) | 2.45 (1.15-5.27) | 2.26 (1.04-4.89) | 2.21 (1.11-4.43) |

APOE

1	+69	1.50 (0.82-2.75)						
2	+78 (1b)	3.10 (1.32-7.29)	3.22 (1.33-7.75)	3.78 (1.50-9.50)	3.88 (1.66-9.08)	4.23 (1.82-9.85)	3.54 (1.65-7.61)	
4	152 (C128R) 290 (R175C)	<i>N.B.: 1 or 2 rare variants on exon 4b.290 (only) = APOE2 (E2/E3 or E2/E2)); on exon 4b.152 (only)= APOE4 (E3/4 or E4/E4); no rare variants on either 4b.152 or 4b.290 = APOE3 (E3/E3); excluded: 1 rare variant on APOE 4b.152 and APOE 4b.290 = E2/E4.</i>						
	→ APOE2	0.20 (0.08-0.46)	0.13 (0.05-0.33)	0.19 (0.08-0.44)	0.15 (0.06-0.37)	0.19 (0.08-0.42)	0.17 (0.08-0.37)	
	APOE3	1.74 (0.96-3.18)						
	→ APOE4	1.82 (0.87-3.78)	3.36 (1.55-7.29)	2.22 (1.09-4.54)	2.42 (1.19-4.93)	2.69 (1.31-5.50)	2.40 (1.26-4.56)	

CETP

1	→ -629	2.38 (1.20-4.72)	2.89 (1.49-5.61)	2.45 (1.23-4.90)	2.34 (1.21-4.53)	2.85 (1.47-5.52)	2.55 (1.41-4.63)	
	+95		1.60 (0.64-4.01)			0.065		
6	→ -56	0.41 (0.22-0.79)	0.49 (0.27-0.90)	0.42 (0.22-0.79)	0.46 (0.25-0.87)	0.37 (0.20-0.70)	0.43 (0.25-0.76)	
7	+8 (1b)	0.41 (0.22-0.78)	0.086	0.41 (0.22-0.76)	0.46 (0.25-0.84)	0.38 (0.21-0.70)	0.42 (0.25-0.73)	
8	+77 (1b)	2.26 (0.59-8.58)		1.70 (0.52-5.60)	1.70 (0.51-5.70)		1.61 (0.54-4.81)	
9	-51		0.098					
	111			1.56 (0.57-4.27)	1.58 (0.59-4.23)			
	→ +24					2.08 (1.13-3.85)	1.51 (0.87-2.62)	
	+29 (1b)	1.61 (0.86-3.01)	1.54 (0.84-2.82)		1.56 (0.86-2.84)	2.08 (1.14-3.82)	1.63 (0.95-2.80)	
13	-14		0.64 (0.35-1.16)					
15	82	1.64 (0.46-5.86)						
16	159	1.66 (0.88-3.13)	0.065		1.53 (0.82-2.87)			

EL

1	+55	1.51 (0.82-2.77)						
	229 (1b)		0.012	0.063		0.066		0.033 (0.62, 2.01)
3	-22			0.57 (0.30-1.08)	0.62 (0.33-1.16)			
	→ & 53 (T111D) &	0.56 &	0.17 &	0.28 &	0.047 &	0.54 &	0.21 (0.70, 1.37) &	
4	+98 &		0.039	0.054	0.014			0.045 (0.60, 1.77)
5	+42		0.079		0.62 (0.34-1.13)			
7	-76				0.61 (0.18-2.09)			
9	-108		0.072		0.039			
10	304			0.65 (0.23-1.87)				
	→ 337	1.64 (0.77-3.47)	1.74 (0.85-3.57)	2.27 (1.06-4.86)	2.06 (0.95-4.49)		1.81 (0.93-3.50)	
	→ 504		0.058		0.0085	0.066		0.064 (1.28, 0.47)
	1349			0.55 (0.20-1.56)	0.56 (0.20-1.54)			

HL

1	-544	0.56 (0.30-1.04)	0.67 (0.37-1.21)		0.66 (0.37-1.21)	0.66 (0.37-1.19)		
	→ -280	0.51 (0.27-0.94)	0.59 (0.33-1.07)			0.63 (0.35-1.14)	0.62 (0.36-1.05)	
3	→ -279	0.0049		0.011	0.038	0.071		0.022 (0.59, 2.22)
	-242	0.093						

→ -46 10 (1b)	0.0042 <i>1.59 (0.54-4.64)</i>	<i>1.87 (0.58-6.00)</i>	0.0033 0.036	0.0075 0.015	0.66 (0.36-1.20)		0.017 (1.85, 0.47) 0.080 (4.16, 0.63)
4 9			0.55 (0.30-1.01)		0.66 (0.37-1.19)		
5 -8 (1b)	0.53 (0.20-1.38)		0.49 (0.19-1.26)	0.55 (0.22-1.39)	0.63 (0.27-1.47)	0.56 (0.25-1.26)	
→ 17	0.38 (0.13-1.09)	0.65 (0.24-1.81)	0.56 (0.22-1.46)	0.46 (0.16-1.34)		0.46 (0.19-1.09)	
→ 98	0.63 (0.32-1.23)	0.025	0.61 (0.31-1.17)	0.59 (0.30-1.15)	0.085	0.65 (0.37-1.14)	
7 +31 (1b)	0.39 (0.12-1.28)	0.048	0.50 (0.19-1.36)	0.59 (0.22-1.61)	0.53 (0.21-1.37)	0.50 (0.21-1.21)	
8 +111	0.099				0.084		
LCAT							
5 171	0.67 (0.15-3.03)			<i>1.54 (0.31-7.57)</i>			
6 → 429		0.067		0.074	0.061		0.079 (1.59, 0.41)
LDLR							
2 → LDLR2 (rs2228671)	0.64 (0.32-1.28)	0.55 (0.28-1.12)	0.44 (0.22-0.88)	0.64 (0.33-1.26)	0.52 (0.27-1.03)	0.55 (0.30-1.02)	
Int 9 rs1003723			0.55 (0.29-1.05)				
11 → LDLR11 (rs5929)	0.61 (0.20-1.84)	0.52 (0.17-1.58)	0.47 (0.16-1.41)	0.36 (0.11-1.17)	0.37 (0.12-1.13)	0.46 (0.17-1.24)	
12 rs5930			0.057				
UTR rs1433099					0.075		
LPL							
3 156	<i>1.90 (0.57-6.29)</i>		0.029				
4 → 6	0.45 (0.18-1.17)			0.46 (0.19-1.14)		0.61 (0.27-1.35)	
5 +33		0.62 (0.34-1.15)		0.65 (0.36-1.20)	0.67 (0.36-1.22)		
→ +37		0.59 (0.32-1.09)		0.63 (0.34-1.17)	0.65 (0.35-1.20)	0.66 (0.38-1.14)	
+103		0.59 (0.32-1.09)					
6 +73 (1b)	0.63 (0.34-1.18)	0.47 (0.26-0.84)	0.64 (0.36-1.15)	0.55 (0.31-0.99)	0.50 (0.28-0.90)	0.56 (0.33-0.94)	
→ +82		<i>2.16 (1.07-4.38)</i>	<i>1.60 (0.79-3.26)</i>		<i>1.74 (0.90-3.38)</i>	<i>1.55 (0.84-2.84)</i>	
+108		0.60 (0.32-1.12)					
8 25	0.55 (0.26-1.15)						
→ +481 (HindIII)	0.54 (0.29-0.98)	0.57 (0.31-1.03)	0.59 (0.32-1.07)	0.60 (0.33-1.08)	0.68 (0.38-1.21)	0.60 (0.36-1.01)	
9 -90 (1b)	0.56 (0.31-1.02)	0.58 (0.32-1.03)		0.61 (0.34-1.08)		0.64 (0.38-1.07)	
→ 99 (S447X)	0.44 (0.21-0.90)	0.30 (0.15-0.62)	0.40 (0.16-0.81)	0.45 (0.23-0.90)	0.37 (0.19-0.75)	0.39 (0.21-0.73)	
10 -11 (1b)	0.45 (0.22-0.90)	0.34 (0.17-0.68)	0.40 (0.20-0.80)	0.43 (0.22-0.84)	0.35 (0.18-0.68)	0.39 (0.21-0.72)	
10 10	0.61 (0.31-1.22)						
PLTP							
1 → -180	0.39 (0.15-1.04)		0.40 (0.16-1.02)	0.63 (0.25-1.63)	0.37 (0.13-1.02)	0.50 (0.22-1.19)	
→ +26	0.099	0.34 (0.16-0.76)	0.29 (0.13-0.68)	0.020	0.030		0.023 (0.64, 0.15)
2 -76				<i>1.57 (0.83-2.97)</i>			
10 → +70	0.21 (0.07-0.61)	0.19 (0.07-0.52)	0.16 (0.06-0.46)	0.053	0.18 (0.07-0.49)	0.21 (0.09-0.51)	
12 +68	<i>1.69 (0.91-3.12)</i>		<i>1.51 (0.83-2.74)</i>				

SR-BI							
1	72 (G2S)		0.064	1.67 (0.77-3.64)			
8	→ 41 (A350A)	0.043	0.019	0.046	0.064	0.022	0.020 (0.40, 1.74)
11	-41		1.86 (0.65-5.30)				

† Adjusted OR ≥ 1.50 (*Atherogenic* SNP), or OR $\leq 1/1.50=0.67$ (*Atheroprotective* SNP), or (SNP x gender) interaction (nominal) $p \leq .10$ and at least one gender-specific OR (men: OR_m; women: OR_w) satisfying *Atherogenic* or *Atheroprotective* criteria (Gender-Dependent SNP). (*N.B.* : Gender-Dependence overrides *Atherogenic* / *Atheroprotective* characterization)

§ Cases: atherogenic lipid profile (low HDL-C, high LDL-C) (186 subjects); controls: non-atherogenic lipid profile (high HDL_C, low LDL-C) (185 subjects).

Relative to first / last exonic base on the 5' / 3' flanking region.

£ Single SNP, case-control OR adjusted for nongenetic covariates [gender, age, BMI, education, country of birth, cigarette smoking, alcohol drinking, dietary fat (%), dietary fiber(g), physical inactivity].

§ Likelihood ratio test of model in £ vs. extended model including SNP x gender interaction.

& EL: exon 3 b.53 (T111I) was substituted for exon 4 b.+98 due to high correlation (total sample $r = 0.96$ (men/women: 0.99/0.93)) in modeling based on the total sample and modeling based on any subsample for which both SNPs were selected in Tier 1.

Appendix Table C. RCT gene Tier 2 (nominal) $p=.10$ stepdown selection final models within Tier 1 SNP groups, with internal cross-validations in five 80%:20% random subsamples.

Atherogenic SNPs in final models	Entry Step [§]					
<i>for total sample or subsamples:</i>	Total Sample	80% random subsample				
		A	B	C	D	E
<i>APOE4</i>	1	4	1	2	1	2
CETP 1b.-629	2	1	3	-	-	1
APOA1 2b.+33	3	3	4	4	2	6
ABCA1 32b.+30	4	6	-	1	-	4
LPL 6b.+82	5	-	2	-	-	3
EL 10b.337	6	-	-	3	3	-
<i>For subsamples only :</i>						
ABCA1 45b.+68	-	-	5	-	-	-
<i>APOE3</i>	-	5	-	-	-	-
CETP 9b.+29	-	2	-	-	-	5
CETP 16b.159	-	2	-	-	-	-
Atheroprotective SNPs in final models	Entry Step [§]					
<i>for total sample or subsamples:</i>	Total Sample	80% random subsample				
		A	B	C	D	E
<i>APOE2</i>	1	1	1	1	1	1
PLTP 10b.+70	2	3	-	-	-	2
LPL S447X	3	9	3	2	3	5
ABCA1 50b.3038	4	4	4	4	2	3
CETP 6b.-56	5	5	-	5	4	4
HL 5b.98	7	10	-	8	-	-
HL 1b.-280	6	2	-	-	-	-
LDLR2 (rs2228671)	8	-	-	9	-	7
<i>For subsamples only :</i>						
ABCA1 2b.+68	-	6	-	10	-	-
ABCA1 24b.54	-	8	-	-	-	-
HL 1b.-544	-	-	-	-	6	-
HL 4b.9	-	-	-	6	-	-
HL 5b.17	-	-	-	7	-	-
HL 5b.+42	-	-	-	-	5	-
PLTP 1b.+26	-	-	2	3	-	-
PLTP 1b.-180	-	7	-	-	-	6
Gender-Dependent						

SNPs in final models <i>for total sample or subsamples:</i>	Entry Step [§]					
	Total Sample	80% random subsample				
		A	B	C	D	E
PLTP 1b.+26	1	1			1	1
+ gender interaction	2	not retained	Athero- protective	Athero- protective	2	2
ABCA1 50b.2037	3	-	-	-	3	
+ gender interaction	4	-	-	-	4	
EL 10b.504	5	-	-	-	5	10
+ gender interaction	6	-	-	-	6	11
SR-BI A350A	7	6	3	5	11	8
+ gender interaction	8	7	4	6	12	9
ABCA1 1b.-1126	9	-	7	3	13	12
+ gender interaction	10	-	8	4	14	13
HL 3b.-279	11	2	-	1	9	6
+ gender interaction	12	3	-	2	10	7
<i>For subsamples only :</i>						
ABCA1 1b.-38	-	-	-	-	-	14
+ gender interaction	-	-	-	-	-	15
ABCA1 6b.53	-	-	-	-	7	-
+ gender interaction	-	-	-	-	8	-
ABCA1 23b.+102	-	4	-	7	-	-
+ gender interaction	-	5	-	8	-	-
ABCA1 24b.54	-	-	-	9	-	-
+ gender interaction	-	-	-	10	-	-
ABCA1 50b.2452	-	8	-	-	-	-
+ gender interaction	-	9	-	-	-	-
HL 5b.98	-	-	1	-	-	3
+ gender interaction	-	-	2	-	-	4
HL 7b.+31	-	-	5	-	-	-
+ gender interaction	-	-	-	-	-	-
LCAT 6b.429	-	-	-	-	-	5
+ gender interaction	-	-	-	-	-	not retained

[§] Order of forced-forward entry of SNPs retained in model after stepdown selection.

Appendix Table D. RCT gene Tier 3 (nominal) $p=.05$ stepdown selection (SNPs only, nongenetic covariates forced into model) final models, with internal cross-validations in five 80%:20% random subsamples.

SNPs in final models <i>for total sample or subsamples:</i>	Total Sample	Entry Step [§] 80% random subsample				
		A	B	C	D	E
<i>APOE2</i>	1	1	1	1	1	1
PLTP 1b.+26	2	2	3	5	3	2
LPL S447X	3	-	-	2	-	3
CETP 6b.-56	4	-	-	-	4	-
ABCA1 50b.3038	5	3	2	8	2	-
LDLR2 (rs2228671)	6	-	-	3	-	4
HL 1b.-280	7	5	-	-	-	-
ABCA1 32b.+30	8	4	-	9	-	-
PLTP 1b.+26 x Gender	9	-	-	-	5	-
SR-BI A350A	10	8	-	17	11	-
SR-BI A350A x Gender	11	9	-	18	12	-
HL 3b.-279	12	10	-	11	13	-
HL 3b.-279 x Gender	13	11	-	12	14	-
<i>For subsamples only :</i>						
ABCA1 1b.-1126	-	-	9	13	6	10
ABCA1 1b.-1126 x Gender	-	-	10	14	7	11
ABCA1 1b.-38	-	-	-	-	-	8
ABCA1 1b.-38 x Gender	-	-	-	-	-	9
ABCA1 23b.+102	-	-	-	15	-	-
ABCA1 23b.+102 x Gender	-	-	-	16	-	-
ABCA1 45b.+68	-	-	5	-	-	-
APOA1 2b.+33	-	-	8	-	-	-
<i>APOE4</i>	-	-	4	10	-	-
CETP 1b.-629	-	6	7	-	-	-
CETP 9b.+29	-	-	-	-	-	5
HL 4b.9	-	-	-	4	-	-
HL 5b.98	-	7	-	-	-	-
HL 5b.17	-	-	-	6	-	-
EL 5b.+42	-	-	-	-	8	-
EL 10b.337	-	-	-	7	-	-
EL 10b.504	-	-	-	-	9	-
EL 10b.504 x Gender	-	-	-	-	10	-
LPL 6b.+82	-	-	6	-	-	-
PLTP 1b.-180	-	-	-	-	-	7

[§] Order of forced-forward entry of SNPs retained in model after stepdown selection.

Appendix Table E. RCT gene Tier 4 (nominal) $p=.05$ stepdown selection (SNPs + nongenetic covariates) final models, with internal cross-validations in five 80%:20% random subsamples.

Covariates/SNPs in final models <i>for total sample or subsamples:</i>	Total Sample	Entry Step [§]				
		A	B	80% random subsample		
				C	D	E
BMI (kg/m ²)	1	1	1	1	1	1
<i>APOE2</i>	2	2	2	5	3	2
PLTP 1b.+26	3	5	4	2	5	5
Alcohol: Medium+High	4	6	3	4	4	10
Alcohol: Low	5	7	7	6	6	11
Current Smoker	6	4	5	3	2	3
ABCA1 50b.3038	7	9	6	11	7	-
LPL S447X	8	-	-	7	-	4
Age (yrs)	9	-	-	12	8	9
Gender	10	3	12	15	10	12
ABCA1 32b.+30	11	8	-	9	-	-
LDLR2 (rs2228671)	12	-	-	8	-	8
HL 1b.-280	13	10	-	-	-	-
HL 3b.-279	14	15	-	20	19	-
HL 3b.-279 x Gender	15	16	-	21	20	-
SR-BI A350A	16	13	-	24	17	-
SR-BI A350A x Gender	17	14	-	25	18	-
<i>For subsamples only :</i>						
Education (Low)	-	12	-	19	-	-
ABCA1 1b.-1126	-	-	11	17	13	14
ABCA1 1b.-1126 x Gender	-	-	13	18	14	15
ABCA1 1b.-38	-	-	-	-	-	16
ABCA1 1b.-38 x Gender	-	-	-	-	-	17
ABCA1 23b.+102	-	-	-	22	-	-
ABCA1 23b.+102 x Gender	-	-	-	23	-	-
ABCA1 45b.+68	-	-	8	-	-	-
APOA1 2b.+33	-	-	-	16	-	-
<i>APOE4</i>	-	-	10	-	-	-
CETP 1b.-629	-	11	-	-	-	-
CETP 6b.-56	-	-	-	-	9	-
CETP 9b.+29	-	-	-	-	-	6
HL 4b.9	-	-	-	10	-	-
HL 5b.17	-	-	-	14	-	-
EL 5b.+42	-	-	-	-	12	-

EL 10b.337	-	-	-	13	-	-
EL 10b.504	-	-	-	-	15	-
EL 10b.504 x Gender	-	-	-	-	16	-
LPL 6b.+82	-	-	9	-	-	-
PLTP 1b.-180	-	-	-	-	-	7
PLTP 1b.+26 x Gender	-	-	-	-	11	13

§ Order of forced-forward entry of SNPs retained in model after stepdown selection.

APPENDIX FIGURE LEGENDS

APPENDIX FIGURE A

Histogram of rare allele frequency (%) differences for 121 RCT gene common SNPs (rare allele frequency $\geq 3\%$) that were assayed in both the resequencing subsample (n=95) and in the remaining case-control sample (n=276). Median frequency difference = 0%, mean = -0.19%, SD = 3.9%.

APPENDIX FIGURE B

Minimum case (n=186) / control (n=185) single-SNP unadjusted odds ratio (OR) detectable with specified statistical power ($1-\beta$) = 60% (10%) 90%, 95%, 99% (2-tailed $\alpha = 5\%$) as a function of the control proportion with rare allele(s) (heterozygote/homozygote) for a given SNP. The power for the corresponding adjusted OR would be greater than for the unadjusted OR.