heterozygotes and homozygotes. We have also confirmed that the incidence of D442G mutation is higher in people with hyperalphalipoproteinemia (2.58 mmol/l or over).

Genetic *CETP* deficiency is the most important and common cause of hyperalphalipoproteinemia in Japanese and the *CETP* deficiency contributes to 60% of hyperalphacholesterolemia [28]. However, the role of CETP in atherogenesis is still under debate. Study in the Japanese Omagari area has shown a relatively increased incidence of coronary atherosclerosis in CETP deficiency [29]. In Copenhagen City Heart Study, increased HDL-cholesterol levels caused by mutations in *CETP* are associated with an increased risk of CAD in white women [30]. In contrast, the B2 allele of TaqIB polymorphism is associated with low CETP mass, higher HDL-cholesterol levels, and a decreased risk for coronary artery disease [16]. The reason for this discrepancy is unknown. It might be due to dose effects of CETP mass or another genetic abnormality can be involved in this difference to explain the risk for CAD. Hirano et al showed that the people with low LIPC activity had a higher incidence of CAD [31]. Therefore, it is possible that the LIPC activity is involved in these differences. Further studies are necessary to determine the role of CETP in CAD in various populations with difference genetic background.

Our study is consistent with other studies in terms of allele frequency of the S447X polymorphism of *LPL* gene [18, 19, 32]. Recent studies show that the X447 mutation is associated with a favorable lipid profile, with lower TG and higher HDL-cholesterol levels, and that it may confer protection against coronary artery disease [18, 19, 33]. We also found similar tendency in

men and women. However, the statistical significance was found in HDL-cholesterol levels of the total population and women, but not in men. Because the X447 mutation is associated with higher LPL activity, the TG levels were lower in heterozygotes and homozygotes as expected, although the significance was not noted in women. Homozygotes seem to have lower TG levels than heterozygotes, which reflects the gene dosage effect. Because the carriers of the S447X have favorable lipid profile in terms of HDL-cholesterol and TG, and several studies have shown a decreased risk of CAD in carriers of the S447X [34, 35], we should examine whether carriers of the S447X have less coronary artery events in the future.

In terms of *LIPC* gene polymorphism, our data clearly indicate that the frequency of the TT genotype is significantly higher in the Japanese than that in Caucasians [36, 37]. However, the higher frequency of the TT genotype is also found in Koreans and Japanese [38-40]. Therefore, this difference might partly explain higher HDL-cholesterol levels in Asians.

Our results on allele frequency of the SstI polymorphism of the *APOC3* gene were almost comparable to the data on Asian Indians [41], but not on Caucasians [42]. Caucasians seem to have less allele frequency of S2. Although the association of higher TG levels with S2 allele has been reported in studies carried out in Caucasians [43-45] and Asians [46-48], our data show that the association was found in the total population and in men, but not in women. Few other studies, however, did not find any significant association between SstI polymorphism and hypertriglyceridemia [49-51]. The linkage disequilibrium between this polymorphism and the

causative mutation might be weakened or absent in some populations [43].

Our data clearly showed that the heterozygotes of D442G mutation, homozygote of LPL S447X mutation, and people with TaqIB2B2 genotype had a higher incidence of hyperalphalipoproteinemia with HDL-cholesterol levels of 2.58 mmol/l or over. Alcohol consumption and smoking can also affect the levels of HDL-cholesterol. Corbex et al showed that the HDL levels of the people with certain polymorphisms of the *CETP* gene are modulated by alcohol consumption [52]. Therefore, it might be necessary to taking account of the environmental effects on the effect of gene polymorphism on HDL-cholesterol levels as well as on the risk of cardiovascular events.

In summary we have provided a largest database of gene polymorphism related to lipid metabolism in the general Japanese population. Prospective study is now under way to determine the contribution of these gene polymorphisms to cardiovascular risk in Japanese.

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Appendix

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References

1. Murray CJ, Lopez AD: Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet 349:1269-1276, 1997

2. Watanabe H, Yamane K, Fujikawa R, Okubo M, Egusa G, Kohno N: Westernization of lifestyle markedly increases carotid intima-media wall thickness (IMT) in Japanese people. Atherosclerosis 166:67-72, 2003

3. Marmot MG, Syme SL, Kagan A, Kato H, Cohen JB, Belsky J: Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: prevalence of coronary and hypertensive heart disease and associated risk factors. Am J Epidemiol 102:514-525, 1975

4. Rader DJ, Cohen J, Hobbs HH: Monogenic hypercholesterolemia: new insights in pathogenesis and treatment. J Clin Invest 111:1795-1803, 2003

5. Austin MA, Hutter CM, Zimmern RL, Humphries SE: Familial hypercholesterolemia and coronary heart disease: a HuGE association review. Am J Epidemiol 160:421-429, 2004

6. Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE: Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. Circulation 96:2520-2525, 1997

7. Yen FT, Deckelbaum RJ, Mann CJ, Marcel YL, Milne RW, Tall AR: Inhibition of cholesteryl ester transfer protein activity by monoclonal antibody. Effects on cholesteryl

ester formation and neutral lipid mass transfer in human plasma. J Clin Invest 83:2018-2024, 1989

8. Brown ML, Inazu A, Hesler CB, Agellon LB, Mann C, Whitlock ME, Marcel YL, Milne RW, Koizumi J, Mabuchi H, et al.: Molecular basis of lipid transfer protein deficiency in a family with increased high-density lipoproteins. Nature 342:448-451, 1989

9. Inazu A, Brown ML, Hesler CB, Agellon LB, Koizumi J, Takata K, Maruhama Y, Mabuchi H, Tall AR: Increased high-density lipoprotein levels caused by a common cholesteryl-ester transfer protein gene mutation. N Engl J Med 323:1234-1238, 1990

10. Hirano K, Yamashita S, Funahashi T, Sakai N, Menju M, Ishigami M, Hiraoka H, Kameda-Takemura K, Tokunaga K, Hoshino T, et al.: Frequency of intron 14 splicing defect of cholesteryl ester transfer protein gene in the Japanese general population--relation between the mutation and hyperalphalipoproteinemia. Atherosclerosis 100:85-90, 1993

11. Nagano M, Yamashita S, Hirano K, Kujiraoka T, Ito M, Sagehashi Y, Hattori H, Nakajima N, Maruyama T, Sakai N, Egashira T, Matsuzawa Y: Point mutation (-69 G-->A) in the promoter region of cholesteryl ester transfer protein gene in Japanese hyperalphalipoproteinemic subjects. Arterioscler Thromb Vasc Biol 21:985-990, 2001

12. Sakai N, Yamashita S, Hirano K, Menju M, Arai T, Kobayashi K, Ishigami M, Yoshida Y, Hoshino T, Nakajima N, et al.: Frequency of exon 15 missense mutation (442D:G) in cholesteryl ester transfer protein gene in hyperalphalipoproteinemic Japanese subjects

Atherosclerosis 114:139-145, 1995

13. Tall AR: Plasma cholesteryl ester transfer protein. J Lipid Res 34:1255-1274, 1993

14. Wang S, Deng L, Milne RW, Tall AR: Identification of a sequence within the C-terminal 26 amino acids of cholesteryl ester transfer protein responsible for binding a neutralizing monoclonal antibody and necessary for neutral lipid transfer activity. J Biol Chem 267:17487-17490, 1992

15. Hannuksela ML, Liinamaa MJ, Kesaniemi YA, Savolainen MJ: Relation of polymorphisms in the cholesteryl ester transfer protein gene to transfer protein activity and plasma lipoprotein levels in alcohol drinkers. Atherosclerosis 110:35-44, 1994

16. Ordovas JM, Cupples LA, Corella D, Otvos JD, Osgood D, Martinez A, Lahoz C, Coltell O, Wilson PW, Schaefer EJ: Association of cholesteryl ester transfer protein-TaqIB polymorphism with variations in lipoprotein subclasses and coronary heart disease risk: the Framingham study. Arterioscler Thromb Vasc Biol 20:1323-1329, 2000

17. Stocks J, Thorn JA, Galton DJ: Lipoprotein lipase genotypes for a common premature termination codon mutation detected by PCR-mediated site-directed mutagenesis and restriction digestion. J Lipid Res 33:853-857, 1992

18. Kuivenhoven JA, Groenemeyer BE, Boer JM, Reymer PW, Berghuis R, Bruin T, Jansen H, Seidell JC, Kastelein JJ: Ser447stop mutation in lipoprotein lipase is associated with elevated HDL cholesterol levels in normolipidemic males. Arterioscler Thromb Vasc Biol

17:595-599, 1997

19. Groenemeijer BE, Hallman MD, Reymer PW, Gagne E, Kuivenhoven JA, Bruin T, Jansen H, Lie KI, Bruschke AV, Boerwinkle E, Hayden MR, Kastelein JJ: Genetic variant showing a positive interaction with beta-blocking agents with a beneficial influence on lipoprotein lipase activity, HDL cholesterol, and triglyceride levels in coronary artery disease patients. The Ser447-stop substitution in the lipoprotein lipase gene. REGRESS Study Group. Circulation 95:2628-2635, 1997

20. Bensadoun A, Berryman DE: Genetics and molecular biology of hepatic lipase. Curr Opin Lipidol 7:77-81, 1996

21. Zambon A, Deeb SS, Hokanson JE, Brown BG, Brunzell JD: Common variants in the promoter of the hepatic lipase gene are associated with lower levels of hepatic lipase activity, buoyant LDL, and higher HDL2 cholesterol. Arterioscler Thromb Vasc Biol 18:1723-1729, 1998

22. Ordovas JM, Civeira F, Genest J, Jr., Craig S, Robbins AH, Meade T, Pocovi M, Frossard PM, Masharani U, Wilson PW, et al.: Restriction fragment length polymorphisms of the apolipoprotein A-I, C-III, A-IV gene locus. Relationships with lipids, apolipoproteins, and premature coronary artery disease. Atherosclerosis 87:75-86, 1991

23. Anderson RA, Burns TL, Lee J, Swenson D, Bristow JL: Restriction fragment length polymorphisms associated with abnormal lipid levels in an adolescent population.

Atherosclerosis 77:227-237, 1989

24 Johnson CL, Rifkind BM, Sempos CT, Carroll MD, Bachorik PS, Briefel RR, Gordon DJ, Burt VL, Brown CD, Lippel K, et al.: Declining serum total cholesterol levels among US adults. The National Health and Nutrition Examination Surveys. Jama 269:3002-3008, 1993

25. Nagano M, Yamashita S, Hirano K, Ito M, Maruyama T, Ishihara M, Sagehashi Y, Oka T, Kujiraoka T, Hattori H, Nakajima N, Egashira T, Kondo M, Sakai N, Matsuzawa Y: Two novel missense mutations in the CETP gene in Japanese hyperalphalipoproteinemic subjects: high-throughput assay by Invader assay. J Lipid Res 43:1011-1018, 2002

26. Inazu A, Jiang XC, Haraki T, Yagi K, Kamon N, Koizumi J, Mabuchi H, Takeda R, Takata K, Moriyama Y, et al.: Genetic cholesteryl ester transfer protein deficiency caused by two prevalent mutations as a major determinant of increased levels of high density lipoprotein cholesterol. J Clin Invest 94:1872-1882, 1994

27. Inazu A, Koizumi J, Haraki T, Yagi K, Wakasugi T, Takegoshi T, Mabuchi H, Takeda R: Rapid detection and prevalence of cholesteryl ester transfer protein deficiency caused by an intron 14 splicing defect in hyperalphalipoproteinemia. Hum Genet 91:13-16, 1993

28. Sakai N, Santamarina-Fojo S, Yamashita S, Matsuzawa Y, Brewer HB, Jr.: Exon 10 skipping caused by intron 10 splice donor site mutation in cholesteryl ester transfer protein gene results in abnormal downstream splice site selection. J Lipid Res 37:2065-2073, 1996

29. Hirano K, Yamashita S, Nakajima N, Arai T, Maruyama T, Yoshida Y, Ishigami M, Sakai N,

Kameda-Takemura K, Matsuzawa Y: Genetic cholesteryl ester transfer protein deficiency is extremely frequent in the Omagari area of Japan. Marked hyperalphalipoproteinemia caused by CETP gene mutation is not associated with longevity. Arterioscler Thromb Vasc Biol 17:1053-1059, 1997

30. Agerholm-Larsen B, Nordestgaard BG, Steffensen R, Jensen G, Tybjaerg-Hansen A: Elevated HDL cholesterol is a risk factor for ischemic heart disease in white women when caused by a common mutation in the cholesteryl ester transfer protein gene. Circulation 101:1907-1912, 2000

31. Hirano K, Yamashita S, Kuga Y, Sakai N, Nozaki S, Kihara S, Arai T, Yanagi K, Takami S, Menju M, et al.: Atherosclerotic disease in marked hyperalphalipoproteinemia. Combined reduction of cholesteryl ester transfer protein and hepatic triglyceride lipase. Arterioscler Thromb Vasc Biol 15:1849-1856, 1995

32. Hata A, Robertson M, Emi M, Lalouel JM: Direct detection and automated sequencing of individual alleles after electrophoretic strand separation: identification of a common nonsense mutation in exon 9 of the human lipoprotein lipase gene. Nucleic Acids Res 18:5407-5411, 1990

33. Mattu RK, Needham EW, Morgan R, Rees A, Hackshaw AK, Stocks J, Elwood PC, Galton DJ: DNA variants at the LPL gene locus associate with angiographically defined severity of atherosclerosis and serum lipoprotein levels in a Welsh population. Arterioscler Thromb

14:1090-1097, 1994

34. Gagne SE, Larson MG, Pimstone SN, Schaefer EJ, Kastelein JJ, Wilson PW, Ordovas JM, Hayden MR: A common truncation variant of lipoprotein lipase (Ser447X) confers protection against coronary heart disease: the Framingham Offspring Study. Clin Genet 55:450-454, 1999

35. Peacock RE, Hamsten A, Nilsson-Ehle P, Humphries SE: Associations between lipoprotein lipase gene polymorphisms and plasma correlations of lipids, lipoproteins and lipase activities in young myocardial infarction survivors and age-matched healthy individuals from Sweden. Atherosclerosis 97:171-185, 1992

36. Anderson JL, Carlquist JF: Genetic polymorphisms of hepatic lipase and cholesteryl ester transfer protein, intermediate phenotypes, and coronary risk: do they add up yet? J Am Coll Cardiol 41:1990-1993, 2003

37. Couture P, Otvos JD, Cupples LA, Lahoz C, Wilson PW, Schaefer EJ, Ordovas JM: Association of the C-514T polymorphism in the hepatic lipase gene with variations in lipoprotein subclass profiles: The Framingham Offspring Study. Arterioscler Thromb Vasc Biol 20:815-822, 2000

38. Yamakawa-Kobayashi K, Somekawa Y, Fujimura M, Tomura S, Arinami T, Hamaguchi H: Relation of the -514C/T polymorphism in the hepatic lipase gene to serum HDL and LDL cholesterol levels in postmenopausal women under hormone replacement therapy.

Atherosclerosis 162:17-21, 2002

39. Somekawa Y, Umeki H, Kobayashi K, Tomura S, Aso T, Hamaguchi H: Effects of hormone replacement therapy and hepatic lipase polymorphism on serum lipid profiles in postmenopausal Japanese women. J Clin Endocrinol Metab 87:4766-4770, 2002

40. Hong SH, Song J, Kim JQ: Genetic variations of the hepatic lipase gene in Korean patients with coronary artery disease. Clin Biochem 33:291-296, 2000

41. Chhabra S, Narang R, Krishnan LR, Vasisht S, Agarwal DP, Srivastava LM, Manchanda SC, Das N: Apolipoprotein C3 SstI polymorphism and triglyceride levels in Asian Indians. BMC Genet 3:9, 2002

42. Hoffer MJ, Sijbrands EJ, De Man FH, Havekes LM, Smelt AH, Frants RR: Increased risk for endogenous hypertriglyceridaemia is associated with an apolipoprotein C3 haplotype specified by the SstI polymorphism. Eur J Clin Invest 28:807-812, 1998

43. Shoulders CC, Grantham TT, North JD, Gaspardone A, Tomai F, de Fazio A, Versaci F, Gioffre PA, Cox NJ: Hypertriglyceridemia and the apolipoprotein CIII gene locus: lack of association with the variant insulin response element in Italian school children. Hum Genet 98:557-566, 1996

44. Dallinga-Thie GM, van Linde-Sibenius Trip M, Rotter JI, Cantor RM, Bu X, Lusis AJ, de Bruin TW: Complex genetic contribution of the Apo AI-CIII-AIV gene cluster to familial combined hyperlipidemia. Identification of different susceptibility haplotypes. J Clin Invest

99:953-961, 1997

45. Paul-Hayase H, Rosseneu M, Robinson D, Van Bervliet JP, Deslypere JP, Humphries SE: Polymorphisms in the apolipoprotein (apo) AI-CIII-AIV gene cluster: detection of genetic variation determining plasma apo AI, apo CIII and apo AIV concentrations. Hum Genet 88:439-446, 1992

46. Ko YL, Ko YS, Wu SM, Teng MS, Chen FR, Hsu TS, Chiang CW, Lee YS: Interaction between obesity and genetic polymorphisms in the apolipoprotein CIII gene and lipoprotein lipase gene on the risk of hypertriglyceridemia in Chinese. Hum Genet 100:327-333, 1997

47. Hong SH, Park WH, Lee CC, Song JH, Kim JQ: Association between genetic variations of apo AI-CIII-AIV cluster gene and hypertriglyceridemic subjects. Clin Chem 43:13-17, 1997

48. Zeng Q, Dammerman M, Takada Y, Matsunaga A, Breslow JL, Sasaki J: An apolipoprotein CIII marker associated with hypertriglyceridemia in Caucasians also confers increased risk in a west Japanese population. Hum Genet 95:371-375, 1995

49. Price WH, Morris SW, Burgon R, Donald PM, Kitchin AH: Apolipoprotein CIII polymorphism and coronary heart disease. Lancet 2:1041, 1986

50. Marcil M, Boucher B, Gagne E, Davignon J, Hayden M, Genest J, Jr.: Lack of association of the apolipoprotein A-I-C-III-A-IV gene XmnI and SstI polymorphisms and of the lipoprotein lipase gene mutations in familial combined hyperlipoproteinemia in French Canadian subjects. J Lipid Res 37:309-319, 1996

51. Bai H, Saku K, Liu R, Imamura M, Arakawa K: Association between coronary heart disease and the apolipoprotein A-I/C-III/A-IV complex in a Japanese population. Hum Genet 95:102-104, 1995

52. Corbex M, Poirier O, Fumeron F, Betoulle D, Evans A, Ruidavets JB, Arveiler D, Luc G, Tiret L, Cambien F: Extensive association analysis between the CETP gene and coronary heart disease phenotypes reveals several putative functional polymorphisms and gene-environment interaction. Genet Epidemiol 19:64-80, 2000

Table 1.

Lipid profile and age of all the participants.

	all	men	women
T-Cho (mmol/l)	5.18 (0.021)	5.23 (0.046)	5.15 (0.046)
TG (mmol/l)	1.31 (0.024)	1.58 (0.050)*	1.11 (0.039)*
HDL-c (mmol/l)	1.53 (0.010)	1.38 (0.020)*	1.65 (0.017)*
LDL-c (mmol/l)	3.00 (0.020)	3.08 (0.044)*	2.93 (0.039)*
Age (years)	47.1 (0.58)	49.5 (0.87)*	45.3 (0.76)*
Men (%)	43		

Data are expressed as mean (SEM). * $p<0.01$, men vs. women.

Table 2

Demographic and lipid profile of all the participants according to genotype

CETP D442G (rs2303790)

genotype	age	%	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
wt	47	91.6	1.53 (0.001)	1.37 (0.025)	3.06 (0.021)
hetero	48.4	8.1	1.75 (0.004)	1.15 (0.061)	2.90 (0.075)
homo	46.5	0.2	1.81 (0.18)	1.60 (0.101)	3.19 (1.580)
			p=0.000	p=0.071	p=0.154

CETP Int14 +1 G → A (rs5742907)

genotype	age	%	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
wt	47	99.4	1.54 (0.009)	1.36 (0.024)	3.06 (0.020)
hetero	58.7	0.6	2.12 (0.262)	1.72 (0.362)	3.08 (0.316)
			p=0.000	p=0.241	p=0.938

CETP TaqIB (rs708272)

genotype	age	%	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
B1B1	46.8	35.8	1.50 (0.016)	1.36 (0.036)	3.00 (0.033)
B1B2	48.4	48.4	1.54 (0.013)	1.38 (0.038)	3.08 (0.030)
B2B2	48.2	15.8	1.66 (0.024)	1.25 (0.043)	3.08 (0.051)
			p=0.000	p=0.160	p=0.362

LPL S447X (rs328)

genotype	age	%	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
wt	47.3	78	1.53 (0.011)	1.37 (0.029)	3.06 (0.023)
hetero	46.2	20.7	1.60 (0.020)	1.24 (0.043)	3.06 (0.046)
homo	48	1.3	1.63 (0.101)	1.08 (0.125)	3.29 (0.189)
			p=0.004	p=0.032	p=0.487

LIPC 514CT (rs1800588)

genotype	age	%	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
CC	49.7	24.9	1.49 (0.018)	1.37 (0.046)	3.11 (0.040)
CT	45.6	50.4	1.53 (0.013)	1.33 (0.034)	3.03 (0.029)
TT	47.6	24.7	1.63 (0.020)	1.39 (0.050)	3.06 (0.040)
			p=0.000	p=0.520	p=0.255

APOC3 SstI (rs5128)

genotype	age	%	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
S1S1	46.6	42	1.56 (0.015)	1.32 (0.039)	3.06 (0.032)
S1S2	47	45.8	1.54 (0.013)	1.34 (0.033)	3.03 (0.029)
S2S2	48.9	12.2	1.52 (0.025)	1.53 (0.070)	3.11 (0.060)
			p=0.413	p=0.021	p=0.434

Data are expressed as mean (SEM). P-value was based on analysis of covariance.

Table 3

Demographic and lipid profile of male participants according to genotype

CETP D442G (rs2303790)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
wt	351	1.36 (0.020)	1.60 (0.052)	3.11 (0.045)
hetero	26	1.60 (0.105)	1.19 (0.176)	2.98 (0.194)
		p=0.003	p=0.035	p=0.453

CETP TaqIB (rs708272)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
B1B1	121	1.33 (0.034)	1.64 (0.087)	3.06 (0.073)
B1B2	203	1.36 (0.026)	1.55 (0.068)	3.11 (0.064)
B2B2	53	1.56 (0.063)	1.53 (0.147)	3.13 (0.107)
		p=0.001	p=0.664	p=0.758

LPL S447X (rs328)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
wt	292	1.36 (0.022)	1.65 (0.060)	3.08 (0.047)
hetero	81	1.43 (0.048)	1.36 (0.082)	3.16 (0.112)
homo	4	1.51 (0.386)	0.95 (0.295)	2.80 (0.513)
		p=0.278	p=0.029	p=0.617

LIPC 514CT (rs1800588)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
CC	99	1.32 (0.032)	1.66 (0.094)	3.08 (0.072)
CT	188	1.40 (0.032)	1.51 (0.075)	3.08 (0.069)
TT	90	1.40 (0.041)	1.60 (0.095)	3.08 (0.085)
		p=0.266	p=0.499	p=0.996

APOC3 SstI (rs5128)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
S1S1	165	1.37 (0.031)	1.50 (0.073)	3.16 (0.072)
S1S2	173	1.40 (0.031)	1.58 (0.076)	3.00 (0.060)
S2S2	39	1.31 (0.054)	1.92 (0.162)	3.13 (0.138)
		p=0.473	p=0.041	p=0.196

Data are expressed as mean (SEM). P-value was based on analysis of covariance.

Table 4

Demographic and lipid profile of female participants according to genotype

CETP D442G (rs2303790)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
wt	440	1.58(0.018)	1.128 (0.0412)	2.93 (0.041)
hetero	34	1.67 (0.074)	1.15 (0.092)	2.98 (0.140)
		p=0.002	p=0.590	p=0.306

CETP TaqIB (rs708272)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
B1B1	183	1.58 (0.028)	1.13 (0.057)	2.93 (0.062)
B1B2	220	1.67 (0.026)	1.15 (0.066)	2.98 (0.059)
B2B2	72	1.75 (0.043)	0.92 (0.057)	2.85 (0.105)
		p=0.004	p=0.127	p=0.461

LPL S447X (rs328)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
wt	369	1.62 (0.020)	1.14 (0.046)	2.95 (0.046)
hetero	102	1.73 (0.038)	0.99 (0.065)	2.85 (0.081)
homo	4	1.97 (0.164)	0.72 (0.177)	3.89 (0.321)
		p=0.010	p=0.185	p=0.054

LIPC 514CT (rs1800588)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
CC	102	1.59 (0.041)	1.15 (0.089)	2.93 (0.086)
CT	249	1.63 (0.022)	1.04 (0.046)	2.90 (0.050)
TT	124	1.73 (0.037)	1.20 (0.091)	3.03 (0.090)
		p=0.014	p=0.210	p=0.406

APOC3 SstI (rs5128)

genotype	n	HDL-c (mmol/l)	TG (mmol/l)	LDL-c (mmo/l)
S1S1	207	1.65 (0.028)	1.05 (0.054)	2.90 (0.062)
S1S2	208	1.62 (0.026)	1.18 (0.067)	2.93 (0.059)
S2S2	60	1.75 (0.045)	1.08 (0.079)	3.03 (0.106)
		p=0.078	p=0.272	p=0.608

Data are expressed as mean (SEM). P-value was based on analysis of covariance.

Table 5.

Incidence of *CETP* TaqIB, D442G, and *LPL* S447X genetypes according to HDL levels.

CETP TaqIB	HDL-c (mmol/l)			
genotype	1.0> (8.3%)	1.0_, 2.58> (89.9%)	2.58_ (1.8%)	
B1B1	72 (9.9%)	644 (88.8%)	9 (1.2%)	p=0.009
B1B2	79 (8.2%)	870 (90.2%)	16 (1.7%)	
B2B2	15 (4.8%)	284 (91.6%)	11 (3.5%)	
CETP D442G				
WT	161 (8.7%)	1671 (89.8%)	29 (1.6%)	p=0.011
Hetero	5(3.6%)	125 (91.2%)	7 (5.1%)	
Homo	0 (0%)	2 (100%)	0 (0%)	
LPL S447X				
WT	134 (8.9%)	1354 (89.4%)	26 (1.7%)	p=0.002
Hetero	21 (5.0%)	390 (93.3%)	7 (1.7%)	
Homo	2 (8.0%)	21 (84.0%)	2 (8.0%)	

Column percentage is shown on top. Each box shows the number of participants in each category and its percentage in each genotype.

Supplemental table

		Age	T-cho (mmol/l)	TG (mmol/l)	HDL-c (mmol/l)	LDL-c (mmol/l)
total	mean	45.9	5.15	1.33	1.52	3.03
n=12,839	median	48.0	5.10	1.06	1.49	2.97
this study	mean	47.1	5.18	1.35	1.53	3.02
n=2,267	median	48.0	5.10	1.06	1.49	2.92