Supplemental Material

Methods

The European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) is a prospective population study of 25,663 male and female inhabitants of Norfolk, United Kingdom, aged between 45 and 79 years who completed a baseline questionnaire survey and attended a clinic visit. EPIC-Norfolk is part of the 10-country collaborative EPIC study designed to investigate dietary and other determinants of cancer. Additional data were obtained to enable assessment of determinants of other diseases.

The study cohort was similar to UK population samples with regard to many characteristics, including anthropometry, blood pressure, and lipids, but with a lower proportion of smokers[1]. Participants were recruited by mail from age-sex registers of general practices. At the baseline survey between 1993 and 1997, participants completed a detailed health and lifestyle questionnaire, and additional data collection was performed by trained nurses at a clinic visit. All individuals have been flagged for mortality at the UK Office of National Statistics, with vital status ascertained for the entire cohort. Death certificates for all decedents were coded by trained nosologists according to the International Classification of Diseases (ICD) 9th revision. Death was considered due to CAD if the underlying cause was coded as ICD 410 to 414. In addition, participants admitted to a hospital were identified by their unique National Health Service number by data linkage with ENCORE (East Norfolk Health Authority database), which identifies all hospital contacts throughout England and Wales for Norfolk residents. Participants were identified as having CAD during follow-up if they had a hospital admission and/or died with CAD listed as an underlying cause. We report results with follow-up up to January 2003, an

average of 6 years. The Norwich District Health Authority Ethics Committee approved the study, and all participants gave written informed consent.

Reference

1. Day N, Oakes S, Luben R, Khaw KT, Bingham S, Welch A, Wareham N. EPIC-Norfolk: study design and characteristics of the cohort. European Prospective Investigation of Cancer. *Br J Cancer*. 1999;80 Suppl 1:95-103.

Supplemental Table I. Odds Ratios for Future CAD Events by MCP-1 Quartile and for MCP-1 as Continuous Variable for men and women only

	MCP-1 quartiles						
	1	**2**	**3**	**4**	**P***	**Ln(MCP-1)†**	**P‡**
Men							
MCP-1 levels (pg/ml)	< 38.4	38.4 to 51.4	51.4 to 67.1	> 67.1	-	-	-
Total no. of patients	436	434	421	453	-	-	-
Cardiovascular events, n (%)	157 (36.0)	154 (35.5)	143 (34.0)	174 (38.4)	-	-	-
Model 1	1	0.97 (0.73 to 1.29)	0.90 (0.68 to 1.21)	1.09 (0.82 to 1.46)	0.606	1.08 (0.85 to 1.37)	0.535
Model 2	1	0.93 (0.68 to 1.27)	0.80 (0.59 to 1.10)	0.88 (0.65 to 1.20)	0.565	0.90 (0.70 to 1.16)	0.418
Model 3	1	0.91 (0.68 to 1.23)	0.81 (0.60 to 1.01)	0.94 (0.69 to 1.27)	0.578	0.96 (0.75 to 1.22)	0.714
Women							
MCP-1 levels (pg/ml)	< 38.0	38.0 to 50.8	50.8 to 66.1	> 66.1	-	-	-
Total no. of patients	253	260	244	262	-	-	-
Cardiovascular events, n (%)	88 (34.8)	94 (36.2)	78 (32.0)	97 (37.0)	-	-	-
Model 1	1	1.08 (0.74 to 1.59)	0.88 (0.60 to 1.31)	1.12 (0.77 to 1.65)	0.605	1.00 (0.73 to 1.37)	0.994
Model 2	1	1.04 (0.69 to 1.58)	0.92 (0.60 to 1.41)	1.21 (0.79 to 1.85)	0.608	1.00 (0.71 to 1.41)	0.994
Model 3	1	0.97 (0.65 to 1.44)	0.80 (0.53 to 1.21)	1.07 (0.71 to 1.60)	0.526	0.98 (0.70 to 1.36)	0.905

Odds ratios and corresponding 95% confidence intervals calculated by conditional logistic regression, taking into account matching for age, and enrollment time, per MCP-1 quartile. CRP, triglycerides and MCP-1 were log-transformed before analysis. Model 1: unadjusted. Model 2: Adjusted for BMI, smoking status, systolic blood pressure, LDL-cholesterol, HDL-cholesterol and CRP. Model 3: adjustment for the FRS. P***** = p value for the association between MCP-1 quartiles and CAD risk. P† = Odds ratios and corresponding 95% confidence intervals calculated by conditional logistic regression, taking into account matching for age and enrollment time, for MCP-1 as continuous variable. P‡ = p value corresponding to Ln(MCP-1). MCP-1 = Monocyte chemoattractant protein-1; LDL = low-density lipoprotein; HDL = high-density lipoprotein; FRS = Framingham Risk Score.

Supplemental Table II. *CCL2* Polymorphism Characteristics

Gene position	RS Number	Nucleotide change	Variant type Location	MAF cohort	MAF control	Genotyping success, %
-2835	2857654	C > A	DRR	0.28	0.27	93.6
-2578	1024611	A > G	DRR	0.28	0.27	94.3
-2136	1024610	A > T	DRR	0.20	0.20	93.5
-1811	3760399	A > G	DRR	0.04	0.05	94.5
-927	3760396	G > C	Promoter	0.21	0.21	94.6
+764	2857657	C > G	Intron 1	0.20	0.19	94.4
+3726	2530797	T > C	3´Flanking	0.38	0.38	93.7

CCL2 polymorphisms characteristics. MAF = minor allele frequency; MAF cohort = minor allele frequencies calculated in the cases and controls and of the controls only (MAF control); HWE = Hardy Weinberg equilibrium; X^2 = Chi-squared distribution with 1 degree of freedom to test for deviations from Hardy–Weinberg equilibrium with corresponding p-value (HWE P); DDR = distal regulatory region.

Supplemental Table III. Distribution of cardiovascular risk factor among the *CCL2* polymorphisms

Gene position		**-2835**			**-2578**			**-2136**			**-1811**
	CC	**CA**	**AA**	**AA**	**AG**	**GG**	**AA**	**AT**	**TT**	**AG**	**GG**
No. of participants	1349	1045	191	1360	1052	194	1679	785	120	232	2378
Age, years	65	65	66	65	65	66	65	65	65	65	65
	(65to66)	(65to66)	(65 to 67)	(65 to 66)	(65 to 66)	(65 to 67)	(65 to 66)	(65 to 66)	(63 to 66)	(64 to 66)	(65 to 66)
Women, %	493 (37)	372 (36)	76 (40)	497 (37)	371 (35)	78 (40)	594 (35)	292 (37)	46 (38)	72 (31)	876 (37)
Body mass index, kg/m^2	26.7	26.6	25.9	26.7	26.6	25.8	26.6	26.6	26.6	26.6	26.6
	(26.5 to 26.9)	(26.4 to 26.8)	(25.4 to 26.3)	(26.5 to 26.9)	(26.4 to 26.8)	(25.3 to 26.3)	(26.4 to 26.7)	(26.3 to 26.8)	(26.1 to 27.2)	(26.2 to 27.0)	(26.4 to 26.7)
Waist circumference, cm	92.2	92.4	90.4	92.2	92.5	90.1	92.3	92.1	91.5	93.4	92.0
	(91.6 to 92.8)	(91.7 to 93.1)	(88.8 to 92.0)	(91.6 to 92.8)	(91.8 to 93.2)	(88.5 to 91.7)	(91.7 to 92.8)	(91.3 to 93.0)	(89.4 to 93.6)	(92.1 to 94.7)	(91.5 to 92.5)
Current Smoker, %	134 (9.9)	130 (12.4)	20 (10.5)	135 (9.9)	131 (12.5)	19 (9.8)	192 (11.4)	77 (9.8)	13 (10.8)	32 (13.8)	256 (10.8)
Diabetes mellitus, %	45 (3.3)	32 (3.1)	6 (3.1)	46 (3.4)	31 (2.9)	194 (3.1)	51 (3.0)	26 (3.3)	5 (4.2)	13 (5.6)	71 (3.0)
Systolic blood pressure,	141	141	139	141	141	139	141	140	141	143	140
mmHg	(140 to 142)	(140 to 142)	(136 to 141)	(140 to 142)	(140 to 142)	(136 to 142)	(141 to 142)	(139 to 141)	(137 to 144)	(141 to 146)	(140 to 141)
Diastolic blood pressure,	84	84	82	84	84	82	84	84	85	86	84
mmHg	(84 to 85)	(84 to 85)	(81 to 84)	(84 to 85)	(84 to 85)	(81 to 84)	(84 to 85)	(83 to 85)	(83 to 87)	(85 to 88)	(84 to 85)
Total cholesterol, mmol/l	6.30	6.33	6.36	6.30	6.34	6.35	6.30	6.36	6.28	6.31	6.31
	(6.24 to 6.37)	(6.26 to 6.40)	(6.19 to 6.54)	(6.24 to 6.36)	(6.27 to 6.41)	(6.18 to 6.52)	(6.24 to 6.35)	(6.28 to 6.44)	(6.07 to 6.48)	(6.18 to 6.45)	(6.27 to 6.36)
LDL-cholesterol, mmol/l	4.14	4.14	4.22	4.14	4.15	4.20	4.14	4.17	4.12	4.20	4.14
	(4.09 to 4.20)	(4.08 to 4.21)	(4.06 to 4.37)	(4.09 to 4.19)	(4.09 to 4.21)	(4.05 to 4.36)	(4.09 to 4.19)	(4.10 to 4.24)	(3.93 to 4.31)	(4.07 to 4.33)	(4.10 to 4.18)
HDL-cholesterol, mmol/l	1.32	1.33	1.35	1.32	1.33	1.36	1.33	1.34	1.33	1.26	1.34
	(1.30 to 1.34)	(1.31 to 1.36)	(1.30 to 1.41)	(1.30 to 1.34)	(1.31 to 1.36)	(1.31 to 1.41)	(1.31 to 1.34)	(1.31 to 1.36)	(1.25 to 1.40)	(1.22 to 1.31)	(1.32 to 1.35)
Triglycerides, mmol/l	1.70	1.70	1.60	1.70	1.70	1.60	1.70	1.70	1.60	1.80	1.70
	(1.20 to 2.30)	(1.20 to 2.40)	(1.20 to 2.10)	(1.20 to 2.30)	(1.20 to 2.40)	(1.20 to 2.10)	(1.20 to 2.30)	(1.20 to 2.40)	(1.20 to 2.30)	(1.23 to 2.40)	(1.20 to 2.30)
C-reactive protein, mg/l	1.60	1.70	1.60	1.60	1.70	1.60	1.70	1.70	1.60	1.60	1.70
	(0.80 to 3.83)	(0.80 to 3.70)	(0.70 to 3.45)	(0.80 to 3.80)	(0.80 to 3.80)	(0.70 to 3.58)	(0.80 to 3.60)	(0.80 to 4.10)	(0.80 to 3.43)	(0.80 to 3.40)	(0.80 to 3.80)

Data are presented as mean with the 95% confidence interval or number with the corresponding percentage. Skewed variables are presented as median with the 25th to 75th percentile. LDL = low-density lipoprotein, HDL = high-density lipoprotein.

Supplemental Table III continued. Distribution of cardiovascular risk factor among the CCL2 polymorphisms

Gene position		**-927**			**+764**			**-3726**	
	GG	**GC**	**CC**	**CC**	**CG**	**GG**	**TT**	**TC**	**CC**
No. of participants	1648	842	123	1689	805	106	984	1214	391
Age, years	65	65	65	65	65	65	65	65	65
	(65 to 66)	(65 to 66)	(64 to 67)	(65 to 66)	(64 to 65)	(63 to 67)	(65 to 66)	(65 to 66)	(64 to 66)
Women, %	625 (38)	285 (34)	36 (29)	600 (35)	301 (37)	39 (37)	340 (35)	443 (37)	157 (40)
Body mass index, kg/m^2	26.6	26.5	26.4	26.6	26.6	26.6	26.4	26.6	26.8
	(26.4 to 26.8)	(26.3 to 26.8	(25.8 to 27.0)	(26.4 to 26.7)	(26.3 to 26.8)	(26.1 to 27.2)	(26.2 to 26.6)	(26.4 to 26.9)	(26.4 to 27.2)
Waist circumference, cm	92.2	92.3	92.4	92.3	92.1	91.8	92.0	92.4	91.8
	(91.6 to 92.7)	(91.5 to 93.1)	(90.5 to 94.3)	(91.7 to 92.8)	(91.3 to 92.9)	(89.6 to 94.0)	(91.3 to 92.8)	(91.8 to 93.0)	(90.6 to 93.0)
Current Smoker, %	189 (11.5)	79 (9.4)	19 (15.4)	194 (11.4)	82 (10.2)	11 (10.4)	118 (12.0)	121 (10.0)	42 (10.7)
Diabetes mellitus, %	50 (3.0)	30 (3.6)	5 (4.1)	52 (3.1)	29 (3.6)	4 (3.8)	32 (3.3)	39 (3.2)	13 (3.3)
Systolic blood pressure,	141	141	139	141	140	141	141	141	140
mmHg	(140 to 141)	(140 to 142)	(136 to 143)	(140 to 142)	(138 to 141)	(137 to 145)	(140 to 142)	(140 to 142)	(138 to 141)
Diastolic blood pressure,	84	84	84	84	84	85	84	84	84
mmHg	(84 to 85)	(83 to 85)	(81 to 86)	(84 to 85)	(83 to 85)	(83 to 87)	(83 to 85)	(84 to 85)	(83 to 85)
Total cholesterol, mmol/l	6.36	6.24	6.25	6.29	6.36	6.33	6.32	6.31	6.33
	(6.30 to 6.41)	(6.17 to 6.32)	(6.04 to 6.46)	(6.23 to 6.35)	(6.28 to 6.44)	(6.10 to 6.56)	(6.25 to 6.39)	(6.24 to 6.37)	(6.22 to 6.44)
LDL-cholesterol, mmol/l	4.18	4.09	4.14	4.13	4.17	4.19	4.20	4.13	4.16
	(4.13 to 4.23)	(4.02 to 4.15)	(3.96 to 4.31)	(4.09 to 4.18)	(4.10 to 4.24)	(3.98 to 4.39)	(4.10 to 4.23)	(4.07 to 4.19)	(4.06 to 4.26)
HDL-cholesterol, mmol/l	1.34	1.33	1.27	1.32	1.33	1.31	1.32	1.34	1.32
	(1.32 to 1.35)	(1.30 to 1.35)	(1.20 to 1.33)	(1.31 to 1.34)	(1.31 to 1.36)	(1.24 to 1.39)	(1.30 to 1.35)	(1.31 to 1.36)	(1.28 to 1.36)
Triglycerides, mmol/l	1.70	1.60	1.80	1.70	1.70	1.60	1.70	1.70	1.70
	(1.20 to 2.30)	(1.20 to 2.40)	(1.20 to 2.40)	(1.20 to 2.30)	(1.20 to 2.40)	(1.30 to 2.30)	(1.20 to 2.40)	(1.20 to 2.30)	(1.30 to 2.40)
C-reactive protein, mg/l	1.80	1.50	1.90	1.70	1.70	1.60	1.60	1.70	1.70
	(0.80 to 3.90)	(0.70 to 3.50)	(0.80 to 3.65)	(0.80 to 3.60)	(0.80 to 4.20)	(1.00 to 3.30	(0.80 to 3.40)	(0.80 to 4.10)	(0.80 to 3.90)

Data are presented as mean with the 95% confidence interval or number with the corresponding percentage. Skewed variables are presented as median with the 25th to 75th percentile. LDL = low-density lipoprotein, HDL = high-density lipoprotein

Supplemental Table IV. MCP-1 Serum Concentrations according to CCL2 Polymorphisms of Male Study Participants

	MCP-1 serum concentration levels, pg/ml						
	Median	**25th Lower percentile**	**75th Upper percentile**	**Beta coefficients (95% CI)**	**P***	**P†**	**P ‡**
-2835 C/A				-1.10 (-2.98 to 0.78)	0.250	0.235	0.241
-2835 AA	51.71	37.85	74.41				
-2835 CA	51.12	38.41	67.09				
-2835 CC	51.71	37.85	74.41				
-2578 A/G				-0.97 (-2.82 to 0.89)	0.306	0.272	0.298
-2578 GG	51.44	37.62	74.19				
-2578 AG	51.12	38.41	66.94				
-2578 AA	51.57	39.16	67.64				
-2136 A/T				1.39 (-0.64 to 3.42)	0.179	0.177	0.153
-2136 AA	51.11	38.09	67.49				
-2136 AT	51.27	38.17	68.08				
-2136 TT	56.45	45.24	75.45				
-1811 A/G				1.72 (-2.20 to 5.65)	0.389	0.342	0.241
-1811 AG	49.69	36.33	66.97				
-1811 GG	51.27	38.37	68.04				
-927 G/C				0.86 (-1.09 to 2.80)	0.388	0.386	0.400
-927 GG	51.17	38.08	67.36				
-927 GC	51.09	39.16	69.86				
-927 CC	55.83	43.30	67.11				
+764 C/G				1.40 (-0.65 to 3.45)	0.179	0.188	0.152
+764 CC	51.15	38.16	67.54				
+764 CG	51.38	38.33	68.43				
+764 GG	56.77	45.29	75.16				
+3726 T/C				-0.69 (-2.38 to 1.01)	0.427	0.407	0.472
+3726 TT	51.46	51.46	69.99				
+3726 TC	50.35	37.54	66.67				
+3726 CC	52.50	40.58	67.92				

Beta coefficients adjusted for age (95 % confidence interval) of MCP-1 serum concentration according to CCL2 polymorphisms with the corresponding p-values. P* = unadjusted p value. P† = p value adjusted for waist circumference, systolic blood pressure and triglycerides; P‡ = p value adjusted for the Framingham Risk Score.

Supplemental Table V. MCP-1 Serum Concentrations according to CCL2 Polymorphisms of Female Study Participants.

	MCP-1 serum concentration levels, pg/ml						
	Median	**25th Lower percentile**	**75th Upper percentile**	**Beta coefficients (95% CI)**	**P***	**P†**	**P ‡**
-2835 C/A				1.35 (-1.02 to 3.71)	0.264	0.300	0.270
-2835 AA	47.86	37.03	67.84				
-2835 CA	49.73	37.32	65.92				
-2835 CC	51.64	38.56	67.44				
-2578 A/G				1.48 (-0.86 to 3.81)	0.216	0.246	0.223
-2578 GG	47.14	36.41	68.58				
-2578 AG	49.68	37.35	64.95				
-2578 AA	52.44	38.84	67.60				
-2136 A/T				1.39 (-1.12 to 3.98)	0.292	0.308	0.290
-2136 AA	49.68	37.13	66.13				
-2136 AT	53.29	40.35	67.75				
-2136 TT	51.51	37.25	64.45				
-1811 A/G				0.67 (-5.03 to 6.37)	0.817	0.764	0.270
-1811 AG	52.69	36.65	65.47				
-1811 GG	50.46	38.16	67.09				
-927 G/C				0.81 (-1.89 to 3.52)	0.556	0.455	0.569
-927 GG	50.00	37.74	66.15				
-927 GC	50.39	38.62	65.45				
-927 CC	61.34	40.51	72.14				
+764 C/G				1.67 (-0.97 to 4.34)	0.213	0.235	0.216
+764 CC	49.59	37.07	66.02				
+764 CG	52.96	40.47	67.79				
+764 GG	54.08	35.94	63.72				
+3726 T/C				0.15 (-2.01 to 2.31)	0.892	0.982	0.879
+3726 TT	51.17	36.86	67.48				
+3726 TC	50.39	39.84	67.30				
+3726 CC	48.49	37.30	64.80				

Beta coefficients adjusted for age (95 % confidence interval) of MCP-1 serum concentration according to CCL2 polymorphisms with the corresponding p-values. P* = unadjusted p value. P† = p value adjusted for waist circumference, systolic blood pressure and triglycerides; P‡ = p value adjusted for the Framingham Risk Score.

Supplemental Table VI. Odds Ratios for Future CAD Events by *CCL2* polymorphism of male study participants.

			P*	P†	P‡
-2835 C/A					
AA (ref) – CA – CC	1.08 (0.72 to 1.64)	0.84 (0.56 to 1.26)	0.054	0.013	0.036
AA vs CA + CC	0.93 (0.63 to 1.39)		0.736	0.356	0.637
CC vs CA + AA	0.78 (0.64 to 0.96)		0.017	0.003	0.011
-2578 A/G					
GG (ref) – GA – AA	1.10 (0.73 to 1.66)	0.87 (0.58 to 1.30)	0.077	0.029	0.069
GG vs GA + AA	0.96 (0.65 to 1.42)		0.841	0.380	0.670
AA vs GA + GG	0.80 (0.65 to 0.97)		0.027	0.008	0.022
-2136 A/T					
AA (ref) – AT – TT	1.00 (0.80 to 1.25)	0.98 (0.58 to 1.64)	0.996	0.749	0.924
AA vs AT + TT	1.00 (0.81 to 1.23)		0.986	0.665	0.720
TT vs AT + AA	0.98 (0.59 to 1.63)		0.931	0.649	0.959
-1811 A/G					
AG vs GG	1.13 (0.80 to 1.61)		0.481	0.244	0.193
-927 G/C					
GG (ref) – GC – CC	0.94 (0.75 to 1.17)	0.95 (0.60 to 1.52)	0.838	0.768	0.803
GG vs GC + CC	0.94 (0.76 to 1.16)		0.555	0.529	0.516
CC vs GC + GG	0.97 (0.61 to 1.54)		0.906	0.592	0.752
+764 C/G					
CC (ref) – CG – GG	1.00 (0.80 to 1.24)	0.92 (0.54 to 1.57)	0.952	0.672	0.907
CC vs CG + GG	0.99 (0.80 to 1.22)		0.914	0.708	0.785
GG vs CG + CC	0.92 (0.54 to 1.56)		0.755	0.509	0.799
+3726 T/C					
TT (ref) – TC – CC	0.93 (0.75 to 1.16)	1.10 (0.80 to 1.53)	0.547	0.939	0.656
TT vs TC + CC	0.97 (0.78 to 1.19)		0.748	0.793	0.901
CC vs TC + TT	1.15 (0.85 to 1.55)		0.369	0.886	0.408

Odds ratios and the corresponding 95% confidence interval calculated by conditional logistic regression, taking into account matching for age, gender, and enrollment time per *CCL2* polymorphism. P* = Unadjusted p value. P† = p value adjusted for body mass index, waist circumference, systolic blood pressure, diastolic blood pressure and triglycerides; P‡ = p value adjusted for the Framingham Risk Score.

Supplemental Table VII. Odds Ratios for Future CAD Events by *CCL2* polymorphism of female study participants.

			P*	P†	P‡
-2835 C/A					
AA (ref) – CA – CC	0.87 (0.52 to 1.48)	1.04 (0.62 to 1.74)	0.506	0.279	0.304
AA vs CA + CC	0.96 (0.58 to 1.58)		0.864	0.327	0.479
CC vs CA + AA	1.16 (0.88 to 1.53)		0.292	0.363	0.269
-2578 A/G					
GG (ref) – GA – AA	0.92 (0.54 to 1.54)	1.06 (0.63 to 1.77)	0.625	0.417	0.407
GG vs GA + AA	0.99 (0.60 to 1.63)		0.966	0.481	0.579
AA vs GA + GG	1.14 (0.86 to 1.50)		0.362	0.396	0.317
-2136 A/T					
AA (ref) – AT – TT	1.13 (0.84 to 1.53)	0.75 (0.38 to 1.48)	0.464	0.608	0.629
AA vs AT + TT	1.07 (0.81 to 1.42)		0.647	0.582	0.688
TT vs AT + AA	0.73 (0.37 to 1.43)		0.349	0.549	0.493
-1811 A/G					
AG vs GG	1.36 (0.80 to 2.32)		0.252	0.144	0.213
-927 G/C					
GG (ref) – GC – CC	0.88 (0.65 to 1.20)	0.69 (0.33 to 1.47)	0.501	0.654	0.467
GG vs GC + CC	0.86 (0.64 to 1.16)		0.318	0.671	0.448
CC vs GC + GG	0.73 (0.35 to 1.52)		0.392	0.365	0.253
+764 C/G					
CC (ref) – CG – GG	1.17 (0.88 to 1.56)	0.90 (0.44 to 1.82)	0.520	0.637	0.529
CC vs CG + GG	1.14 (0.86 to 1.50)		0.370	0.359	0.390
GG vs CG + CC	0.86 (0.428 to 1.74)		0.681	0.960	0.671
+3726 T/C					
TT (ref) – TC – CC	1.05 (0.77 to 1.44)	1.64 (1.10 to 2.43)	0.037	0.054	0.045
TT vs TC + CC	1.20 (0.90 to 1.60)		0.215	0.213	0.170
CC vs TC + TT	1.59 (1.11 to 2.27)		0.011	0.017	0.015

Odds ratios and the corresponding 95% confidence interval calculated by conditional logistic regression, taking into account matching for age, gender, and enrollment time per *CCL2* polymorphism. P* = Unadjusted p value. P† = p value adjusted for body mass index, waist circumference, systolic blood pressure, diastolic blood pressure and triglycerides; P‡ = p value adjusted for the Framingham Risk Score.

Supplemental Table VIII. Estimated *CCL2* Polymorhism Combination Frequencies.

-2835	-2578	-2136	-1811	-927	+764	+3726	Haplotype	Frequency, %
A	G	A	A	G	C	T	H1	27.8
C	A	A	A	C	C	T	H2	21.0 (48.8)
C	A	T	A	G	G	C	H3	19.6 (68.4)
C	A	A	A	G	C	C	H4	18.5 (86.9)
C	A	A	A	G	C	T	H5	7.9 (94.8)
C	A	A	G	G	C	T	H6	4.4 (99.3)

Supplemental Table IX. MCP-1 Serum Concentration Ratios according to *CCL2* Haplotypes

Haplotype	Ratio (95% CI)	P*	P†	P‡
Men				
H1	Ref	-	-	-
H2	-0.04 (-2.36 to 2.28)	0.971	0.937	0.947
H3	0.37 (-2.06 to 2.80)	0.766	0.777	0.724
H4	-2.54 (-4.95 to -0.13)	0.039	0.031	0.038
H5	-2.71 (-6.02 to 0.60)	0.109	0.111	0.098
H6	-2.27 (-6.40 to 1.87)	0.282	0.255	0.237
Women				
H1	Ref	-	-	-
H2	1.61 (-1.48 to 4.71)	0.308	0.275	0.316
H3	2.63 (-0.45 to 5.70)	0.095	0.121	0.100
H4	-0.65 (-3.74 to 2.45)	0.684	0.599	0.690
H5	4.05 (-0.14 to 8.25)	0.058	0.077	0.062
H6	0.95 (-5.09 to 6.98)	0.759	0.903	0.792

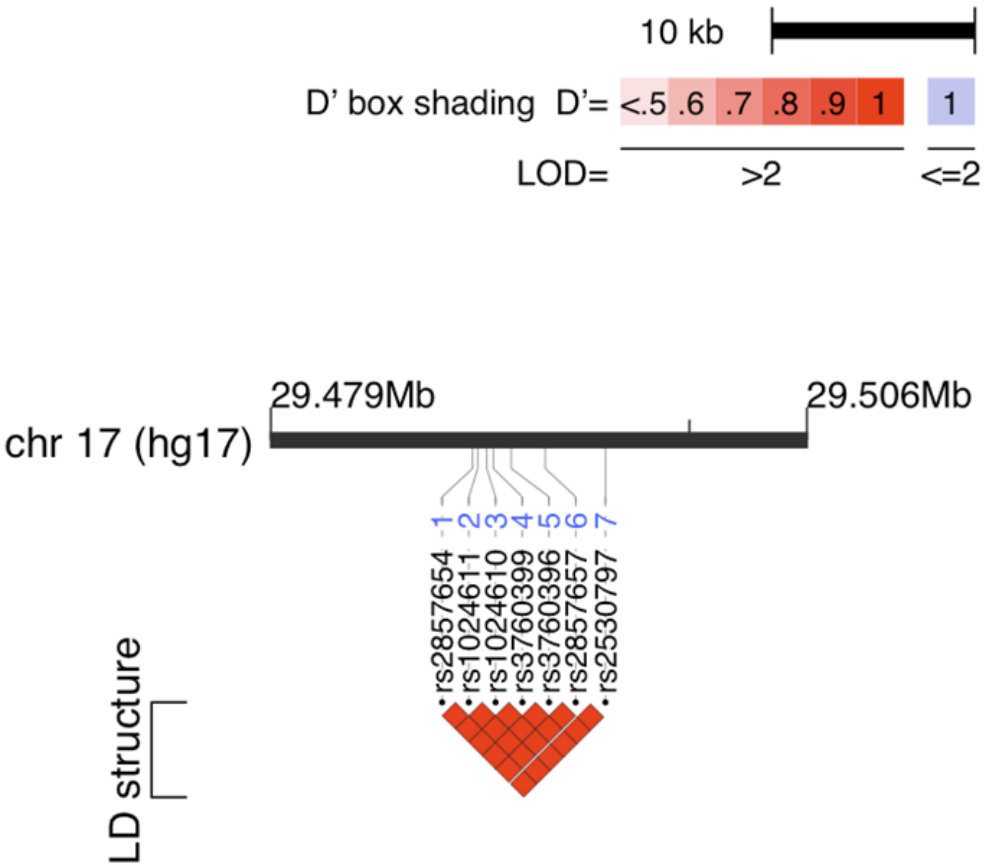
Age and sex corrected MCP-1 serum concentration ratios with the corresponding 95 % confidence interval for the most six common *CCL2* haplotypes. MCP-1 serum concentration ratios are corrected for age only in the separate analysis for men and women. The haplotype with the highest frequency (H1) is used as reference haplotype. P* = p value adjusted for age and sex, or age in the men and women analysis only. P† = p value adjusted for age and sex, or age in the men and women analysis only, waist circumference, systolic blood pressure and triglycerides; P‡ = p value adjusted for the Framingham Risk Score.

Supplemental Table X. CAD Ratios by *CCL2* haplotypes

	Ratio (95% CI)	P*	P†	P‡
Men				
H1	Ref	-	-	-
H2	0.85 (0.69 to 1.04)	0.115	0.072	0.095
H3	0.86 (0.69 to 1.06)	0.151	0.122	0.207
H4	0.94 (0.76 to 1.16)	0.564	0.388	0.562
H5	0.70 (0.52 to 0.94)	0.019	0.011	0.011
H6	0.86 (0.60 to 1.23)	0.403	0.179	0.252
Women				
H1	Ref	-	-	-
H2	0.98 (0.74 to 1.30)	0.892	0.920	0.801
H3	1.12 (0.85 to 1.48)	0.404	0.442	0.511
H4	0.31 (0.99 to 1.73)	0.055	0.061	0.042
H5	0.92 (0.63 to 1.35)	0.683	0.583	0.549
H6	0.80 (0.45 to 1.40)	0.429	0.217	0.245

Age and sex adjusted ratios for CAD events with the corresponding 95 % confidence interval for the most six common MCP-1 haplotypes. CAD ratios are corrected for age only in the separate analysis for men and women. The haplotype with the highest frequency (H1) is used as reference haplotype. P* = p value adjusted for age and sex, or age in the men and women analysis only. P† = p value adjusted for age and sex, or age in the men and women analysis only, waist circumference, systolic blood pressure and triglycerides; P‡ = p value adjusted for the Framingham Risk Score.

Supplementary Figure I.



Positions of the 7 SNPs at the *CCL2* locus and LD structure for the 7 *CCL2* typed single nucleotide polymorphisms labeled by 1 to 7 and just below their unique RS numbers. SNP 1 refers to gene position -2835, 2 to -2578, 3 to -2136, 4 to -1811, 5 to -927, 6 to +764 and 7 to +3726. The bottom of the figure depicts an LD plot for the locus with pairwise LD values (D') presented. See the key for details. The figure was generated using LocusView (T. Petryshen, A. Kirby, M. Ainscow, unpublished software, available from the Broad Institute, Cambridge, MA. www.broad.mit.edu/mpg/locusview/).