SUPPLEMENTARY MATERIAL

Supplementary Table 1. Minor allele frequency comparisons for controls versus each CAD-affected case group for all *TNFR1* SNPs

			Older Normal (CATHGEN)	All Affected (CATHGEN)		Younger Affected (CATHGEN)		Older Affected (CATHGEN)		GENECARD Probands	
SNP name[a]	Chromosome 12 location (bp)	Alleles[c]	MAF[d] (%)	MAF (%)	*p* value[†]	MAF (%)	*p* value[†]	MAF (%)	*p* value[†]	MAF (%)	*p* value[†]
rs36037566	6,307,433	**D**/I	47.7	50.9	0.476	52.8[‡]	0.743	46.9	0.698	46.8	0.871
rs12426675[b]	6,309,731	**A**/G	16.9	20.0	0.171	17.8	0.836	24.6	0.004	21.7	0.025
rs1800693[b]	6,310,270	**C**/T	41.3	42.8	0.638	44.9	0.350	38.7	0.752	40.7	0.797
rs4149586	6,312,121	**C**/A	2.1	1.7	0.275	1.4	0.149	2.2	0.542	1.2	0.065
rs1800692[b]	6,312,607	**G**/A	41.6	38.6	0.872	38.9	0.538	38.1	0.812	39.2	0.559
rs4149584[b]	6,312,904	**C**/T	1.6	1.7	0.137	1.7	0.125	1.5	0.363	2.0	0.356
rs4149579	6,317,618	**C**/T	10.0	8.0	0.094	8.0	0.367	7.9	0.119	7.5	0.175
rs4149578	6,317,698	**C**/T	6.9	8.3	0.093	6.5	0.757	12.0	0.001	9.5	0.037
rs4149577	6,317,783	**A**/G	48.6	46.0	0.869	46.0	0.718	45.9	0.974	47.7	0.802
rs4149576	6,319,376	**C**/T	42.1	44.3	0.385	46.2	0.355	40.6	0.848	41.3	0.908
rs4149573	6,319,645	**C**/G	5.7	7.3	0.083	5.8	0.814	10.5	0.002	9.1	0.018
rs767455[b]	6,321,206	**T**/C	42.8	45.3	0.427	46.9	0.391	42.0	0.795	41.9	0.824
rs2234649[b]	6,321,624	**T**/G	1.0	1.1	0.873	0.8	0.752	1.8	0.429	0.8	0.872
rs4149621[b]	6,321,822	**T**/C	2.1	1.7	0.763	1.5	0.365	2.2	0.875	1.4	0.712
rs4149570[b]	6,321,851	**C**/A	41.6	39.4	0.967	39.1	0.802	40.1	0.881	39.2	0.378
rs11064145	6,325,359	**T**/G	46.0	47.3	0.152	48.5	0.310	44.8	0.078	44.1	0.801

[a]For SNP location, please see Supplementary Figure 1. [b]These SNPs were included in the study of Poirier et al.[11] (see Supplementary Table 3).

[c]Major allele is bold, D=deletion, I=insertion; basepair position determined using NCBI build 36. [d]MAF = minor allele frequency.

[†]The *p* value is for the comparison of Caucasian cases and controls using logistic regression adjusting for gender and CAD risk factors. *P* values are not adjusted for multiple comparisons; however, a *p* value of < 0.0031 would be significant after Bonferroni correction for 16 comparisons.

[‡]The minor allele in the controls is the major allele in the younger affected sample.

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Supplementary Table 2. Family-based association tests for *TNFR1* SNPs and CAD in 1101 GENECARD families

SNP Name	APL[a] *p* value	PDT[b]	
		chi-square statistic	*p* value[c]
rs36037566	0.7154	1.81	0.1789
rs12426675	0.8300	1.34	0.2468
rs1800693	0.0900	3.65	0.0561
rs4149586	0.5247	0.33	0.5637
rs1800692	0.2623	1.76	0.1845
rs4149584 (R92Q)	0.6081	4.26	0.0389
rs4149579	0.1749	1.31	0.2526
rs4149578	0.1040	0.63	0.4281
rs4149577	0.4672	2.96	0.0852
rs4149576	0.0846	4.04	0.0445
rs4149573	0.7681	1.23	0.2674
rs767455	0.0845	3.45	0.0634
rs2234649	0.2427	0.06	0.8084
rs4149621	0.9945	0.31	0.5791
rs4149570	0.3364	1.42	0.2330
rs11064145	0.2458	4.13	0.0421

[a]APL, association in the presence of linkage. [b]PDT, pedigree disequilibrium test. [c]The p values were not adjusted for multiple comparisons; however, a *p* value of < 0.0031 would be significant after Bonferroni correction for 16 comparisons.

SUPPLEMENTARY MATERIAL

Supplementary Table 3. Description of novel polymorphisms in *TNFRSF1A* from Poirier *et al.*[11]

Polymorphism	Position	Alleles[a]	Chromosome 12 location (bp)	Known SNP[b]
G-609T	5' of gene	**G**/T	6,321,851	rs4149570
G-580A	5' of gene	**G**/A	6,321,822	rs4149621
A-383C	5' of gene	**A**/C	6,321,624	rs2234649
P12P	Exon 1	**A**/G	6,321,206	rs767455
G+212/in2 (212th nucleotide of intron 2)	Intron 2	**G**/A	6,313,305	TNFRSF1AI2[†]
R92Q	Exon 4	**G**/A	6,312,904	rs4149584
G+147/in4 (147th nucleotide of intron 4)	Intron 4	**G**/A	6,312,646	TNFRSF1AI4[†]
C+186/in4T (186th nucleotide of intron 4)	Intron 4	**C**/T	6,312,607	rs1800692
G+10/in6A (10th nucleotide of intron 6)	Intron 6	**G**/A	6,310,270	rs1800693
T+294/in7C (294th nucleotide of intron 7)	Intron 7	**T**/C	6,309,731	rs12426675

[a]Major allele is in bold typeface. [b]For minor allele frequencies of these SNPs in the current study, please see Supplementary Table 1.
[†]Monomorphic in our sample; basepair position determined using NCBI build 36

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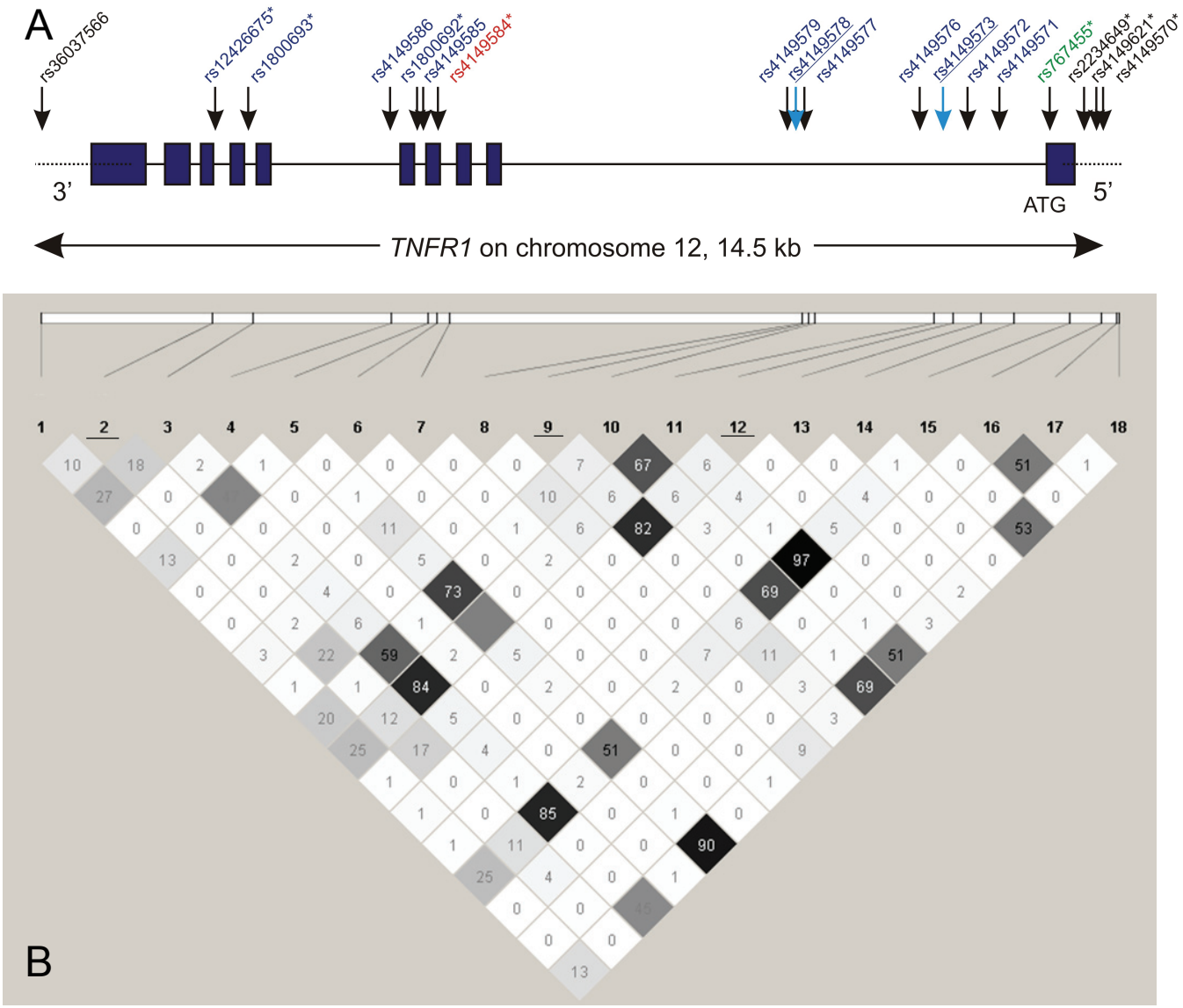

Supplementary Figure 1. Location and linkage disequilibrium plot for the *TNFR1* SNPs genotyped in CATHGEN. (**A**) The human *TNFR1* gene (chromosome 12) is depicted with lavender rectangles signifying exons, solid lines signifying introns, dotted lines signifying non-coding regions, and arrows indicating the 16 SNPs genotyped in the CATHGEN cohort. SNPs are color-coded to represent functional status: red, non-synonymous coding; green, synonymous coding; blue, intronic; black, flanking region. The 2 SNPs significantly associated with CAD are underlined (designated by blue arrows), with the following *p* values: r4149578, 0.001; rs4149573, 0.002. Asterisks denote *TNFR1* SNPs evaluated by Poirier *et al* (11). The full results for all SNPs are shown in Supplemental Table 2. (**B**) Pair-wise linkage disequilibrium (LD) plot for all SNPs in *TNFR1*. Shading indicates the level of LD, with darker shading representing higher LD. As expected in light of the procedure for SNP selection , LD is limited. Numbers in the boxes represent r^2 (×100) values for all Caucasians. The LD pattern is similar for ethnicities and controls (data not shown).

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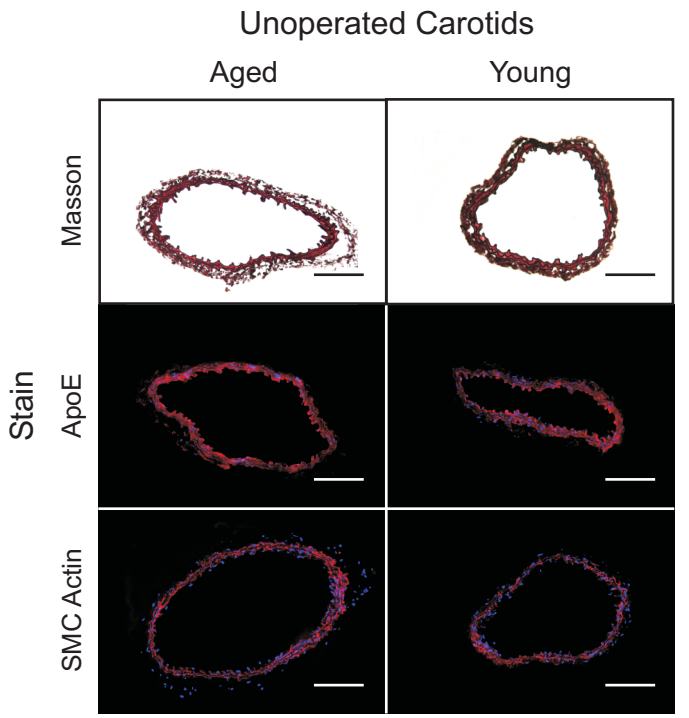

Supplementary Figure 2. Young and aged carotid arteries are indistinguishable prior to grafting. Common carotid arteries from aged and young mice were harvested and processed either for paraffin embedding and morphometry (top panels) or OCT embedding and immunofluorescence (lower 4 panels). Specimens were stained with either a modified connective tissue stain (”Masson”) or with IgG reactive with apolipoprotein E (apoE) or SMC actin, as indicated. Cognate sections stained with negative control IgG yielded no immunofluorescence. Shown are individual samples representative of 5 independent carotid arteries in each age group. Scale bars = 100 m.

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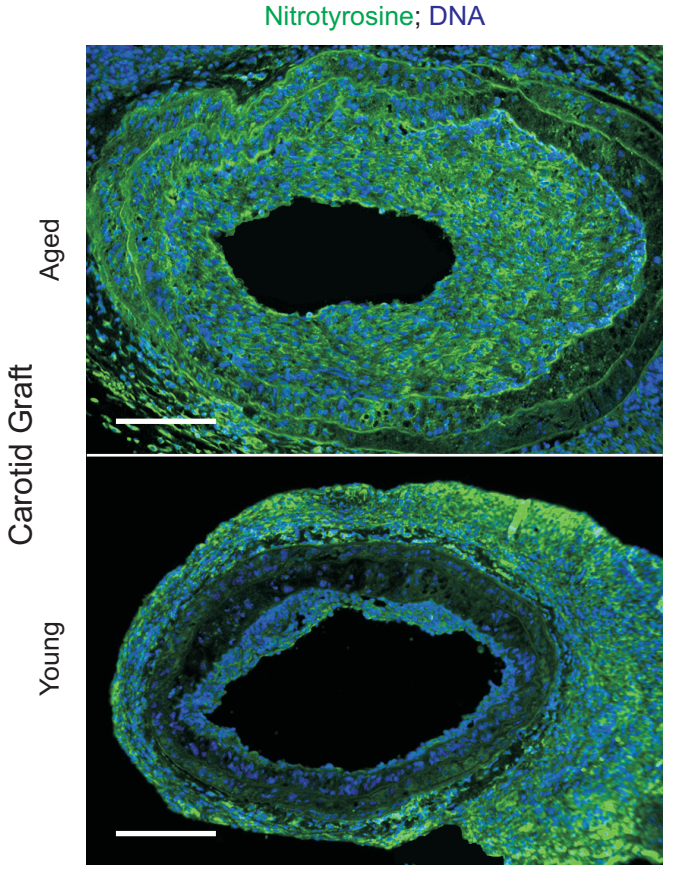

Supplementary Figure 3. Aged arteries demonstrate greater atherosclerosis-associated oxidative damage than youg arteries. Carotid grafts from Figure 5 were immunostained for nitrotyrosine (green) and counterstained for DNA (blue). Shown are samples representative of four arteries analyzed, with similar results. Scale bars = 100 m.

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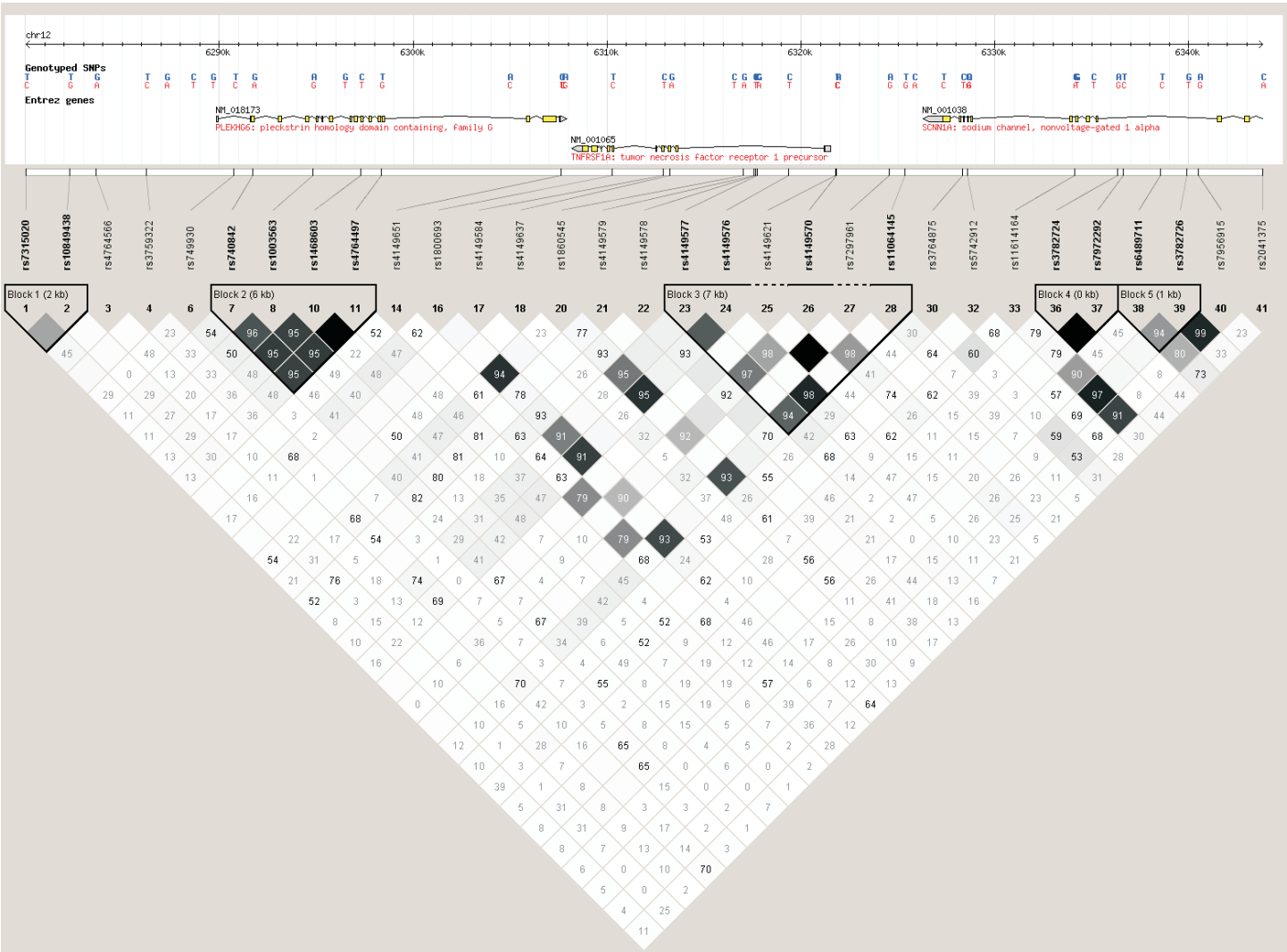
SUPPLEMENTARY MATERIAL



Supplementary Figure 4. LD (r^2) for the 65kb region surrounding *TNFR1*, generated from the International HapMap Project (http://hapmap.ncbi.nlm.nih.gov/) and displayed using the HaploView software (http://www.broadinstitute.org/mpg/haploview).