

## Supplemental Material

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## Materials and Methods

### Study population

The IMPROVE study is an observational, multi-center, longitudinal study. In brief, participants (N=3,711), aged from 55 to 79 years, with at least three established vascular risk factors (male sex or at least 5 years after menopause for women, smoking, hypertension, diabetes, dyslipidemia, or family history of cardiovascular disease), but asymptomatic for cardiovascular diseases were recruited from 7 centers in 5 European countries: Finland (n=1,050, recruited in two centers in Kuopio), Sweden (n=533, recruited in Stockholm), the Netherlands (n=532, recruited in Groningen), France (n=501, recruited in Paris), and Italy (n=553, recruited in Milan and n=542 in Perugia). The recruitment took place between March 2004 and April 2005. The study was designed to investigate whether C-IMT independently predicts vascular events in a high-risk European population. The IMPROVE data include information about lifestyle, medical history, socioeconomic status, and biochemical measurements from blood samples <sup>14,76</sup>.

### C-IMT assessment

C-IMT were measured through B-mode ultrasound in different segments of the carotid artery tree. Details of the procedure including precision and validity of the method are reported elsewhere <sup>14</sup>. For the present study, we employed the composite measure of C-IMT corresponding to the maximum of the values measured at the different locations of the whole carotid tree (C-IMT<sub>max</sub>). The reason for choosing C-IMT<sub>max</sub> (among other C-IMT measurements available), is it was associated with current smoking <sup>14</sup> and risk of future manifest CVD <sup>77</sup> in previous studies performed on this study material. Further, it is a commonly used measure in this field. Our chosen methodology for analyzing interactions requires the use of a binary variable for the outcome considered <sup>78</sup>. Hence, C-IMT was dichotomized; we used the cut-point value at the 75<sup>th</sup> percentile of the C-IMT<sub>max</sub> to define abnormal C-IMT in accordance with recommendations from the American Society of Echocardiography <sup>79</sup>. In additional analyses, we also used the 50% cut-point value of C-IMT<sub>max</sub> as it means a broader definition of abnormal C-IMT.

### Smoking assessment

We classified participants in 2 groups: “current smokers’ and “non-smokers” according

to the information reported by the participants at baseline. “Current smokers” included participants who reported current smoking or having smoked regularly in the past but quitting within 2 years of their enrolment. “Non-smokers” included participants who reported that they never had smoked. A total of 495 participants had missing information on smoking status.

#### Genotype data

From the DNA extracted from stored blood samples, genetic information was measured using Illumina Cardio-Metabo- 200k<sup>80</sup> and Immuno- Chips<sup>81</sup> bead array at one of the participating centers (Karolinska Institutet). Standard quality control (QC) procedures were applied for the separate chips as well as for their combination. All individuals were genotyped with both chips and when variants were present on both chips, the QC results were cross-checked. Due to QC, we excluded single nucleotide polymorphisms (SNPs) for any of the following: low call rate, (<95%), low minor allele frequency (MAF<0.05), and deviation from Hardy-Weinberg equilibrium ( $p < 1 \times 10^{-6}$ ). Also, we excluded participants with low call rates (<95%), relatedness, discrepancy between sex chromosome and registered sex, and participants with an outlier value in the multi-dimensional scaling used to explore population stratification<sup>82</sup>.

#### Statistical analysis

For descriptive purposes, categorical variables were reported as percentages, whereas continuous variables were reported as mean values with standard deviations (SD).

For the gene-smoking interactions analysis, we defined interaction as departure from additivity of effects from each of the two factors (smoking and genetic risk variant) considered, consistent with how Rothman defined interaction<sup>83</sup>. A dominant model of inheritance was chosen for the classification of risk genotypes; individuals who carry either one or two copies of the risk allele are considered to carry the risk variant. Using logistic regression, odds ratios (OR) with 95% confidence intervals (CI) of having C-IMT above the 75<sup>th</sup> percentile value (and above the 50<sup>th</sup> percentile value as supplementary analyses) were calculated for: 1) double exposure: smoking and carrying the genetic risk variant (OR11), 2) smoking without carrying the genetic risk

variant (OR01) and 3) carrying the genetic risk variant without being a smoker (OR10). The reference category was the group with neither of the two exposures. These three ORs formed the basis for the calculation of the Synergy index (S), a measure used to evaluate interaction on the additive scale, as follows:  $S = (OR11-1) / (OR10-1) + (OR01-1)$  <sup>78,83</sup>. The 95% CI and p-value for S were calculated using Hosmer and Lemeshow's delta method <sup>84</sup>. Adjustments were made for age, sex, education, physical inactivity, Mediterranean diet score <sup>85</sup>, and population stratification. The GEIRA software code (SAS version), which incorporated SAS procedures for logistic regression analysis and for calculations of the Synergy index, was used for these analyses <sup>86</sup>. The GEIRA software procedure classified the risk variant based on a comparison of MAF between those having abnormal C-IMT (cases) and those without (controls); if the MAF in the cases was greater than or equal to that in controls, the minor allele in the cases was assigned the risk allele, otherwise the major allele. This approach, i.e. that we determine the reference group based on MAF in the cases in comparison with the controls, means that all OR point estimates we obtain are above 1.0 <sup>86</sup>. For main analyses, we chose to only consider results based on data where the minimum number of individuals for each of the possible exposure combinations was at least 10. That pre-defined cut-off was arbitrarily chosen. However, we also performed interaction analyses on the remaining data available. We also tested interactions on the multiplicative scale using the cross-product between smoking and each SNPs considered, assessing its p-value for significance. To address the multiple testing problem, we used the Bonferroni correction: p-values of  $<2.4 \times 10^{-7}$  for S and for cross-product terms were considered significant (0.05 alpha test/207,586 SNPs).

Upon obtaining a significant result, a manual search was performed in the Single Nucleotide Polymorphism database (dbSNP), included in the National Center for Biotechnology Information (NCBI), to determine which gene can be linked to the SNP in question.

Statistical analysis was performed using SAS 9.4 (SAS institute, Cary NC, USA).

Supplemental Table I: Synergy index (S) point estimates with 95% confidence intervals (CI) for the significant gene-smoking interaction results\* after Bonferroni adjustment for multiple testing in relation to C-IMT<sub>max</sub> with cut-off at the 75<sup>th</sup> percentile

	<b>S (95% CI)</b>
<b>Chr 1</b>	
rs12134420	5.39 (1.33;21.83)
rs2446622	4.89 (1.60;14.94)
rs72676073	3.69 (1.45;9.38)
rs73009101	3.87 (1.35;11.07)
<b>Chr 2</b>	
rs6758414	4.63 (1.45;14.82)
rs9789490	5.82 (1.50;22.59)
<b>Chr 3</b>	
rs9877192	4.44 (1.37;14.41)
<b>Chr 4</b>	
rs11736632	3.47 (1.34;9.01)
<b>Chr 5</b>	
rs13176964	3.32 (1.34;8.27)
rs2278392	4.11 (1.34;12.63)
rs4867490	4.12 (1.46;11.66)
rs7722352	4.06 (1.36;12.12)
<b>Chr 7</b>	
rs28695838	5.63 (1.86;17.04)
<b>Chr 8</b>	
rs12545167	4.52 (1.38;14.81)
rs4301463	4.08 (1.51;11.02)
rs6997802	4.06 (1.50;10.95)
rs752039	5.26 (1.40;19.74)
<b>Chr 9</b>	
rs10810371	3.34 (1.35;8.25)
rs143207461	4.36 (1.48;12.80)

Chr 10

rs12244483 4.05 (1.39;11.80)  
rs12251673 4.11 (1.32;12.75)  
rs7068194 4.10 (1.32;12.69)  
rs7092757 4.21 (1.38;12.85)  
rs72826094 5.44 (1.33;22.31)

Chr 11

rs1002171 3.73 (1.33;10.46)  
rs2434468 4.19 (1.46;12.01)  
rs2511241 4.68 (1.65;13.30)  
rs3741392 4.29 (1.42;12.97)  
rs61899280 4.63 (1.58;13.60)

Chr 12

rs10506726 4.96 (1.78;13.80)  
rs11171745 3.64 (1.33;9.94)  
rs11171773 3.84 (1.34;11.02)  
rs116378618 3.88 (1.34;11.23)  
rs1689512 3.64 (1.33;9.94)  
rs17118317 3.95 (1.34;11.64)  
rs35436573 4.09 (1.42;11.77)  
rs4762693 4.57 (1.31;15.91)  
rs773643 3.72 (1.37;10.10)  
rs7956913 4.16 (1.39;12.42)

Chr 13

rs12872592 4.63 (1.51;14.20)

Chr 14

rs4981312 4.60 (1.37;15.48)  
rs7155978 4.00 (1.37;11.72)  
rs915064 4.13 (1.35;12.66)

Chr 16

rs1003341 5.07 (1.27;20.22)

Chr 17

rs3744761 4.11 (1.32;12.74)

rs4362432 3.64 (1.41;9.38)

Chr 20

rs6032180 4.13 (1.47;11.61)

\* Synergy index results were considered significant at p-values  $<2.4 \times 10^{-7}$

Supplemental Table II: Significant gene-smoking interaction results\* after Bonferroni adjustment for multiple testing in relation to C-IMT<sub>max</sub> with cut-off at the 50<sup>th</sup> percentile. A dominant genetic model was assumed<sup>†</sup>.

	Number of observations								Odds Ratio (95% Confidence Interval) <sup>‡</sup>					
	Non-smokers without the risk variant		Non-smokers with the risk variant		Smokers without the risk variant		Smokers with the risk variant		Reference group: Non-smokers without the risk variant					
	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Risk allele	MAF (%)	Non-smokers with the risk variant	Smokers without the risk variant	Smokers with the risk variant	p Synergy index
Chr 1														
rs11208009	1150	184	1098	247	158	15	152	46	T	35	1.04 (0.81;1.33)	1.68 (1.35;2.09)	4.44 (2.4;8.22)	9.85x10 <sup>-16</sup>
rs11582097	773	135	722	151	534	63	528	142	A	23	1.06 (0.9;1.25)	1.45 (1.12;1.89)	2.92 (2.11;4.05)	8.19x10 <sup>-10</sup>
rs7529090	741	129	696	139	567	69	554	154	A	25	1.04 (0.89;1.22)	1.4 (1.06;1.83)	2.85 (2.08;3.9)	5.11x10 <sup>-10</sup>
rs12068067	839	145	780	169	469	54	470	124	A	20	1.07 (0.91;1.26)	1.5 (1.17;1.94)	3.01 (2.13;4.27)	5.41x10 <sup>-10</sup>
rs12569167	1152	187	1095	255	156	11	154	38	A	6	1.06 (0.83;1.36)	1.74 (1.4;2.16)	4.49 (2.2;9.17)	2.01x10 <sup>-10</sup>
rs143013938	1151	188	1096	255	156	11	154	38	A	6	1.06 (0.83;1.36)	1.73 (1.39;2.15)	4.49 (2.2;9.16)	1.10x10 <sup>-10</sup>
rs12024343	1152	188	1095	255	156	11	155	38	T	6	1.07 (0.84;1.37)	1.73 (1.39;2.15)	4.5 (2.2;9.18)	1.86x10 <sup>-10</sup>
rs6681152	1147	188	1094	253	158	11	156	38	T	6	1.06 (0.83;1.36)	1.72 (1.38;2.14)	4.49 (2.2;9.16)	7.54x10 <sup>-11</sup>
rs76647137	1153	188	1095	255	155	11	155	38	A	6	1.07 (0.84;1.37)	1.73 (1.4;2.15)	4.5 (2.2;9.18)	2.65x10 <sup>-10</sup>
rs150990100	1150	184	1099	247	158	15	151	46	T	35	1.03 (0.8;1.32)	1.68 (1.35;2.09)	4.43 (2.4;8.2)	3.49x10 <sup>-16</sup>
rs164155	1174	185	1115	253	134	14	135	40	A	32	1.11 (0.85;1.43)	1.73 (1.39;2.15)	4.06 (2.13;7.72)	2.00x10 <sup>-7</sup>
rs17573783	1148	184	1093	251	160	15	157	42	G	6	1.07 (0.84;1.36)	1.73 (1.39;2.15)	3.92 (2.1;7.31)	1.00x10 <sup>-7</sup>
rs282001	1147	177	1089	239	161	22	161	54	T	7	1.03 (0.81;1.31)	1.68 (1.35;2.1)	3.61 (2.09;6.21)	1.83x10 <sup>-8</sup>
rs4915853	1151	184	1098	247	157	15	152	46	A	35	1.05 (0.82;1.34)	1.68 (1.35;2.09)	4.44 (2.4;8.22)	2.03x10 <sup>-15</sup>
rs6679002	1150	184	1099	247	158	15	151	46	T	35	1.03 (0.8;1.32)	1.68 (1.35;2.09)	4.43 (2.4;8.2)	3.49x10 <sup>-16</sup>
rs7548334	1151	188	1100	256	153	11	149	37	T	6	1.04 (0.81;1.34)	1.73 (1.39;2.15)	4.37 (2.13;8.93)	6.97x10 <sup>-10</sup>
Chr 2														
rs10171234	1135	181	1078	238	172	17	171	54	A	7	1.03 (0.81;1.3)	1.7 (1.36;2.12)	3.79 (2.13;6.74)	2.24x10 <sup>-9</sup>
rs11691338	895	151	841	183	413	48	409	110	G	18	1.13 (0.95;1.34)	1.57 (1.22;2)	3.16 (2.19;4.57)	2.43x10 <sup>-9</sup>
rs1319213	957	162	911	201	351	37	339	92	T	15	1.07 (0.9;1.28)	1.58 (1.24;2)	3.34 (2.23;5.02)	1.10x10 <sup>-11</sup>
rs1509099	984	166	935	202	324	33	315	91	C	14	1.1 (0.91;1.32)	1.55 (1.23;1.96)	3.73 (2.44;5.7)	2.45x10 <sup>-17</sup>
rs3754956	957	162	910	201	351	37	340	92	C	15	1.08 (0.9;1.29)	1.58 (1.24;2)	3.35 (2.23;5.02)	1.37x10 <sup>-11</sup>
rs3769874	957	162	911	201	351	37	339	92	T	15	1.07 (0.9;1.28)	1.58 (1.24;2)	3.34 (2.23;5.02)	1.10x10 <sup>-11</sup>
rs3769889	985	165	934	202	323	34	316	91	C	14	1.1 (0.91;1.32)	1.56 (1.24;1.98)	3.62 (2.38;5.5)	4.6x10 <sup>-15</sup>
rs3820989	971	162	925	196	337	37	325	97	T	14	1.06 (0.89;1.28)	1.53 (1.2;1.94)	3.57 (2.38;5.36)	5.63x10 <sup>-17</sup>
rs7574791	982	166	934	204	326	33	316	89	T	14	1.09 (0.9;1.31)	1.57 (1.24;1.98)	3.64 (2.38;5.57)	1.18x10 <sup>-15</sup>
rs79916544	982	166	934	204	326	33	316	89	T	14	1.09 (0.9;1.31)	1.57 (1.24;1.98)	3.64 (2.38;5.57)	1.18x10 <sup>-15</sup>
rs16857518	1164	185	1105	247	143	13	143	45	A	6	1.08 (0.84;1.39)	1.71 (1.38;2.13)	4.33 (2.26;8.28)	1.10x10 <sup>-10</sup>
rs1869325	1154	184	1093	246	154	15	157	47	G	6	1.08 (0.84;1.38)	1.72 (1.38;2.14)	4.02 (2.17;7.44)	8.21x10 <sup>-9</sup>
rs2854386	1173	189	1102	257	135	10	148	36	G	6	1.2 (0.93;1.55)	1.75 (1.41;2.18)	4.81 (2.34;9.9)	5.61x10 <sup>-9</sup>
rs4667744	901	156	863	182	407	43	387	111	C	17	1.01 (0.85;1.2)	1.48 (1.16;1.89)	3.33 (2.28;4.88)	7.12x10 <sup>-17</sup>
rs550619	1068	175	1012	227	240	24	238	66	G	10	1.05 (0.85;1.29)	1.67 (1.33;2.09)	3.38 (2.08;5.49)	6.21x10 <sup>-8</sup>
rs570877	1068	175	1012	227	240	24	238	66	T	10	1.05 (0.85;1.29)	1.67 (1.33;2.09)	3.38 (2.08;5.49)	6.21x10 <sup>-8</sup>



rs7588461	728	137	688	162	580	61	561	130	G	25	1 (0.85;1.18)	1.49 (1.15;1.93)	2.75 (1.97;3.84)	1.87x10 <sup>-7</sup>
Chr 3														
rs11130290	993	161	948	206	315	38	302	87	A	13	1.04 (0.87;1.26)	1.61 (1.27;2.04)	3.1 (2.06;4.67)	5.00x10 <sup>-8</sup>
rs115766450	992	161	948	206	316	38	302	87	G	13	1.04 (0.86;1.25)	1.61 (1.27;2.04)	3.1 (2.06;4.67)	4.13x10 <sup>-8</sup>
rs13088462	1179	188	1120	256	129	11	130	37	C	5	1.11 (0.85;1.45)	1.74 (1.4;2.16)	4.51 (2.21;9.21)	4.27x10 <sup>-9</sup>
rs13097744	1178	188	1119	256	129	11	130	37	G	5	1.11 (0.85;1.44)	1.74 (1.4;2.16)	4.5 (2.2;9.2)	4.24x10 <sup>-9</sup>
rs1383252	1052	171	991	225	252	27	252	67	C	10	1.10 (0.90;1.34)	1.68 (1.34;2.11)	3.44 (2.13;5.54)	1.60x10 <sup>-7</sup>
rs4974108	993	161	948	206	315	38	302	87	T	13	1.04 (0.87;1.26)	1.61 (1.27;2.04)	3.1 (2.06;4.67)	5.00x10 <sup>-8</sup>
rs6445455	1054	171	997	224	254	28	253	69	T	10	1.09 (0.89;1.33)	1.67 (1.33;2.09)	3.4 (2.13;5.44)	7.57x10 <sup>-8</sup>
rs6445601	993	161	947	206	315	38	302	87	T	13	1.05 (0.87;1.26)	1.61 (1.27;2.04)	3.11 (2.06;4.68)	5.16x10 <sup>-8</sup>
rs6445604	993	161	948	206	315	38	302	87	A	13	1.04 (0.87;1.26)	1.61 (1.27;2.04)	3.1 (2.06;4.67)	5.00 x 10 <sup>-8</sup>
rs6445611	993	161	948	206	315	38	302	87	T	13	1.04 (0.87;1.26)	1.61 (1.27;2.04)	3.1 (2.06;4.67)	5.00 x 10 <sup>-8</sup>
rs7640083	993	161	948	206	315	38	302	87	G	13	1.04 (0.87;1.26)	1.61 (1.27;2.04)	3.1 (2.06;4.67)	5.00 x 10 <sup>-8</sup>
rs7648012	912	153	862	191	396	46	388	102	G	17	1.07 (0.90;1.28)	1.58 (1.24;2.02)	3.04 (2.08;4.45)	4.43 x 10 <sup>-8</sup>
rs7649069	992	161	946	206	316	38	304	87	A	13	1.04 (0.87;1.26)	1.61 (1.27;2.04)	3.1 (2.06;4.67)	5.01 x 10 <sup>-8</sup>
rs9877188	993	161	948	206	315	38	302	87	T	13	1.04 (0.87;1.26)	1.61 (1.27;2.04)	3.1 (2.06;4.67)	5 x 10 <sup>-8</sup>
rs6777719	1054	171	997	224	254	28	253	69	T	10	1.09 (0.89;1.33)	1.67 (1.33;2.09)	3.4 (2.13;5.44)	7.57 x 10 <sup>-8</sup>
rs181877	1093	177	994	224	215	22	256	69	G	10	1.24 (1.01;1.53)	1.69 (1.35;2.12)	3.98 (2.39;6.63)	3.7 x 10 <sup>-9</sup>
rs6773525	867	145	780	172	441	54	470	120	G	20	1.19 (1.01;1.41)	1.56 (1.21;2.01)	3.18 (2.23;4.52)	5.4 x 10 <sup>-9</sup>
rs7632761	953	157	883	199	355	42	367	94	T	15	1.06 (0.89;1.27)	1.61 (1.27;2.05)	3.05 (2.05;4.55)	2.21 x 10 <sup>-7</sup>
Chr 4														
rs10454793	1145	179	1087	240	163	20	163	53	A	7	1.01 (0.8;1.29)	1.7 (1.36;2.11)	3.57 (2.05;6.21)	6.42 x 10 <sup>-8</sup>
rs11731522	917	156	850	192	391	43	400	101	A	17	1.09 (0.91;1.29)	1.59 (1.25;2.02)	3.12 (2.12;4.59)	1.21 x 10 <sup>-8</sup>
rs2175586	1144	187	1089	256	164	12	161	37	A	6	1.04 (0.82;1.32)	1.74 (1.4;2.16)	4.05 (2.04;8.06)	8.18 x 10 <sup>-8</sup>
Chr 5														
rs1392279	1100	181	1045	237	205	18	204	56	C	8	1.05 (0.84;1.3)	1.68 (1.35;2.1)	3.73 (2.15;6.46)	1.03 x 10 <sup>-9</sup>
rs17415614	974	161	929	204	334	38	321	89	G	14	1.02 (0.85;1.23)	1.57 (1.24;1.99)	3.27 (2.17;4.94)	8.30 x 10 <sup>-12</sup>
rs1858432	655	113	599	119	653	86	650	174	G	30	1.09 (0.93;1.28)	1.38 (1.03;1.84)	2.73 (2.03;3.67)	2.17 x 10 <sup>-7</sup>
rs2063564	925	148	853	179	383	51	397	114	C	17	1.1 (0.92;1.3)	1.55 (1.21;1.98)	3.08 (2.14;4.43)	2.67 x 10 <sup>-9</sup>
rs2594849	969	154	905	187	339	45	345	106	T	15	1.11 (0.93;1.33)	1.57 (1.23;2.01)	3.1 (2.13;4.52)	2.16 x 10 <sup>-8</sup>
rs746215	807	141	765	157	501	58	485	136	C	22	1 (0.85;1.18)	1.4 (1.08;1.82)	3.08 (2.19;4.33)	8.91 x 10 <sup>-15</sup>
rs756452	1145	188	1087	255	163	11	163	38	A	6	1.03 (0.81;1.31)	1.72 (1.39;2.14)	4.25 (2.13;8.47)	3.55 x 10 <sup>-10</sup>
Chr 6														
rs1265045	860	152	806	180	448	47	444	113	A	19	1.04 (0.88;1.23)	1.51 (1.18;1.93)	3.21 (2.21;4.66)	4.19 x 10 <sup>-13</sup>
rs1265100	934	155	878	197	374	44	372	96	G	16	1.04 (0.87;1.24)	1.59 (1.25;2.02)	3.01 (2.04;4.44)	7.64 x 10 <sup>-8</sup>
rs2844633	848	151	796	175	454	48	443	116	T	20	1.03 (0.87;1.22)	1.48 (1.15;1.9)	3.19 (2.21;4.61)	7.01 x 10 <sup>-14</sup>
rs1933650	1093	177	1047	233	215	22	203	60	T	9	1.04 (0.83;1.28)	1.68 (1.34;2.1)	3.48 (2.08;5.83)	3.34 x 10 <sup>-08</sup>
rs3957146	1063	178	1007	236	245	21	243	57	C	10	1.03 (0.84;1.26)	1.68 (1.34;2.1)	3.68 (2.16;6.3)	3.26 x 10 <sup>-10</sup>
rs3957148	1055	178	1003	237	253	21	247	56	G	10	1.01 (0.83;1.24)	1.67 (1.34;2.09)	3.66 (2.14;6.27)	1.66 x 10 <sup>-10</sup>
rs3998159	1052	178	1002	236	256	21	248	57	C	10	1.01 (0.82;1.23)	1.67 (1.33;2.09)	3.66 (2.14;6.26)	5.73 x 10 <sup>-11</sup>
rs41282644	1141	183	1077	242	167	16	173	51	A	7	1.03 (0.81;1.3)	1.7 (1.36;2.11)	3.81 (2.13;6.8)	1.48 x 10 <sup>-09</sup>
rs7454108	1061	178	1005	235	245	21	242	57	C	10	1.03 (0.84;1.26)	1.68 (1.34;2.1)	3.69 (2.16;6.3)	2.65 x 10 <sup>-10</sup>
rs9275184	1053	177	1003	235	238	21	239	57	C	10	1.04 (0.85;1.28)	1.68 (1.34;2.1)	3.69 (2.16;6.3)	6.23 x 10 <sup>-10</sup>

rs9275206	1061	177	1004	235	243	20	243	57	G	10	1.04 (0.85;1.28)	1.68 (1.34;2.11)	3.87 (2.24;6.67)	1.31 x 10 <sup>-11</sup>
rs9275221	1057	177	998	233	242	21	238	57	C	10	1.02 (0.83;1.26)	1.66 (1.33;2.08)	3.7 (2.16;6.32)	6.03 x 10 <sup>-11</sup>
rs9275334	1061	177	1003	235	247	22	246	58	C	10	1.04 (0.85;1.27)	1.68 (1.34;2.11)	3.56 (2.11;6.02)	9.64 x 10 <sup>-9</sup>
rs9275383	1033	174	978	224	275	25	272	69	T	11	1.02 (0.84;1.24)	1.64 (1.3;2.05)	3.6 (2.21;5.87)	4.43 x 10 <sup>-12</sup>
rs9275495	1060	177	1003	235	247	22	246	58	T	10	1.04 (0.85;1.27)	1.68 (1.34;2.1)	3.56 (2.1;6.01)	9.05 x 10 <sup>-9</sup>
rs9275530	1061	177	1004	235	247	22	246	58	C	10	1.04 (0.85;1.27)	1.68 (1.34;2.1)	3.56 (2.11;6.02)	9.13 x 10 <sup>-9</sup>
rs9275532	1061	177	1004	235	247	22	246	58	G	10	1.04 (0.85;1.27)	1.68 (1.34;2.1)	3.56 (2.11;6.02)	9.13 x 10 <sup>-9</sup>
rs9321228	1118	186	1068	247	190	13	182	46	T	7	1.03 (0.82;1.29)	1.66 (1.34;2.07)	5.37 (2.74;10.54)	2.23 x 10 <sup>-28</sup>
rs9359725	1037	176	973	223	271	23	277	70	C	11	1.04 (0.86;1.27)	1.63 (1.3;2.04)	3.84 (2.34;6.29)	3.28 x 10 <sup>-15</sup>
rs9396195	1188	184	1126	249	120	15	124	44	A	5	1.03 (0.78;1.36)	1.71 (1.38;2.13)	3.84 (2.1;7.03)	2.9 x 10 <sup>-8</sup>
Chr 7														
rs56006970	1108	178	1056	237	200	21	194	56	T	8	1 (0.8;1.25)	1.68 (1.34;2.1)	3.53 (2.08;6.01)	5.46 x 10 <sup>-9</sup>
rs651841	977	159	917	201	331	40	333	92	A	14	1.04 (0.87;1.25)	1.56 (1.23;1.98)	3.3 (2.21;4.93)	3.43 x 10 <sup>-12</sup>
rs663911	950	153	889	194	358	46	361	99	T	15	1.06 (0.89;1.27)	1.57 (1.23;2)	3.11 (2.12;4.56)	2.40 x 10 <sup>-9</sup>
rs6958510	1030	164	954	207	278	34	296	86	T	12	1.15 (0.95;1.39)	1.63 (1.29;2.06)	3.5 (2.27;5.39)	9.91 x 10 <sup>-10</sup>
rs77327146	1182	187	1102	255	126	12	148	38	G	5	1.13 (0.87;1.47)	1.74 (1.4;2.16)	4.44 (2.23;8.86)	1.14 x 10 <sup>-8</sup>
Chr 8														
rs10110877	1136	185	1082	250	166	14	163	42	C	7	1.02 (0.8;1.3)	1.71 (1.37;2.12)	3.92 (2.1;7.33)	2.37 x 10 <sup>-9</sup>
rs10217099	1164	184	1092	246	144	15	158	47	C	6	1.15 (0.9;1.48)	1.73 (1.39;2.15)	4.1 (2.21;7.6)	1 x 10 <sup>-7</sup>
rs2941652	1094	174	1012	219	214	25	238	74	G	10	1.14 (0.92;1.4)	1.65 (1.31;2.07)	3.67 (2.28;5.89)	4.45 x 10 <sup>-10</sup>
rs7818319	1093	175	1038	229	215	24	212	64	A	9	1.04 (0.84;1.29)	1.67 (1.34;2.1)	3.37 (2.06;5.54)	1.91 x 10 <sup>-7</sup>
rs8192330	1116	176	1048	231	192	23	202	62	A	8	1.01 (0.81;1.26)	1.65 (1.32;2.07)	3.58 (2.16;5.93)	6.92 x 10 <sup>-11</sup>
Chr 9														
rs6478342	877	156	813	187	431	43	437	106	C	18	1.08 (0.92;1.28)	1.55 (1.21;1.98)	3.29 (2.24;4.83)	3.35 x 10 <sup>-12</sup>
rs7025754	1016	164	961	204	292	35	289	89	C	12	1.03 (0.85;1.25)	1.58 (1.25;2)	3.28 (2.16;4.98)	4.24 x 10 <sup>-11</sup>
rs9406646	949	153	912	199	359	46	338	94	T	15	1.01 (0.84;1.2)	1.57 (1.24;2)	2.93 (2;4.29)	7.63 x 10 <sup>-8</sup>
Chr 10														
rs16930144	1146	178	1081	240	162	20	169	53	G	7	1.07 (0.84;1.36)	1.7 (1.36;2.13)	3.61 (2.1;6.21)	2.29 x 10 <sup>-7</sup>
rs7072256	938	152	883	186	369	47	367	107	A	16	1.02 (0.85;1.21)	1.54 (1.21;1.97)	2.98 (2.05;4.32)	3.50 x 10 <sup>-9</sup>
rs17875327	1037	166	978	208	270	33	272	85	G	12	1.04 (0.85;1.26)	1.6 (1.27;2.02)	3.27 (2.14;5.01)	5.32 x 10 <sup>-10</sup>
rs2245348	1154	186	1091	252	154	13	159	41	G	6	1.06 (0.83;1.35)	1.72 (1.38;2.14)	4.35 (2.24;8.44)	2.79 x 10 <sup>-11</sup>
rs1862082	1154	186	1090	251	154	13	160	42	T	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs2474754	1154	186	1090	252	154	13	160	41	C	6	1.07 (0.84;1.36)	1.72 (1.39;2.14)	4.35 (2.24;8.46)	5.78 x 10 <sup>-11</sup>
rs2474755	1154	186	1089	251	154	13	160	42	C	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.7 x 10 <sup>-12</sup>
rs2474756	1154	186	1090	251	154	13	160	42	T	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs2474757	1154	186	1090	251	154	13	160	42	G	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs2474758	1154	186	1090	251	154	13	160	42	A	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs2474759	1154	186	1090	251	154	13	160	42	C	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs2506107	1154	186	1090	251	154	13	160	42	A	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs2506108	1154	186	1090	251	154	13	160	42	G	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs2506109	1154	186	1090	251	154	13	160	42	G	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs2506110	1154	186	1090	251	154	13	160	42	G	6	1.07 (0.84;1.36)	1.72 (1.38;2.13)	4.44 (2.29;8.61)	4.41 x 10 <sup>-12</sup>
rs56668170	1147	183	1089	248	161	16	161	45	A	7	1.03 (0.81;1.31)	1.71 (1.38;2.13)	3.83 (2.09;7)	1.47 x 10 <sup>-08</sup>

Chr 11														
rs11603873	1070	175	1019	233	237	24	231	60	G	9	1 (0.81;1.23)	1.67 (1.34;2.09)	3.31 (2.01;5.47)	1.26 x 10 <sup>-7</sup>
rs58858617	1071	175	1019	233	237	24	231	60	C	9	1 (0.81;1.23)	1.67 (1.34;2.1)	3.32 (2.01;5.47)	1.29 x 10 <sup>-7</sup>
rs16938342	1166	185	1111	251	142	14	139	42	T	6	1.08 (0.84;1.39)	1.72 (1.39;2.14)	3.91 (2.1;7.29)	2.1 x 10 <sup>-7</sup>
rs2237898	1144	183	1086	245	164	16	164	48	C	7	1.06 (0.84;1.35)	1.7 (1.37;2.12)	3.98 (2.19;7.22)	8.71 x 10 <sup>-10</sup>
rs3758768	1063	169	1012	215	245	30	238	78	C	10	1.02 (0.83;1.25)	1.62 (1.29;2.04)	3.3 (2.11;5.16)	1.3 x 10 <sup>-09</sup>
rs4909953	1155	184	1103	248	153	15	147	45	A	6	1.05 (0.82;1.35)	1.71 (1.37;2.13)	4.04 (2.18;7.49)	9.94 x 10 <sup>-10</sup>
Chr 12														
rs12318758	1123	177	1067	232	185	22	182	61	T	8	1.01 (0.8;1.27)	1.66 (1.33;2.08)	3.59 (2.14;6.02)	3.03 x 10 <sup>-10</sup>
rs12829836	1100	179	1043	239	208	20	207	54	G	8	1.05 (0.84;1.3)	1.7 (1.36;2.12)	3.72 (2.11;6.55)	1.04 x 10 <sup>-8</sup>
rs12831974	1006	163	945	209	302	36	305	84	C	13	1.03 (0.85;1.25)	1.59 (1.26;2.01)	3.32 (2.17;5.08)	2.22 x 10 <sup>-11</sup>
rs2555296	1080	178	1014	234	228	21	236	59	A	10	1.05 (0.85;1.29)	1.66 (1.33;2.08)	3.85 (2.27;6.53)	1.61 x 10 <sup>-12</sup>
rs874619	932	155	885	197	376	44	365	96	A	16	1.03 (0.87;1.23)	1.59 (1.25;2.02)	2.96 (2.01;4.35)	2.13 x 10 <sup>-7</sup>
Chr 13														
rs11841001	1057	169	1004	223	251	30	246	70	A	10	1.05 (0.85;1.28)	1.64 (1.3;2.06)	3.4 (2.14;5.39)	1.74 x 10 <sup>-9</sup>
rs11841544	1056	169	1004	222	252	30	246	71	A	10	1.04 (0.85;1.27)	1.63 (1.3;2.05)	3.43 (2.17;5.45)	1.66 x 10 <sup>-10</sup>
rs1414320	1037	173	985	227	271	25	265	66	G	11	1.06 (0.87;1.29)	1.67 (1.33;2.1)	3.42 (2.11;5.52)	3.1 x 10 <sup>-8</sup>
Chr 14														
rs17109084	1064	169	1000	208	244	30	250	85	A	11	1.04 (0.85;1.28)	1.6 (1.27;2.02)	3.35 (2.17;5.19)	1.2 x 10 <sup>-10</sup>
rs17175304	1153	187	1101	252	155	12	149	41	A	6	1.04 (0.81;1.33)	1.71 (1.37;2.12)	4.51 (2.33;8.75)	4.62 x 10 <sup>-14</sup>
rs1775671	1120	184	1061	245	188	15	189	48	C	7	1.12 (0.89;1.41)	1.72 (1.38;2.15)	3.93 (2.16;7.13)	1.39 x 10 <sup>-07</sup>
Chr 15														
rs12148293	1118	175	1062	233	190	24	188	60	T	8	1.01 (0.8;1.26)	1.67 (1.33;2.08)	3.44 (2.08;5.68)	6.16 x 10 <sup>-9</sup>
Chr 16														
rs1552273	887	152	843	182	419	47	407	110	A	18	1 (0.84;1.19)	1.53 (1.2;1.96)	2.91 (2.01;4.2)	1.24 x 10 <sup>-8</sup>
rs2549732	1121	182	1064	249	187	17	186	44	A	7	1.05 (0.84;1.32)	1.72 (1.38;2.14)	3.71 (2.06;6.7)	2.29 x 10 <sup>-7</sup>
rs258160	964	158	899	191	342	41	351	102	C	15	1.05 (0.88;1.26)	1.57 (1.23;2)	3.09 (2.1;4.57)	3.59 x 10 <sup>-9</sup>
rs8049897	1013	168	953	221	295	31	297	72	A	12	1.02 (0.84;1.23)	1.64 (1.31;2.07)	3.14 (2.02;4.89)	1.5 x 10 <sup>-7</sup>
Chr 17														
rs11867392	1123	174	1058	236	185	25	192	57	T	8	1.11 (0.89;1.39)	1.68 (1.35;2.1)	3.91 (2.29;6.7)	2.07 x 10 <sup>-10</sup>
rs12938678	871	146	822	182	437	53	428	111	A	19	1.04 (0.87;1.23)	1.55 (1.21;1.99)	2.89 (2.02;4.15)	1.17 x 10 <sup>-7</sup>
rs3744761	1190	189	1131	253	118	10	119	40	T	5	1.01 (0.76;1.33)	1.72 (1.38;2.13)	4.52 (2.22;9.21)	6.95 x 10 <sup>-13</sup>
rs9901525	857	148	815	179	451	51	435	114	C	19	1.02 (0.86;1.2)	1.52 (1.19;1.95)	2.94 (2.05;4.2)	2.84 x 10 <sup>-9</sup>
Chr 18														
rs17082725	1125	180	1072	244	183	18	178	49	T	7	1.05 (0.83;1.32)	1.71 (1.37;2.14)	3.79 (2.14;6.7)	1.12 x 10 <sup>-8</sup>
Chr 19														
rs10426583	767	133	735	145	539	64	515	148	C	24	1.01 (0.86;1.19)	1.39 (1.06;1.82)	2.86 (2.07;3.93)	9.85 x 10 <sup>-11</sup>
Chr 20														
rs17329208	1157	182	1096	249	151	17	154	44	C	6	1.12 (0.88;1.44)	1.72 (1.38;2.14)	3.98 (2.18;7.28)	1.03 x 10 <sup>7</sup>
rs6032180	1085	172	1030	230	223	27	220	63	T	9	1.05 (0.85;1.29)	1.67 (1.33;2.09)	3.38 (2.07;5.52)	9.66 x 10 <sup>-8</sup>
rs6037397	1104	185	1029	240	204	14	221	53	T	8	1.16 (0.93;1.43)	1.68 (1.35;2.1)	4.98 (2.67;9.29)	2.5 x 10 <sup>-18</sup>
rs6048171	1179	189	1128	255	129	10	122	38	C	5	1.04 (0.8;1.36)	1.7 (1.37;2.12)	5.37 (2.55;11.29)	1.36 x 10 <sup>-20</sup>
rs6118390	1010	170	968	218	298	29	282	75	C	12	1.04 (0.86;1.26)	1.61 (1.28;2.03)	3.54 (2.24;5.57)	6.15 x 10 <sup>-13</sup>

rs731428	1163	187	1101	254	145	12	149	39	C	6	1.13 (0.88;1.45)	1.75 (1.41;2.17)	4.43 (2.17;9.04)	5.92 x 10 <sup>-8</sup>
Chr 21														
rs2837461	1087	175	1013	219	221	24	237	74	G	10	1.18 (0.96;1.45)	1.67 (1.33;2.1)	3.63 (2.23;5.91)	7.85 x 10 <sup>-8</sup>
rs3788061	1123	177	1071	243	185	22	179	50	A	7	1.03 (0.82;1.3)	1.68 (1.35;2.1)	3.75 (2.17;6.48)	4.86 x 10 <sup>-10</sup>

MAF: minor allele frequency

\* Synergy index results were considered significant at p-values <2.4x10<sup>-7</sup>; Minimum number of subjects in each group:10

† Individuals who carry either one or two copies of the risk allele are considered to carry the risk variant

‡ Model adjusted for sex, age, education (categorical), physical activity (categorical), Mediterranean diet score and population structure (MDS1-3 continuous)

Supplemental Table III: Genes in proximity to the genetic variants included in the significant gene-smoking interaction results observed for C-IMT<sub>max</sub> with cut-off at the 50<sup>th</sup> percentile

	Position	Function	Gene in proximity to the genetic variant
Chr 1			
rs11208009	62730021	Intergenic variant	None
rs11582097	246871729	Intron variant	<i>AHCTF1</i>
rs7529090	246905930	Intron variant	<i>AHCTF1</i>
rs12068067	246862636	Intron variant	<i>AHCTF1</i>
rs12569167	91986652	Intron variant	<i>BRDT</i>
rs143013938	91989182-91989200	Intron variant	<i>BRDT</i>
rs12024343	91998118	Intron variant	<i>BRDT</i>
rs6681152	92013275	Intron variant	<i>BRDT</i>
rs76647137	92013746	Intron variant	<i>BRDT</i>
rs150990100	62733677	Intergenic variant	None
rs164155	162372551	Intergenic variant	None
rs17573783	108181218	Intron variant	<i>SLC25A24</i>
rs282001	91321022	Intron variant	<i>HFM1</i>
rs4915853	62725906	Intergenic variant	None
rs6679002	62734265	Intergenic variant	None
rs7548334	92027662	Intergenic variant	None
Chr 2			
rs10171234	106688521	Intergenic variant	None
rs11691338	164783678	Intron Variant	<i>COBLL1</i>
rs1319213	164718780	Intron Variant	<i>COBLL1</i>
rs1509099	164771494	Intron Variant	<i>COBLL1</i>
rs3754956	164719135	Intron Variant	<i>COBLL1</i>
rs3769874	164712075	Intron Variant	<i>COBLL1</i>
rs3769889	164744447	Intron Variant	<i>COBLL1</i>
rs3820989	164780775	Intron Variant	<i>COBLL1</i>
rs7574791	164733949	Intron Variant	<i>COBLL1</i>
rs79916544	164728852	Intron Variant	<i>COBLL1</i>
rs16857518	170044398	Intron Variant	<i>UBR3</i>
rs1869325	137327004	Intron variant	<i>THSD7B</i>
rs2854386	218162779	Downstream transcript variant	<i>CXCR1</i>
rs4667744	164305368	Intergenic variant	None
rs550619	21037729	Intron variant	<i>APOB</i>
rs570877	21028168	Intron variant	<i>APOB</i>
rs7588461	230370064	Intron variant	<i>SP140L</i>
Chr 3			
rs11130290	51311103	Intron variant	<i>DOCK3</i>

rs115766450	51307891	Intron variant	<i>DOCK3</i>
rs13088462	51034282	Intron Variant	<i>DOCK3</i>
rs13097744	50957594	Intron Variant	<i>DOCK3</i>
rs1383252	51223655	Intron Variant	<i>DOCK3</i>
rs4974108	51305640	Intron Variant	<i>DOCK3</i>
rs6445455	51163181	Intron Variant	<i>DOCK3</i>
rs6445601	51297167	Intron Variant	<i>DOCK3</i>
rs6445604	51298161	Intron Variant	<i>DOCK3</i>
rs6445611	51306999	Intron Variant	<i>DOCK3</i>
rs7640083	51309674	Intron Variant	<i>DOCK3</i>
rs7648012	51317140	Intron Variant	<i>DOCK3</i>
rs7649069	51313625	Intron Variant	<i>DOCK3</i>
rs9877188	51306291	Intron Variant	<i>DOCK3</i>
rs6777719	51163981	Intron Variant	<i>DOCK3</i>
rs181877	138376056	Intron Variant	<i>MRAS</i>
rs6773525	190803931	Intergenic variant	None
rs7632761	117481408	Intergenic variant	None
Chr 4			
rs10454793	117481408	Intergenic variant	None
rs11731522	26048425	Intergenic variant	None
rs2175586	144575789	Intergenic variant	None
Chr 5			
rs1392279	166293601	Intergenic variant	None
rs17415614	143761457	Intergenic variant	None
rs1858432	19398208	Intergenic variant	None
rs2063564	19337298	Intergenic variant	None
rs2594849	173760886	Intergenic variant	None
rs746215	173584350	Non-coding transcript variant	<i>LOC285593 and LOC105377735</i>
rs756452	86372315	Intron Variant	<i>LOC105379064</i>
Chr 6			
rs1265045	31117563	Intron variant	<i>CDSN and PSORS1C1</i>
rs1265100	31137533	Intron variant; downstream variant	<i>PSORS1C1 and PSORS1C2</i>
rs2844633	31128412	Intron variant; downstream variant	<i>PSORS1C1</i>
rs1933650	749311	Intron variant	<i>LOC105374873</i>
rs3957146	32713753	Intergenic variant	None
rs3957148	32714360	Intergenic variant	None
rs3998159	32714242	Intergenic variant	None
rs41282644	43785985	Intron variant; prime UTR* variant	<i>POLR1; CVEGFA</i>
rs7454108	32713706	Intergenic variant	None
rs9275184	32686937	Intergenic variant	None
rs9275206	32689788	Intergenic variant	None
rs9275221	32691322	Intergenic variant	None
rs9275334	32699330	Intergenic variant	None

rs9275383	32701069	Intergenic variant	None
rs9275495	32705797	Intergenic variant	None
rs9275530	32707746	Intergenic variant	None
rs9275532	32707857	Intergenic variant	None
rs9321228	130460110	Intergenic variant	None
rs9359725	87043599	Intergenic variant	None
rs9396195	56298323	Intron variant	<i>COL21A1</i>
Chr 7			
rs56006970	128924100-128924110	Intergenic variant	None
rs651841	4153005	Intron variant	<i>SDK1</i>
rs663911	4152536	Intron variant	<i>SDK1</i>
rs6958510	142272000	Non-coding transcript variant	<i>TRY2P</i>
rs77327146	14457730	Intron variant	<i>DGKB</i>
Chr 8			
rs10110877	61236173	Intron variant	<i>CLVS1</i>
rs10217099	27164195	Intergenic variant	None
rs2941652	105351844	Intergenic variant	<i>ZFPM2</i>
rs7818319	127597397	Intergenic variant	None
rs8192330	22163617	Intron variant; upstream variant	<i>BMP1 and SFTPC</i>
Chr 9			
rs6478342	117970446	Intergenic variant	None
rs7025754	4784933	Intergenic variant	None
rs9406646	16405575	Intergenic variant	None
Chr 10			
rs16930144	29311311	Intron variant	<i>LYZL1</i>
rs7072256	29298594	Intron variant	<i>LYZL1</i>
rs17875327	92515052	Intron variant	<i>IDE</i>
rs2245348	35587790	Intergenic variant	None
rs1862082	35586427	Downstream variant	<i>LOC107984221</i>
rs2474754	35586803	Downstream variant	<i>LOC107984221</i>
rs2474755	35585967	Non-coding transcript variant	<i>LOC107984221</i>
rs2474756	35585451	Non-coding transcript variant	<i>LOC107984221</i>
rs2474757	35584565	Non-coding transcript variant	<i>LOC107984221</i>
rs2474758	35584527	Non-coding transcript variant	<i>LOC107984221</i>
rs2474759	35584146	Non-coding transcript variant	<i>LOC107984221</i>
rs2506107	35585734	Non-coding transcript variant	<i>LOC107984221</i>
rs2506108	35585711	Non-coding transcript variant	<i>LOC107984221</i>
rs2506109	35584717	Non-coding transcript variant	<i>LOC107984221</i>
rs2506110	35584461	Non-coding transcript variant	<i>LOC107984221</i>
rs56668170	35337642	Non-coding transcript variant	<i>CCNY</i>
Chr 11			
rs11603873	15075456	Intron variant	<i>CALCB</i>
rs58858617	15076171	Intron variant	<i>CALCB</i>

rs16938342	45684744	Intergenic variant	None
rs2237898	2842590	Intron variant	<i>KCNQ1 and KCNQ1-AS1</i>
rs3758768	128803284	Intron variant	<i>FLI1</i>
rs4909953	10798837	Intron variant	<i>EIF4G2</i>
Chr 12			
rs12318758	54433784	Intron variant	<i>LOC102724050</i>
rs12829836	62828365	Intron variant	<i>PPM1H</i>
rs12831974	72330254	Intron variant	<i>TRHDE</i>
rs2555296	119216510	Intron variant	<i>LOC105370026</i>
rs874619	130448207	Intron variant	<i>RIMBP2</i>
Chr 13			
rs11841001	75674967	Intron variant	<i>LMO7</i>
rs11841544	75687060	Intron variant	<i>LMO7</i>
rs1414320	109882745	Intergenic variant	None
Chr 14			
rs17109084	71153222	Intergenic variant	None
rs17175304	79877374	Intron variant	<i>LOC105370582</i>
rs1775671	86837576	Intergenic variant	None
Chr 15			
rs12148293	82097824	Downstream; intron variant	<i>LINC01583 and LOC105370924</i>
Chr 16			
rs1552273	85417119	Intron variant	<i>GSE1</i>
rs2549732	80827779	Intergenic variant	None
rs258160	63780910	Intergenic variant	None
rs8049897	89957794	Intron variant	<i>DEF8</i>
Chr 17			
rs11867392	2018522	Intron variant	<i>RTN4RL1. LOC105371485. LOC105371486</i>
rs12938678	29383409	Intergenic variant	None
rs3744761	45118646	Intron variant	<i>PLCD3</i>
rs9901525	6191015	Upstream variant	<i>LOC105371508</i>
Chr 18			
rs17082725	70506308	Intergenic variant	<i>LOC105376872</i>
Chr 19			
rs10426583	4650006	Intron variant	<i>TNFAIP8L</i>
Chr 20			
rs17329208	53041791	Intron variant	<i>TSHZ2</i>
rs6032180	45428246	Intron variant	<i>LOC105372631</i>
rs6037397	2774414	Intergenic variant	None
rs6048171	22534857	Intergenic variant	None
rs6118390	8938100	Intergenic variant	None
rs731428	52943621	Intergenic variant	None
Chr 21			
rs2837461	40150682	Intron variant	<i>DSCAM</i>



rs3788061

43171012

Intron variant

*CRYAA and LOC107987300*

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\* UTR: untranslated region

Supplemental Table IV: Significant gene-smoking interaction results\* after Bonferroni adjustment for multiple testing in relation to C-IMT<sub>max</sub> with cut-off at 75<sup>th</sup> percentile. A dominant genetic model was assumed†. Results presented are limited to those produced from analyzes where the minimum number of 10 subjects has not been achieved‡.

	Number of observations								Odds Ratio (95% Confidence Interval) <sup>  </sup>					
	Non-smokers without the risk variant		Non-smokers with the risk variant		Smokers without the risk variant		Smokers with the risk variant		Reference group: Non-smokers without the risk variant					
	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Risk allele	MAF (%)	Non-smokers with the risk variant	Smokers without the risk variant	Smokers with the risk variant	p Synergy index
Chr 1														
rs11208756	1922	614	17	5	334	155	1	2	T	8	1(0.36;2.77)	1.69(1.35;2.11)	10.07(0.89;113.87)	1.39x10 <sup>-16</sup>
rs11578418	1923	613	16	6	334	153	1	4	G	10	1.22(0.46;3.23)	1.67(1.34;2.09)	12.28(1.34;112.86)	7.11x10 <sup>-19</sup>
rs11804222	1920	613	19	6	334	153	1	4	G	9	1.01(0.39;2.62)	1.67(1.34;2.09)	11.48(1.24;106.18)	9.53x10 <sup>-26</sup>
rs17371694	1899	604	40	15	332	150	3	7	C	14	1.26(0.68;2.33)	1.65(1.32;2.07)	9.26(2.29;37.52)	1.69x10 <sup>-22</sup>
rs17602729	1911	607	28	12	331	148	4	9	G	13	1.31(0.65;2.63)	1.63(1.3;2.04)	9.4(2.82;31.4)	5.62x10 <sup>-25</sup>
rs76000797	1902	607	37	12	333	153	2	4	C	14	1.16(0.59;2.28)	1.67(1.34;2.09)	9.89(1.76;55.58)	1.01x10 <sup>-21</sup>
Chr 2														
rs113407226	1918	610	21	9	334	153	1	4	G	11	1.39(0.62;3.13)	1.67(1.34;2.09)	14.81(1.64;133.61)	1.77x10 <sup>-22</sup>
rs1598279	1919	613	20	6	334	155	1	2	T	10	1.14(0.45;2.89)	1.69(1.35;2.11)	12.99(1.12;150.16)	1.13x10 <sup>-21</sup>
rs17594260	1913	610	24	9	332	152	2	5	C	9	1.02(0.46;2.23)	1.67(1.33;2.09)	7.77(1.45;41.69)	5.319x10 <sup>-17</sup>
rs2300963	1917	612	20	7	334	154	1	3	T	10	1.06(0.44;2.56)	1.68(1.35;2.1)	10.6(1.02;109.98)	3.06x10 <sup>-18</sup>
Chr 3														
rs10433607	1902	608	37	11	333	153	2	4	G	13	1.17(0.58;2.33)	1.68(1.34;2.1)	8.42(1.48;47.92)	1.05x10 <sup>-14</sup>
rs13320534	1901	608	38	11	333	153	2	4	G	13	1.13(0.57;2.24)	1.68(1.34;2.1)	8.41(1.48;47.88)	5.90x10 <sup>-16</sup>
rs1497891	1882	599	57	20	332	148	3	9	C	17	1.07(0.62;1.86)	1.62(1.3;2.04)	11.99(3.14;45.75)	1.34x10 <sup>-69</sup>
rs16849578	1914	610	25	9	334	154	1	3	T	11	1.14(0.52;2.49)	1.68(1.35;2.1)	11.59(1.18;114.21)	4.94x10 <sup>-20</sup>
rs2133007	1879	599	60	20	330	148	4	9	T	18	1.01(0.58;1.74)	1.63(1.3;2.04)	9.02(2.69;30.23)	8.09x10 <sup>-48</sup>
rs2713621	1888	601	51	18	329	150	6	7	G	15	1.15(0.65;2.01)	1.66(1.32;2.07)	6.18(1.92;19.86)	2.83x10 <sup>-14</sup>
rs904241	1880	599	59	20	332	148	3	9	A	18	1.02(0.59;1.76)	1.62(1.29;2.03)	11.97(3.14;45.68)	1.26x10 <sup>-78</sup>
rs9845228	1900	607	39	12	332	152	2	5	G	13	1.01(0.52;1.99)	1.67(1.34;2.09)	6.78(1.26;36.43)	3.16x10 <sup>-13</sup>
Chr 5														
rs10043169	1904	608	21	7	332	150	1	4	A	10	1.1(0.46;2.64)	1.65(1.31;2.06)	13.33(1.46;121.58)	5.43x10 <sup>-32</sup>
rs10512634	1908	605	31	14	333	153	2	4	G	13	1.3(0.67;2.52)	1.68(1.34;2.1)	14.55(1.59;133.3)	1.81x10 <sup>-26</sup>
rs10515808	1916	610	23	9	334	153	1	4	C	10	1.34(0.6;2.95)	1.68(1.34;2.1)	13.37(1.46;121.97)	8.76x10 <sup>-20</sup>
rs12522290	1890	602	49	17	331	151	4	6	C	15	1(0.56;1.8)	1.66(1.32;2.08)	5.85(1.57;21.78)	3.15x10 <sup>-14</sup>
rs1347118	1923	614	16	5	334	154	1	3	G	9	1.01(0.36;2.88)	1.68(1.34;2.1)	11.62(1.2;112.24)	2.96x10 <sup>-24</sup>
rs295044	1870	597	66	22	329	150	5	7	C	18	1.06(0.64;1.75)	1.66(1.32;2.07)	6.42(1.83;22.56)	9.03x10 <sup>-18</sup>
rs400196	1914	610	25	9	333	153	2	4	G	11	1.09(0.5;2.42)	1.67(1.34;2.09)	7.98(1.39;45.73)	2.56x10 <sup>-14</sup>
rs4438916	1915	610	24	9	334	153	1	4	G	10	1.26(0.57;2.76)	1.68(1.34;2.09)	13.35(1.46;121.81)	8.57x10 <sup>-23</sup>
rs72814378	1916	610	23	9	334	153	1	4	A	10	1.34(0.6;2.95)	1.68(1.34;2.1)	13.37(1.46;121.97)	8.76x10 <sup>-20</sup>

rs79791419	1915	610	24	9	334	153	1	4	A	10	1.26(0.57;2.76)	1.68(1.34;2.09)	13.35(1.46;121.81)	8.57x10-23
Chr 6														
rs111663960	1910	609	29	10	334	154	1	3	A	12	1.26(0.59;2.68)	1.69(1.35;2.11)	12.86(1.29;127.77)	1.01x10-19
rs113600760	1908	609	31	10	333	151	2	6	C	12	1.05(0.5;2.18)	1.65(1.32;2.07)	9.28(1.84;46.67)	1.95x10-26
rs12199718	1913	611	26	8	334	154	1	3	C	10	1.04(0.46;2.34)	1.68(1.34;2.1)	12.63(1.29;123.92)	6.65x10-30
rs1266071	1920	612	19	7	334	154	1	3	C	10	1.07(0.44;2.63)	1.68(1.34;2.1)	9.89(0.99;98.57)	1.51x10-15
rs190761	1908	609	31	10	333	151	2	6	C	12	1.05(0.5;2.18)	1.65(1.32;2.07)	9.28(1.84;46.67)	1.95x10-26
rs512685	1893	604	40	14	330	149	4	8	G	14	1.1(0.58;2.05)	1.64(1.31;2.06)	7.55(2.24;25.48)	1.83x10-23
rs557411	1908	609	31	10	333	151	2	6	T	12	1.05(0.5;2.18)	1.65(1.32;2.07)	9.28(1.84;46.67)	1.95x10-26
rs576899	1908	609	31	10	333	151	2	6	G	12	1.05(0.5;2.18)	1.65(1.32;2.07)	9.28(1.84;46.67)	1.95x10-26
rs579544	1908	609	31	10	333	151	2	6	A	12	1.05(0.5;2.18)	1.65(1.32;2.07)	9.28(1.84;46.67)	1.95x10-26
rs6940832	1908	609	31	10	333	151	2	6	G	12	1.05(0.5;2.18)	1.65(1.32;2.07)	9.28(1.84;46.67)	1.95x10-26
rs707974	1921	612	18	7	334	154	1	3	A	10	1.15(0.46;2.84)	1.68(1.35;2.1)	9.9(0.99;98.64)	3.16x10-13
rs72832602	1910	607	28	12	334	154	1	3	T	12	1.54(0.76;3.14)	1.69(1.35;2.11)	12.9(1.3;128.21)	9.89x10-13
rs72834621	1910	608	28	11	334	154	1	3	A	12	1.45(0.69;3.02)	1.69(1.35;2.11)	12.88(1.3;127.99)	1.66x10-14
rs72834627	1912	608	27	11	334	154	1	3	G	12	1.52(0.72;3.19)	1.69(1.35;2.11)	12.9(1.3;128.16)	5.59x10-13
rs72834643	1911	608	28	11	334	154	1	3	C	12	1.45(0.7;3.04)	1.69(1.35;2.11)	12.89(1.3;128.09)	2.50x10-14
rs72834647	1911	608	28	11	334	154	1	3	G	12	1.45(0.7;3.04)	1.69(1.35;2.11)	12.89(1.3;128.09)	2.51x10-14
rs7766267	1909	607	29	12	334	154	1	3	G	12	1.54(0.76;3.14)	1.69(1.35;2.11)	12.9(1.3;128.18)	1.00x10-12
rs78227802	1908	609	31	10	333	151	2	6	C	12	1.05(0.5;2.18)	1.65(1.32;2.07)	9.28(1.84;46.67)	1.95x10-26
rs9477109	1915	611	24	8	332	154	2	3	A	11	1.14(0.5;2.57)	1.69(1.35;2.11)	11.48(1.16;113.77)	4.12x10-19
rs9482260	1887	597	52	22	334	154	1	3	G	15	1.48(0.88;2.5)	1.7(1.36;2.13)	12.87(1.32;125.87)	2.03x10-14
rs9487678	1927	615	12	4	334	155	1	2	G	8	1.08(0.34;3.43)	1.69(1.35;2.11)	10.01(0.89;112.49)	4.81x10-13
Chr 7														
rs10256347	1912	608	27	11	333	153	2	4	C	12	1.22(0.6;2.52)	1.68(1.34;2.1)	8.47(1.42;50.56)	1.08x10-12
rs16868830	1917	610	22	9	334	154	1	3	T	9	1.15(0.5;2.64)	1.68(1.34;2.1)	12.4(1.2;127.83)	2.22x10-21
rs2191886	1914	609	25	10	333	152	2	5	C	11	1.26(0.59;2.68)	1.66(1.33;2.08)	10.06(1.89;53.43)	3.77x10-19
rs2271032	1893	604	46	15	332	152	3	5	A	15	1.06(0.58;1.95)	1.67(1.33;2.09)	6.5(1.53;27.58)	9.17x10-14
Chr 8														
rs10091991	1909	608	29	11	334	152	1	5	G	12	1.56(0.75;3.26)	1.67(1.33;2.09)	21.43(2.46;186.9)	8.31x10-40
rs17778118	1921	612	18	7	333	150	2	7	A	10	1.31(0.53;3.21)	1.64(1.31;2.06)	11.97(2.43;58.94)	1.55x10-25
Chr 9														
rs12380395	1887	602	52	17	328	147	7	10	C	17	1.01(0.57;1.78)	1.63(1.3;2.04)	5.85(2.15;15.92)	1.10x10-20
Chr 10														
rs10887807	1903	605	36	14	332	150	3	7	T	12	1.32(0.7;2.51)	1.65(1.32;2.07)	8.75(2.19;34.93)	1.12x10-17
rs10905959	1913	609	26	10	333	152	2	5	C	11	1.3(0.61;2.75)	1.66(1.33;2.08)	20.63(2.35;181.01)	3.89x10-57
rs11202726	1898	605	41	14	331	149	4	8	A	13	1.1(0.59;2.07)	1.64(1.31;2.05)	8.19(2.39;28.12)	1.50x10-27
rs11598623	1898	605	41	14	331	149	4	8	A	13	1.1(0.59;2.07)	1.64(1.31;2.05)	8.19(2.39;28.12)	1.50x10-27
rs12356363	1911	609	28	10	330	149	5	8	C	12	1.02(0.47;2.21)	1.64(1.31;2.06)	6.09(1.95;18.98)	1.36x10-15
rs12411339	1916	611	23	8	334	154	1	3	C	11	1.06(0.46;2.42)	1.68(1.35;2.1)	9.1(0.91;90.85)	9.47x10-14
rs1571026	1906	609	33	10	334	154	1	3	T	12	1.02(0.49;2.12)	1.68(1.35;2.11)	8.94(0.87;91.55)	1.69x10-14
rs2274356	1907	609	32	10	334	154	1	3	A	12	1.08(0.52;2.24)	1.69(1.35;2.11)	8.95(0.87;91.63)	8.11x10-13
rs4457667	1912	608	27	11	334	154	1	3	C	10	1.24(0.59;2.62)	1.68(1.35;2.1)	16.49(1.68;162.19)	2.33x10-35

rs74149704	1898	605	41	14	331	149	4	8	A	13	1.1(0.59;2.07)	1.64(1.31;2.05)	8.19(2.39;28.12)	1.50x10-27
rs963244	1915	611	24	8	334	154	1	3	A	11	1.09(0.48;2.49)	1.68(1.35;2.1)	9.86(1.00;97.65)	2.27x10-15
Chr 11														
rs10082672	1875	598	63	21	328	146	7	11	T	19	1.04(0.62;1.74)	1.61(1.28;2.02)	6.55(2.44;17.58)	1.02x10-27
rs10082701	1876	598	63	21	328	146	7	11	C	19	1.04(0.62;1.74)	1.61(1.29;2.03)	6.56(2.44;17.59)	1.12x10-27
rs11214260	1894	606	45	13	334	153	1	4	G	14	1.05(0.56;1.99)	1.67(1.34;2.09)	14.97(1.65;136.2)	1.69x10-48
rs11232958	1903	603	36	15	333	151	2	6	C	14	1.41(0.75;2.64)	1.66(1.33;2.08)	13.61(2.68;69.04)	4.20x10-32
rs11232966	1903	604	36	15	333	151	2	6	A	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs11246161	1892	604	47	15	333	152	2	5	C	13	1.01(0.55;1.85)	1.66(1.33;2.07)	11.25(2.15;58.90)	2.66x10-46
rs11820515	1903	604	36	15	333	151	2	6	G	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs11827684	1902	604	36	15	333	151	2	6	A	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.58(2.68;68.92)	3.43x10-32
rs11827708	1903	604	36	15	332	151	2	6	A	14	1.4(0.75;2.63)	1.67(1.33;2.09)	13.59(2.68;68.95)	6.81x10-32
rs2919706	1903	604	36	15	333	150	2	7	G	14	1.41(0.75;2.64)	1.65(1.32;2.06)	16.48(3.35;81.03)	4.32x10-51
rs2919707	1903	604	36	15	333	151	2	6	C	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs2919708	1903	604	36	15	333	151	2	6	A	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs2919710	1903	604	36	15	333	151	2	6	G	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs2919713	1903	604	36	15	333	151	2	6	T	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs2919718	1903	604	36	15	333	151	2	6	C	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs3020039	1903	604	36	15	333	151	2	6	T	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs3020044	1903	604	36	15	333	151	2	6	G	14	1.4(0.75;2.63)	1.66(1.33;2.08)	13.59(2.68;68.96)	3.56x10-32
rs4284411	1903	604	35	15	333	151	2	6	T	14	1.42(0.76;2.68)	1.66(1.33;2.08)	13.59(2.68;68.94)	3.92x10-31
rs963167	1910	605	29	14	333	150	2	7	G	14	1.39(0.71;2.70)	1.65(1.32;2.07)	14.03(2.84;69.32)	3.77x10-36
Chr 12														
rs1040213	1924	614	15	5	333	153	2	4	T	8	1.02(0.36;2.89)	1.67(1.34;2.09)	7.69(1.38;42.87)	1.40x10-13
rs10505859	1850	590	89	29	329	148	6	9	G	19	1.07(0.69;1.65)	1.63(1.30;2.05)	6.77(2.33;19.73)	6.11x10-27
rs10851044	1921	613	18	6	333	152	2	5	A	10	1.18(0.46;3.05)	1.66(1.33;2.08)	10.35(1.94;55.32)	6.91x10-21
rs11169949	1830	582	109	37	328	147	6	10	T	23	1.04(0.70;1.55)	1.64(1.30;2.05)	6.14(2.14;17.59)	1.80x10-23
rs12371260	1920	613	18	6	333	152	2	5	A	10	1.18(0.46;3.04)	1.66(1.33;2.08)	10.35(1.94;55.31)	5.88x10-21
rs1468624	1881	597	58	22	333	153	1	4	G	16	1.16(0.69;1.93)	1.68(1.34;2.10)	13.77(1.46;129.53)	1.11x10-31
rs1718302	1892	605	47	14	329	150	6	7	A	15	1.08(0.58;2.00)	1.65(1.32;2.07)	6.34(1.95;20.62)	1.50x10-16
rs632151	1904	606	35	13	333	153	2	4	G	12	1.18(0.61;2.28)	1.68(1.34;2.10)	8.38(1.51;46.59)	1.01x10-14
Chr 13														
rs4771411	1917	614	12	4	332	152	1	5	A	9	1.1(0.34;3.59)	1.67(1.33;2.08)	16.41(1.87;143.78)	1.12x10-41
Chr14														
rs709932	1883	599	56	20	333	152	2	5	C	16	1.15(0.68;1.96)	1.67(1.34;2.09)	8.33(1.53;45.22)	1.42x10-16
Chr 15														
rs12899074	1920	612	19	7	334	154	1	3	G	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.25x10-29
rs12899456	1889	602	50	17	332	151	3	6	A	14	1.15(0.65;2.04)	1.66(1.33;2.08)	7.63(1.81;32.28)	2.52x10-17
rs12899581	1920	612	19	7	334	154	1	3	A	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.25x10-29
rs12905302	1888	602	50	17	331	151	3	6	G	14	1.15(0.65;2.04)	1.67(1.33;2.09)	7.63(1.81;32.27)	3.40x10-17
rs12906675	1920	612	19	7	334	154	1	3	G	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.25x10-29
rs12907202	1917	611	19	7	334	154	1	3	G	9	1.12(0.46;2.71)	1.67(1.34;2.09)	13.74(1.36;138.66)	4.50x10-29
rs12907472	1920	612	19	7	334	154	1	3	G	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.25x10-29

rs12907922	1920	612	19	7	334	154	1	3	A	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.25x10-29
rs12916113	1919	612	20	7	334	154	1	3	A	9	1.09(0.45;2.64)	1.68(1.34;2.09)	13.73(1.36;138.64)	1.88x10-30
rs12916122	1919	612	20	7	334	154	1	3	T	9	1.09(0.45;2.64)	1.68(1.34;2.09)	13.73(1.36;138.64)	1.88x10-30
rs16968518	1916	610	23	9	334	154	1	3	T	13	1.42(0.64;3.15)	1.69(1.35;2.11)	12.29(1.25;121.05)	1.72x10-13
rs181447504	1888	602	50	17	332	151	3	6	C	14	1.15(0.65;2.04)	1.66(1.33;2.08)	7.63(1.8;32.25)	2.40x10-17
rs2928138	1920	612	19	7	334	154	1	3	T	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.25x10-29
rs34073905	1879	599	60	20	333	152	2	5	G	16	1.12(0.66;1.89)	1.67(1.33;2.09)	9.8(1.78;53.87)	7.24x10-26
rs34359839	1890	599	49	20	331	149	4	8	A	16	1.36(0.79;2.35)	1.65(1.32;2.07)	8.04(2.32;27.92)	6.28x10-17
rs35396991	1889	602	50	17	332	151	3	6	A	14	1.15(0.65;2.04)	1.66(1.33;2.08)	7.63(1.81;32.28)	2.52x10-17
rs531366	1920	612	19	7	334	154	1	3	G	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.24x10-29
rs540257	1920	612	19	7	334	154	1	3	T	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.24x10-29
rs600724	1903	608	19	7	331	154	1	3	C	9	1.12(0.46;2.71)	1.68(1.34;2.10)	13.7(1.36;138.07)	1.02x10-28
rs615835	1920	611	19	7	334	154	1	3	A	9	1.12(0.46;2.71)	1.68(1.34;2.10)	13.78(1.37;139.09)	6.27x10-29
rs623722	1920	611	19	7	334	154	1	3	T	9	1.12(0.46;2.71)	1.68(1.34;2.10)	13.78(1.37;139.09)	6.27x10-29
rs6495133	1857	591	82	28	327	146	8	11	C	20	1.14(0.73;1.80)	1.63(1.30;2.05)	5.08(1.98;13.07)	3.79x10-13
rs687549	1920	612	19	7	334	154	1	3	A	9	1.12(0.46;2.71)	1.68(1.34;2.09)	13.74(1.36;138.67)	6.24x10-29
rs71401605	1890	600	49	19	331	150	4	7	G	16	1.3(0.75;2.27)	1.66(1.33;2.08)	7.24(2.02;25.98)	6.75x10-14
rs71401676	1889	602	50	17	332	151	3	6	C	15	1.15(0.65;2.04)	1.66(1.33;2.08)	7.63(1.81;32.28)	2.52x10-17
rs7173321	1919	612	19	7	334	154	1	3	C	9	1.12(0.46;2.71)	1.67(1.34;2.09)	13.73(1.36;138.63)	5.13x10-29
rs75969957	1889	599	49	20	331	149	4	7	A	16	1.36(0.79;2.35)	1.65(1.32;2.07)	7.24(2.02;25.97)	6.65x10-13
rs8033883	1857	591	82	28	327	146	8	11	A	20	1.14(0.73;1.8)	1.63(1.30;2.05)	5.08(1.98;13.07)	3.79x10-13
rs8038911	1889	601	50	18	332	151	3	6	A	14	1.22(0.69;2.14)	1.66(1.33;2.08)	7.65(1.81;32.34)	2.60x10-15
Chr 16														
rs12596139	1927	615	12	4	334	155	1	2	G	7	1.27(0.4;4.04)	1.69(1.35;2.11)	12.89(1.12;147.88)	2.90x10-15
rs12933423	1908	608	30	11	332	154	2	3	G	12	1.08(0.53;2.19)	1.69(1.35;2.11)	7.8(1.26;48.43)	1.56x10-13
rs16973748	1906	608	32	11	334	154	1	3	G	12	1.04(0.51;2.1)	1.68(1.34;2.1)	10.58(1.08;103.44)	2.43x10-21
rs1805007	1933	616	6	3	334	154	1	3	C	6	1.25(0.31;5.06)	1.68(1.34;2.1)	13.33(1.35;131.91)	1.03x10-16
rs1863985	1892	606	29	11	329	149	2	4	C	12	1.25(0.61;2.58)	1.65(1.32;2.07)	8.59(1.52;48.64)	1.80x10-13
rs7203264	1852	589	87	30	326	143	9	14	G	20	1.14(0.74;1.76)	1.62(1.28;2.03)	5.01(2.12;11.86)	7.12x10-15
Chr 18														
rs112812977	1901	606	37	13	334	153	1	4	T	13	1.11(0.58;2.14)	1.67(1.34;2.09)	13.36(1.44;124.41)	5.32x10-32
rs12607452	1923	614	16	5	334	154	1	3	C	8	1.08(0.39;3.04)	1.68(1.34;2.1)	10.12(1.03;99.53)	2.58x10-15
rs16978345	1923	614	16	5	334	154	1	3	A	8	1.08(0.39;3.04)	1.68(1.34;2.1)	10.12(1.03;99.53)	2.58x10-15
rs4605263	1909	608	22	9	333	153	1	3	G	11	1.32(0.59;2.93)	1.69(1.35;2.11)	16.32(1.57;169.44)	6.16x10-28
rs8097973	1911	607	28	12	330	149	5	8	T	13	1.44(0.71;2.9)	1.65(1.31;2.06)	7.93(2.35;26.81)	1.71x10-13
Chr 20														
rs17092385	1912	610	27	9	333	152	2	5	T	11	1.05(0.48;2.28)	1.66(1.33;2.08)	9.44(1.78;50.16)	3.43x10-25
rs73139727	1922	612	17	7	334	153	1	4	T	8	1.4(0.57;3.45)	1.67(1.34;2.09)	19.02(2.1;172.06)	2.24x10-36
Chr 21														
rs2835673	1924	612	15	7	334	153	1	4	C	9	1.33(0.53;3.33)	1.68(1.34;2.1)	12.46(1.33;116.77)	3.57x10-16
Chr 22														
rs12170612	1904	607	35	12	333	153	2	4	G	12	1.09(0.55;2.13)	1.67(1.34;2.09)	8.3(1.43;48.38)	1.05x10-16
rs9607434	1905	607	34	12	333	153	2	4	G	12	1.13(0.58;2.23)	1.67(1.34;2.09)	8.31(1.43;48.42)	4.16x10-15

MAF: minor allele frequency;

\* Synergy index results were considered significant at p-values  $<2.4 \times 10^{-7}$

† Individuals who carry either one or two copies of the risk allele are considered to carry the risk variant

‡ Results from observations where the number of subjects in any subgroup is 0 are not shown (n=268)

|| Model adjusted for sex, age, education (categorical), physical activity (categorical), Mediterranean diet score and population structure (MDS1-3 continuous)

Supplemental Table V: Significant gene-smoking interaction results\* after Bonferroni adjustment for multiple testing in relation to C-IMT<sub>max</sub> with cut-off at 50<sup>th</sup> percentile. A dominant genetic model was assumed<sup>†</sup>. Results presented are limited to those produced from analyzes where the minimum number of 10 subjects has not been achieved<sup>‡</sup>.

	Number of observations								Odds Ratio (95% Confidence Interval) <sup>  </sup>					
	Non-smokers without the risk variant		Non-smokers with the risk variant		Smokers without the risk variant		Smokers with the risk variant		Risk allele	MAF (%)	Reference group: Non-smokers without the risk variant			
	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases			Non-smokers with the risk variant	Smokers without the risk variant	Smokers with the risk variant	p Synergy index
Chr1														
rs10889363	1267	1208	41	42	196	278	3	15	C	17	1.15(0.73;1.82)	1.8(1.46;2.22)	6.78(1.93;23.9)	1.91x10-13
rs11208008	1267	1208	41	42	196	278	3	15	T	17	1.15(0.73;1.82)	1.8(1.46;2.22)	6.78(1.93;23.9)	1.91x10-13
rs11208010	1267	1208	41	42	196	278	3	15	T	17	1.15(0.73;1.81)	1.8(1.46;2.22)	6.78(1.93;23.89)	1.61x10-13
rs12130333	1267	1208	41	42	196	278	3	15	C	17	1.15(0.73;1.82)	1.8(1.46;2.22)	6.78(1.93;23.9)	1.91x10-13
rs12566784	1292	1234	16	16	198	284	1	9	T	11	1.13(0.55;2.31)	1.82(1.47;2.24)	11.32(1.42;90.33)	4.30x10-18
rs1336474	1259	1195	47	55	198	285	1	8	A	20	1.22(0.8;1.84)	1.83(1.48;2.25)	12.2(1.51;98.82)	3.62x10-19
rs16840422	1284	1224	24	26	198	283	1	10	C	14	1.16(0.65;2.07)	1.81(1.47;2.23)	14.21(1.81;111.88)	7.30x10-30
rs2818765	1282	1223	26	27	197	284	1	9	T	13	1.06(0.61;1.87)	1.83(1.49;2.26)	9.95(1.22;81.08)	1.57x10-15
rs3766404	1283	1221	24	26	198	283	1	10	T	14	1.16(0.65;2.07)	1.81(1.47;2.23)	14.2(1.8;111.83)	9.34x10-30
rs4245713	1281	1227	27	23	198	283	1	10	A	14	1(0.56;1.79)	1.81(1.47;2.23)	12.7(1.59;101.54)	9.43x10-32
rs486453	1208	1154	100	96	194	265	5	28	C	28	1.04(0.77;1.4)	1.73(1.4;2.14)	6.86(2.62;17.92)	2.42x10-31
rs4949623	1202	1151	106	99	193	262	6	31	A	28	1.01(0.75;1.36)	1.72(1.39;2.13)	6.16(2.55;14.91)	3.57x10-29
Chr 2														
rs1520399	1274	1217	34	33	195	277	3	16	T	18	1.01(0.61;1.66)	1.79(1.45;2.21)	6.97(2;24.28)	7.78x10-19
rs2043075	1273	1212	35	38	198	285	1	8	G	14	1.08(0.66;1.75)	1.82(1.48;2.25)	9.94(1.22;81.33)	1.57x10-15
rs62621191	1276	1216	32	34	197	284	2	9	C	15	1.17(0.71;1.95)	1.82(1.48;2.24)	10.58(1.32;84.99)	4.25x10-15
rs6751950	1256	1194	52	56	195	279	4	14	C	20	1.07(0.72;1.6)	1.8(1.46;2.22)	6.82(1.93;24.1)	3.67x10-16
rs964582	1251	1194	57	56	195	273	4	20	A	22	1.04(0.7;1.53)	1.78(1.44;2.2)	5.47(1.84;16.23)	6.03x10-13
Chr 3														
rs1602474	1299	1242	9	8	198	282	1	11	G	10	1.04(0.39;2.77)	1.8(1.46;2.22)	13.16(1.67;103.53)	4.82x10-28
rs2889390	1254	1192	54	58	195	280	4	13	T	21	1.03(0.7;1.51)	1.8(1.46;2.22)	8.1(1.8;36.58)	4.81x10-20
Chr 4														
rs1439471	1198	1145	110	105	191	262	8	31	C	28	1.04(0.78;1.38)	1.74(1.4;2.15)	4.88(2.21;10.76)	2.48x10-17
rs727633	1216	1157	92	93	192	267	7	26	C	26	1.17(0.86;1.59)	1.76(1.42;2.18)	5.35(2.29;12.49)	5.38x10-15
Chr 5														
rs10039050	1296	1237	12	13	198	283	1	10	A	13	1.08(0.48;2.43)	1.81(1.47;2.23)	13.3(1.68;105.41)	8.96x10-28
rs17708750	1264	1210	44	40	196	274	3	19	C	17	1.01(0.64;1.57)	1.77(1.43;2.19)	7.86(2.29;26.96)	1.61x10-27
rs2731798	1186	1126	122	124	191	264	7	29	A	29	1.06(0.8;1.38)	1.76(1.42;2.18)	5.15(2.22;11.97)	2.49x10-17
rs6881772	1296	1237	12	13	198	284	1	9	T	13	1.08(0.48;2.43)	1.82(1.47;2.24)	12.35(1.54;98.92)	3.13x10-23
rs7725668	1273	1213	34	37	198	286	1	7	T	16	1.2(0.74;1.96)	1.83(1.49;2.26)	10.32(1.25;85.36)	3.64x10-13

Chr 6														
rs1474642	1272	1219	36	31	198	283	1	10	A	15	1.01(0.61;1.67)	1.81(1.47;2.23)	12.57(1.57;100.31)	6.25x10-31
rs17802893	1299	1241	9	9	198	285	1	8	T	8	1.04(0.4;2.71)	1.82(1.48;2.24)	10.64(1.31;86.68)	7.27x10-17
rs3094682	1279	1219	29	31	198	282	1	11	C	15	1.25(0.74;2.12)	1.82(1.48;2.24)	11.77(1.49;93.24)	8.64x10-17
Chr 7														
rs5024722	1262	1204	46	46	194	277	4	16	A	20	1.1(0.72;1.68)	1.8(1.46;2.23)	6.49(1.86;22.63)	1.26x10-13
rs509834	1284	1226	20	21	197	282	1	10	T	12	1.1(0.58;2.08)	1.8(1.46;2.22)	13.63(1.73;107.75)	1.29x10-30
Chr 8														
rs10095737	1251	1190	57	60	195	272	4	21	G	21	1.11(0.76;1.63)	1.77(1.43;2.18)	7.34(2.46;21.93)	1.32x10-23
rs10097531	1233	1179	75	71	192	268	7	25	C	24	1.03(0.73;1.46)	1.77(1.43;2.19)	4.67(1.97;11.09)	1.12x10-12
rs10107180	1241	1186	67	64	194	268	5	25	C	23	1.02(0.71;1.47)	1.75(1.42;2.16)	6.51(2.43;17.44)	1.42x10-25
rs10107303	1233	1180	75	70	192	268	7	25	C	24	1.01(0.72;1.43)	1.77(1.43;2.19)	4.68(1.97;11.11)	2.94x10-13
rs167999	1258	1198	48	50	195	273	4	20	A	20	1.1(0.73;1.67)	1.77(1.44;2.19)	6.6(2.22;19.65)	3.91x10-18
rs2116096	1241	1185	67	65	194	268	5	25	G	22	1.03(0.72;1.48)	1.75(1.42;2.17)	6.49(2.42;17.38)	7.03x10-25
rs28592638	1233	1180	74	70	191	268	7	25	C	24	1.03(0.73;1.46)	1.78(1.43;2.2)	4.69(1.98;11.14)	9.66x10-13
rs4610751	1175	1121	132	127	190	264	8	29	C	31	1(0.77;1.31)	1.77(1.42;2.19)	4.57(1.96;10.63)	1.06x10-13
rs6601520	1223	1168	85	82	192	263	7	30	T	25	1.05(0.76;1.46)	1.72(1.39;2.13)	7(2.85;17.18)	1.52x10-35
rs6601524	1242	1186	66	64	195	269	4	24	G	22	1.03(0.71;1.49)	1.75(1.41;2.16)	8.1(2.74;23.9)	1.52x10-37
rs6985218	1234	1180	74	70	192	268	7	25	C	24	1.03(0.73;1.46)	1.77(1.43;2.19)	4.7(1.98;11.15)	6.44x10-13
rs7001206	1226	1175	80	74	192	267	6	26	G	24	1.05(0.75;1.47)	1.76(1.42;2.18)	5.92(2.38;14.76)	2.09x10-21
rs7014168	1251	1190	57	60	195	272	4	21	G	21	1.11(0.76;1.63)	1.77(1.43;2.18)	7.34(2.46;21.93)	1.32x10-23
rs73196893	1271	1206	37	44	196	280	3	13	G	18	1.28(0.81;2.01)	1.81(1.47;2.23)	9.21(2.03;41.67)	1.77x10-16
rs73196895	1264	1194	39	44	193	272	3	14	C	18	1.19(0.76;1.86)	1.8(1.46;2.23)	10.11(2.25;45.32)	5.92x10-24
rs73198940	1296	1236	12	14	197	284	2	9	G	11	1.34(0.61;2.98)	1.82(1.48;2.24)	11.63(1.44;93.73)	5.55x10-13
rs7823088	1241	1186	67	64	195	269	4	24	G	22	1.02(0.7;1.46)	1.75(1.41;2.16)	8.09(2.74;23.89)	8.41x10-39
rs891554	1232	1178	76	72	192	267	7	26	C	24	1.02(0.73;1.44)	1.76(1.43;2.18)	4.82(2.04;11.4)	3.07x10-14
rs9644730	1233	1179	75	71	192	268	7	25	G	24	1.03(0.73;1.46)	1.77(1.43;2.19)	4.67(1.97;11.09)	1.12x10-12
Chr 9														
rs12686329	1282	1221	26	29	198	287	1	6	C	13	1.11(0.64;1.93)	1.83(1.49;2.25)	10.46(1.24;88.1)	2.02x10-15
rs2472508	1271	1216	37	34	196	280	2	13	G	18	1.04(0.64;1.7)	1.81(1.47;2.23)	8.31(1.83;37.63)	1.47x10-19
rs2487049	1271	1216	37	34	197	280	2	13	A	18	1.04(0.63;1.7)	1.8(1.46;2.22)	8.31(1.83;37.64)	7.58x10-20
rs7851754	1205	1152	103	98	190	261	9	32	G	28	1.05(0.78;1.42)	1.73(1.39;2.14)	5.89(2.55;13.62)	9.78x10-26
rs930340	1245	1190	63	59	193	274	6	19	A	21	1.01(0.69;1.47)	1.78(1.44;2.2)	5.26(1.94;14.25)	2.95x10-14
rs9406465	1191	1128	117	119	189	259	9	34	A	31	1.11(0.84;1.47)	1.74(1.4;2.16)	5.1(2.41;10.82)	2.97x10-18
Chr 10														
rs55749454	1278	1220	30	30	198	283	1	10	G	14	1.08(0.64;1.83)	1.81(1.47;2.23)	12.94(1.62;103.09)	1.69x10-28
rs7081222	1240	1193	68	57	193	274	6	19	C	21	1(0.69;1.45)	1.77(1.44;2.19)	5.72(2.09;15.66)	6.24x10-18
Chr 11														
rs11221388	1284	1223	24	27	197	285	2	8	G	14	1.14(0.64;2.02)	1.83(1.48;2.25)	10.29(1.27;83.4)	1.09x10-14
rs12362809	1272	1213	36	37	195	281	4	12	G	16	1.09(0.67;1.76)	1.81(1.47;2.23)	7.75(1.7;35.38)	4.35x10-15
rs12363819	1284	1223	24	27	197	285	2	8	A	14	1.14(0.64;2.02)	1.83(1.48;2.25)	10.29(1.27;83.4)	1.09x10-14
rs198459	1264	1205	44	45	196	285	2	8	G	19	1.11(0.72;1.72)	1.83(1.49;2.26)	10.6(1.31;86.05)	1.27x10-16
rs61907787	1285	1226	23	24	197	285	2	8	G	14	1.09(0.6;1.98)	1.82(1.48;2.25)	10.28(1.27;83.34)	5.69x10-16



rs835839	1279	1217	29	33	198	284	1	9	C	15	1.26(0.74;2.13)	1.83(1.48;2.25)	11.02(1.38;88.29)	2.97x10-14
Chr 12														
rs1463863	1262	1205	46	45	198	282	1	11	C	18	1.07(0.69;1.65)	1.82(1.47;2.24)	10.95(1.39;85.96)	8.26x10-21
rs17466339	1278	1223	29	27	198	286	1	7	C	15	1.02(0.59;1.76)	1.83(1.48;2.25)	10.11(1.23;83.08)	1.05x10-17
Chr 13														
rs11840638	1272	1211	36	39	196	282	3	11	C	16	1.21(0.75;1.94)	1.82(1.47;2.24)	12.48(1.59;97.66)	3.28x10-21
rs1331752	1234	1182	74	68	196	275	3	18	A	23	1.04(0.73;1.48)	1.77(1.43;2.18)	11.43(2.61;50.03)	1.43x10-47
rs2094196	1260	1200	48	50	196	278	3	15	T	19	1.1(0.72;1.66)	1.79(1.45;2.21)	9.77(2.21;43.2)	9.32x10-28
rs4592537	1262	1205	46	45	198	282	1	11	C	18	1.06(0.69;1.63)	1.81(1.47;2.23)	12.79(1.62;100.98)	5.11x10-30
rs500574	1241	1185	67	65	196	277	3	16	G	22	1.13(0.79;1.63)	1.79(1.45;2.21)	10.26(2.32;45.41)	1.95x10-29
rs9525841	1272	1211	36	39	196	282	3	11	T	16	1.21(0.75;1.94)	1.82(1.47;2.24)	12.48(1.59;97.66)	3.28x10-21
rs9533613	1272	1211	36	39	196	282	3	11	T	16	1.21(0.75;1.94)	1.82(1.47;2.24)	12.48(1.59;97.66)	3.28x10-21
Chr 14														
rs10142781	1245	1190	61	59	193	274	5	19	C	20	1.06(0.72;1.55)	1.79(1.44;2.21)	5.42(2;14.7)	9.2x10-14
rs10151371	1229	1179	79	71	193	270	6	23	G	24	1.04(0.74;1.47)	1.78(1.44;2.2)	4.92(1.96;12.34)	5.87x10-13
rs17124043	1248	1195	60	55	196	279	3	14	C	21	1.1(0.75;1.62)	1.81(1.46;2.23)	6.45(1.81;22.92)	4.06x10-13
rs17124045	1248	1195	60	55	196	279	3	14	A	21	1.1(0.75;1.62)	1.81(1.46;2.23)	6.45(1.81;22.92)	4.06x10-13
rs17203608	1248	1196	60	54	196	279	3	14	T	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs17798173	1248	1196	60	54	196	279	3	14	C	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs17798179	1248	1196	60	54	196	279	3	14	C	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs17798191	1248	1196	60	54	196	279	3	14	C	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs4303414	1248	1196	60	54	196	279	3	14	C	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs4483792	1248	1196	60	54	196	279	3	14	T	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs4904423	1248	1195	60	55	196	279	3	14	G	21	1.1(0.75;1.62)	1.81(1.46;2.23)	6.45(1.81;22.92)	4.06x10-13
rs4904424	1248	1196	60	54	196	279	3	14	G	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs59644163	1248	1196	60	54	196	279	3	14	A	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs61975760	1248	1196	60	54	196	279	3	14	A	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs61975777	1248	1196	60	54	196	279	3	14	C	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs61975778	1248	1196	60	54	196	279	3	14	C	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs61975779	1248	1196	60	54	196	279	3	14	G	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs61975782	1248	1196	60	54	196	279	3	14	G	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs61977336	1248	1196	60	54	196	279	3	14	C	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
rs72693891	1248	1196	60	54	196	279	3	14	G	21	1.07(0.73;1.58)	1.8(1.46;2.23)	6.44(1.81;22.88)	7.70x10-14
Chr 15														
rs11638662	1190	1138	118	112	191	262	8	31	C	29	1.06(0.8;1.4)	1.73(1.4;2.14)	5.79(2.5;13.37)	1.83x10-24
rs12439792	1291	1238	17	12	198	287	1	6	T	9	1(0.46;2.18)	1.83(1.49;2.25)	9.92(1.16;84.81)	5.01x10-16
rs4395027	1277	1218	29	27	198	282	1	11	G	15	1.01(0.58;1.73)	1.8(1.46;2.22)	15.31(1.94;120.91)	3.24x10-49
rs7165170	1262	1201	46	49	198	282	1	11	A	20	1.05(0.69;1.61)	1.8(1.46;2.22)	18.14(2.27;144.85)	3.04x10-66
rs76414746	1284	1226	24	24	198	284	1	9	A	13	1.27(0.71;2.29)	1.82(1.48;2.24)	14.04(1.75;112.86)	4.19x10-23
rs922507	1258	1193	50	57	195	275	4	18	C	20	1.18(0.79;1.77)	1.79(1.45;2.21)	6.16(2.05;18.45)	6.01x10-13
Chr 16														
rs2716596	1271	1210	37	40	198	285	1	8	G	17	1.16(0.73;1.85)	1.83(1.49;2.25)	10.39(1.28;84.41)	9.48x10-15
rs34550882	1278	1222	30	28	198	283	1	10	C	14	1.06(0.62;1.8)	1.82(1.47;2.24)	10.82(1.35;86.46)	8.58x10-20

rs4787317	1288	1230	20	20	198	283	1	10	G	13	1.06(0.56;2.01)	1.81(1.47;2.24)	11.19(1.39;89.79)	1.06x10-20
rs8059494	1289	1230	18	20	198	285	1	8	T	12	1.29(0.66;2.53)	1.82(1.48;2.25)	10.95(1.35;88.73)	9.21x10-13
Chr 17														
rs4793460	1292	1232	16	18	198	285	1	8	T	12	1.32(0.65;2.67)	1.82(1.48;2.25)	11.5(1.42;93.38)	2.15x10-13
rs60399446	1288	1226	20	23	197	285	1	8	G	13	1.15(0.61;2.16)	1.84(1.49;2.26)	10.3(1.26;84)	6.54x10-14
Chr 19														
rs10417472	1280	1221	28	29	198	286	1	7	T	14	1.06(0.61;1.84)	1.83(1.48;2.25)	10.08(1.21;83.76)	4.41x10-16
rs1041992	1173	1108	135	142	190	252	9	41	T	5	1.09(0.84;1.41)	1.69(1.36;2.1)	5.79(2.77;12.1)	6.66x10-30
rs2665586	1279	1221	29	29	198	286	1	7	G	14	1.03(0.6;1.79)	1.83(1.48;2.25)	10.07(1.21;83.72)	6.06x10-17
rs6510126	1263	1198	45	52	197	279	2	14	C	19	1.18(0.77;1.79)	1.81(1.47;2.23)	8.42(1.87;38.01)	5.23x10-16
rs73064150	1279	1219	29	31	198	283	1	10	A	17	1.15(0.68;1.96)	1.81(1.47;2.23)	13.04(1.64;103.53)	4.11x10-25
Chr 20														
rs182390	1221	1143	87	107	191	264	8	29	C	28	1.29(0.95;1.75)	1.77(1.43;2.19)	5.62(2.42;13.06)	3.78x10-14
rs6044009	1269	1215	39	35	198	286	1	7	G	17	1.14(0.7;1.84)	1.83(1.49;2.26)	10.2(1.24;83.81)	1.80x10-14
rs6130615	1287	1229	21	21	198	286	1	7	C	13	1.03(0.55;1.93)	1.83(1.48;2.25)	9.89(1.19;82.29)	6.44x10-16
Chr 22														
rs5756557	1247	1193	61	57	195	279	4	14	C	22	1.04(0.71;1.51)	1.8(1.46;2.22)	6.63(1.87;23.42)	2.41x10-16
rs6000602	1250	1194	56	55	195	278	4	14	C	21	1.1(0.74;1.62)	1.79(1.45;2.21)	6.63(1.87;23.42)	1.57x10-14
rs6000609	1247	1192	61	58	195	279	4	14	T	21	1.03(0.71;1.51)	1.8(1.46;2.22)	6.63(1.87;23.42)	2.29x10-16

MAF: minor allele frequency

\* Synergy index results were considered significant at p-values <2.4x10-7

† Individuals who carry either one or two copies of the risk allele are considered to carry the risk variant

‡ Results from observations where the number of subjects in any subgroup is 0 are not shown (n=20)

|| Model adjusted for sex, age, education (categorical), physical activity (categorical), Mediterranean diet score and population structure (MDS1-3 continuous)

Supplemental Table VI: Genes in proximity to the genetic variants included in the significant gene-smoking interactions from analyses limited to data where at least one subgroup includes less than 10 individuals.

	Position	Function	Gene in proximity to the genetic variant
<b>C-IMT<sub>max</sub> with cut-off at the 75<sup>th</sup> percentile</b>			
Chr 1			
rs11208756	65803628	Intron variant	<i>PDE4B</i>
rs11578418	151820508	Intron variant	<i>RORC</i>
rs11804222	11876457	Intergenic variant	<i>None</i>
rs17371694	61843890	Intron variant	<i>PATJ</i>
rs17602729	114693436	Stop gained	<i>AMPD1</i>
rs76000797	230273106	Intron variant	<i>GALNT2</i>
Chr 2			
rs113407226	27263266	Intron variant	<i>SLC30A3</i>
rs1598279	134473632	Intron variant	<i>TMEM163</i>
rs17594260	33476565	Non-coding transcript variant	<i>RASGRP3</i>
rs2300963	206569780	Intron variant	<i>ADAM23</i>
Chr 3			
rs10433607	46131216	Non-coding transcript variant	<i>LOC105377067</i>
rs13320534	46130208	Upstream variant	<i>LOC105377067</i>
rs1497891	180464236	Intergenic variant	<i>None</i>
rs16849578	180464236	Intergenic variant	<i>None</i>
rs2133007	180512734	Intron variant	<i>LOC101928856</i>
rs904241	180546955	Intron variant	<i>LOC101928856</i>
rs2713621	3:129505288	Intron variant	<i>IFT122</i>
rs9845228	7801970	Intergenic variant	<i>None</i>
Chr 5			
rs10043169	160406190	Intron variant	<i>SLU7</i>
rs10512634	35987449	Intron variant	<i>UGT3A1</i>
rs10515808	160393924	Missense variant	<i>ZBED8</i>
rs12522290	153418096	Intergenic variant	<i>None</i>
rs1347118	156035250	Intron variant	<i>SGCD</i>
rs295044	106864274	Intergenic variant	<i>LINC01950</i>
rs400196	25717398	Intergenic variant	<i>None</i>
rs4438916	160400918	Intron variant	<i>ZBED8</i>
rs72814378	160397311	Intron variant	<i>ZBED8</i>
rs79791419	160414486	Intron variant	<i>SLU7</i>
Chr 6			
rs111663960	26081992	Intergenic variant	<i>None</i>
rs113600760	50986966	Intergenic variant	<i>None</i>

rs12199718	169859976	Intergenic variant	<i>None</i>
rs1266071	31701719	Intron variant; upstream variant	<i>ABHD16A; MIR4646</i>
rs190761	51011974	Intergenic variant	<i>None</i>
rs512685	149471889	Intron variant	<i>ZC3H12D</i>
rs557411	50998902	Intergenic variant	<i>None</i>
rs576899	50985929	Intergenic variant	<i>None</i>
rs579544	50985602	Intergenic variant	<i>None</i>
rs6940832	51012532	Intergenic variant	<i>None</i>
rs707974	31661722	3 Prime UTR* variant; upstream variant	<i>GPANK1; BAG6; C6orf47</i>
rs72832602	25978174	Intron variant, downstream transcript variant	<i>TRIM38</i>
rs72834621	26004795	Intergenic variant	<i>None</i>
rs72834627	26019183	Upstream variant	<i>H1-1. H3C1</i>
rs72834643	:26041758	Intergenic variant	<i>None</i>
rs72834647	26043165	Downstream variant	<i>H2BC3</i>
rs7766267	25990246	Intron variant	<i>TRIM38</i>
rs78227802	50995403	Intergenic variant	<i>None</i>
rs9477109	16387177	Intron variant	<i>ATXN1</i>
rs9482260	122606981	Intron variant	<i>PKIB</i>
rs9487678	111598059	Non-coding transcript variant;intron variant	<i>TRAF3IP2-AS1; TRAF3IP2</i>
Chr 7			
rs10256347	116243531	Intron variant	<i>TES</i>
rs16868830	95585346	Prime UTR*variant	<i>PDK4</i>
rs2191886	31401276	Intergenic variant	<i>None</i>
rs2271032	69359109	Intergenic variant	<i>None</i>
Chr 8			
rs10091991	9402217	Intergenic variant	<i>LOC105379231</i>
rs17778118	134660104	Intron variant	<i>ZFAT</i>
Chr 9			
rs12380395	17877300	Intergenic variant	<i>None</i>
Chr 10			
rs10905959	11458048	Intergenic variant	<i>None</i>
rs10887807	88344239	Intron variant	<i>RNLS; LOC101929727</i>
rs11202726	88343172	Intron variant	<i>RNLS; LOC101929727</i>
rs11598623	88342668	Intron variant	<i>RNLS; LOC101929727</i>
rs12356363	20159357	Intron variant	<i>PLXDC2</i>
rs12411339	121308291	Intron variant	<i>LOC105378523</i>
rs1571026	6093062	Intron variant	<i>RBM17</i>
rs2274356	6113913	Intron variant	<i>RBM17</i>
rs4457667	118466441	Intergenic variant	<i>None</i>
rs74149704	88342862	Intron variant	<i>RNLS; LOC101929727</i>
rs963244	66555465	Downstream transcript variant, intron variant	<i>CTNNA3</i>
Chr 11			
rs10082672	1635752	Intergenic variant	<i>None</i>

rs10082701	1635752	Intergenic variant	<i>None</i>
rs11214260	112589295	Intergenic variant	<i>None</i>
rs11232958	71280639	Intergenic variant	<i>None</i>
rs11232966	71282505	Intergenic variant	<i>None</i>
rs11246161	441140	Intron variant; 500B downstream variant	<i>ANO9; LOC105376506</i>
rs11820515	71274752	Intergenic variant	<i>None</i>
rs11827684	71274571	Intergenic variant	<i>None</i>
rs11827708	71274677	Intergenic variant	<i>None</i>
rs2919706	71271759	Intergenic variant	<i>None</i>
rs2919707	71271796	Intergenic variant	<i>None</i>
rs2919708	71271932	Intergenic variant	<i>None</i>
rs2919710	71272305	Intergenic variant	<i>None</i>
rs2919713	71274499	Intergenic variant	<i>None</i>
rs2919718	71278894	Intergenic variant	<i>None</i>
rs3020039	71272077	Intergenic variant	<i>None</i>
rs3020044	71274371	Intergenic variant	<i>None</i>
rs4284411	71275850	Intergenic variant	<i>None</i>
rs963167	9090011	Intron variant; downstream variant	<i>SCUBE2; MIR5691</i>
Chr 12			
rs1040213	76148815	Intergenic variant	<i>None</i>
rs10505859	20263760	Intergenic variant	<i>None</i>
rs10851044	118878894	Intron variant	<i>LOC105370019</i>
rs12371260	118884736	Intron variant	<i>LOC105370019</i>
rs11169949	51892962	Intergenic variant	<i>None</i>
rs1468624	564688	Intron variant	<i>NINJ2</i>
rs1718302	102878908	Intron variant	<i>PAH</i>
rs632151	49895440	Intron variant	<i>FAIM2</i>
Chr 13			
rs4771411	101961195	Intron variant	<i>FGF14</i>
Chr 14			
rs709932	94382864	Missense variant	<i>SERPINA1</i>
Chr 15			
rs12899456	75072408	Intergenic variant	<i>None</i>
rs12905302	75103493	Intergenic variant	<i>None</i>
rs12899074	50649787	Intron variant	<i>TRPM7</i>
rs12899581	50628649	Intron variant	<i>TRPM7</i>
rs12906675	50646137	Intron variant	<i>TRPM7</i>
rs12907202	50639226	Intron variant	<i>TRPM7</i>
rs12907472	50647806	Intron variant	<i>TRPM7</i>
rs12907922	50633900	Intron variant	<i>TRPM7</i>
rs12916113	50661819	Intron variant	<i>TRPM7</i>
rs12916122	50682650	Intron variant	<i>TRPM7</i>
rs531366	50576582	Intron variant	<i>TRPM7</i>

rs540257	50595978	Intron variant	<i>TRPM7</i>
rs600724	50622623	Intron variant	<i>TRPM7</i>
rs615835	50604141	Intron variant	<i>TRPM7</i>
rs623722	50620154	Intron variant	<i>TRPM7</i>
rs2928138	50605915	Intron variant	<i>TRPM7</i>
rs7173321	50630403	Intron variant	<i>TRPM7</i>
rs687549	50576828	Intron variant	<i>TRPM7</i>
rs16968518	39239539	Intergenic variant	<i>None</i>
rs181447504	75087334	Intergenic variant	<i>None</i>
rs34073905	75123784	Intergenic variant	<i>None</i>
rs34359839	74982328	Intergenic variant	<i>None</i>
rs35396991	75078284	Intergenic variant	<i>None</i>
rs6495133	74963117	Intron variant	<i>LOC107984731</i>
rs71401605	74960708	Intergenic variant	<i>None</i>
rs71401676	75098000	Intergenic variant	<i>None</i>
rs75969957	74977570	Intergenic variant	<i>None</i>
rs8033883	74965147	Upstream variant	<i>LOC107984731</i>
rs8038911	75092427	Intergenic variant	<i>None</i>
Chr 16			
rs12596139	54128472	Intergenic variant	<i>None</i>
rs12933423	4037511	Coding sequence variant, synonymous variant	<i>ADCY9</i>
rs16973748	86796209	Intergenic variant	<i>None</i>
rs1805007	89919709	Missense variant	<i>MC1R</i>
rs1863985	58590190	Intergenic variant	<i>CNOT1</i>
rs7203264	69091066		<i>None</i>
Chr 18			
rs112812977	12862914	Intron variant	<i>PTPN2</i>
rs12607452	45348204	Intron variant	<i>SLC14A2</i>
rs16978345	45345030	Intron variant	<i>SLC14A2</i>
rs4605263	69259177	Intergenic variant	<i>None</i>
rs8097973	59398950		<i>LOC107985156</i>
Chr 20			
rs17092385	35151451	Intron variant	<i>MMP24-AS1-EDEM2</i>
rs73139727	63709681	Intron variant; upstream variant	<i>ZGPAT. ARFRP1</i>
Chr 21			
rs2835673	37209209	Intron variant	<i>DSCR9</i>
Chr 22			
rs12170612	37236140	Intron variant	<i>RAC2</i>
rs9607434	37240909	Intron variant	<i>RAC2</i>
<b>C-IMT<sub>max</sub> with cut-off at the 50<sup>th</sup> percentile</b>			
Chr 1			
rs10889363	62728338	Intergenic variant	<i>None</i>

rs11208008	62725123	Intergenic variant	<i>None</i>
rs11208010	62737550	Intergenic variant	<i>None</i>
rs12130333	62726106	Intergenic variant	<i>None</i>
rs12566784	214955060	Intergenic variant	<i>None</i>
rs1336474	65225566	Intron variant	<i>AK4</i>
rs16840422	196683704	Intron variant	<i>CFH</i>
rs2818765	216995141	Intron variant	<i>ESRRG</i>
rs3766404	196682702	Intron variant	<i>CFH</i>
rs4245713	202809133	Prime UTR <sup>a</sup> variant; upstream variant	<i>KDM5B; PCAT6</i>
rs486453	76146148	Intron variant	<i>ST6GALNAC3</i>
rs4949623	76152308	Intron variant	<i>ST6GALNAC3</i>
Chr 2			
rs1520399	176398745	Intergenic variant	<i>None</i>
rs2043075	7442631	Intron variant	<i>LOC100506274</i>
rs62621191	240557353	Splice acceptor variant; 2KB upstream variant	<i>ANKMY1; DUSP28</i>
rs6751950	70333807	Intergenic variant	<i>None</i>
rs964582	100751914	Intergenic variant	<i>None</i>
Chr 3			
rs1602474	163772877	Intergenic variant	<i>None</i>
rs2889390	160991223	Intron variant	<i>PPM1L</i>
Chr 4			
rs1439471	41708560	Intergenic variant	<i>None</i>
rs727633	21918920	Intron variant	<i>KCNIP4</i>
Chr 5			
rs10039050	150339295	Intron variant	<i>LOC105378225</i>
rs17708750	174085431	Intron variant and non-coding transcript	<i>NSG2 -LOC102724551</i>
rs2731798	17095241	Intergenic variant	<i>None</i>
rs6881772	150341244	Upstream variant	<i>LOC105378225</i>
rs7725668	126663642	Intron variant	<i>LOC105379162</i>
Chr 6			
rs1474642	170543473	Intron variant	<i>PSMB1</i>
rs17802893	12716327	Upstream variant; intron variant	<i>PHACTR1, LOC107984015</i>
rs3094682	31296684	Intron variant	<i>LINC02571, LOC112267902</i>
Chr 7			
rs5024722	142158888	Intron variant	<i>MGAM2</i>
rs509834	71673017	Intron variant	<i>GALNT17</i>
Chr 8			
rs10095737	10783642	Intron variant	<i>PINX1</i>
rs10097531	10801382	Intron variant	<i>PINX1</i>
rs10107180	10791576	Intron variant	<i>PINX1</i>
rs10107303	10791682	Intron variant	<i>PINX1</i>
rs2116096	10778377	Intron variant	<i>PINX1</i>
rs28592638	10797063	Intron variant	<i>PINX1</i>

rs6601520	10771198	Intron variant	<i>PINX1</i>
rs6601524	10777712	Intron variant	<i>PINX1</i>
rs6985218	10797906	Intron variant	<i>PINX1</i>
rs7014168	10784455	Intron variant	<i>PINX1</i>
rs7823088	10781532	Intron variant	<i>PINX1</i>
rs891554	10793270	Intron variant	<i>PINX1</i>
rs9644730	10795981	Intron variant	<i>PINX1</i>
rs167999	55880126	Intron variant	<i>LYN</i>
rs4610751	9594578	Intron variant	<i>TNKS</i>
rs7001206	10734019	Intron variant	<i>LOC102723313</i>
rs73196893	11023727	Intron variant	<i>XKR6</i> , <i>LOC112268405</i>
rs73196895	11027222	Intron variant	<i>XKR6</i>
rs73198940	11134055	Intron variant	<i>XKR6</i>
Chr 9			
rs12686329	110193988	Intron variant	<i>None</i>
rs2472508	104921972	Intron variant	<i>ABCA1</i>
rs2487049	104922005	Intron variant	<i>ABCA1</i>
rs7851754	108613871	Intergenic variant	<i>None</i>
rs930340	84048599	Intergenic variant	<i>None</i>
rs9406465	1386357	Intron variant	<i>LOC102723803</i>
Chr 10			
rs55749454	88339382	Intron variant	<i>RNLS</i> , <i>LOC101929727</i>
rs7081222	9879580	Upstream variant	<i>LINC02663</i>
Chr 11			
rs11221388	128605106	Intergenic variant	<i>LOC105369568</i>
rs12362809	114475848	Intergenic variant	<i>NXPE2</i>
rs12363819	128608431	Intergenic variant	<i>LOC105369568</i>
rs198459	61757548	Non-coding transcript; intron variant	<i>MYRF-AS1</i> ; <i>MYRF</i>
rs61907787	128610401	Non-coding transcript	<i>LOC105369568</i>
rs835839	44880352	Intron variant	<i>TSPAN18</i>
Chr 12			
rs1463863	118745833	Intergenic variant	<i>None</i>
rs17466339	40318557	Intron variant	<i>LRRK2</i>
Chr 13			
rs11840638	43774384	Intron variant	<i>ENOX1</i>
rs1331752	57248074	Intergenic variant	<i>None</i>
rs2094196	47939422	Intergenic variant	<i>None</i>
rs4592537	62001158	Intergenic variant	<i>None</i>
rs500574	57226507	Intergenic variant	<i>None</i>
rs9525841	43772927	Intergenic variant	<i>ENOX1</i>
rs9533613	43773493	Intergenic variant	<i>ENOX1</i>
Chr 14			
rs10142781	46837078	3 prime UTR <sup>a</sup> variant	<i>MDGA2</i>



rs10151371	88028231	Intron variant; 2KB upstream variant	<i>LINC01146; LINC01147</i>
rs17124043	88084433	Intron variant	<i>LINC01146</i>
rs17124045	88084580	Intron variant	<i>LINC01146</i>
rs17203608	88080126	Intron variant	<i>LINC01146</i>
rs17798173	88077653	Intron variant	<i>LINC01146</i>
rs17798179	88078202	Intron variant	<i>LINC01146</i>
rs17798191	88089912	Intergenic variant	<i>None</i>
rs4303414	88062456	Intron variant	<i>LINC01146</i>
rs4483792	88062707	Intron variant	<i>LINC01146</i>
rs4904423	88084632	Intron variant	<i>LINC01146</i>
rs4904424	88085048	Intron variant	<i>LINC01146</i>
rs59644163	88079131	Intron variant	<i>LINC01146</i>
rs61975760	88062229	Intron variant	<i>LINC01146</i>
rs61975777	88066797	Intron variant	<i>LINC01146</i>
rs61975778	88069792	Intron variant	<i>LINC01146</i>
rs61975779	88069792	Intron variant	<i>LINC01146</i>
rs61975782	88080381	Intron variant	<i>LINC01146</i>
rs61977336	88050993	Intron variant	<i>LINC01146</i>
rs72693891	88087009	Non-coding transcript variant	<i>LINC01146</i>
Chr 15			
rs11638662	40254473	Intron variant; 2KB upstream variant	<i>BUB1B-PAK6; PAK6; PAK6-AS1</i>
rs12439792	67145047	Intron variant	<i>SMAD3</i>
rs4395027	93110051	Intron variant	<i>LOC101927025</i>
rs7165170	90638257	Intron variant	<i>CRTC3; CRTC3-AS1</i>
rs76414746	63076515	Intergenic variant	<i>None</i>
rs922507	94663407	Intergenic variant	<i>None</i>
Chr 16			
rs2716596	74045220	Intergenic variant	<i>None</i>
rs34550882	31263554	Intron variant	<i>ITGAM</i>
rs4787317	25341946	Intergenic variant	<i>None</i>
rs8059494	25243921	Missense variant	<i>ZKSCAN2</i>
Chr 17			
rs4793460	72622702	Intron variant	<i>LINC00511; LOC107985006</i>
rs60399446	42756585	Intron variant	<i>RAMP2-AS1</i>
Chr 19			
rs10417472	48594630	Intron variant	<i>SULT2B1</i>
rs1041992	41625899	Synonymous variant	<i>CEACAM4</i>
rs2665586	48596124	Intron variant	<i>SULT2B1</i>
rs6510126	58164549	Intergenic variant	<i>None</i>
rs73064150	54482485	Intergenic variant	<i>None</i>
Chr 20			
rs182390	39683827	Intergenic variant	<i>None</i>
rs6044009	16485758	Intron variant	<i>KIF16B</i>

rs6130615	44430797	3 Prime UTR*variant	<i>HNF4A</i>
chr 22			
rs5756557	37209757	Intron variant	<i>SSTR3</i>
rs6000609	37213302	Intron variant	<i>SSTR3</i>
rs6000602	37194509	Intron variant	<i>C1QTNF</i>

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\* UTR: untranslated region

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