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Table I. Characteristics of study subjects

Category	Group	No.	Age (Mean±SD)	Sex (% male)	Smoking habit (%)		Pack-years of smokers (Mean±SD)
					Non-smoker	Smoker	
NCCH set	Case	2,343	59±9	65	34	66	51±30
	Adenocarcinoma	1,656	58±9	56	46	54	43±27
	Squamous cell carcinoma	390	62±7	91	3	97	61±29
	Small cell carcinoma	297	62±9	80	5	95	62±32
	Control	1,173	48±14	58	63	37	27±21
NNGH set	Case	136	68±10	74	27	73	55±29
	Adenocarcinoma	84	67±10	64	39	61	48±25
	Squamous cell carcinoma	52	70±9	90	6	94	62±32
	Control	145	64±14	71	33	67	45±35

Table II. GWAS and validation studies to identify loci associated with lung adenocarcinoma risk

Stage	Subject (No.)		Polymorphic loci analyzed	Genotyping method	Result					
	Case	Control			Loci/Allele	Crude OR (95% CI)	P value	Adjusted OR ^a (95% CI)	P value	
GWAS	1st ^b	Patients of NCCH (200)	Volunteers enrolled in Tokai University (200)	23,010 microsatellites	Pooled DNA typing	1,328 loci	ND	$P_{2 \times m} < 0.05$	ND	ND
	2nd ^c	Patients of NCCH (200)	Volunteers enrolled in Keio University (200)	431 microsatellites	Pooled DNA typing	17 loci	ND	$P_{2 \times m} < 0.05$	ND	ND
	3rd ^d	Patients of NCCH (576) consisting of 192 1st set, 192 2nd set and 192 another subjects	Tokai and Keio volunteers and non-cancer NCCH patients (576) consisting of 192 1st and 192 2nd set volunteers; and 192 non-cancer NCCH patients	17 microsatellites	Individual DNA typing	D6S0067i and other 5 loci	ND	$P_{2 \times m} = 2.4 \times 10^{-7}$ at D6S0067i $P_{2 \times m} = 0.012 - 0.0011$ at 5 other loci	ND	ND
SNP analysis ^e	Randomly selected 3rd stage GWAS subjects (525)	Randomly selected 3rd stage GWAS subjects (525)	56 SNPs	24 SNPs by sequencing 32 SNPs by Taqman PCR	rs17426593 DQA1*03 DQA1*01	1.51 (1.27-1.80) 1.50 (1.26-1.79) 0.69 (0.58-0.82)	4.2×10^{-6} 6.6×10^{-6} 2.8×10^{-5}	ND	ND	ND
	Same as above	Same as above	rs17426593 and rs34843907	-	DQA1*03 DQA1*01	1.32 (1.27-1.81) 0.69 (0.58-0.82)	3.4×10^{-6} 2.3×10^{-5}	ND	ND	ND
Validation	Other patients of NCCH (1,131)	Other subjects (648) consisting of 9 Tokai and 478 Keio volunteers; and 161 non-cancer NCCH patients	Same as above	Taqman PCR	DQA1*03 DQA1*01	1.27 (1.11-1.45) 0.86 (0.75-0.99)	5.6×10^{-4} 0.030	ND	ND	ND
(Combined analysis)	Patients of NCCH (1,656)	Subjects (1,173) consisting of 200 Tokai and 635 Keio volunteers and 338 non-cancer NCCH patients	Same as above	-	DQA1*03 DQA1*01	1.35 (1.21-1.51) 0.78 (0.70-0.87)	5.6×10^{-8} 6.0×10^{-6}	1.36 (1.20-1.54) 0.77 (0.68-0.87)	5.3×10^{-7} 1.4×10^{-5}	
Validation in another set	Patients of NINGH (84)	Non-cancer patients of NINGH (145)	Same as above	Taqman PCR	DQA1*03 DQA1*01	1.57 (1.07-2.30) 0.77 (0.52-1.13)	0.022 0.18	1.70 (1.14-2.53) 0.68 (0.49-1.09)	0.0087 0.12	

ND: not determined.

^aadjusted for sex, age, and smoking.

^b23,010 microsatellite loci containing repeat units of 2-6-bp were examined, and 1,328 loci showed significant differences in allele distribution.

^cAmong 1,328 loci selected in the 1st GWAS stage, 431 loci that contained repeat units of 3-6-bp were examined, and 17 loci showed significant differences in allele distribution.

^d17 loci selected in the 2nd GWAS stage were examined, and 6 loci showed significant differences in allele distribution. Only the D6S0067i locus was identified as being significantly different after Bonferroni correction (i.e., $P < 0.05/23,010 = 2.2 \times 10^{-6}$). In this stage, 576 subjects consisted of two sets of 192 subjects which were chosen from two sets of 200 subjects examined in the 1st and 2nd GWAS stages, respectively, and another 192 subjects were examined.

^eIn this stage, 525 cases and 525 controls, which were randomly chosen from the 576 cases and 576 controls examined in the 3rd GWAS stage, were examined for 56 SNPs.

Table IV. Differences in the distribution of the HLA class II alleles between 525 lung adenocarcinoma cases and 525 controls

Gene	No.	Allele ^a	Frequency		OR	(95% CI)	P value by χ^2 test
			Control	Case			
DRB1	1	DRB1*1502	0.148	0.125	0.82	(0.64 - 1.05)	0.12
	2	<u>DRB1*0901</u>	0.117	0.157	1.40	(1.09 - 1.81)	0.0079
	3	<u>DRB1*0405</u>	0.106	0.154	1.53	(1.18 - 1.98)	0.0012
	4	<u>DRB1*1302</u>	0.097	0.058	0.58	(0.42 - 0.81)	0.0011
	5	<u>DRB1*1501</u>	0.091	0.055	0.58	(0.41 - 0.81)	0.0013
	6	DRB1*0803	0.073	0.075	1.02	(0.74 - 1.42)	0.90
	7	DRB1*0101	0.057	0.033	0.56	(0.37 - 0.86)	0.0077
	8	DRB1*1401/1405/1406/1412/1429	0.057	0.069	1.24	(0.87 - 1.77)	0.23
	9	DRB1*0802	0.052	0.037	0.70	(0.46 - 1.07)	0.10
	10	DRB1*0403/0404/0406	0.044	0.073	1.73	(1.19 - 2.52)	0.0040
	11	DRB1*1201/1202	0.040	0.050	1.25	(0.82 - 1.89)	0.30
	12	DRB1*1101	0.026	0.022	0.81	(0.46 - 1.42)	0.47
	13	DRB1*0410	0.021	0.016	0.78	(0.41 - 1.48)	0.44
	Total		0.929	0.924			
DQA1	1	DQA1*01	0.530	0.438	0.69	(0.58 - 0.82)	2.8x10 ⁻⁵
	2	DQA1*03	0.348	0.444	1.50	(1.26 - 1.79)	6.6x10 ⁻⁶
	3	DQA1*04/05/06	0.122	0.118	0.88	(0.68 - 1.14)	0.43
	Total		1.000	1.000			
DQB1	1	DQB1*0601	0.218	0.205	0.92	(0.75 - 1.14)	0.46
	2	DQB1*0303	0.139	0.164	1.22	(0.96 - 1.54)	0.11
	3	<u>DQB1*0401</u>	0.104	0.153	1.54	(1.19 - 2.00)	0.0010
	4	<u>DQB1*0604</u>	0.097	0.058	0.57	(0.41 - 0.79)	7.4x10 ⁻⁴
	5	DQB1*0301	0.093	0.093	1.01	(0.75 - 1.35)	0.97
	6	<u>DQB1*0602</u>	0.086	0.053	0.59	(0.42 - 0.84)	0.0028
	7	DQB1*0302	0.081	0.092	1.15	(0.85 - 1.57)	0.35
	8	DQB1*0501	0.061	0.059	0.96	(0.67 - 1.37)	0.82
	9	DQB1*0402	0.042	0.051	1.21	(0.80 - 1.82)	0.36
	10	DQB1*0502	0.030	0.027	0.90	(0.54 - 1.51)	0.70
	11	DQB1*0503	0.028	0.028	1.03	(0.61 - 1.72)	0.93
	Total		0.979	0.983			
DR-DQ	1	DRB1*1502-DQA1*01-DQB1*0601	0.150	0.130	0.85	(0.66 - 1.09)	0.19
	2	DRB1*0901-DQA1*03-DQB1*0303	0.119	0.153	1.34	(1.05 - 1.73)	0.021
	3	<u>DRB1*0405-DQA1*03-DQB1*0401</u>	0.101	0.144	1.51	(1.16 - 1.96)	0.0022
	4	<u>DRB1*1302-DQA1*01-DQB1*0604</u>	0.094	0.057	0.58	(0.42 - 0.81)	0.0013
	5	<u>DRB1*1501-DQA1*01-DQB1*0602</u>	0.082	0.051	0.60	(0.42 - 0.85)	0.0042
	6	DRB1*0803-DQA1*01-DQB1*0601	0.070	0.072	1.02	(0.73 - 1.43)	0.89
	7	DRB1*0101-DQA1*01-DQB1*0501	0.047	0.034	0.72	(0.46 - 1.12)	0.14
	8	<u>DRB1*0403/0404/0406-DQA1*03-DQB1*0302</u>	0.040	0.068	1.72	(1.17 - 2.54)	0.0058
	9	DRB1*1201/1202-DQA1*04/05/06-DQB1*0301	0.032	0.032	0.99	(0.61 - 1.61)	0.97
	10	DRB1*1401/1405/1406/1412/1429-DQA1*01-DQB1*0503	0.028	0.031	1.13	(0.68 - 1.88)	0.64
	11	DRB1*1101-DQA1*04/05/06-DQB1*0301	0.025	0.017	0.68	(0.37 - 1.25)	0.21
	12	DRB1*0802-DQA1*04/05/06-DQB1*0402	0.024	0.026	1.10	(0.64 - 1.91)	0.73
	Total		0.812	0.815			

^aDRB1 and DQB1 alleles linked to the DQA1*03 or DQA1*01 alleles and DR-DQ alleles containing the DQA1*03 or DQA1*01 alleles, which were significantly associated with lung ADC risk, are underlined.

Figure 1

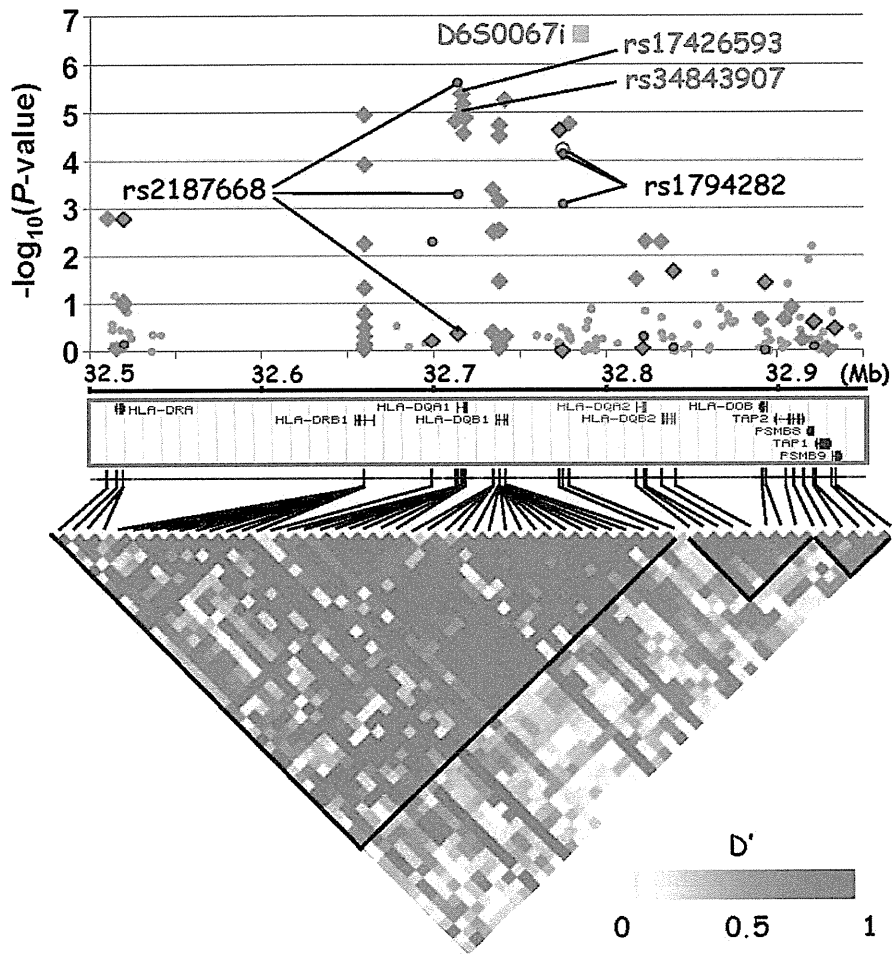


Figure 2a

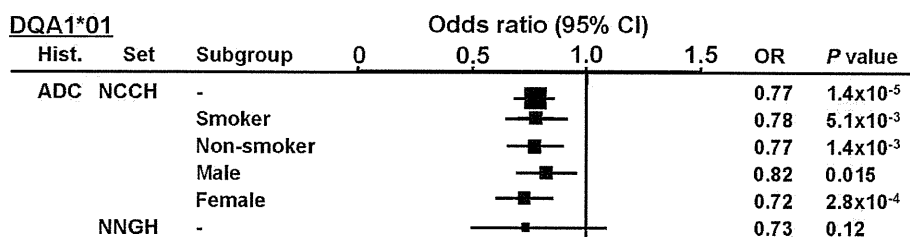
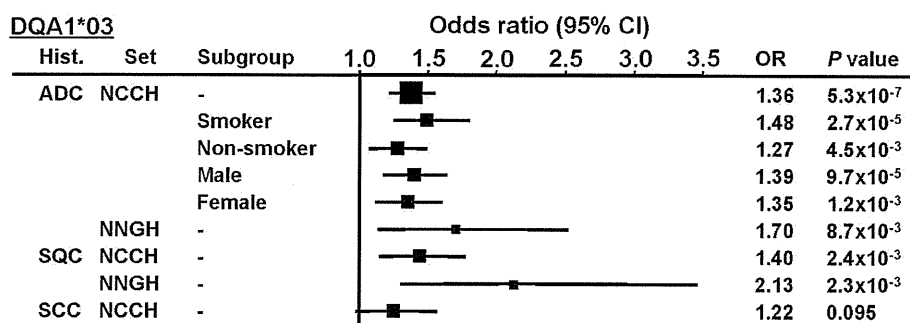
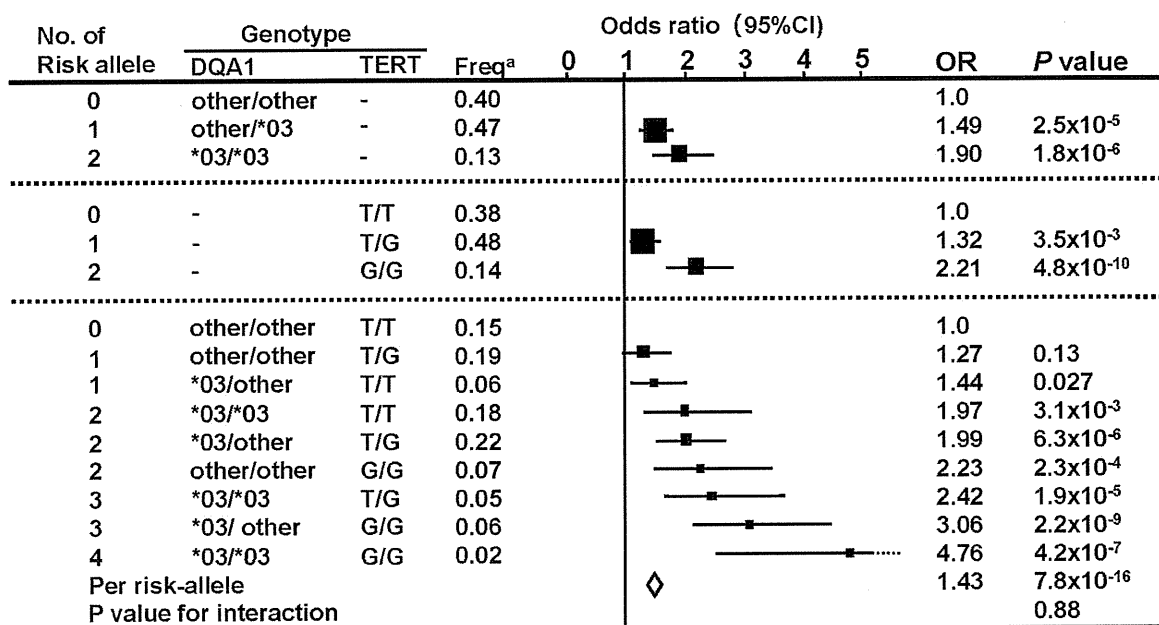


Figure 2b



^aFrequency in controls.

Supplementary Table I. Inflation factors for the 1st and 2nd stages of GWAS

Repeat unit	1st stage		2nd stage	
	No. of markers	Inflation factor ^a	No. of markers	Inflation factor ^a
All	23,010	0.639	1,328	-
2-bp	16,545	0.520	897	-
3-bp	1,295	0.919	86	0.812
4-bp	4,502	0.958	303	1.026
5-bp	648	1.022	41	1.265
6-bp	20	0.947	1	-
3~6-bp	6,465	0.955	431	1.010

^aThe mean of the lower 90% of the test statistics ($-\log P$ values by Fisher's exact test) divided by the mean of the lower 90% of the expected values.

Supplementary Table II. Linkage disequilibrium between the D6S0067i polymorphisms and SNPs/alleles in the 6p21.31 locus

SNP/Allele	Controls		ADC cases	
	D'	R ²	D'	R ²
rs17426593	0.516	0.225	0.603	0.349
rs34843907	0.531	0.152	0.688	0.280
DQA1_2_145	0.514	0.223	0.607	0.352
DQA1_2_150	0.531	0.152	0.689	0.283
DQA1*01	0.531	0.152	0.689	0.283
DQA1*03	0.516	0.225	0.607	0.352

Supplementary Table III. Linkage disequilibrium between exonic and intronic *HLA-DQA1* SNPs among case and control populations

Population	DQA1_2_145 and rs17426593		DQA1_2_150 and rs34843907	
	D'	R ²	D'	R ²
Controls	1.000	0.983	1.000	0.996
ADC cases	1.000	0.996	0.996	0.992

Supplementary Table IV. Correlation coefficients of HLA-*DQA1* alleles determined by exonic SNPs and intronic SNPs

Population	R^2	
	DQA1*01	DQA1*03
Controls	1.000	0.983
ADC cases	0.996	0.996

Supplementary Table V. ORs of the DQA1*03 and DQA1*01 alleles for lung cancer risk

Allele	Category	Histological type	Subgroup	No.		Crude			Adjusted		
				Case	Control ^a	OR	(95% CI)	P value	OR	(95% CI)	P value
DQA1*03	NCCH	ADC		1,656	1,173	1.35	(1.21 - 1.51)	5.6x10 ⁻⁸	1.36 ^b	(1.20 - 1.54)	5.3x10 ⁻⁷
			Smoker	896	363	1.46	(1.22 - 1.75)	2.9x10 ⁻⁵	1.48 ^c	(1.23 - 1.77)	2.7x10 ⁻⁵
			Non-smoker	760	610	1.27	(1.09 - 1.48)	0.0022	1.27 ^c	(1.08 - 1.50)	0.0045
			Male	924	675	1.35	(1.16 - 1.57)	1.4x10 ⁻⁴	1.39 ^d	(1.18 - 1.65)	9.7x10 ⁻⁵
			Female	732	498	1.27	(1.09 - 1.49)	0.0021	1.35 ^d	(1.12 - 1.61)	0.0012
		SQC	390	1,173	1.27	(1.08 - 1.50)	0.0047	1.40 ^b	(1.13 - 1.74)	0.0024	
		SCC	297	1,173	1.17	(0.98 - 1.41)	0.089	1.22 ^b	(0.97 - 1.54)	0.095	
		NNGH	ADC	84	145	1.57	(1.07 - 2.30)	0.022	1.70 ^b	(1.14 - 2.53)	0.0087
	SQC		52	145	2.07	(1.32 - 3.27)	0.0016	2.13 ^b	(1.31 - 3.49)	0.0023	
	DQA1*01	NCCH	ADC		1,656	1,173	0.78	(0.70 - 0.87)	6.0x10 ⁻⁶	0.77 ^b	(0.68 - 0.87)
Smoker				896	363	0.78	(0.65 - 0.92)	0.0040	0.78 ^c	(0.65 - 0.93)	0.0051
Non-smoker				760	610	0.78	(0.67 - 0.91)	0.0016	0.77 ^c	(0.65 - 0.90)	0.0014
Male				924	675	0.83	(0.72 - 0.96)	0.0150	0.82 ^d	(0.69 - 0.96)	0.0150
Female				732	498	0.74	(0.62 - 0.87)	4.6x10 ⁻⁴	0.72 ^d	(0.60 - 0.86)	2.8x10 ⁻⁴
		NNGH	ADC	84	145	0.77	(0.52 - 1.13)	0.18	0.73 ^b	(0.49 - 1.09)	0.12

^aInformation on smoking was not available for 200 subjects.

^bAdjusted for age, sex and smoking.

^cAdjusted for age and sex.

^dAdjusted for sex and smoking.

Supplementary Table VI. Differences in the allele distribution of SNPs in lung cancer susceptibility loci identified by GWASs

Allele	Chromosomal location	Position	Gene	Category	Minor allele frequency		OR (95% CI, <i>P</i>)
					Control	Case	
rs2736100-G	5p15.33	1339516	<i>TERT</i> (intron 2)	All	0.377	0.444	1.38 (1.23 - 1.56, 6.3×10^{-8}) ^a
				ADC		0.465	1.46 (1.30 - 1.65, 6.6×10^{-10}) ^a
				SQC		0.382	0.95 (0.77 - 1.19, 0.68) ^a
				SCC		0.407	1.07 (0.85 - 1.35, 0.58) ^a
				Non-smoker	0.380	0.470	1.47 (1.25 - 1.73, 4.1×10^{-6}) ^b
				Smoker	0.372	0.431	1.29 (1.08 - 1.53, 4.2×10^{-3}) ^b
rs401681-T	5p15.33	1375087	<i>CLPTM1L</i> (intron 13)	All	0.334	0.312	0.88 (0.78 - 0.99, 0.044) ^a
				ADC		0.314	0.89 (0.79 - 1.01, 0.077) ^a
				SQC		0.300	0.88 (0.70 - 1.10, 0.27) ^a
				SCC		0.315	0.87 (0.68 - 1.11, 0.27) ^a
				Non-smoker	0.333	0.297	0.81 (0.68 - 0.96, 0.014) ^b
				Smoker	0.336	0.319	0.96 (0.80 - 1.15, 0.65) ^b
rs1051730-T	15q25.1	76681394	<i>CHRNA3</i> (Y215Y)	All	0.015	0.032	1.79 (1.19 - 2.78, 9.5×10^{-3}) ^a
				ADC		0.030	1.72 (1.14 - 2.69, 9.5×10^{-3}) ^a
				SQC		0.033	2.29 (1.14 - 4.72, 0.020) ^a
				SCC		0.037	2.22 (1.09 - 4.58, 0.027) ^a
				Non-smoker	0.015	0.030	1.65 (0.94 - 3.02, 0.083) ^b
				Smoker	0.017	0.033	1.94 (1.09 - 3.79, 0.023) ^b

^aAdjusted for sex, age and smoking.

^bAdjusted for sex and age.

Supplementary Table VII. ORs for genotypes of the *HLA-DQA1*, *TERT* and *CHRNA3* loci

Locus	Number of risk allele	Genotype	Control (%)	Case (%)	OR* (95% CI)	P
HLA-DQA1	0	other/other	389 (40.2)	509 (30.7)	Reference	
	1	*03/other	455 (47.0)	859 (51.9)	1.49 (1.24 - 1.79)	2.5 x 10 ⁻⁵
	2	*03/*03	124 (12.8)	288 (17.4)	1.90 (1.45 - 2.48)	1.8 x 10 ⁻⁶
rs2736100 (<i>TERT</i>)	0	T/T	373 (38.5)	488 (29.5)	Reference	
	1	T/G	460 (47.5)	796 (48.0)	1.32 (1.10 - 1.60)	3.5 x 10 ⁻³
	2	G/G	135 (14.0)	372 (22.5)	2.21 (1.72 - 2.86)	4.8 x 10 ⁻¹⁰
rs1051730 (<i>CHRNA3</i>)	0	G/G	939 (97.0)	1,558 (94.1)	Reference	
	1	G/A	28 (2.9)	95 (5.7)	1.82 (1.18 - 2.89)	6.4 x 10 ⁻³
	2	A/A	1 (0.1)	3 (0.2)	0.94 (0.11 - 19.0)	0.960

^aAdjusted for sex, age and smoking.

Supplementary Table VIII. Risk of combined *HLA-DQA1*, *TERT* and *CHRNA3* genotypes for lung adenocarcinoma

Gene	Number Risk allele	Genotype	Control (%)	Case (%)	OR* (95% CI)	P	
2		rs2736100 (<i>TERT</i>) *03 (<i>HLA-DQA1</i>)					
	0	T/T	other/other	148 (15.3)	149 (9.0)	Reference	
	1	T/G	other/other	188 (19.4)	249 (15.0)	1.27 (0.93 -1.74)	0.13
	1	T/T	*03/other	176 (18.2)	243 (14.7)	1.44 (1.04 -1.99)	0.027
	2	T/T	*03/*03	49 (5.1)	96 (5.8)	1.97 (1.25 -3.13)	3.1 × 10 ⁻³
	2	T/G	*03/other	212 (21.9)	415 (25.1)	1.99 (1.47 -2.70)	6.3 × 10 ⁻⁶
	2	G/G	other/other	53 (5.5)	111 (6.7)	2.23 (1.45 -3.45)	2.3 × 10 ⁻⁴
	3	T/G	*03/*03	60 (6.2)	132 (8.0)	2.42 (1.61 -3.68)	1.9 × 10 ⁻⁵
	3	G/G	*03/other	67 (6.9)	201 (12.1)	3.06 (2.11 -4.48)	2.2 × 10 ⁻⁹
	4	G/G	*03/*03	15 (1.5)	60 (3.6)	4.76 (2.53 -9.47)	4.2 × 10 ⁻⁷
Per risk-allele					1.43 (1.31 -1.56)	7.8 × 10 ⁻¹⁶	
P value for interaction						0.88	
2		rs2736100 (<i>TERT</i>)	rs1051730 (<i>CHRNA3</i>)				
	0	T/T	G/G	362 (37.4)	457 (39.7)	Reference	
	1 or 2		G/A + A/A	11 (1.1)	31 (2.7)	1.73 (0.84 -3.80)	0.14
	1	T/G	G/G	445 (46.0)	749 (65.0)	1.32 (1.09 -1.60)	4.5 × 10 ⁻³
	2 or 3		G/A + A/A	15 (1.5)	47 (4.1)	2.40 (1.30 -4.69)	4.9 × 10 ⁻³
	2	G/G	G/G	132 (13.6)	352 (30.6)	2.22 (1.71 -2.88)	9.3 × 10 ⁻¹⁰
	3 or 4		G/A + A/A	3 (0.3)	20 (1.7)	4.27 (1.38 -18.8)	9.9 × 10 ⁻³
Per risk-allele					1.48 (1.33 -1.66)	3.9 × 10 ⁻¹¹	
P value for interaction						0.73	
2		*03 (<i>HLA-DQA1</i>)	rs1051730 (<i>CHRNA3</i>)				
	0	other/other	G/G	380 (39.3)	470 (40.8)	Reference	
	1	*03/other	G/G	440 (45.5)	809 (70.2)	1.53 (1.26 -1.84)	1.1 × 10 ⁻⁵
	2 or 3		G/A + A/A	15 (1.5)	50 (4.3)	2.47 (1.36 -4.74)	2.5 × 10 ⁻³
	2	*03/*03	G/G	119 (12.3)	279 (24.2)	2.01 (1.54 -2.65)	2.9 × 10 ⁻⁷
	3 or 4		G/A + A/A	5 (0.5)	9 (0.8)	1.37 (0.44 -4.77)	0.59
Per risk-allele					1.35 (1.21 -1.50)	5.1 × 10 ⁻⁷	
P value for interaction						0.083	
3	0			144 (14.9)	132 (8.0)	Reference	
	1			356 (36.8)	479 (28.9)	1.45 (1.08 -1.94)	0.013
	2			319 (33.0)	619 (37.4)	2.15 (1.60 -2.88)	3.0 × 10 ⁻⁷
	3			127 (13.1)	349 (21.1)	3.11 (2.24 -4.35)	9.3 × 10 ⁻¹²
	4			22 (2.3)	73 (4.4)	4.16 (2.39 -7.50)	2.0 × 10 ⁻⁷
	5			0 (0)	4 (0.2)	- (- - -)	-
	6			0 (0)	0 (0)	- (- - -)	-
Per risk-allele					1.45 (1.40 -1.50)	2.5 × 10 ⁻¹⁷	

^aAdjusted for sex, age and smoking.

Supplementary Table IX. Association of 10 SNPs commonly analyzed in the present and other GWASs with lung cancer risk

SNP	Genome location	Gene	Position	Allele	Minor allele frequency		Allele OR		P value	
					Japanese*	Others	Japanese ^a	Others	Japanese*	Others
rs7192	32,519,624	<i>HLA-DRA</i>	exon 4	G/T	0.444	0.370	0.76	0.98 ^b	0.0016	0.65
rs3129763	32,698,903			G/A	0.064	0.270	1.10	1.14 ^b	0.60	0.0048
rs2187668	32,713,862	<i>HLA-DQA1</i>	intron 1	G/A	0.033	0.100	1.21	1.11 ^e	0.42	3.6x10 ⁻⁷
								1.27 ^b		5.0x10 ⁻⁴
								1.22 ^c		2.3x10 ⁻⁶
rs2647012	32,772,436			G/A	0.214	0.330	0.61	1.00 ^b	2.3x10 ⁻⁵	0.95
rs1794282	32,774,504			G/A	0.000	0.080	-	1.18 ^e	-	6.9x10 ⁻¹⁰
		1.29 ^b	8.0x10 ⁻⁴							
		1.20 ^c	7.2x10 ⁻⁵							
		1.26 ^d	6.0x10 ⁻⁵							
rs2239800	32,821,245	<i>HLA-DQA2</i>	intron 2	T/C	0.289	0.130	1.01	1.20 ^e	0.88	0.47
rs1573649	32,839,236			T/C	0.426	0.420	0.81	0.95 ^b	0.021	0.82
rs2071469	32,892,761	<i>HLA-DOB</i>	5'UTR	G/A	0.424	0.430	1.20	1.01 ^b	0.037	0.95
rs1057373	32,921,257	<i>TAP1</i>	3'UTR	G/T	0.105	0.080	1.18	1.00 ^b	0.23	0.78
rs17587	32,933,068	<i>PSMB9</i>	exon 3	G/T	0.243	0.280	0.90	0.98 ^b	0.33	0.33

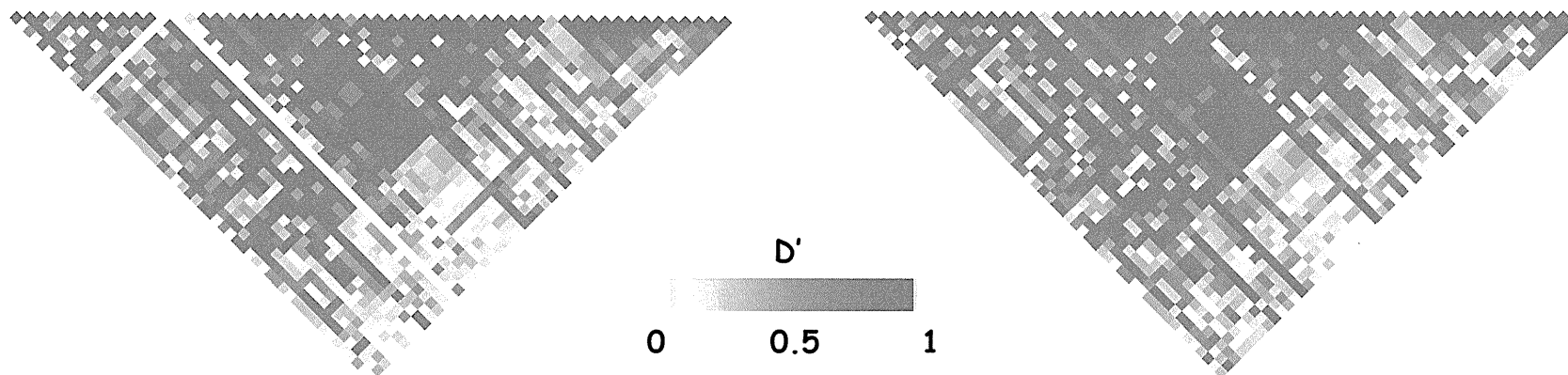
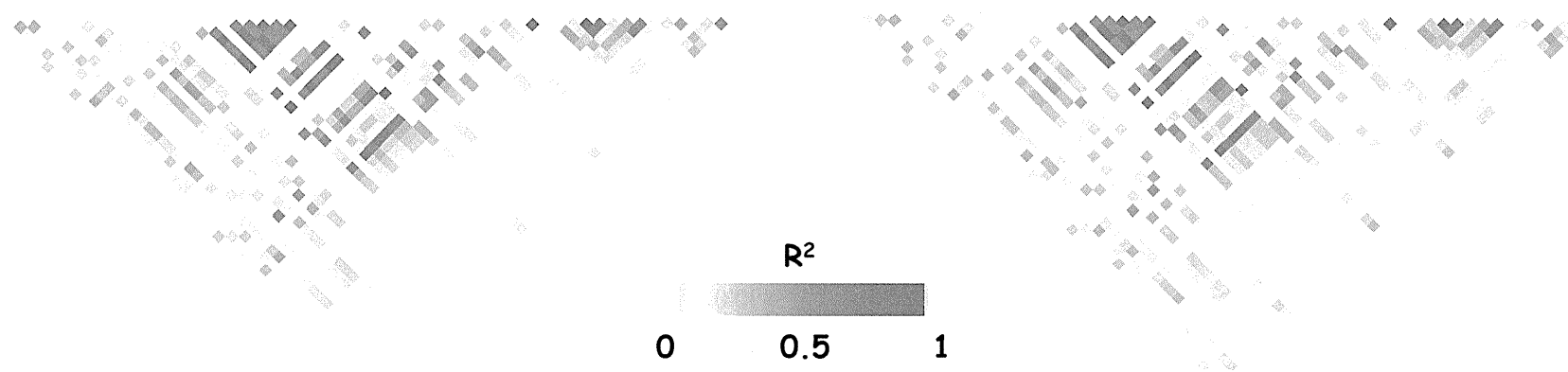
^aAssociation with lung adenocarcinoma risk on 525 cases and 525 controls.

^bAssociation with lung cancer risk on 1,989 cases and 2,625 controls in European countries⁸.

^cAssociation with lung cancer risk on 5,095 cases and 5,200 controls in European countries and USA⁴.

^dAssociation with lung cancer risk on 2,971 cases and 3,746 controls in European countries, Canada and USA⁵.

^eAssociation with lung cancer risk on 13,300 cases and 19,666 controls in European countries and USA¹¹.

A**B**

Supplementary Fig. 1. Linkage disequilibrium among 55 SNPs in the 6p21.31 locus.

(A) D' value. (B) R^2 value. Results in 525 cases (left) and 525 controls (right) are shown. Boxes are shaded according to the pair-wise D' or R^2 values. A SNP, DRB1_2_61, was monomorphic in the cases, therefore, D' and R^2 values were not plotted in the cases.