

	UParis (A29 EUR Carriers)				GHS cohort #1 (A29 EUR)		
	Cases n=286	Ctrls n=108	OR (LCI-UCI)	p-val	Carriers n=4014	OR (LCI-UCI)	p-val
Second HLA-A Allele							
Aw19 co-susceptible (29,30,31,33)	41	4	4.44 (1.55-17.53)	2.20E-03	247	2.63 (1.80-3.78)	1.29E-06
A3002	13	1	5.19 (0.76-222.84)	0.12	45	4.31 (2.11-8.26)	6.15E-05
A3301	9	0	Inf (0.77-Inf)	0.07	39	3.40 (1.43-7.23)	3.2E-03
A0301	26	15	0.63 (0.31-1.35)	0.20	592	0.59 (0.38-0.90)	0.01
A0101	71	17	1.81 (0.99-3.48)	0.04	662	1.73 (1.29-2.31)	2.67E-04
A3201	3	4	0.28 (0.04-1.70)	0.10	152	0.28 (0.06-0.83)	0.01
A0201	64	24	1.03 (0.59-1.85)	1.00	1085	0.80 (0.59-1.08)	0.14
A2902	10	1	3.95 (0.55-173.12)	0.30	48	3.07 (1.37-6.24)	3.6E-03
A2601	8	3	1.03 (0.24-6.13)	1.00	115	1.00 (0.42-2.07)	1.00

Figure 1

	UParis (A29 EUR Carriers)				GHS cohort #1 (A29 EUR)		
Second HLA-A Allele	Cases n=286	Ctrl n=108	OR (LCI-UCI)	p-val	Carriers n=4014	OR (LCI-UCI)	p-val
A2501	3	2	0.57 (0.06-6.96)	0.62	101	0.42 (0.08-1.28)	0.16
A2402	23	11	0.79 (0.35-1.86)	0.55	356	0.92 (0.57-1.44)	0.83
A3101	9	2	1.75 (0.35-16.95)	0.73	115	1.13 (0.50-2.26)	0.71
A1101	14	10	0.52 (0.21-1.34)	0.16	255	0.78 (0.41-1.36)	0.44
A2301	6	2	1.16 (0.20-11.91)	1.00	94	0.92 (0.33-2.10)	1.00
A6801	9	8	0.42 (0.14-1.27)	0.09	128	1.01 (0.45-2.01)	0.86
A19 all (29,30,31,32,33)	44	8	2.07 (0.92-4.64)	0.08	399	1.49 (1.02-2.18)	0.04

Figure 1 (cont.)

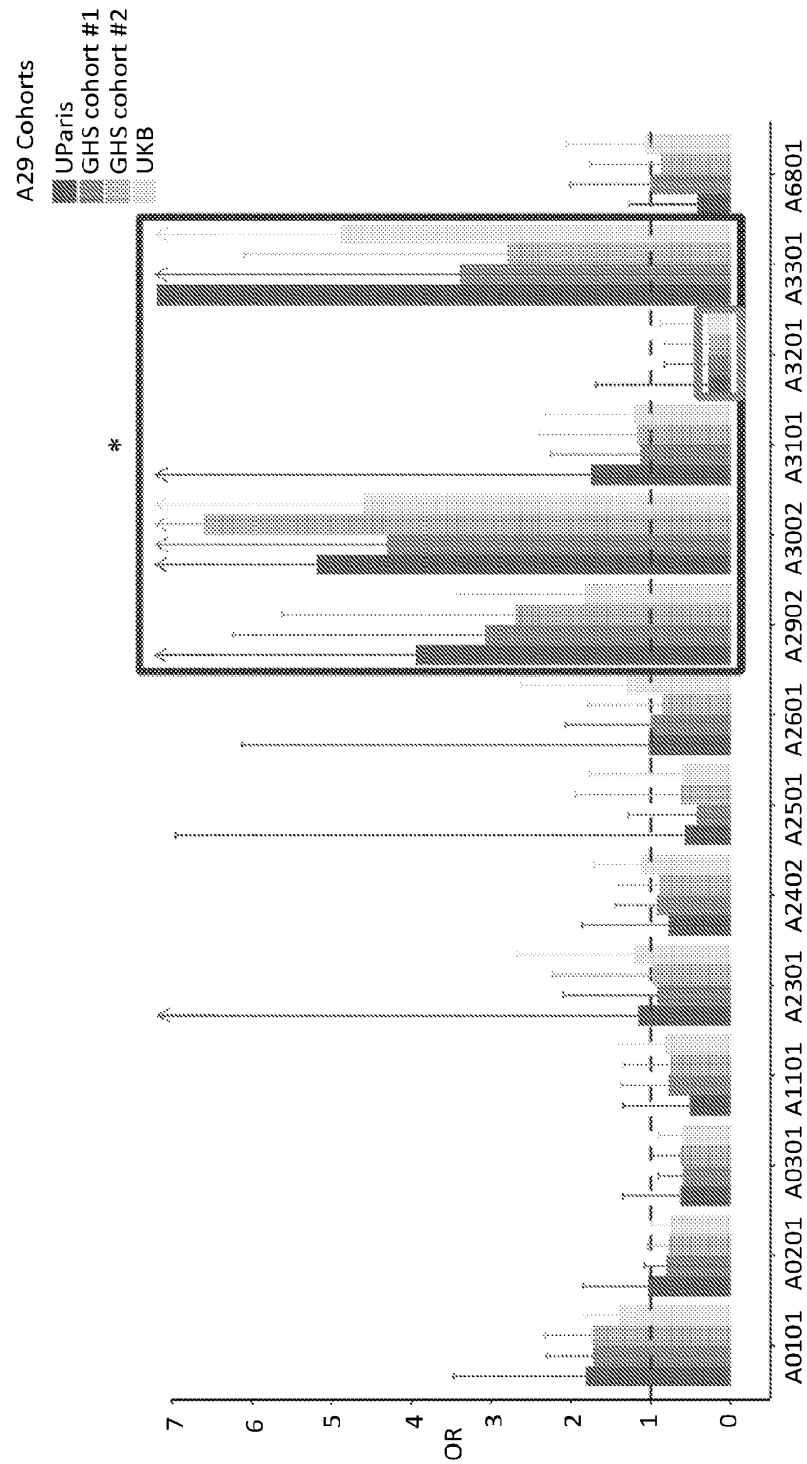
	GHS cohort #2 (A29 EUR)			UKB (A29 EUR)		
	Carriers n=2829	OR (LCI-UCI)	p-val	Carriers n=38,543	OR (LCI-UCI)	p-val
Second HLA-A Allele						
Aw19 co-susceptible (29,30,31,33)	164	2.69 (1.81-3.92)	1.07E-06	2416	2.51 (1.75-3.52)	9.62E-07
A3002	20	6.60 (2.98-14.13)	3.03E-06	396	4.60 (2.39-8.09)	1.25E-05
A3301	32	2.80 (1.16-6.09)	0.01	255	4.89 (2.19-9.56)	1.63E-04
A0301	380	0.63 (0.40-0.97)	0.03	5497	0.60 (0.38-0.90)	0.01
A0101	448	1.74 (1.28-2.33)	3.21E-04	7411	1.39 (1.05-1.83)	0.02
A3201	105	0.27 (0.05-0.82)	0.02	1323	0.30 (0.06-0.88)	0.02
A0201	756	0.78 (0.57-1.04)	0.09	10680	0.75 (0.56-1.00)	0.05
A2902	37	2.70 (1.18-5.61)	9.43E-03	750	1.83 (0.86-3.43)	0.08



Figure 1 (cont.)

	GHS cohort #2 (A29 EUR)			UKB (A29 EUR)		
Second HLA-A Allele	Carriers n=2829	OR (LCI-UCI)	p-val	Carriers n=38,543	OR (LCI-UCI)	p-val
A2601	91	0.85 (0.35-1.78)	0.86	834	1.30 (0.55-2.62)	0.41
A2501	47	0.62 (0.12-1.94)	0.62	673	0.60 (0.12-1.77)	0.50
A2402	249	0.89 (0.55-1.40)	0.74	2801	1.12 (0.69-1.72)	0.57
A3101	75	1.18 (0.51-2.39)	0.57	1015	1.20 (0.54-2.33)	0.58
A1101	177	0.76 (0.40-1.33)	0.44	2278	0.82 (0.44-1.40)	0.61
A2301	61	0.96 (0.34-2.24)	1.00	672	1.21 (0.44-2.68)	0.65
A6801	100	0.87 (0.38-1.76)	0.87	1142	1.07 (0.48-2.06)	0.86
A19 all (29,30,31,32,33)	269	1.58 (1.07-2.34)	0.02	3739	1.51 (1.04-2.18)	0.03

Figure 1 (cont.)



HLA-A alleles

Figure 2

	UParis (A29 EUR Carriers)				GHS cohort #1 (A29 EUR)		
	Cases n=286	Ctrl's n=108	OR (LCI-UCI)	p-val	Carriers n=4014	OR (LCI-UCI)	p-val
Second HLA-A Allele							
Aw19 co-susceptible (29,30,31,33)	41	4	4.05 (1.40-11.77)	0.01	247	2.21 (1.47-3.33)	1.55E-04
A3002	13	1	4.32 (0.55-33.79)	0.16	45	2.78 (1.31-5.88)	7.66E-03
A3301	9	0	6204540.00 (0.00-Inf)	0.98	39	3.12 (1.29-7.58)	0.01
A0301	26	15	0.71 (0.35-1.45)	0.35	592	0.69 (0.45-1.08)	0.11
A0101	71	17	1.84 (1.01-3.35)	0.05	662	1.57 (1.15-2.16)	0.00
A3201	3	4	0.22 (0.05-1.04)	0.06	152	0.30 (0.09-0.97)	4.38E-02
A0201	64	24	0.97 (0.56-1.68)	0.92	1085	0.87 (0.64-1.20)	0.41
A2902	10	1	3.26 (0.40-26.32)	0.27	48	1.83 (0.80-4.20)	0.15
A2601	8	3	1.09 (0.28-4.26)	0.90	115	0.87 (0.39-1.91)	0.72

Figure 3

	UParis (A29 EUR Carriers)				GHS cohort #1 (A29 EUR)		
Second HLA-A Allele	Cases n=286	Ctrl n=108	OR (LCI-UCI)	p-val	Carriers n=4014	OR (LCI-UCI)	p-val
A2501	3	2	0.55 (0.08-3.61)	0.54	101	0.57 (0.16-2.01)	0.38
A2402	23	11	0.85 (0.39-1.85)	0.67	356	0.99 (0.61-1.61)	0.97
A3101	9	2	1.75 (0.37-8.33)	0.48	115	1.42 (0.68-2.97)	0.35
A1101	14	10	0.55 (0.23-1.34)	0.19	255	0.81 (0.45-1.48)	0.50
A2301	6	2	1.06 (0.21-5.47)	0.94	94	0.85 (0.34-2.17)	0.74
A6801	9	8	0.42 (0.16-1.15)	0.09	128	0.95 (0.45-2.04)	0.90
A19 all (29,30,31,32,33)	44	8	2.07 (0.92-4.64)	0.08	399	1.49 (1.02-2.18)	0.04

Figure 3 (cont.)

	GHS cohort #2 (A29 EUR)			UKB (A29 EUR)		
	Carriers n=2829	OR (LCI-UCI)	p-val	Carriers n=38,543	OR (LCI-UCI)	p-val
Second HLA-A Allele						
Aw19 co-susceptible (29,30,31,33)	164	2.49 (1.63-3.81)	2.34E-05	2416	2.24 (1.52-3.30)	4.57E-05
A3002	20	4.26 (1.83-9.92)	7.68E-04	396	4.01 (2.05-7.84)	4.99E-05
A3301	32	2.69 (1.15-6.28)	0.02	255	2.00 (0.80-5.01)	0.14
A0301	380	0.72 (0.46-1.14)	0.16	5497	0.65 (0.43-1.01)	0.05
A0101	448	1.59 (1.15-2.19)	0.01	7411	1.82 (1.35-2.45)	0.00
A3201	105	0.22 (0.06-0.83)	2.52E-02	1323	0.28 (0.08-0.90)	3.33E-02
A0201	756	0.87 (0.63-1.20)	0.41	10680	0.82 (0.61-1.11)	0.20
A2902	37	1.94 (0.84-4.46)	0.12	750	2.10 (1.05-4.23)	0.04

Figure 3 (cont.)

	GHS cohort #2 (A29 EUR)			UKB (A29 EUR)		
	Carriers n=2829	OR (LCI-UCI)	p-val	Carriers n=38,543	OR (LCI-UCI)	p-val
Second HLA-A Allele						
A2601	91	0.91 (0.40-2.09)	0.82	834	0.73 (0.33-1.61)	0.44
A2501	47	0.69 (0.18-2.62)	0.59	673	0.66 (0.20-2.15)	0.49
A2402	249	1.06 (0.65-1.74)	0.81	2801	1.00 (0.63-1.59)	0.99
A3101	75	1.57 (0.72-3.41)	0.25	1015	1.24 (0.58-2.64)	0.57
A1101	177	0.83 (0.45-1.53)	0.54	2278	0.82 (0.46-1.45)	0.49
A2301	61	0.73 (0.28-1.95)	0.53	672	0.85 (0.35-2.10)	0.73
A6801	100	0.76 (0.35-1.67)	0.50	1142	1.43 (0.70-2.91)	0.33
A19 all (29,30,31,32,33)	269	1.58 (1.07-2.34)	0.02	3739	1.51 (1.04-2.18)	0.03

Figure 3 (cont.)

ERAP1	Function	UParis				P
		F cases	F controls	OR		
	rs27044 5:96783148:C:G	Q730E				
	rs17482078 5:96783162:C:G	R725Q				
	rs10050860 5:96786506:C:T	D575N				
	rs30187 5:96788627:T:C	K528R				
	rs2287987 5:96793832:T:C	M349V				
	rs27895 5:96793840:C:T	G346D				
	rs26618 5:96795133:T:C	I276M				
	rs3734016 5:96803761:C:T	E56K				
	rs72773968 5:96803892:G:A	I12T				
Hap 1	I	E	E	E	E	E
Hap 2	T	E	E	E	E	E
Hap 3	T	E	E	E	E	E
Hap 5	T	E	E	E	E	E
Hap 6	T	E	E	E	E	E
Hap 7	T	K	E	E	E	E
Hap 8	T	E	E	E	E	E
Hap 10	T	E	E	E	E	E
		0.17	0.35	0.41	0.48	0.11
		0.28	0.17	1.78		8.0E-3

Figure 4

Gene	Variant	Variant type	Study	OR (LCI-UCI)	p-value	Hom OR	Case MAF	Control MAF	Meta OR (LCI-UCI)	Meta p- value
ERAP2- LNPEP	rs10044354 5:96984791:C:T	Intronic	Kuiper et al.	2.3 (1.69-3.61)	1.21E-06		0.63	0.42	1.95 (1.55-2.44)	6.20E-09
			UParis	1.55 (1.13-2.11)	5.80E-03	2.6 (1.3-5.15)	0.52	0.41		
			LD between rs10044354 (ERAP2-LNPEP) and rs27432 (ERAP1): D' = 0.79 R2 = 0.18							
ERAP1	rs27432 5:96783569:A:G*	Intronic	Kuiper et al.	2.26 (2.05-2.47)	7.20E-05		0.85	0.71	2.46 (1.85-3.26)	4.07E-10
			UParis	2.58 (1.78-3.76)	6.60E-07	4.77 (1.98-11.51)	0.83	0.65		

Figure 5

Gene	Variant	Variant type	Study	OR (LCI-UCI)	p-value	Hom OR	Case MAF	Control MAF	Meta OR (LCI-UCI)	Meta p-value
ERAP2	rs2248374 5:96900192:A:G	Splice region	Kuiper et al.	0.44 (0.31-0.63)	6.60E-06		0.33	0.53	0.56 (0.45-0.70)	2.39E-07
			UParis	0.68 (0.5-0.92)	1.40E-02	0.45 (0.23-0.87)	0.43	0.53		

Figure 6

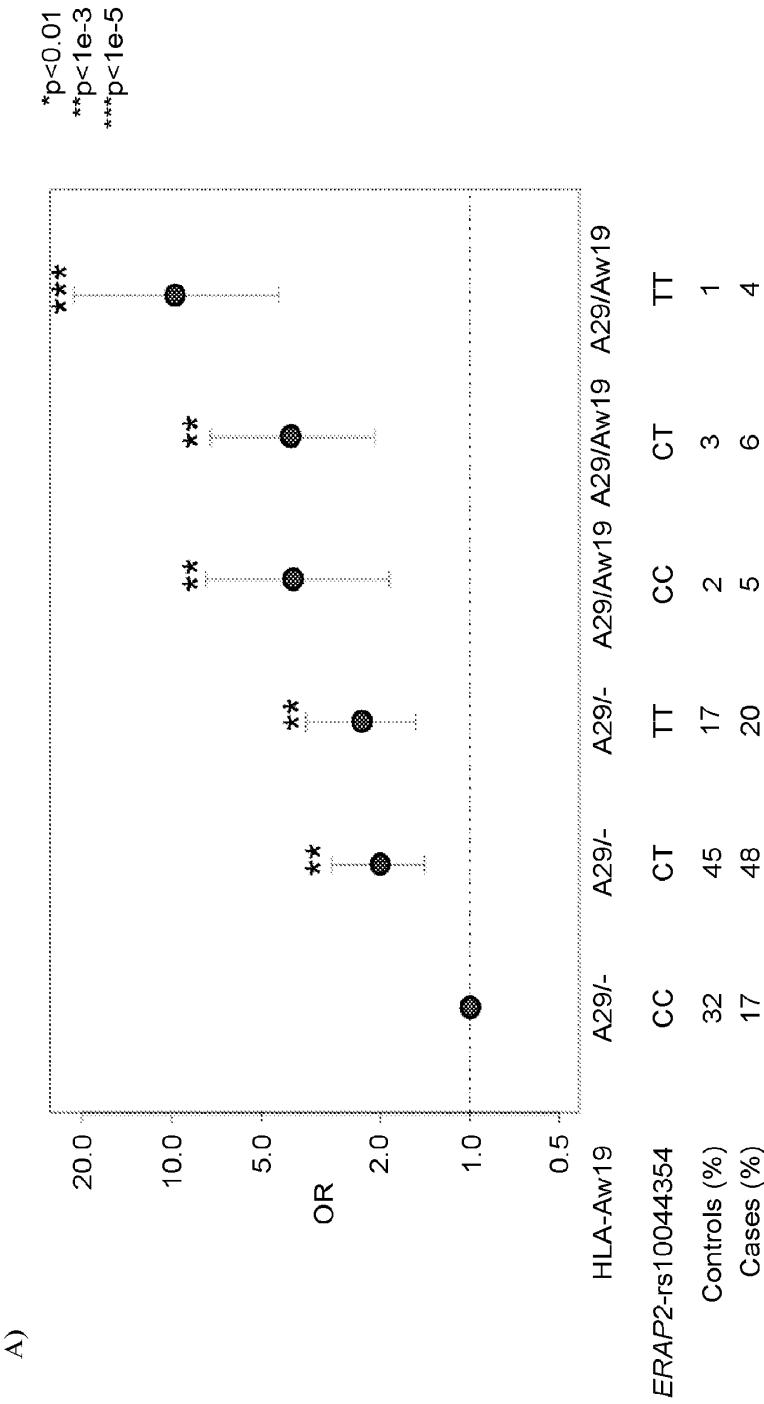


Figure 7

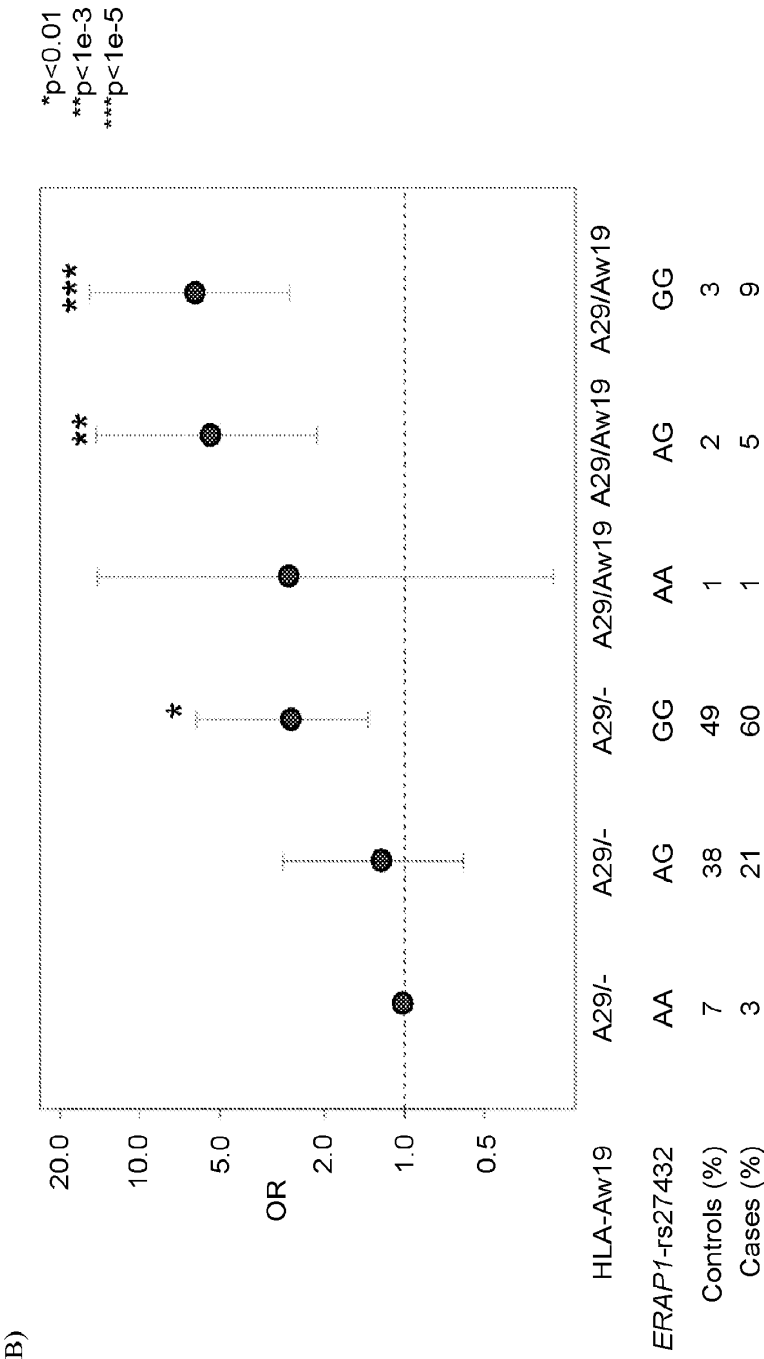
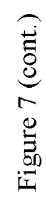


Figure 7 (cont.)



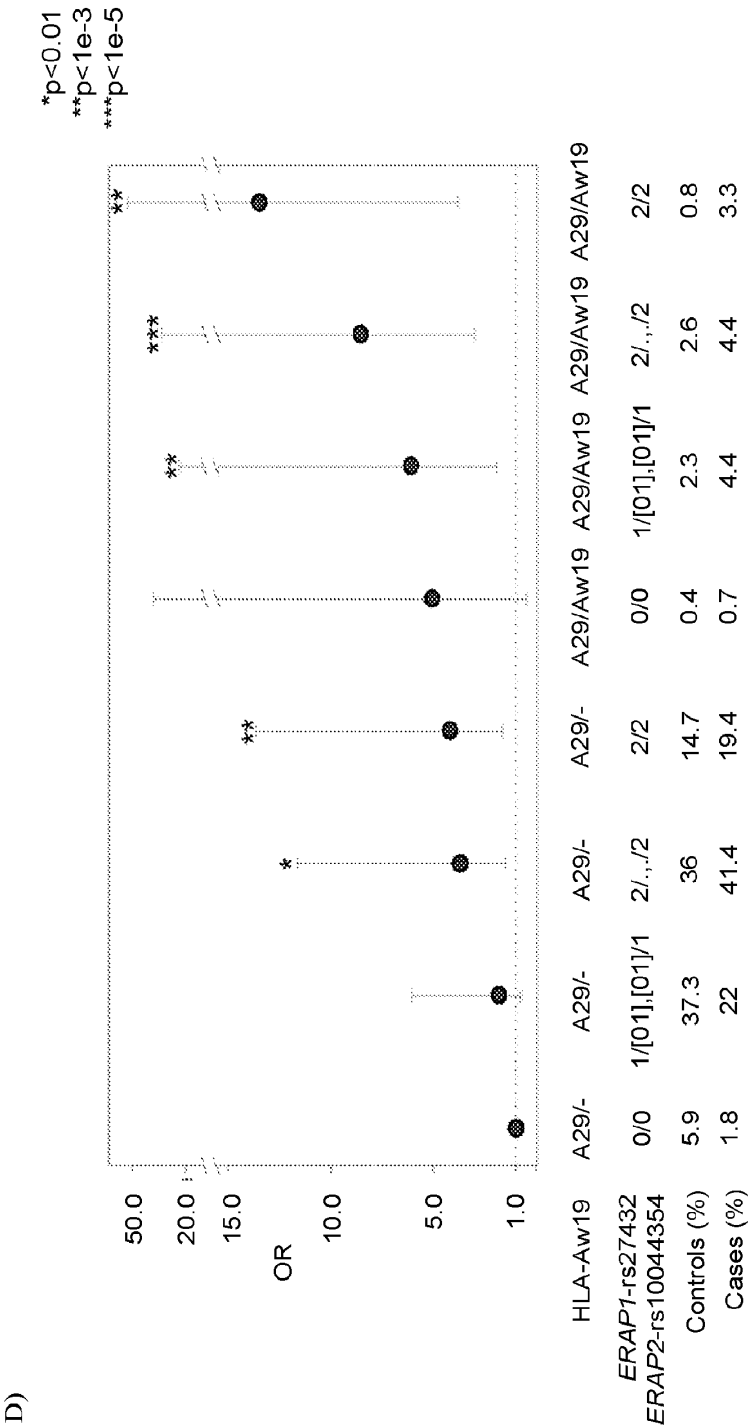


Figure 7 (cont.)

Aw19	ERAP2- rs10044354	Case_n	Contr_n	Case_F	ControlF	OR	OR CI_low	OR CI_high	P
A29/-	CC	46	1296	0.167	0.319	1.000	NA	NA	NA
A29/-	CT	132	1842	0.478	0.453	2.019	1.421	2.911	3.95E-05
A29/-	TT	56	681	0.203	0.167	2.316	1.522	3.539	4.51E-05
A29/Aw19	CC	13	94	0.047	0.023	3.891	1.861	7.644	2.13E-04
A29/Aw19	CT	17	119	0.062	0.029	4.019	2.092	7.413	2.32E-05
A29/Aw19	TT	12	34	0.043	0.008	9.902	4.378	21.197	1.16E-07

Figure 8

Aw19	ERAP1- rs27432	Cases number	Control number	Case freq.	Controls freq.	OR	OR CI_low	OR CI_high	P
A29/-	AA	9	298	0.033	0.073	1.000	NA	NA	NA
A29/-	AG	58	1550	0.212	0.378	1.239	0.601	2.876	0.734
A29/-	GG	164	2001	0.601	0.488	2.713	1.374	6.105	1.72E-03
A29/Aw19	AA	2	24	0.007	0.006	2.747	0.274	14.391	0.209
A29/Aw19	AG	15	91	0.055	0.022	5.430	2.144	14.579	9.32E-05
A29/Aw19	GG	25	133	0.092	0.032	6.196	2.708	15.515	1.54E-06

Figure 9

ERAP1- rs27432	ERAP2- rs10044354	Cases number	Control number	Cases freq.	Controls freq.	OR	OR_Cllo	OR_Clhi	P
AA	CC	7	255	0.026	0.063	1.000	NA	NA	NA
AA	CT	4	60	0.015	0.015	2.420	0.503	9.885	0.236
AA	TT	0	2	0.000	0.000	0.000	0.000	208.116	1.000
AG	CC	19	687	0.070	0.170	1.007	0.400	2.871	1.000
AG	CT	49	856	0.180	0.212	2.084	0.924	5.521	0.072
AG	TT	5	86	0.018	0.021	2.113	0.515	7.964	0.197
GG	CC	32	443	0.118	0.109	2.628	1.118	7.160	0.024
GG	CT	94	1030	0.346	0.255	3.323	1.525	8.594	8.29E-04
GG	TT	62	627	0.228	0.155	3.598	1.617	9.446	4.03E-04

Figure 10

AW19	ERAP1- rs27432	ERAP2- rs10044354	Cases number	Control number	Cases freq.	Controls freq.	OR	OR_Clo	OR_Chi	P	Absolute risk
A29/-	0	0	5	237	0.018	0.059	NA	NA	NA	NA	3.43E-05
A29/-	0/1	0/1	60	1510	0.220	0.373	1.883	0.752	6.071	0.197	6.45E-05
A29/-	2_either	2_either	113	1457	0.414	0.360	3.674	1.506	11.653	1.16E-03	1.26E-04
A29/-	2_both	2_both	53	596	0.194	0.147	4.211	1.666	13.665	6.26E-04	1.44E-04
A29/Aw19	0	0	2	18	0.007	0.004	5.204	0.465	34.701	0.092	1.78E-04
A29/Aw19	0/1	0/1	12	93	0.044	0.023	6.079	1.929	22.651	5.23E-04	2.08E-04
A29/Aw19	2_either	2_either	19	104	0.070	0.026	8.604	3.002	30.314	3.09E-06	2.95E-04
A29/Aw19	2_both	2_both	9	31	0.033	0.008	13.527	3.791	54.766	1.17E-05	4.63E-04

Figure 11

Allele/position	9	17	56	62	63	70	73	76	77	79	80	81	82	83	97	105	109	114	116	152
A*01:01:01:01	F	R	G	Q	E	H	T	A	N	G	T	L	R	G	I	P	F	R	D	A
A*29:02:01:01	T	-	-	L	Q	Q	-	-	-	-	-	-	-	-	M	S	-	-	-	V
A*30:02:01:01	S	S	R	-	-	-	-	E	-	-	-	-	-	-	-	S	-	E	H	R
A*31:01:02:01	T	-	R	-	-	-	I	V	D	-	-	-	-	-	M	S	-	Q	-	V
A*32:01:01:01	-	-	-	-	-	-	-	E	S	R	I	A	L	R	M	-	L	Q	-	V
A*33:01:01:01	T	-	-	R	N	-	I	V	D	-	-	-	-	-	M	S	-	Q	-	V
A*74:01:01:01	-	-	-	-	-	-	-	V	D	-	-	-	-	-	M	-	L	Q	-	V
Ex2															Ex3					

Figure 12