

Supplementary Materials: HLA-DQB1 and HLA-DRB1 variants confer susceptibility to latent autoimmune diabetes in adults: relative predispositional effects among allele groups

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Table S1. Quality assessment scheme for the included literature (Newcastle-Ottawa Scale).

Literature	Selection				Comparability	Exposure			Total
	I	II	III	IV	V	VI	VII	VIII	
Yin N.N. (2017)	*	*	*	*	*	*	*	*	*****
Cejkova P. (2008)	*	*	*		*	*	*	*	*****
Katarina K. (2007)	*	*	*		*		*	*	*****
Desai M. (2007)		*	*	*	*		*	*	*****
Li Q. (2005)	*		*	*	*		*	*	*****
Hosszufalusi N. (2003)	*		*	*	*		*	*	*****
Cerna M. (2003)	*		*	*	*	*	*	*	*****
Vatay A. (2002)	*		*	*	*	*	*	*	*****
Xiao J.Z. (1997)	*		*	*	*		*	*	*****

I: Adequacy of the case definition; II: Representativeness of the cases; III: Selection of controls; IV: Definition of controls; V: Comparability of cases and controls on the basis of the design or analysis; VI: Ascertainment of exposure; VII: Same method of ascertainment for cases and controls; VIII: Nonresponse rate.

Table S2. The main characteristics of LADA patients and controls.

First Author, Year	Male/Female		Mean Age (years)		BMI (kg/m²)		No Treatment Diagnosis (months)	Insulin after	Mean C-peptide (pmol/L)	GADA (ng/mL)	IA-2A	ICAs
	LADA	Control	LADA	Control	LADA	Control						
Yin N.N., 2017	370/282	640/541	50.6±11.3	41.9±16.4			6			+ / –	+ / –	
Cejkova P., 2008					31.6 (26.6-45.4)		6	At onset:		554.5(50.4–2000)		
Katarina K., 2007	17/14						6		478.0 (4.4–1522)	392.0 (5–2800)		
Desai M., 2007		150/177		55.3±19.8(20–91)		25.4±4.0						

Li Q., 2005	UKPDS	110/101		25.1±4.8	3		+		
	W2	74/56		28.6±5.3	12		+		
	YT2D	16/21		27.5±5.8	3		+ / -		+ / -
		23/16	37.5		6		+		
At onset:									
530.0 (240–1400)									
Hosszufalusi N., 2003		25/29	59.0 (47.5–67.0)	23.5 (22.6–27.1)	6	After onset, 1–10 years:	+ / -	+ / -	+ / -
						340.0 (210–1870)			
						After onset, >10 years:			
400.0 (160–1170)									
Cerna M., 2003		30/40		27 (22–37)	6	609.0 (51–2800)	193.0 (3–3000)	+ / -	
Vatay A., 2002		20/22	56.9±2.3		6		+ / -		+ / -
Xiao J.Z., 1997					6		+ / -	+ / -	

BMI: body mass index; GADA: antigitamic acid decarboxylase antibody; IA-2A: islet antigen 2A; ICAs: antibodies against islet cells; + : positive reaction; - : negative reaction; + / - : some patients were positive for GADA, IA-2A or ICAs.

Table S3. Meta-regression with concomitant variables for the heterogeneity analysis.

Allele Group	N	Publication Year		Ethnicity		Sample Size		NOS Score	
		β	p	β	p	β	p	β	p
<i>DQB1*02</i>	8	1.019	0.489	1.781	0.079	1.000	0.193	0.964	0.871
<i>DQB1*03</i>	9	0.996	0.887	0.880	0.724	1.000	0.580	0.780	0.244
<i>DQB1*04</i>	6	1.063	0.052	1.304	0.659	1.001	0.090	1.689	0.028
<i>DQB1*05</i>	5	1.013	0.878	0.345	0.539	0.999	0.478	1.570	0.253
<i>DQB1*06</i>	7	0.974	0.509	1.872	0.075	1.000	0.675	0.830	0.551
<i>DRB1*03</i>	6	0.985	0.617	0.712	0.299	1.000	0.234	0.814	0.271
<i>DRB1*04</i>	6	0.981	0.543	0.922	0.849	1.000	0.709	1.014	0.953
<i>DRB1*07</i>	4	1.064	0.697	0.538	0.139	1.002	0.069	0.447	0.250
<i>DRB1*08</i>	5	0.919	0.181	0.398	0.313	0.999	0.136	0.922	0.902
<i>DRB1*11</i>	4	1.079	0.717	0.727	0.468	0.998	0.288	1.783	0.615
<i>DRB1*12</i>	5	1.108	0.120	2.917	0.139	1.001	0.132	1.732	0.279
<i>DRB1*15</i>	4	0.882	0.471	0.477	0.130	0.998	0.055	3.595	0.055

Note: β , regression coefficient in the form of an index; p , the p value of the meta-regression; Bold: statistically significant p value.

Table S4. Leave-one-out sensitivity analysis for *HLA-DQB1*05*, *HLA-DRB1*08* and *HLA-DRB1*09*.

Allele Group	Leave-one-out study	OR	95% CI	p	I^2	p_h
<i>DQB1*05</i>	Cejkova P. 2008	0.719	0.567-0.913	0.007	19.60%	0.292
	Desai M. 2007	0.919	0.627-1.256	0.594	12.90%	0.328
	Cerna M. 2003	0.883	0.552-1.410	0.601	50.90%	0.107
	Vatay A. 2002	0.706	0.551-0.904	0.006	22.40%	0.276
	Xiao J.Z. 1997	0.769	0.612-0.964	0.023	48.40%	0.121
<i>DRB1*08</i>	Yin N.N. 2017	1.454	0.620-3.412	0.390	67.70%	0.026
	Cejkova P. 2008	1.038	0.484-2.225	0.925	81.50%	0.001
	Desai M. 2007	1.401	0.511-3.839	0.512	83.30%	0.000
	Cerna M. 2003	0.623	0.490-0.792	0.000	37.00%	0.190
	Vatay A. 2002	1.065	0.485-2.340	0.875	81.90%	0.001
<i>DRB1*09</i>	Yin N.N. 2017	1.050	0.474-2.328	0.904	18.60%	0.297
	Cejkova P. 2008	1.344	1.150-1.571	0.000	25.10%	0.261
	Desai M. 2007	1.372	1.173-1.606	0.000	0.00%	0.702
	Cerna M. 2003	1.334	1.141-1.559	0.000	0.00%	0.444
	Vatay A. 2002	1.346	1.152-1.573	0.000	26.20%	0.255

Note: OR, odds ratio; CI, confidence interval; p , probability for overall effect test; p_h , probability for heterogeneity test; Bold: statistically significant p value.

Table S5. Test for publication bias in the association between the *DQB1* and *DRB1* allele groups and the risk of developing LADA.

Allele Group	<i>n</i>	<i>p</i> -Begg	<i>p</i> -Egger
<i>DQB1</i> *02	8	0.902	0.382
<i>DQB1</i> *03	9	0.175	0.229
<i>DQB1</i> *04	6	0.707	0.281
<i>DQB1</i> *05	5	0.462	0.642
<i>DQB1</i> *06	7	0.368	0.322
<i>DRB1</i> *03	6	0.707	0.560
<i>DRB1</i> *04	6	1.000	0.321
<i>DRB1</i> *08	5	0.221	0.127
<i>DRB1</i> *09	5	0.806	0.947

Note: *n*, the number of studies for the corresponding allele group; *p*-Begg, the *p* value of Begg's test; *p*-Egger, the *p* value of Egger's test.

Table S6. The frequencies of *DQB1* and *DRB1* allele groups among populations originating from Asia and Europe.

Allele	Asian		European	
	Count (2 <i>n</i>)	Frequency	Count (2 <i>n</i>)	Frequency
<i>DQB1</i> *02	393	0.101	973	0.318
<i>DQB1</i> *03	1566	0.403	1189	0.310
<i>DQB1</i> *04	239	0.065	68	0.024
<i>DQB1</i> *05	4	0.036	459	0.163
<i>DQB1</i> *06	471	0.121	522	0.186
<i>DRB1</i> *01			265	0.096
<i>DRB1</i> *03	275	0.075	614	0.203
<i>DRB1</i> *04	266	0.073	567	0.187
<i>DRB1</i> *07			408	0.147
<i>DRB1</i> *08	304	0.083	95	0.034
<i>DRB1</i> *09	825	0.226	28	0.010
<i>DRB1</i> *10			18	0.006
<i>DRB1</i> *11			355	0.128
<i>DRB1</i> *12	408	0.112	51	0.018
<i>DRB1</i> *13			278	0.100
<i>DRB1</i> *14			65	0.023
<i>DRB1</i> *15			295	0.106
<i>DRB1</i> *16			95	0.034