Supplementary Material - Genetic discrimination between LADA and childhood-onset type 1 diabetes within the MHC

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Supplementary Note

The Bone Mineral Density in Childhood Study (BMDCS)

BMDCS IS a multicenter, longitudinal study of bone accrual in healthy children. Authors and affiliations are listed below.

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Figure 1. Flow Chart of datasets and overall analysis

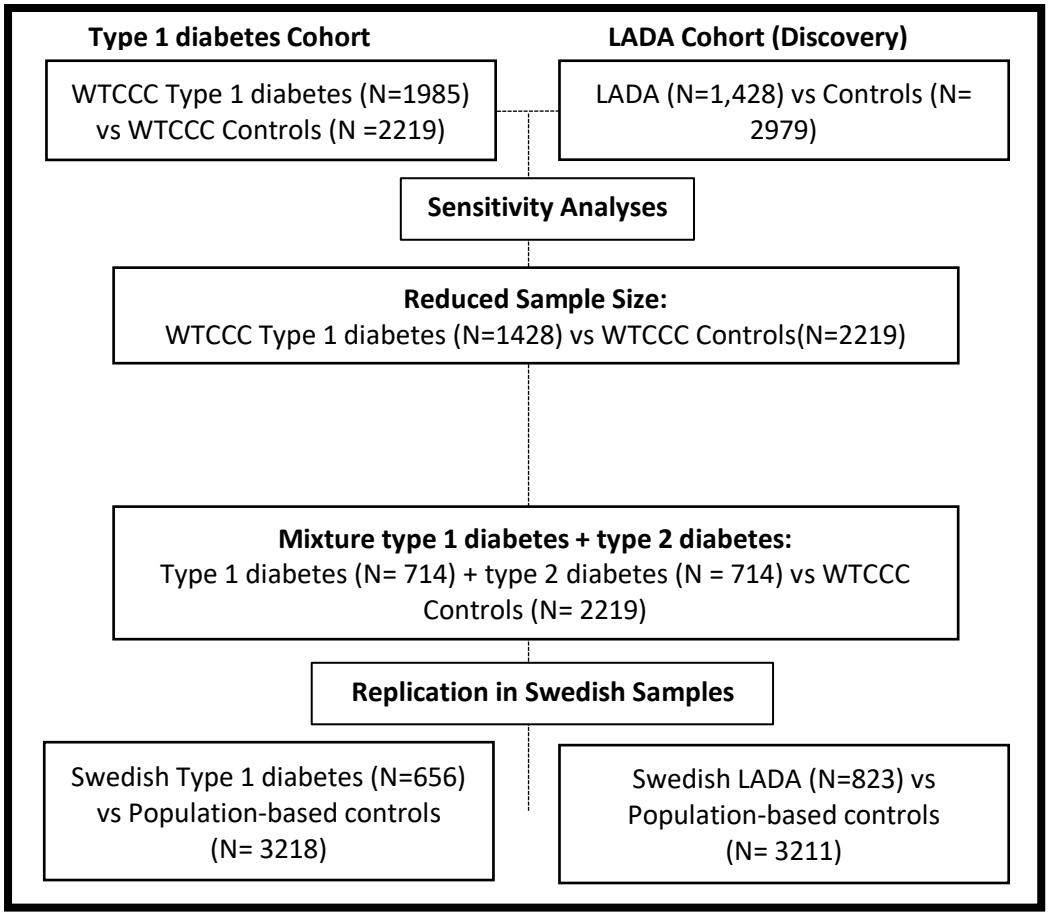
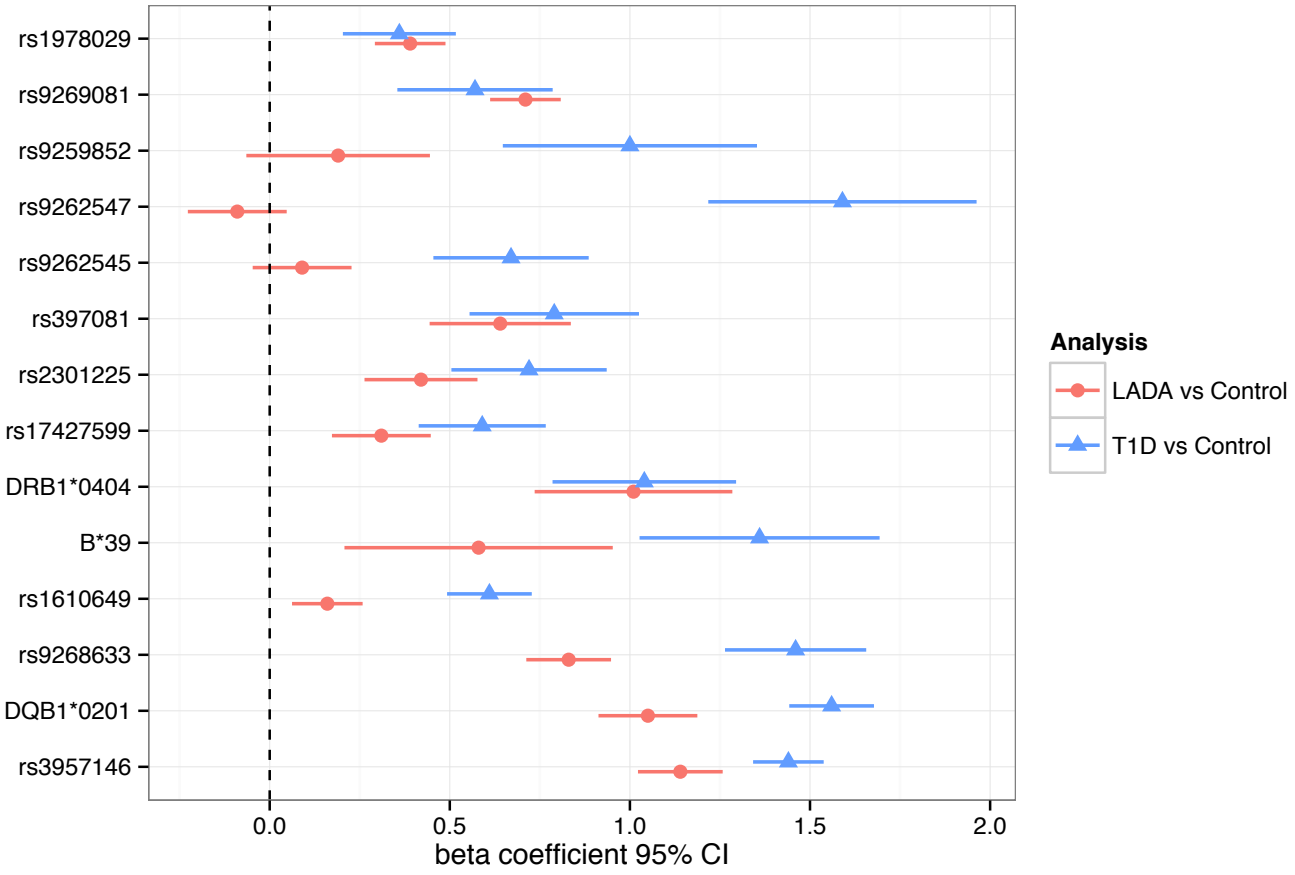


Figure 2. Forest plot of beta coefficient between analyses



Supplementary Table 1. Cohort Information & Quality Control Details

Cohort	LADA, T1D, T2D, or population controls	Population	Details	N	Genotyping chip	Genotyping QC	Imputation QC
ActionLada	LADA	British, German	Aged 30-70 Patients were designated with diabetes according to standard criteria, and LADA was defined as follows: patients 1) aged 30–70 years, 2) with diabetes associated autoantibodies, and 3) who did not require insulin treatment for at least 6 months post diagnosis. Only samples of European ancestry were included. Cohort overlaps with Cousminer DL et al. Diabetes Care (2018)	1051	Illumina Infinium II Omni Express	Individuals with ambiguous sex, genotype missingness > 5%, and relatedness (pi_hat > 0.2) were excluded. PCA was performed to exclude individuals of non-European ancestry.	MAF <0.01
ActionLada 'Plus'	LADA	American and British	LADA was defined as follows: patients 1) aged 30–70 years, 2) with diabetes associated autoantibodies, and 3) who did not require insulin treatment for at least 6 months post diagnosis. A description of participants and study design can be found in Hawa MI et al. Diabetes Care (2013). More details such as exclusion criteria, etc can be found in Cousminer DL et al. Diabetes Care (2018)	441	Illumina Infinium II Omni Express	Individuals with ambiguous sex, genotype missingness > 5%, and relatedness (pi_hat > 0.2) were excluded. PCA was performed to exclude individuals of non-European ancestry.	MAF <0.01
Bone Mineral Density in Childhood Study (BMDCS)	Population controls	American of diverse ethnic backgrounds	Samples of European descent only were included. More details such as recruitment, exclusion criteria, etc can be found in Cousminer DL et al. Diabetes Care (2018)	1296	Illumina Infinium II Omni Express	Individuals with ambiguous sex, genotype missingness > 5%, and relatedness (pi_hat > 0.2) were excluded. PCA was performed to exclude individuals of non-European ancestry.	MAF <0.01
Non-hodgkin lyphomia Controls (dbGaP)	Population controls	USA, Multiple European countries, Australia	More details such as recruitment, inclusion and exlusion, etc can be found in Berndt et al	1683	Illumina Omni Express	Individuals with genotype missingness > 5% were excluded. PCA was performed to exclude individuals of non-European ancestry.	MAF <0.01
Wellcome Trust Case Control Consortium	1958 British Birth Control Cohort	England, Scotland and Wales	More details such as recruitment, inclusion and exclusion criteria, etc can be found in WTCCC Nature (2007)	3000	Illumina 1.2 M	Individuals with ambiguous sex, genotype missingness > 5%, and duplicates and relatedness (pi_hat > 0.2) were excluded. PCA was performed to exclude individuals of non-European ancestry.Single nucleotide polymorphisms (SNPs) with a call rate <95%, Hardy-Weinberg equilibrium P<10-5 and with A/T and G/C alleles were removed.	MAF <0.01
	T1D	England, Scotland and Wales	More details such as recruitment, inclusion and exclusion criteria, etc can be found in WTCCC Nature (2007). Type 1 diabetes cases were insulin dependent since diagnosis, with a minimum period of at least 6 months, and an age of diagnosis below 17 years.	2000	Affymetrix 500 M	Individuals with ambiguous sex, genotype missingness > 5%, and rduplicates were excluded. PCA was performed to exclude individuals of non-European ancestry.Single nucleotide polymorphisms (SNPs) with a call rate <95%, Hardy-Weinberg equilibrium P<10-5 and with A/T and G/C alleles were removed.	MAF <0.01
	T2D	England, Scotland and Wales	More details such as recruitment, inclusion and exclusion criteria, etc can be found in WTCCC Nature (2007)	1999	Affymetrix 500 M	Individuals with ambiguous sex, duplicates, and genotype missingness > 5%. PCA was performed to exclude individuals of non-European ancestry.Single nucleotide polymorphisms (SNPs) with a call rate <95%, Hardy-Weinberg equilibrium P<10-5 and with A/T and G/C alleles were removed.	MAF <0.01

All New Diabetics In Scania (ANDIS), and Scania Diabetes Registry (SDR)	LADA	Scania, Sweden	**ANDIS**: GAD (ELISA: Negative:< 5 U/ml, Positive:=> 10 U/ml, RIA: Negative:0-34 U/ml, Positive:> 50 U/ml); LADA: Age at onset ≥ 35 years, GAD (ELISA) > 10 kE/L, GAD (RIA) >50 U/ml, Cohort reference: http://andis.ludc.med.lu.se/; **SDR**: GAD (Wallenberg lab (AU ref < 5.0), GAD (Wallenberg lab (IU/ml ref <32); LADA: Age at onset ≥ 35, GAD ≥ 10 AU, GAD ≥ 50 IU/ml, For patients that did not fulfill the criteria for any of the above, the diagnosis given by their physician was used, Cohort reference: Lindholm E, Agardh E, Tuomi T, Groop L, Agardh CD. Classifying diabetes according to the new WHO clinical stages. Eur J Epidemiol. 2001;17(11):983-9. Epub 2002/10/17	823	Illumina Infinium Omni Express Exome	Exclude individuals: Call rate < 95%; ambiguous gender; genome-wide heterozygosity (3 SD from mean); duplicates or related individuals (pi-hat >= 0.2); average pi-hat outliers; population outliers. Exclude SNPs: monomorphic; (MAF >= 0.05 and SNP missing rate > 0.05); (MAF < 0.05 and SNP missing rate > 0.01); (MAF >= 0.05 and HWE <= 0.00000057); (MAF < 0.05 and HWE <= 0.0001)	MAF <0.01
Scania Diabetes Registry (SDR)	T1D	Scania, Sweden	GAD (Wallenberg lab (AU ref < 5.0), GAD (Wallenberg lab (IU/ml ref <32), C-peptide (Klin kem (RIA) ref 0.25-0.75), C-peptide (Klin kem ref 0.3-1.3), C-peptide (Lund (ref 0.25-0.75); T1D: Age at onset < 35, GAD ≥ 20 AU, GAD ≥ 100 IU/ml, C-peptide ≥ 0.25 (Klin kem (RIA)), C-peptide ≥ 0.3 (Klin kem), C-peptide ≥ 0.25 (Lund), For patients that did not fulfill the criteria for any of the above, the diagnosis given by their physician was used, Cohort reference: Lindholm E, Agardh E, Tuomi T, Groop L, Agardh CD. Classifying diabetes according to the new WHO clinical stages. Eur J Epidemiol. 2001;17(11):983-9. Epub 2002/10/17	656	Illumina Infinium Omni Express	Exclude individuals: Call rate < 95%; ambiguous gender; genome-wide heterozygosity (3 SD from mean); duplicates or related individuals (pi-hat >= 0.2); average pi-hat outliers; population outliers. Exclude SNPs: monomorphic; (MAF >= 0.05 and SNP missing rate > 0.05); (MAF < 0.05 and SNP missing rate > 0.01); (MAF >= 0.05 and HWE <= 0.00000057); (MAF < 0.05 and HWE <= 0.0001)	
Malmö Diet and Cancer Study–Cardiovascular Cohort (MDC-CC)	Population controls	Malmö, Sweden	More details such as recruitment, inclusion and exclusion criteria, etc can be found in Rosvall M, Persson M, Ostling G, et al. Risk factors for the progression of carotid intima-media thickness over a 16-year follow-up period: the Malmo Diet and Cancer Study. Atherosclerosis. Apr 2015;239(2):615-621.	3218	Illumina Infinium Omni Express Exome	Exclude individuals: Call rate < 95%; ambiguous gender; genome-wide heterozygosity (3 SD from mean); duplicates or related individuals (pi-hat >= 0.2); population outliers. Exclude SNPs: monomorphic; SNP missing rate > 0.05; HWE <= 10e-6	

Supplementary Table 2. Power Calculation to detect significant signals in LADA cohort

Assumptions multiplicative model (log additive model) for non-MHC Class II signals, Significance level: 0.00000883,LADA cases=1428, Controls = 2979

	Odds Ratio					
Disease allele frequency	**3**	**2**	**1.8**	**1.6**	**1.4**	**1.35**
0.01	**89.70%**	14.50%	5.30%	1.30%	0.20%	0.10%
0.03	**100%**	**90.90%**	64.90%	25.80%	3.80%	1.90%
0.05	**100%**	**99.80%**	**95.60%**	65.10%	14.70%	7.60%
0.1	**100%**	**100%**	**100%**	**98.50%**	58.10%	37.60%
0.2	**100%**	**100%**	**100%**	**100%**	**95.40%**	**84.30%**
0.3	**100%**	**100%**	**100%**	**100%**	**99.4%**	**95.9%**

Supplementary Table 3. Independent association signals from the conditional analysis in type 1 diabetes cases vs WTCCC controls.

Conditional P-value, beta, and standard error(SE) are calculated from stepwise regression conditional on all SNP/HLA-Alleles in rows above (first column) in 1985 type 1 diabetes cases vs. 2219 controls. *Conditional P-value from stepwise regression conditional on all SNPs/HLA-Alleles (column 1) in rows above. Position is base pair position according to build 36 of the human genome reference. Linkage disequilibrium (LD) (r^2) is between the SNP/HLA allele and most significant (top) classical HLA allele. "P" in the allele column indicates that the HLA allele is present and "A" indicates absent.A*24 did not reach significance after conditioning on all variants in the first column.

SNP/HLA-Allele	Locus	Position	Alleles (Major/ Minor)	Minor Allele Frequency		Odds Ratio (95% CI)	Single Marker P-value	Conditional			Top Classical HLA allele	LD (r^2)
				Cases	Controls			P-value	Beta	SE		
rs3957146	*HLA-DQA2*	32789508	T/C	0.385	0.113	4.91 (4.39- 5.50)	8.94E-165	8.94E-165	1.44	0.05	*DQB1*0302*	0.99
DQB1*0201	*HLA-DQB1*	32739039	A/P	0.338	0.140	3.13 (2.81-3.49)	1.02E-91	7.98E-153	1.56	0.06	*DQB1*0201*	1.00
rs9268633	*HLA-DRA*	32514451	A/G	0.017	0.197	0.07 (0.06-0.09)	5.94E-132	5.62E-53	-1.46	0.10	*DRB1*1501*	0.59
rs1610649	*HLA-G*	29876896	A/G	0.384	0.418	0.87 (0.79-0.94)	5.59E-04	6.89E-23	-0.61	0.06	*B*39*	0.00
B*39	*HLA-B*	31431272	A/P	0.043	0.016	2.73 (2.07-3.62)	1.82E-12	1.06E-15	1.36	0.17	*B*39*	1.00
DRB1*0404	*HLA-DRB1*	32660042	A/P	0.082	0.048	1.75 (1.47-2.09)	5.47E-09	6.17E-15	1.04	0.13	*DRB1*0404*	1.00
rs17427599	*HLA-DQB1*	32775342	C/T	0.151	0.245	0.55 (0.49-0.61)	2.16E-23	7.97E-12	-0.59	0.09	*DPB1*0402*	0.00
rs2301225	*HLA-DPA1*	33143838	C/T	0.059	0.109	0.51 (0.44-0.60)	1.07E-16	9.56E-12	-0.72	0.11	*DPB1*0402*	0.96
rs397081	*NOTCH4*	32300595	T/C	0.095	0.045	2.22 (1.86-2.65)	2.20E-18	1.11E-10	0.79	0.12	*A*3201*	0.00
rs9262545	*MUC22*	31101041	G/A	0.087	0.119	0.70 (0.61 -0.81)	4.89E-06	7.83E-11	-0.67	0.11	*A*3201*	0.00
rs9262547	*MUC22*	31101206	T/A	0.135	0.119	1.16 (1.02-1.32)	0.034	7.17E-17	1.59	0.19	*A*3201*	0.00
rs9259852	*HLA-A*	30004400	T/C	0.023	0.041	0.55 (0.43-0.72)	3.04E-06	2.04E-08	-1.00	0.18	*A*3201*	0.96
rs9269081	*HLA-DRA*	32549078	C/A	0.110	0.265	0.34 (0.30-0.39)	1.19E-62	1.61E-07	-0.57	0.11	*DQB1*0602*	0.00
rs1978029	*HLA-DQB2*	32839688	T/C	0.349	0.463	0.62 (0.57-0.68)	2.53E-22	1.92E-06	-0.36	0.08	*A*24*	0.00

Supplementary Table 4. Independent association signals from the conditional analysis in LADA cases vs controls.

Conditional P-value, beta, and standard error(SE) are calculated from stepwise regression conditional on all SNP/HLA-alleles in rows above (first column) in 1428 LADA cases vs. 2979 controls. Conditional P-value from stepwise regression conditional on all SNPs/HLA-Alleles (column 1) in rows above. Position is base pair position according to build 36 of the human genome reference. LD (r^2) is between the SNP/HLA allele and the most significant (top) classical HLA allele. "P" in the allele column indicates the HLA allele is present and "A" indicates absent. ^DPB1*0402 did not reach significance after conditioning on all variants in the first column. For conditional association analysis results for *HLA-B*39* and rs1619379 see **Supplementary Table 3**.

SNP/HLA-Allele	Locus	Position	Alleles (Major /Minor)	Minor Allele Frequency		Odds Ratio (95% CI)	Single Marker P-value	Conditional			Top Classical HLA allele	LD (r^2)
				Cases	Controls			P-value*	Beta	SE		
rs3957146	*HLA-DQA2*	32789508	T/C	0.251	0.101	3.03 (2.63-3.33)	1.80E-68	1.80E-68	1.14	0.06	DQB1*0302	0.99
DRB1*03	*HLA-DRB1*	32660042	A/P	0.209	0.118	1.99 (1.76-2.24)	5.31E-35	3.23E-52	1.07	0.07	DRB1*03	1
rs9269081	*HLA-DRA*	32549078	C/A	0.179	0.315	0.47 (0.42 -0.53)	1.40E-42	3.54E-16	-0.49	0.06	DQB1*0604	0.01
DRB1*0404	*HLA-DRB1*	32660042	A/P	0.037	0.035	1.04 (0.82-1.33)	0.328084	3.08E-11	0.95	0.14	DRB1*0404	1
DQB1*0604	*HLA_DQB1*	32739039	A/P	0.059	0.035	1.75 (1.43-2.17)	5.73E-07	1.55E-10	0.81	0.13	DQB1*0604	1
rs2143462	*C6orf10*	32443182	C/T	0.221	0.167	1.42 (1.26-1.58)	1.39E-08	8.24E-08	0.47	0.09	DPA1*02	0.01
DPA1*02	*HLA-DPA1*	33145064	A/P	0.148	0.186	0.76 (0.67-0.86)	1.23E-04	1.62E-06	-0.34	0.07	DPA1*02	1
rs3130192	*HLA-DPB1*	33169908	C/T	0.066	0.103	0.62 (0.52-0.73)	3.96E-08	5.32E-06	-0.42	0.09	^DPB1*0402	0.85

Supplementary Table 5. Independent association signals from the conditional analysis in the downsampled cohort of type 1 diabetes cases (n=1,428) vs controls.

Conditional P-value calculated from stepwise regression conditional on all SNP/HLA-alleles in rows above (first column) in 1428 type 1 diabetes cases versus 2219 controls. Shaded rows denote that this MHC Class I signal appeared in the full type 1 diabetes vs WTCCC dataset but not in LADA vs control set. *rs1619379 is in LD with rs1610649 (r2=0.822), which is consistent in the full type 1 diabetes vs WTCCC dataset. "P" in the allele column indicates the HLA allele is present and "A" indicates absent. ^C*07 did not reach significance after conditioning on all variants in the first column.

SNP/HLA-Allele	Locus	Position	Allele (Major /Minor)	Minor Allele Frequency		Odds Ratio	Single Marker	Conditional			Top Classical	LD
				Cases	Controls	(95% CI)	P-value	P-value*	Beta	Standard Error	HLA allele	(r2)
rs3957146	*HLA-DQA2*	32789508	T/C	0.39	0.113	5.02 (4.45-5.66)	2.98E-157	2.98E-157	1.57	0.06	DQB1*0302	0.99
DQB1*0201	*HLA-DQB1*	32739039	A/P	0.338	0.14	3.14 (2.80-3.528)	7.33E-81	3.27E-136	1.67	0.07	DQB1*0201	1
rs9268633	*HLA-DRA*	32514451	G/A	0.02	0.197	0.08 (0.06-0.11)	6.40E-102	2.02E-37	-1.35	0.11	DQB1*0602	0.53
rs1619379	*HLA-G*	29893214	G/A	0.398	0.432	0.87 (0.79-0.95)	0.002	1.37E-17	-0.56	0.07	DRB1*0404	0
DRB1*0404	*HLA-DRB1*	32660042	A/P	0.083	0.048	1.78 (1.47-2.15)	1.54E-08	9.91E-13	0.98	0.14	DRB1*0404	1
B*39	*HLA-B*	31431272	A/P	0.043	0.016	2.79 (2.08-3.75)	5.09E-12	5.58E-14	1.43	0.19	B*39	1
rs2301225	*HLA-DPA1*	33143838	C/T	0.057	0.109	0.49 (0.41-0.59)	1.60E-14	3.96E-12	-0.81	0.12	DPB1*0402	0.96
rs9267665	*C2*	31978835	C/T	0.082	0.03	2.92 (2.35-3.64)	1.86E-21	1.73E-09	0.88	0.15	DQB1*0602	0
rs9269081	*HLA-DRA*	32549078	C/A	0.11	0.265	0.34 (0.30-0.39)	1.60E-54	1.79E-13	-0.8	0.11	DQB1*0602	0.31
rs9262545	*MUC22*	31101041	G/A	0.087	0.119	0.70 (0.60-0.82)	8.07E-06	3.36E-09	-0.67	0.11	A*24	0
rs9262547	*MUC22*	31101206	T/A	0.133	0.119	1.13 (0.98-1.31)	0.16388	9.69E-14	1.64	0.22	B*14	0
rs549182	*NOTCH4*	32313023	G/A	0.074	0.02	3.93 (3.05-5.06)	5.59E-28	1.20E-06	1.33	0.27	B*14	0
rs2853928	*HLA-C*	31365490	G/T	0.372	0.295	1.42 (1.28-1.57)	3.22E-11	1.26E-06	0.48	0.1	^C*07	0.79

Supplementary Table 6. Independent association signals from the conditional analysis in the downsampled cohort of type 1 diabetes cases (n=714) vs controls.

Conditional P-value calculated from stepwise regression conditional on all SNP/HLA-alleles in rows above (first column) in 714 type 1 diabetes cases versus 2219 controls. Shaded rows denote that this MHC Class I signal appeared in the full type 1 diabetes vs WTCCC dataset but not in LADA vs control set. "P" in the allele column indicates the HLA allele is present and "A" indicates absent. ^DPB1*0402 did not reach significance after conditioning on all variants in the first column.

SNP/HLA-Allele	Locus	Position	Allele (Major /Minor)	Minor Allele Frequency		Odds Ratio (95% CI)	Single Marker P-value	Conditional			Top Classical HLA allele	LD (r2)
				Cases	Controls			P-value	Beta	SE		
rs3957146	*HLA-DQA2*	32789508	T/C	0.399	0.112	5.25 (4.55-6.06)	3.69E-112	3.69E-112	1.75	0.08	DQB1*0302	0.99
rs2187668	*HLA-DQA1*	32713862	G/A	0.319	0.14	2.88 (2.50-3.32)	2.33E-48	6.42E-88	1.83	0.09	DRB1*0301	0.99
rs9268633	*HLA-DRA*	32514451	G/A	0.014	0.197	0.06 (0.04-0.09)	1.61E-57	3.77E-24	-1.35	0.13	DRB1*1501	0.59
B*39	*HLA-B*	31431272	A/P	0.047	0.015	3.20 (2.26-4.53)	1.26E-10	4.75E-15	1.94	0.25	B*39	1
DRB1*0404	*HLA-DRB1*	32660042	A/P	0.076	0.049	1.62 (1.27-2.06)	1.68E-04	1.23E-13	1.19	0.16	DRB1*0404	1
rs1610649	*HLA-G*	29876896	A/G	0.374	0.418	0.83(0.74-0.83)	0.002	2.17E-12	-0.6	0.09	DPB1*0402	0
rs9262545	*MUC22*	31101041	G/A	0.08	0.119	0.64 (0.52-0.80)	1.57E-05	2.81E-08	-0.72	0.13	DPB1*0402	0
rs2249168	*MUC21*	31066233	C/T	0.131	0.124	1.06 (0.89-1.27)	0.81	2.65E-09	1.38	0.23	^DPB1*0402	0

Supplementary Table 7. Independent association signals from the conditional analysis in a sample of randomly selected type 1 diabetes and type 2 diabetes cases vs controls.

Conditional P-value calculated from stepwise regression conditional on all SNP/HLA-alleles in rows above (first column) in 714 type 1 diabetes cases + 714 type 2 diabetes cases versus 2219 controls. Shaded rows highlight the MHC Class I signals that appear in the full type 1 diabetes vs WTCCC conditional analysis. "P" in the allele column indicates that the HLA allele is present and "A" indicates absent. ^B*39 did not reach significance after conditioning on all variants in the first column.

SNP/HLA-Allele	Locus	Position	Allele (Major /Minor)	Minor Allele Frequency		Odds Ratio (95% CI)	Single Marker P-value	Conditional			Top Classical HLA allele	LD (r2)
				Cases	Controls			P-value	Beta	Standard Error		
rs3957146	*HLA-DQA2*	32789508	T/C	0.256	0.112	2.72 (2.40-3.09)	1.16E-52	1.16E-52	0.99	0.07	DQB1*0302	0.99
rs2187668	*HLA-DQA1*	32713862	G/A	0.234	0.14	1.88 (1.66-2.12)	2.71e-27	1.03E-38	0.89	0.07	DRB1*0301	0.99
DRB1*0404	*HLA-DRB1*	32660042	A/P	0.059	0.049	1.22 (0.99-1.51)	0.075	2.11E-10	0.85	0.13	DRB1*0404	1
rs1619379	*HLA-G*	29893214	G/A	0.4	0.43	0.88(0.800.97)	0.014	1.60E-07	-0.3	0.06	B*39	0
rs9262545	*MUC22*	31101041	G/A	0.083	0.119	0.67 (0.57-0.79)	3.43E-07	6.42E-07	-0.44	0.09	B*39	0
rs9262547	*MUC22*	31101206	T/A	0.117	0.118	0.99 (0.85-1.14)	0.548	3.03E-16	1.63	0.2	B*39	0
HLA_B_39	*HLA-B*	31431272	A/P	0.03	0.015	1.99 (1.44-2.77)	4.73E-05	2.61E-06	0.88	0.19	^B*39	1

Supplementary Table 8. Independent association signals from the conditional analysis in type 1 diabetes vs controls in the Swedish replication cohort.

Conditional P-value calculated from stepwise regression conditional on all SNP/HLA-Alleles in rows above (first column) in 656 type 1 diabetes cases versus 3218 controls. Position is base pair position according to build 36 of the human genome reference. Shaded rows denote this signal appeared in the full type 1 diabetes vs WTCCC dataset. LD (r^2) is between the SNP/HLA allele and top classical HLA allele. "P" in the allele column indicates the HLA allele is present and "A" indicates absent. ^DQB1*0503 did not reach significance after conditioning on all variants in the first column.

SNP/HLA-Allele	Locus	Position	Alleles (Major /Minor)	Minor Allele Frequency		Odds Ratio (95% CI)	Single Marker P-value	Conditional			Top Classical HLA allele	LD (r2)
				Cases	Controls			P-value*	Beta	Standard Error		
rs9275206	*HLA-DQA1*	32765543	A/G	0.393	0.147	3.70 (3.33-4.34)	6.35E-89	6.35E-89	1.57	0.08	DQB1*0302	0.99
DQB1*0201	*HLA-DQB1*	32739039	A/P	0.312	0.129	3.07 (2.67-3.52)	2.17E-58	1.96E-135	1.98	0.08	DQB1*0201	1
DQB1*0602	*HLA-DQB1*	32739039	A/P	0.005	0.138	0.03 (0.02-0.07)	2.41E-43	1.85E-40	-1.26	0.09	DQB1*0602	1
rs9269081	*HLA-DRA*	32549078	C/A	0.076	0.262	0.23(0.19-0.29)	1.60E-45	1.99E-30	-0.82	0.07	DRB1*0401	0.06
rs3129871	*HLA-DRA*	32514320	C/A	0.095	0.335	0.21(0.17-0.25)	1.27E-65	3.33E-22	-0.63	0.07	DRB1*0401	0.06
rs9784758	*TAP2*	32896489	T/C	0.212	0.091	2.70(2.27-3.13)	2.02E-34	1.03E-23	0.97	0.1	DRB1*0401	0.11
rs805294	*LY6G6C*	31796196	C/T	0.53	0.359	2.01(1.78-2.27)	6.41E-30	8.02E-20	0.55	0.06	B*39	0
rs707919	*LY6G5B*	31749118	T/C	0.333	0.31	1.11(0.98-1.27)	0.04	5.61E-16	0.42	0.05	DRB1*0401	0.13
rs3130192	*HLA-DPB1*	33169908	C/T	0.049	0.107	0.43(0.33-0.56)	6.17E-10	8.83E-15	-0.77	0.1	DPB1*0402	0.88
rs11969522	*PSMB9*	32967803	G/C	0.081	0.033	0.44 (0.39-0.49)	5.98E-16	6.45E-13	-1.1	0.15	B*39	0
rs9275425	*HLA-DQB1*	32778852	C/A	0.487	0.293	2.22(2.04-2.56)	1.33E-40	2.54E-12	0.37	0.05	B*39	0.01
rs1053924	*PRRT1*	32228693	G/A	0.144	0.305	0.38(0.32-0.45)	1.16E-32	8.02E-11	-0.43	0.07	B*39	0
B*39	HLA-B	31431272	A/P	0.034	0.013	2.75(1.90-3.98)	6.80E-09	1.74E-10	1.54	0.24	B*39	1
rs2735028	*HLA-G*	29893517	G/A	0.319	0.335	0.93(0.82-1.05)	0.315203	1.10E-09	-0.39	0.06	A*0101	0.42
rs3104407	*HLA-DQA2*	32790430	A/G	0.244	0.457	0.38(0.33-0.44)	5.10E-45	3.01E-10	-0.36	0.06	DRB1*0401	0.12
rs3104406	*HLA-DQA2*	32790421	G/A	0.143	0.339	0.33(0.28-0.38)	2.23E-39	9.71E-11	-0.37	0.06	DQB1*0301	0.11
rs2239803	HLA-DRA	32519811	G/A	0.543	0.436	1.54(1.37-1.72)	3.33E-13	3.67E-09	0.32	0.05	DQB1*0503	0.01
rs3117099	*BTNL2*	32466248	C/T	0.361	0.246	1.73(1.53-1.97)	3.29E-17	7.95E-11	0.35	0.05	DQB1*0604	0.06
rs549182	*NOTCH4*	32313023	G/A	0.04	0.017	2.44(1.75-3.41)	9.09E-09	1.37E-06	0.97	0.2	DQB1*0503	0.01
rs3135392	*HLA-DRA*	32517220	G/T	0.446	0.417	1.13(1.00-1.27)	0.04	3.23E-07	0.15	0.03	DRB1*0401	0.15
rs3132132	*HLA-DMB*	33009912	G/A	0.082	0.116	0.68(0.55-0.84)	6.15E-04	1.81E-06	-0.46	0.1	DRB1*0401	0.01
rs3129727	*HLA-DQA2*	32787668	C/T	0.001	0.021	0.04(0.01-0.26)	1.44E-06	7.31E-06	-1.09	0.24	^DQB1*0503	0.99

Supplementary Table 9. Independent association signals from the conditional analysis in LADA vs controls in the Swedish replication cohort.

Conditional P-value calculated from stepwise regression conditional on all SNP/HLA-Alleles in rows above (first column) in 823 LADA cases versus 3211 controls. “P” in the allele column indicates the HLA allele is present and “A” indicates absent. The HLA-B*39 frequency is 0.025 in cases and 0.013 in controls. The frequency of rs1619379 is 0.392 in cases and 0.387 in controls.

SNP/HLA-Allele	Locus	Position	Allele (Major /Minor)	Minor Allele Frequency		Odds Ratio (95% CI)	Single Marker P-value	Conditional			Top Classical HLA allele	LD (r2)	HLA-B*39			rs1619379 (HLA-G)		
				Cases	Controls			P-value*	Beta	Standard Error			P-value	Beta	SE	P-value	Beta	SE
rs3129882	*HLA-DRA*	32517508	A/G	0.223	0.378	0.47(0.42-0.54)	3.51E-10	3.51E-10	-0.84	0.13	DRB1*15	0.2	0.2	0.507	0.396	0.764	0.039	0.13
rs2596560	*MICA*	31463297	A/G	0.586	0.747	0.48 (0.43-0.53)	3.67E-08	4.19E-07	-0.67	0.13	DQB1*0201	0.35	0.122	0.61	0.395	0.52	0.082	0.13