

SUPPLEMENTARY DATA

**Supplementary Table S1.** Clinical and demographic characteristics and median serum levels of inflammatory markers in the studied sample

Variable*	Type 1 diabetes (N=67)	LADA (N=75)	Type 2 diabetes (N=390)	P-value for group comparisons			
				All	Type 1 diabetes vs. LADA	Type 2 diabetes vs. LADA	Type 1 diabetes vs. Type 2 diabetes
Age, years	46.0 [36.0;52.5]	56.0 [46.0;65.0]	57.0 [49.0;64.0]	<0.001	<0.001	0.424	<0.001
Gender, n (%)				0.123	0.171	0.835	0.171
Male	35 (52.2%)	50 (66.7%)	252 (64.6%)				
Female	32 (47.8%)	25 (33.3%)	138 (35.4%)				
Age at diagnosis, years	40.0 [33.5;49.0]	49.0 [39.5;60.0]	55.0 [46.0;61.0]	<0.001	0.001	0.017	<0.001
DM duration, years	1.50 [0.12;5.07]	3.42 [1.02;5.95]	2.13 [0.53;4.18]	0.017	0.045	0.018	0.527
BMI, kg/m <sup>2</sup>	24.0 [22.2;26.7]	26.1 [23.5;28.8]	28.5 [25.8;32.0]	<0.001	0.02	<0.001	<0.001
WHR, cm	0.89 [0.84;0.92]	0.93 [0.89;0.99]	0.95 [0.90;0.99]	<0.001	<0.001	0.193	<0.001
SBP, mmHg	121 [115;134]	132 [118;145]	137 [125;153]	<0.001	0.017	0.017	<0.001
DBP, mmHg	74.0 [67.0;80.0]	79.0 [72.2;84.0]	81.0 [74.2;89.0]	<0.001	0.007	0.025	<0.001
FPG, mmol/L	7.95 [6.31;11.0]	8.04 [6.82;10.4]	7.50 [6.37;9.22]	0.05	0.654	0.061	0.342
HbA1c, %	8.20 [6.93;9.00]	7.60 [6.57;8.85]	6.90 [6.30;8.40]	<0.001	0.304	0.012	0.002
HbA1c, mmol/mol	66.1 (52.2;74.9)	59.6 (48.4;73.2)	51.9 (45.4;68.3)	<0.001	0.304	0.011	0.001
Triglycerides, mmol/L	0.84 [0.64;1.18]	1.08 [0.81;1.52]	1.46 [1.08;2.08]	<0.001	0.001	<0.001	<0.001
Total-c, mmol/L	4.76 [4.27;5.53]	5.07 [4.31;5.62]	5.14 [4.50;5.81]	0.078	0.222	0.602	0.075
HDL-c, mmol/L	1.86 [1.48;2.22]	1.57 [1.26;1.82]	1.23 [1.04;1.49]	<0.001	0.002	<0.001	<0.001
LDL-c, mmol/L	2.62 [2.16;3.30]	2.91 [2.42;3.50]	3.11 [2.53;3.69]	0.006	0.089	0.299	0.005
Autoantibodies (U/mL)							
GAD65 <sup>†</sup> positive	44 (83%)	57 (91.9%)	0 (0%)				
GAD65	117 [15.5;755]	45.0 [8.94;217]	2.34 [1.84;2.75]	<0.001	0.157	<0.001	<0.001
IA-2Ab <sup>‡</sup> positive	12 (30%)	6 (15.4%)	0 (0%)				
IA-2Ab	10.0 [10.0;34.6]	10.0 [10.0;10.0]	10.0 [10.0;10.0]	0.065	0.282	0.441	0.065
Inflammatory markers							
Leukocytes (x10 <sup>9</sup> /L)	6230 [5115; 7588]	6310 [5278; 7320]	6715 [5752; 8040]	0.005	0.872	0.017	0.053
Adiponectin (µg/mL)	8.30 [5.23;12.0]	6.22 [3.42;11.1]	4.82 [3.10;7.52]	<0.001	0.08	0.030	<0.001
sTNFRII (ng/mL)	2.06 [1.85;2.53]	2.73 [2.18;3.60]	3.05 [2.31;3.90]	<0.001	0.001	0.084	<0.001
IL6 (pg/mL)	1.10 [0.34;1.92]	0.70 [0.46;1.05]	0.94 [0.38;2.02]	0.537	0.553	0.553	0.553
hsCRP (mg/L)	1.47 [0.76;3.17]	1.28 [0.47;2.67]	2.03 [0.80;3.60]	0.018	0.371	0.022	0.261

\*Variables are expressed as median and interquartile range, unless otherwise specified

†Data available for 489 patients

‡Data available for 145 subjects

BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; GAD65, glutamic acid decarboxylase autoantibodies; HDL-c, highdensity lipoprotein cholesterol; hsCRP high-sensitivity C-reactive protein; IA-2Ab, anti-tyrosine phosphatase (IA-2Ab) autoantibodies LDL-c, low-density

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lipoprotein cholesterol; IL-6, interleukin-6; SBP systolic blood pressure; sTNFRII, soluble receptor for tumor necrosis factor type II; Total-c, total cholesterol; WHR, waist-hip ratio

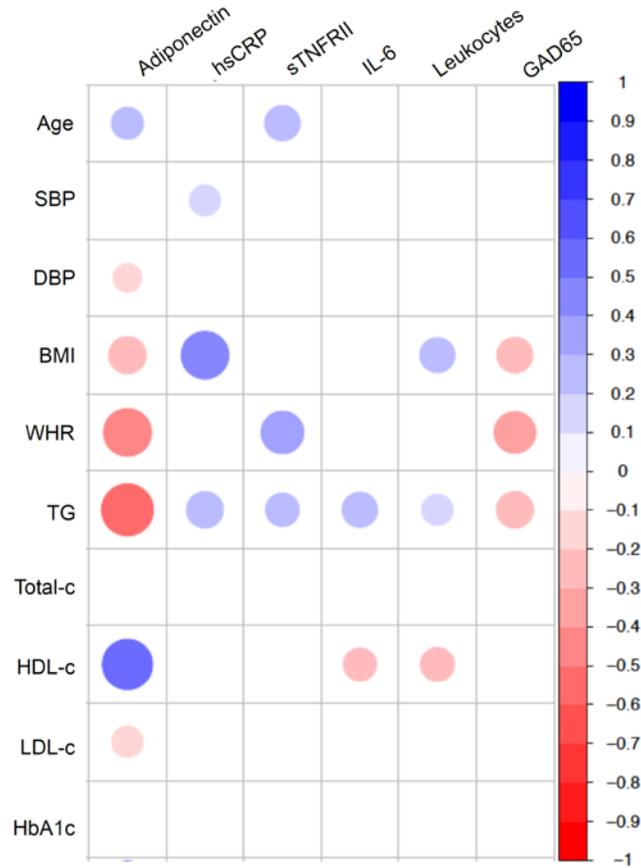
**Supplementary Table S2.** Clinical and demographic characteristics and median serum levels of inflammatory markers in autoimmune diabetes (classic type 1 diabetes and LADA) vs. T2D.

	T2D (N=390)	Autoimmune (N=142)	P-value
Age, years	57.0 [49.0;64.0]	50.0 [40.0;61.0]	<0.001
Gender, n (%)			0.365
Male,	252 (64.6%)	85 (59.9%)	
Female	138 (35.4%)	57 (40.1%)	
Age at diagnosis, years	55.0 [46.0;61.0]	44.5 [36.0;56.0]	<0.001
DM Duration, years	2.13 [0.53;4.18]	2.88 [0.53;5.40]	0.142
BMI, kg/m <sup>2</sup>	28.5 [25.8;32.0]	24.6 [22.8;28.0]	<0.001
WHR, cm	0.95 [0.90;0.99]	0.91 [0.86;0.94]	<0.001
SBP, mmHg	137 [125;153]	128 [116;140]	<0.001
DBP, mmHg	81.0 [74.2;89.0]	75.0 [70.0;83.0]	<0.001
FPG, mmol/L	7.50 [6.37;9.22]	8.04 [6.49;10.5]	0.019
HbA1c, %	6.90 [6.30;8.40]	7.85 [6.73;9.00]	<0.001
HbA1c, mmol/mol	51.9 [45.4;68.3]	62.3 [50.0;74.9]	<0.001
Triglycerides, mmol/L	1.46 [1.08;2.08]	0.98 [0.70;1.32]	<0.001
Total-c, mmol/L	5.14 [4.50;5.81]	4.97 [4.29;5.61]	0.076
HDL-c, mmol/L	1.23 [1.04;1.49]	1.66 [1.35;2.01]	<0.001
LDL-c, mmol/L	3.11 [2.53;3.69]	2.79 [2.33;3.49]	0.007
<b>Inflammatory markers</b>			
Leukocytes (x10 <sup>7</sup> /L)	67.2 [57.5;80.4]	62.7 [52.0;75.7]	0.001
Adiponectin (µg/mL)	4.82 [3.10;7.52]	7.14 [3.96;11.3]	<0.001
sTNFRII (ng/mL)	3.05 [2.31;3.90]	2.46 [1.98;3.43]	<0.001
IL6 (pg/mL)	0.94 [0.38;2.02]	0.81 [0.40;1.72]	0.822
hsCRP (mg/L)	2.03 [0.80;3.60]	1.40 [0.55;3.07]	0.007

BMI, body mass index; DBP, diastolic blood pressure; HDL-c, high-density lipoprotein; FPG, fasting plasma glucose; hsCRP, high-sensitivity C-reactive protein; IL-6, interleukin 6; sTNFRII, soluble receptor for tumor necrosis factor type II; WHR, waist-hip ratio.

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**Supplementary Figure S1.** Graphical display of the correlation analyses between metabolic variables and median serum circulating proinflammatory markers for autoimmune diabetes (LADA and classic adult-onset type 1). The areas of circles show the absolute value of the corresponding correlation coefficient and are colored according to the value (blue=positive correlation; red=negative correlation).

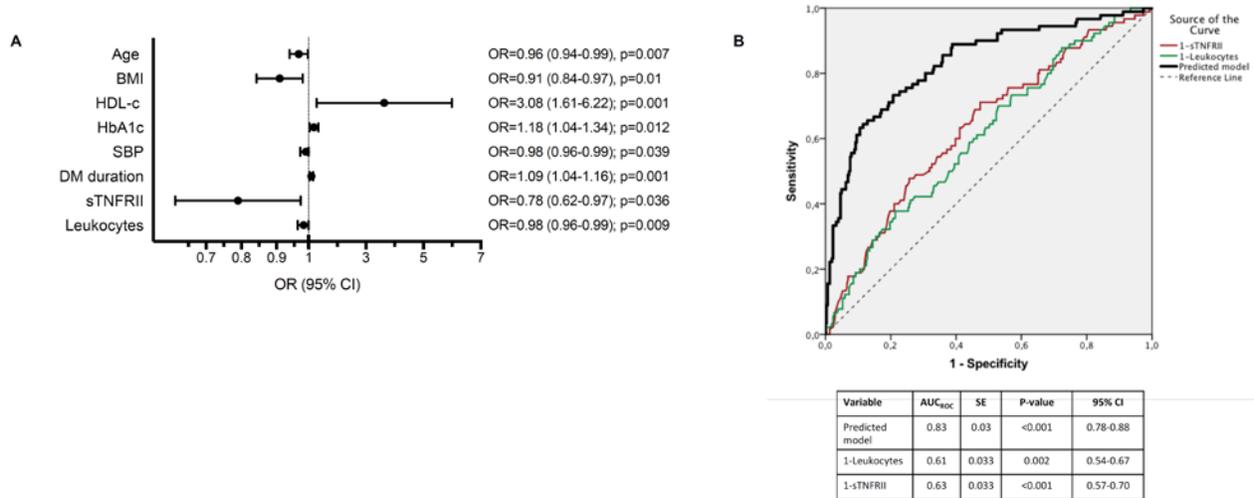


\*p<0.05; \*\*p<0.01; \*\*\*p<0.001; †, adjusted by diabetes duration

BMI, body mass index; DBP, diastolic blood pressure; HDL-c, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-c, low-density lipoprotein cholesterol; IL-6, interleukin 6; SBP, systolic blood pressure; sTNFRII, soluble receptor for tumor necrosis factor type II; TG, triglycerides; Total-c, total cholesterol; WHR, waist-hip ratio

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**Supplementary Figure S2.** A) Logistic regression model\* for autoimmune diabetes (LADA and classic adult-onset type 1) vs. type 2 (Hosmer and Lemeshow test p-value = 0.12). B) Receiver operating characteristics (ROC) curve showing the relationship between sensitivity (true positive) and 1-specificity (true negative) in determining the discriminatory ability of the logistic regression model and the single biomarkers as predictors for LADA vs. type 2 diabetes. The model explained 37% of the dependent variable.



\*Models adjusted by age, gender, WHR, BMI, SBP, DBP, FPG, HbA1c, TG, HDL-c, LDL-c and diabetes duration

Figure footnote: AUCROC, area under the ROC curve, CI, confidence interval; hsCRP, high-sensitivity C-reactive protein; BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; FPG, fasting plasma glucose; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; OR, odds ratio; SBP, systolic blood pressure; sTNFRII, soluble receptor for tumor necrosis factor type II; TG, triglycerides; WHR, waist-hip ratio