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Supplementary Table S1. Human genes associated with T1D: overlap with other autoimmune diseases and animal models of T1D. Human association data were extracted from the Immunobase database (www.immunobase.org) and from references (1-4). Light blue shading indicates that the same marker (single nucleotide polymorphism) is shared between the disease and T1D, while dark blue shading indicates that a different marker within or around the gene is associated with the disease, or in a few cases, that the gene has been associated without the exact marker being defined. Markers that are not associated with particular genes or that are associated with lincRNA were excluded from the table. The number of overlaps for each disease is shown after the disease abbreviation (out of a total of 64 loci listed for T1D). For rodent genetic studies, dark orange shading indicates that the gene(s) in the susceptibility region (Idd for NOD mice and Iddm for BB rats) has been implicated, while lighter shading simply denotes that the gene is within the susceptibility region, but has not been formally implicated. Mouse and rat association data were from t1dbase.org and from references (5; 6). At time of submission, however, the t1dbase.org database was no longer accessible, although a fraction of it has been archived with over 2,300 URLs accessible on https://web.archive.org/web/*/t1dbase.org/*. Abbreviations: AA, Alopecia areata; AS, Ankylosing spondylitis; ATD, Autoimmune thyroid disease; CEL, Celiac disease; CRO, Crohn's disease; IBD, Inflammatory bowel disease; JIA, Juvenile Idiopathic Disease; MS, Multiple sclerosis; PBC, Primary biliary cirrhosis; PSC, Primary sclerosing cholangitis; PSO, Psoriasis; RA, Rheumatoid arthritis; SJO, Sjogren syndrome; SLE, Systematic lupus erythematosus; SSC, Systematic scleroderma; T1D, Type 1 diabetes, UC, Ulcerative colitis; VIT, Vitiligo.

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Loci	Main genes	T1D	CRO (32)	IBD (31)	UC (30)	MS (25)	RA (24)	CEL (23)	JIA (16)	SLE (15)	PBC (11)	VIT (11)	AA (10)	PSO (9)	PSC (8)	SSC (7)	AS (6)	ATD (5)	SJO (5)	NOD	BB
1p13.2	PTPN22, PHTF1																			Idd18.2	Iddm26
1p31.1	PGM1																				
1q31.2	RGS1																			Idd5.4	
1q32.1	IL10																			Idd5	
2p23.3	EFR3B																				
2q11.2	AFF3																			Idd26	
2q12.1	IL18RAP																				
2q24.2	IFIH1																				
2q32.3	STAT4																			Idd5	
2q33.2	CTLA4																			Idd5.1	
2q33.2	SLC11A1																			Idd5.2	
3p21.31	CCR5																				
4q27	IL2, IL21, ADAD1																			Idd3	Iddm32
5p13.2	IL7R																				
5p15	ERAP1																				
6q15	BACH2																				
6p21.3	PRSS16																				
MHC	HLA-DR, HLA-DQ																			Idd1	Iddm1
6q21	FYN																				
6q22.32	CENPW																				
6q23.3	TNFAIP3																				
6q25.3	TAGAP																			Idd23	
7p12.1	COBL																				
7p12.2	IKZF1																				
7p15.2	SKAP2																				Iddm14

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8p23.1	CTSB																				
9p24.2	GLIS3																				
10p11.22	NRP1, ITGB1																				
10p15.1	IL2RA, RBM17																				
10p15.1	PRKCQ																				
10q23.31	RNLS																				
11p15.5	INS, IGF2																				Iddm25
11q13.1	BAD																				
12p13.31	CD69																				
12q13.2	ERBB3, IKZF4																				
12q13.2	DGKA, RAB5B																				
12q13.13	ITGB7																				Iddm34
12q14.1	CYP27B1																				
12q24.12-13	SH2B3, NAA25																				
13q22	LMO7																				
13q32.3	GPR183																				
14q24.1	ZFP36L1																				
14q32.2	DLK1																				Iddm4/8
15q14	RASGRP1																			Idd13	Iddm27
15q25.1	CTSH																			Idd2	
16p11.2	IL27, NUPR1																				Iddm10
16p13.13	CLEC16A, DEXI																				
16q23.1	CTRB1																				
17p13.2	UBE2G1																				
17q12	GSDMB, ORMDL3																			Idd4	
17q21.2	CCR7, SMARCE1																			Idd4	
17q21.31	MAP3K14																				
18p11.21	PTPN2																			Idd21.2	
18q22.2	CD226																			Idd21.1	
19p13.2	TYK2																				
19q13.32	PRKD2																				
19q13.33	FUT2																				
20p13	SIRPG																				
21q22.3	UBASH3A																				
22q12.2	HORMAD2																				
22q12.3-13.1	C1QTNF6, RAC2																				Iddm34
22q12.3	IL2RB																				
Xp22.2	TLR8																				
Xq28	GAB3																				

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Supplementary Table S2. Human genes associated with T1D: known markers or SNPs, and function or potential function in APCs (under parenthesis if function known in other cell types). Markers that are not associated with particular genes or that are associated with lincRNA were excluded. Genes that are known or expected to affect APC function are highlighted.

Loci	Main genes	SNPs	List of SNPs	Potential role in APCs	Refs
1p13.2	**PTPN22**, PHTF1	2	rs2476601, rs6679677	PTPN22 regulates type I interferon responses to TLR agonists	(7; 8)
1p31.1	PGM1	1	rs2269241	(unknown)	
1q31.2	RGS1	2	rs2209014, rs2816316	(T cells)	
1q32.1	**IL10**	2	rs3024493, rs3024505	IL-10 inhibits T cell effector response and supports regulatory T cell functions	(2)
2p23.3	EFR3B	1	rs478222	(unknown)	
2q11.2	AFF3	3	rs6740838, rs9653442, rs13415583	May play a role in monocytes	(9)
2q12.1	IL18RAP	1	rs917997	(IFNg secretion)	
2q24.2	**IFIH1**	4	rs1990760, rs2111485, rs35667974, rs72871627	IFIH1 regulates the production of type I interferon in response to viruses and RNA	(10)
2q32.3	**STAT4**	2	rs6744380, rs7574865	STAT4 is key to IL-12 signaling and is required for T1D development	(11; 12)
2q33.2	CTLA4	2	rs3087243, rs11571316	(T cells, Tregs)	
2q33.2	**SLC11A1**	1	rs3731685	Nramp1, endosomal protein (DCs, MΦs) enhances MHC-II expression and antigen presentation, silencing reduces disease incidence in NOD mice; also influences the IL-12/IL-10 balance	(13-18)
3p21.31	**CCR5**	4	rs333, rs11711054, rs17078977, rs113010081	DC / macrophage homing to inflamed sites Association controversial for certain variants	(19-23)
4q27	IL2, IL21, ADAD1	5	rs2069763, rs4505848, rs6827756, rs17388568, rs75793288	(T cells)	
5p13.2	IL7R	2	rs1445898, rs11954020	(lymphocytes)	
5p15	**ERAP1**	1	rs30187	Antigen processing: trimming of MHC class I peptides; effect on proinflammatory cytokines / chemokines	(24-26)
6q15	BACH2	3	rs597325, rs11755527, rs72928038	(lymphocytes)	
6p21.3	**PRSS16**	0	unconfirmed	Antigen processing (thymus)	(27-30)
MHC	**HLA-DR, HLA-DQ**	3	rs6916742, rs9272346, rs9268645	Antigen presentation: susceptibility conferred by HLA-DR3/DR4 and DQ8/DQ2, protection from DQ6	(31; 32)
6q21	FYN	1	rs11964650	(unknown)	
6q22.32	CENPW	3	rs9388489, rs1538171, rs9375435	(unknown)	
6q23.3	**TNFAIP3**	3	rs1878658, rs2327832, rs6920220	Encodes A20, a negative regulator of NF-kB and TLR signaling; expression of A20 is reduced in LADA	(33; 34)
6q25.3	**TAGAP**	2	rs212402, rs1738074	Macrophages from Tagap-deficient mice produce less type I interferons, TNF-α, IL-6 and inflammatory chemokines in response to HSV infection	(19; 35)
7p12.1	COBL	1	rs4948088	(actin regulation)	
7p12.2	**IKZF1**	3	rs62447205, rs10272724, rs201847125	IKAROS, encoded by IKZF1, regulates the development and differentiation of mDCs and pDCs	(36; 37)
7p15.2	**SKAP2**	2	rs7804356, rs12533947	Required for MΦ migration and chemotaxis	(38)
8p23.1	**CTSB**	1	rs1296023	Protease contributing to antigen processing	(39)
9p24.2	GLIS3	3	rs6476839, rs7020673, rs10758593	(pancreatic beta cells)	
10p11.22	**NRP1, ITGB1**	3	rs722988, rs1557150, rs2666236	NRP1: expressed at high levels on pDCs; it is unclear whether its ligation can potentiate tolerogenic functions as seen with Tregs; ITGB1-encoded CD29 is an adhesion molecule expressed on some myeloid cells and involved in the proliferation of β-cells	(39-41)
10p15.1	IL2RA, RBM17	6	rs2104286, rs7090530, rs10795791, rs12251307, rs41295121, rs61839660	(T cells, Tregs)	
10p15.1	PRKCQ	2	rs2236380, rs11258747	(T cells, NF-kB signaling downstream of TCR)	
10q23.31	RNLS	2	rs10509540, rs12416116	May play a role in monocytes	(9)

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11p15.5	**INS**, IGF2	5	rs689, rs3741208, rs7111341, rs7928968, rs72853903	INS: autoantigen; level of expression in thymic epithelial cells influences selection of insulin-reactive T cells; mutations can favor binding of INS DRiP on MHC.	(42-44)
11q13.1	BAD	1	rs694739	(apoptosis)	
12p13.31	**CD69**	3	rs917911, rs4763879, rs10492166	Regulates tissue retention and egress, including that of DCs	(2; 45)
12q13.2	**ERBB3**, IKZF4	5	rs705704, rs705705, rs705708, rs2292239, rs11171739	ERBB3: expressed in maturing DCs and monocytes, with higher expression being more protective; (IKZF4: role in T cells and Tregs,)	(46)
12q13.2	DGKA, RAB5B	1	rs11171710	(T cells)	
12q13.13	**ITGB7**	1	rs11170466	The protein associates with CD103 (ITGAE) or CD49d (ITGA4) to regulate leukocyte homing	(39)
12q14.1	**CYP27B1**	2	rs4760341, rs10877012	Responsible for the production of bioactive vitamin D, which potentiates the tolerogenic function of DCs	(47)
12q24.12-13	**SH2B3**, NAA25	3	rs653178, rs3184504, rs17696736	Lnk (encoded by SH2B3) regulates the number of DCs and their response to GM-CSF	(19; 48; 49)
13q22	LMO7	1	rs539514	(unknown)	
13q32.3	**GPR183**	2	rs6491500, rs9585056	Stimulation of GPR183-encoded EBI2 regulates cell migration and positioning of macrophages and DCs	(9; 50; 51)
14q24.1	**ZFP36L1**	1	rs1465788	Regulated monocyte / macrophage differentiation	(52)
14q32.2	DLK1	2	rs941576, rs56994090	Expressed on mucosal DCs	
15q14	RASGRP1	4	rs7171171, rs12908309, rs17574546, rs72727394	(lymphocytes)	
15q25.1	**CTSH**	3	rs3825932, rs12148472, rs34593439	Protease contributing to antigen processing	(53)
16p11.2	**IL27**, NUPR1	3	rs151234, rs4788084, rs9924471	IL-27: induces IL-10+ Tr1 cells and also potentiate Foxp3+ Tregs	(2; 54; 55)
16p13.13	**CLEC16A**, DEXI	3	rs193778, rs12708716, rs12927355	CLEC16A regulates autophagy and antigen processing in APCs; DEXI may play a role in monocytes	(9; 56-58)
16q23.1	CTRB1	1	rs7202877	(pancreas)	
17p13.2	UBE2G1	1	rs9906760	(unknown)	
17q12	GSDMB, ORMDL3	3	rs2290400, rs12150079, rs12453507	(asthma ORMDL3)	
17q21.2	**CCR7**, SMARCE1	1	rs757411	CCR7: enable DC homing to lymph nodes; SMARCE1: may play a role in monocytes	(9; 49)
17q21.31	**MAP3K14**	1	rs17759555	Encodes the NF-kB-inducing kinase (NIK), which regulates the NF-kB pathway and cross-priming by DCs	(39; 59)
18p11.21	**PTPN2**	3	rs1893217, rs2542151, rs12971201	Besides a major role in T cells, it also regulates M-CSF receptor signaling and macrophage differentiation	(60)
18q22.2	**CD226**	3	rs763361, rs1615504, rs1790575	CD226 cross-linking enhances MHC-II, CD80 and CD86 on CD8α+ DCs, but not CD8α- DCs	(9; 61)
19p13.2	**TYK2**	3	rs1051738, rs12720356, rs34536443	TYK2 regulates the production of IL-12 by DCs, as well as the response to IL-12	(12)
19q13.32	PRKD2	2	rs425105, rs60652743	(mostly implicated in tumor invasion); may play a role in monocytes	(9)
19q13.33	FUT2	3	rs516246, rs601338, rs602662	(intestinal epithelial cells)	
20p13	SIRPG	1	rs2281808	(T cells)	
21q22.3	UBASH3A	2	rs11203202, rs11203203	(T cells: inhibition of NF-kB signaling under TCR)	
22q12.2	HORMAD2	1	rs5753037	(unknown)	
22q12.3-13.1	**C1QTNF6**, **RAC2**	2	rs229533, rs229541	C1QTNF6: regulation of IL-10 production; RAC2: encodes a small GTPase that controls phagosome pH and cross-presentation	(62; 63)
22q12.3	IL2RB	1	rs229526	(T cells)	
Xp22.2	**TLR8**	1	rs5979785	Response of DCs and other APCs to ssRNA	(64)
Xq28	**GAB3**	1	rs2664170	Encodes an adaptor protein that binds GRB2 and SHP2 tyrosine phosphatase and regulated monocyte / macrophage differentiation,; functions downstream of M-CSF receptor	(65)

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Supplementary Table S3. Selected rodent genes associated with T1D with a known or putative role in APCs. The table shows a limited selection of relevant genes from the reviews by Driver et al. (5) and Wallis et al. (6). Genes present in Idd regions are NOD mice, while those in Iddm regions are from diabetes-prone BB rats.

Main genes	Region	Potential role in APCs	Refs
B2m	Idd13.1, Iddm27	Component of MHC-I, β2m variation can influence the selection of peptides for MHC-I binding and susceptibility to disease	(66; 67)
C1qtnf6	Iddm34	Enhances IL-10 production by MΦs, see Table S2	(63)
Cd101	Idd10/Idd18.4	Crosslinking induces IL-10 secretion by DCs	(5; 68)
Csf1	Idd18.3	Encodes M-CSF, a growth factor for MΦs	Table S6
Csf2	Idd4.3	Encodes GM-CSF, a growth factor for DCs	Table S6
Iapp	Idd6.2	Autoantigen, for tolerance induction? Accumulation in islets contributes to inflammation and macrophage activation	(69)
Il1a / Il1b	Idd13, Iddm27	Proinflammatory cytokines	(5; 6)
Il10	Idd5	Immunoregulatory cytokine produced by DCs	Table S2
Il27	Iddm10	Immunoregulatory cytokine produced by DCs	Table S2
Ins1 / Ins2	Iddm25	Autoantigen, for tolerance induction	Table S2
MHC-II	Idd1, Iddm1	Permissible haplotype I-A^{g7} (NOD mouse) and $RT1^{u}$ (BB rat)	
Nfkb1	Iddm33	Encodes subunit 1 of NF-κB	Table S11
Sirpa	Idd13.2	NOD variant on BM-DCs binds more strongly to CD47	(70)
Slc11a1	Idd5.2	Influences antigen presentation and cytokine production	Table S2
Vdr	Iddm34	Encodes the vitamin D receptor	(6)
Unindentified	Idd4	Controls overproduction of IL-12 by MΦs	(71)
Unindentified	Idd10/17/18	Controls overproduction of IL-12 by DCs arrested in maturing phase	(72)

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Supplementary Table S4. Altered number of DC and monocyte populations in T1D. The table is divided in two sections: A) blood DCs and monocytes and B) in vitro differentiated DCs from monocytes. Abbreviations: mDCs: myeloid DCs; pDCs: plasmacytoid DCs; MoDCs: monocyte-derived DCs; ctrl: control; NO: new onset T1D; LT: long-term T1D; AAb: autoantibodies; A: adults; C: children; YA: young adults; ↗ increased in T1D; ↘ decreased in T1D; ≡ no change.
(*) Trend for more mDCs and less pDCs in T1D (not significant). Lin- cells typically exclude lymphocytes, NK cells and monocytes.

APC		Phenotype	Subject	Age group	Frequency / cell count	Refs
A	Blood DCs	Lin- HLA-DR+	T1D vs ctrl	A	Frequency ≡ Cell count ≡	(73)
	Blood DCs	Lin- HLA-DR+	T1D At-risk, NO vs LT, ctrl	All	Frequency ↗	(74)
	Blood mDCs	Lin- HLA-DR+ CD11c+ CD123lo	T1D vs ctrl	A	Frequency ≡ (*)	(73)
	Blood mDCs	CD1c+ CD19-	T1D vs ctrl	C/YA	Frequency ≡	(75)
	Blood mDCs	CD1c+ CD19-	AAb+ vs ctrl	All	Frequency ≡	(76)
	Blood mDCs	Lin- HLA-DR+ CD11c+ CD123-	T1D At-risk, NO, LT vs ctrl	YA	Cell count ≡	(77)
	Blood mDCs	Lin- HLA-DR+ CD11c+ CD123-	T1D At-risk, NO, LT vs ctrl	All	Frequency ↘	(74)
	Blood mDCs	HLA-DR+ CD11c+ CD1c+	T1D vs ctrl	C	Frequency ↘ Cell count ↘	(78)
	Blood mDCs	Lin- HLA-DR+ CD11c+	T1D NO, LT vs ctrl	C	Frequency ↘ Cell count ↘	(79)
	Blood mDCs	cDC1: Lin- CD1c+	T1D NO vs ctrl	All	Frequency ↘	(80)
	Blood mDCs	cDC1: Lin- CD1c+	T1D LT vs ctrl	All	Frequency ≡	(80)
	Blood pDCs	Lin- HLA-DR+ CD11c- CD123lo	T1D vs ctrl	A	Frequency ≡ (*)	(73)
	Blood pDCs	CD304+	T1D vs ctrl	C/YA	Frequency ≡	(75)
	Blood pDCs	CD304+	AAb+ vs ctrl	All	Frequency ≡	(76)
	Blood pDCs	Lin- HLA-DR+ CD11c- CD123+	T1D At-risk, NO, LT vs ctrl	All	Frequency ↗	(74)
	Blood pDCs	HLA-DR+ CD123+ CD303+	T1D vs ctrl	C	Frequency ↘ Cell count ↘	(78)
	Blood pDCs	Lin- HLA-DR+ CD123+ CD304+	T1D NO, LT vs ctrl	C	Frequency ↘ Cell count ↘	(79)
	Blood pDCs	Lin- CD303+ CD304+	T1D NO, LT vs ctrl	All	Frequency ↘ Cell count ↘	(80)
	Blood pDCs	Lin- HLA-DR+ CD11c- CD123+	T1D At-risk, NO, LT vs ctrl	YA	Frequency ↗ Cell count ≡	(77)
	Blood monocytes	CD14+	T1D vs ctrl	C/YA	Frequency ≡	(75)
	Blood monocytes	CD14+	AAb+ vs ctrl	All	Frequency ≡	(76)
	Blood monocytes	HLA-DR+ CD14+ CD19-	T1D NO vs ctrl	C	Frequency ↗ Cell count ↗	(79)
	Blood monocytes	HLA-DR+ CD14+ CD19-	T1D LT vs ctrl	C	Frequency ≡ Cell count ↘	(79)
B	MoDCs	N/A	T1D vs ctrl	All	Yield ↘	(81)
	MoDCs	HLA-DR+ CD14-	AAb+ vs ctrl	All	Yield ↘	(82)
	MoDCs	HLA-DR+ CD11c+	At-risk, NO vs ctrl	C	Yield ↘	(83)

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Supplementary Table S5. Altered frequency and yield of DCs from NOD mice compared to other mouse strains. The table is divided in two sections: A) freshly isolated DCs and B) in vitro differentiated DCs from bone marrow. The cytokines listed are those used for in vitro differentiation of the DCs. "Not seen in" means that the reduced frequency of CD8α+ DCs observed in the spleen was not seen in the indicated tissues. Abbreviations: BM-DCs: bone marrow-derived DCs; PLN: pancreatic lymph node; ↗ increased in NOD; ↘ decreased in NOD. (*) Phenotype: CD11c^{low} mPDCA (CD317)+.

APC		Mouse strains	Frequency / yield	Notes	Refs
A	Splenic CD8α+ DCs	NOD vs B6, B10.DR	Frequency ↘		(84)
	Splenic CD8α+ DCs	NOD vs NOR, B6, BALB/c	Frequency ↘	Not seen in PLNs	(85)
	Splenic CD8α+ DCs	NOD vs NOR, B6	Frequency ↘	Not seen in thymus	(86)
	Splenic CD8α+ DCs	NOD.H-2k vs B10.H-2k	Frequency ↘	In favor of CD8α- DCs; Idd1-independent	(87)
	Splenic pDCs (*)	NOD (young vs diabetic)	Frequency ↘		(88)
	Splenic DCs	NOD vs CBA, DBA/2	Frequency ↘		(89)
	Splenic DCs	NOD vs DBA/2	In vitro yield ↘	FLT3L	(89)
	PLN merocytic DCs	NOD vs B6, BALB/c	Frequency ↗	CD11c+ CD8α- CD11b-/low	(90)
	Liver B220+ DCs	NOD vs NOR, BALB/c (females)	Yield ↘	Defective in vitro propagation	(91)
B	BM-DCs	NOD vs B6, CBA, DBA/2	Yield ↘	GM-CSF/IL-4	(89)
	BM-DCs	NOD vs B6, DBA/2	Yield ↘	GM-CSF/IL-4; bias toward granulocytes	(92)
	BM-DCs	NOD vs B6	Yield ↘	GM-CSF ± IL-4	(93)
	BM-DCs	NOD vs B10.DR	Yield ↘	GM-CSF/IL-4	(94)
	BM-DCs	NOD vs B10.DR, B6, DBA/2	Yield ↘	GM-CSF ± IL-4	(95)
	BM-DCs	NOD vs NOR, B6, BALB/c	Yield ↘	GM-CSF; bias toward MΦ-like cells	(96)
	BM-DCs	NOD.H-2k vs B10.H-2k	Yield ↘	GM-CSF/IL-4; Idd1-independent	(97)
	BM-DCs	NOD vs NOR, B6, BALB/c	Yield ↗	GM-CSF/IL-4	(98)

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SUPPLEMENTARY DATA

Supplementary Table S6. Role of growth factors in APC alterations and defects in NOD mice.

Cytokine	Role / effect	Refs
FLT3L	Treatment with FLT3L corrects deficiency in CD8α+ DC numbers in NOD mice	(84; 86)
	Treatment with FLT3L expands pDC precursors and restore their function in NOD mice	(99)
GM-CSF	Greater number of granulocyte-macrophage colony-forming cells (NOD vs B6)	(100)
	Reduced response of myeloid progenitors to GM-CSF (NOD vs BALB/c)	(101)
	Enhanced proliferation of pancreatic DC precursors to GM-CSF (NOD vs B6)	(102)
	Over-production of GM-CSF linked to *Csf2* polymorphism (Idd4.3) in monocytes and MΦs (NOD vs B6)	(103)
	Persistent STAT5 stimulation by GM-CSF that is impervious to regulation by IL-10 (NOD vs B6; T1D / high-risk patients vs healthy controls)	(104)
	Increased GM-CSF production and STAT5 phosphorylation in monocytes from T1D patients and at-risk subjects	(105)
M-CSF	Reduced yield of MΦs from bone marrow cells with M-CSF (NOD vs NON and congenics)	(106)

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SUPPLEMENTARY DATA

Supplementary Table S7. Distribution of extra-pancreatic expression of major β-cell antigens. The cell-specific and tissue-specific expression of autoantigens (outside the pancreas) is reported according to published reports and gene expression databases including the Immunological Genome Project (ImmGen, www.ImmGen.org), BioGPS (www.biogps.org) and the Genotype-Tissue Expression Project (GTEx, www.gtexportal.org). Although not a β-cell antigen, GAD67 is listed because several epitopes are identical (cross-reactive) between GAD65 and GAD67.

Islet autoantigen	Extra-pancreatic tissue	Notes, other sources	Refs
Proinsulin (*INS*)	Thymus	In mTECs, AIRE-dependent	(107-109)
	Lymph nodes (fibroblastic reticular cells)	In FRCs (mice), nodes in mice and humans	(110-113)
	Blood myeloid cells	Humans (monocytes, DCs)	(114)
	Peripheral DCs	Human and mouse	(115-118)
	Liver, bone marrow, adipose tissue	Under hyperglycemic conditions (mice)	(119)
Chromogranin A (*CHGA*)	Adrenal and pituitary glands, stomach	BioGPS (mouse) and GTEx (human)	
	Adrenal, pituitary and thyroid glands	BioGPS (human)	
	mTECs	ImmGen (mouse)	
IA-2 (*PTPRN*)	Brain, pituitary and adrenal glands	BioGPS (mouse) and GTEx (human)	
	Brain / pineal gland	BioGPS (human)	
	Thymus, spleen	Splice variant missing exon 13 only	(120)
	mTECs	ImmGen (mouse)	(109)
IAPP (*IAPP*)	mTECs	ImmGen (mouse)	
	pDCs (?)	BioGPS (mouse)	
IGRP (*G6PC2*)	mTECs (low)	ImmGen (mouse)	
	Thymus, spleen	Splice variants differ from pancreas	(121; 122)
	Testis?	GTEx (human)	
GAD65 (*GAD2*)	Brain (NOT expressed in mTECs)	BioGPS and GTEx (human)	(109)
GAD67 (*GAD1*)	Brain	BioGPS (mouse, human) and GTEx (human)	
	mTECs and lymph node stromal cells	ImmGen (mouse)	(109; 111; 123)
ZnT8 (*SLC30A8*)	Testis	GTEx (human)	

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SUPPLEMENTARY DATA

Supplementary Table S8. Alterations in antigen processing and peptide loading in T1D.

Process	Gene product	Association with T1D and relevant functions	Refs
Antigen processing	CLEC16A	Polymorphism associated with T1D	(9; 56)
		Regulates autophagy in humans	(57)
		Knockdown of CLEC16A in NOD mice protects from T1D by impacting autophagy in mTECs and T cell selection	(58)
	CTSB	Polymorphism associated with T1D	(39)
		Regulates antigen processing, autophagy and lysosomal dynamics	(124; 125)
	CTSH	Polymorphism associated with T1D	(53)
		Regulates antigen processing	(125)
		Polymorphism associated with lower insulin production in β cells (a role in mTECs and other cells?)	(126)
	ERAP1	Polymorphism associated with T1D	(24)
		Regulates processing of antigens to MHC class I and influencing recognition by CD8+ T cells; associated with multiple autoimmune diseases	(25)
		Effect on proinflammatory cytokine expression	(26)
	PRSS16	Polymorphism associated with T1D	(27; 28)
		PRSS16 knock-out NOD mice were protected from disease, in part due to a more effective deletion of certain diabetogenic CD4+ T cells in the thymus	(29; 30)
Peptide loading	CLIP	Elevated levels of I-A^{g7}-associated CLIP on splenic B cells (NOD vs other strains)	(127)
		Increased % of CLIP+ monocytes in T1D patients (vs control and T2D patients)	(128)
		Increased density of empty HLA-DR on B cells from T1D patients (vs control twins)	(129)
		Poor HLA-DM editing leads to persistence of CLIP	(130)
		HLA-DQ2 and DQ8 are more resistant to CLIP release by HLA-DM	(131)
	INS-DRiP	Polymorphism in the 3'UTR of INS leads to better binding of the insulin defective ribosomal product (DRiP) to HLA-DQ8/DQ2 molecules. T1D patients who carry both susceptible DQ8/DQ2 and INS-DRiP alleles have T cell responses to this neoantigen, while subjects carrying the protective DQ6 or INS-DRiP allele alone do not show any response.	(44)
	HIP	Hybrid insulin peptides: fusion products between the C-terminus of InsC-derived peptide and the N-terminus of a peptide from another β-cell antigen (chromogranin A or IAPP) fit the I-A^{g7} MHC particularly well. Such peptides were also identified in T1D patients as HLA-DQ8 or DQ8/DQ2-restricted.	(132; 133)

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SUPPLEMENTARY DATA

Supplementary Table S9. Altered expression of MHC and costimulatory molecules in APCs from NOD mice compared to other mouse strains. The table is divided in two sections: A) MHC, and B) Costimulatory molecules CD40, CD80 and CD86. Abbreviations: pDCs: Plasmacytoid DCs; LPS: lipopolysaccharides; PIC: poly I:C; ↗ increased in NOD; ↘ decreased in NOD; ≡ no change. Data refer to mean fluorescence intensity, except (#) based on % cells positive for the cytokine and (*) based on mRNA levels. (**) pDCs defined as SiglecH^{+} BST2 (CD317)$^{+}$ B220^{+}.

	APC	Mouse strains	Stimulation	MHC and costimulation	Refs
MHC molecules	Splenic DCs (ex vivo)	NOD vs DBA/2	None	MHC-II ↘	(89)
	Splenic DCs (cultured)	NOD vs DBA/2	None	MHC-II ↘	(89)
	BM-DCs	NOD vs B6	None	MHC-II ↘	(96)
	BM-DCs	NOD vs B6	None	MHC-II ↘	(93)
	BM-DCs	NOD vs DBA/2	None	MHC-II ↘	(89)
	BM-DCs	NOD vs DBA/2	None	MHC-II ↘	(92)
	BM-DCs	NOD vs CBA	None, LPS/IFN-γ	MHC-II ↘	(134)
	BM-DCs	NOD vs B10.DR	None	MHC-II ≡	(94)
	BM-DCs	NOD.H-2k vs B10.H-2k	None	MHC-II ↘ (#)	(97)
	BM-DC	NOD vs B6	LPS, CD40L	MHC-II ↘	(72)
	Pre-DCs	NOD vs NOR	CpG	MHC-II ↘	(99)
	Splenic MΦs	NOD vs NOR, BALB/c	None, LPS	MHC-I ↗ MHC-II ≡	(135)
	Peritoneal MΦs	NOD vs NOR, B6	IFN-γ	MHC-I ↘	(106)
Costimulatory molecules	Splenic CD8α+ DCs	NOD vs B6	None	CD40 ↗	(136)
	Splenic CD8α+ DCs	NOD vs B6	None	CD80, CD86 ≡ CD40 ↗	(137)
	Splenic CD8α+ DCs	NOD vs B6	CpG	CD80, CD86 ↘ CD40 ↗	(137)
	Splenic CD8α+ DCs	NOD vs NOR, BALB/c	None, LPS, PIC	CD40, CD80, CD86 ≡	(85)
	Splenic CD8α- DCs	NOD vs NOR, BALB/c	None, LPS, PIC	CD40, CD80, CD86 ≡	(85)
	Splenic CD8α- DCs	NOD vs B6	None, CpG	CD80, CD86 ≡ CD40 ↗	(137)
	Splenic DCs (ex vivo)	NOD vs DBA/2	None	CD40 ↗ CD80, CD86 ≡	(89)
	Splenic DCs (in vitro)	NOD vs DBA/2	None	CD80 ↘ (#) CD40, CD86 ≡	(89)
	Splenic pDCs (**)	NOD vs B6	None	CD40, CD80, CD86 ≡	(137)
	Splenic pDCs (**)	NOD vs B6	CpG	CD40 ≡ CD80, CD86 ↘	(137)
	Pancreatic CD8α- DCs	NOD vs B6	None	CD40, CD86 ↘	(138)
	BM-DCs	NOD vs NOR, B6, BALB/c	None	CD40, CD80, CD86 ≡	(96)
	BM-DCs	NOD vs BALB/c	None	CD40, CD80, CD86 ≡	(139)
	BM-DCs	NOD vs BALB/c, B6	None	CD40, CD80, CD86 ≡	(140)
	BM-DCs	NOD vs BALB/c, B6	None	CD80 ↘ CD40, CD86 ≡	(141)
	BM-DCs	NOD vs B6	None	CD40, CD80, CD86 ↘	(93)
	BM-DCs	NOD vs CBA	None	CD40, CD80, CD86 ↘	(134)
	BM-DCs	NOD vs DBA/2	None	CD40, CD86 ↘	(92)
	BM-DCs	NOD vs B10.DR, B6	None	CD40, CD80, CD86 ↗	(95)
	BM-DCs	NOD vs B10.DR	None	CD40 ↗	(94)
	BM-DCs	NOD vs BALB/c, B6	None	CD40, CD80 ↗	(142)
	BM-DCs	NOD, NOR vs BALB/c, B6	None	CD40, CD80, CD86 ↗	(139)
	BM-DCs	NOD vs DBA/2	None	CD80 ↘ (#) CD40, CD86 ≡	(89)
	BM-DCs	NOD vs NON	LPS	CD80, CD86 ↘ (*)	(143)
	BM-DCs	NOD vs CBA	LPS/IFN-γ	CD40 ≡ CD80, CD86 ↘	(134)
	BM-DCs	NOD vs BALB/c	LPS	CD40, CD80, CD86 ≡	(139)
	BM-DCs	NOD vs BALB/c, B6	LPS	CD40, CD80, CD86 ≡	(140)
	BM-DCs	NOD vs B6	LPS, CD40L	CD86 ↘	(72)
	BM-DCs	NOD vs BALB/c, B6	LPS/IFN-γ	CD40,80,86 ≡	(141)
	BM-DCs	NOD vs BALB/c, B6	With T cells	CD80,86 ↗	(141)
	Pre-DCs	NOD vs NOR	CpG	CD80,86 ↘	(99)
	Splenic MΦs	NOD vs NOR, BALB/c	None	CD40, CD80, CD86 ≡	(135)
	Splenic MΦs	NOD vs NOR, BALB/c	LPS	CD40, CD80 ≡ CD86 ↗	(135)
	B cells	NOD vs BALB/c, B6, B6g7	None	CD40, CD80 ↗	(142)

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SUPPLEMENTARY DATA

Supplementary Table S10. Altered expression of MHC and costimulatory molecules in APCs from T1D patients compared to various controls. The table is divided in two sections: A) MHC, and B) Costimulatory molecules CD40, CD80 and CD86. Abbreviations: MoDCs: monocyte-derived DCs; mDCs: myeloid DCs; pDCs: plasmacytoid DCs; NO: new onset; ctrl: control; FDR: first degree relative; LPS: lipopolysaccharides; ↗ increased in T1D; ↘ decreased in T1D; ≡ no change. Data refer to mean fluorescence intensity, except (#) based on % cells positive for the cytokine and (*) based on mRNA levels.

	APC	Subject	Stimulation	MHC and costimulation	Refs
MHC molecules	Blood DCs	T1D NO vs ctrl (children)	None	HLA-DR ≡	(79)
	Blood mDCs	T1D vs ctrl	None	HLA-DR ↗	(74)
	Blood mDCs	T1D vs ctrl	None	HLA-DR ↗	(77)
	Blood pDCs	T1D vs ctrl	None	HLA-DR ↗	(74)
	Blood pDCs	T1D vs ctrl	None	HLA-DR ↗	(77)
	MoDCs	T1D, At-Risk vs ctrl (children)	None	HLA-DR ↘ (#)	(83)
	MoDCs	T1D vs ctrl (children)	None, LPS	HLA-DR ≡	(144)
	MoDCs	T1D vs ctrl, T2D, RA	LPS	HLA-DR ≡	(145)
	MoDCs	T1D vs ctrl, T2D, RA	LPS	MHC-I ↘	(145)
Costimulatory molecules	PBMCs	T1D NO vs ctrl (children)	None	CD80 ↗ CD40, 86 ≡ (*)	(146)
	PBMCs	T1D NO vs ctrl (adults)	None	CD86 ↗ CD40, 80 ≡ (*)	(146)
	Blood DCs	T1D NO vs ctrl (children)	None	CD40, CD86 ≡	(79)
	Blood mDCs	T1D vs ctrl	None	CD40, CD80, CD86 ≡	(77)
	Blood mDCs	T1D vs ctrl	None	CD40, CD80, CD86 ≡ (#)	(73)
	Blood pDCs	T1D vs ctrl	None	CD40, CD80, CD86 ≡	(77)
	Blood pDCs	T1D vs ctrl	None	CD40, CD80, CD86 ≡ (#)	(73)
	MoDCs	T1D vs ctrl, T2D	None	CD80 ≡ CD86 ↗	(147)
	MoDCs	T1D vs ctrl (children)	None	CD80 ↘ (#)	(83)
	MoDCs	At-Risk FDR vs ctrl	None	CD80, CD86 ↘ (#)	(82)
	MoDCs	T1D vs ctrl	None	CD40, CD80, CD86 ≡	(148)
	MoDCs	T1D vs ctrl (children)	None	CD80, CD86 ≡	(144)
	MoDCs	T1D vs ctrl,T2D	None, TNF/IL-1/IL-6	CD40, CD80, CD86 ≡	(149)
	MoDCs	T1D vs ctrl (children)	LPS	CD80, CD86 ↘	(144)
	MoDCs	T1D vs ctrl, T2D, RA	LPS	CD40 ↘	(145)
	MoDCs	T1D vs ctrl, T2D, RA	LPS	CD80, CD86 ≡	(145)
	MoDCs	T1D vs ctrl	TNF-α	CD80 ↗ CD40, CD86 ≡	(148)

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SUPPLEMENTARY DATA

Supplementary Table S11. Evidence of the implication of the NF-κB pathway in the abnormal maturation of DCs and MΦs in T1D.

Species	Role / effect	Refs
NOD mice	Hyperactive IκB kinase and NF-κB in splenic DCs and BM-DCs (NOD vs B6 and BALB/c)	(140)
	Excessive NF-κB activity enhances costimulation and cytokine secretion (NOD vs NOR, BALB/c)	(139)
	Overexpression of IL-12 by MΦs is due to abnormal regulation by NF-κB and linked to Idd4	(71; 150)
	Excessive NF-κB activity in BM-DCs and B cells (NOD vs BALB/c, B6)	(142)
	Lower expression of p65/p50/p52 and RelB in BM-DCs (NOD vs NON)	(143)
BB rats	Polymorphism in the *NFKB1* gene (Iddm33)	(6)
T1D patients	Excessive NF-κB activity in monocytes and monocyte-derived DCs from T1D patients	(145)
	Susceptibility gene *MAP3K14* encodes NIK, a positive regulator of NF-κB pathway	Table S2
	Susceptibility gene *TNFAIP3* encodes A20, a negative regulator of NF-κB pathway	Table S2

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SUPPLEMENTARY DATA

Supplementary Table S12A. Altered cytokine expression in APCs from NOD mice compared to other mouse strains. The table is divided in four sections: IL-10, IL-12, proinflammatory cytokines, and Type I interferons (T1). Abbreviations: LPS: lipopolysaccharides; PIC: poly I:C; PGN; peptidoglycan; SAC: Staph. aureus Cowan extract; ↗ increased in NOD; ↘ decreased in NOD; ≡ no change. Data refer to MFI or amount secreted, except (*) indicating mRNA levels.

APC		Mouse strains	Stimulation	Cytokines	Refs
IL-10	Splenic CD8α+ DCs	NOD vs NOR, BALB/c	PIC	IL-10 ≡	(85)
	Splenic CD8α+ DCs	NOD vs NOR, BALB/c	CD40L/LPS	IL-10 ↗	(85)
	Splenic CD8α- DCs	NOD vs NOR, BALB/c	PIC, CD40L/LPS	IL-10 ≡	(85)
	Pancreatic CD8α+ DCs	NOD vs B6	None	IL-10 ↘ (*)	(151)
	Pancreatic CD8α- DCs	NOD vs B6	None	IL-10 ↘ (*)	(138)
	Pancreatic CD8α- DCs	NOD vs B6	LPS	IL-10 ≡	(138)
	Pancreatic CD8α- DCs	NOD vs B6	LPS	IL-10 ↗ (*)	(138)
	BM-DCs	NOD vs B6	LPS	IL-10 ↘	(72)
	Macrophages	NOD vs B6, B10	LPS	IL-10 ↘	(152)
	Macrophages	NOD vs NOR	LPS	IL-10 ↗	(152)
IL-12	Splenic CD8α+ DCs	NOD vs B6	CpG	IL-12p40 ↘	(86)
	Splenic CD8α+ DCs	NOD vs NOR, BALB/c	PIC, CD40L/LPS	IL-12 ↘	(85)
	Splenic CD8α+ DCs	NOD vs B6	LPS, PIC, SAC	IL-12p40 ↘	(84)
	Splenic CD8α- DCs	NOD vs NOR, BALB/c	PIC, CD40L/LPS	IL-12 ≡	(85)
	Splenic DCs	NOD vs NOR, BALB/c	PIC	IL-12 ↘ IL-12p40 ↘	(85)
	Splenic DCs	NOD vs NOR	CD40L/LPS	IL-12 ↘ IL-12p40 ↘	(85)
	Splenic DCs	NOD vs B6, B10.BR	SAC, TNF-α	IL-12p40 ↘	(84)
	Splenic DCs	NOD vs B6	CpG	IL-12	(137)
	Pancreatic CD8α- DCs	NOD vs B6	None	IL-12b ↘ (*)	(138)
	Pancreatic CD8α- DCs	NOD vs B6	LPS	IL-12 ≡	(138)
	Pancreatic CD8α- DCs	NOD vs B6	LPS	IL-12a ↗ (*)	(138)
	BM-DCs	NOD vs BALB/c, B6	CD40L, LPS	IL-12 ↗	(140)
	BM-DCs	NOD vs NOR, BALB/c	CD40L, LPS	IL-12 ↗	(139)
	BM-DCs	NOD vs DBA/2	LPS/CD40L	IL-12 ↗	(89)
	BM-DCs	NOD vs B6	LPS	IL-12 ↗	(72)
	BM-DCs	NOD vs B6	LPS/T cells	IL-12 ↗	(141)
	BM-DCs	NOD vs B10.DR	None	IL-12p40 ↗	(94)
	BM-DCs	NOD vs B10.DR	LPS	IL-12p40 ≡	(94)
	BM-DCs	NOD vs NON	LPS	IL-12a ↘ (*)	(143)
	BM-DCs	NOD vs B6, B10.DR	CD40L or LPS/IFN-γ	IL-12 ↘	(95)
	BM-DCs	NOD vs B6	LPS/IFN-γ	IL-12 ↘	(93)
	Macrophages	NOD vs NOR	LPS	IL-12 ↗	(85)
	Macrophages	NOD vs B6	LPS	IL-12 ↗	(153)
	Macrophages	NOD vs B6, B10, NOR	LPS	IL-12 ↗	(152)
	Macrophages	NOD vs A/J, B6, BALB/c	LPS	IL-12 ↗ IL-12p40 ↗	(150)
	Macrophages	NOD vs A/J, B6, BALB/c	LPS	IL-12p40 ↗	(71)
	Macrophages	NOD vs NOR, BALB/c	LPS, TNF-α, CD40L	IL-12 ↗	(135)
	Macrophages	NOD vs NOR, BALB/c	LPS	IL-12p40 ↗ (*)	(135)

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SUPPLEMENTARY DATA

Supplementary Table S12B. Altered cytokine expression in APCs from NOD mice compared to other mouse strains. The table is divided in four sections: IL-10, IL-12, proinflammatory cytokines, and Type I interferons (T1). Abbreviations: LPS: lipopolysaccharides; PIC: poly I:C; PGN; peptidoglycan; SAC: Staph. aureus Cowan extract; ↗ increased in NOD; ↘ decreased in NOD; ≡ no change. Data refer to MFI or amount secreted, except (*) indicating mRNA levels.

APC		Mouse strains	Stimulation	Cytokines	Refs
Pro-inflammatory cytokines	Splenic CD8α+ DCs	NOD vs B6	LPS, PIC, SAC	IL-6 ≡	(84)
	Splenic CD8α- DCs	NOD vs B6	LPS, PIC, SAC	IL-6 ↗	(84)
	Splenic DCs	NOD vs NOR	PIC	TNF-α ≡	(85)
	Splenic DCs	NOD vs B6	CpG	TNF-α ↗	(137)
	Pancreatic CD8α- DCs	NOD vs B6	LPS	IL-6 ↗ TNF-α ≡	(138)
	Pancreatic CD8α- DCs	NOD vs B6	LPS	IL-1b, IL-6, TNF ↗ (*)	(138)
	BM-DCs	NOD vs NON	LPS	IL-1a, IL-1b, IL-6 ↘ (*)	(143)
	BM-DCs	NOD vs B6, B10.DR	LPS/IFN-γ	IL-6 ≡	(95)
	Pre-DCs	NOD vs NOR	CpG	IL-6, TNF-α ↘	(99)
	Macrophages	NOD vs B6	PGN	TNF-α ↘	(153)
	Macrophages	NOD vs NOR, BALB/c	LPS	IL-1α, TNF-α ↗	(135)
	Macrophages	NOD vs NOR, BALB/c	CD40L	TNF-α ↗ IL-1α ≡	(135)
	Macrophages	NOD vs NOR	LPS	IL-1, TNF-α ↘ IL-6 ≡	(152)
	Macrophages	NOD vs B6, B10	LPS	IL-1, TNF-α ≡ IL-6 ↗	(152)
IFN-I	Splenic DCs	NOD vs B6	CpG	IFN-α ↗ IFN-β ↗	(137)
	Splenic pDCs	NOD (young vs diabetic)	None (basal)	IFN-α ↘	(88)
	BM-DC (Flt3L)	NOD vs B6g7	CpG	IFN-α ↗	(137)

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SUPPLEMENTARY DATA

Supplementary Table S13. Altered cytokine expression in APCs from T1D patients compared to various controls. The table is divided in four sections: A) IL-10, B) IL-12, C) proinflammatory cytokines, and D) Type I interferons. Abbreviations: MoDCs and MoMΦs: monocyte-derived DCs and macrophages; mDCs: myeloid DCs; LPS: lipopolysaccharides; PIC: poly I:C; PC4: Pam3CSK4; ctrl: control; AAb: autoantibody; FDR: first degree relative; ↗ increased in T1D; ↘ decreased in T1D; ≡ no change. Data refer to mean fluorescence intensity or amount secreted, except (#) based on % cells positive for the cytokine and (*) based on mRNA levels.

APC		Subjects	Stimulation	Cytokines	Refs
IL-10	Blood DCs	New onset T1D (children)	PIC	IL-10 ≡ (#)	(79)
	MoDCs	T1D vs ctrl, T2D, RA	LPS	IL-10 ≡	(145)
	MoDCs	T1D or At-Risk vs ctrl	IL-1β	IL-10 =	(83)
	MoDCs	T1D vs ctrl (children)	LPS	IL-10 ↗	(144)
	Blood monocytes	T1D vs ctrl, T2D (adults)	LPS	IL-10 ↗	(147)
	Blood monocytes	New onset T1D (children)	PIC	IL-10 ≡ (#)	(79)
	Blood monocytes	T1D vs ctrl,T2D	IFN-γ	IL-10 ≡ (*)	(154)
	B cells	T1D vs ctrl	IL-21	IL-10 ≡ (#)	(155)
	B cells	T1D, LADA vs ctrl, T2D	None	B10 cells ↘ (#)	(156)
	B cells	T1D vs ctrl	Anti-IgM	IL-10 ↘ (#) IL-10 ↘	(157)
	B cells	T1D vs ctrl	PC4, LPS, CpG	IL-10 ↘	(157)
IL-12	Blood DCs	T1D vs ctrl, T2D	CD40L, LPS	IL-12 ↘	(73)
	Blood DCs	New onset T1D (children)	PIC	IL-12 ≡ (#)	(79)
	MoDCs	T1D vs ctrl (children)	LPS	IL-12 ↘	(144)
	MoDCs	T1D vs ctrl	IL-1β	IL-12 ≡	(83)
	MoDCs	At-Risk vs ctrl	IL-1β	IL-12 ↘	(83)
	Blood monocytes	New onset T1D (children)	PIC	IL-12 ≡ (#)	(79)
	Blood monocytes	T1D vs ctrl,T2D	LPS	IL-12 ≡	(147)
	Blood monocytes	T1D vs ctrl,T2D	IFN-γ	IL-12 ↗ (*)	(154)
Proinflammatory cytokines	Blood DCs	New onset T1D (children)	PIC	IL-6, TNF-α ≡ (#)	(79)
	Blood mDCs	New onset T1D (children)	LPS, PIC, R848	IL-1β ≡ (#)	(75)
	Blood mDCs	New onset T1D (children)	LPS	IL-6 ↘ (#)	(75)
	Blood mDCs	New onset T1D (children)	PIC, R848	IL-6 ≡ (#)	(75)
	Blood mDCs	AAb+ vs AAb-	None, LPS, PIC	IL-1β, IL-6 ≡ (#)	(76)
	Blood mDCs	AAb+ vs AAb-	R848	IL-1β ↗ (#) IL-6 ≡ (#)	(76)
	MoDCs	T1D vs ctrl, T2D, RA	LPS	IL-1β, IL-6, TNF-α ≡	(145)
	MoDCs	T1D vs ctrl	TNF-α	IL-6 ↗	(148)
	MoDCs	T1D or At-Risk vs ctrl	IL-1β	TNF-α ↘ IL-6 ≡	(83)
	Blood monocytes	New onset T1D (children)	None, LPS	IL-1β ↗ (#) IL-6 ≡ (#)	(75)
	Blood monocytes	New onset T1D (children)	PIC, R848	IL-1β, IL-6 ≡ (#)	(75)
	Blood monocytes	AAb+ vs AAb-	None, LPS	IL-1β ↗ (#) IL-6 ≡ (#)	(76)
	Blood monocytes	AAb+ vs AAb-	PIC, R848	IL-1β ↗ (#) IL-6 ↘ (#)	(76)
	Blood monocytes	New onset T1D (children)	PIC	IL-6 ≡ (#)	(79)
	Blood monocytes	New onset T1D (children)	PIC	TNF-α ↗ (#)	(79)
	Blood monocytes	T1D vs ctrl	None, LPS, PC4	IL-1β ↗ TNF-α ↗	(158)
	Blood monocytes	T1D vs ctrl,T2D	LPS	IL-6 ↗ IL-1β, TNF-α ≡	(147)
	MoMΦs	DQ8/DQ2 T1D vs ctrls	LPS	IL-1β, IL-6, TNF-α ↗	(159)
	B cells	T1D vs ctrl	Anti-IgM	TNF-α ↗ (#) TNF-α ↘	(157)
IFN-I	Blood DCs	T1D, T2D vs ctrl	CD40L	IFN-α ↘	(73)
	Blood pDCs	New onset T1D (children)	R848 (TLR7/8)	IFN-α ↗ (#)	(75)
	Blood pDCs	FDR vs T1D, ctrl	CpG	IFN-α ↗	(160)
	PBMCs	T1D patients	Flu virus	IFN-α ↗	(74)
	PBMCs	T1D patients	Flu virus	IFN-α ↗	(77)

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SUPPLEMENTARY DATA

Supplementary Table S14. Other mechanisms of tolerance that are altered in APCs in T1D. The column H/M/R indicates whether the data refers to humans, mice or rats. Abbreviations: IDO: indoleamine 2,3-dioxygenase; MS; multiple sclerosis.

Mechanism	Role / effect	H/M/R	Refs
Galectin-1	Inhibitor of T cell proliferation and Th1/Th17 responses Monocytes produce less galectin-1 in T1D patients compared to controls	H	(161)
IDO	Inhibitor of T cell proliferation and effector T cell response in favor of Treg responses	H/M/R	(162)
	Contribute to the protective role of pDCs in NOD mice	M	(163)
	DCs from young female NOD mice have an impaired induction of IDO in response to IFN-γ, relative to male NOD mice or B6 mice	M	(164)
	Defects due to inhibited Stat1 signaling, corrected by peroxynitrite inhibitor or a Stat1-independent inducer (chorionic gonadotrophin)	M	(164; 165)
	Defective IDO induction by IFN-γ in NOD mice extends to dermal fibroblasts	M	(166)
Vitamin D	Regulator of the tolerogenic function of DCs	H/M/R	(167)
	CYP27B1, encoding a critical enzyme for the generation of vitamin D, is associated with T1D and MS	H	Table S1 Table S2
	CYP27B1 polymorphism can lead to reduced expression in DCs (MS)	H	(168)
	CYP27B1 polymorphism leads to reduced expression in PBMCs (T1D)	H	(169)
	One *CYP27B1* polymorphism is associated with lower Treg frequency (T1D)	H	(170)
	VDR, encoding the vitamin D receptor, is associated with T1D in BB rats	R	Table S3

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SUPPLEMENTARY DATA

Supplementary Table S15. Defects in adhesion and homing of APCs. The table is divided in two sections: A) cell adhesion, and B) chemotaxis. The column H/M indicates whether the data refers to humans (H) or mice (M). Abbreviations: AAb: autoantibodies; MoDCs: monocyte-derived DCs; mDCs: myeloid DCs.

	Molecule	Role / effect	H/M	Refs
Adhesion molecules	ICAM-1	Expressed at lower level on MoDCs from T1D patients (vs T2D and controls)	H	(147)
	ITGB7	Recruitment by adhesion of T cells and APCs expressing CD103 or CD49d, particularly important for recruitment to islets in humans and NOD mice	M	(171-173)
		ITGB7 is associated with human T1D	H	Table S2
	ITGB1	*ITGB1* is associated with human T1D	H	Table S2
		ITGB1 may also be required for β-cells to proliferate	M	(41)
	ITGB7 / ITGB1	ITGA4/B7 and ITGB1 can bind fibronectin	H/M	
		BM-DCs have increased adhesion to fibronectin in vitro (NOD vs B6, BALB/c)	M	(174)
	SLAM	Reduced SLAM expression in NOD mice leads to diminished homotypic interaction between mDCs and NKT cells (NOD vs B6) and to defective secretion of IL-4 and IL-10 by NKT cells, which play a regulatory role in T1D	M	(175; 176)
	SIRPα	The protein encoded by the NOD allele of *Sirpa* on DCs binds more strongly to CD47, which results in enhanced T cell proliferation	M	(70)
Chemokines and receptors	Chemotaxis	Impaired migration toward inflamed tissue sites (NOD vs B6, BALB/c)	M	(177)
	CCR2	Reduced expression on CD11c+ CD8α- DCs (NOD vs B6, ± LPS)	M	(138)
		CCL2 (CCR2 ligand) recruits tolerogenic CD11c+ CD11b+ DCs to islets (NOD)	M	(178)
		CCR2-deficient NOD mice have lower incidence of disease diabetes	M	(179)
		Reduced on mDCs and pDCs from children with T1D (vs controls)	H	(78)
		Blood levels of CCL2 (CCR2 ligand) are reduced in subjects with multiple AAb.	H	(180)
		CCR2 association with T1D is controversial	H	(21-23)
	CCR5	Reduced expression on CD11c+ CD8α- DCs (NOD vs B6, ± LPS)	M	(138)
		Involved in the recruitment of leukocytes, including DCs, to inflamed islets	M	(181; 182)
		CCR5-deficient NOD mice have accelerated diabetes	M	(179)
		Blockade of CCL5 (one of CCR5 ligands) ameliorates diabetes	M	(181)
		Levels of CCL3 and CCL4 (other CCR5 ligands) are increased in blood of subjects with multiple AAb	H	(180)
		CCR5 is associated with human T1D	H	Table S2
	CCR7	*CCR7* is associated with human T1D	H	Table S2
		Defective migration of mature NOD BM-DCs toward CCL19 (a CCR7 ligand)	M	(174)
	CXCL12	Association of *CXCL12* with early onset of T1D	H	(183; 184)
		Increased expression of CXCL12 in NOD pancreas recruits pDCs (NOD vs NOR,B6)	M	(185)

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SUPPLEMENTARY DATA

Supplementary Table S16. Preclinical studies featuring exogenous APCs ± antigen provision. Abbreviations: BM-DCs bone marrow-derived DCs; IV intravenous; IP intraperitoneal; ID intradermal; MPLA monophosphoryl lipid A.

Study details	Outcome	Refs
Feili-Hariri et al. 1999. BM-DCs (4 days with GM-CSF +/- IL-4), unpulsed or pulsed with (HSP60(437-460), GAD65(509-528), GAD65(524-543), 60 μg/ml); 4-8x10^5 DCs injected IV in NOD mice (three weekly injections at 5-7 weeks)	DCs were protective with no added benefit from antigen provision	(186)
Papaccio et al. 2000. Splenic DCs, unpulsed or pulsed with human gamma globulin (100 μg/ml); 3x10^5 DCs injected IV in NOD mice (one injection at 8 wks)	Protection required antigen pulsing (irrelevant antigen)	(187)
Krueger et al. 2003. Spleen-derived DC line, unpulsed or pulsed with insulin (400 μg/ml); 4x10^5 APCs injected IP in cyclophosphamide-treated NOD mice (one injection at 8 weeks)	Protection with insulin-DCs, no protection with OVA as antigen	(188)
Lo et al. 2006. BM-DCs (6 days with GM-CSF and IL-4), unpulsed or pulsed with 3 μM InsB(9-23) or InsC19-A3 or GAD65(78-97) peptide; 1x10^5 DCs injected in footpad of NOD mice (three injections from 9 to 11 weeks)	Only DCs with GAD65 peptide had a significant protection	(189)
Marin-Gallen et al. 2010. BM-DCs (7 days with GM-CSF), co-cultured with apoptotic bodies from NIT-1 cells (beta cell line); 1x10^6 DCs injected IP in RIP-IFN-β NOD mice (one single injection at 12-14 days of age)	Only DCs loaded with beta cell apoptotic cells protected, compared to unpulsed or pulsed with apoptotic cells from non-beta cells.	(190)
Haase et al. 2010. BM-DCs (8 days with GM-CSF and IL-10, 1.5% mouse serum), pulsed with InsB(9-23) and InsB(15-23) at 10 μg/ml; 1x10^6 DCs injected IP in NOD mice (weekly injections from 5 to 12 weeks of age)	Only DCs pulsed with insulin peptides were protective	(191)
Gibson et al. 2015. BM-DCs (6 days with GM-CSF, IL-4 and vitamin D3), matured with LPS for 24h, pulsed with InsC19-A3 (10 μg/ml); 2x10^5 DCs injected ID in humanized HLA-DR4 Tg mice (two injections two weeks apart)	Reduced proliferation and IFNγ, increased IL-10 in ex vivo recall response	(192)
Lo et al. 2018. BM-DCs (5-6 days with GM-CSF and IL-4), used immature and pulsed with 3 μM InsB(9-23), GAD65(78-97) or GAD65(260-279) peptide; 1x10^5 DCs injected in footpad of NOD mice (three weekly injections starting at 9 weeks of age).	Pulsing with certain subdominant and ignored epitopes conferred better protection than unpulsed	(193)
Funda et al. 2018. BM-DCs (7 days with GM-CSF and IL-4, 10% FBS or serum-free medium; vitamin D2 and dexamethasone added on day 6), unpulsed or pulsed with GAD65 (1-2 μg/ml) or OVA (1 μg/ml), and activated with MPLA for another day; 3x10^6 DCs injected IP in NOD.SCID mice along with 5x10^6 splenocytes from diabetic NOD mice. Also 3x10^6 DCs injected IP in NOD mice (one single injection at 4 weeks of age).	Protective response with unpulsed DCs, which was lost when DCs were pulsed with GAD65 or OVA	(194)

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