

Supporting Information

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SI Materials and Methods

Mice. The list of mice is provided in the accompanying paper. For experiments using STZ (Sigma-Aldrich), a dose of 50 mg/kg i.p. was administered for 2 consecutive d before T-cell transfer. This dose provided the minimal requirements to induce leukocyte infiltration (1). The institutional animal care committee approved these studies.

T-Cell Transfers. Isolation and transfer of CD4 T cells were done as described. All cells were first activated in vitro before i.v. injection. Detailed procedures are provided in the accompanying paper (2). NOD and NOD.IFN- γ R^{-/-} mice received a sublethal dose of irradiation (6.5 Gy) before T-cell injection. PTx treatment on activated CD4 T cells was performed as previously described (3).

Antibody Treatments. Mice received 500 μ g i.p. anti-IFN- γ -neutralizing mAb (clone H22; provided by R. Schreiber, Washington University School of Medicine, St. Louis, MO) or 400 μ g anti-VCAM-1 (clone M/K-2.7; ATCC). Isotype control rat IgG (Sigma-Aldrich) antibodies were used.

Islet Isolation and Handling. Islets isolation, staining for immunofluorescence analysis by standard microscope with epi-illumination, and confocal and two-photon microscopy were performed as described, and results are provided in the accompanying paper (2).

Microarray, qRT-PCR, and Evaluation. Islets of Langerhans were isolated from six to eight mice, yielding an average of 500 islets per isolation. For experiments using IP-HEL recipients, all mice

(T-cell-transferred and non-T-cell-transferred) received equal doses of sublethal irradiation. Total RNA was purified using RNAqueous Kit (Life Technologies). Samples were biotin-labeled and hybridized to Gene 1.0 ST microarrays (Affymetrix) using standard Affymetrix protocols (www.affymetrix.com) from the Siteman Cancer Center Molecular and Genomic Analysis Core Facility. Evaluation of differential gene expression was done using Arraystar Software (DNASTar). At least two independent RNA isolations and hybridizations were used to determine the significance of gene expression differences between the samples. Statistical significance was determined using moderated *t* test with Benjamini-Hochberg False Discovery Rate Analysis. Heat maps were generated using hierarchical clustering with Euclidean or Standard Pearson metric. K-means clustering was performed using Standard Pearson metric. GO term analysis was performed by hypergeometric probability distribution (4). Validation of microarray results was performed by qRT-PCR using the Fast SYBR Green kit and $\Delta\Delta C_t$ calculate on a StepOnePlus Instrument (Applied Biosystems). All primers were designed by Primer Bank (<http://pga.mgh.harvard.edu/primerbank/>), and actin was used as the qRT-PCR standard.

Statistical Analysis. The Mann-Whitney *u* test was used to determine the level of significant differences between samples, and these levels were plotted using GraphPad Prism 5 (GraphPad Software, Inc). *****P* < 0.0001; ****P* < 0.001; ***P* < 0.01; **P* < 0.05; ns, *P* \geq 0.05. Median numbers of T cells per infiltrated islets in all experiments were obtained by including only islets containing infiltrating T cells.

1. Calderon B, Suri A, Unanue ER (2006) In CD4+ T-cell-induced diabetes, macrophages are the final effector cells that mediate islet beta-cell killing: Studies from an acute model. *Am J Pathol* 169:2137-2147.
2. Calderon B, Carrero JA, Miller MJ, Unanue ER (2011) Cellular and molecular events in the localization of diabetogenic T cells to islets of Langerhans. *Proc Natl Acad Sci USA*, 10.1073/pnas.1018973108.

3. Cyster JG, Goodnow CC (1995) Pertussis toxin inhibits migration of B and T lymphocytes into splenic white pulp cords. *J Exp Med* 182:581-586.
4. Draghici S (2003) *Data Analysis Tools for DNA Microarrays* (Chapman & Hall, London).

Table S1. IFN-dependent gene changes

Gene name	Recipient mouse			
	NOD <i>Rag1</i> ^{-/-}		NOD.IFN- γ R	
	Fold change	<i>P</i> value	Fold change	<i>P</i> value
BC023105	102.303	0.000015	-1.062	0.762000
<i>Cxcl10</i>	78.554	0.000003	10.978	0.000041
<i>ligp1</i>	54.037	0.000017	-1.315	0.503000
<i>Mpa2l</i>	40.955	0.000002	5.355	0.000248
<i>Gbp2</i>	33.738	0.000015	3.794	0.002080
<i>Tgtp2</i>	24.446	0.000033	-1.052	0.901000
<i>Cxcl9</i>	24.433	0.000009	1.151	0.479000
<i>Gbp4</i>	24.164	0.000032	2.249	0.007740
<i>Tgtp1</i>	23.918	0.000048	-1.086	0.831000
<i>ligp2</i>	20.831	0.000008	1.509	0.246000
<i>Gbp8</i>	20.083	0.000002	2.571	0.006940
<i>Gbp5</i>	14.231	0.000129	5.007	0.000983
<i>Ifit3</i>	13.078	0.001420	1.412	0.527000
<i>Irgm1</i>	12.416	0.000113	1.259	0.362000
<i>Gbp8</i>	12.343	0.000090	1.922	0.019700
<i>Irgb10</i>	11.609	0.000041	-1.18	0.437000
<i>Irg47</i>	10.409	0.000021	1.519	0.097100
<i>Gbp6</i>	10.356	0.000073	1.624	0.135000
<i>Gbp3</i>	9.927	0.002740	1.381	0.283000
<i>Serpin3A*</i>	9.907	0.000798	22.119	0.000479
Gm4951	9.202	0.000040	-1.184	0.377000
<i>Cd274</i>	9.094	0.000062	1.451	0.226000
<i>Gbp6</i>	9.016	0.000032	1.843	0.059200
<i>GzmA*</i>	8.432	0.001150	9.632	0.003170
AW1120100	8.214	0.000248	2.71	0.022300
<i>Psmb9</i>	8.121	0.000700	2.013	0.110000
<i>Gzmb*</i>	7.666	0.002460	9.086	0.000086
<i>Psmb8</i>	7.625	0.001010	2.783	0.045100
<i>Stat1</i>	6.776	0.000101	1.308	0.147000
<i>Herc5</i>	6.719	0.000030	2.305	0.010200
<i>Rtp4</i>	6.481	0.000044	1.24	0.440000
<i>Ccl24*</i>	6.455	0.003270	8.1	0.000123
<i>Ifit2</i>	6.415	0.000079	1.182	0.517000
<i>Ly6a</i>	6.138	0.002220	2.114	0.032600
<i>Gdap10</i>	5.772	0.035800	2.757	0.240000
<i>Samd9l</i>	5.767	0.002060	2.877	0.057800
<i>Psmc2</i>	5.539	0.000393	3.132	0.022200
<i>Mkl1</i>	5.537	0.000105	1.797	0.013600
<i>Bcl2a1a*</i>	5.431	0.016900	4.952	0.062600
<i>Ifit1</i>	5.418	0.000360	1.37	0.351000
<i>Casp1</i>	5.376	0.002790	2.905	0.010900
<i>Bcl2a1b*</i>	5.277	0.011500	4.792	0.055000
<i>Zbp1</i>	5.202	0.000725	1.098	0.653000
G530012D1	5.195	0.275000	1.806	0.669000
<i>Ube2l6</i>	4.999	0.009030	2.448	0.056900
<i>Oasl2</i>	4.991	0.000290	1.456	0.110000
<i>Tnfrsf10</i>	4.976	0.002470	1.482	0.078400
<i>Ifi204</i>	4.965	0.000168	1.133	0.582000
<i>Gm5431</i>	4.926	0.000613	-1.015	0.937000
ENSMUSG00000057445	4.823	0.000697	1.436	0.254000
<i>Serping1*</i>	4.813	0.004770	3.232	0.007510
<i>Bcl2a1d*</i>	4.759	0.022300	4.472	0.073200
<i>Xzfl1</i>	4.599	0.000432	1.12	0.712000
<i>Gbp1</i>	4.594	0.000096	1.308	0.153000
<i>Rsad2</i>	4.546	0.000780	-1.074	0.660000
<i>Ch25h</i>	4.544	0.003850	1.782	0.048000
I830012O16	4.487	0.001670	1.482	0.199000
<i>Irf1</i>	4.47	0.004580	1.77	0.197000
<i>Ifi44</i>	4.47	0.000032	-1.165	0.488000

Table S1. Cont.

Gene name	Recipient mouse			
	NOD <i>Rag1</i> ^{-/-}		NOD.IFN- γ R	
	Fold change	<i>P</i> value	Fold change	<i>P</i> value
<i>Ddx60</i>	4.456	0.000047	1.747	0.027100
<i>Defb1</i> *	4.449	0.022000	3.584	0.088400
<i>Nampt</i>	4.447	0.000145	1.84	0.055200
<i>Il2rg</i> *	4.44	0.002790	3.895	0.000507
<i>Crybb3</i> *	4.426	0.004950	7.951	0.000201
<i>Parp14</i>	4.356	0.000364	1.889	0.008090
<i>Serpin3f</i>	4.3	0.001840	1.702	0.032300
<i>Psmc2</i> *	4.263	0.002260	2.333	0.081300
<i>Ms4a6d</i> *	4.235	0.001920	2.636	0.010500
<i>Il6</i>	4.214	0.003380	1.553	0.225000
<i>Cd53</i> *	4.194	0.001840	5.465	0.000495
<i>Tmem140</i>	4.19	0.000106	1.93	0.016700
<i>Ubd</i>	4.178	0.010200	1.15	0.689000
<i>Cd52</i> *	4.144	0.015800	3.868	0.014400
<i>Ppa1</i> *	4.1	0.000671	2.101	0.058500
<i>Cfb</i> *	4.087	0.045600	7.181	0.009380
<i>Lsm5</i>	4.024	0.182000	2.679	0.403000
<i>Ifi203</i>	4.01	0.002490	1.15	0.730000

*Genes not reduced in IFN- γ ^{-/-} recipients.

Table S2. Leukocyte-depleted gene changes

Gene name	Unpurified β -cells Fold change	Purified β -cells Fold change
BC023105	102.303	104.3
<i>Cxcl10</i>	78.554	105.556
<i>ligp1*</i>	54.037	45.606
<i>Mpa2l</i>	40.955	76.64
<i>Gbp2</i>	33.738	86.261
<i>Tgtp2</i>	24.446	33.231
<i>Cxcl9*</i>	24.433	14.937
<i>Gbp4</i>	24.164	60.639
<i>Tgtp1</i>	23.918	30.365
<i>ligp2</i>	20.831	22.422
<i>Gbp8</i>	20.083	55.652
<i>Gbp5</i>	14.231	38.876
<i>Ifit3*</i>	13.078	10.242
<i>Irgm1</i>	12.416	14.62
<i>Gbp8</i>	12.343	47.104
<i>Irgb10</i>	11.609	12.401
<i>Irg47</i>	10.409	12.902
<i>Gbp6</i>	10.356	15.576
<i>Gbp3</i>	9.927	39.44
<i>Serpin3A</i>	9.907	16.538
Gm4951	9.202	10.5
<i>Cd274</i>	9.094	13.692
<i>Gbp6</i>	9.016	20.686
<i>Gzma*</i>	8.432	1.248
AW1120100	8.214	13.414
<i>Psmb9*</i>	8.121	4.44
<i>Gzmb*</i>	7.666	1.345
<i>Psmb8</i>	7.625	6.031
<i>Stat1</i>	6.776	11.725
<i>Herc5</i>	6.719	7.934
<i>Rtp4</i>	6.481	5.194
<i>Ccl24*</i>	6.455	-1.037
<i>Ifit2</i>	6.415	6.224
<i>Ly6a</i>	6.138	6.322
<i>Gdap10*</i>	5.772	1.673
<i>Samd9l*</i>	5.767	3.67
<i>Psmc2</i>	5.539	5.575
<i>Mkl1</i>	5.537	7.303
<i>Bcl2a1a*</i>	5.431	-1.299
<i>Ifit1</i>	5.418	8.677
<i>Casp1*</i>	5.376	2.646
<i>Bcl2a1b*</i>	5.277	-1.273
<i>Zbp1</i>	5.202	3.699
G530012D1*	5.195	1.446
<i>Ube2l6</i>	4.999	8.507
<i>Oasl2</i>	4.991	10.833
<i>Tnfrsf10</i>	4.976	10.581
<i>Ifi204*</i>	4.965	2.288
Gm5431	4.926	4.452
ENSMUSG00000057445*	4.823	2.614
<i>Serping1</i>	4.813	5.472
<i>Bcl2a1d*</i>	4.759	-1.007
<i>Xzfp1</i>	4.599	4.074
<i>Gbp1</i>	4.594	6.626
<i>Rsad2</i>	4.546	5.06
<i>Ch25h*</i>	4.544	1.621
I830012O16	4.487	3.731
<i>Irf1</i>	4.47	4.565
<i>Ifi44</i>	4.47	6.973
<i>Ddx60</i>	4.456	5.05
<i>Defb1</i>	4.449	3.533
<i>Nampt</i>	4.447	3.317

Table S2. Cont.

Gene name	Unpurified β -cells Fold change	Purified β -cells Fold change
<i>Il2rg*</i>	4.44	1.385
<i>Crybb3</i>	4.426	3.49
<i>Parp14</i>	4.356	8.631
<i>Serpin3f</i>	4.3	3.559
<i>Psme2</i>	4.263	3.459
<i>Ms4a6d*</i>	4.235	1.193
<i>Il6</i>	4.214	2.721
<i>Cd53*</i>	4.194	1.08
<i>Tmem140</i>	4.19	5.556
<i>Ubd</i>	4.178	2.688
<i>Cd52*</i>	4.144	1.569
<i>Ppa1</i>	4.1	2.465
<i>Cfb</i>	4.087	9.973
<i>Lsm5*</i>	4.024	1.493
<i>Ifi203</i>	4.01	2.129

*Leukocyte-associated genes.