SUPPLEMENTARY DATA

Distinct roles of beta cell mass and function during type 1 diabetes onset and remission

Helena Chmelova[1,2], Christian M. Cohrs[1,2], Julie A. Chouinard[1,2], Cathleen Petzold[1], Matthias Kuhn[3], Chunguang Chen[1,2], Ingo Roeder[3], Karsten Kretschmer[1,2] and Stephan Speier[1,2]

[1]DFG-Research Center for Regenerative Therapies Dresden, Technische Universität Dresden, Germany; [2]Paul Langerhans Institute Dresden, German Center for Diabetes Research (DZD), Germany; [3]Institute for Medical Informatics and Biometry, Technische Universität Dresden, Germany.

Supplementary Table 1. Effect of donor and recipient genotype on intraocular islet environment. Combining the RIP-HA mouse model and the AC imaging platform allows modifying the environment for intraocular islets by different arrangements of islet donor and recipient genotypes. Thereby, intraocular islets can be studied *in vivo* in the presence or absence of autoimmune infiltration in combination with a normo- or hyperglycemic environment.

		recipient mouse islets	
		RIP-HA$^+$	**RIP-HA$^-$**
donor islets	**RIP-HA$^+$**	• Intraocular islet infiltration • Hyperglycemic environment	• Intraocular islet infiltration • Normoglycemic environment
	RIP-HA$^-$	• Intact intraocular islets • Hyperglycemic environment	• Intact intraocular islets • Normoglycemic environment

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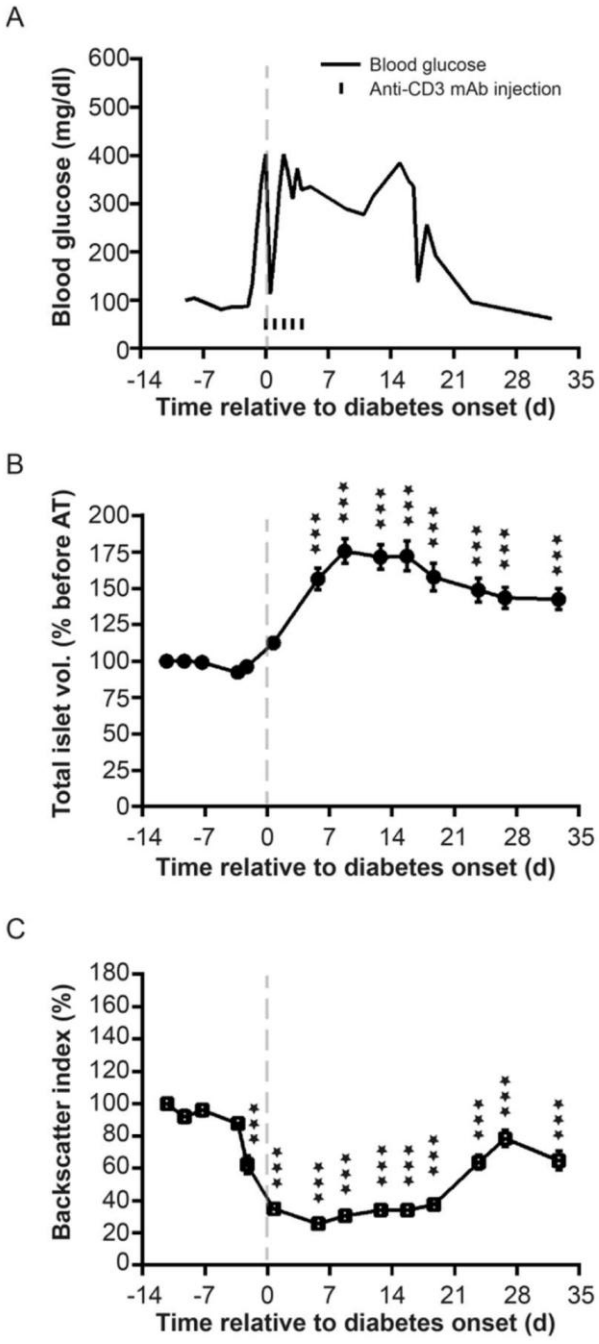
Supplementary Figure 1. NOD.SCID islets transplanted to the AC of NOD.SCID mice show similar changes in total islet volume and islet backscatter in response transient hyperglycemia. (A) Non-fasting blood glucose of NOD.SCID recipient mice in response to adoptive transfer of NOD.BDC2.5 T cells and anti-CD3 mAb treatment (mean of 3 mice). (B) Total islet volume of intraocular NOD.SCID islets in response to adoptive T cell transfer and anti-CD3 mAb treatment in the same NOD.SCID recipient mice as in panel A (n = 19 islets from 3 mice; mean ± SEM). (C) Backscatter index of the same islets analyzed in panel B (mean ± SEM). Significant changes from before adoptive transfer were analyzed by a linear mixed model and are indicated by * ($p < 0.05$), ** ($p < 0.01$) or *** ($p < 0.005$).



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Induction of autoimmune diabetes in NOD.SCID mice by adoptive transfer of BDC2.5 T cells. Single cell suspensions from pooled spleen and lymph nodes (cervical, axillary, brachial, inguinal, popliteal, and mesenteric) of NOD-BDC2.5 mice were prepared using 70 µm cell strainers (BD, NJ, USA). Cells were subsequently washed in Hank's Balanced Salt Solution (Life Technologies, CA, USA) supplemented with 10 mM HEPES and 5% fetal bovine serum. Cells were labeled with biotin-conjugated CD4 (Clone RM4-5), PE-conjugated Vβ4-TCR (Clone KT4), APC-conjugated CD62L (Clone MEL-14) and PerCP-Cy5.5-conjugated CD25 (Clone PC61) monoclonal antibodies (mAbs) and with Pacific Blue-conjugated streptavidin (all eBioscience, CA, USA or BD). The autoMACSTM magnetic cell separation system and streptavidin-conjugated magnetic microbeads (Miltenyi Biotec, Germany) were used to enrich CD4+ T cells. The sample was sorted on a FACS Aria (BD). For adoptive transfer, 2 x 106 FACS-purified CD4+Vβ4+CD62LhighCD25- BDC2.5 T cells in PBS were injected i.v. into recipient NOD.SCID mice. Non-fasting blood glucose levels were closely monitored after adoptive transfer. Diabetes onset was defined as non-fasting blood glucose > 400 mg / dl and normoglycemia as non-fasting blood glucose levels < 200 mg / dl. Arrest of autoimmune attack was achieved by treatment with anti-CD3 mAb. Mice received intravenous injections of 10 µg / day anti-CD3 mAb (Clone 145-2C11; eBioscience) for 5 consecutive days starting at diabetes onset. To achieve restoration of normoglycemia, mice were additionally implanted with 1 insulin pellet at >2 weeks after diabetes onset (LinBit; LinShin Canada Inc., Canada).