

SUPPLEMENTAL MATERIAL

Pancreas tissue slices from organ donors enable in situ analysis of type 1 diabetes pathogenesis

Julia K. Panzer^{1,2,3,#}, Helmut Hiller^{4,#}, Christian M. Cohrs^{1,2,3,#}, Joana Almaca^{5,#}, Stephen J. Enos^{1,2,3}, Maria Beery⁴, Sirlene Cechin⁶, Denise M. Drotar^{1,2,3}, John R. Weitz⁵, Jorge Santini⁷, Mollie K. Huber^{4,7}, Mirza Muhammad Fahd Qadir^{6,8}, Ricardo L. Pastori⁶, Juan Domínguez-Bendala^{6,8}, Edward A. Phelps⁷, Mark A. Atkinson⁴, Alberto Pugliese^{5,6,9}, Alejandro Caicedo⁵, Irina Kusmartseva⁴ and Stephan Speier^{1,2,3*}

¹Paul Langerhans Institute Dresden (PLID) of the Helmholtz Zentrum München at the University Clinic Carl Gustav Carus of Technische Universität Dresden, Helmholtz Zentrum München, Neuherberg, Germany

²Institute of Physiology, Faculty of Medicine, Technische Universität Dresden, Germany

³German Center for Diabetes Research (DZD)

⁴Department of Pathology, Immunology and Laboratory Medicine, University of Florida Diabetes Institute, Gainesville, FL, USA

⁵Department of Medicine, Division of Metabolism, Endocrinology and Diabetes, University of Miami Miller School of Medicine, Miami, FL, USA

⁶Diabetes Research Institute, University of Miami Miller School of Medicine, Miami, FL, USA

⁷J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, USA

⁸Department of Cell Biology and Anatomy, University of Miami Miller School of Medicine, Miami, FL, USA

⁹Department of Microbiology and Immunology, University of Miami Miller School of Medicine, Miami, FL, USA

JKP's present address is: Department of Medicine, Division of Metabolism, Endocrinology and Diabetes, University of Miami Miller School of Medicine, Miami, FL, USA

JRW's present address is Department of Pediatrics, university of California San Diego, CA, USA

[#]These authors contributed equally to this work

*Corresponding Author:

Stephan Speier

Tatzberg 47/49

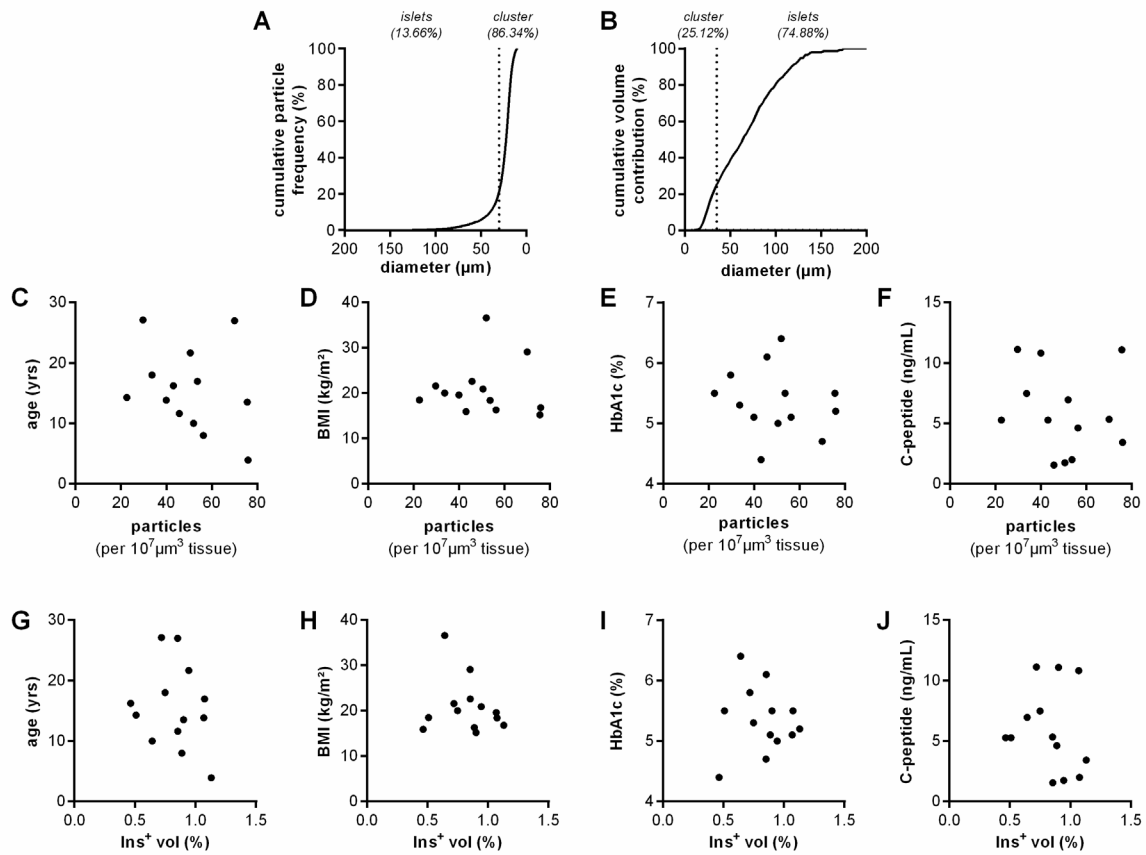
01307 Dresden

Germany

Stephan.Speier@tu-dresden.de

Tel: +49 (0)351-796-36617

Fax: +49 (0)351-796-36699



Supplemental Figure 1. Endocrine cell volume distribution and regression analyses

(A) Cumulative frequency distribution of all endocrine objects found in studied pancreas tissue slices by diameter.

(B) Cumulative volume contribution of all endocrine objects found in studied pancreas tissue slices by diameter. Dotted line indicates the separation of small cell clusters (≤ 10 cells) and islets (>11 cells).

(C-F) Correlation analysis of endocrine object counts against age (C), BMI (D), HbA1c (E) and plasma C-peptide (F).

(G-J) Correlation analysis of total Ins^+ volume in % of total slice volume against age (G), BMI (H), HbA1c (I) and plasma C-peptide (J).

POD CaseID	Age (y)	T1D diabetes duration (y)	Histopathology Report - nPOD
6456	30.49	0	Ins+ islets, numerous with range in sizes and compact morphologies. Low numbers of insulin-negative islets and also insulinitis present (aggregates and peri-islet). Rare islet hyperplasia (>500um). No exocrine infiltrates. HLA class I- low to moderate islet infiltrating lymphocytes otherwise normal low levels.
6469	27.06	1.5	Ins+/Gluc+ islets are in majority though with varying numbers between pancreas regions and lobules within sections. Single beta-cells observed in exocrine regions or in islets or as clusters. Normal numbers of islets with regular morphology (spherical profiles). Insulinitis present- <8 islets overall with peri-islet CD3+ cells in low numbers. Islet fibrosis, mild. Mild global CD3+ exocrine infiltrates all regions. Mild focal interstitial fibrosis, acinar atrophy, and duct obstruction.
6472	10.25	4	Ins+/Gluc+ islets, lobular distribution in 1 paraffin block and rare islets in other blocks. Majority of islets are INS- with irregular morphologies and reduced numbers in most blocks. Insulinitis in INS+ (majority) and INS- islets. Moderate increases in acinar Ki67+ cell numbers and mild increase in islet Ki67+ cell numbers. Mild to moderate diffuse exocrine CD3+ infiltrates. Elevated to hyperexpression of HLA-I in INS+ islets of blocks 02 and 05. Focal mixed polymorphonuclear and mononuclear infiltrates in one block (06). 01 and 02 blocks contain ventral lobe eg. PanHead region.
6459	20.95	10	Ins-/Gluc+ islets, reduced numbers, mostly small to medium sized, diffuse morphologies (irregular outlines). Variable moderate exocrine atrophy. None to very mild CD3+ exocrine and periductal infiltrates.

Supplemental Table 1. Histopathology reports of the nPOD OPPC Aperio database for the studied T1D cases