

Legends to Supplementary Figures

Supplementary Figure S1 (related to Figure 1): specificity, sensitivity and linearity of the assay for detection of pancreas cell types.

- A. Specificity of acinar cell markers. Note that one of the islet preparations is apparently contaminated with acinar cells. All sorted cell types, n=2-4; except sorted endothelial and leukocytes, n=1.
- B. Specificity of duct cell markers. All sorted cell types, n=3; except sorted endothelial and leukocytes, n=1.
- C. Specificity of delta cell markers. All sorted cell types, n=3; Sorted alpha, n=2; Sorted endothelial and leukocytes, n=1.
- D. Specificity of vascular endothelial cell markers. As expected, a clear signal is present in islet preparations (containing endothelial cells) but not in sorted non-endothelial cells. All sorted cell types, n=2; Sorted endothelial and leukocytes, n=1.
- E. The average of all 3 beta-cell markers when taking all unmethylated molecules (All T), above it the average when taking all unmethylated molecules except 1 methylated C (AllT-1) above it the average when taking all unmethylated molecules except 2 methylated C (All T-2). Sorted beta, n=6; sorted alpha, n=8; sorted delta, n=6; sorted acinar, n=4; sorted duct, n=4; sorted endothelial cells and leukocytes, n=1.
- F-G. Alpha and beta-cell markers in material sorted from islets of patients with T2D. ND, non-diabetic donor. In F, ND alpha, n=6; T2D alpha, n=3; ND beta, n=4; T2D beta, n=4; ND delta, n=6; T2D delta n=3. In G, ND alpha, n=8; T2D alpha, n=3; ND beta, n=6; T2D beta, n=5; ND delta, n=6; T2D delta n=3.
- H-K. Sensitivity and linearity of assay in detecting DNA from acinar cells, duct cells, delta cells and vascular endothelial cells, n=1. DNA from the cell type of interest was diluted into DNA of Leukocytes and the methylation assay was performed to determine the contribution of the cell of interest. Dots represent the average of all markers used for each cell type.

Supplementary Figure S2 (related to Figure 3): HPAP islet composition, shown separately for each cell type.

- A-C, percentage of DNA from each cell type in islet preparations. Each dot is the average of signal from methylation markers in one islet preparation, for acinar cells (A), alpha-cells (B) and beta-cells (C). ND Aab-, n =41; ND Aab+, n=15; T2D, n=26; T1D, n=10. Black dots in ND Aab+ represents donors that have more than 1 positive autoantibody.
- D-F, normalization of insulin secretion in high glucose for the number of islets (D), for insulin content (E) and for beta-cell DNA content (F). ND Aab-, n =41; ND Aab+, n=12; T2D, n=25; T1D, n=9. Black dots in ND Aab+ represents donors that have more than 1 positive autoantibody.
- G, correlation between beta-cell DNA and insulin secretion in high glucose, shown separately for the different donor groups. ND Aab-, n =39; ND Aab+, n=12; T2D, n=25; T1D, n=9.

Supplementary Figure S3 (related to Figure 4): beta-cell fraction (inferred from methylation analysis in nPOD sections) as a function of duration of disease (A) or age of onset (B). T1D, n=18.

Legends to Supplementary Tables

Supplementary Table S1: HPAP and nPOD cohorts

Age, race, sex, BMI, HbA1c, C-peptide, diagnosis, duration of disease and autoantibodies data for each HPAP donor.
Age, sex, BMI, race, C-peptide, diagnosis, duration of disease and age of onset data for each nPOD donor.

Supplementary Table S2: Alberta Islet Distribution Program and Islets from Integrated Islet Distribution Program (IIDP) center cohorts.

Islet preparations were used to purify the endocrine and exocrine cell types. Age, BMI, sex, purity, diagnosis and duration of disease data for each donor.

Supplementary Table S3: Antibodies for sorting or immunofluorescence staining.

List of antibodies used for sorting or immunofluorescence staining, company and their catalog number.

Supplementary Table S4: Markers for Next Generation Sequencing (NGS) and ddPCR.

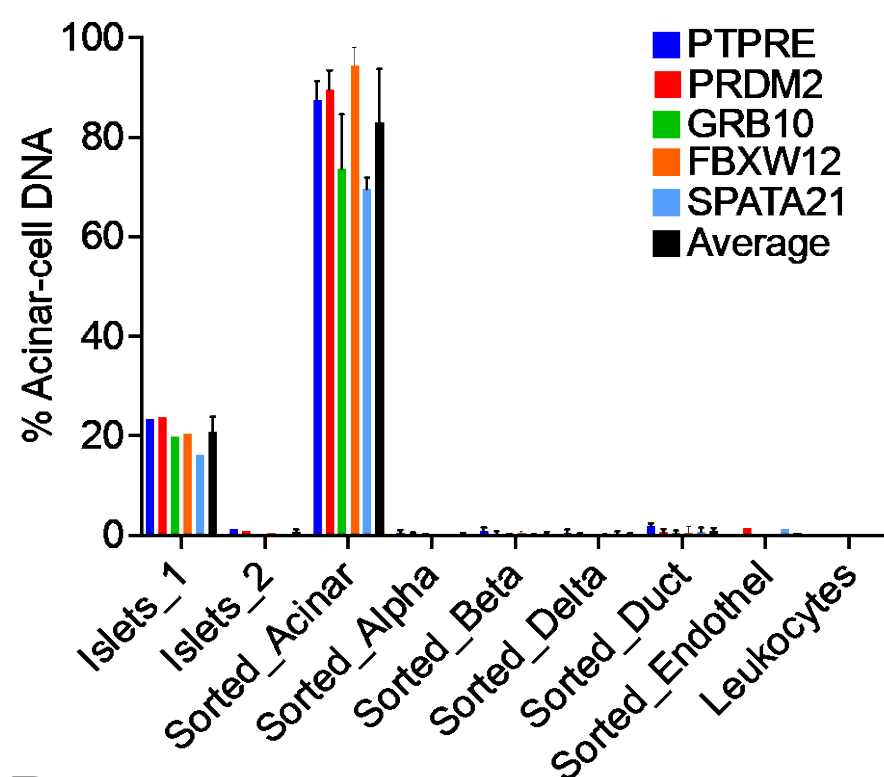
List of all markers used for next generation sequencing and ddPCR. Data about the location in gene browser, the number of CpG sites, fully unmethylated or methylated, the original sequence, the length of the sequence and the primers designed for each marker.

Supplementary Table S5: Primary data for all figures.

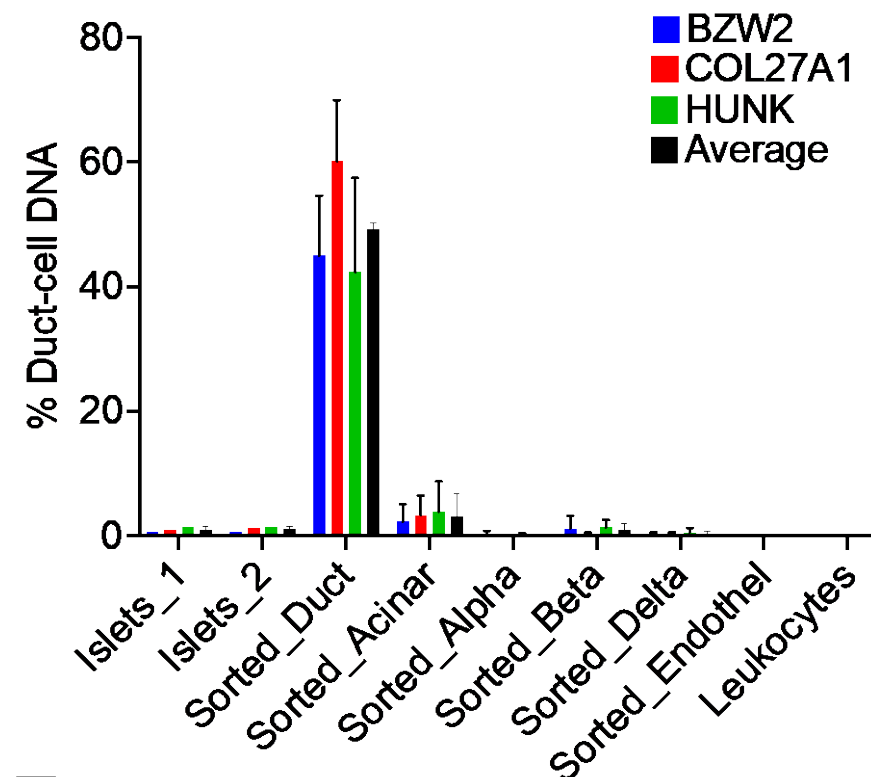
Supplemental File: a detailed protocol.

Supplementary Figure 1 (related to Figure 1)

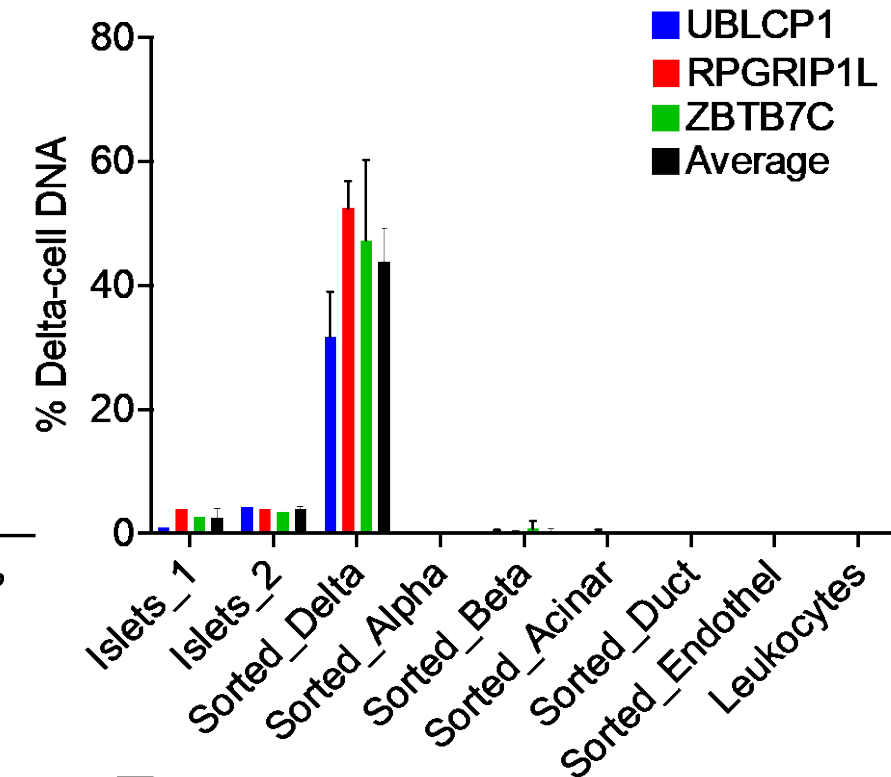
A



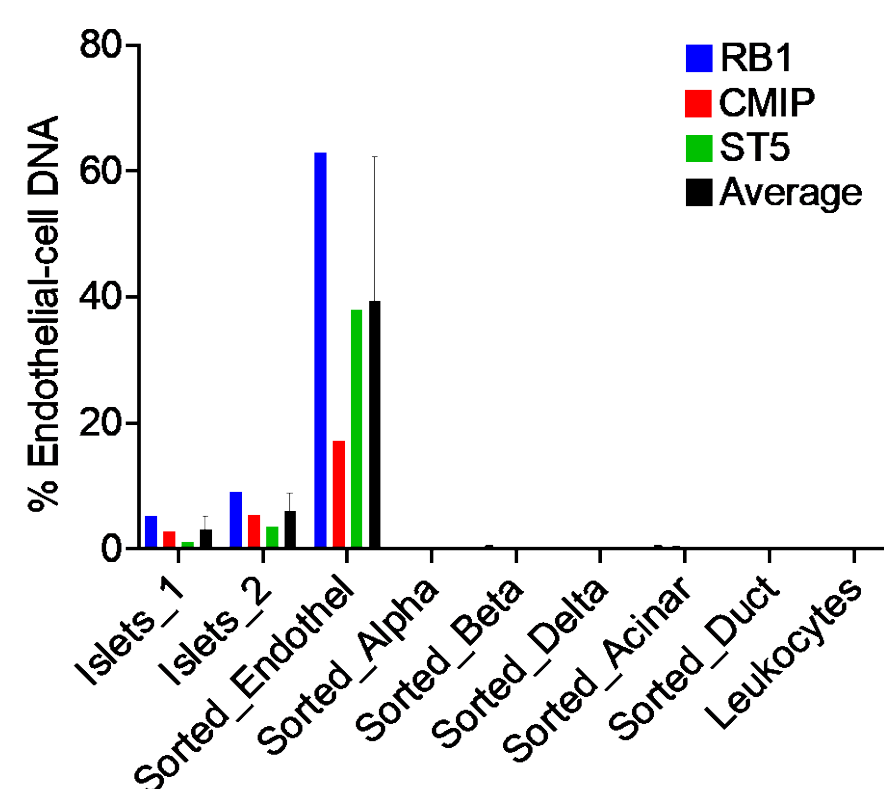
B



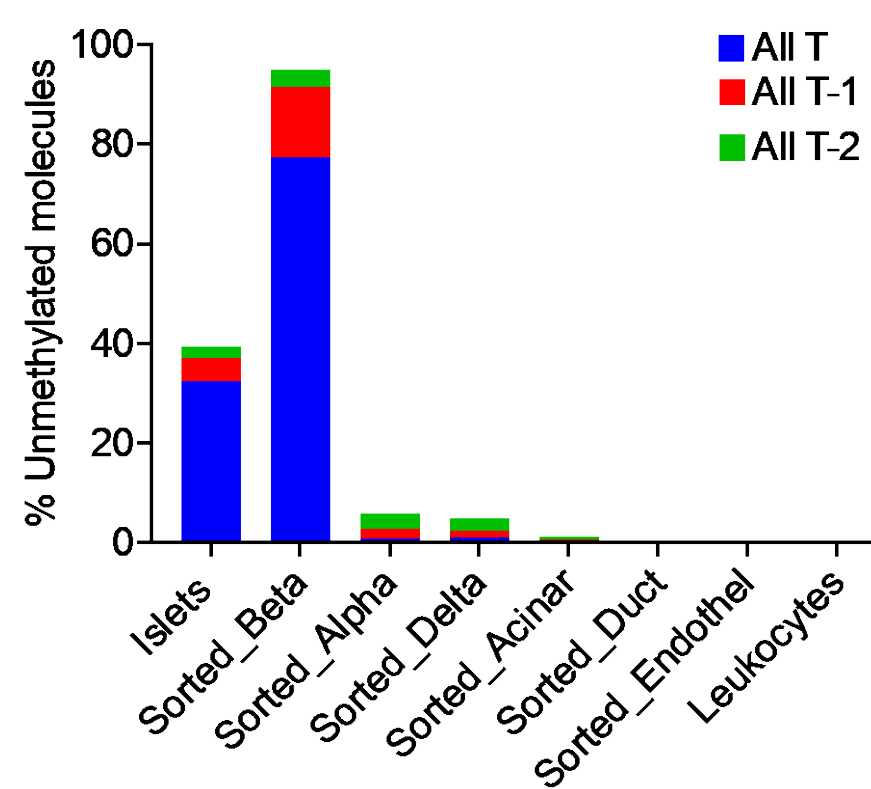
C



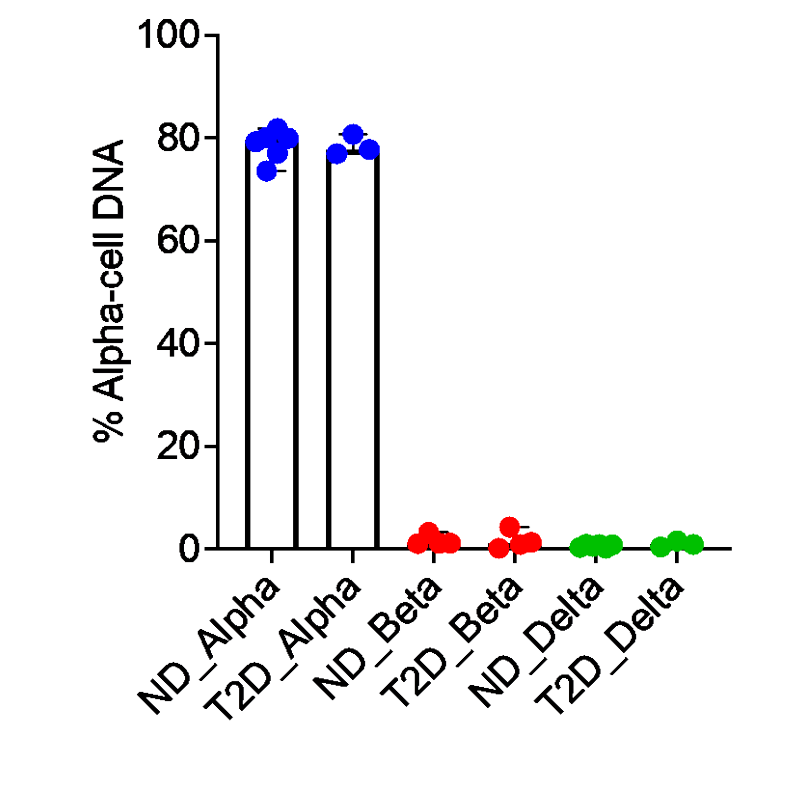
D



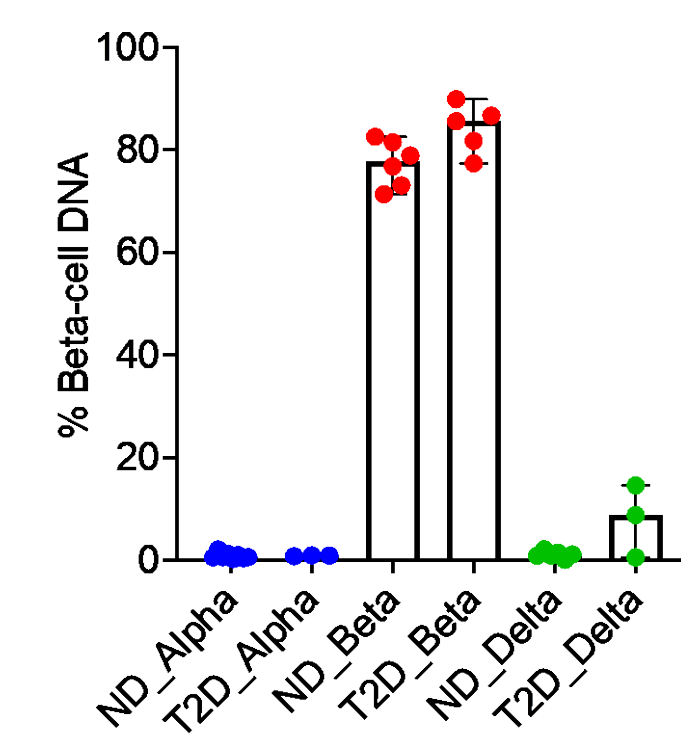
E



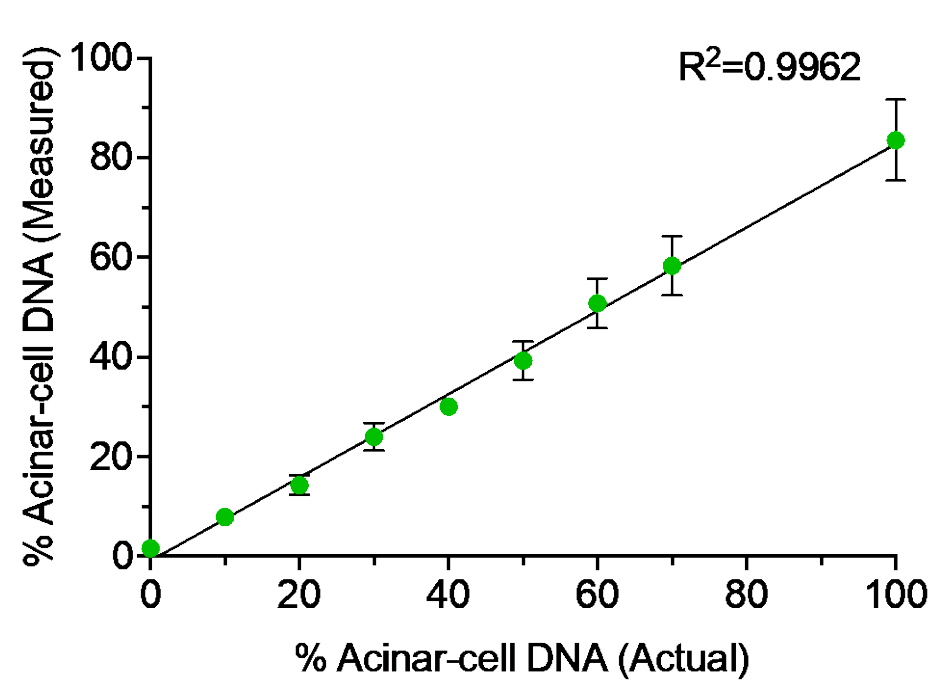
F



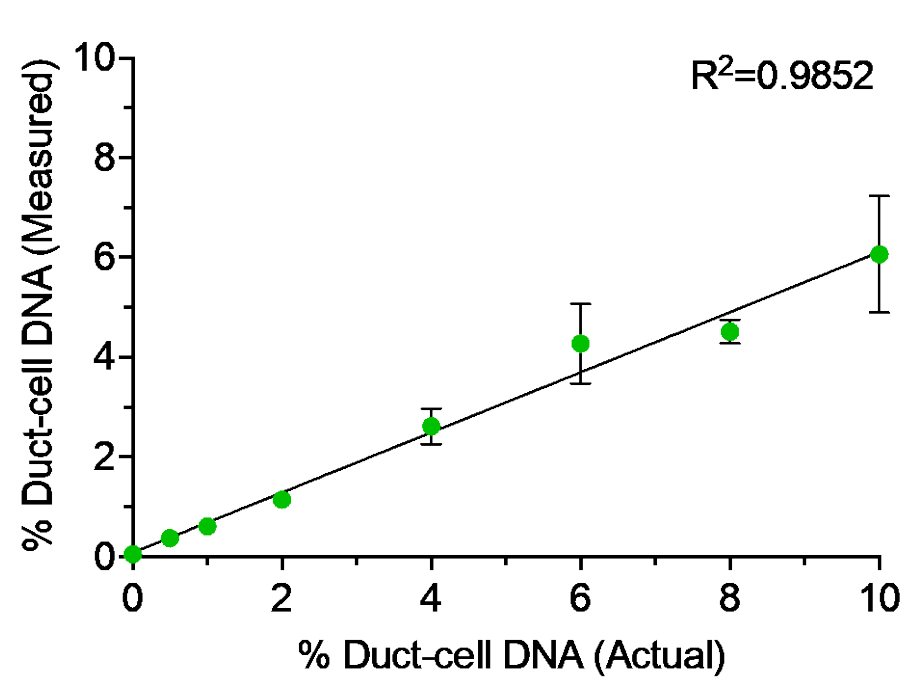
G



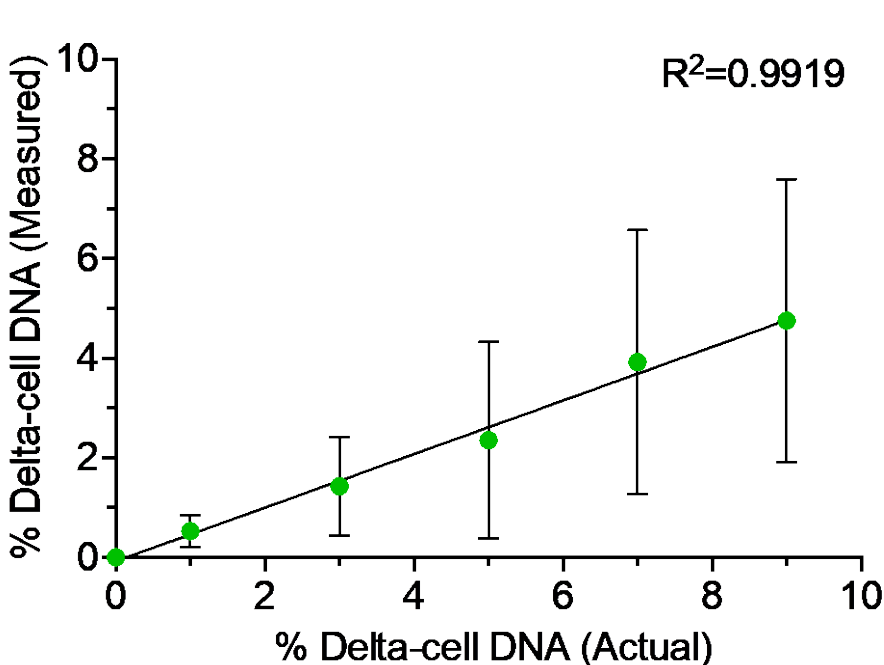
H



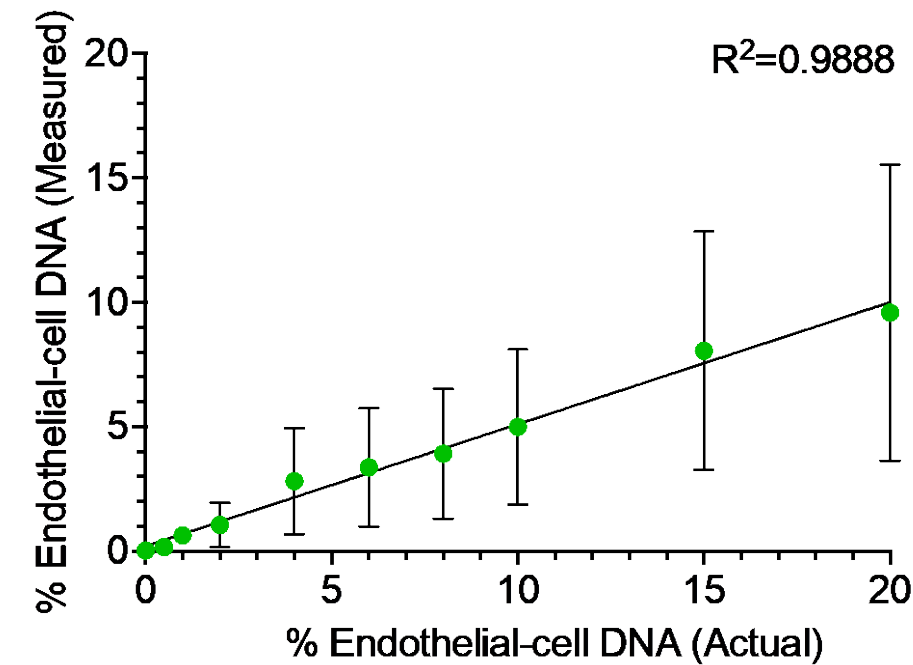
I



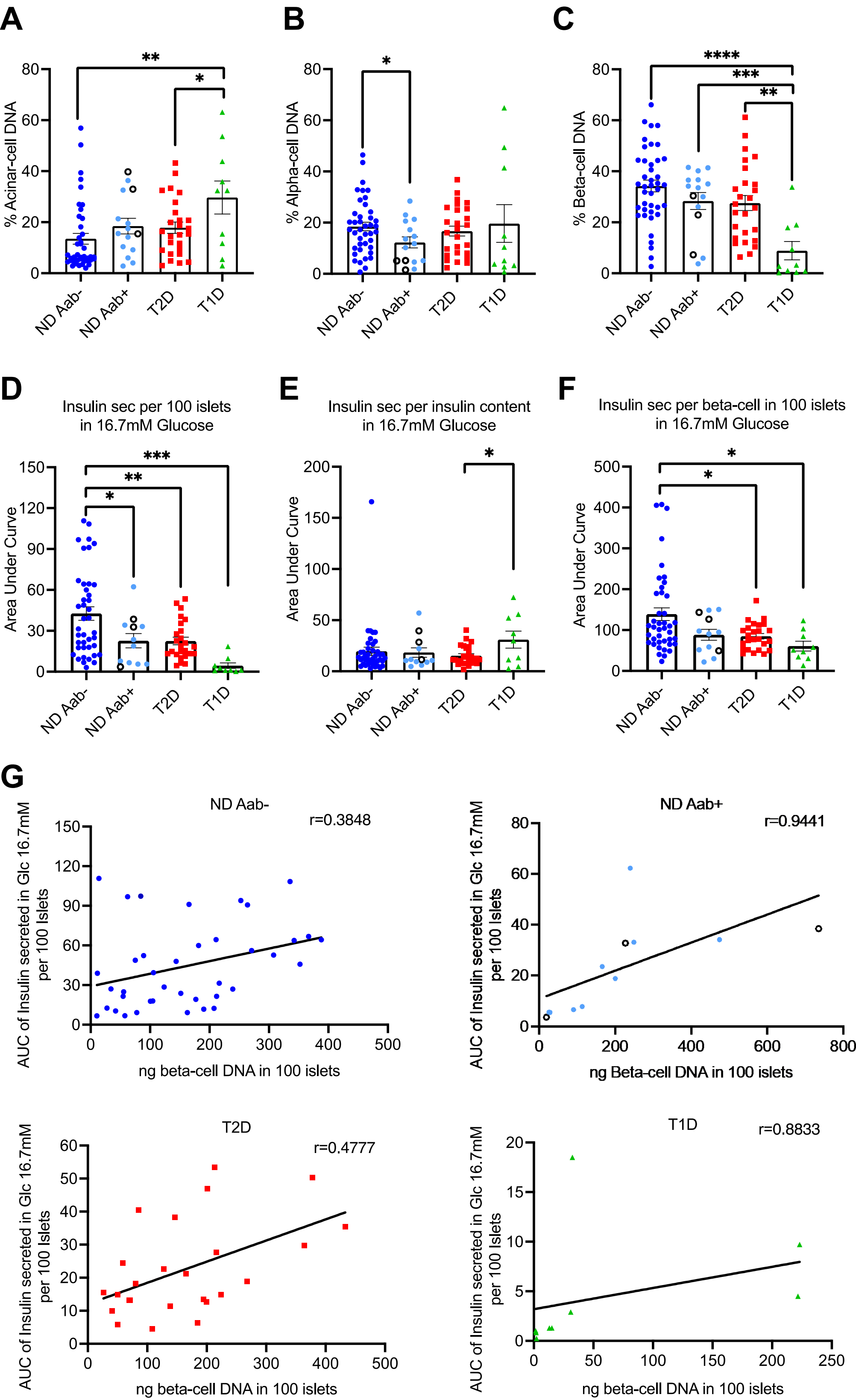
J



K

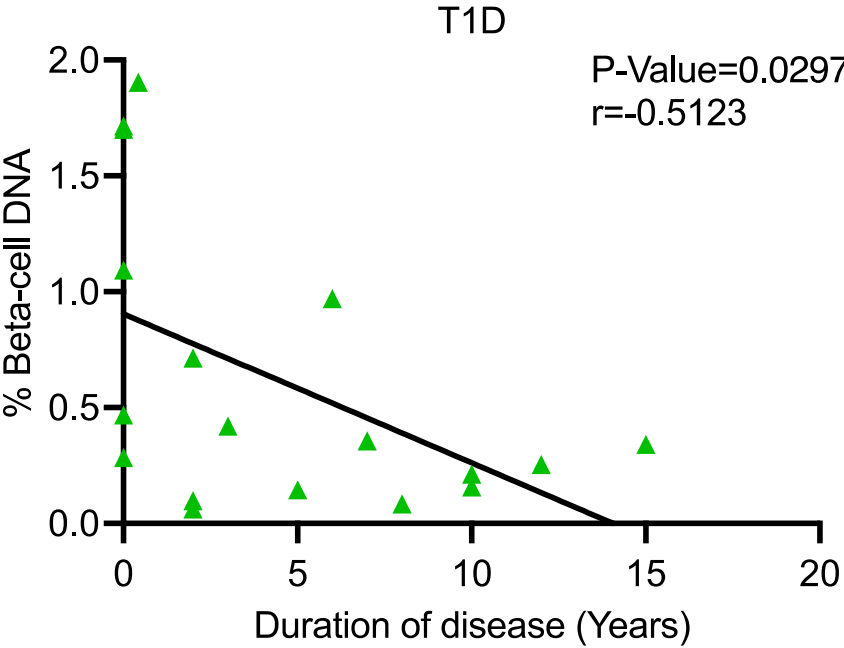


Supplementary Figure 2 (related to Figure 3)



Supplementary figure 3 (related to Figure 4)

A



B

