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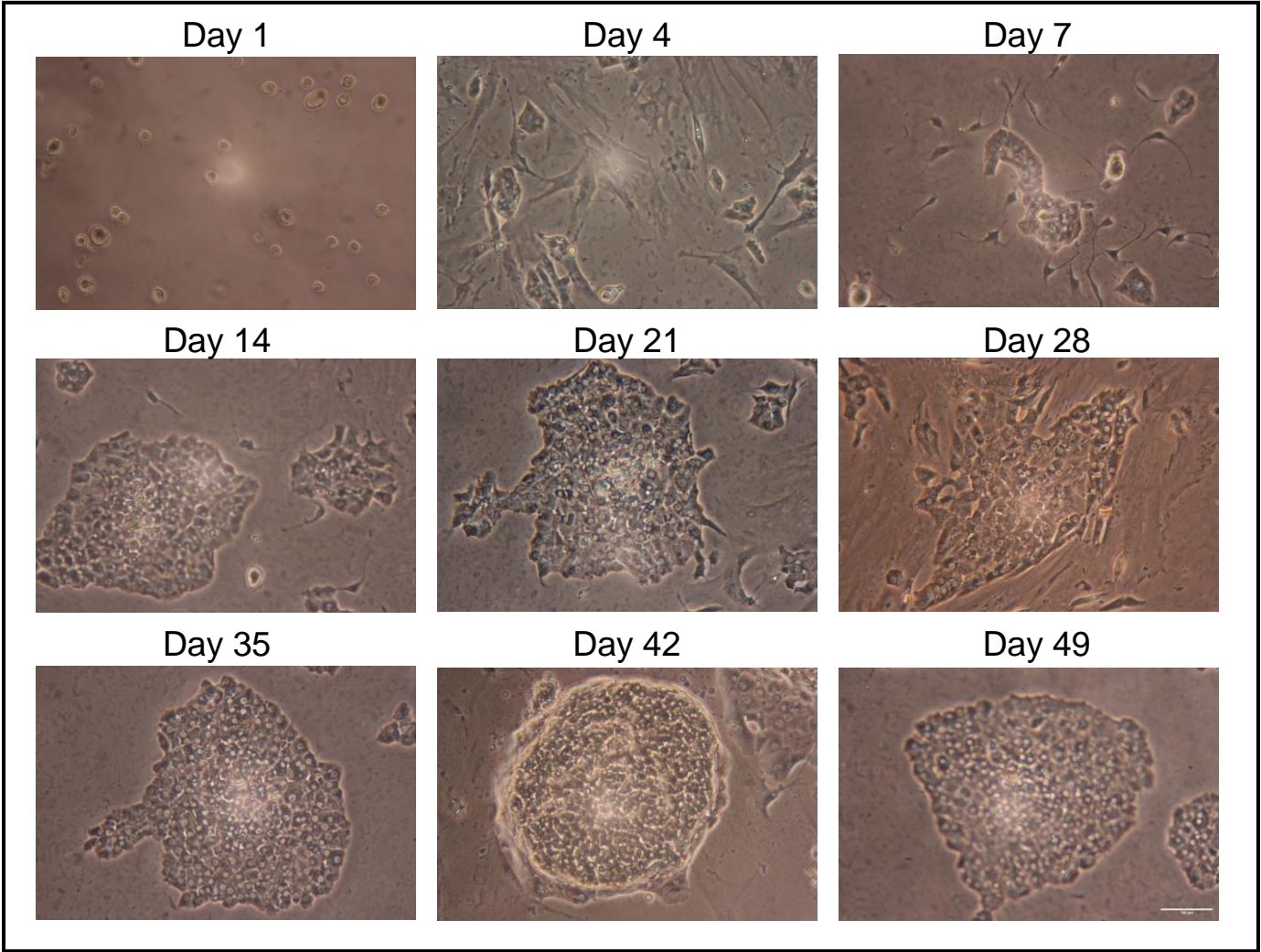
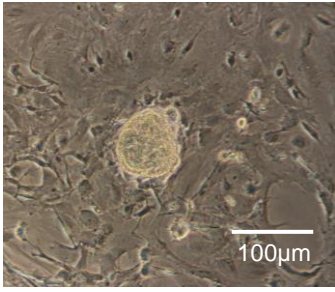
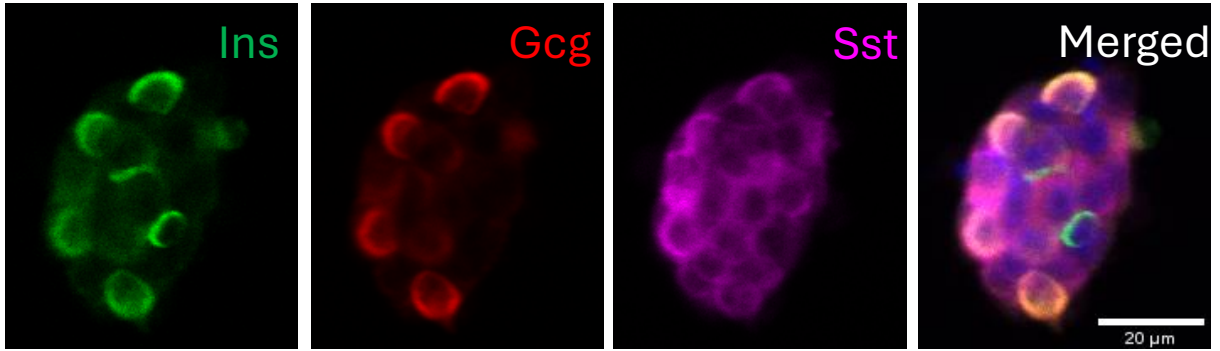


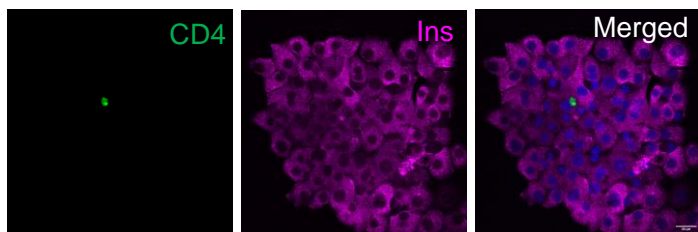
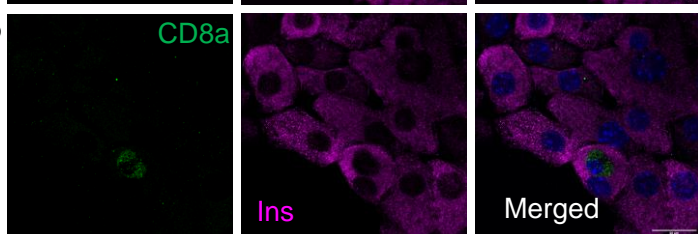
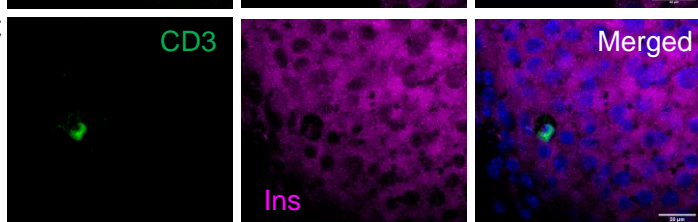
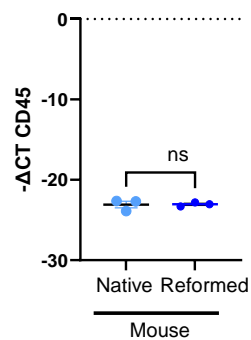
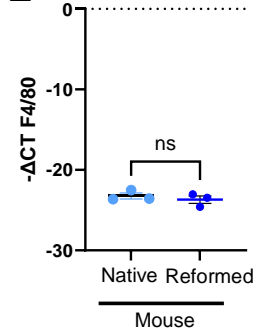
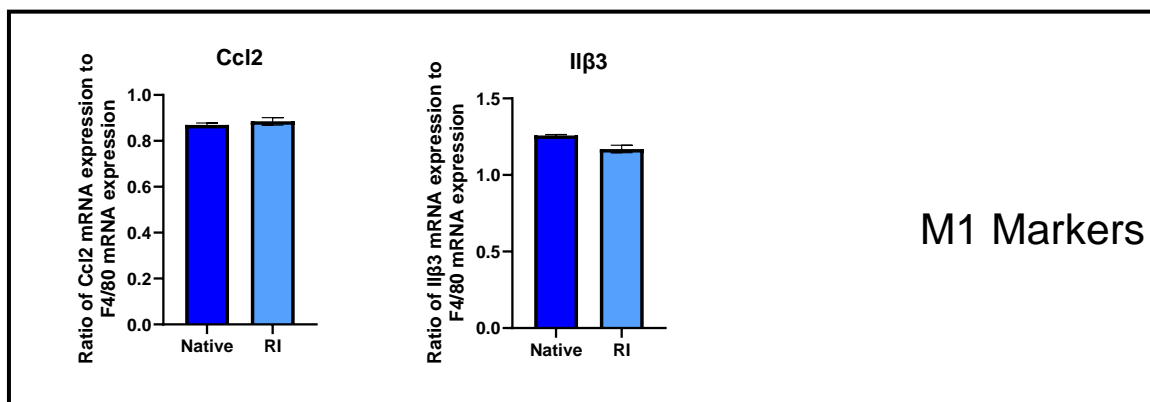
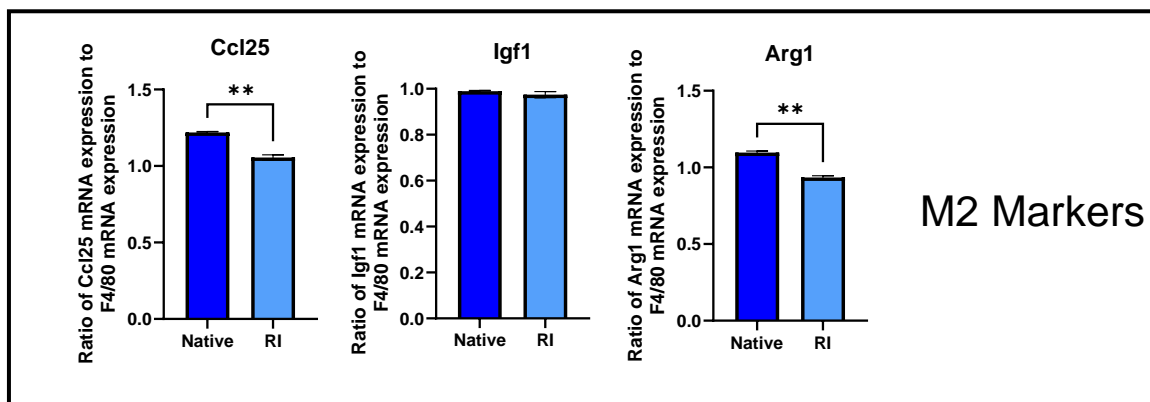
Fig. S1

A



B



A**B****C****D****E****F****G**

A

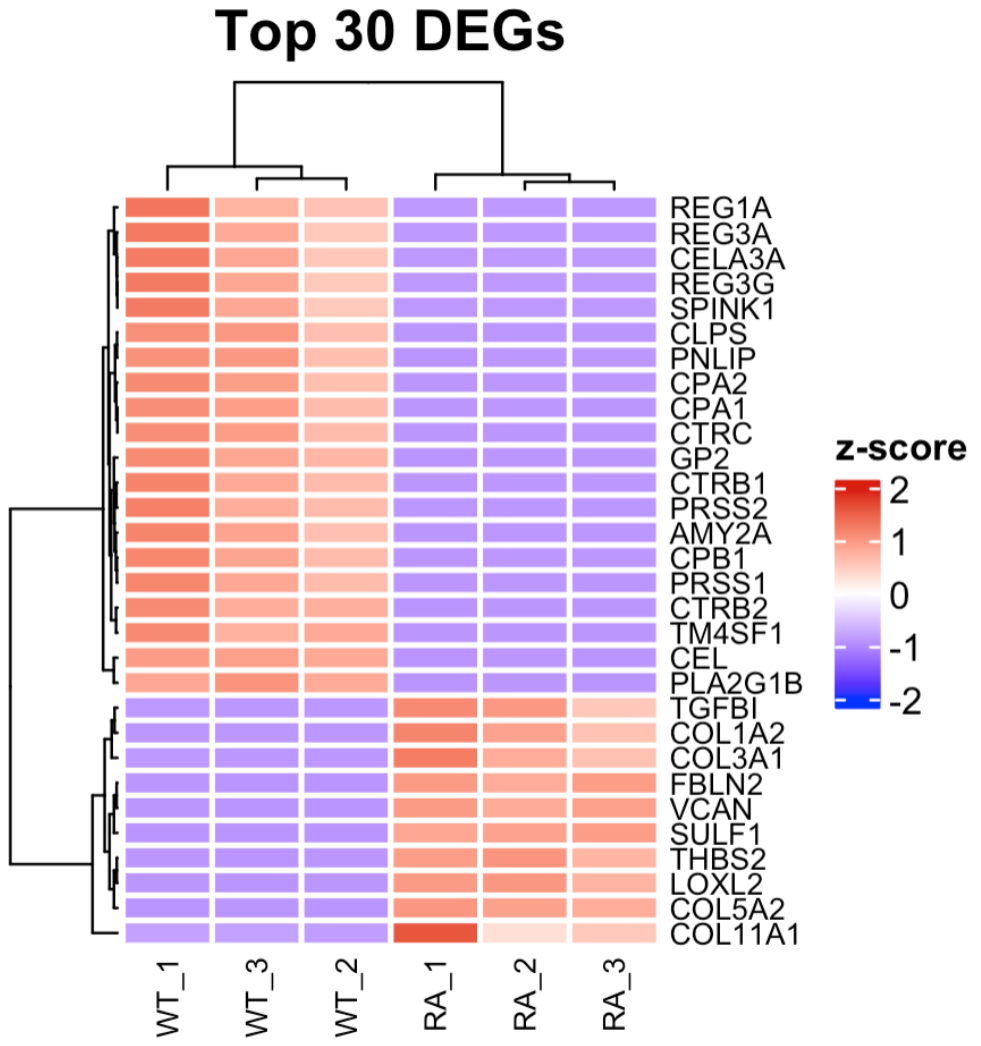
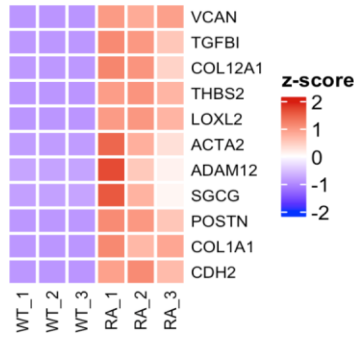
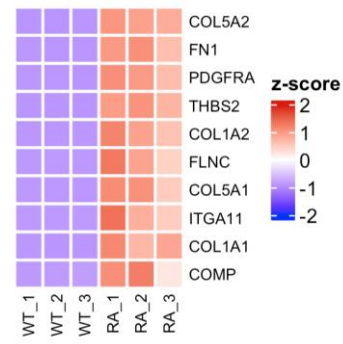


Fig. S4

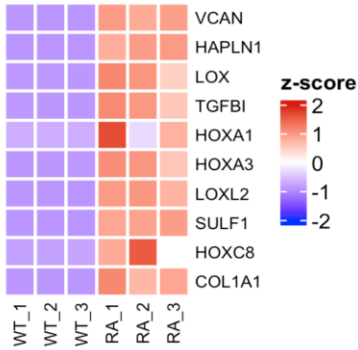
B Epithelial Mesenchymal Transition



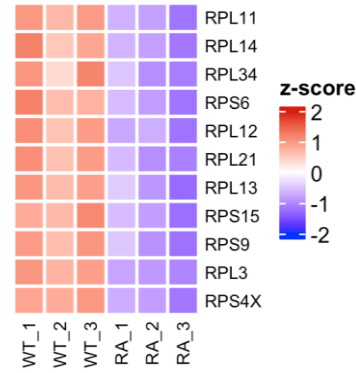
C Focal Adhesions



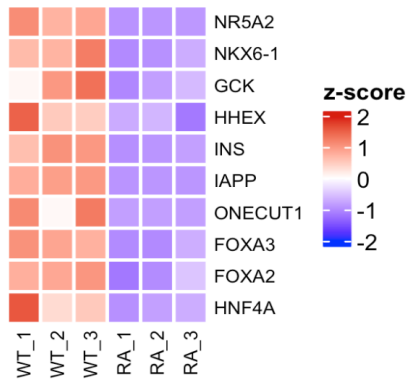
D Skeletal System Development



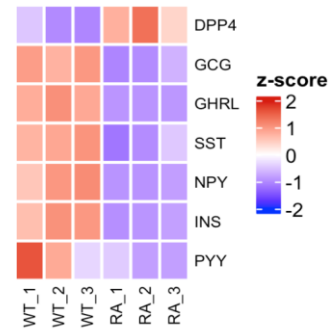
E Ribosome



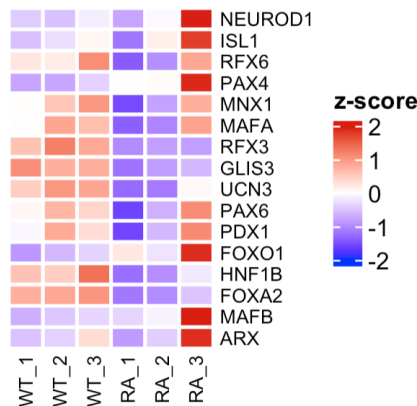
F Maturity Onset Diabetes of the Young



G Islet Hormones



H Islet-Enriched Transcription Factors



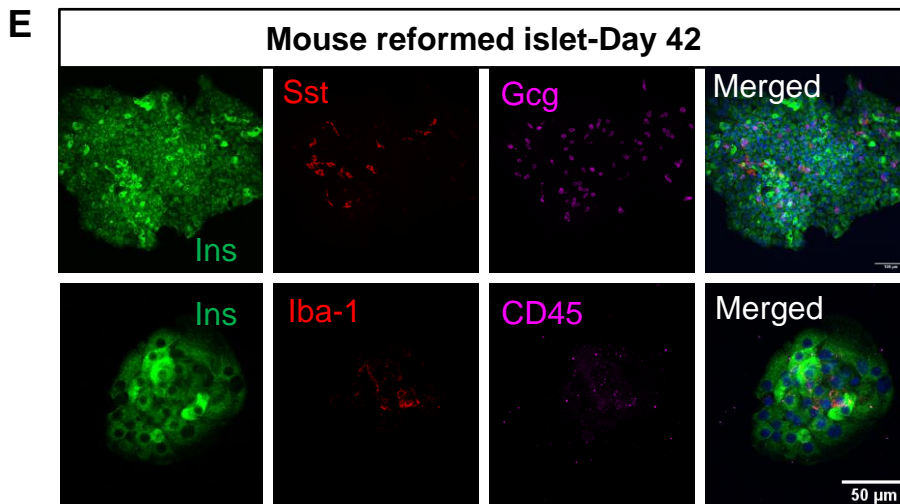
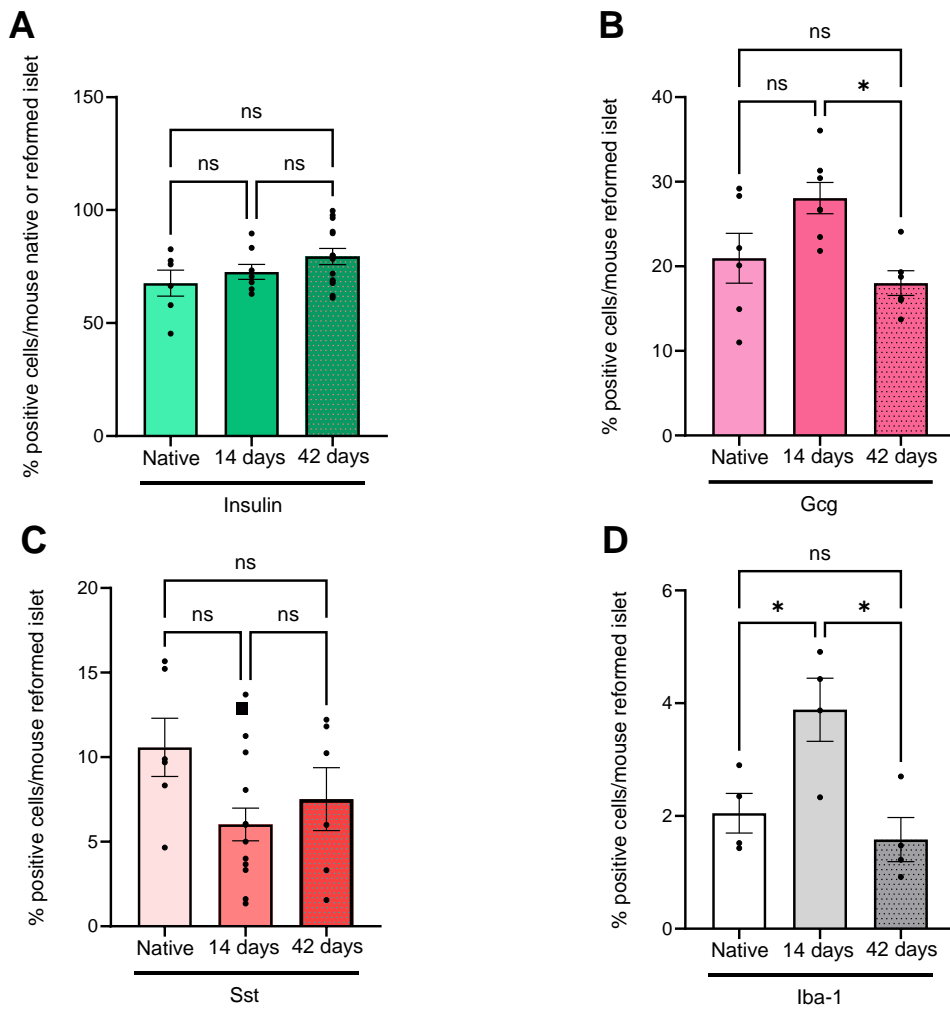


Fig. S6

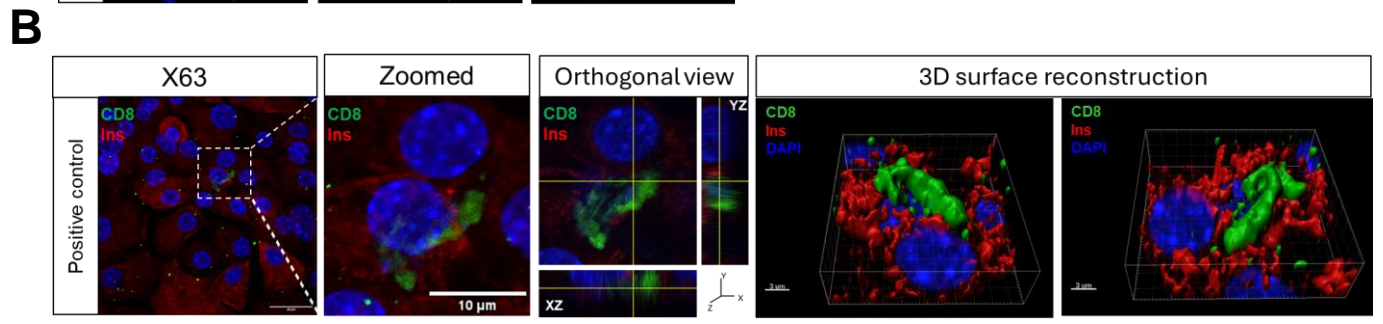
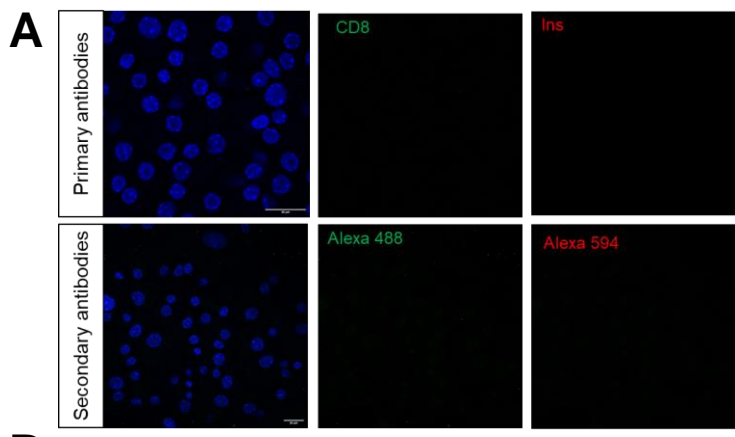


Fig. S7

Supplementary Figure Legends

Figure S1. Brightfield images of reformed islets from day 1 to day 49. Light microscopy images illustrate the formation reformed islets from day 1. By day 14 the islets are fully formed and are maintained till day 49.

Figure S2. Reformed islet formation after 7 days. Light microscopy images show that mouse islet cells formed 3-dimensional spheroid structures after 7 days of seeding. Scale bar is 100 μ m (A). Immunofluorescence detection by confocal microscopy of islet hormones in maturing mouse reformed at day 7 confirmed that developing reformed islets expressed insulin (Ins; green), glucagon (Gcg; red) and somatostatin (Sst; purple). Scale bar is 20 μ m.

Figure S3. Immune population in reformed islets. Immunostaining of the reformed islets with antibodies directed against insulin (Ins; purple) and immune markers CD4 (A), CD8a (B) and CD3 (C) (green) confirmed the presence of both resident macrophages and resident T-cells in reformed islets. Scale bar is 20 μ m. (D, E) Negative delta Ct values distribution graphs of Ptpcr (CD45, all immune cell marker) and Adgre1 (F4/80, macrophage marker) in native and reformed mouse islets detected by quantitative PCR. The macrophage polarity (pro-inflammatory-M1, anti-inflammatory-M2) of reformed islets are evaluated by quantitative PCR of *Ccl2*, and *Ii β 3* (M1) (F) and *Ccl25*, *Igf1* and *Arg1* (M2) (G). Quantification of M1 and M2 markers are mean \pm SEM relative to F4/80 mRNA expression of native and reformed islets respectively. **p < 0.01; unpaired t test with Welch's correction.

Figure S4. Transcriptomic analyses of native and reformed human islets. (A) Heatmap illustrating top 30 differentially expressed genes in reformed islets. (B, C, D) Heatmaps illustrating genes differentially enriched in EMT, Focal adhesion and Skeletal development pathway process. (E) KEGG enriched pathways related to ribosome biogenesis. (F) Pathways enriched in Maturity Onset of the Diabetes of the Young. (G) Heatmap of mRNA expression of islets hormones. (H) Heatmap of selected subset of islet-enriched transcription factors between native and reformed islets.

Figure S5. Depletion of resident macrophages affect migratory response of T cells. Mouse reformed islets derived from BALB/c were exposed to 600ug/ml of clodronate liposome for 48h before co-culturing them with haplotype matched CD8⁺T cells, derived from diabetic NOD mice. Bar graph shows mean total percentage of CD8⁺T cells migrating when cocultured with haplotype matched BALB/c reformed islets (S A). Two-way ANOVA or unpaired Student t-test were performed to assess significance. ****p < 0.0001. (B) represents images of invasion of reformed islets in presence and absence of CD8⁺T cells. In invasion experiments, the reformed islets were immunolabelled with antibodies against insulin (Ins; purple), CD8

(green), CD80 (red) and a nuclear stain DAPI. Scale bars represent 20 μ m for fluorescence microscopy.

Figure S6. Comparative and quantitative analyses of cell composition of native islets, reformed islets at day14 and day 42.

Percentages of different cell types in mouse reformed islets at day 14 and day 42 were calculated using the cell counter plugin in ImageJ software and compared to native mouse islets (A-D). Numerical data are presented as the mean \pm SEM, n=4-14 observations (no. of islets per experiment) in 6-10 coverslips containing reformed islets. *ns* represents $p>0.05$, unpaired Student t-test or One-way ANOVA, Šídák's multiple comparisons test. Reformed islets at day 42 were immunolabelled for insulin (Ins; green), somatostatin (Sst; red), glucagon (Gcg; purple) (E-upper panel), and resident macrophages (Iba-1; red) (E-lower panel). DAPI nuclear staining is shown in blue. Scale bars are 100 μ m (upper panel) and 50 μ m (lower panel).

Figure S7. The primary, secondary and positive controls to determine the specificities of antibodies.

The primary antibodies alone, secondary antibodies and positive control indicate the specificity of the primary antibodies. For positive control, reformed islets were immunolabelled with CD8, insulin and counterstained with DAPI. (A) The first panel illustrates reformed islets that were probed with primary antibodies while the second panel shows reformed islets treated with secondary antibodies only (Alexa 488 and Alexa 594). (B) For positive control, reformed islets were immunolabelled with CD8, insulin and counterstained with DAPI. The orthogonal views represent the XZ and the YZ planes of the positive control (B) while the 3D surface reconstruction illustrates the position of CD8 cells and insulin positive cells (C).