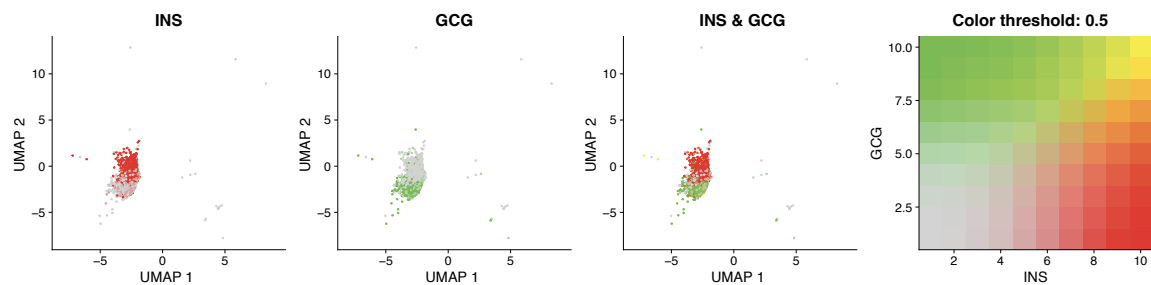
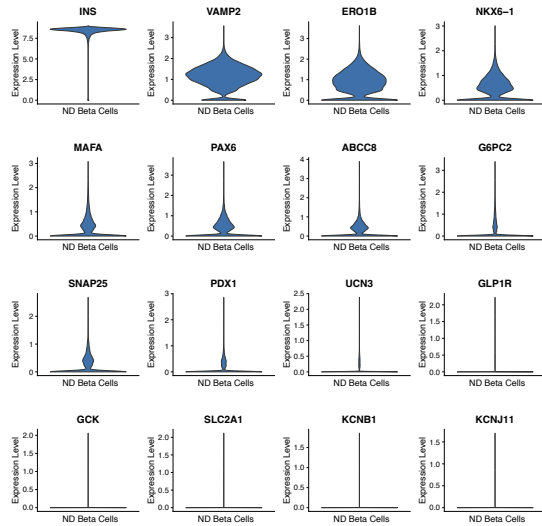


Supplementary Figure 1. Sample representation per cluster. Proportion of cells in each cluster from all donor samples in HPAP. No clusters have representation from only a small number of donors.



Supplementary Figure 2. Marker gene expression in alpha+beta cluster. Expression level of insulin and glucagon separately, as well as overlaid together, in the alpha+beta cluster. The insulin and glucagon expressing cells within this cluster appear largely distinct.

A

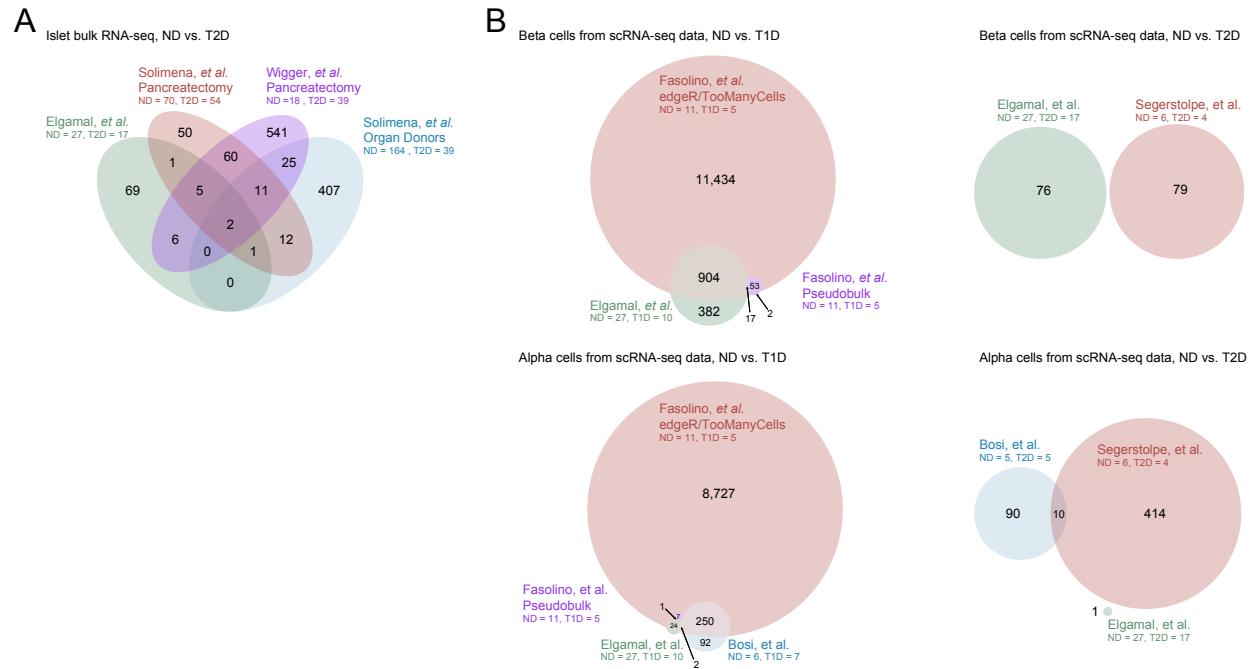


B

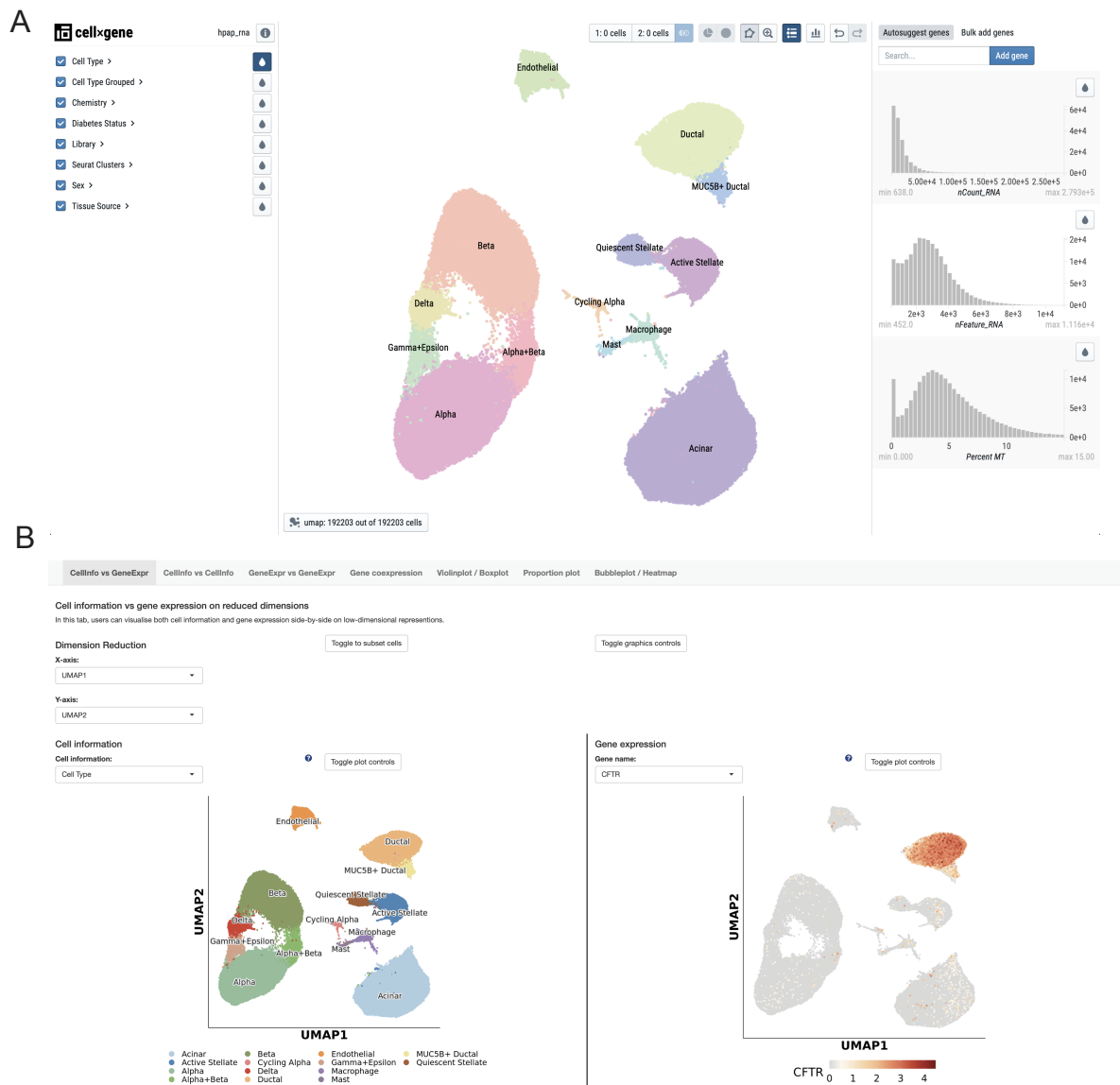
Gene	Non-Diabetic Beta Cell Mean Transcript Counts	Non-Diabetic Beta Cells Expressing Transcript (%)	Non-Diabetic Samples Expressing Transcript (%)
INS	13645.52	99.68	100
VAMP2	7.18	92.27	100
ERO1B	5.22	82.75	100
NKX6-1	2.3	72.19	100
MAFA	1.79	50.41	100
PAX6	1.76	57.27	100
ABCC8	1.4	52.11	100
G6PC2	1.36	33.07	100
SNAP25	0.94	44.09	100
PDX1	0.61	34.12	100
UCN3	0.39	25.45	100
GLP1R	0.25	18.05	100
GCK	0.14	12.09	100
SLC2A1	0.1	9.01	100
KCNB1	0.08	7.22	96.3
KCNJ11	0.07	6.1	100

Supplementary Figure 3. Expression of canonical beta cell genes in non-diabetic donors.

(A) Violin plots showing expression levels of 16 canonical beta cell genes across all beta cells from non-diabetic donors. (B) Table representing mean transcript counts, percentage of cells expressing transcript, and percentage of samples expressing transcript for 16 canonical beta cell genes in beta cells from non-diabetic donors.

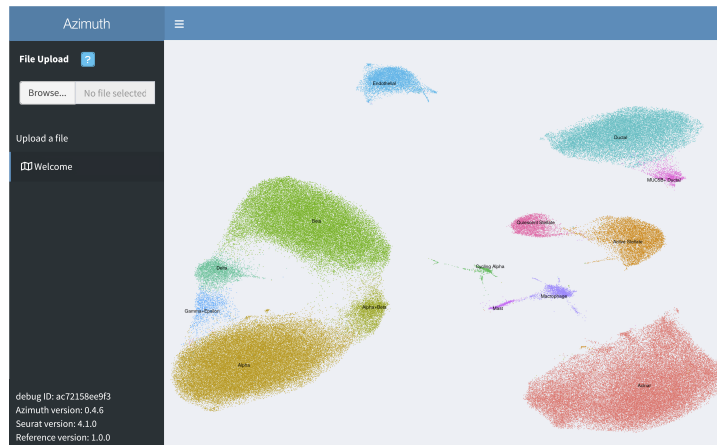


Supplementary Figure 4. Concordance of differential gene expression analyses across studies of pancreatic islets from bulk or single cell RNA-sequencing. (A) Venn diagram comparing significant differentially expressed genes between our study and two others using bulk RNA-sequencing to study changes in gene expression between type 2 diabetic and non-diabetic islets. Samples were either collected from organ donors or from pancreatectomy of living donors as noted. (B) Euler diagrams comparing significant differentially expressed genes in either beta cells or alpha cells from studies using single cell RNA-sequencing technologies. If a single study used more than one analysis method, each method is noted in the diagram. Where raw data was available, significant genes were determined using an adjusted p-value of < 0.1 .

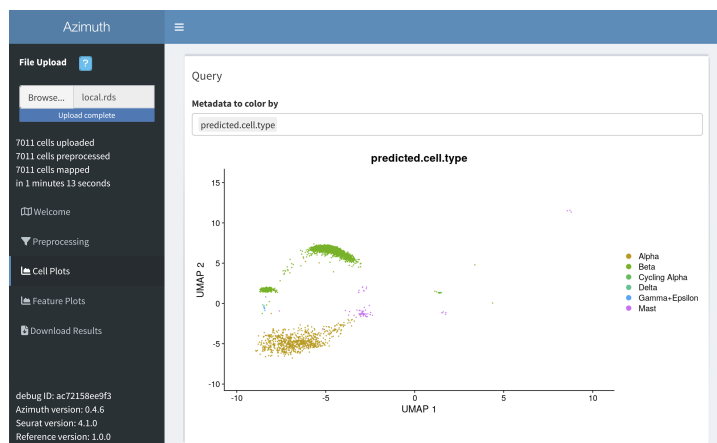


Supplementary Figure 5. Visualizing single cell profiles in islet cell types. (A) Islet single cell object in Cellxgene browser including cell type labels and technical features. (B) Islet single cell object in ShinyCell including cell type labels and expression of selected gene.

A



B



Supplementary Figure 6. Reference mapping of islet single cell gene expression. (A) Screenshot of islet cell type expression in the Azimuth application which enables users to upload their own data and perform annotation of cell type identity. (B) Screenshot of predicted cell types from Azimuth after mapping a publicly available mouse islet dataset to our reference map.

A

Gene Expression **Gene Expression by Diabetes Status** Gene Expression by Samples

Show 25 entries

Gene	Acinar	Alpha	Beta	Delta	Ductal	Endothelial	Gamma.Epsilon	Macrophage	Mast	Stellate
AIBG	3.27261e-02	4.67307e-01	2.84725e-01	33.6654833	1.086773e-02	6.285702e1	45.46133081	4.548223e-01	42.3782157	4.586825e-01
AIBG-AS1	2.320169e-01	3.400949e-02	1.841105e-02	2.9532227	1.244174e-01	1.04959459	3.54291173	5.364167e-02	1.3627215	4.622447e-02
AICF	4.82839e-01	4.86233e-02	4.115999e-01	1.9589922	1.830135e-01	0.21819325	3.48709175	3.037363e-01	0.1312187	1.402195e-01
A2M	1.808825e-01	3.933422e-01	6.079455e-02	0.01745652	1.525623e-01	90.6589108	0.05574615	1.025682e-02	5.0701892	1.054939e-02
A2M-AS1	1.879183e-01	2.791525e-01	1.444395e-01	0.39860154	3.725872e-01	1.19519589	0.28253513	2.292314e-02	6.9657428	6.839012e-01
A2M.L1	2.405591e-03	1.549727e-02	3.989762e-03	0.00000000	1.719030e-03	0.02021480	0.00000000	7.533076e-03	0.00000000	1.494029e-02
A2M.L1-AS1	4.543127e-03	4.980638e-02	1.541875e-02	0.10890336	3.179456e-02	0.00033053	0.29445625	0.000000e-02	0.00000000	2.637036e-02
A2M.L1-AS2	3.574406e-04	1.167072e-02	0.000000e-02	0.00000000	1.992946e-02	0.00000000	0.00000000	0.000000e-02	0.00000000	0.000000e-02
A3GALT2	2.697417e-04	2.968884e-03	1.668846e-03	0.00000000	0.000000e-02	0.05488237	0.00000000	1.835194e-01	0.00000000	5.348300e-02
A4GALT	1.478048e-01	8.363854e-01	1.355326e-01	0.66743200	1.195134e-01	83.85668240	2.18426302	3.063457e-02	0.6775548	2.583378e-01
A4GNT	0.000000e-02	3.551897e-03	3.267596e-04	0.00000000	5.401534e-02	0.00000000	0.00000000	0.000000e-02	0.00000000	3.154541e-03
AAAS	1.809300e-02	4.000879e-02	1.854512e-02	2.93225558	5.206393e-02	4.8989147	3.01089727	3.971746e-02	1.9164218	4.704056e-02
AACS	1.786550e-02	1.260717e-01	5.985727e-02	7.3805129	6.520071e-02	3.45589617	8.81303437	3.334672e-02	6.2701593	3.630304e-02
AACD	2.330674e-01	2.674009e-01	1.063461e-01	0.32911268	7.674036e-01	0.19558696	0.12992847	1.383664e-02	0.00000000	1.672720e-02
AACDL2	3.856332e-04	8.978823e-04	0.000000e-02	0.00000000	0.000000e-02	0.00000000	0.00000000	0.000000e-02	0.00000000	0.000000e-02
AACDL2-AS1	0.000000e-02	0.000000e-02	0.000000e-02	0.00000000	5.780649e-02	0.00000000	0.00000000	0.000000e-02	0.00000000	0.000000e-02
AACDL3	0.000000e-02	0.000000e-02	0.000000e-02	0.00000000	5.175520e-04	0.00000000	0.00000000	0.000000e-02	0.00000000	0.000000e-02

Gene Acinar Alpha Beta Delta Ductal Endothelial Gamma.Epsilon Macrophage Mast Stellate

Showing 1 to 25 of 24,319 entries

Previous 1 2 3 4 5 ... 973 Next

B



Supplementary Figure 7. Querying and visualizing islet cell type-specific expression. (A) Interactive table showing normalized expression levels of genes in each identified cell type. (B) Interactive visualization of differential cell type expression in disease states.