Supplemental Information

Expression of SARS-CoV-2 Entry Factors in the Pancreas of Normal Organ Donors and Individuals with COVID-19

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Supplemental Figure 1. Expression patterns of SARS-CoV-2 associated genes, Related to Figure 1.

(A-B) Violin plot showing \textit{ACE2} and \textit{TMPRSS2} normalized gene expression in β-cells from donors with \((n = 694 \text{ cells})\) and without type 2 diabetes \((n = 2,985 \text{ cells})\). \textit{ACE2} and \textit{TMPRSS2} expression were not significantly different between groups, Wilcoxon rank sum tests. ND: No Diabetes, T2D: Type 2 Diabetes

(C) Violin plot showing the distribution of \textit{TMPRSS4} normalized expression in the pancreas of donors without diabetes \((n = 12,185 \text{ cells})\).

(D) Bar graphs showing the percentage of pancreatic cells with detectable \textit{TMPRSS4} in donors with \((n = 2,705 \text{ cells})\) and without type 2 diabetes \((n = 12,185 \text{ cells})\). T2D: Type 2 Diabetes.

(E-G) Violin plots showing the distribution of \textit{TMPRSS11D}, \textit{CTSL}, and \textit{ADAM17} normalized expression in the pancreas of donors without diabetes \((n = 12,185 \text{ cells})\).

(H) Violin plot showing \textit{CTSL} normalized gene expression in β-cells from donors with \((n = 694 \text{ cells})\) and without type 2 diabetes \((n = 2,985 \text{ cells})\). \textit{CTSL} expression was higher in beta cells from donors with type 2 diabetes, Wilcoxon rank sum tests, adjusted \(P = 8.94 \times 10^{-32}, \ast\ast\ast P < 0.001\). ND: No Diabetes, T2D: Type 2 Diabetes. Violin plot limits show maxima and minima, and the dots represent individual data points.
Supplemental Figure 2. Detection of SARS-CoV-2 associated gene expression in human pancreas using single molecular fluorescence in situ hybridization (smFISH), Related to Figure 2 and STAR Methods.

(A) Validation of smFISH probes in control human tissues. Single molecular fluorescent in-situ hybridization (smFISH) images of human duodenum, ileum, and kidney used as a positive controls to test the specificity of the probe sets used to determine the expression of ACE2 and TMPRSS2.

(B) Validation of smFISH probes in control human tissues. smFISH images of human duodenum and kidney used as a positive controls to test the specificity of the probe sets used to determine the expression of ACE2, TMPCR4, TMPRSS11D, CTSL, and ADAM17.

(C-F) Representative images of smFISH for (C) ACE2 and TMPRSS11D; (D) ACE2 and CTSL; (E) ACE2 and ADAM17; (F) ACE2 and TMPRSS4; mRNA in human pancreatic tissue sections counter stained for insulin. Inset highlights mRNA distribution in pancreatic islets; scale bar: 20µm.
Supplemental Figure 3. Detection of ACE2 protein in human pancreatic tissue, Related to Figure 3 and STAR Methods.

(A) Detection ACE2 in protein lysate from three organ donors. Full immunoblot images of data presented in Figure 3A. Membranes were incubated with primary antibodies against ACE2 (as indicated on the figure), washed, and incubated with the corresponded secondary antibody. Protein bands were visualized using the Odyssey Li-Cor infrared imager. The molecular weight ladder (Bio-Rad, Cat.No. 1610373) was run in each gel to confirm the correct size of the ACE2 band.

(B) Total protein on the membrane for the corresponding blots shown above. Pancreas lysates were run in TGX stain-free gels (Bio-Rad). After electrophoresis, gels were activated under UV light for 5 minutes using a Gel Doc EZ imaging system (Bio-Rad) to label all tryptophan residues on proteins. Once photoactivated, proteins were transferred to nitrocellulose membranes. The stain-free signal from proteins on the membrane was imaged using the Gel Doc EZ system.

(C) Validation of ACE2 antibodies for immunohistochemistry. IHC images of human duodenum and kidney were used as positive controls to test the specificity of four commercially available ACE2 antibodies as indicated on the figure.

(D) ACE2 blocking peptide (Abcam, Cat# 198988) was used to confirm the specificity of Abcam rabbit monoclonal ACE2 antibody (Cat# ab108252). The image of pancreas tissue section stained for ACE2 showing absence of staining with the neutralized antibody. Scale bars: 300µm.
Supplemental Figure 3

A

|   | GEL 1 | GEL 2 | GEL 3 | GEL 4 |
|---|-------|-------|-------|-------|
|   | human pancreas | human pancreas | human pancreas | human pancreas |
| p1 | p2 | p3 | p1 | p2 | p3 | p1 | p2 | p3 |
| 250 | 180 | 120 | 150 | 100 | 70 | 250 | 180 | 120 |
| 180 | 120 | 70 | 150 | 100 | 70 | 180 | 120 | 70 |
| 120 | 70 | 40 | 100 | 60 | 30 | 120 | 70 | 40 |
| 70 | 40 | 20 | 60 | 30 | 20 | 70 | 40 | 20 |

B

1st Ab: Rabbit monoclonal to ACE2 (ab108252, 1:1000)
1st Ab: Rabbit polyclonal to ACE2 (ab15348, 1:5000)
1st Ab: Mouse monoclonal to ACE2 (MAB933, 1:1000)
1st Ab: Goat polyclonal to ACE2 (AF933, 1:5000)

Total protein Gel1 Total protein Gel2 Total protein Gel3 Total protein Gel4

C

Duodenum

ACE2, ab108252
ACE2, ab15348
ACE2, MAB933
ACE2, AF933

Kidney

D

Pancreas

ACE2, ab108252
ACE2 peptide, ab198988
Supplemental Figure 4. ACE2 is highly expressed in microvasculature of the human pancreas, Related to Figure 3 and Figure 4.

(A) Representative image of pancreatic tissue section from SARS-CoV-2 negative donor without diabetes stained for ACE2 and Insulin. ACE2 positivity was associated with microvasculature in the acinar and islet regions Scale bars: 200µm.

(B) Representative immunofluorescence images showing lack of ACE2 protein expression in pancreatic blood vessels from control donors across different age groups. Scale bars (left to right): 100µm, 200µm, 200µm, 200µm, 200µm, 100µm.

(C) ACE2 expression by endothelial cells in the human pancreas. Representative immunofluorescence image of pancreatic tissue section stained for ACE2 (Abcam, ACE2 antibody Cat# ab108252) and endothelial cell marker CD34 (Novus Biological, mouse monoclonal CD34 antibody Cat# NBP2-32932). Endothelial cell positive for both ACE2 and CD34 markers are shown. Scale bars: 50µm.
Supplemental Figure 4

A

ACE2:INS

acinar microvasculature

islet microvasculature

B

AGE (years)

| Age Range | Images |
|-----------|--------|
| 0 - ≤ 0.25 | ![Image](ace2__dapi_0_0_0_0.png) |
| >0.25 - < 2 | ![Image](ace2__dapi_0_0_0_1.png) |
| ≥2 - < 11 | ![Image](ace2__dapi_0_0_2_0.png) |
| ≥11 - ≤ 15 | ![Image](ace2__dapi_0_0_2_1.png) |
| >20 - ≤ 33 | ![Image](ace2__dapi_0_0_2_2.png) |
| ≥51 - ≤ 72 | ![Image](ace2__dapi_0_0_2_3.png) |

C

ACE2

CD34

ACE2:CD34
Supplemental Figure 5. Detection of SARS-CoV-2 nucleocapsid protein (NP) in the pancreas from individual with COVID-19, Related to Figure 5 and STAR Methods.

(A) Representative IHC image showing ACE2 protein expression in the pancreatic duct of COVID-19 Case 1. Scale bar: 200µm.

(B) IHC image of the human lung tissue sample known to be positive for SARS-CoV-2 used as positive control to test specificity of antibody against SARS-CoV-2 NP (clone B46F, Invitrogen, Cat# MA-1-7404). Scale bars: 50µm.

(C) Tissue section from pancreas of COVID-19 Case 1 showing the presence of SARS-CoV-2 NP in ductal epithelial cells. Scale bar: 200µm.

(D) Tissue section from pancreas of COVID-19 Case 1 stained with ductal cell marker cytokeratin 19 (CK 19) and SARS-CoV-2 NP. Scale bar: 200µm.
Supplemental Figure 5

A. ACE2:INS – Pancreas, COVID-19 Case 1

B. SARS-CoV-2 NP – Lung

C. Pancreas, COVID-19 Case 1

D. SARS-CoV-2 NP/ CK 19
### Supplemental Tables

**Table S1. Gene expression by donor group and pancreatic cell type, Related to Figure 1A-D and Figure S1.** From an integrated analysis of five public scRNAseq datasets (GSE84133 (Baron et al., 2016), GSE81076 (Grün et al., 2016), GSE85241 (Muraro et al., 2016), GSE86469 (Lawlor et al., 2017), and E-MTAB-5061 (Segerstolpe et al., 2016)), the number and percentage (presented as n (%)) of cells expressing *ACE2*, *TMPRSS2*, *TMPRSS4*, *CTSL*, *ADAM17*, *TMPRSS11D* are listed for each cell type from isolated islets from donors without diabetes (no diabetes; ND) or with type 2 diabetes (T2D).

| Gene       | Donor Group | Alpha | Beta | Delta | Epsilon | Gamma | Acinar | Ductal | Endothelial | Activated stellate | Quiescent stellate | Schwann | Macrophage | Mast |
|------------|-------------|-------|------|-------|---------|-------|--------|--------|-------------|-------------------|-------------------|----------|-------------|------|
| **ACE2**   | ND          | 15 (0.40) | 17 (0.57) | 7 (0.83) | 0 (0.00) | 6 (1.41) | 70 (4.11) | 81 (5.54) | 0 (0.00) | 1 (0.26) | 2 (1.17) | 0 (0.00) | 1 (1.54) | 0 (0.00) |
|            | T2D         | 1 (0.12) | 2 (0.29) | 1 (0.57) | 0 (0.00) | 3 (1.52) | 13 (8.07) | 40 (8.13) | 0 (0.00) | 1 (1.19) | 0 (0.00) | 0 (0.00) | 0 (0.00) | 0 (0.00) |
| **TMPRSS2**| ND          | 624 (16.55) | 163 (5.46) | 24 (2.86) | 1 (3.85) | 18 (4.22) | 915 (53.73) | 739 (50.55) | 8 (2.88) | 10 (2.56) | 2 (1.17) | 3 (14.29) | 70 (4.11) | 81 (5.54) |
|            | T2D         | 271 (32.07) | 73 (10.52) | 9 (5.17) | 0 (0.00) | 11 (5.56) | 115 (7.143) | 289 (58.74) | 8 (44.44) | 8 (9.52) | 0 (0.00) | 2 (50.00) | 0 (0.00) | 0 (0.00) |
| **TMPRSS4**| ND          | 134 (3.55) | 151 (5.06) | 16 (1.91) | 1 (3.85) | 11 (2.58) | 31 (1.82) | 46 (3.15) | 6 (2.16) | 5 (1.28) | 1 (0.58) | 3 (14.29) | 1 (1.54) | 3 (6.25) |
|            | T2D         | 89 (10.53) | 81 (11.67) | 9 (5.17) | 0 (0.00) | 5 (2.53) | 13 (8.07) | 40 (8.13) | 7 (38.89) | 7 (8.33) | 0 (0.00) | 1 (25.00) | 0 (0.00) | 0 (0.00) |
| **CTSL**   | ND          | 1375 (36.47) | 1006 (33.70) | 206 (24.55) | 11 (42.31) | 145 (33.96) | 353 (20.73) | 344 (23.53) | 98 (35.25) | 228 (58.46) | 123 (71.93) | 9 (42.86) | 42 (64.62) | 7 (14.58) |
|            | T2D         | 617 (73.02) | 409 (58.93) | 97 (55.75) | 3 (75.00) | 147 (74.24) | 91 (56.52) | 318 (64.63) | 9 (50.00) | 70 (83.33) | 7 (77.78) | 3 (75.00) | 13 (92.86) | 2 (25.00) |
| **ADAM17** | ND          | 709 (18.81) | 512 (17.15) | 140 (16.69) | 3 (11.54) | 97 (22.72) | 409 (33.04) | 483 (38.78) | 80 (28.78) | 116 (29.74) | 12 (7.02) | 8 (38.10) | 24 (36.92) | 6 (12.50) |
|            | T2D         | 370 (43.79) | 214 (30.84) | 61 (35.06) | 2 (50.00) | 97 (48.99) | 90 (55.90) | 316 (64.23) | 12 (66.67) | 39 (46.43) | 3 (33.33) | 2 (50.00) | 6 (42.86) | 3 (37.50) |
| **TMPRSS11D** | ND    | 17 (0.45) | 2 (0.07) | 3 (0.36) | 0 (0.00) | 0 (0.00) | 4 (0.23) | 5 (0.34) | 0 (0.00) | 0 (0.00) | 1 (4.76) | 0 (0.00) | 0 (0.00) | 0 (0.00) |
|            | T2D         | 16 (1.89) | 7 (1.01) | 0 (0.00) | 0 (0.00) | 5 (2.53) | 2 (1.24) | 8 (1.63) | 0 (0.00) | 1 (1.19) | 0 (0.00) | 0 (0.00) | 0 (0.00) | 0 (0.00) |
Table S2. ACE2 and viral entry protein co-expression patterns, Related to Figure 1. From an integrated analysis of five public scRNAseq datasets (GSE84133 (Baron et al., 2016), GSE81076 (Grün et al., 2016), GSE85241 (Muraro et al., 2016), GSE86469 (Lawlor et al., 2017), and E-MTAB-5061 (Segerstolpe et al., 2016)), the number and percentage (presented as n (%)) of cells co-expressing ACE2 with *TMPRSS2*, *TMPRSS4*, *CTSL*, *ADAM17*, *TMPRSS11D* are listed for each cell type from isolated islets from donors without diabetes (no diabetes; ND) or with type 2 diabetes (T2D).

| Gene Pairs       | Donor Group | Alpha   | Beta     | Delta    | Epsilon  | Gamma   | Acinar   | Ductal   | Endothelial | Activated Stellate | Quiescent stellate | Schwann | Macrophage | Mast    |
|------------------|-------------|---------|----------|----------|----------|---------|----------|----------|-------------|-------------------|-------------------|----------|-------------|---------|
| ACE2+/TMPRSS2+   | ND          | 9 (0.24)| 3 (0.10) | 2 (0.24) | 0 (0.00) | 0 (0.00)| 65 (3.82)| 63 (4.31)| 0 (0.00)    | 0 (0.00)          | 0 (0.00)          | 0 (0.00) | 1 (1.54)   | 0 (0.00) |
| ACE2+/TMPRSS4+   | T2D         | 0 (0.00)| 0 (0.00) | 1 (0.57) | 0 (0.00) | 0 (0.00)| 13 (8.07)| 30 (6.10)| 0 (0.00)    | 0 (0.00)          | 0 (0.00)          | 0 (0.00) | 0 (0.00)   | 0 (0.00) |
| ACE2+/CTSL      | ND          | 3 (0.08)| 2 (0.07) | 2 (0.24) | 0 (0.00) | 0 (0.00)| 4 (0.23) | 5 (0.34) | 0 (0.00)    | 0 (0.00)          | 0 (0.00)          | 0 (0.00) | 0 (0.00)   | 0 (0.00) |
| ACE2+/ADAM17+   | T2D         | 0 (0.00)| 1 (0.14) | 1 (0.57) | 0 (0.00) | 0 (0.00)| 2 (1.24) | 2 (0.41) | 0 (0.00)    | 0 (0.00)          | 0 (0.00)          | 0 (0.00) | 0 (0.00)   | 0 (0.00) |
| ACE2+/TMPRSS11D+| ND          | 9 (0.24)| 10 (0.34)| 2 (0.24) | 0 (0.00) | 5 (1.17)| 25 (1.47)| 47 (3.21)| 0 (0.00)    | 0 (0.00)          | 1 (0.58)          | 0 (0.00) | 0 (0.00)   | 0 (0.00) |
| ACE2+/ADAM17+   | T2D         | 1 (0.12)| 2 (0.29) | 1 (0.57) | 0 (0.00) | 3 (1.52)| 11 (6.83)| 40 (8.13)| 0 (0.00)    | 1 (1.19)          | 0 (0.00)          | 0 (0.00) | 0 (0.00)   | 0 (0.00) |
| ACE2+/CTSL      | ND          | 8 (0.21)| 7 (0.23) | 4 (0.48) | 0 (0.00) | 5 (1.17)| 41 (2.41)| 45 (3.08)| 0 (0.00)    | 1 (0.26)          | 0 (0.00)          | 0 (0.00) | 1 (1.54)   | 0 (0.00) |
| ACE2+/ADAM17+   | T2D         | 1 (0.12)| 2 (0.29) | 0 (0.00) | 0 (0.00) | 3 (1.52)| 12 (7.45)| 37 (7.52)| 0 (0.00)    | 0 (0.00)          | 0 (0.00)          | 0 (0.00) | 0 (0.00)   | 0 (0.00) |
| ACE2+/TMPRSS11D+| ND          | 0 (0.00)| 0 (0.00) | 1 (0.12) | 0 (0.00) | 0 (0.00)| 0 (0.00) | 0 (0.00) | 0 (0.00)    | 0 (0.00)          | 0 (0.00)          | 0 (0.00) | 0 (0.00)   | 0 (0.00) |
Table S3. Donor characteristics, Related to Figure 3, Figure 4, and STAR Methods. Tissues from 56 non-diabetic, SARS-CoV-2 negative donors were selected from the nPOD biobank and subjected to assays as detailed in the far-right column. Abbreviations: nPOD ID, Network for Pancreatic Organ donors with Diabetes Identification Number; yrs, years; BMI, body mass index; IHC, chromogen-based immunohistochemistry; IF, immunofluorescence; smFISH, single molecule fluorescence in situ hybridization.

*Some donors had hypertension in their anamnesis, but none of the donors evaluated received ACE inhibitors or angiotensin II receptor.

| nPOD ID | Age (yrs) | Sex | Race/Ethnicity | BMI (kg/m^2) | Histopathology by nPOD | Technique Performed |
|---------|-----------|-----|----------------|--------------|------------------------|---------------------|
| 6012*   | 68        | Female | Caucasian      | 23.7         | Ins+/Gluc+ normal islets, high density tail. Mild chronic pancreatitis, IPMN in PanHead (gastric type). Moderate exocrine fatty infiltrate. | IHC                 |
| 6013    | 65        | Male   | Caucasian      | 24.2         | Ins+/Gluc+ normal islets. Focal, moderate ductular metaplasia. | IHC, IF, smFISH     |
| 6017*   | 59        | Female | Caucasian      | 24.8         | Ins+/Gluc+ normal islets. Fatty infiltration-mild | IHC                 |
| 6021*   | 72        | Female | Hispanic       | 24.5         | Ins+/Gluc+ normal islets. Extra-acinar islets. Low Ki67. Mucinous ductal dysplasia. Multifocal mild acinar atrophy and fatty infiltration. | IHC, IF             |
| 6030    | 30.1      | Male   | Caucasian      | 27.1         | Ins+/Gluc+ islets. Moderate Ki67 islets and other compartments. Sludge in ducts PanHead 05 and 10. Infrequent ductal islet units. | IHC                 |
| 6057    | 22        | Male   | Caucasian      | 26           | Ins+/Gluc+ normal islets, High Ki67+ most compartments | IHC                 |
| 6091    | 27.1      | Male   | Caucasian      | 35.6         | Ins+/Gluc+ normal islets, many large especially in head and body. Degree of fatty infiltrate moderate. No infiltrates identified. | IHC                 |
| 6092    | 0.5       | Female | African Am     | 13.8         | Ins+ normal. High Ki67+ islets and acinar. | IHC                 |
| 6106    | 2.9       | Male   | Caucasian      | 17.4         | Ins+/Gluc+ normal islets. Low Ki67 acinar and islet but multifocal, mild duct proliferation. | IHC                 |
| 6126    | 25.2      | Male   | Hispanic       | 25.1         | Ins+/Gluc+ islets, normal. Moderate Ki67 acinar cells and occ. islets. | IHC                 |
| 6125    | 0.42      | Male   | Caucasian      | 18.9         | Ins+/Gluc+ normal islets. High acinar Ki67+. | IHC                 |
| 6130    | 5.2       | Male   | Caucasian      | 18.5         | Ins+ normal islets; low Ki67 in acinar and islets. No infiltrates. | IHC                 |
| 6131    | 24.2      | Male   | Caucasian      | 24.8         | Ins+/Gluc+ islets. Occ. high islet Ki67. | IHC                 |
| 6134    | 26.7      | Male   | Caucasian      | 20.1         | Ins+/Gluc+ islets plentiful, some with vascular stasis. Low Ki67. | IHC                 |
| 6137    | 8.9       | Female | Hispanic       | 24.2         | Ins+ islets. Occ. islet with 3 or more Ki67+ cell. Mild fatty infiltrate. No inflammatory infiltrates. | IHC                 |
| 6162    | 22.7      | Male   | African Am     | 28.9         | Ins+/Gluc+ islets, plentiful. Very mild, focal acinar atrophy. | IHC                 |
| 6160    | 22.1      | Male   | Caucasian      | 23.9         | Ins+/Gluc+ islets present, all sizes. No infiltrates. Low Ki67. | IHC                 |
| 6164    | 0         | Male   | Caucasian      | 16.5         | Ins+/Gluc+ islets, plentiful. Multifocal lymphoid (high CD3+) aggregates or early PLN. High Ki67 islets and acinar regions. | IHC                 |
| 6168    | 51        | Male   | Hispanic       | 25.2         | Ins+/Gluc+ islets, all sizes. Normal density. Low Ki67. Variable fatty infiltrates acinar regions. | IHC, IF             |
| 6174    | 20.9      | Male   | Caucasian      | 19.5         | Ins+/Gluc+ islets, plentiful. Low Ki67. No infiltrates. | IHC                 |
| 6178    | 24.5      | Female | Caucasian      | 27.5         | Ins+/Gluc+ normal islets. Low Ki67. No infiltrates. | IHC                 |
| 6179    | 20        | Female | Caucasian      | 20.7         | Ins+/Gluc+ islets, normal range of sizes, morphologies and density. Very high acinar Ki67. No other significant abnormalities observed. | IHC                 |
| ID  | Age | Sex  | Race     | Ins/Gluc+ Status | Description                                                                 | IHC/IF/SmFISH |
|-----|-----|------|----------|------------------|-----------------------------------------------------------------------------|----------------|
| 6187| 17.1| Male | Caucasian| Ins+Gluc+ normal islets, numerous. No inflammation. Low islet Ki67, moderate acinar Ki67. | IHC, IF         |
| 6218| 0.4 | Female| Male     | Ins+Gluc+ islets, normal. No abnormalities observed.                          | IHC, IF         |
| 6222| 18  | Male  | Caucasian| Ins+Gluc+ islets, numerous. High exocrine Ki67 with focal high duct Ki67+. Islets with Ki67+ cells in occ. islets head and body with more in tail region | IHC            |
| 6229| 20  | Female| African Am| Ins+Gluc+ islets, no abnormalities observed. Occasional islet hyperemia. | IHC            |
| 6232| 20  | Female| African Am| Ins+Gluc+ islets, numerous. Significant findings. 0-4 Ki67+ cells per islet, some non-insulin, as expected for this age. Low acinar Ki67. | IHC            |
| 6234| 2.5 | Female| Caucasian| Ins+Gluc+ islets. No abnormalities observed. Low Ki67 all compartments. | IHC            |
| 6238| 20  | Male  | African Am| Ins+Gluc+ islets, normal numbers. Low Ki67. No major infiltrates. Focal hemorrhage and compression of acinar tissue. | IHC            |
| 6251| 33  | Female| Caucasian| Ins+Gluc+ islets, numerous, including single cells. Infrequent islet with 1-3 Ki67+ cells. No significant lesions. | IHC, IF, Western Blot |
| 6282| 14  | Male  | Caucasian| Ins+Gluc+ islets, numerous, small to large islet size range. High islet Ki67+ (2-5+ cells/islet). | IHC, IF         |
| 6290| 58  | Male  | Caucasian| Ins+Gluc+ islets, numerous. Multifocal extra- and intracinac regions with moderate fat content. Very mild chronic pancreatitis, focal (PanTail). | IHC            |
| 6313| 0.25| Male  | Caucasian| Ins+Gluc+ islets, mostly small, numerous islets. Moderate acinar and islet Ki67+. No CD3 infiltrates observed. | IHC, IF, smFISH |
| 6315| 1.6 | Male  | African Am| Ins+Gluc+ islets, normal sizes and morphologies. Moderate acinar Ki67+ while islets have low Ki67+. Low acinar Ki67. | IHC, IF, smFISH |
| 6339| 23.3| Male  | Caucasian| Ins+Gluc+ islets, normal morphologies and sizes including rare islets with reduced ratio beta to alpha cells. Very mild sporadic CD3+ periductal infiltrates. Mild to moderate interlobular fat. Mild increase acinar Ki67. | IHC            |
| 6348| 0.03| Female| African Am| Ins+Gluc+ islets, clusters, single cells. Well formed acini and lobules throughout. Very high Ki67 acini and islets. | IHC            |
| 6353| 13  | Male  | African Am| Ins+Gluc+ islets, range of normal sizes with rare islet >500um. Moderate islet Ki67+. Mild extra-pancreatic fat. Low acinar Ki67+ and CD3+ cell numbers. | IHC, IF         |
| 6356| 0.58| Female| Caucasian| Ins+Gluc+ islets, normal range of sizes and morphologies. Very mild focal islet hyperplasia ventral lobe. Acinar Ki67+ cell numbers mild with very Ki67+ islets for donor age. | IHC, IF, SmFISH |
| 6370| 0   | Male  | Caucasian| Ins+Gluc+ islets, expected numbers and morphologies including numerous single cells and clusters. High exocrine Ki67+ cell numbers but infrequent Ki67+ beta cells. Minimal exocrine CD3+ cell numbers. | IHC            |
| 6375| 28.7| Male  | Caucasian| Ins+Gluc+ islets, normal numbers and sizes. Highly variable islet Ki67+ numbers with some having very high Ki67+. Low acinar Ki67+. Low with focally increased intralobular fat. Low exocrine infiltrates. | IHC            |
| 6376| 0.6 | Female| Caucasian| Ins+Gluc+ islets, expected range of small to medium sized islets with regular morphology. Moderate Ki67+ acinar cells with focally high numbers in tail region. Low islet Ki67+ cells. Tail region has multifocal, very mild CD3+ infiltrates. | IHC            |
| 6387| 18.1| Male  | Caucasian| Ins+Gluc+ islets, density, sizes, and morphologies within normal range. Low Ki67 except for few islets with mild increases, often non-beta cell. Low (normal) exocrine infiltrates. | IHC            |
| 6406| 4.9 | Male  | Caucasian| Ins+Gluc+ islets within normal range of sizes, shapes and density per region. | IHC, IF, SmFISH |
| 6415| 10.9| Male  | African Am| Ins+Gluc+ islets range of normal sizes, numbers and morphologies. Acinar and islet Ki67+ cell numbers low (0-2) to occasional low-moderate (3-10). | IHC            |
| 6453| 23.44| Male | Hispanic| Ins+Gluc+ islets, wide range sizes, including very small to clusters, large islets (>500um) with predominance of alpha-cells and diffuse spreading. Mild islet fibrosis. Mild variable fat infiltration lobules. Slight autolysis (<20%). | IHC            |
| 6461| 14.29| Male | Caucasian| Ins+Gluc+ islets, mostly small to medium with regular morphology. Rare possible Ins- islet and small islets or clusters of alpha cells. No significant lesions observed. | IF, SmFISH     |
| Sample | Age  | Sex  | Ethnicity | Ins/Glu+ islets, expected range of sizes, morphologies and densities with single beta-cells widely scattered. | Method(s) |
|--------|------|------|-----------|--------------------------------------------------------------------------------------------------|-----------|
| 6467   | 13.83| Male | Caucasian | Ins/Glu+ islets expected range of sizes, morphologies and densities with single beta-cells widely scattered. | IHC       |
| 6474   | 21.12| Male | African Am| Ins/Glu+ islets, numerous medium to large (400-500 um) with widely scattered alpha cells in periphery of several islets. Scattered foci GCG+ cells acinar regions. Mild increase islet Ki67+ cell numbers (2-5/islet). Widely scattered, mild increase in CD3+ cells within acinar regions. Various other examples of normal endocrine populations including ductal islet units of all endocrine populations and single and clustered PP+ cells in PanTail blocks. | IHC       |
| 6479   | 21.67| Female| Hispanic  | Ins/Glu+ islets, normal range of sizes, morphologies and densities. Mild (head, body) to moderate lobular fatty infiltration. | IHC       |
| 6488   | 4.6  | Female| Caucasian | Ins/Glu+ islets, normal range of sizes, morphologies and densities. Abundant single beta- and alpha-cells. Mild increase exocrine Ki67+ cell numbers due to mild leukocytic infiltrate as often seen. | IHC       |
| 6492   | 28.56| Male | Hispanic  | Ins/Glu+ islets, a wide range of sizes with mostly spherical morphologies including numerous single endocrine cells or clusters. Few islets with high Ki67 and CD3+ cell numbers. | IHC       |
| 6493   | 18.84| Male | Caucasian | Ins/Glu+ islets, normal sizes and morphologies including single endocrine cells in acinar regions. No significant lesions observed. | IHC, IF, Western Blot |
| 6495   | 9.6  | Male | Caucasian | Ins/Glu+ islets, normal range of sizes including some large (800um) with regular morphologies and densities per region. No significant lesions. | Western Blot |
| 6500   | 14.14| Female| African Am| Ins/Glu+ islets, wide range of sizes and mostly spherical morphologies. No significant lesions. | IHC       |
| 6516   | 20.75| Male | Caucasian | Ins/Glu+ islets, normal range of sizes, numbers and shapes. No significant findings. | IF, smFISH |
| 6518   | 21.86| Male | Caucasian | (Preliminary): islets plentiful, normal numbers, morphology. | IHC       |
Table S4. Demographic and clinical information for COVID-19 cases, Related to Figure 5 and Figure S5C-D. Pancreas was obtained at autopsy from three patients with fatal coronavirus disease 2019 (COVID-19). Abbreviations: yr, years; African Am, African American; BMI, body mass index; Type 2 DM, Type 2 diabetes; appx, approximately.

|                        | COVID-19 Case 1 | COVID-19 Case 2 | COVID-19 Case 3 |
|------------------------|-----------------|-----------------|-----------------|
| Age at Death (yr)      | 72              | 45              | 71              |
| Sex                    | Male            | Male            | Male            |
| Race                   | Caucasian       | African Am      | African Am      |
| BMI (kg/m²)            | 14.9            | 49.0            | 26.3            |
| Diabetes Status        | No diabetes     | Type 2 DM       | Type 2 DM       |
| Diabetes Duration      | ----            | unknown         | unknown         |
| Blood Glucose (mg/dL)  |                 |                 |                 |
| at admission           | 94              | 156             | 264             |
| at death               | 121             | 238             | 134             |
| Reported Days Ill      | Unknown         | 2               | 4               |
| Prior to Hospital      |                 |                 |                 |
| Admission              | (appx 1 week nursing home) |          |                 |
| Days from Admission to |                 |                 |                 |
| Death                  | 51              | 8               | 39              |