### Supplementary Table 1. Major gross pathologies identified at necropsy.

| Tissue | Pathology | Wt (52/%) | Wt T4 (14/%) | Pax8 +/- (17/%) | Pax8 +/- T4 (18/%) | Pax8 +/- (8/%) | Pax8 +/- T4 (5/%) |
|--------|-----------|-----------|--------------|-----------------|------------------|----------------|------------------|
| Heart  | Enlarged  | 4/ 8%     | 1/ 7%        | 1/ 7%           | 4/ 22%           | 0/ 0%          | 0/ 0%            |
| Kidney | Necrotic  | 4/ 8%     | 0/ 0%        | 1/ 7%           | 0/ 0%            | 0/ 0%          | 0/ 0%            |
| Liver  | Cancer    | 9/ 17%    | 0/ 0%        | 8/ 47%*         | 0/ 0%            | 0/ 0%          | 0/ 0%            |
| Liver  | Enlarged  | 14/ 27%   | 0/ 0%        | 9/ 53%          | 2/ 11%           | 0/ 0%          | 0/ 0%            |
| Spleen | Enlarged  | 9/ 17%    | 0/ 0%        | 7/ 41%          | 3/ 17%           | 0/ 0%          | 0/ 0%            |

The percentage of mice presenting with various pathologies is represented. *p < 0.05 compared to Wt. Analysed using Fisher’s Exact Test.

### Supplementary Table 2. List of the most modulated transcripts in pancreatic islets isolated from Pax8 +/- and Wt mice.

| Gene Symbol | Fold Change | p-value |
|-------------|-------------|---------|
| Scgn        | 30.08       | 0.0253  |
| Gm11096     | 28.36       | 0.0035  |
| Pcsk1n      | 15.77       | 0.0450  |
| Slc2a5      | 12.74       | 0.0440  |
| Mxipl       | 12.64       | 0.0461  |
| Wdr83os     | 12.49       | 0.0310  |
| Abat        | 12.43       | 0.0202  |
| Slc25a42    | 11.52       | 0.0277  |
| Insrr       | 11.46       | 0.0420  |
| Cfap126     | 11.24       | 0.0204  |
| Serpin12    | -10.51      | 0.0278  |
| Galnt3      | -10.7       | 0.0335  |
| Ero1l       | -10.99      | 0.0183  |
| Tm4sf1      | -13.3       | 0.0471  |
| Igfbp3      | -16.46      | 0.0464  |
| Ak4         | -21.78      | 0.0363  |
| Hmox1       | -24.1       | 0.0341  |
| Reg2        | -29.21      | 0.0465  |
| Pfkbp3      | -31.12      | 0.0393  |
| Slc2a1      | -42.5       | 0.0461  |
Supplementary Table 3. Antibodies used in this study.

| Antibody                                           | Dilution | Vendor              | Catalog number                     |
|----------------------------------------------------|----------|---------------------|------------------------------------|
| Alexa fluor 647 donkey anti-mouse                  | 1:800    | Thermofisher        | Cat# A-31571, RRID:AB_162542)      |
| Alexa fluor 555 donkey anti-rabbit                 | 1:800    | Thermofisher        | Cat# A-31572, RRID:AB_162543      |
| Alexa fluor 488 donkey anti-goat                   | 1:800    | Thermofisher        | Cat# A-11055, RRID:AB_2534102     |
| Anti-insulin                                       | 1:500    | Sigma-Aldrich       | Cat# I2018, RRID:AB_260137        |
| Anti-insulin                                       | 1:500    | Santa Cruz Biotechnology | Cat# sc-9168, RRID:AB_2126540     |
| Anti-glucagon                                      | 1:150    | Cell Signaling      | Cat# 2760, RRID:AB_659831         |
| Anti-glucagon                                      | 1:100    | Sigma-Aldrich       | Cat# G2654, RRID:AB_259852        |
| Anti-somatostatin                                  | 1:150    | Santa Cruz Biotechnology | Cat# sc-7819, RRID:AB_2302603     |
| Anti-pSer473 Akt                                   | 1:500    | Cell Signaling      | Cat# 9271, RRID:AB_329825         |
| Anti-Akt                                           | 1:1000   | Cell Signaling      | Cat# 9272, RRID:AB_329827         |
| Anti-Gapdh                                         | 1:1000   | Cell Signaling      | Cat# 2118, RRID:AB_561053         |
| Anti-pThr172 Ampk                                  | 1:1000   | Cell Signaling      | Cat# 2535, RRID:AB_331250         |
| Anti-Amk                                          | 1:1000   | Cell Signaling      | Cat# 2532, RRID:AB_330331         |
| Anti-Lc3b                                          | 1:1000   | Cell Signaling      | Cat# 2775, RRID:AB_915950)        |
| Anti-Ucp2                                          | 1:200    | Santa Cruz Biotechnology | Cat# ab15895, RRID:AB_2214787     |
| Anti-Vdac1                                         | 1:1000   | Abcam               | Cat# sc-517380, RRID:AB_2755043   |
| Anti-Pgc1-α                                       | 1:1000   | Santa Cruz Biotechnology | Cat# A21363, RRID:AB_1501848     |
| Anti-cytochrome c oxidase subunit Va               | 1:1000   | Molecular probes    | Cat# A-6403, RRID:AB_221582       |
| Anti-cytochrome c oxidase subunit I                | 1:1000   | Molecular probes    | Cat# 393206-100UL, RRID:AB_211975 |
| Anti-4hne                                          | 1:1000   | MilliPore           | Cat# sc-55580, RRID:AB_2231427    |
| Anti-Fas                                           | 1:200    | Santa Cruz Biotechnology | Cat# sc-100847, RRID:AB_2219392  |
| Anti-Acaa2                                         | 1:200    | Santa Cruz Biotechnology | Cat# ALX-804-549-C100, RRID:AB_2050978 |
| Anti-Ccl2                                          | 1:200    | ENZO                | Cat# ab32536, RRID:AB_776751      |
| Anti-NfkB                                          | 1:1000   | Abcam               | Cat# 3033, RRID:AB_331284         |
| Anti-pSer536 NfkB                                  | 1:1000   | Cell Signaling      | Cat# ab13498, RRID:AB_300402      |
| Anti-Sod1                                          | 1:2000   | Abcam               | Cat# G1160, RRID:AB_259845        |
| Anti-Gst                                           | 1:1000   | Sigma-Aldrich       | Cat# sc-575, RRID:AB_631365       |
| Anti-Gadd153                                       | 1:200    | Santa Cruz Biotechnology | Cat# sc-53090, RRID:AB_2147279   |
| Anti-Myh7                                          | 1:150    | Santa Cruz Biotechnology | Cat# A5045, RRID:AB_257896       |
| HRP-goat anti-rabbit                               | 1:5000   | Sigma-Aldrich       | Cat# A9044, RRID:AB_258431        |
| HRP-rabbit anti-mouse                              | 1:5000   | Sigma-Aldrich       | Cat# sc-516102, RRID:AB_2687626   |
| HRP-IgGκ light chain binding protein anti-mouse    | 1:1000   | Santa Cruz Biotechnology | Cat# 705-036-147, RRID:AB_2340392|
| HRP-donkey anti-goat                               | 1:2000   | Jackson ImmunoResearch Labs | Cat# 705-036-147, RRID:AB_2340392|
| Gene       | Forward primer sequence            | Reverse primer sequence            |
|------------|------------------------------------|------------------------------------|
| Mouse mtNd1| 5′-CCTATACCCCTGCTCCTCATC-3′       | 5′-GAGGCTGTGTGTTGTGTGAC-3′         |
| Mouse nPecam| 5′-ATGGAAAGCCTGCCATCAG-3′       | 5′-TCCTTTGGTTTCAGCATC-3′          |
| Mouse Pgc1-α| 5′-GGGTGACAGAGGAAAGAAT-3′      | 5′-CACCAAAACCAAGAAGCAG-3′         |
| Mouse Pax8 | 5′-GTTTGAGCGCCGACATTAC-3′       | 5′-GTAAGGGCAGTGGTACGAC-3′         |
| Mouse Rps29| 5′-GGAGTCACCCACGGAAAGT-3′       | 5′-CATGTTCAAGGGATTTGTC-3′         |
| Mouse Ucp2 | 5′-GGATGGCATTCCAGCCTCCT-3′       | 5′-AGCATCTCTCCTGCACACTA-3′        |
| Mouse Srebp1-c| 5′-GCATGCCGACGGAAGGTAC-3'  | 5′-CCAGGTGATGCCCCCTCA-3'          |
| Mouse Srebp2| 5′-ACCGGTCTCCCTCATCAACG-3′      | 5′-TCCTGAATCAGCCCACG-3′           |
| Mouse Fasn | 5′-TGATGGACGGCAGCAGCCT-3′       | 5′-TGGAATCTGGAGGTTGTA-3′          |
| Mouse Soc2 | 5′-AGACAAGAACCCCAATCCTCC-3′      | 5′-GGTAAAGGGAGTCCCCAGA-3′         |
| Mouse Il-1β| 5′-AAGCTTGGTGAGGAATGTG-3′       | 5′-ACACCCATGAGCGAGTCC-3′          |
| Mouse Tnf-α| 5′-CCCTCAGCCTACATCAT-TTCT-3′    | 5′-GCTACGAGCTGGGTACAG-3′          |
| Mouse Cpt1 | 5′-AGACAAGAACCCCAATCCTCC-3′      | 5′-CCAGGTGATGCCCCCTCA-3′          |
| Mouse Lcad | 5′-GGATGGACGGCAGCAGCCT-3’       | 5′-TGGAATCTGGAGGTTGTA-3′          |
| Mouse Mcad | 5′-TGATGGACGGCAGCAGCCT-3’       | 5′-GGTAAAGGGAGTCCCCAGA-3′         |
| Mouse Atp5a1| 5′-AGACAAGAACCCCAATCCTCC-3′     | 5′-CCAGGTGATGCCCCCTCA-3′          |
| Mouse Cox5b| 5′-ACCCCTATCTAGTCCTCC-3′       | 5′-CCAGCAAAACCAAGATGACAG-3′       |
| Mouse Uqrc1 | 5′-ATCAAGGCACCTAGCCCAAG-3’      | 5′-TCATTCTGATCATCTCCCCG-3’        |
| Mouse Ndufab5| 5′-GGAGTCACCCACGGAAAGT-3’      | 5′-AAACCCAAATTCGCTTCCCATG-3’      |
| Mouse Cish | 5′-GCATGCCGACGGAAGGTAC-3’       | 5′-ATTCCTGCAACCGATTTGCTTCC-3’     |