

Tab. S1: Quantification of endocrine cells per embryo (Mean + SEM)

Ins

| Stage | Control | n | <i>isl1</i> ^{-/-} | n |
|--------|--------------|----|----------------------------|----|
| 28 hpf | 18.67 ± 0.46 | 16 | 10.43 ± 0.64 | 7 |
| 48 hpf | 23.90 ± 0.50 | 10 | 9.66 ± 0.80 | 10 |
| 76 hpf | 29.85 ± 0.87 | 13 | 15.40 ± 0.68 | 13 |

Sst

| Stage | Control | n | <i>isl1</i> ^{-/-} | n |
|--------|--------------|----|----------------------------|----|
| 28 hpf | 15.87 ± 0.45 | 16 | 8.57 ± 0.42 | 7 |
| 48 hpf | 23.30 ± 0.74 | 10 | 5.83 ± 0.54 | 10 |
| 76 hpf | 25.23 ± 0.54 | 13 | 7.33 ± 0.62 | 13 |

Gcg

| Stage | Control | n | <i>isl1</i> ^{-/-} | n |
|--------|--------------|----|----------------------------|---|
| 48 hpf | 27.86 ± 0.40 | 7 | 3.75 ± 0.41 | 8 |
| 76 hpf | 34.73 ± 0.67 | 11 | 7.12 ± 0.89 | 8 |
| 96 hpf | 33.71 ± 0.94 | 7 | 10.80 ± 0.86 | 5 |

Tab. S2: Quantification of *isl1* and *pax6b* expressing cells per embryo (Mean + SEM)*isl1*

| Stage | Control | n | <i>isl1</i> ^{-/-} | n |
|--------|--------------|---|----------------------------|---|
| 48 hpf | 42.88 ± 1.10 | 8 | 43.04 ± 1.23 | 6 |
| 76 hpf | 56.86 ± 2.44 | 9 | 54.50 ± 1.67 | 7 |

pax6b

| Stage | Control | n | <i>isl1</i> ^{-/-} | n |
|--------|--------------|----|----------------------------|----|
| 24 hpf | 38.60 ± 1.06 | 10 | 39.80 ± 0.74 | 10 |

Tab. S3: Quantification of *ins*⁺ cells per embryo (Mean + SEM)

| Stage | <i>isl1</i> ^{-/-} | n | <i>isl1</i> ^{-/-} + MO ^{<i>isl2a</i>} | n |
|--------|----------------------------|---|---|---|
| 30 hpf | 8.80 ± 0.66 | 8 | 8.2 ± 0.66 | 6 |
| 72 hpf | 9.62 ± 0.88 | 9 | 10.25 ± 0.70 | 7 |

Tab. S4: Length of the exocrine pancreas [μm] (Mean + SEM)

| Genotype | Length [μm] | n |
|--|--------------------------|----|
| Control | 235.6 \pm 15.86 | 9 |
| Control + MO ^{isl2a} | 162.6 \pm 5.9 | 14 |
| Control + MO ^{isl2b} | 188.7 \pm 8.87 | 21 |
| Control + MO ^{isl2a/b} | 131.4 \pm 9.83 | 21 |
| | | |
| <i>isl1</i> ^{-/-} | 182.0 \pm 7.56 | 21 |
| <i>isl1</i> ^{-/-} + MO ^{isl2a} | 125.6 \pm 11.41 | 14 |
| <i>isl1</i> ^{-/-} + MO ^{isl2b} | 120.7 \pm 16.06 | 11 |
| <i>isl1</i> ^{-/-} + MO ^{isl2a/b} | 74.56 \pm 5.2 | 17 |

Tab. S5: Quantification of EdU assay (Mean + SEM)

| | Control | n | <i>isl1</i> ^{-/-} | n |
|--------------------------------------|------------------|---|----------------------------|---|
| total Ins | 35.23 \pm 1.45 | 7 | 14.25 \pm 0.99 | 8 |
| Ins ⁺ /EdU ⁺ | 2.14 \pm 0.50 | 7 | 0.75 \pm 0.31 | 8 |
| % Ins ⁺ /EdU ⁺ | 6.10 \pm 1.38 | 7 | 4.54 \pm 1.90 | 8 |

Tab. S6: Quantification of DBCs and VBCs per Embryo (Mean + SEM)

DBC_s (H2B-RFP⁺)

| | Control | n | <i>isl1</i> ^{-/-} | n |
|-----|------------------|----|----------------------------|---|
| Ins | 21.00 \pm 1.36 | 6 | 5.6 \pm 0.60 | 5 |
| Sst | 19.90 \pm 0.45 | 10 | 4.57 \pm 0.57 | 7 |
| Gcg | 22.71 \pm 1.22 | 7 | 2.8 \pm 0.66 | 5 |

VBC_s (H2B-RFP⁻)

| | Control | n | <i>isl1</i> ^{-/-} | n |
|-----|------------------|----|----------------------------|---|
| Ins | 10.17 \pm 0.94 | 6 | 9.00 \pm 0.70 | 5 |
| Sst | 10.06 \pm 0.65 | 10 | 1.85 \pm 0.40 | 7 |
| Gcg | 11.00 \pm 0.78 | 7 | 8.00 \pm 1.14 | 5 |

Tab. S7: Primer for qPCR

| Gene | Pimer (5'-3' Orientation) | |
|----------------|---------------------------|--------------------------|
| <i>EF1a</i> | TCTCTACCTACCCTCCTCTTGGTC | TTGGTCTTGGCAGCCTTCTGTG |
| <i>ins</i> | GCCCAACAGGCTTCTTCTACAAC | GCAGATTTAGGAGGAAGGAAACCC |
| <i>sst2</i> | GCACTTCTGCGGATGAAGAGATAC | TGTAGCGATCCCAGAGATGAGC |
| <i>gcga</i> | AGCGAGGAGACGATCCAAACAC | GCTGAGTCTTCCAACACACACCAG |
| <i>pax6b</i> | GCCAGGACAACCAAATCAAGACG | GTGAAGGACGTTCTGTTTCTCTGC |
| <i>mnx1</i> | TGATGCTAACAGAGACGCAGGTG | TACTGCGCTTCCATTTTCATGCG |
| <i>neuroD</i> | CTTTCAACACACCCTAGAGTTCCG | GCATCATGCTTTCCTCGCTGTATG |
| <i>isl1</i> | CGAGACCTTTACAAATGGCAGCAG | TGTGCACATGAGGTCAAGC |
| <i>trypsin</i> | ACCAGCTGTCTGATCTCTGGATGG | CAGACGGCTTGGGTAATTGCTTC |
| <i>ela3l</i> | GTTGTCGCTGGATGCAATGGAG | TGCCGTCAGAGTTCTTGCAGTTC |

Tab. S8: qPCR, fold expression in relation to control embryos (Mean + SEM)

Whole mounts (Fig.1)

| Gene | Stage | <i>isl1</i> ^{-/-} |
|-------------|--------|----------------------------|
| <i>ins</i> | 28 hpf | 0.11 ± 0.02 |
| | 96 hpf | 0.32 ± 0.03 |
| <i>sst2</i> | 28 hpf | 0.19 ± 0.02 |
| | 96 hpf | 0.41 ± 0.02 |
| <i>gcga</i> | 28 hpf | 0.52 ± 0.06 |
| | 96 hpf | 0.62 ± 0.15 |

Isolated pancreata (Fig. 2)

| Gene | <i>isl1</i> ^{-/-} |
|---------------|----------------------------|
| <i>ins</i> | 0.32 ± 0.02 |
| <i>sst2</i> | 0.51 ± 0.14 |
| <i>gcga</i> | 0.20 ± 0.04 |
| <i>pax6b</i> | 1.02 ± 0.21 |
| <i>neuroD</i> | 1.05 ± 0.06 |
| <i>isl1</i> | 0.94 ± 0.12 |
| <i>mnx1</i> | 0.97 ± 0.11 |
| <i>arx</i> | 0.15 ± 0.01 |

Whole mounts (Fig. 5)

| Gene | Genotype | fold expression |
|----------------|---|-----------------|
| <i>trypsin</i> | Control + MO ^{<i>isl2a/b</i>} | 0.77 ± 0.13 |
| | <i>isl1</i> ^{-/-} | 0.37 ± 0.02 |
| | <i>isl1</i> ^{-/-} + MO ^{<i>isl2a/b</i>} | 0.33 ± 0.02 |
| <i>ela3l</i> | Control + MO ^{<i>isl2a/b</i>} | 0.88 ± 0.16 |
| | <i>isl1</i> ^{-/-} | 0.04 ± 0.01 |
| | <i>isl1</i> ^{-/-} + MO ^{<i>isl2a/b</i>} | 0.04 ± 0.00 |