

SUPPLEMENTARY DATA

Mafa enables Pdx1 to effectively convert pancreatic islet progenitors and committed islet α -cells into β -cells *in vivo*

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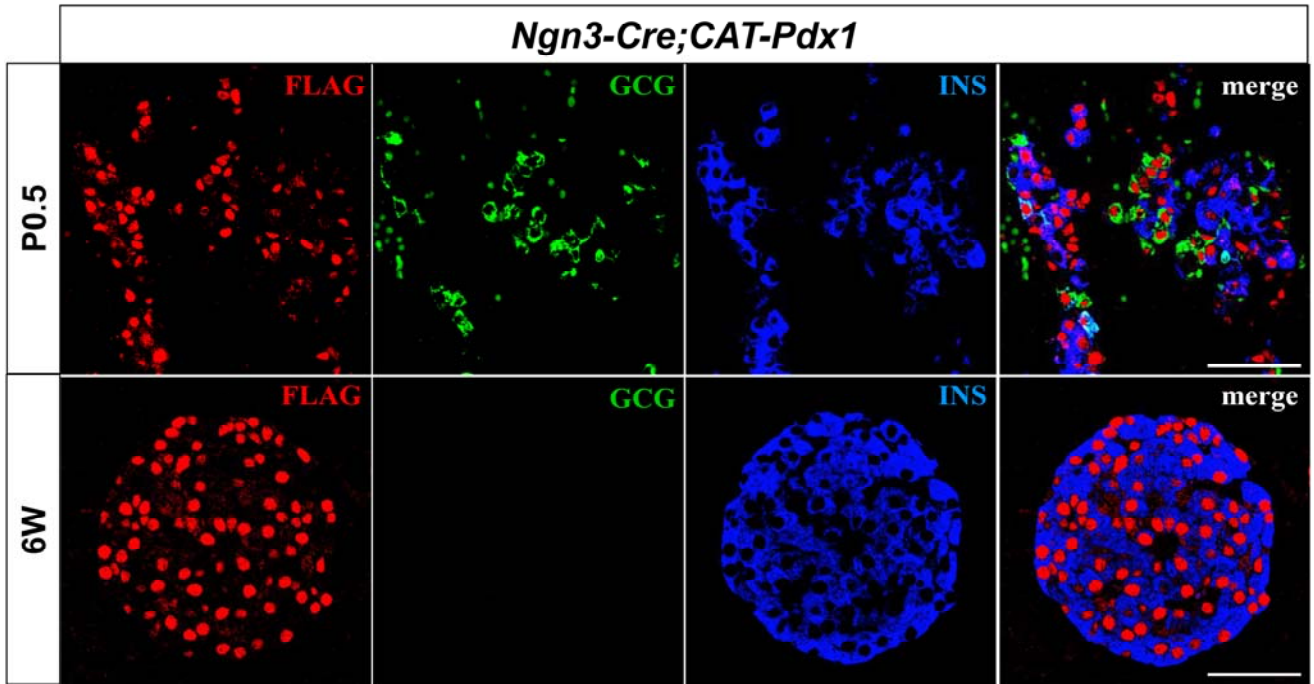
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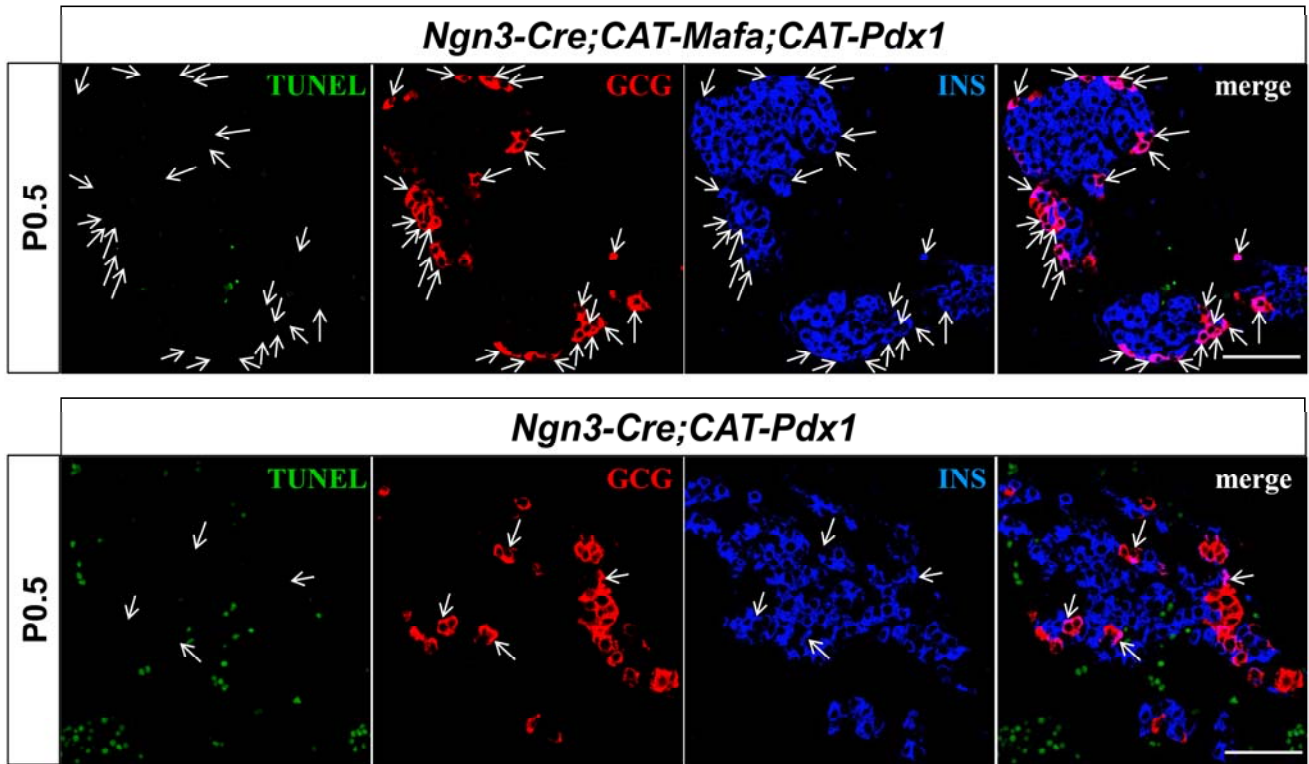
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Supplementary Figure 1. $Pdx1^{flag}$ is expressed in most P0.5 and 6W *Ngn3-Cre;CAT-Pdx1* islet cells. Flag staining (red) was observed in most of *Ngn3-Cre;CAT-Pdx1* insulin⁺(blue) and glucagon⁺(green) cells at P0.5 and 6W; the Crepenetrance rate was a maintained at approximately 95%. Scale bars: 50 μ m.

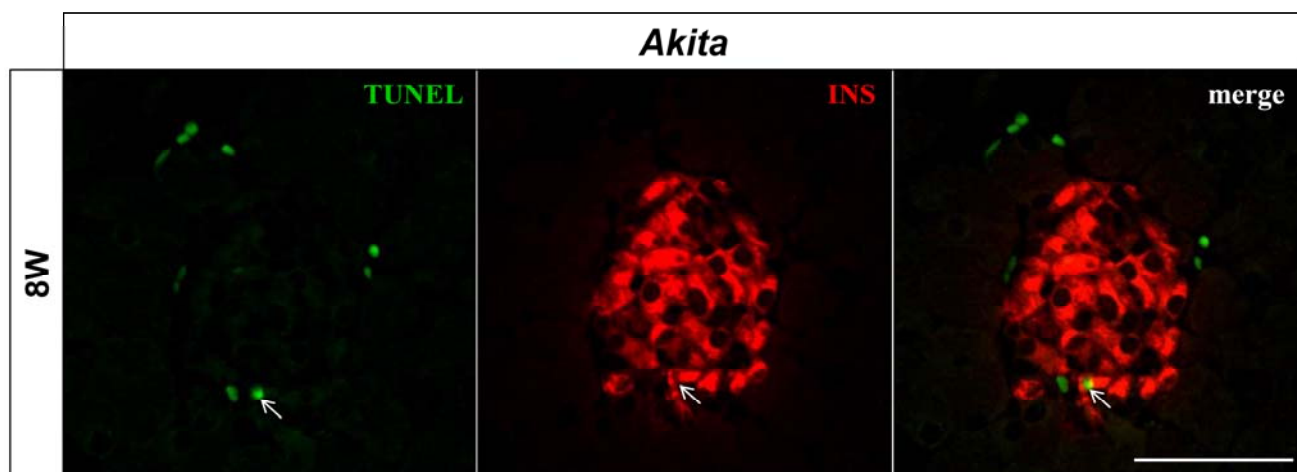
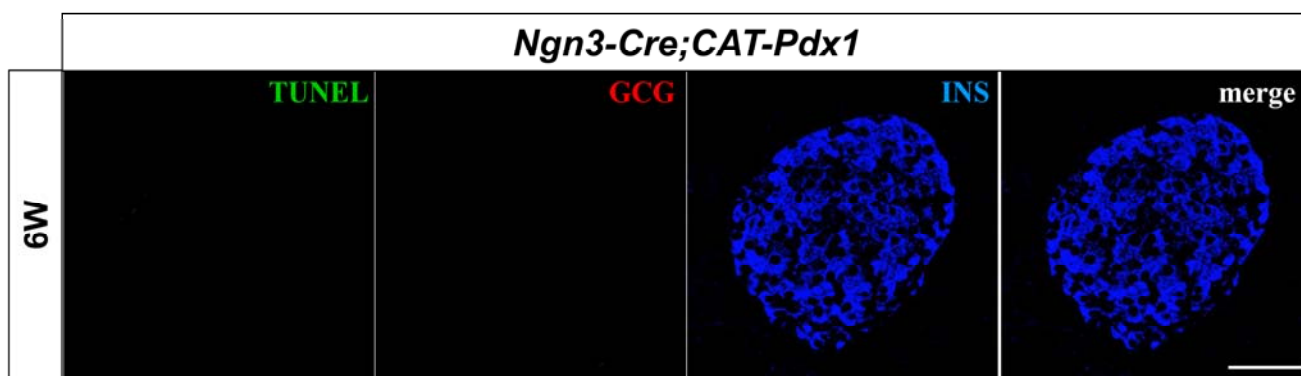
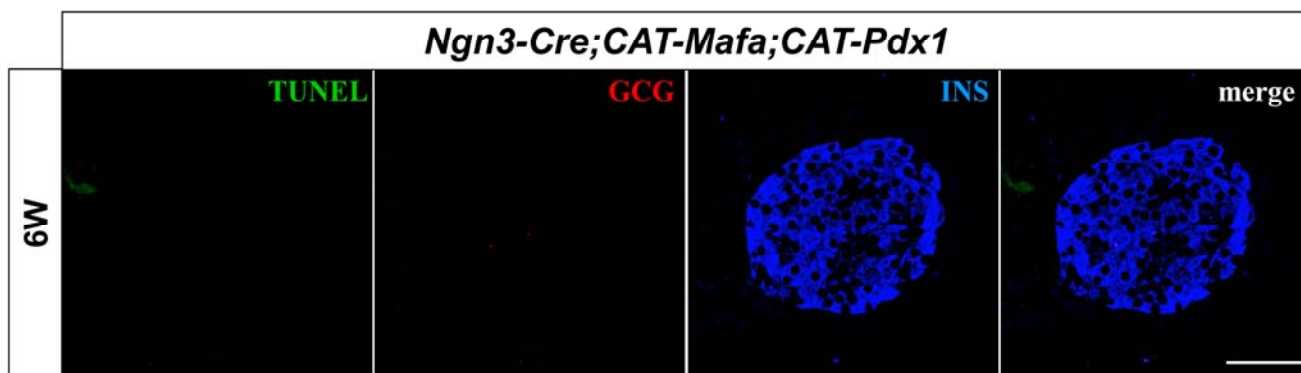


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Supplementary Figure 2. There were not any TUNEL⁺ apoptosis observed within Mafa^{myc} and/or Pdx1^{flag} expressing islet cells. TUNEL staining was performed with (A) P0.5, and (B) 6W *Ngn3-Cre;CAT-Mafa;CAT-Pdx1* and *Ngn3-Cre;CAT-Pdx1* mice. The arrows mark the insulin and glucagon double positive cells. No TUNEL⁺ cells (green) were found within islet glucagon⁺ (red) or insulin⁺ (blue) cells. Note: the green staining was shown to be within red blood cells. (C) The C57BL/6 *Ins2^{Akita}* (Akita) mouse, an ER stress induced apoptosis model, was used as a control to observe TUNEL⁺ β-cells. Scale bars: 50 μm.

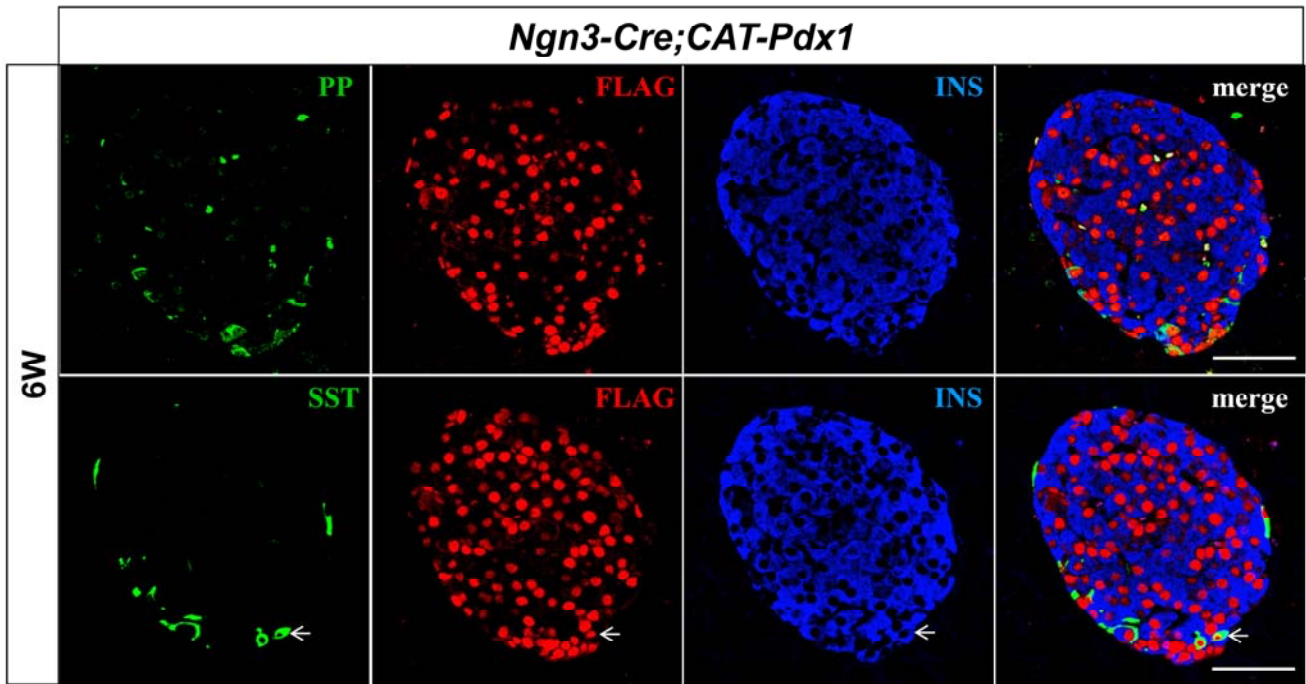


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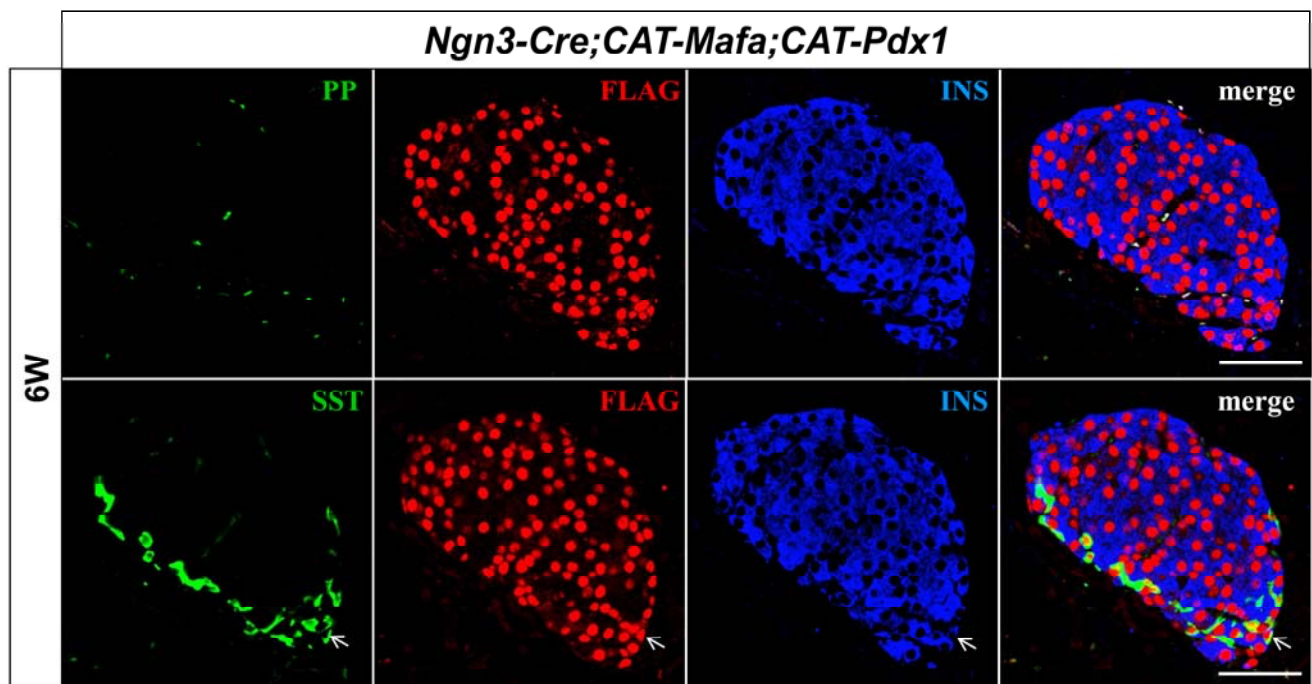


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Supplementary Figure 3. PP and d cells produce Pdx1^{flag} in *Ngn3-Cre;CAT-Pdx1* and *Ngn3-Cre;CAT-Mafa;CAT-Pdx1* islets. Pdx1^{flag} epitope staining (red) was observed in most A) *Ngn3-Cre;CAT-Pdx1* and B) *Ngn3-Cre;CAT-Mafa;CAT-Pdx1* islets. Pdx1^{flag} (red), insulin (blue), PP (green), and somatostatin (green) cells in 6W islets. However, PP⁺ cells are seldom observed in 6W *Ngn3-Cre;CAT-Pdx1;CAT-Mafa* islets. The green staining for PP in 6W *Ngn3-Cre;CAT-Pdx1;CAT-Mafa* islets was only found in red blood cells. The arrows mark insulin and somatostatin double positive cell. Scalebars: 50 μm.

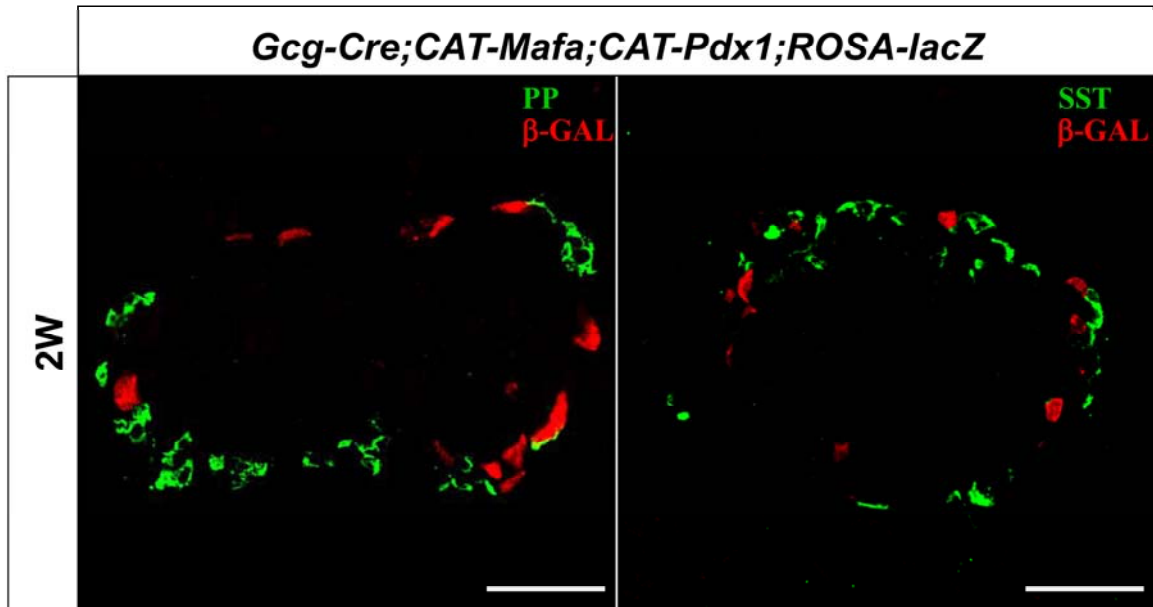


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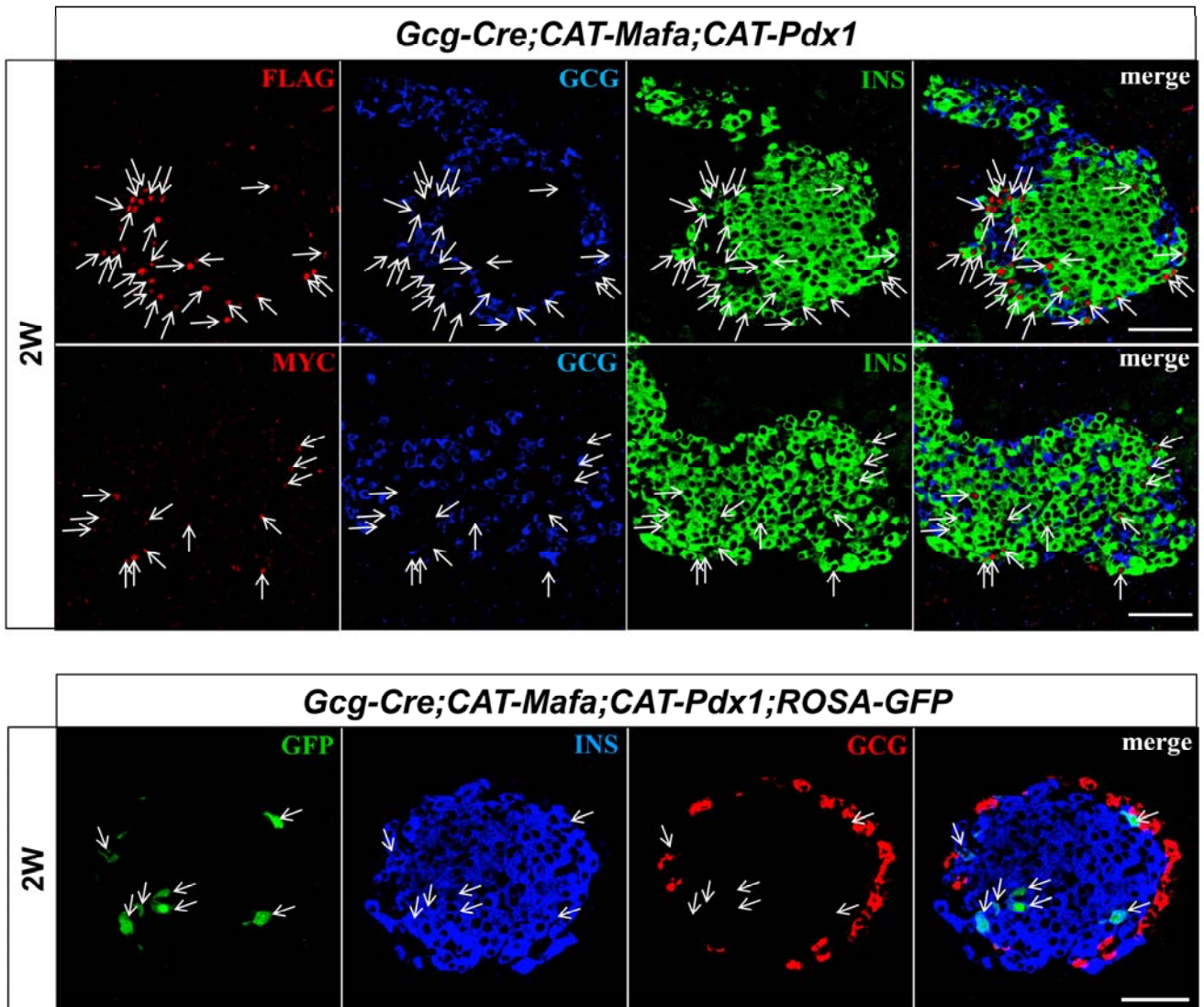
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Supplementary Figure 4. *Mafa*^{myc} + *Pdx1*^{flag} expression does not affect islet PP- and δ -cell levels in *Gcg-Cre;CAT-Mafa;CAT-Pdx1* islets. The *ROSA26*-driven β -gal (red) was used to trace the α -cell fate in PP (green) and somatostatin (SST,green) cells. Notably, there was no evidence of β -gal expression in these 2 week-old *Gcg-Cre;CAT-Mafa;CAT-Pdx1* islet cells. Scale bars: 50 μ m.



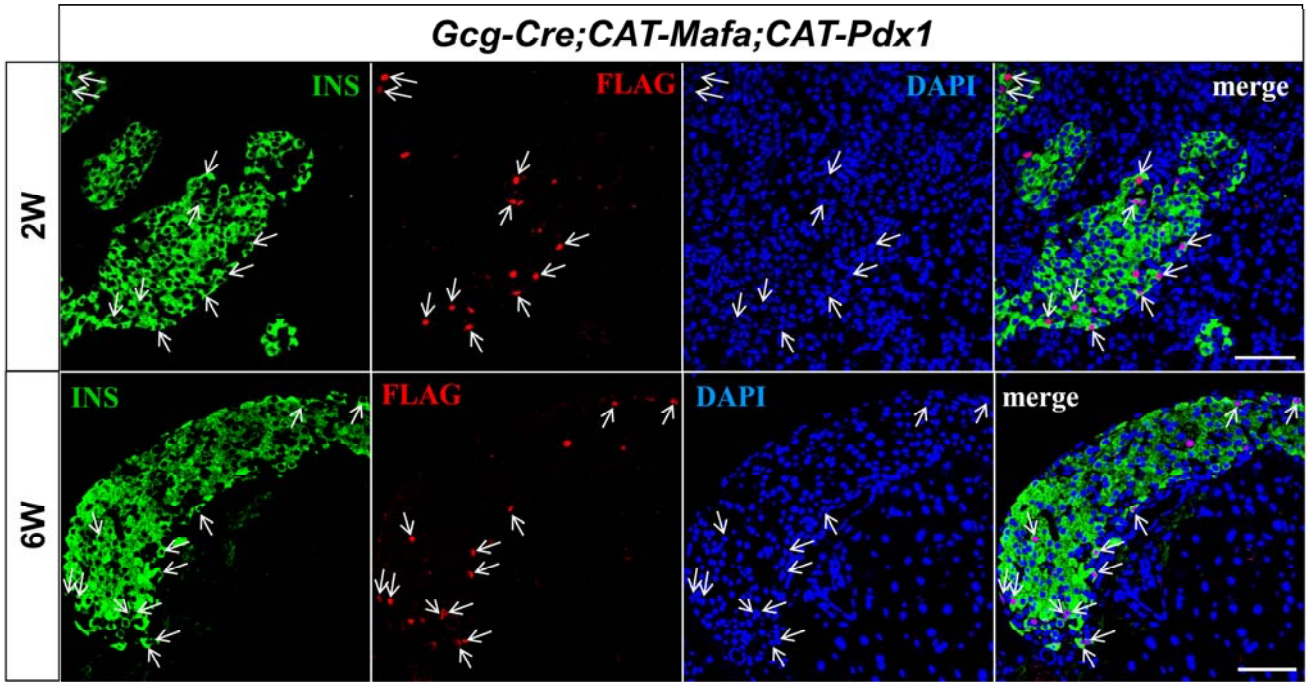
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Supplementary Figure 5. MafA^{myc} + Pdx1^{flag} induces insulin production in pancreatic α -cells. To trace the cell fate of the α -cell smisexpressing MafA^{myc} + Pdx1^{flag} in *Gcg-Cre;CAT-Mafa;CAT-Pdx1* mice , (A) flag- and myc-tagged staining (red) was compared in glucagon (blue) and insulin (green). (B) Tagged Mafa- and Pdx1- expressing α -cells were also traced by immunostaining for GFP (green), insulin (blue) , and glucagon (red) in *Gcg-Cre;CAT-Mafa;CAT-Pdx1;ROSA-GFP* mice. Significantly ,most of Pdx1^{flag}, MafA^{myc}, and GFP co-positive cells are only insulin⁺ in 2 week-old *Gcg-Cre;CAT-Mafa;CAT-Pdx1* islets (indicated by arrows).Scale bars: 50 μ m.



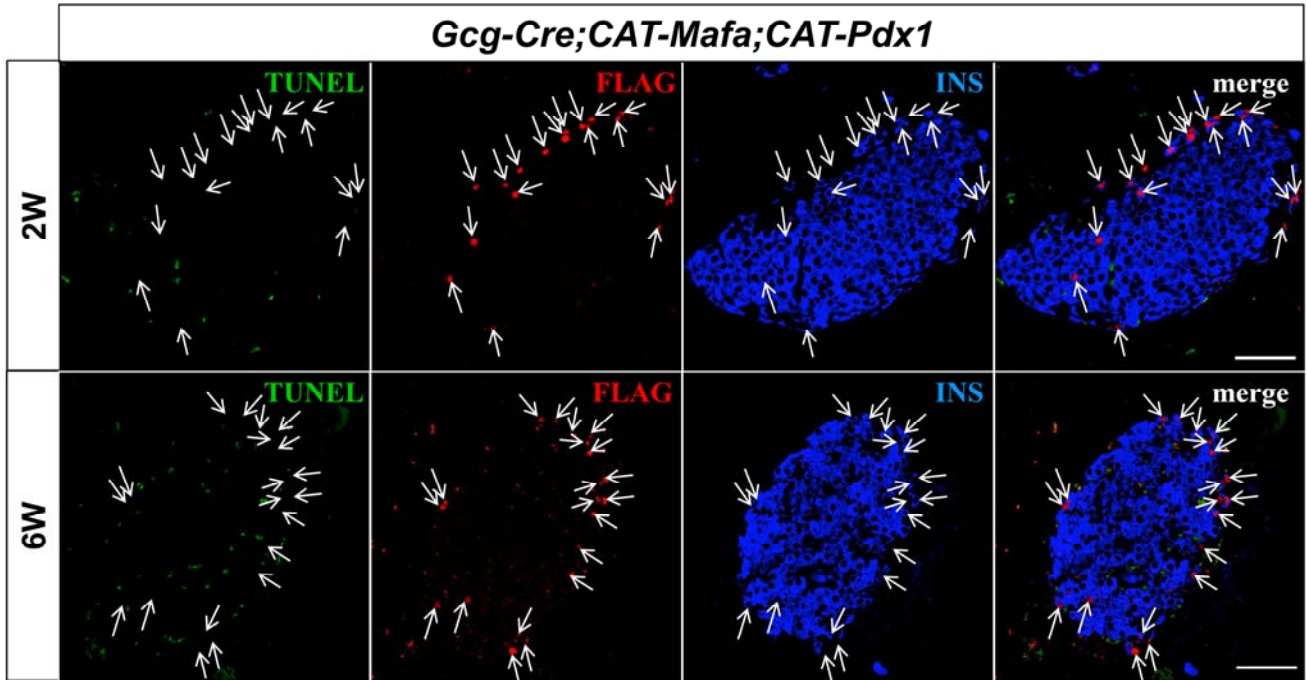
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Supplementary Figure 6. There was not a marked change in the level of a-cell transdifferentiation between 2W and 6W *Gcg-Cre; CAT-Mafa; CAT-Pdx1* islets. Approximately 75% of $Pdx1^{flag}$ expressing cells were insulin⁺ in *Gcg-Cre; CAT-Mafa; CAT-Pdx1* islets. The arrows indicate flag and insulin double positive cells. Scale bars: 50 μ m.



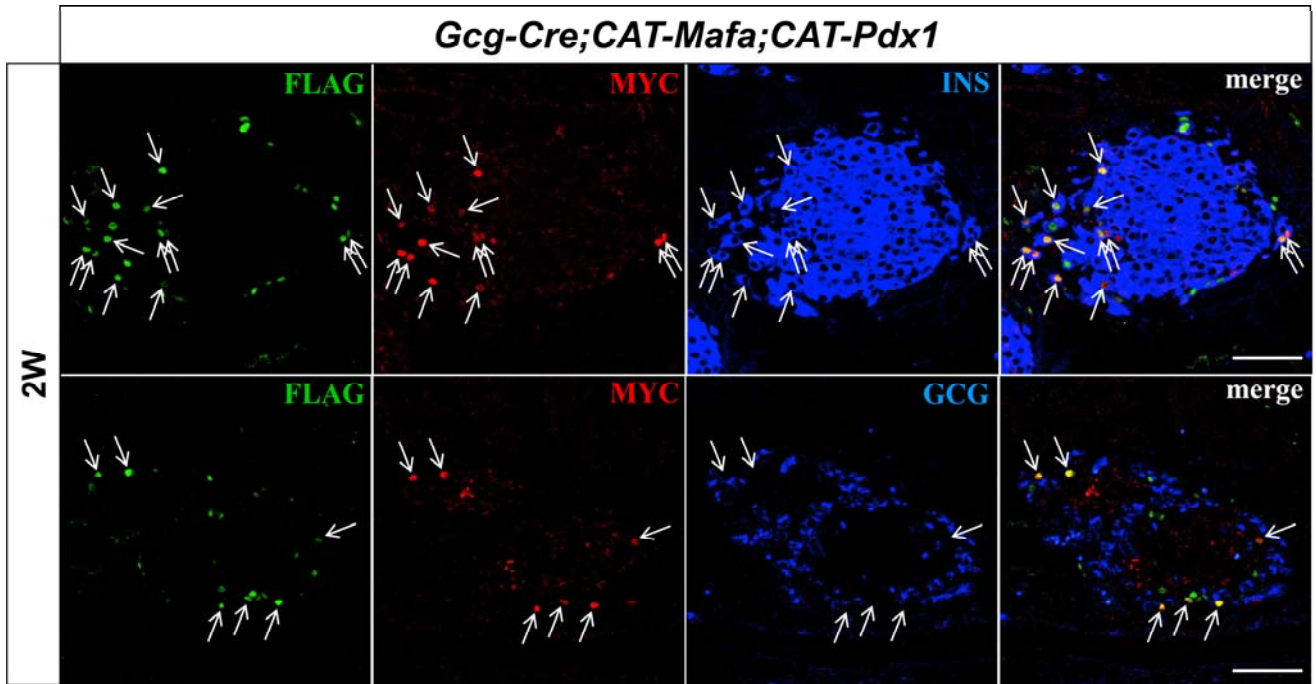
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Supplementary Figure 7. There were no TUNEL⁺ Pdx1^{flag} expressing cells in 2W and 6W *Gcg-Cre;CAT-Mafa;Cat-Pdx1* islets. TUNEL⁺ (green) , flag⁺ (red) ,and insulin⁺ (blue) staining is shown. Flag⁺ cells were indicated by arrows. The green staining cells was only found in red blood cells. Scale bars: 50μm.



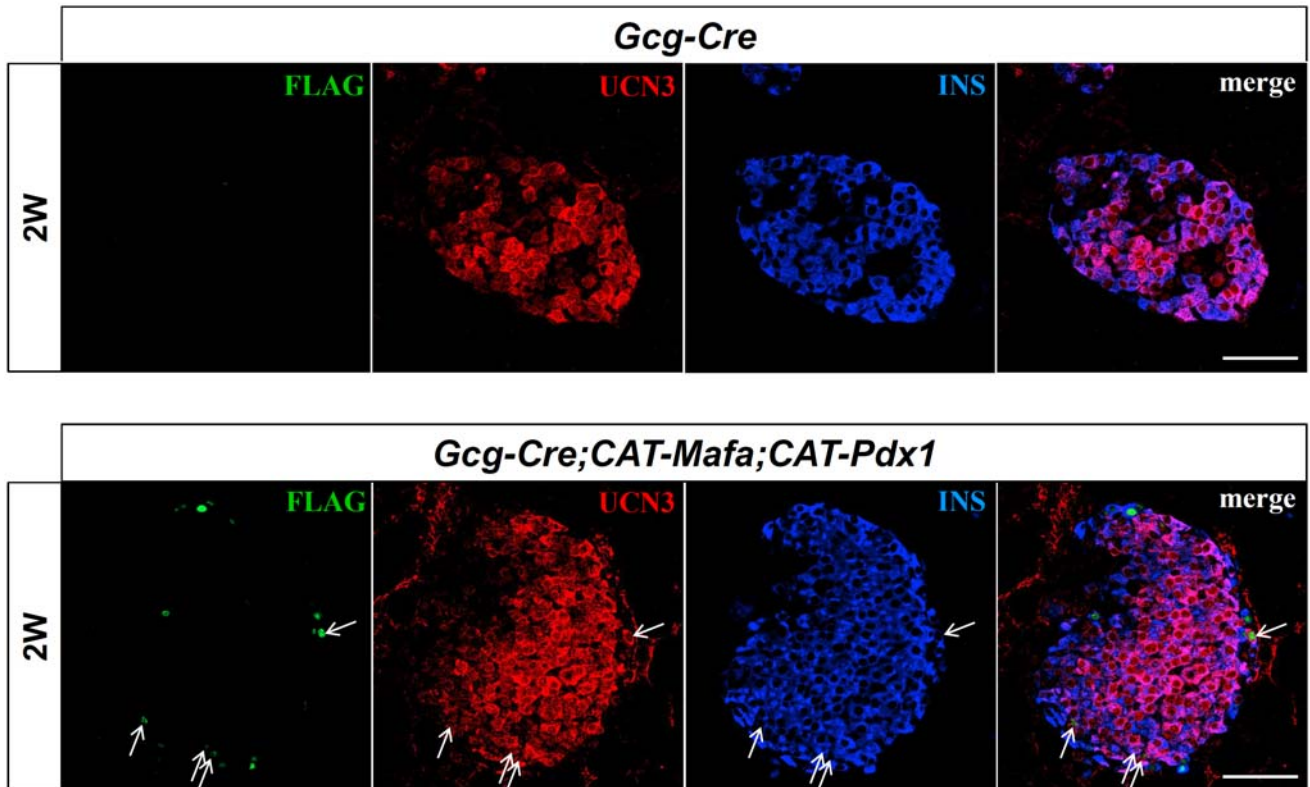
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Supplementary Figure 8. Only monohormonal islet insulin⁺ cells are generated upon MafA^{myc} + Pdx1^{flag} expression in embryonic α -cells. Flag (green), myc (red), insulin (blue), and glucagon (blue) immunostaining was performed in *Gcg-Cre;CAT-Mafa;CAT-Pdx1* islets. Only insulin⁺ cells were produced upon simultaneous production of the tagged transcription factors (indicated by arrows) in developing α -cells. Scale bars: 50 μ m.



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Supplementary Figure 9. Ucn3 expression is gained and Arx compromised upon α -cell conversion to β -like cells in *Gcg-Cre;CAT-Mafa;CAT-Pdx1* islets. (A) The islet Ucn3 (red) β -cell-enriched and GSIS-regulating protein is detectable in 46% of Pdx1 flag (green) cells within 2W *Gcg-Cre;CAT-Mafa;CAT-Pdx1* islets (indicated by arrows). (B) The α -cell-specific Arx transcription factor (green) was present in roughly 21% of FLAG⁺(red) cells. FLAG⁺ and Arx-cells are marked by arrows. Notably, Arx expression was eventually silenced in the islet β -cells produced upon misexpressing Pdx1 in Ngn3⁺ progenitors (19). Scale bars: 50 μ m.



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Gcg-Cre;CAT-Mafa;CAT-Pdx1 (2W)

