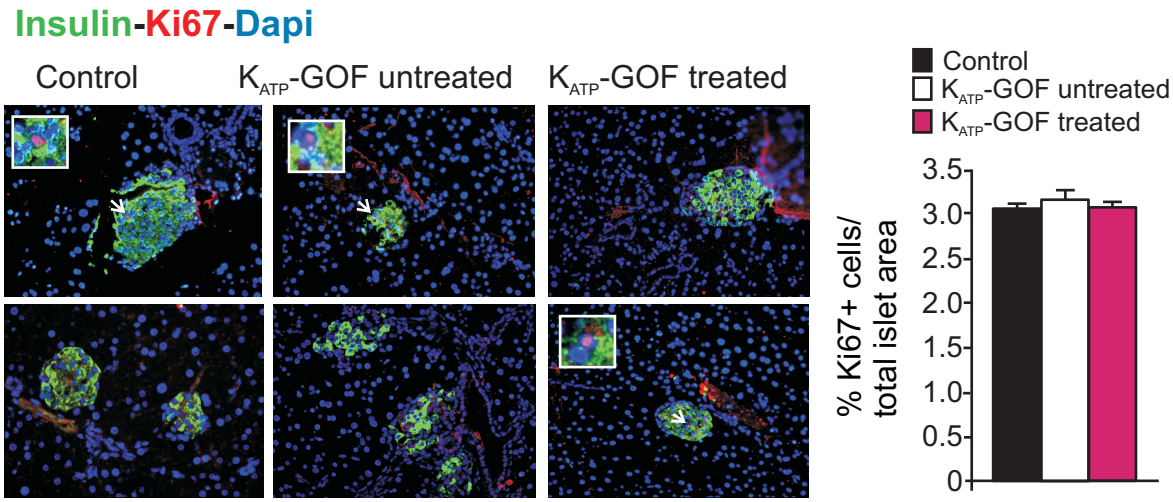
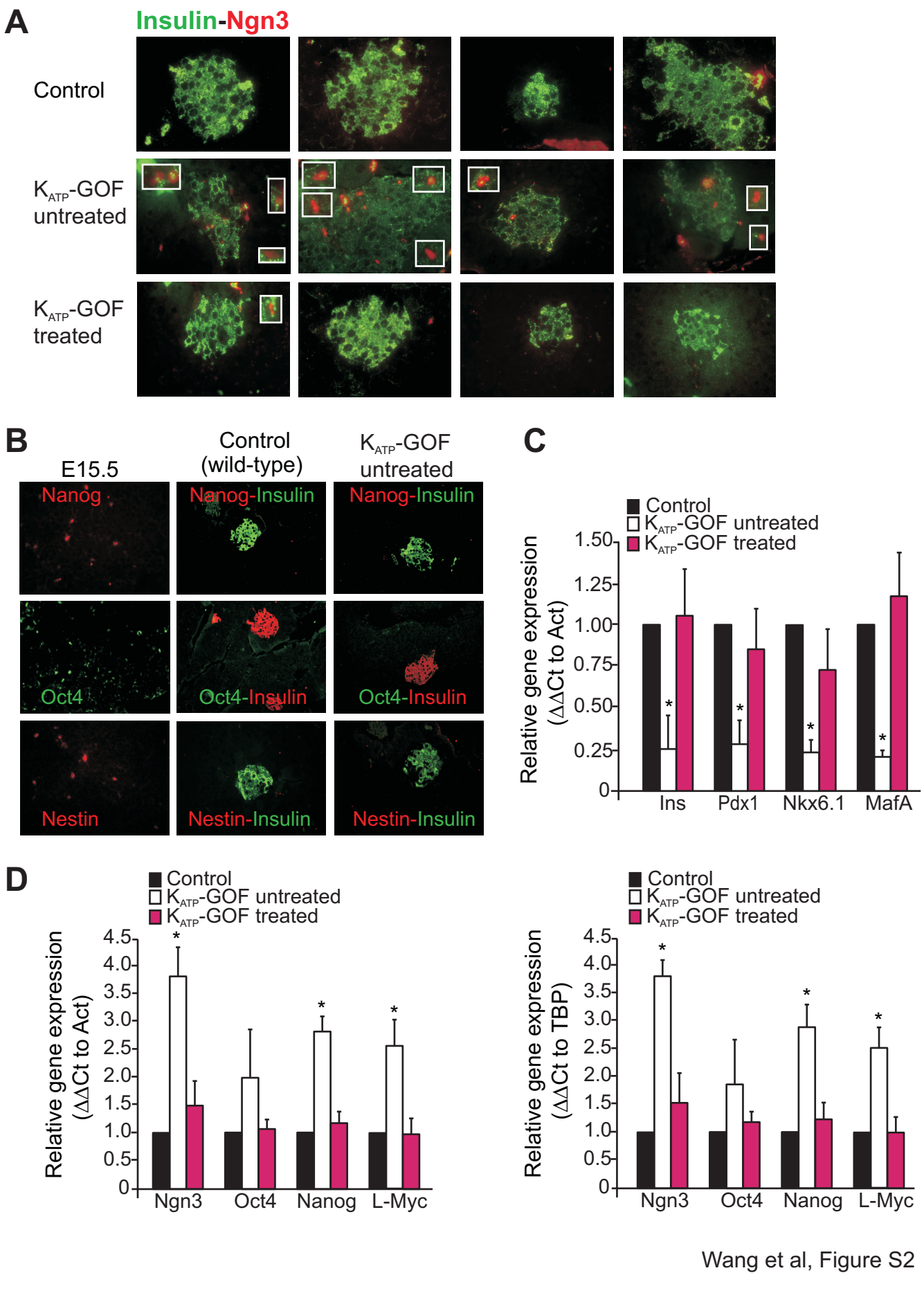

Insulin-Ki67-Dapi
Control
KATP-GOF untreated
KATP-GOF treated
Control
KATP-GOF untreated
KATP-GOF treated
% Ki67+ cells/
total islet area
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0



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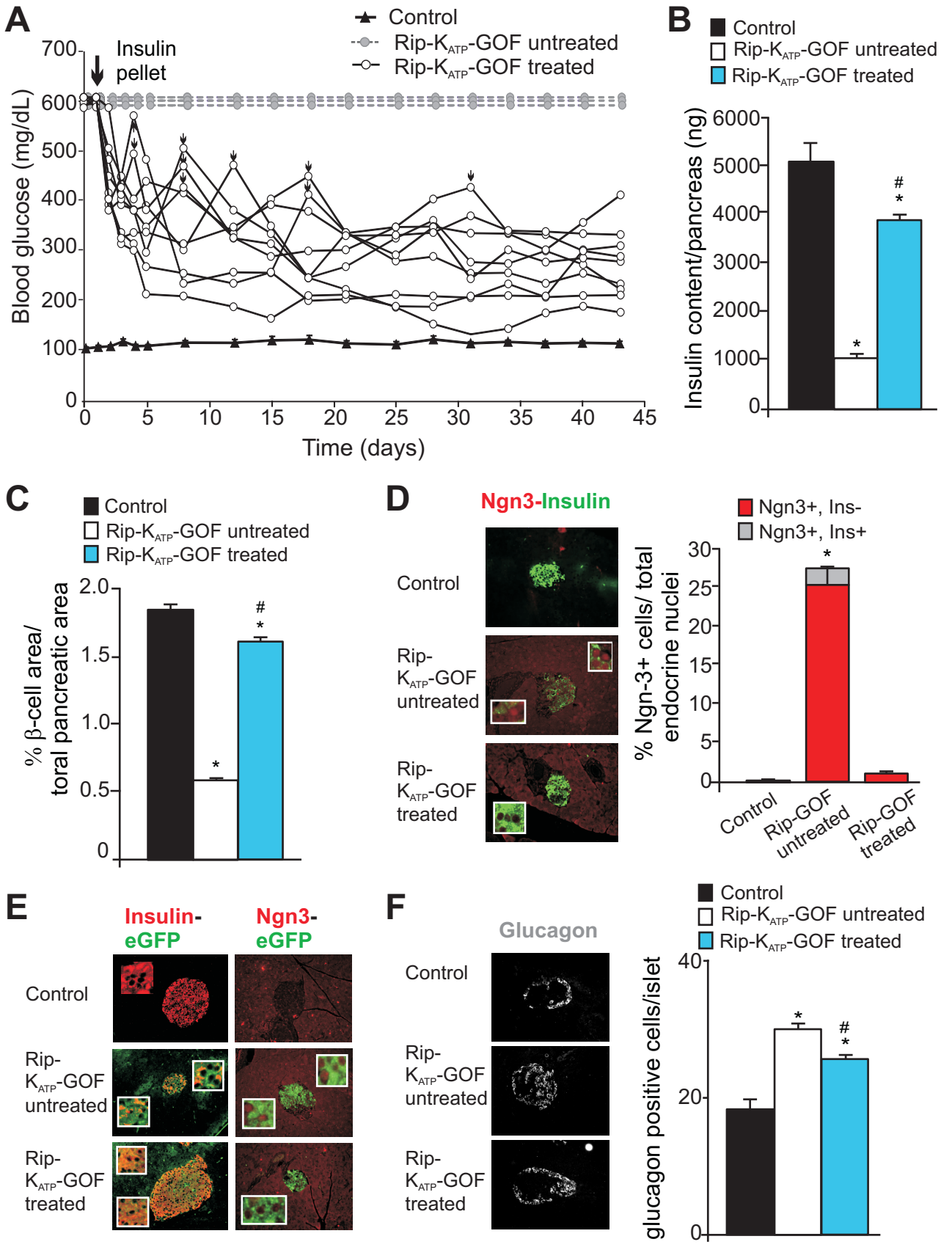

Wang et al, Figure S3

Supplemental information

Figure S1. Similar rate of proliferation in K_{ATP}-GOF untreated and insulin-treated mice, related to Figure 3. (left panels) Representative images of mouse pancreatic sections immunostained for insulin (green) and Ki67 (red), co-stained nuclei with Dapi; and (right panel) percentage of Ki67 positive cells per total islet area of control (black) and K_{ATP}-GOF untreated (white) and insulin-treated (pink) (mean ± SEM). Data represent n=5 mice per group, 5 pancreatic sections per mouse. While bordered insets show β-cell nuclei co-stained for both Ki67 and Dapi.

Figure S2. Increases in cell dedifferentiation markers and reduction of specific β-cell markers in diabetic islets, related to Figure 4. **(A)** Representative pancreatic sections from control and K_{ATP}-GOF untreated and insulin-treated mice double immunostained for insulin (green) and Ngn3 using BCBC antibody (red). **(B)** Representative images of mouse pancreatic sections from E15.5 fetal tissue, control (wild type), and untreated K_{ATP}-GOF mice immunostained for Nanog, Oct4, Nestin and insulin as indicated. **(C,D)** Real-time PCR mRNA levels on islets from control, and K_{ATP}-GOF diabetic and insulin-treated mice. Message levels are shown as relative values using β-actin (Act) as reference gene for β-cell markers **(C),** and β-actin (Act, left panel) and TATA Binding Protein (TBP, right panel) as reference genes for stem cell markers **(D).** Data represent mean ± SEM, n=4 mice per group, samples processed in triplicates. Significant differences *$p<0.05$ with respect to control.

Figure S3. Similar loss of insulin-contening cells and β-cell dedifferentiation is present in another mouse model of neonatal diabetes, related to Figures 2, 4, 5 and 7. **(A)** Fed blood glucose in control (average, black triangles) and in Rip-K_{ATP}-GOF untreated (individual traces grey circles, dashed line) and insulin-treated (individual

traces, white circles, solid line). Big arrow indicates first insulin pellet implantation, and small arrows a second insulin pellet implanted in individual mice as necessary (blood glucose >400mg/dl) (n= 3-9 mice per group). **(B,C)** Total insulin content per pancreas **(B)** and pancreatic β-cell mass **(C)** in control (black) and in Rip-K_{ATP}-GOF untreated (white) and insulin-treated (blue) mice. **(D)** (left panels) Representative pancreatic sections from control and Rip-K_{ATP}-GOF untreated and insulin-treated mice double immunostained for insulin (green) and Ngn3 (red) and (right panel) percentage of Ngn3 positive cells, either insulin negative (red) or insulin positive (grey). Data represent n=3-6 mice per group, 5 pancreatic sections per mouse, mean $\pm$ SEM *Significant differences $p<0.05$ with respect to control and K_{ATP}-GOF insulin treated mice. **(E)** Representative pancreatic sections from control and Rip-K_{ATP}-GOF untreated and insulin-treated mice double immunostained for e-GFP (indicating transgene expression in pancreatic β-cells, green) and insulin or Ngn3 (red) Data represent n=3-6 mice per group, 5 pancreatic sections per mouse**.** **(F)** (left panels) Representative pictures of glucagon immunostaining on pancreatic sections from control and untreated and insulin-treated Rip-K_{ATP}-GOF mice and (right panel) quantification of glucagon positive cells. N= 3-6 mice per group, 5 pancreatic sections per mouse, mean $\pm$ SEM Significant differences *$p<0.05$ with respect to control and $^{\#}p<0.05$ with respect to untreated Rip-K_{ATP}-GOF mice.