SUPPLEMENTARY FIGURE LEGENDS

Figure S1. Normoglycemia in islet-specific β-catenin knockout mice. (A) Glucose tolerance tests were performed on control and *Ctnnb1*$^{\Delta/lox}$*; Ngn3-Cre* (IsBKO) mice at 4 or 12 months of age (n=4-9 mice per genotype and timepoint, as indicated). **(B)** Net area-under-curve (AUC) calculations indicate no significant difference between control and ABKO at 4 or 12 months (*P*=0.57 and 0.30, respectively, by two-tailed, unpaired t-test).

Figure S2. Transient acinar-ductal metaplasia induced by caerulein. (A-B) Anti-CK19 immunohistochemistry reveals weak staining in terminal duct cells (arrowheads) of saline-treated mice. **(C-J)** Immunofluorescence indicates that EYFP$^+$ acinar cells do not stain for CK19 (white) in saline treated mice, regardless of genotype. Magnified areas depict EYFP$^+$/amylase$^+$ acinar clusters containing EYFP-negative /CK19$^+$ terminal duct/centroacinar cells. **(K-L)** At 2 days post-caerulein treatment, both control and ABKO pancreata exhibit widespread upregulation of CK19 (arrowheads). **(M-T)** CK19 is upregulated in EYFP$^+$/amylase$^+$ acinar cells, 2 days post-caerulein, regardless of genotype. **(U-V)** At 14 days post-caerulein, CK19 has been equivalently downregulated in control and ABKO pancreata, although expression remains slightly elevated in terminal duct cells (arrowheads). Abbreviations: is, islet; du, duct. Scale bars: 100μm.

Figure S3. Loss of β-catenin does not affect acinar cell differentiation status during metaplasia. Immunofluorescence for Pdx1 (red) and β-catenin (green) in control **(A-C)** and ABKO **(D-F)** pancreata 2 days after caerulein treatment. Dotted lines indicate areas magnified in

smaller panels. Pdx1 expression is maintained in acinar cells that retain β-catenin expression (closed arrowheads) as well as those deleted for β-catenin (open arrowheads). Similarly, staining for Ptf1a (red) and β-catenin (green) in control **(G-I)** and ABKO **(J-L)** pancreata, 2 days post-caerulein, reveals no difference in Ptf1a expression between β-catenin^{+} and β-catenin-deficient acinar cells (closed and open arrowheads, respectively). Scale bar: 100μm.

Figure S4. Elevated serum amylase associated with caerulein-induced pancreatitis. Amylase enzymatic assays were performed on serum drawn 1 hour or 1 day after the final injection of saline or caerulein (values represent the fold change for each genotype and treatment group, normalized to samples drawn before injections began). Regardless of genotype, caerulein-treated mice exhibit significantly increased serum amylase immediately post-injection, with levels returning to baseline one day later (n=3-7 mice per genotype and treatment group).

Figure S5. Persistence of β-catenin-deficient acinar cells after caerulein-induced pancreatitis. Immunofluorescence staining for amylase (red), EYFP (green) and β-catenin (white) in control **(A-C)** and ABKO **(D-F)** pancreata, 14 days after caerulein treatment. Dotted lines indicate areas magnified in smaller panels. EYFP^{+} cells co-express β-catenin in control but not ABKO pancreata (closed and open arrowheads, respectively), but retain amylase expression regardless of genotype. Scale bar: 100 μm.

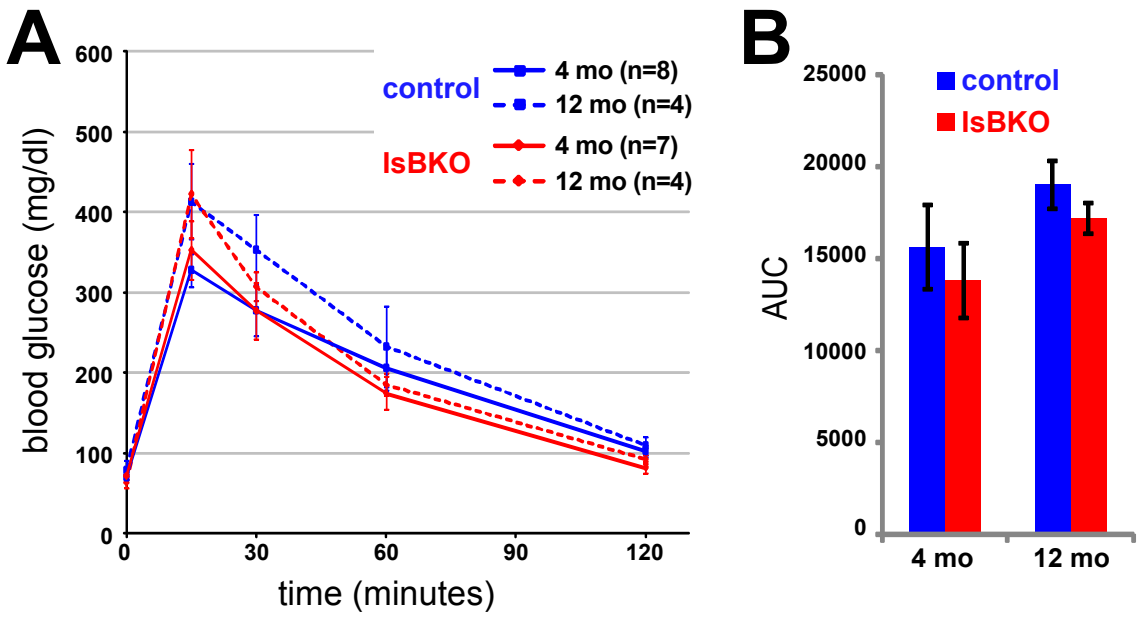
A
600
500
400
300
200
100
0
blood glucose (mg/dl)
0
30
60
90
120
time (minutes)
control
4 mo (n=8)
12 mo (n=4)
lsBKO
4 mo (n=7)
12 mo (n=4)
B
25000
20000
15000
10000
5000
0
AUC
control
lsBKO
4 mo
12 mo

Figure S1

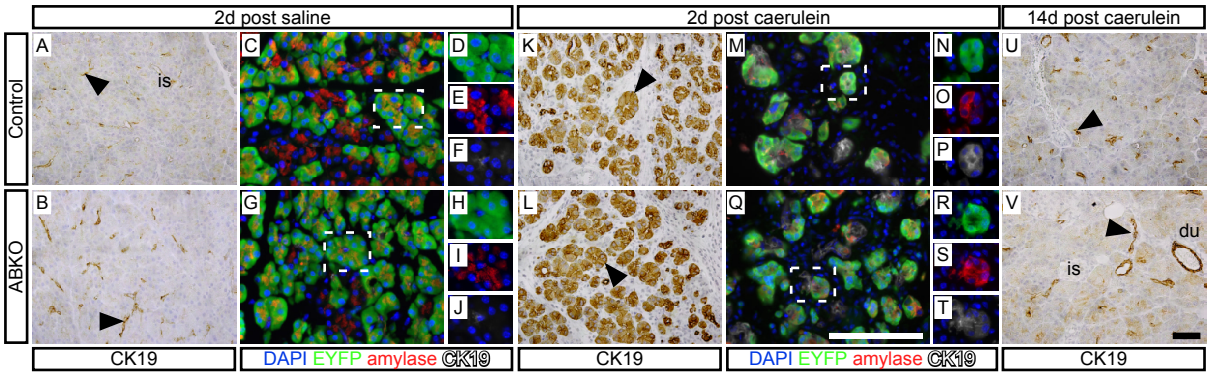
2d post saline
2d post caerulein
14d post caerulein
Control
ABKO
A
B
C
D
E
F
G
H
I
J
K
L
M
N
O
P
Q
R
S
T
U
V
is
du
CK19
DAPI EYFP amylase CK19
CK19
DAPI EYFP amylase CK19
CK19

Figure S2

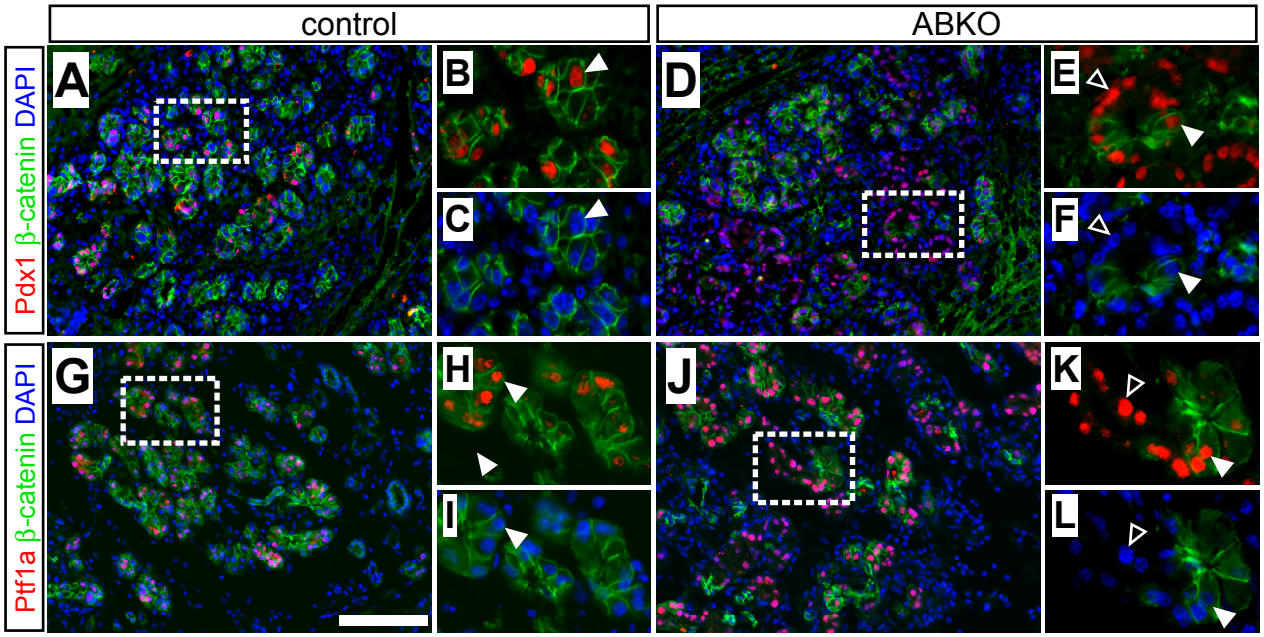
control
ABKO
Pdx1 β-catenin DAPI
Ptf1a β-catenin DAPI
A
B
C
D
E
F
G
H
I
J
K
L

Figure S3

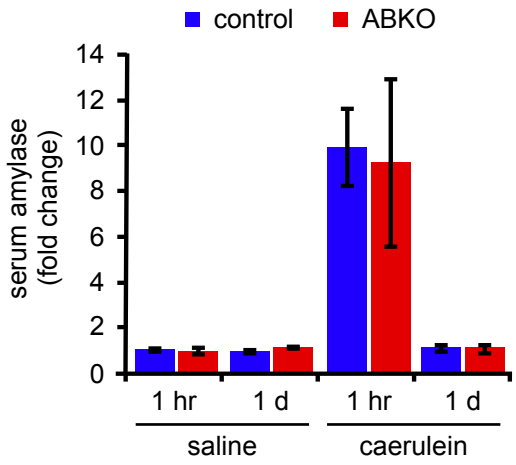
control
ABKO
serum amylase
(fold change)
14
12
10
8
6
4
2
0
1 hr
1 d
1 hr
1 d
saline
caerulein

Figure S4

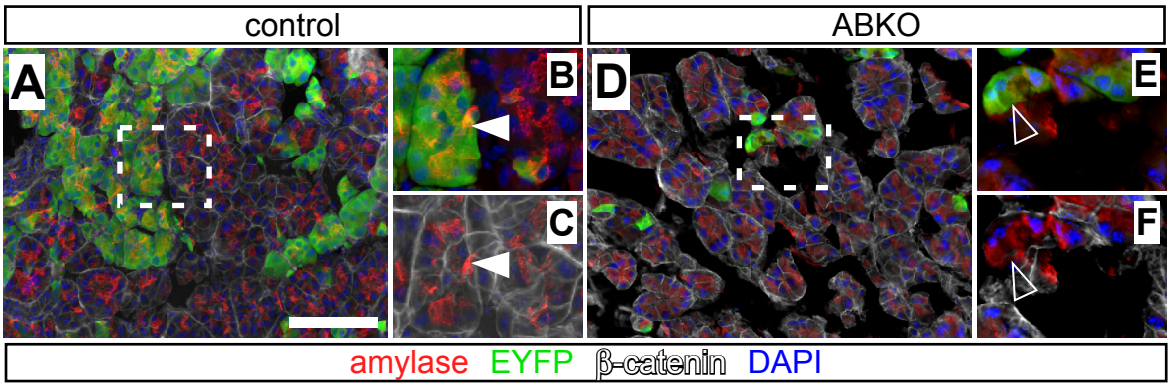

Figure S5