SUPPLEMENTARY LEGENDS

Supplementary Figure 1. Low magnification scans showing pancreas sections with immunohistochemical insulin staining. Each picture represents a whole section of 14-month-old shown genotypes. Insets are magnifications of dashed areas.

Supplementary Figure 2. Tracing of *Men1* invalidation in pancreatic *βMen1* tumors. Representative result of Insulin (green), ChromograninA (red) and Menin (gray) triple-immunofluorescent analysis of 1, 6, 14-months control and *βMen1* pancreas. Insets represent higher magnifications. Note that while all ChromograninA^{+}/Insulin^{+} cells have lost Menin expression in *βMen* pancreas, most of the Chormogranin^{+}/insulin^{-} cells demonstrate this loss. The residual Menin staining seen in ChromograninA^{+} cells (insets) correspond to the expression of Menin in non β-islet-cell lineages (*i.e.* Glucagon-, Somatostatin- and Pancreatic Polypeptide-expressing cells).

Supplementary Figure 3. Quantification of *Men1* invalidation in pancreatic islet lineages. Quantification of Menin disruption in α- and β-cells. Representative picture of triple-Immunofluorescent analysis performed on pancreas sections from 1-month-old *βMen1* and control mice. Right panels represent higher magnifications of dashed areas. Graph shows the percentage of α or β-cells, expressing Menin or not. 3 mice per genotype were analyzed. For control mice, 743 β-cells and 284 α-cells were counted and for *βMen1* mice, 3217 β-cells and 308 α-cells. Data are represented as mean of mice percentage ± SEM. ***: $p<0.001$; Student-t test.

Supplementary Figure 4. Validation of the ActivinB immunohistochemical staining obtained with 2 independent antibodies. Serial sections of 14-month-old mixed tumors and control pancreas were used to test the immunoreactivity of Abcam (ab56059) and Abnova (H00003625-D01P) commercial antibodies. Note the similar expression pattern seen for the tested antibodies in both control and tumor islet.

Supplementary Figure 5. Validation of ActivinB targeted disruption by immunohistochemistry within 14-months-old *InhβB-βMen1* tumors. Dashed lines delineate the islets location.

SUPPLEMENTAL MATERIALS AND METHODS

List of used Primary antibodies:

Antigen	Species	Source	Dilution		
			IHC	IF	WB
ActivinB	Rabbit	Abnova (H00003625-D01P)	1/2000	1/2000*	/
ActivinB	Rabbit	Abcam (ab56059)	1/2000	1/2000*	/
ChromograninA	Rabbit	Immunostar	1/2000	1/100	/
Glucagon	Rabbit	Cell Signaling	1/750	/	/
Glut2	Rabbit	Chemicon	/	1/200	/
Insulin	Guinea-Pig	Dako	1/5000	1/200	/
Ki67	Goat	Santa Cruz Biotech.	/	1/1000*	/
MafA	Rabbit	Abcam	/	1/4000*	1/1000
Ngn3	Goat	Beta Cell Biol. Consortium	/	1/10000*	/
Nkx2.2	Mouse	DHSB	/	/	1/1000
Nkx6.1	Mouse	DHSB	/	1/5000*	1/1000
Pax4	Rabbit	Dr B. Sosa-Pineda	/	1/30000*	1/5000
Pdx1	Goat	Abcam	/	1/500	1/10000
PP	Goat	Imgenex	1/500	/	/
Somatostatin	Goat	Santa Cruz Biotech.	1/5000	/	/
Sox9	Rabbit	Sigma Aldrich	/	1/500	/

* Combined with a Tyramide Signal Amplification (TSA system, Perkin-Elmer)

List of used secondary antibodies:

Antigen	Species	Source	Dilution
Biotinylated anti-rabbit IgG	Horse	Vector	1/200
Biotinylated anti-goat IgG	Horse	Vector	1/200
Biotinylated anti-mouse IgG	Goat	Vector	1/200
Biotinylated anti-guinea-pig IgG	Goat	Vector	1/200
Anti-Guinea Pig Alexa Fluor® 488	Donkey	Jackson Immunoresearch	1/200
Anti-Rabbit Alexa Fluor® 555	Donkey	Invitrogen	1/200

Primer used for real-time quantitative RT-PCR:

Primers	Forward	Reverse
Tbp	5'-TGG TGT GCA CAG GAG CCA AG-3'	5'-TTC ACA TCA CAG CTC CCC AC-3'
Ins1	5'-AGG ACC CAC AAG TGG AAC AAC-3'	5'-GTG CAG CAC TGA TCC ACA ATG-3'
Ins2	5'-GCT CTC TAC CTG GTG TGT GGG-3'	5'-CTC CAC CCA GCT CCA GTT GTG-3'
Mafa	5'-TCA GCA AGG AGG AGG TCA TCC GA-3'	5'-TGG CTC TGG AGC TGG CAC TTC T-3'
Mafb	5'-AGC AGG TGT GAC TCA CGA TG-3'	5'-AGA AGC GGT CCT CCA CAC TA-3'
Scl2a2	5'-TTT GGT GGG TGG CTC GGG GA-34	5'-GGG CGT GTG CCG GTC CAA AT-3'
Nkx6.1	5'-ACT TGG CAG GAC CAG AGA GA-3'	5'-AGA GTT CGG GTC CAG AGG TT-3'
Nkx2.2	5'-TTG TCA TTG TCC GGT GAC TC-3'	5'-TCT ACG ACA GCA GCG ACA AC-3'
Pdx1	5'-AGG TGC TTA CAC AGC GGA AC-3'	5'-GGG TCC CGC TAC TAC GTT TC-3'
Pax4	5'-TGG ACA CCC GAC AGC ACA T-3'	5'-CTT AAG GCT CCG TGA GAT GTC A-3'