Recapitulation of Pancreatic Neuroendocrine Tumors in Human Multiple Endocrine Neoplasia Type I (MEN1) Syndrome via Pdx1-directed Inactivation of Men1

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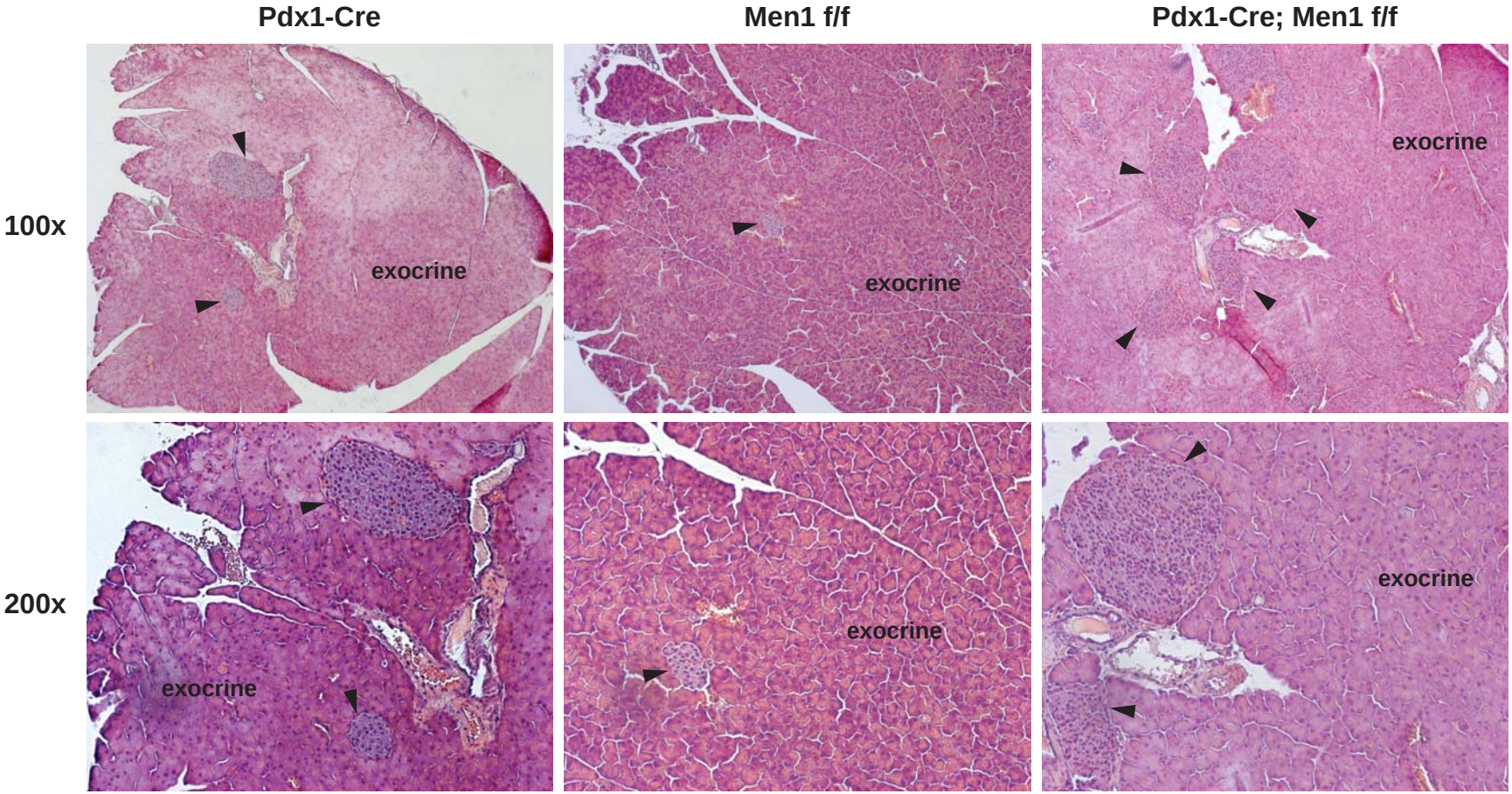
Supplementary Data

Supplementary Data A

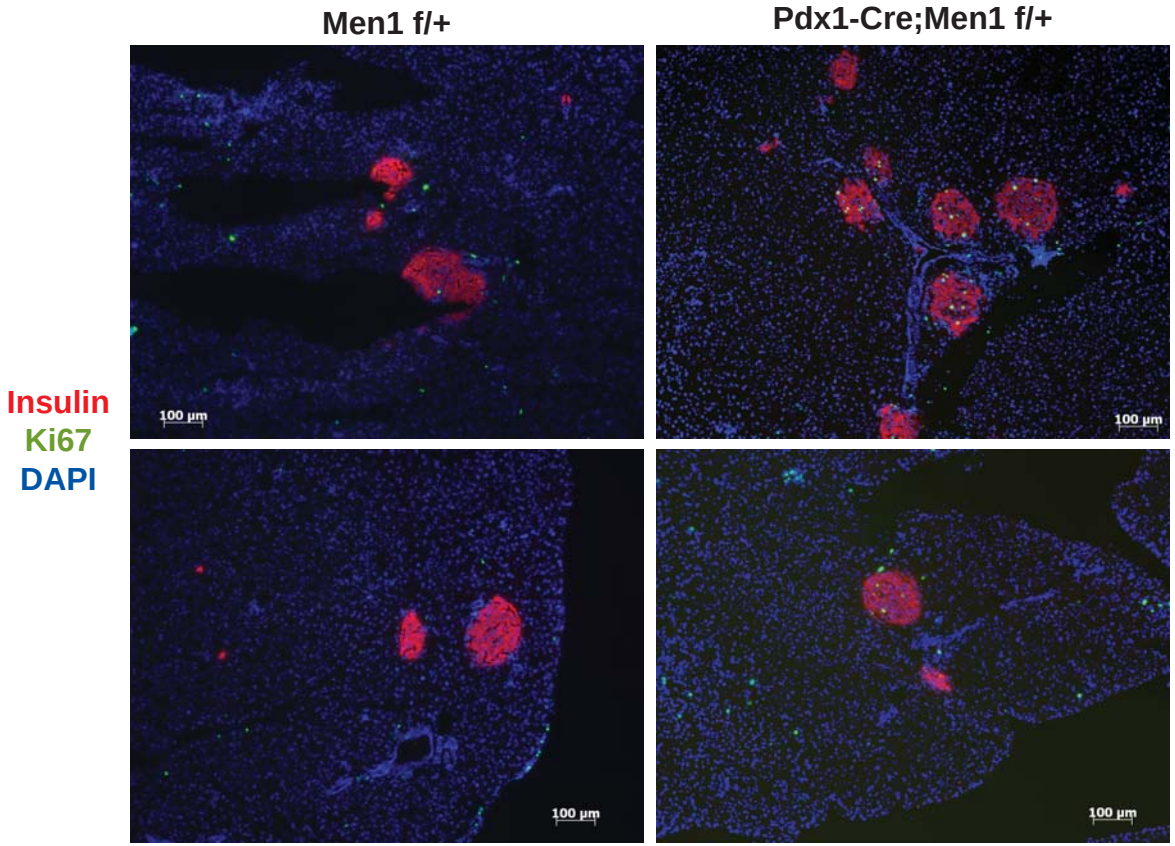
H&E staining of representative control Pdx1-Cre, Men1 f/f pancreas and mutant Pdx1-Cre;Men1 f/f pancreas at 2-3 months (mo) of age. Pancreatic exocrine tissues are as indicated, and islets in control and mutant animals are indicated by arrows. Images are shown at both 100x and 200x



Shen et al., Supplementary data A

Supplementary Data B

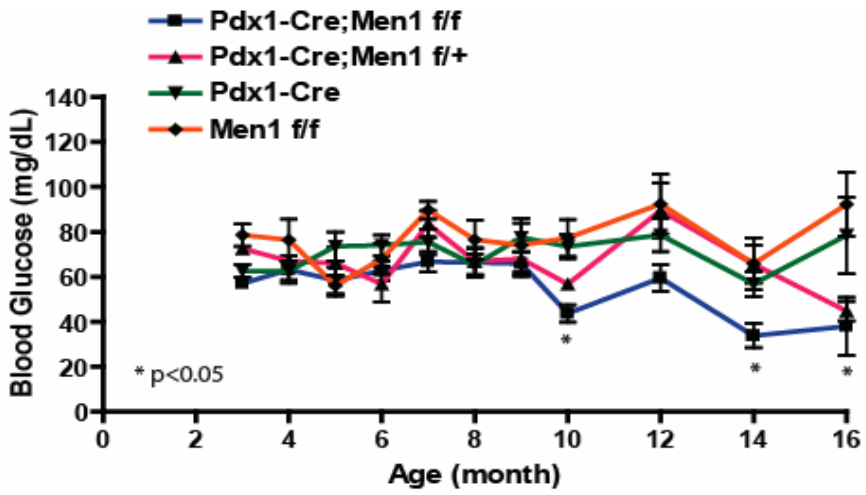
Immuno-fluorescent staining for cell nuclei (DAPI, blue), insulin (red) and Ki-67 (green) of representative control Men1 f/+ and mutant Pdx1-Cre;Men1 f/f islets of 2-3 month old mice. Two representative images for each genotype are shown at 100x.



Shen et al., Supplementary data B

Supplementary Data C

Fasted plasma glucose levels in mice of indicated genotype.



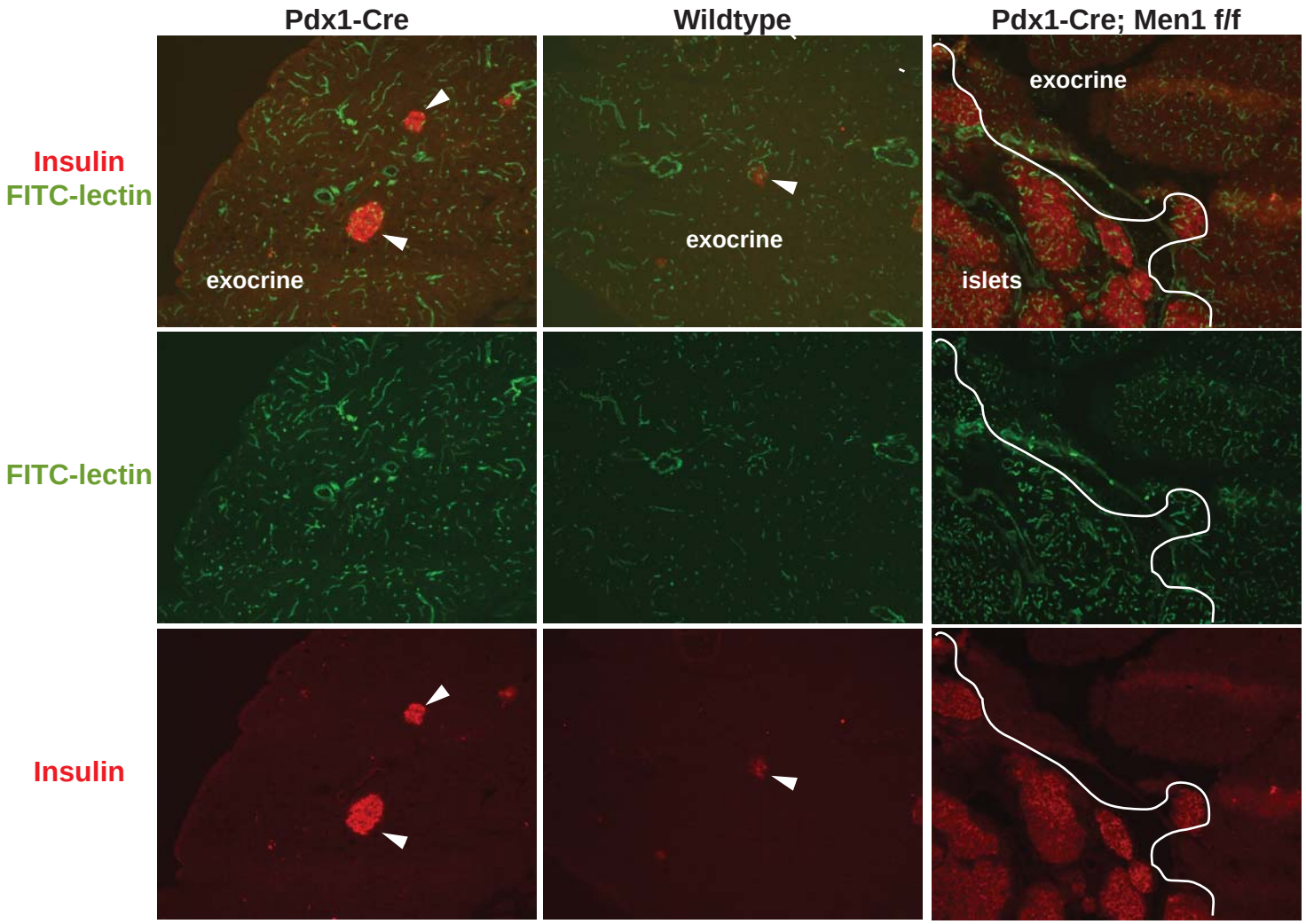
Number of animals represented in graph

Age (month)	3	4	5	6	7	8	9	10	12	14	16
Pdx1-Cre;Men1 f/f	9	9	11	10	13	11	9	6	9	6	4
Pdx1-Cre;Men1 f/+	8	10	7	5	8	7	6	4	8	5	5
Pdx1-Cre	9	10	9	9	10	9	9	5	9	6	5
Men1 f/f	5	6	8	7	8	7	5	3	6	6	5
Total	31	35	35	31	41	34	29	18	32	23	19
p-values	NS	NS	NS	NS	NS	NS	NS	0.0006	0.0832	0.0358	0.0306

NS: not significant by one-way ANOVA analysis

Supplementary Data D

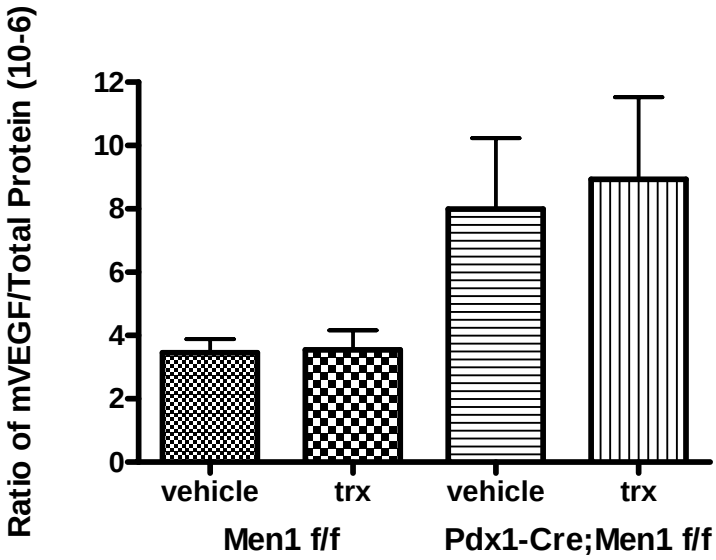
Representative immuno-fluorescent images of pancreatic exocrine tissues from control Pdx1-Cre, wildtype mice, and mutant Pdx1-Cre;Men1 f/f mice at 12 months of age. Blood vessels are visualized via FITC-lectin injection (green) while pancreatic islets are identified using an anti-insulin antibody (red, arrows). Pancreatic exocrine tissues are as indicated, and the extensive islet tumors in Pdx1-Cre;Men1 f/f are outlined in the far right panels.



Shen et al., Supplementary data D

Supplementary Data E

Pancreatic VEGF protein expression in vehicle or sunitinib treated (trx) animals of control Men1 f/f and mutant Pdx1-Cre;Men1 f/f genotypes. Each bar represents the average of multiple animals (n, as shown in supplementary data – Table 2) for each genotypes.



Supplementary Data - Tables

Table 1 - Genotype ratio from Pdx1-Cre;Men1 f/+ mice breeding with each other.

	Men1 +/+	**Men1 f/+**	**Men1 f/f**	
Mendelian %	25.0%	50.0%	25.0%	N
Pdx1-Cre	26.4%	52.7%	20.9%	110
Cre Negative	30.8%	44.2%	25.0%	52

Table 2 – Numbers (#) of animals utilized in sunitinib treatment study, and subsequent images of pancreas analyzed for these animals.

Mouse Genotype		**# of mice**	**# of images**
Men1 f/f	**vehicle**	4	14
	sunitinib	4	15
Pdx1-Cre;Men1 f/f	**vehicle**	6	35
	sunitinib	8	40