**Supplemental information**

**Supplemental Figure legends**

**Supplemental Table 1.**

Incidence of PanNETs formation.

**Supplemental Figure 1.**

A, Representative images of LacZ staining in the pancreas in *Pdx1-Cre;Rosa26R* mice. Scale bars: 100 μm. B, H&E staining and immunohistochemical staining for amylase and cytokeratin in *Pdx1-Cre* and *Pdx1-Cre;Rbf/f* mouse pancreas. Scale bars: 100 μm. C, Percentage of Ki67-positive acinar cells in *Pdx1-Cre* and *Pdx1-Cre;Rbf/f* mice at 2, 4, 6, and 8 months of age (N=3–4). D, Percentage of Ki67-positive duct cells in *Pdx1-Cre* and *Pdx1-Cre;Rbf/f* mice at 2, 4, 6, and 8 months of age (N=3–4). E, Body weight of *Pdx1-Cre* and *Pdx1-Cre;Rbf/f* mice at 1–8 months of age (N=10–21). F, Pancreas weight per body weight of *Pdx1-Cre* and *Pdx1-Cre;Rbf/f* mice at 2, 4, 6, and 8 months of age (N=4–5). G, Immunofluorescence staining for synaptophysin, somatostatin, and PP in *Pdx1-Cre* and *Pdx1-Cre;Rbf/f* islet cells at 4 months of age. Scale bars: 100 μm. H, δ-cells per islet cells in *Pdx1-Cre* and *Pdx1-Cre;Rbf/f* mice at 2, 4, 6, and 8 months of age (N=4). I, PP-cells per islet cells in *Pdx1-Cre* and *Pdx1-Cre;Rbf/f* mice at 2, 4, 6, and 8 months of age (N=4–6).

**Supplemental Figure 2.**

A, Experimental strategy for generation of *Pdx1-Cre;Trp53R172H* mice. Arrow indicates the direction of transcription, and arrowheads indicate *loxP* sites. B, H&E, immunohistochemical and immunofluorescence staining of islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H* mice at 2 months of age. Arrowheads indicate Ki67-positive cells. Scale bars: 100 μm. C, α-cell/β-cell ratio in islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H* mice at 2, 4, 6, and 8 months of age (N=3–5). D, Ki67-positive islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H* mice at 2, 4, 6, and 8 months of age (N=3–5). E, δ-cells per islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H* mice at 2, 4, 6, and 8 months of age (N=4). F, PP-cells per islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H* mice at 2, 4, 6, and 8 months of age (N=4–6). G, Blood glucose levels after 4 h fasting in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H* mice at 2, 4, 6, and 8 months of age (N=7–14). H, Body weight of *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H* mice at 1–8 months of age (N=6–17). I, Pancreas weight per body weight of *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H* mice at 2, 4, 6, and 8 months of age (N=3–4).

**Supplemental Figure 3.**

A,H&E, immunohistochemical and immunofluorescence staining of islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H;Rbf/f* mice at 2 months of age. Arrowheads indicate Ki67-positive cells. Scale bars: 100 μm. B, The α-cell/β-cell ratio in islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H;Rbf/f* mice at 2 and 4 months of age (N=3–5). C, Ki67-positive islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H;Rbf/f* mice at 2 and 4 months of age (N=3–5). D, H&E and immunohistochemical staining for Ki67 of islet cells in *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H;Rbf/f* mice at 2 months of age. Scale bars: 100 μm**.** E and F, Representative microscopic images of PanNETs in *Pdx1-Cre;Trp53R172H;Rbf/f* that have invasiveness to surrounding tissues. Scale bars: 100 μm. G**,** Body weight of *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H;Rbf/f* mice at 1–8 months of age (N=6–21). H, Pancreas weight per body weight of *Pdx1-Cre* and *Pdx1-Cre;Trp53R172H;Rbf/f* mice at 2, 4, 6, and 8 months of age (N=5–6).