

Fig. S1 Real-time RT-PCR analysis of hormone genes expression in E15.5 pancreas. Data are expressed as mean \pm SD; two-tailed unpaired Student's t-test was used to compare between control and null and between control and delSNAG mutants ; ns: $p > 0.05$, $*p < 0.05$, $***p < 0.001$. Animal number $n = 3$.

Fig.S2. Impaired differentiation of pancreatic endocrine cells in *Insm1^{delSNAG/delSNAG}* mice at E18.5. Immunofluorescence analysis of insulin (Ins) (A, A', A''), glucagon (Gcg) (B, B', B''), somatostatin (Sst) (C, C', C''), pancreatic polypeptide (Pp) (D, D', D'') and ghrelin (Ghrl) (E, E', E'') in *Insm1^{+/+}* (A, B, C, D, E), and *Insm1^{delSNAG/delSNAG}* (A', B', C', D', E') mice. The proportion of the indicated endocrine cell types are presented (A'', B'', C'', D'', E''). *Insm1* stained red and hormones stained green. Eight to twelve sections and 600–1300 endocrine cells were counted per hormone per mouse (animal numbers, $n = 5$). Data are expressed as mean \pm SD; two-tailed unpaired Student's t-test is used to examine the significance between control and delSNAG mutants; ns: $p > 0.05$, $**p < 0.01$, $***p < 0.001$.

Fig. S3. Impaired differentiation of pancreatic endocrine cells in *Insm1^{delSNAG/delSNAG}* mice at E15.5. Immunofluorescence analysis of insulin (Ins) (A, A', A''), glucagon (Gcg) (B, B', B''), somatostatin (Sst) (C, C', C''), pancreatic polypeptide (Pp) (D, D', D'') and ghrelin (Ghrl) (E, E', E'') in *Insm1^{+/+}* (A, B, C, D, E), and *Insm1^{delSNAG/delSNAG}* (A', B', C', D', E') mice. The proportion of the indicated endocrine cell types are presented (A'', B'', C'', D'', E''). *Insm1* stained red and hormones stained green. Six to ten sections and 500–1100 endocrine cells were counted per hormone per mouse (animal numbers, $n = 5$). Data are expressed as mean \pm SD; two-tailed unpaired Student's t-test is used to examine the significance between control and delSNAG mutants; ns: $p > 0.05$, $*p < 0.05$, $***p < 0.001$.

Fig. S4. Analysis of proliferation of pancreatic delta cells. Ki67 (green), Sst (red) and DAPI (blue) staining of the pancreas of *Insm1^{+/-lacZ}*, *Insm1^{lacZ/lacZ}* and *Insm1^{delSNAG/lacZ}* mice at E18.5 (A) and E15.5 (B). Statistical analysis is shown in the right. Data are expressed as mean \pm SD; two-tailed unpaired Student's t-test are used to examine the significance between two groups, control vs null mutants and control vs delSNAG mutants; ns: $p > 0.05$. $n = 4$, 300-500 Sst+ cells were counted for each animal.

Fig. S5. TUNEL staining and counting in β -gal+, Ins+ and Sst+ cells. A. Positive and negative controls of TUNEL staining. B. Insulin, TUNEL and β -gal staining in *Insm1^{+/-lacZ}*, *Insm1^{lacZ/lacZ}* and *Insm1^{delSNAG/lacZ}* mice. C. Somatostatin, TUNEL and β -gal staining in *Insm1^{+/-lacZ}*, *Insm1^{lacZ/lacZ}* and *Insm1^{delSNAG/lacZ}* mice. D. Counting results of the TUNEL+ cells in β -gal+, Ins+ and Sst+ cells.

Fig.S6. Co-staining of Sst with Ins and Gcg in *Insm1delSNAG*. Staining of Sst (red), Gcg (green) and DAPI (blue) in pancreas of E15.5 (A) and E18.5 (B) embryos. Staining of Sst (red), Ins (green) and DAPI (blue) in pancreas of E15.5 (C) and E18.5 (D) embryos. Cell counting was showed in the right. Data are expressed as mean \pm SD; two-tailed unpaired Student's t-test are used to examine the significance between two groups, delSNAG vs wt and delSNAG vs het; ns: $p > 0.05$. $n = 6$ (A, B, C), $n = 8$ (D), 1000-2000 Ins+ or 800-1500 Gcg+ cells were counted per animal. (E) Immunostaining of NKX6.1 with Ins, Gcg, Sst, Pp and Ghrl in pancreas of wildtype embryos at E18.5.

Fig.S7. Gene expression analysis using real-time RT-PCR in the islets treated with the Lsd1 inhibitor II, S2101 (Sigma, 489477). Data are expressed as mean \pm SD; two-tailed unpaired Student's t-test; ns: $p > 0.05$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Neonatal animal number $n = 6$ for each treatment.