Supplemental Table 1. Overview of Experimental Groups.

Genotype	Diet	Surgery	Number
1. GcgRA-VilCreERT2 mouse cohort: Various nutrient-stimulated GLP-1 study			
a. VilCreERT2	Chow	N/A	17
b. GcgRA$^{\Delta VilCreERT2}$	Chow	N/A	10
2. GcgRA-Pdx1Cre mouse cohort: Chow vs. HFD study			
a. Pdx1Cre	Chow	N/A	7
b. Pdx1Cre	HFD	N/A	6
c. GcgRA$^{\Delta Null}$	Chow	N/A	7
d. GcgRA$^{\Delta Null}$	HFD	N/A	5
e. GcgRA$^{\Delta Pdx1Cre}$	Chow	N/A	8
f. GcgRA$^{\Delta Pdx1Cre}$	HFD	N/A	11
3. GcgRA-VilCre mouse cohort: Chow vs. HFD study			
a. VilCre	Chow	N/A	7
b. VilCre	HFD	N/A	7
c. GcgRA$^{\Delta Null}$	Chow	N/A	6
d. GcgRA$^{\Delta Null}$	HFD	N/A	6
e. GcgRA$^{\Delta VilCre}$	Chow	N/A	7
f. GcgRA$^{\Delta VilCre}$	HFD	N/A	7
4. GcgRA-Pdx1Cre mouse cohort: Sham vs. VSG study			
a. Pdx1Cre	HFD	Sham	8
b. Pdx1Cre	HFD	VSG	8
c. GcgRA$^{\Delta Pdx1Cre}$	HFD	Sham	8
d. GcgRA$^{\Delta Pdx1Cre}$	HFD	VSG	9
5. GcgRA-VilCre mouse cohort: Sham vs. VSG study			
a. VilCre	HFD	Sham	7
b. VilCre	HFD	VSG	9
c. GcgRA$^{\Delta Null}$	HFD	Sham	7
d. GcgRA$^{\Delta Null}$	HFD	VSG	7
e. GcgRA$^{\Delta VilCre}$	HFD	Sham	6
f. GcgRA$^{\Delta VilCre}$	HFD	VSG	6

All male mice; experiments starting age between 2 mon- 4 mon old.

Supplementary Figure 1. GcgRA mouse cohorts validation.

(A-H) Gcg gene expression from duodenum, jejunum, ileum, and hindbrain of Sham or VSG GcgRA-Pdx1Cre (A-D) and GcgRA-VilCre (E-H) mouse cohorts. Pdx1Cre: Sham (n=8), VSG (n=8); GcgRA$^{\Delta Pdx1Cre}$: Sham (n=8), VSG (n=9); VilCre: Sham (n=7), VSG (n=9); GcgRA$^{\Delta Null}$: Sham (n=7), VSG (n=7); GcgRA$^{\Delta VilCre}$: Sham (n=6), VSG (n=6). (I) Representative (of n=4/surgery/genotype) immunofluorescence images of pancreatic islets (bar = 100 μm). The transcription stop-cassette innervating in the *Gcg* gene expresses GFP. Glucagon is observed in GcgRA$^{\Delta Pdx1Cre}$ mice whereas GFP is not observed. GFP, but not glucagon, is observed in GcgRA$^{\Delta Null}$ and GcgRA$^{\Delta VilCre}$ mice.

Supplementary Figure 2. VSG-induced weight loss in GcgRA mouse cohorts.

BW change during the 10 weeks after sham or VSG surgery in Pdx1Cre (A), GcgRA$^{\Delta Pdx1Cre}$ (B), VilCre (C), GcgRA$^{\Delta Null}$ (D), GcgRA$^{\Delta VilCre}$ (E) mice. All data were obtained from cohorts 4 & 5 and are represented as Mean ± SEM. *P<0.05; **P<0.01 (surgery × time). Pdx1Cre: Sham (n=8), VSG (n=8); GcgRA$^{\Delta Pdx1Cre}$: Sham (n=8), VSG (n=9); VilCre: Sham (n=7), VSG (n=9); GcgRA$^{\Delta Null}$: Sham (n=7), VSG (n=7); GcgRA$^{\Delta VilCre}$: Sham (n=6), VSG (n=6).

A — Duodenum; Relative *Gcg* expression Normalized to *B2m*; Pdx1Cre, RA^ΔPdx1Cre; Sham, VSG

B — Jejunum; Relative *Gcg* expression Normalized to *B2m*; Pdx1Cre, RA^ΔPdx1Cre; Sham, VSG

C — Ileum; Relative *Gcg* expression Normalized to *B2m*; Pdx1Cre, RA^ΔPdx1Cre; Sham, VSG

D — Hindbrain; Relative *Gcg* expression Normalized to B2m; Pdx1Cre, RA^ΔPdx1Cre; Sham, VSG

E — Duodenum; Relative *Gcg* expression Normalized to *B2m*; VilCre, GcgRA^ΔNull, GcgRA^ΔVilCre; Sham, VSG

F — Jejunum; Relative *Gcg* expression Normalized to *B2m*; VilCre, GcgRA^ΔNull, GcgRA^ΔVilCre; Sham, VSG

G — Ileum; Relative *Gcg* expression Normalized to *B2m*; VilCre, GcgRA^ΔNull, GcgRA^ΔVilCre; Sham, VSG

H — Hindbrain; Relative *Gcg* expression Normalized to B2m; VilCre, GcgRA^ΔNull, GcgRA^ΔVilCre; Sham, VSG

I — Glucagon/GFP/DAPI; Sham, VSG; Pdx1Cre, GcgRA^ΔPdx1Cre, VilCre, GcgRA^ΔNull, GcgRA^ΔVilCre

A

Pdx1Cre-Sham
Pdx1Cre-VSG

BW Changes (%) vs Post-surgery days

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B

GcgRA$^{\Delta Pdx1Cre}$-Sham
GcgRA$^{\Delta Pdx1Cre}$-VSG

BW Changes (%) vs Post-surgery days

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C

VilCre-Sham
VilCre-VSG

BW Changes (%) vs Post-surgery days

*

D

GcgRA$^{\Delta Null}$-Sham
GcgRA$^{\Delta Null}$-VSG

BW changes (%) vs Post-surgery days

*

E

GcgRA$^{\Delta VilCre}$-Sham
GcgRA$^{\Delta VilCre}$-VSG

BW changes (%) vs Post-surgery days

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