

Supplementary Information for:

**Vertical sleeve gastrectomy lowers SGLT2/Slc5a2 expression in the mouse
kidney**

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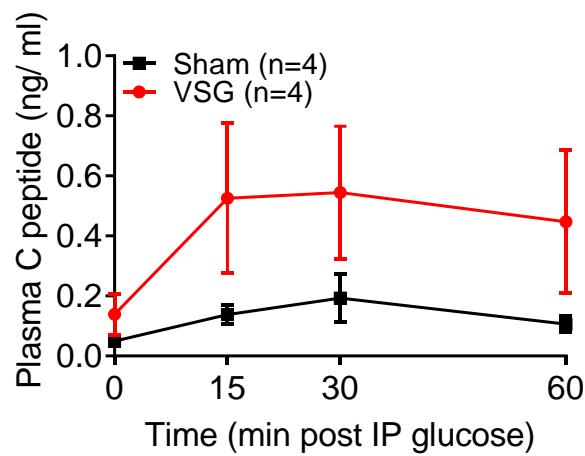
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This PDF includes:

Supplementary text

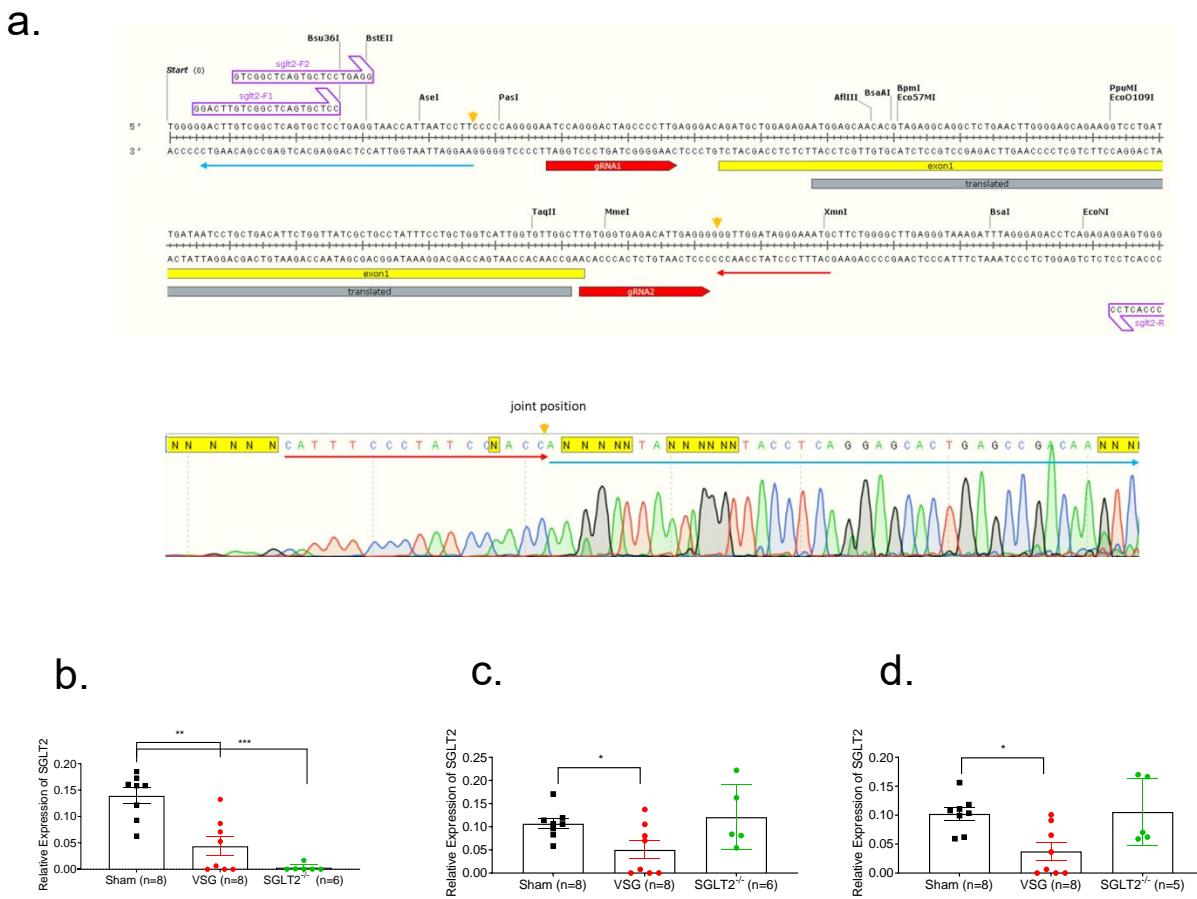
Supplementary Figures 1-6

Supplementary Figure 1



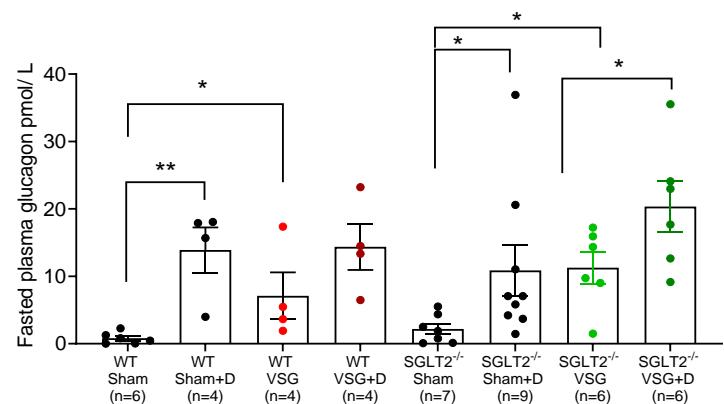
Supp Figure 1. Concentration of c peptide in lean mice following intraperitoneal glucose injection (3g/kg) (shown in Fig 1b). Data are expressed as means \pm SD.

Supplementary Figure 2



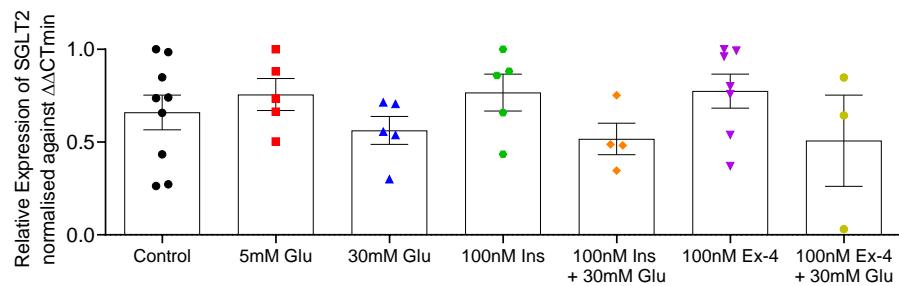
Supp Figure 2. a. Diagram of gene deletion via CRISPR/Cas9 technology. Two gRNAs flanking exon1 of Stlg2 gene were designed to delete entire exon1. b. Quantitative PCR levels of SGLT2 gene expression exon 1 in kidney cortex. *p<0.05, **p<0.01, by Student t-test. c. Quantitative PCR levels of SGLT2 gene expression exons 2-3 in kidney cortex. (black: WT, Sham, red: WT VSG, green: SGLT2^{-/-}) *p<0.05, by Student t-test d. Quantitative PCR levels of SGLT2 gene expression exons 4-5 in kidney cortex. *p<0.05, by two-sided unpaired Student t-test . Data are expressed as means \pm SEM. Abbreviations: VSG: Vertical Sleeve Gastrectomy, SGLT2: Sodium-glucose transporter 2

Supplementary Figure 3



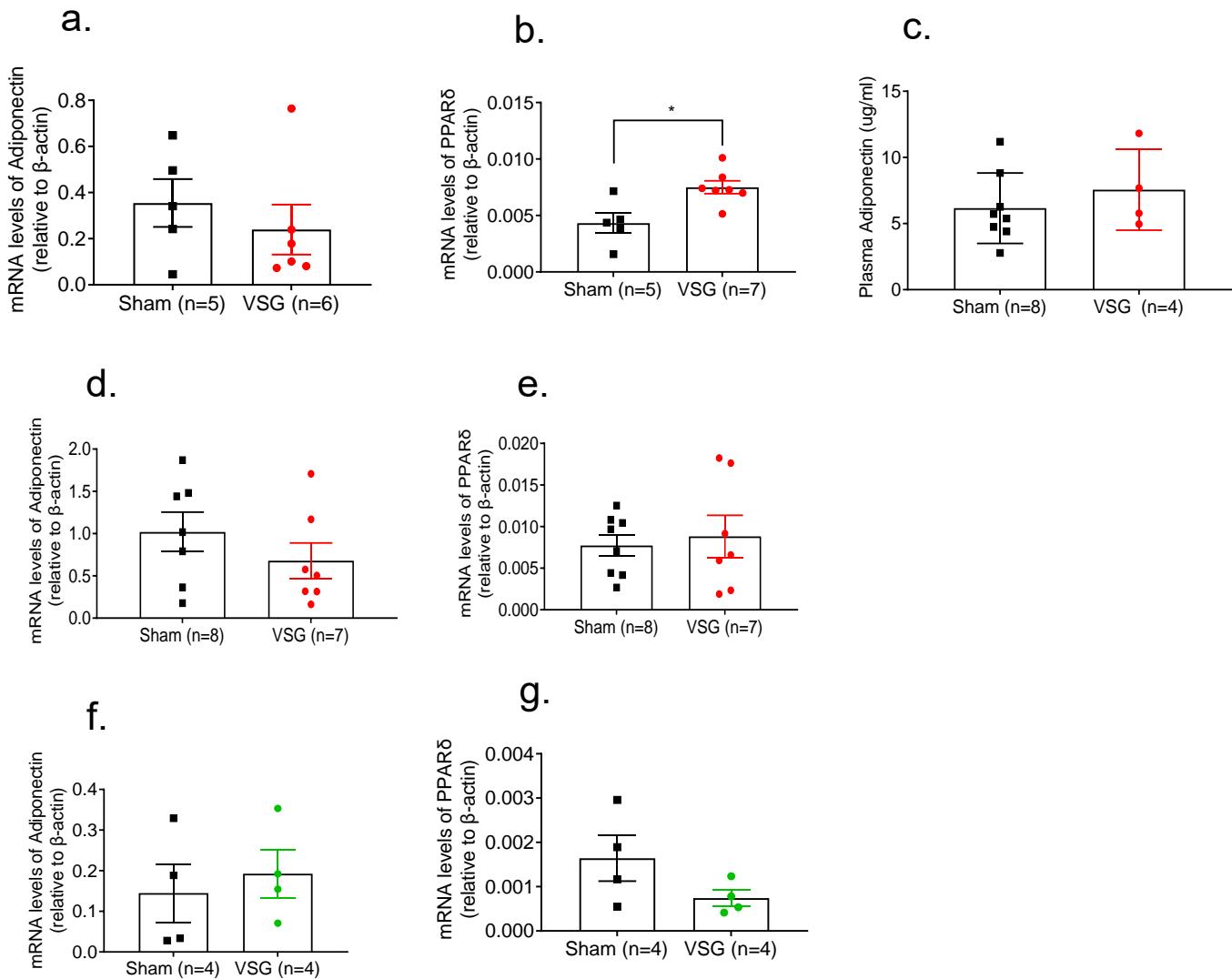
Supp Figure 3. Glucagon plasma levels in 16hr fasted mice following dapagliflozin or vehicle oral gavage (black: WT, SGLT2^{-/-} Sham, red: WT VSG, green: SGLT2^{-/-}). *p<0.05, **p<0.001 by two-sided unpaired Student's t-test. Abbreviations: VSG: Vertical Sleeve Gastrectomy, WT: wild-type, SGLT2: Sodium-glucose transporter 2, D: Dapagliflozin

Supplementary Figure 4



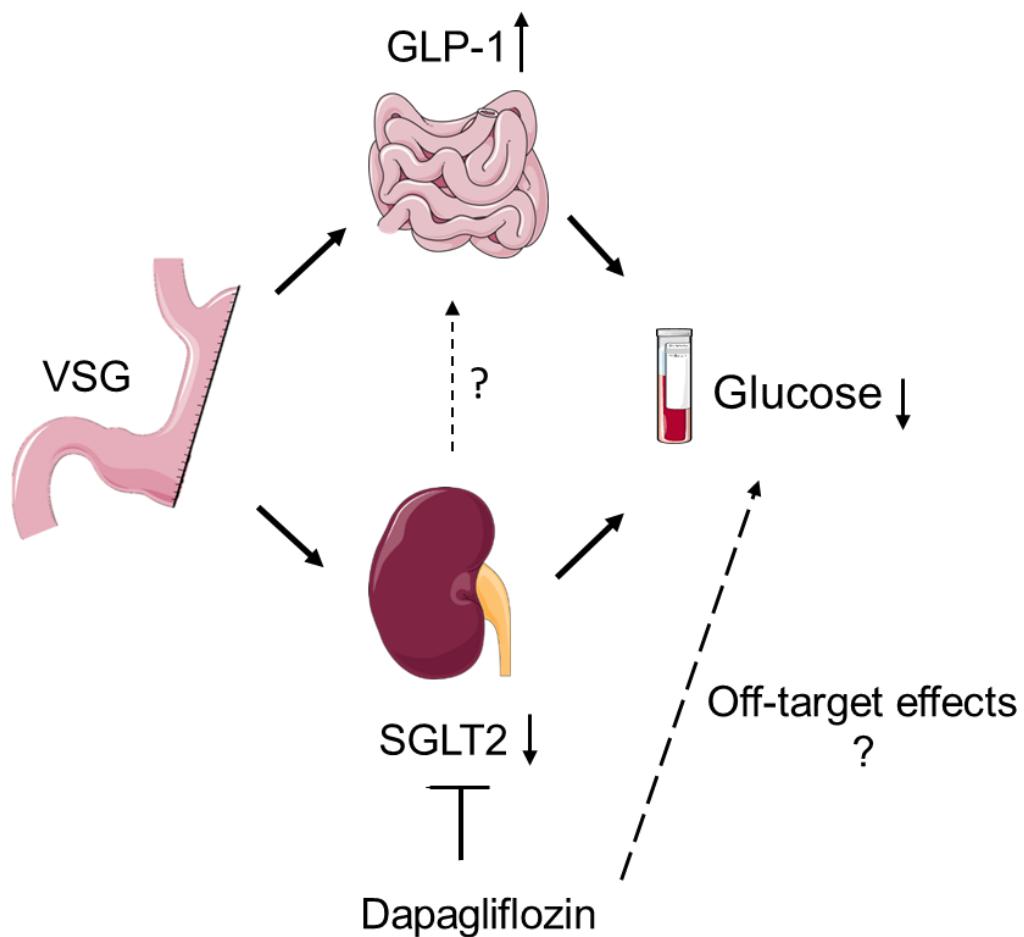
Supp Figure 4. HK-2 cells do not display SGLT2 inhibition following different glucose lowering treatments. Quantitative PCR levels of SGLT2 gene expression in HK-2 cells following 24hrs treatment with medium changed every 12 hours. Abbreviations: Glu: glucose, Ins: insulin, Ex-4: exendin-4

Supplementary Figure 5



Supp Figure 5 a. Quantitative PCR levels of PPAR δ gene expression in lean SC adipose tissue * $P<0.05$, by two-sided unpaired Student's t-test (red: VSG, black: sham) b. Quantitative PCR levels of adiponectin gene expression in lean SC adipose tissue c. Circulating adiponectin was measured in the plasma of 16hr fasted lean mice, 4 weeks post VSG d. Quantitative PCR levels of PPAR δ gene expression in HFD SC adipose tissue e. Quantitative PCR levels of adiponectin gene expression in HFD SC adipose tissue f. Quantitative PCR levels of PPAR δ gene expression in HFD SGLT2 $^{-/-}$ SC adipose tissue (green: SGLT2 $^{-/-}$ VSG, black: SGLT2 $^{-/-}$ sham) g. Quantitative PCR levels of adiponectin gene expression in HFD SGLT2 $^{-/-}$ SC adipose tissue . Data are expressed as means \pm SEM. Abbreviations: VSG: Vertical Sleeve Gastrectomy, PPAR δ : Peroxisome proliferator-activated receptor delta

Supplementary Figure 6



Supp Figure 6. Bariatric surgery effects both incretin production and SGLT2 expression in the kidney to influence blood glucose levels. We show that in addition to previously defined effects in incretins release, VSG lowers SGLT2 expression in the kidney to accelerate glucose excretion thus lowering glucose levels. We also show that the actions of the pharmacological SGLT2 inhibitor dapagliflozin are in part independent of actions of SGLT2. Abbreviations: VSG: Vertical Sleeve Gastrectomy. SGLT2: Sodium-glucose transporter 2