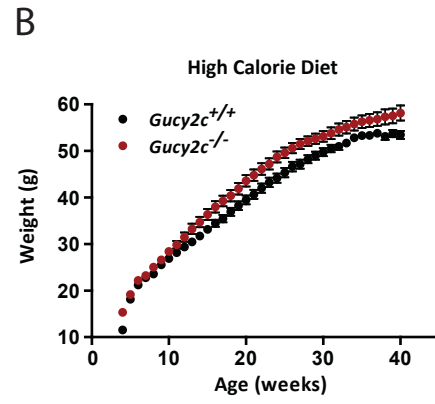
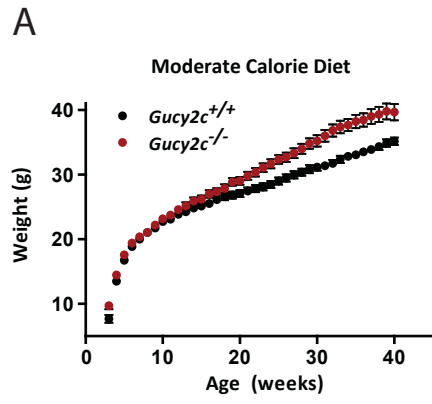
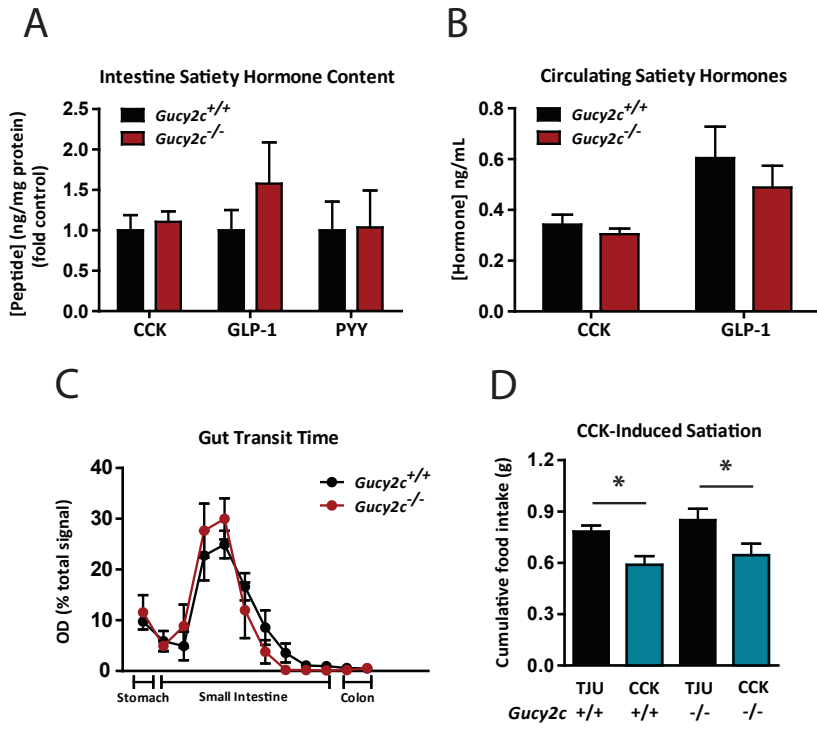


Supplemental Figure 1

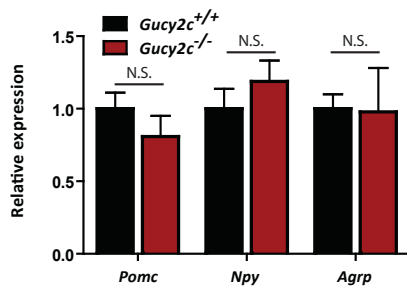


Supplemental Figure 2

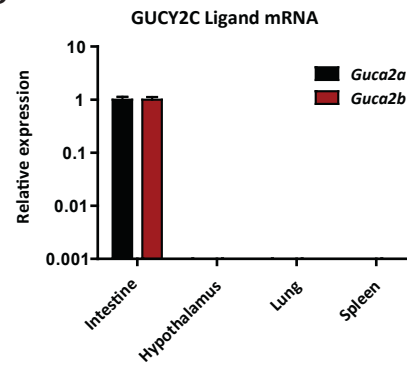


Supplemental Figure 3

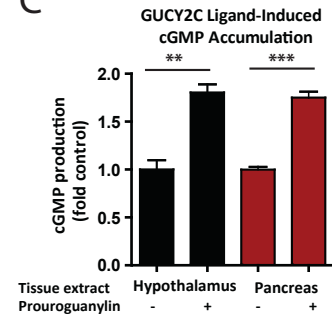
A



B



C



Supplemental Figure Legends

Supplemental Figure 1. (A-B) Growth curves of male *Gucy2c*^{+/+} and *Gucy2c*^{-/-} mice raised on MCD (n = 20-26) and HCD (n = 27-34) (p<0.001 for all diets). All data are mean ± SEM.

Supplemental Figure 2. (A) Protein content of the satiety peptides CCK (jejunum), GLP-1 (ileum), and PYY (ileum) (n = 4-10) in intestine. **(B)** Circulating levels of CCK and GLP-1 in *Gucy2c*^{+/+} and *Gucy2c*^{-/-} mice (n = 5-10). **(C)** Gut transit of fasted mice 10 min following oral gavage with FITC-dextran + lipid (1:1) (n = 4). **(D)** Cumulative food intake of fasted *Gucy2c*^{+/+} and *Gucy2c*^{-/-} mice injected IV with 1 µg of TJU or CCK (n = 10 per group). All data are mean ± SEM. * P<0.05.

Supplemental Figure 3. (A) Hypothalamic expression of appetite-regulating neuropeptides, normalized to β-actin (*Actb*) expression, in fasted *Gucy2c*^{+/+} and *Gucy2c*^{-/-} mice (n = 5 per group). **(B)** Expression of the GUCY2C ligands, guanylin (*Guca2a*) and uroguanylin (*Guca2b*), determined by qRT-PCR, normalized to *Actb* expression (n = 3). **(C)** cGMP production of CT26-GUCY2C cells treated with hypothalamic protein (350 µg), prouroguanylin (5 µg) + hypothalamic protein (350 µg), pancreatic protein (350 µg), or prouroguanylin (5 µg) + pancreatic protein (350 µg) (n = 4-10 per group). All data are mean ± SEM. N.S. = not significant (P>0.05). ** P<0.01, *** P<0.001.