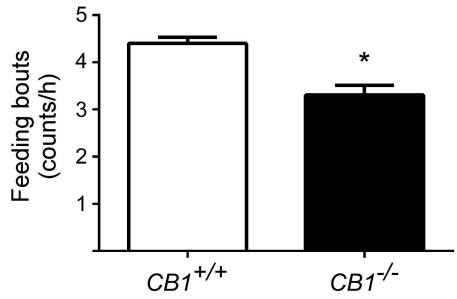

Figure S1. Food consumption of CB1$^{-/-}$ mice. CB1$^{+/+}$ (white bar) and CB1$^{-/-}$ (black bar) mice were placed in metabolic cages for 48 h. Feeding behaviors were recorded and analyzed as feeding bouts per hour in a total period of 24 h. Data are mean +/- SEM (n=5-7/group). *p < 0.05.

Supplemental Figure 1

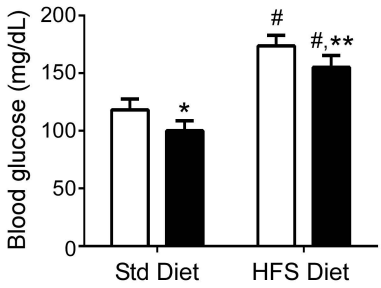

Figure S2. Fasting blood glucose in CB1$^{-/-}$ mice. CB1$^{+/+}$ (white bars) and CB1$^{-/-}$ (black bars) mice maintained on a standard diet (SD) or high fat/high sugar diet (HFS) were fasted overnight. Data are mean +/- SEM (n=5-7/group). *p < 0.05 and **p < 0.01 compared to CB1$^{+/+}$ mice; #p < 0.01 compared to SD.

Supplemental Figure 2

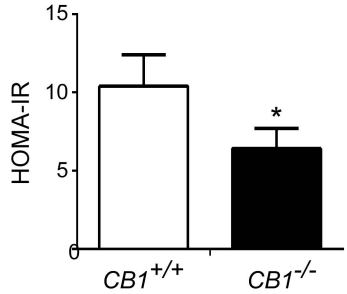

Figure S3. HOMA-IR in CB1$^{-/-}$ mice fed a high fat/high sugar diet. CB1$^{+/+}$ (white bar) and CB1$^{-/-}$ (black bar) mice maintained on a high fat/high sugar diet were fasted overnight and HOMA-IR calculated. Data are mean +/- SEM (n=5-7/group). *p < 0.05.

Supplemental Figure 3

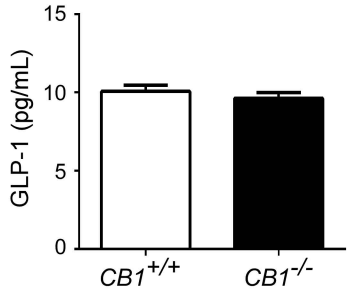

Figure S4. Fasting plasma GLP-1 levels after GLP-1 infusion are similar in WT and CB1KO. WT and CB1KO mice infused with 1.5 pmol/kg·h of GLP-1 for 36 h were fasted and plasma collected. Plasma levels of GLP-1 were measured by ELISA. Data are mean ± SEM, n=3.

Supplemental Figure 4

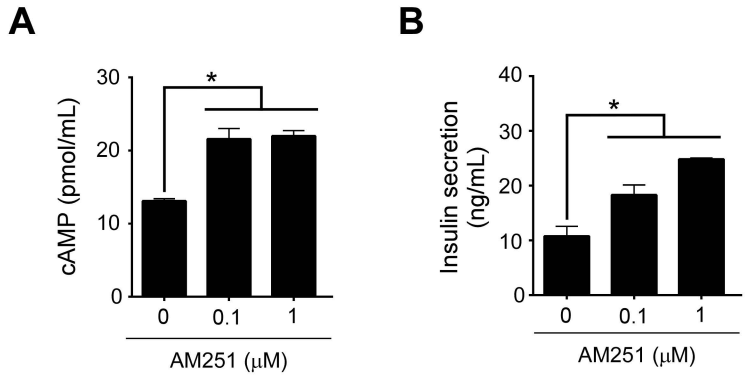

Figure S5. CB1 inverse agonists increase intracellular cAMP accumulation in ßTC6 cells. Relative intracellular cAMP concentrations (A) and insulin secretion (B) from ßTC6 cells treated with the inverse agonist AM251. All values were normalized to protein concentration. Data are mean ± SEM, n=3. *p < 0.05.

Supplemental Figure 5

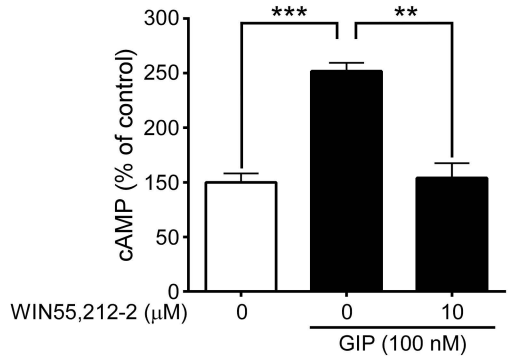

Figure S6. The CB1 specific agonist WIN55,212-2 modulates GIP-mediated intracellular cAMP accumulation in ßTC6 cells. Relative intracellular cAMP concentrations from ßTC6 cells treated with the synthetic cannabinoid WIN55,212-2 before subsequent addition of GIP (100 nM). All values were normalized to protein concentration and represented as percentage to unstimulated cells. Data are mean ± SEM, n=3. **p < 0.01; ***p < 0.001.

Supplemental Figure 6

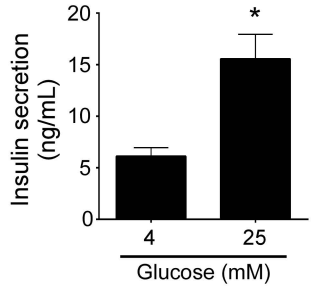

Figure S7. Basal and stimulatory insulin secretion from MIN6 cells. MIN6 cells were cultured with 4 mM of glucose or stimulated with 25 mM of glucose and media was analyzed for insulin. Data are mean +/- SEM (n=3). *p < 0.05.

Supplemental Figure 7

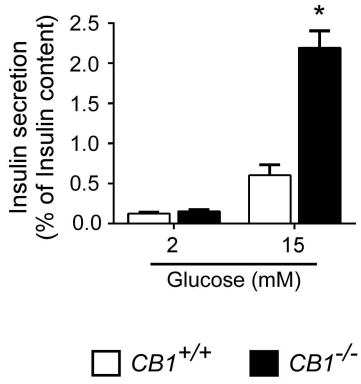

Figure S8. Insulin secretion from CB1$^{-/-}$ isolated islets. Islets isolated from CB1$^{+/+}$ (white bar) and CB1$^{-/-}$ (black bar) mice pre-cultured at 2 mM glucose were stimulated with 15 mM of glucose and media was analyzed for insulin. Data are mean +/- SEM (n=3). *p < 0.05.

Supplemental Figure 8