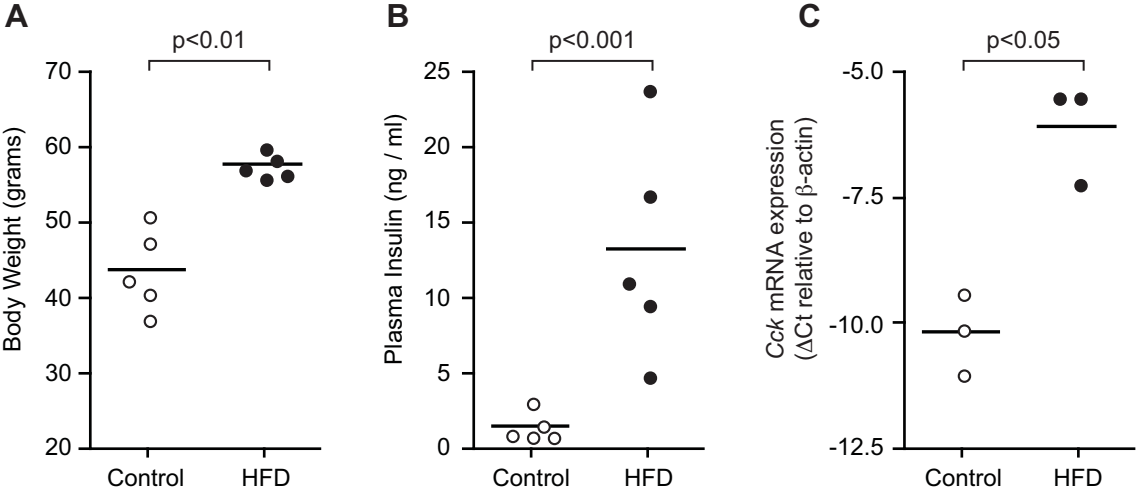
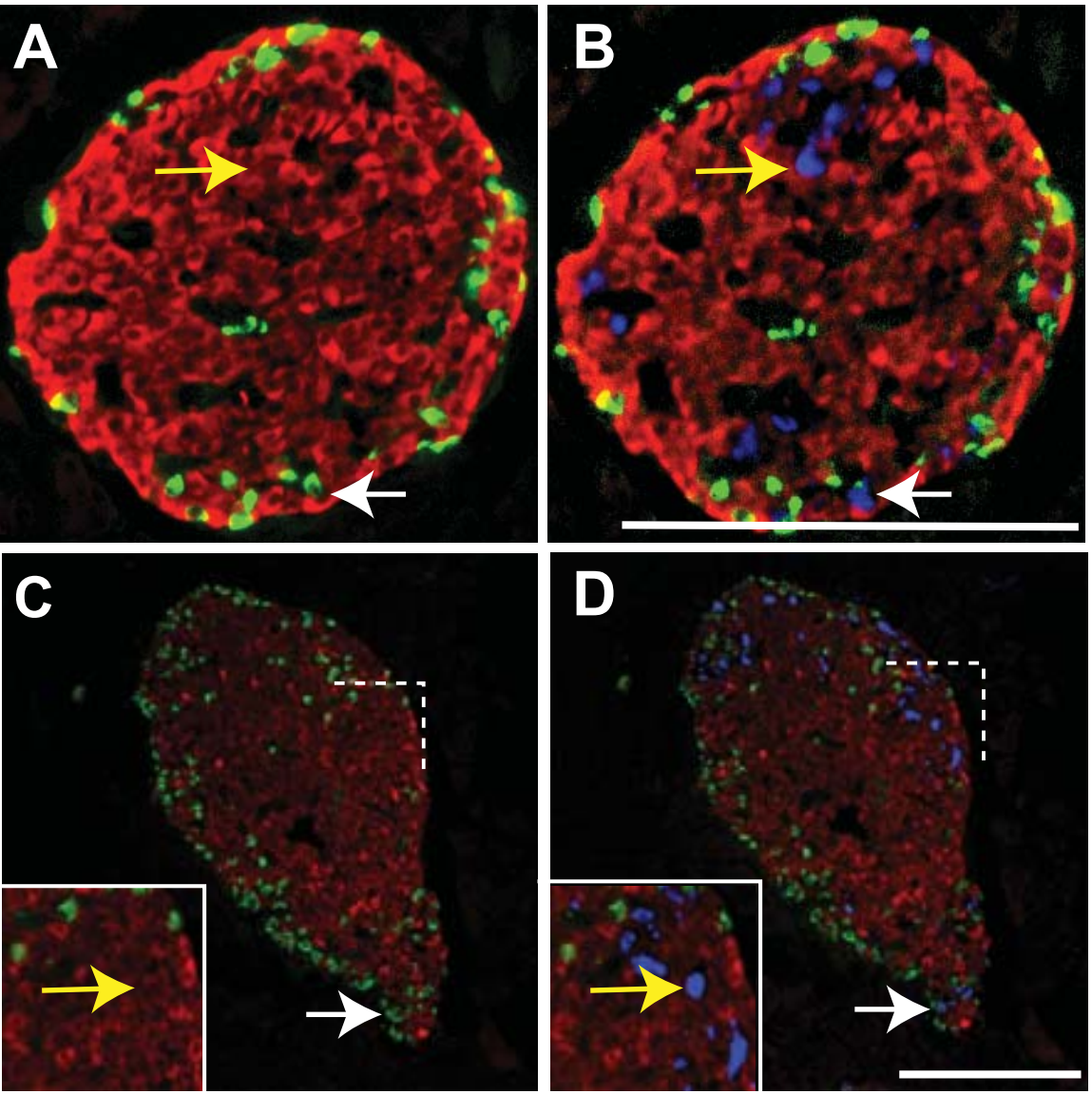
Supplementary Figure 1. High fat diet induced obesity increased islet *Cck* expression. BTBR mice were placed on 60% saturated fat (HFD) or semi-purified (control) diet for 33 weeks at the time of weaning. Body weight (A) and fasting plasma insulin (B) levels increased with diet-induced obesity (N=5). (C) *Cck* mRNA abundance was measured by quantitative RT-PCR with Taqman probes and normalized to β-actin levels (N=3). Plasma insulin levels were $\log_{10}$ transformed. All comparisons were made by Student's unpaired t-tests.

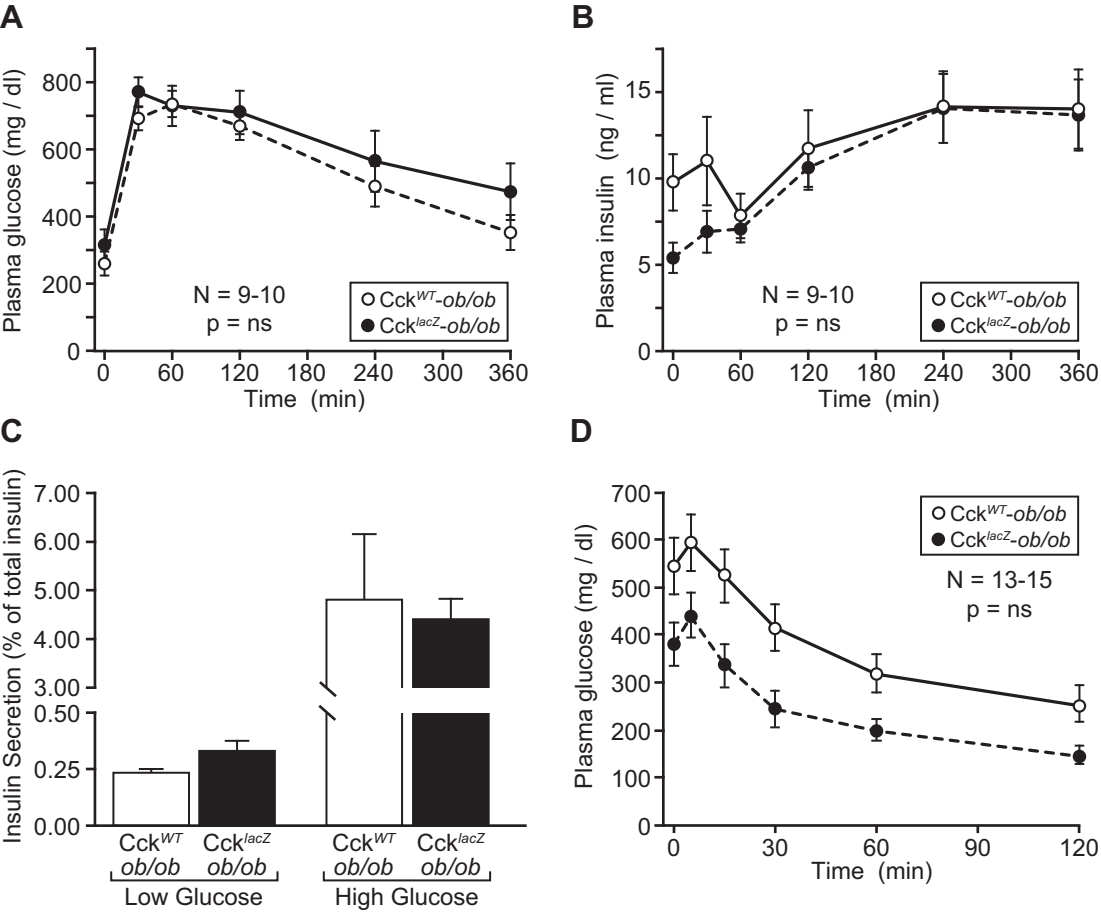
Supplementary Figure 2. CCK is expressed in α- and β-cells of obese mice. Immunofluorescence imaging of insulin (red) and glucagon (green) in a representative islet from two $Cck^{lacZ/+}$-*ob/ob* mice (A, C). X-gal staining (blue) was subsequently performed and imaged on identical sections and overlayed with immunofluorescence images (B, D). White arrows indicate X-gal positive α-cells and yellow arrows indicated X-gal positive β-cells.

Supplementary Figure 3. Loss of CCK does not affect glucose tolerance, insulin secretion, or insulin sensitivity. Glucose (A) and insulin (B) curves on overnight fasted 10 week old male Cck^{WT}-*ob/ob* (N=9) and Cck^{lacZ}-*ob/ob* mice (N=10) after IP-GTT. (C) Glucose-stimulated insulin secretion of statically incubated 14 week old female Cck^{WT}-*ob/ob* (N=4) and Cck^{lacZ}-*ob/ob* (N=5) islets. Comparisons were made by Student's unpaired t-test. (D) ITT on fed 14 week old male and female Cck^{WT}-*ob/ob* (N=15) and Cck^{lacZ}-*ob/ob* (N=13) mice. GTT and ITT data were analyzed using a mixed model approach. Sex, genotype, and starting values were used as covariate adjustments. ITT data was also analyzed by the trapezoidal area under the curve method. No significant differences were detected between genotypes using either method.


A
p<0.01
Body Weight (grams)
70
60
50
40
30
20
Control
HFD
B
p<0.001
Plasma Insulin (ng / ml)
25
20
15
10
5
0
Control
HFD
C
p<0.05
Cck mRNA expression
(ΔCt relative to β-actin)
-5.0
-7.5
-10.0
-12.5
Control
HFD

Supplementary Figure 2




A
Plasma glucose (mg / dl)
800
600
400
200
0
N = 9-10
p = ns
Cck^WT-ob/ob
Cck^lacZ-ob/ob
0
60
120
180
240
300
360
Time (min)
B
Plasma insulin (ng / ml)
15
10
5
0
N = 9-10
p = ns
Cck^WT-ob/ob
Cck^lacZ-ob/ob
0
60
120
180
240
300
360
Time (min)
C
Insulin Secretion (% of total insulin)
7.00
6.00
5.00
4.00
3.00
0.50
0.25
0.00
Cck^WT ob/ob
Cck^lacZ ob/ob
Cck^WT ob/ob
Cck^lacZ ob/ob
Low Glucose
High Glucose
D
Plasma glucose (mg / dl)
700
600
500
400
300
200
100
0
Cck^WT-ob/ob
Cck^lacZ-ob/ob
N = 13-15
p = ns
0
30
60
90
120
Time (min)