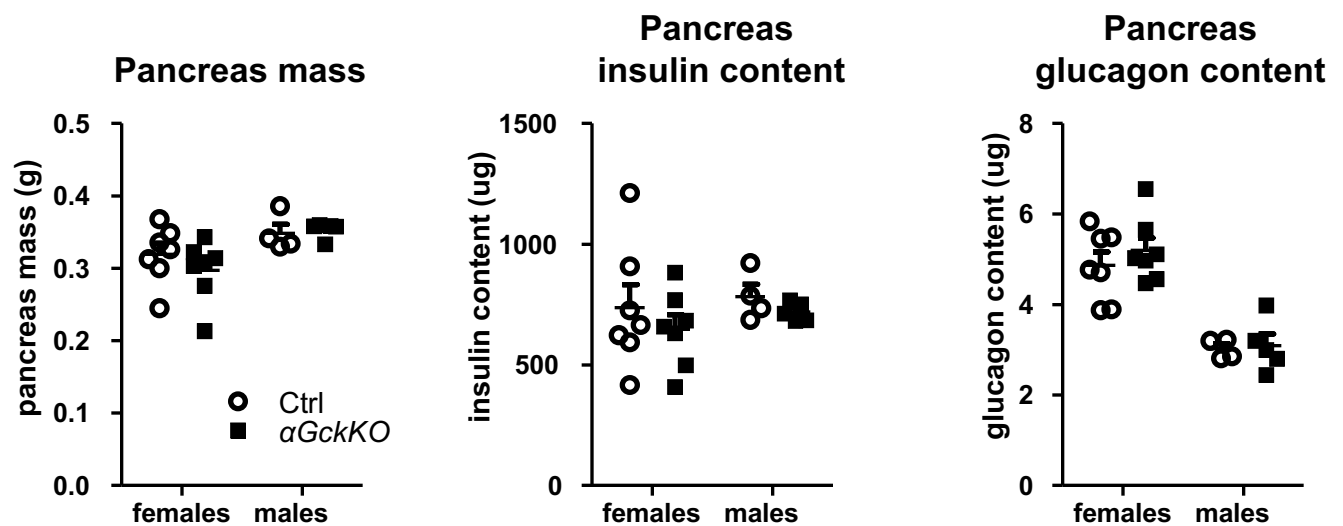
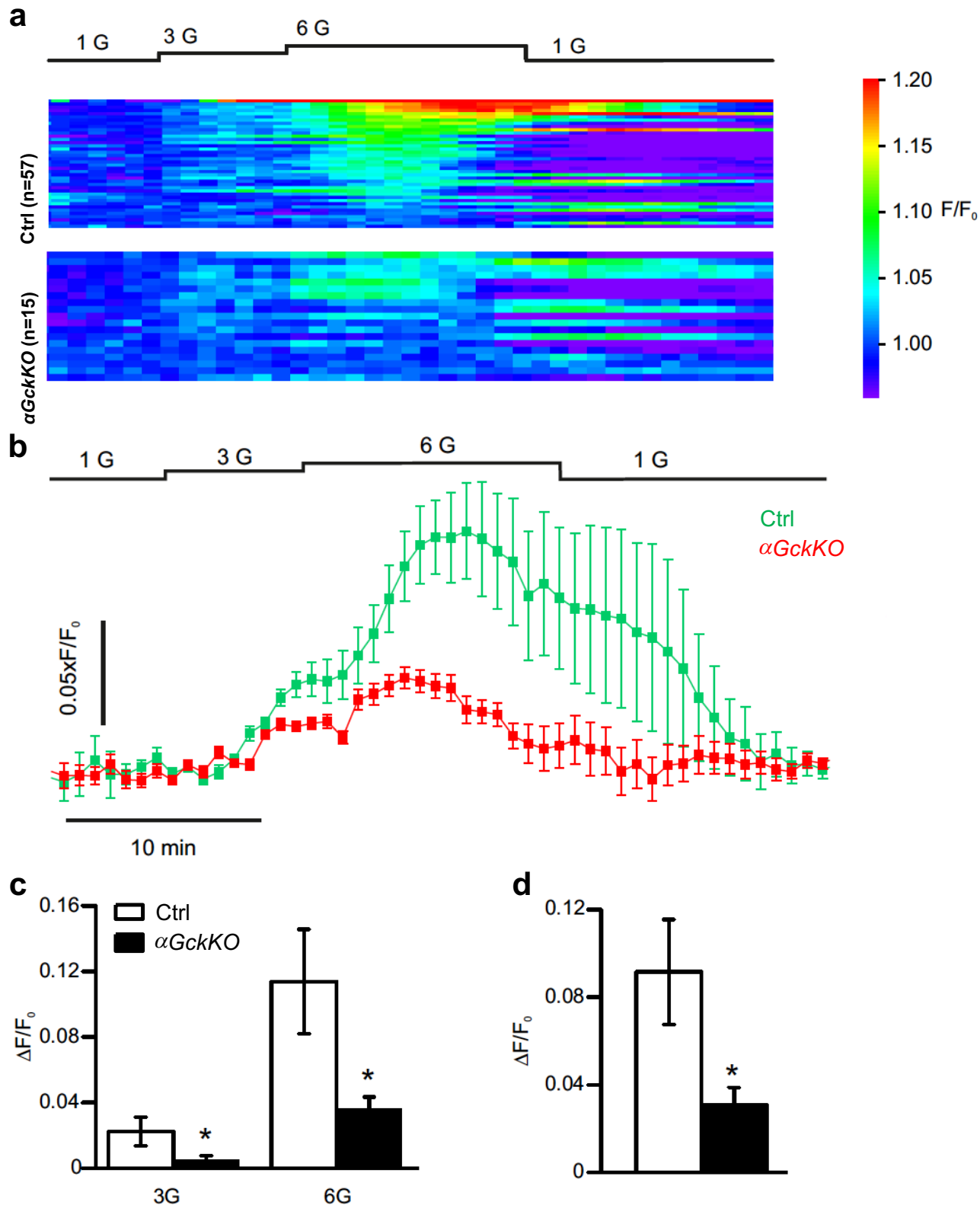
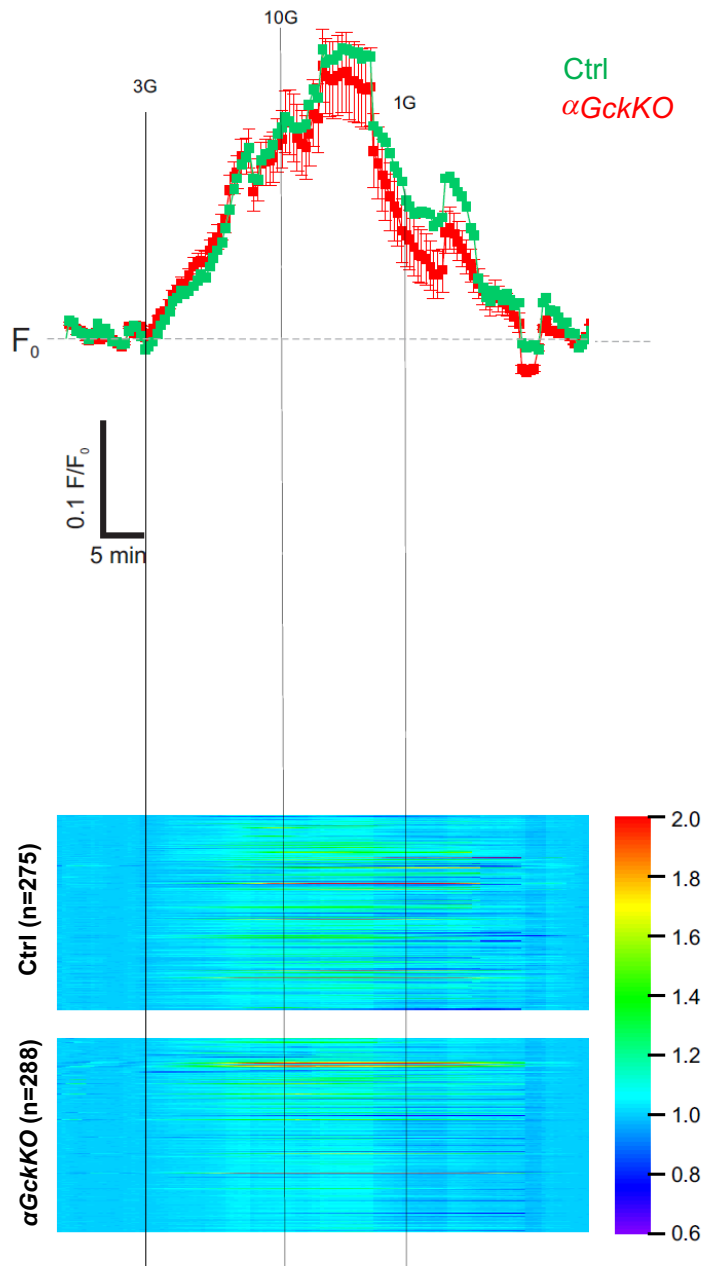




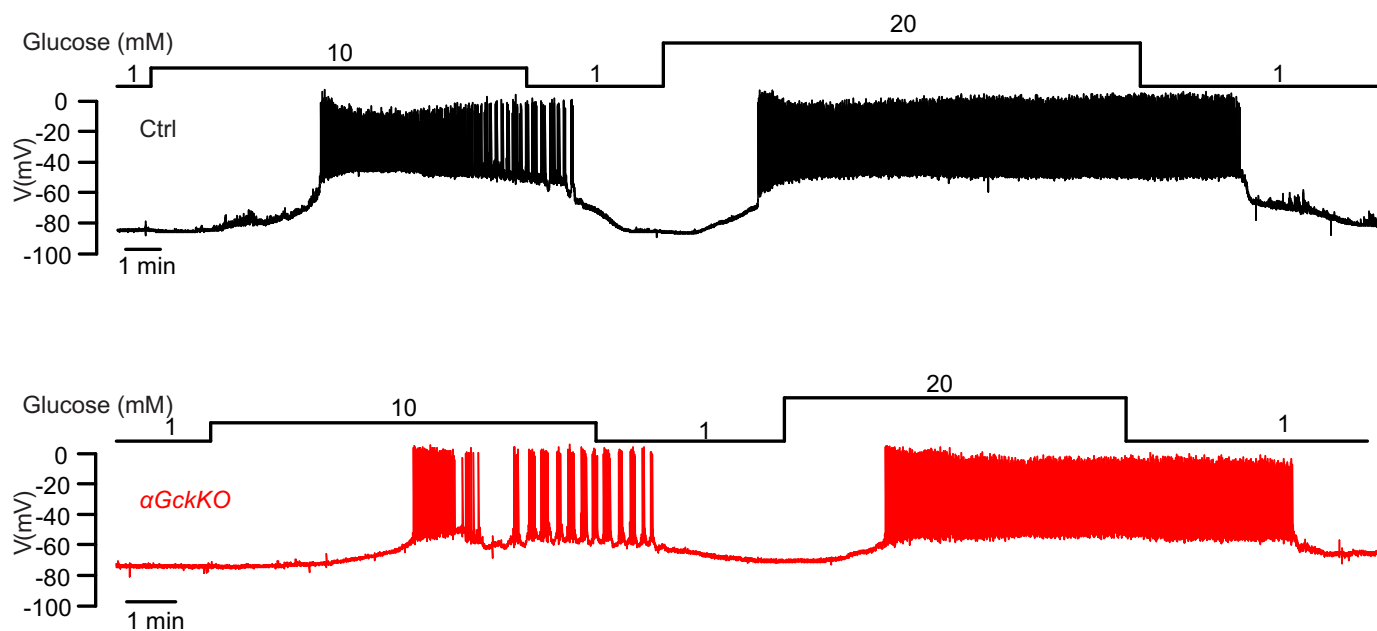
Supplementary Figure 1. Pancreas mass, pancreatic insulin and glucagon content in 18 week-old Ctrl and $\alpha GckKO$ male and female mice. (related to figure 1). N=5 males and n=7 females per genotype.



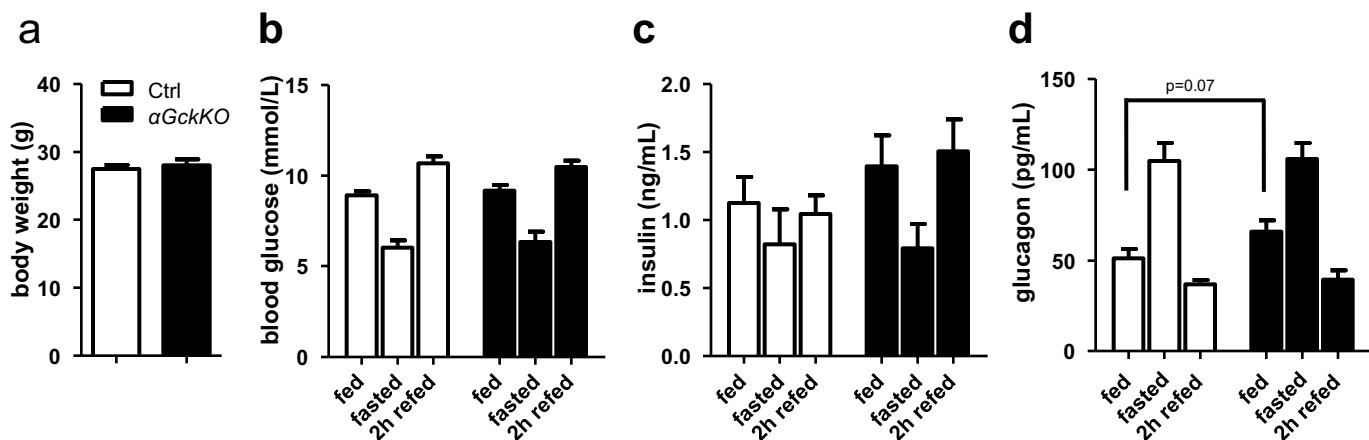
Supplementary figure 2. ATP/ADP ratio in α -cells from 18-20 week-old Ctrl and α GckKO female mice (related to figure 1). **a**) Heat map of Perceval fluorescence in α -cells in the presence of the indicated glucose concentrations (mM). n=57 for Ctrl and n=15 for α GckKO. **b**) Summary of Perceval fluorescence changes in Ctrl and α GckKO α -cells. n=57 for Ctrl and n=15 for α GckKO. **c**) Perceval fluorescence in Ctrl and α GckKO α -cells when glucose was elevated from 1 mM to 3 or 6 mM. * $p < 0.05$; Student t -test. **d**) Perceval fluorescence in Ctrl and α GckKO α -cells when glucose was elevated from 3 to 6 mM. * $p < 0.05$; Student t -test. Data are represented as mean $\pm$ s.e.m.



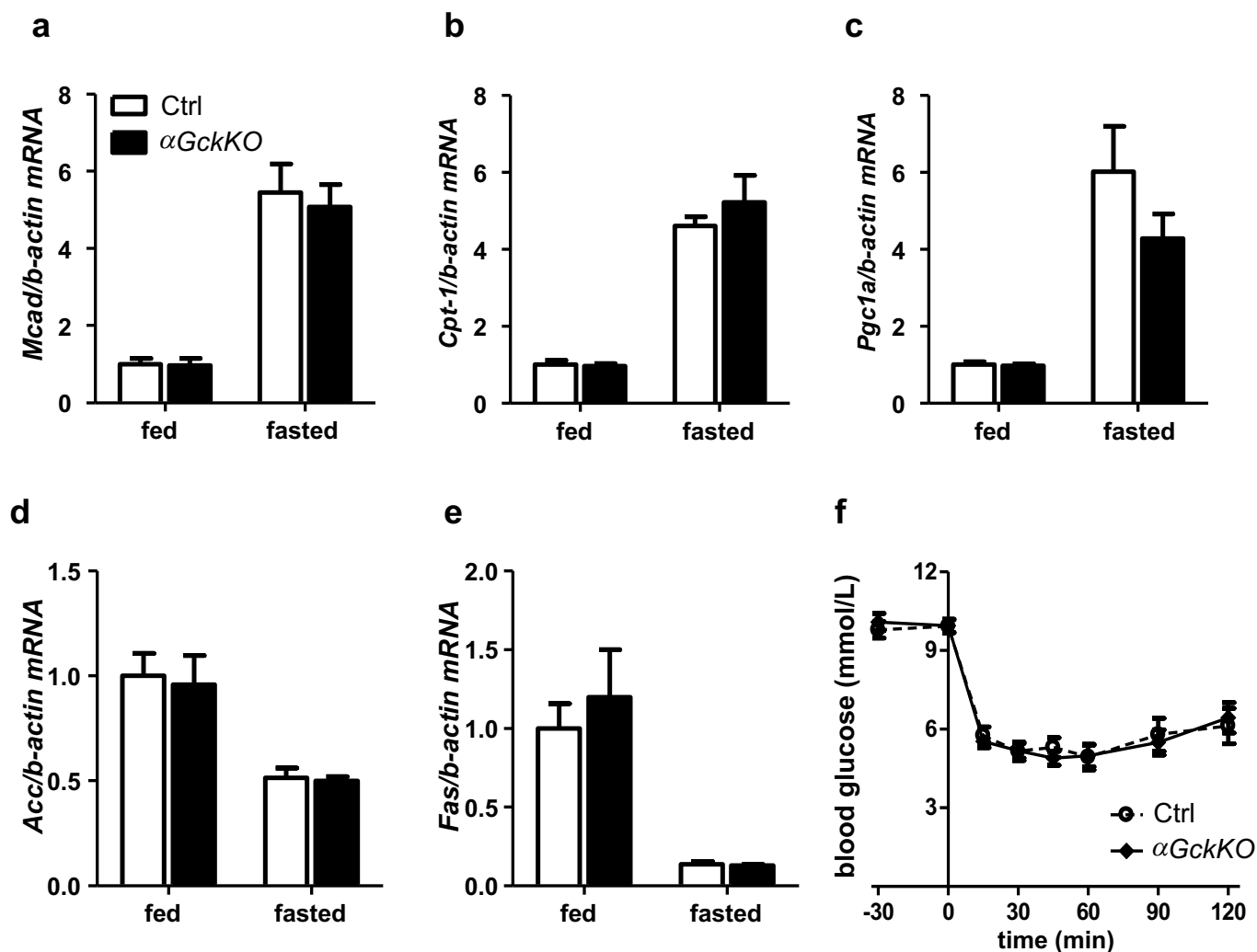
Supplementary figure 3. ATP/ADP ratio in β -cells from 18-20 week-old Ctrl and $\alpha GckKO$ female mice (related to figure 1). Heat map of Perceval fluorescence in β -cells in the presence of the indicated glucose concentrations (mM). n=275 for Ctrl and n=288 for $\alpha GckKO$. Data are represented as mean $\pm$ s.e.m.



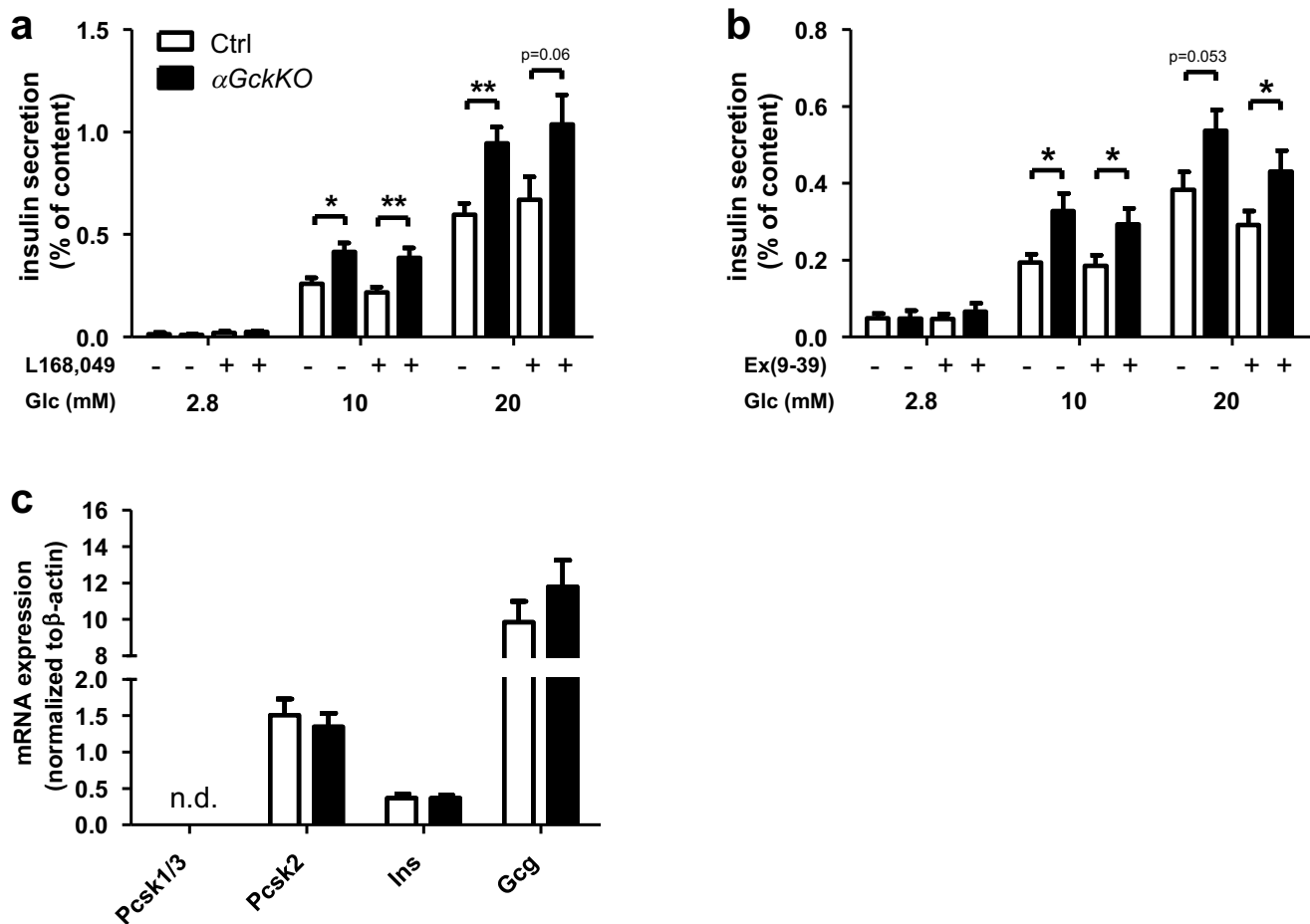
Supplementary figure 4. Example of β -cell electrical activity measured in whole islets from 18 week-old Ctrl (black, $n=4$) and $\alpha GckKO$ (red, $n=4$) female mice (related to figure 2).



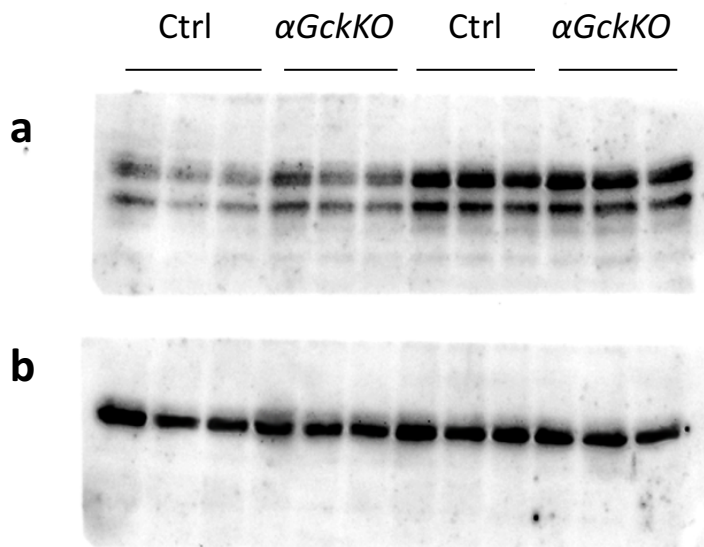
Supplementary figure 5. Metabolic profile of 20 week-old Ctrl and $\alpha GckKO$ male mice (related to figure 3). **(a)** Body weight, **(b)** Blood glucose, **(c)** Plasma insulin, and **(d)** Plasma glucagon. N=11 Ctrl and n=11 $\alpha GckKO$ mice. Student's t-test. Data are represented as mean $\pm$ s.e.m.



Supplementary Figure 6. (a-c) Fatty acid oxidation (*Mcad*, *Cpt1*, *Pgc1a*) and (d,e) synthesis (*Acc*, *Fas*) gene expression in the liver of 18 week-old Ctrl and $\alpha GckKO$ analyzed by qRT-PCR (related to figure 3). f) Intraperitoneal insulin tolerance test in 18 week-old female mice. 6 hrs fasted mice were injected with 0.7 U/kg i.p. insulin. N=9 Ctrl and 11 $\alpha GckKO$ mice. Data are represented as mean $\pm$ s.e.m.



Supplementary Figure 7. Increased glucose-stimulated insulin secretion by α GckKO mouse islets is not reduced by glucagon and GLP-1 antagonism (related to figure 4). **a**) Glucose stimulated insulin secretion in islets isolated from 36 week-old female mice in presence of the GcgR antagonist, L168,049 100nM. **b**) Same as **a**) but in presence of the Glp1R antagonist, Ex(9-39) 100nM. **c**) *Pcsk1/3*, *Pcsk2*, *Ins1*, and *Gcg* expression levels in FACS-purified α -cells from 36 week-old female mice. Data represent the average of four independent experiments, each performed in duplicate. * $p < 0.05$; ** $p < 0.01$; Student *t*-test. Data are represented as mean $\pm$ s.e.m.



Supplementary Figure 8. Uncropped images of pCREB and CREB immunoblotting in liver lysates. **a)** Uncropped image of immunoblotting for pCREB (43 kDa - upper image) and **(b)** CREB (43 kDa - lower image) in liver samples in random fed state and under ON fasting from 18 week-old Ctrl and *αGckKO* female mice (related to figure 3).

Supplementary Table 1. Primer sequences for genotyping (Gck) and for q-RT-PCR analysis.

Primer	Forward 5'-3'	Reverse 5'-3'
Gck (genotyping)	G TTCAGGTTATAGTACATCACAGCAG	ATTG CCTTGTCAACTTGTCC
Gck	ACTGCGGAGATGCTCTTTGA	TCTCGGAGAAGTCCCACGAT
G6Pase	TCCTGGGACAGACACACAAG	CAACTTTAATATACGCTATTGG
Pepck	CTTCTCTGCCAAGGTCATCC	TTTTGGGGATGGGCAC
Mcad	GCTCGTGAGCACATTGAAAA	CATTGTCCAAAAGCCAAACC
Cpt-1	ATCATGTATCGCCGCAAAC	CCATCTGGTAGGAGCACATGG
Pgc1α	AGACAAATGTGCTTCCAAAAAGAA	GAAGAGATAAAGTTGTTGGTTTGGC
Acc	ATTGGGCACCCAGAGCTA	CCCGCTCCTTCAACTTGCT
Fas	CGTATATGTGAACAGCGC	AGGTCTCGGATGCCTA
β-actin	GCTTCTTTGCAGCTCCTTCGT	ATATCGTCATCCATGCGCAAC
Pcsk 1/3	ACCAGGTGCTGCATATCTCG	CACAATGACTGCACGGAGAC
Pcsk2	TTTCGGTCAAATCCTTCCTG	TGCAAAGGCCAAGCGAAGAC
Ins1	CCATCAGCAAGCAGGTCATTGTT	AACGCCAAGGTCTGAAGGTCC
Gcg	CCAAGATTTTGTGCAGTGGTT	GGTAAAGGTCCCTTCAGCAT