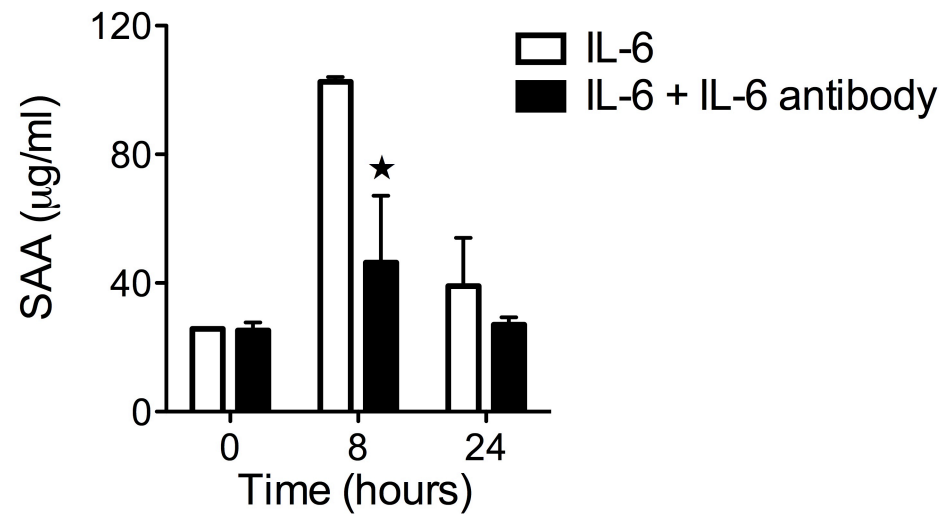


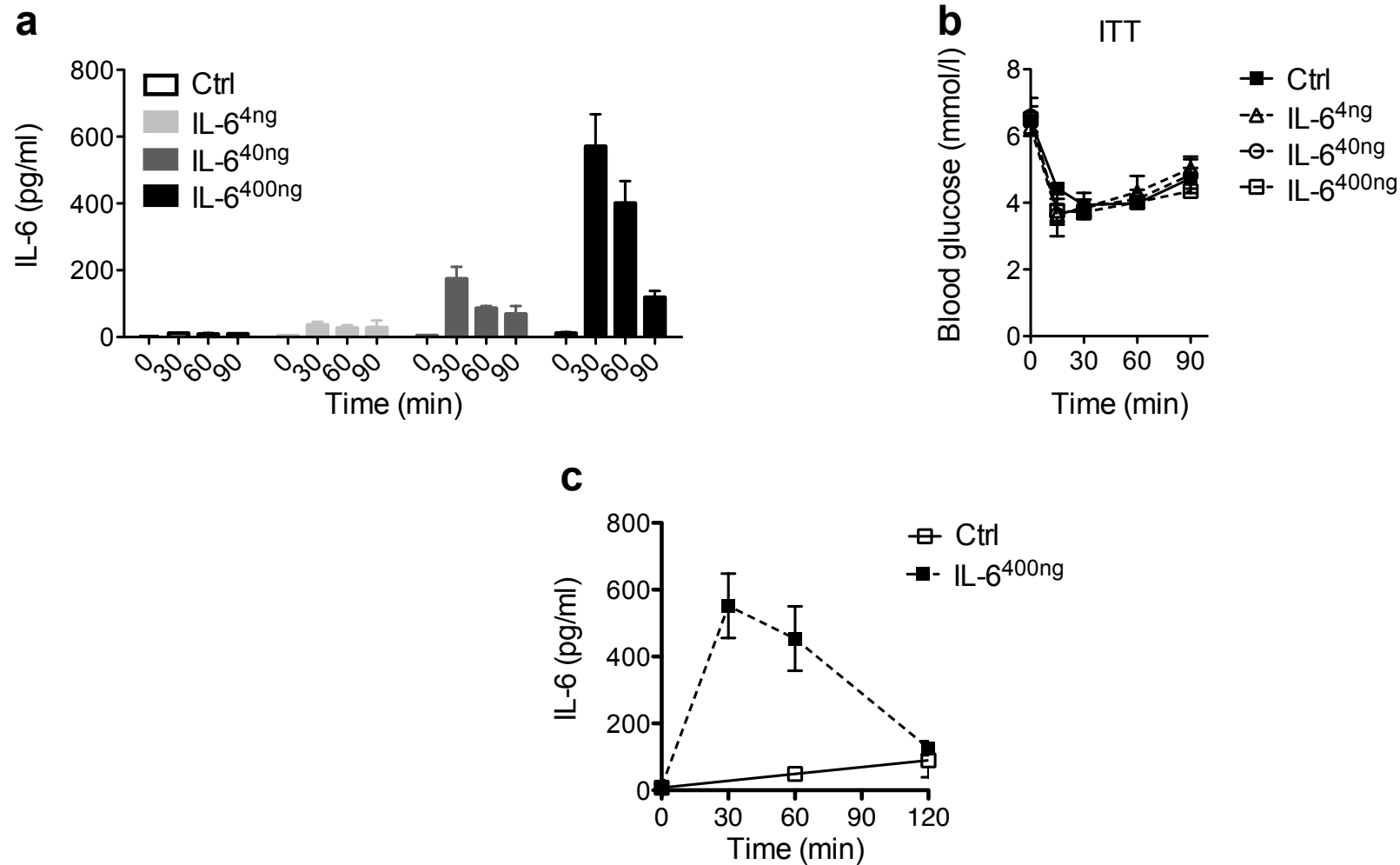
Supplementary Figure 1



Supplementary figure 1. Validation of IL-6 antibody.

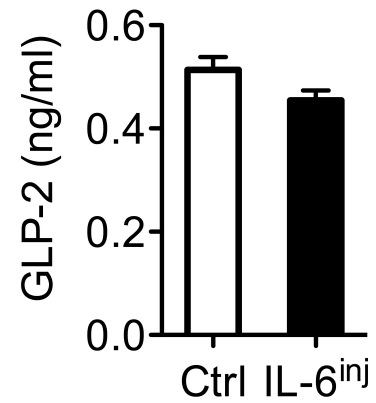
Plasma Serum Amyloid A (SAA) in response to a single injection of 100 ng IL-6 in the presence of an isotype control antibody or an IL-6 neutralizing antibody ($n=3$ per group). Data represents mean \pm s.e.m. * $p < 0.05$ by Student's t test.

Supplementary Figure 2



Supplementary figure 2. Plasma IL-6 levels and insulin tolerance after injection with IL-6. (a) Plasma IL-6 levels in response to a single intraperitoneal injection of IL-6 ($n=6$ per group). (b) Insulin tolerance test after a single injection of IL-6. (c) Plasma IL-6 in response to a single IL-6 injection ($n=4-6$). Data represents mean \pm s.e.m.

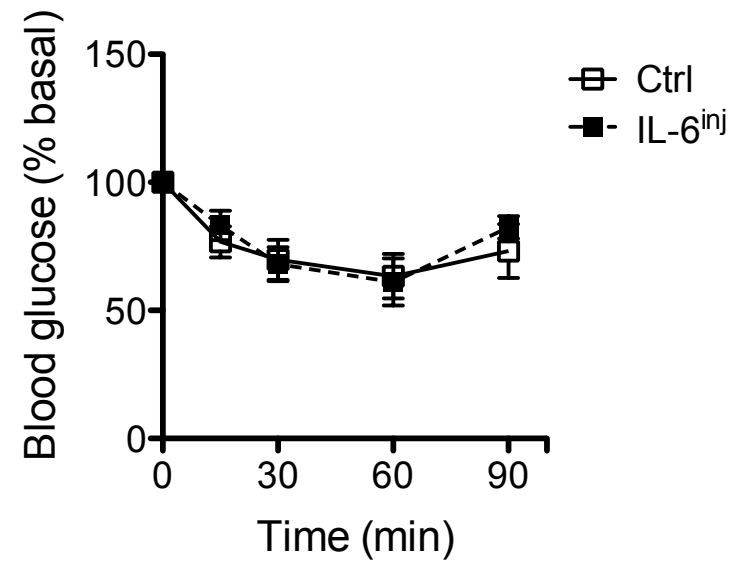
Supplementary Figure 3



Supplementary figure 3. IL-6 effects on GLP-2.

Fasting plasma GLP-2 in mice injected with or without 400 ng IL-6 twice daily for 7 days ($n=10$ per group). Data represents mean \pm s.e.m.

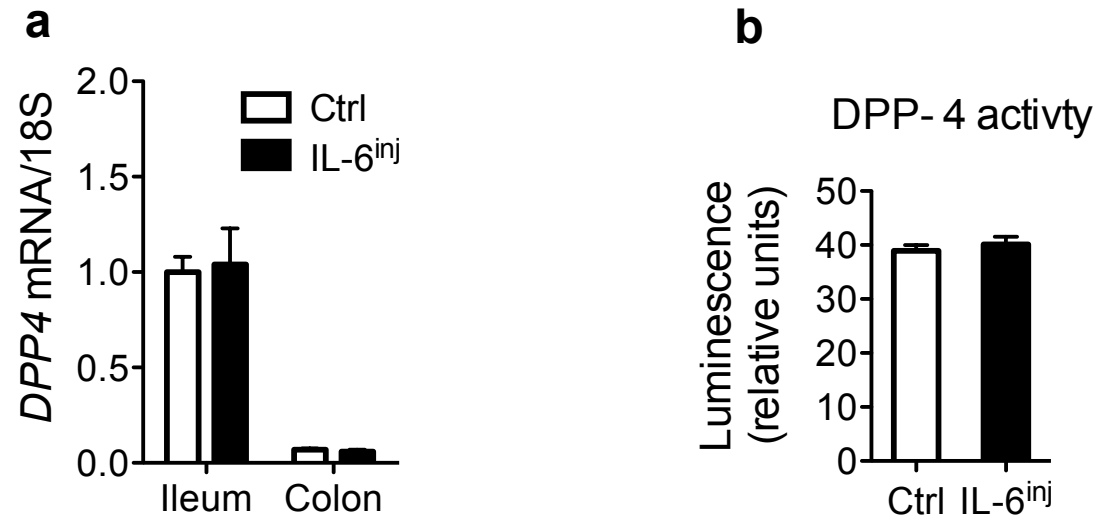
Supplementary Figure 4



Supplementary figure 4. Insulin tolerance test.

Insulin tolerance test in mice injected with or without 400 ng IL-6 twice daily for 7 days ($n=8$ per group). Data represents mean \pm s.e.m.

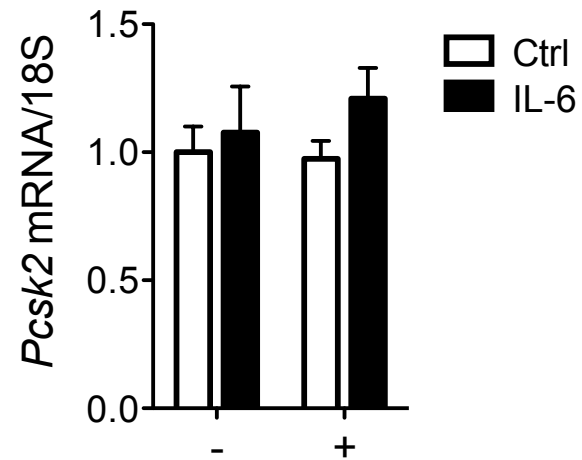
Supplementary Figure 5



Supplementary figure 5. IL-6 effects on DPP-4 expression and activity.

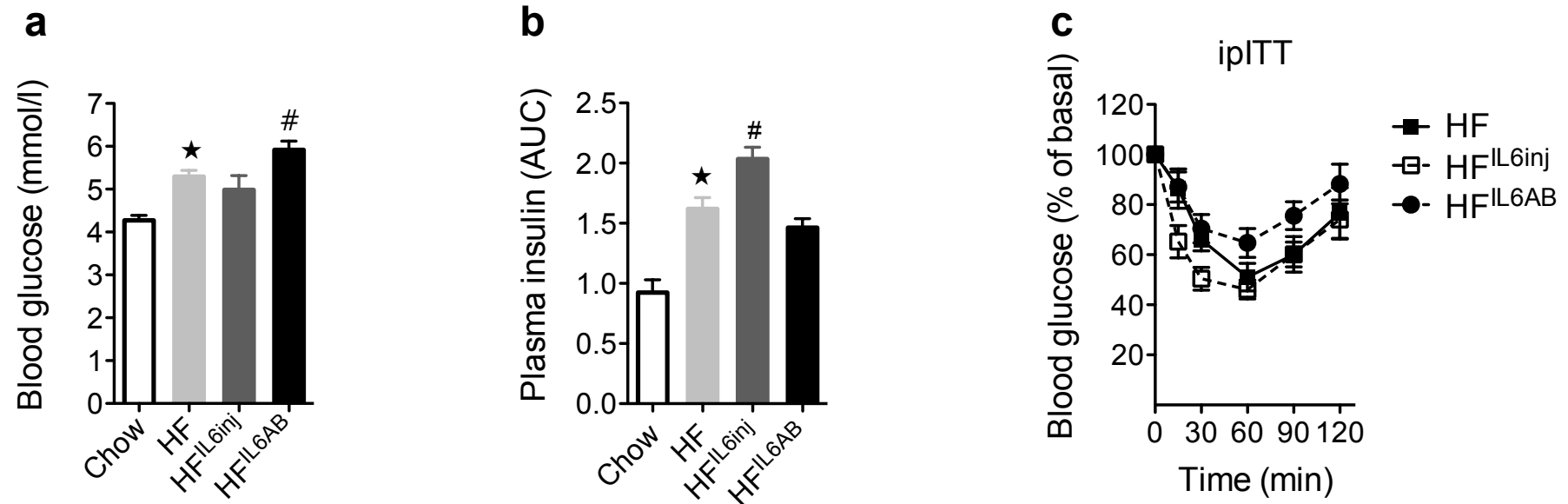
(a) Intestinal mRNA expression in mice injected with or without 400 ng IL-6 twice daily for 7 days ($n=6-8$). Data expressed relative to ileum control. (b) DPP-4 activity in plasma from mice 30 min after a single injection of 400 ng IL-6 ($n=5$). Data represents mean \pm s.e.m.

Supplementary Figure 6



Supplementary figure 6. *Pcsk2* (PC2) mRNA expression in GLUTag cells. GLUTag mRNA expression after 24 h treatment +/- 100 ng/ml IL-6 in the absence (-) or presence (+) of 50 μ mol/l AG490 ($n=3$ per group). Data represents mean \pm s.e.m.

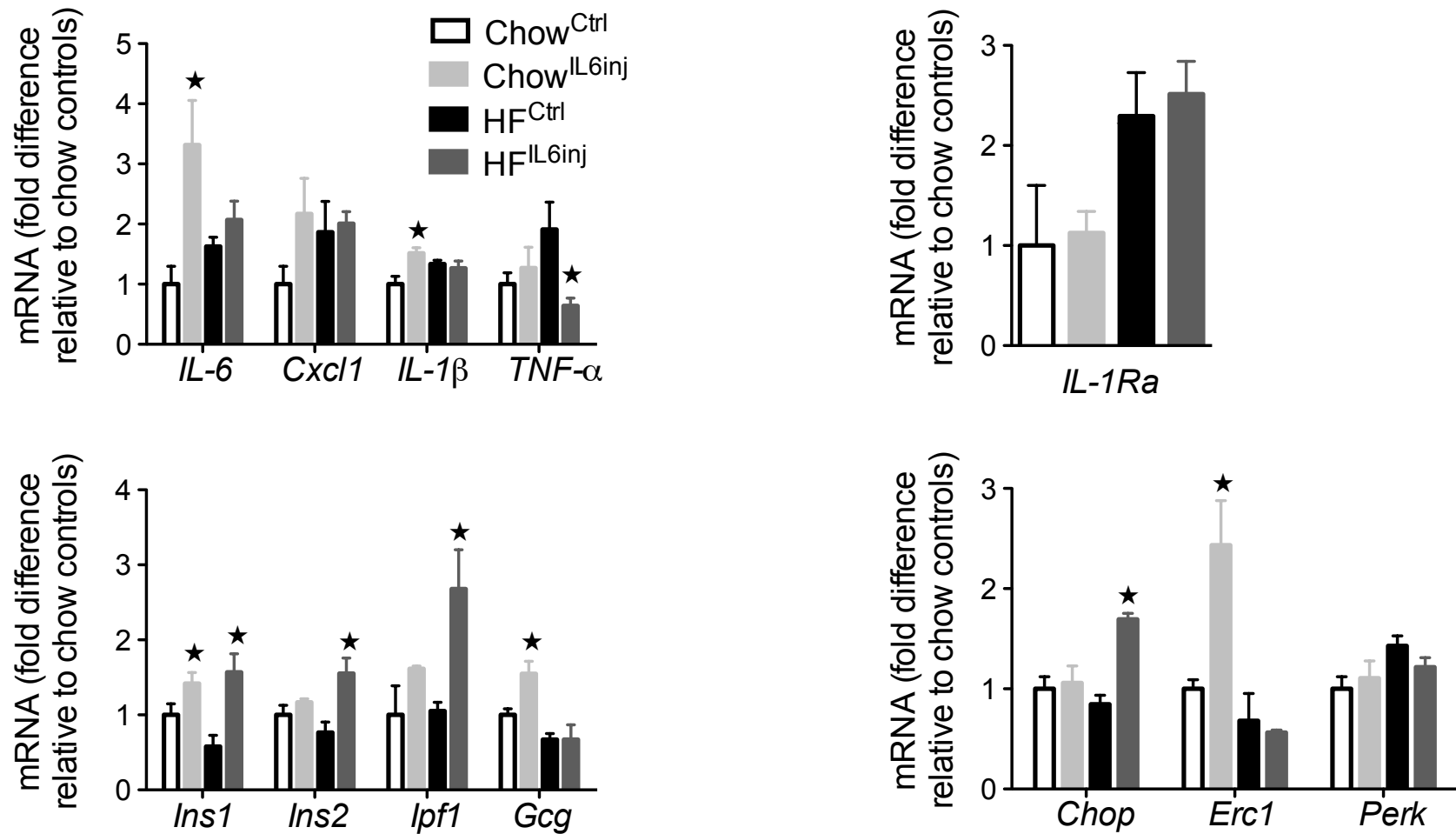
Supplementary Figure 7



Supplementary figure 7. IL-6 interventions in HF diet fed mice.

(a) Fasting blood glucose. (b) Insulin secretion in response to intraperitoneal glucose (c) Insulin tolerance test. Mice were fed chow or HF diet for 15 weeks, HF^{IL6inj} mice were injected twice daily with 400 ng IL-6 for the last 7 days of the study, whereas HF^{IL6AB} mice were injected twice weekly with a neutralizing IL-6 antibody for the last four weeks of the study ($n=7-8$). Data represents mean \pm s.e.m. * $p < 0.05$ by Anova comparing chow vs. HF and # comparing HF vs. HF^{IL6AB} (panel a) and HF vs. HF^{IL6inj} (panel b).

Supplementary Figure 8



Supplementary figure 8. Pancreatic islet gene expression.

mRNA expression in islets from mice fed chow or HF diet for 18 weeks and injected with 400 ng IL-6 or NaCl (Ctrl) twice daily for the last 7 days of the experiment ($n=4$ per group). Data represents mean \pm s.e.m. * $p < 0.05$ by Student's t test comparing changes from baseline (chow controls and HF controls respectively).

Supplementary Table 1

Time (hours)	Active GLP-1 (nmol/l)	Glucagon (nmol/l)
0 - 24	3.1 ± 0.6	2.0 ± 0.7
24 - 48	2.7 ± 0.5	2.4 ± 0.8
48 - 72	3.2 ± 0.6	3.2 ± 1.2
72 - 96	3.7 ± 1.0	3.6 ± 1.4
Content	17.6 ± 3.4	35.0 ± 4.6

Supplementary table 1. GLP-1 and glucagon in FACS sorted human α cells. Active GLP-1 and glucagon accumulation into culture media is provided for four consecutive 24 h intervals. Cellular content was extracted after 96 h ($n=4$). Data represents mean \pm s.e.m