

Expanded View Figures

Figure EV1. GR^{BATKO} BAT and iWAT are not significantly different from Flox controls under cold exposure.

- A GR mRNA levels in BAT after 1 week of cold exposure at 5°C ($n = 5-6$ mice per group).
- B GR expression in BAT separated into adipocytes and stromal vascular fraction ($n = 4$ animals per group).
- C Amplification plots for GR and Nr3c2, indicating lower levels of Nr3c2 being present in BAT ($n = 9$ animals per group).
- D Nr3c2 expression is unaffected upon knockdown of GR in BAT ($n = 5-6$ mice per genotype).
- E Body weight loss over the 1-week cold exposure ($n = 5-6$ animals per group).
- F Weight of white adipose depots ($n = 5-6$ animals per group).
- G Representative images of H&E-stained sections from iWAT. Scale bar 200 μm .
- H qRT-PCR analysis of thermogenic marker gene expression in iWAT ($n = 5-6$ mice per group).
- I-L Blood glucose, insulin, triglycerides, and NEFA levels in Flox and GR^{BATKO} animals after 1 week of exposure to 5°C ($n = 6$ animals per group).

Data information: Data were analyzed with two-tailed Student's *t*-test. ** $P < 0.01$. Error bars denote SEM.

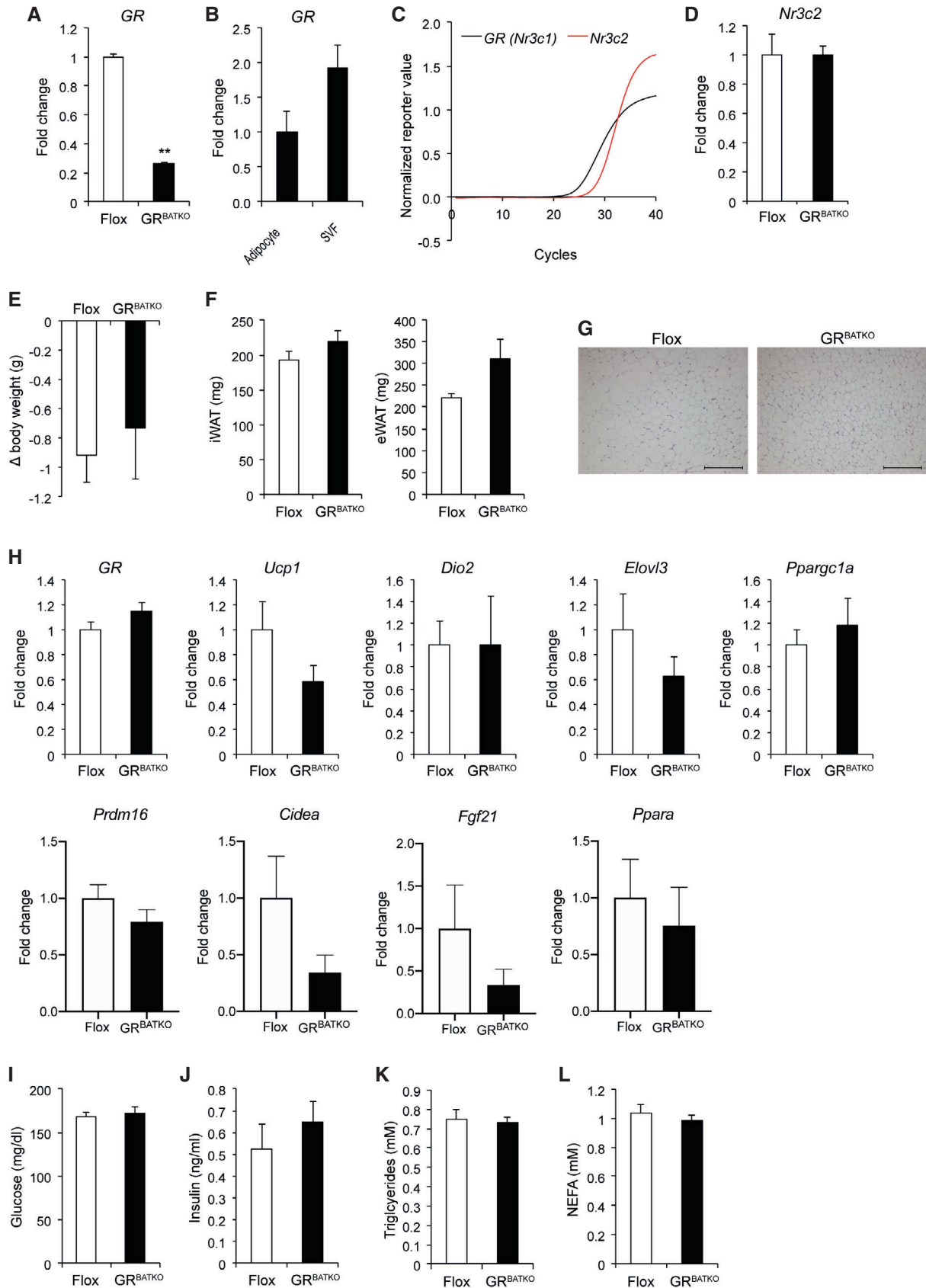


Figure EV1.

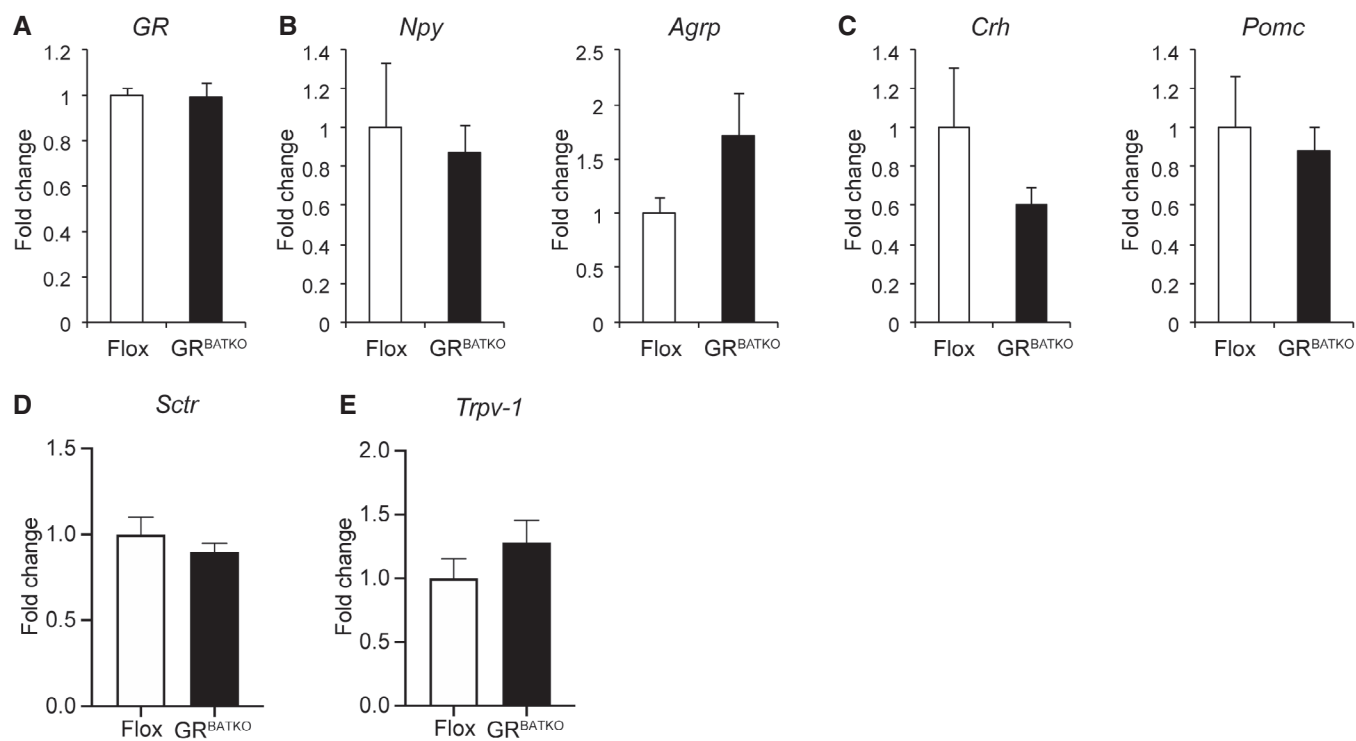


Figure EV2. Hypothalamic gene expression signature is comparable between GR^{BATKO} and Flox control mice.

A GR mRNA levels in hypothalamus of Flox and GR^{BATKO} animals after 24 weeks of high-fat feeding ($n = 5-9$ samples per group).

B qRT-PCR analysis of orexigenic markers *Npy* and *Agrp* ($n = 5-9$ animals per group).

C *Crh* and *Pomc* mRNA levels in hypothalamus of Flox and GR^{BATKO} mice determined by qRT-PCR ($n = 5-9$ animals per group).

D *Sctr* mRNA levels in BAT of Flox and GR^{BATKO} mice determined by qRT-PCR ($n = 9-11$ animals per group).

E *Trpv-1* mRNA levels in BAT of Flox and GR^{BATKO} mice determined by qRT-PCR ($n = 5-9$ animals per group).

Data information: Error bars represent SEM.

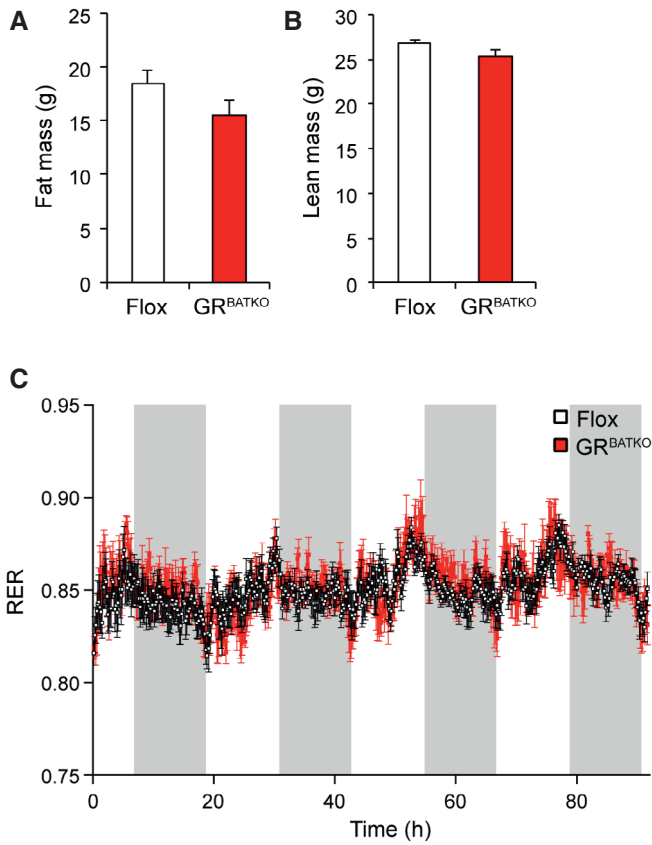


Figure EV3. GR knockdown in BAT does not significantly change body composition or respiratory exchange ratio.

A Fat mass measured with echoMRI in conscious Flox and GR^{BATKO} mice ($n = 6-8$ animals per group).
 B Lean mass in Flox and GR^{BATKO} mice after indirect calorimetry ($n = 6-8$ animals per genotype).
 C Respiratory exchange ratio (RER) in Flox and GR^{BATKO} mice measured over a 90-h period ($n = 6-8$ animals per genotype).

Data information: Error bars represent SEM.

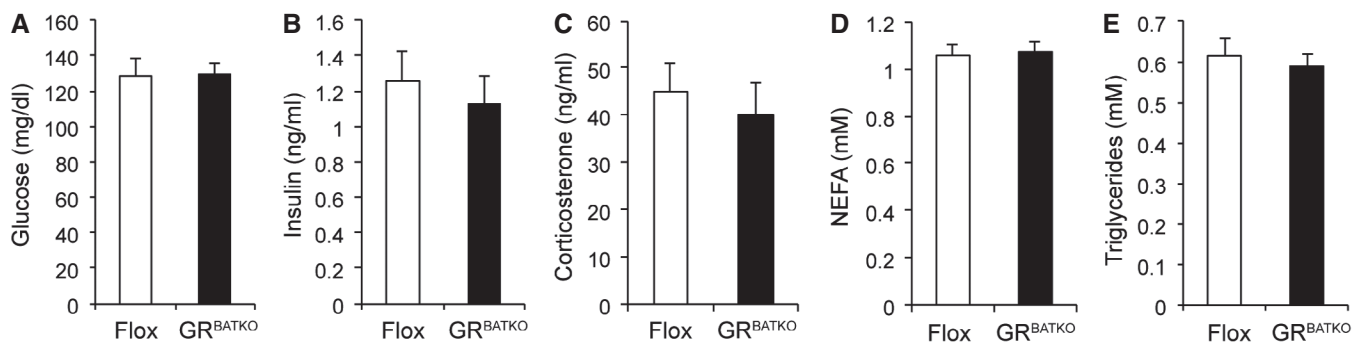


Figure EV4. GR^{BATKO} react comparably to Flox controls to an overnight fast.

A-E Plasma metabolites in Flox and GR^{BATKO} mice fed HFD for 16 weeks. Blood collected after an overnight fast ($n = 13-14$ mice per group). Error bars represent SEM.

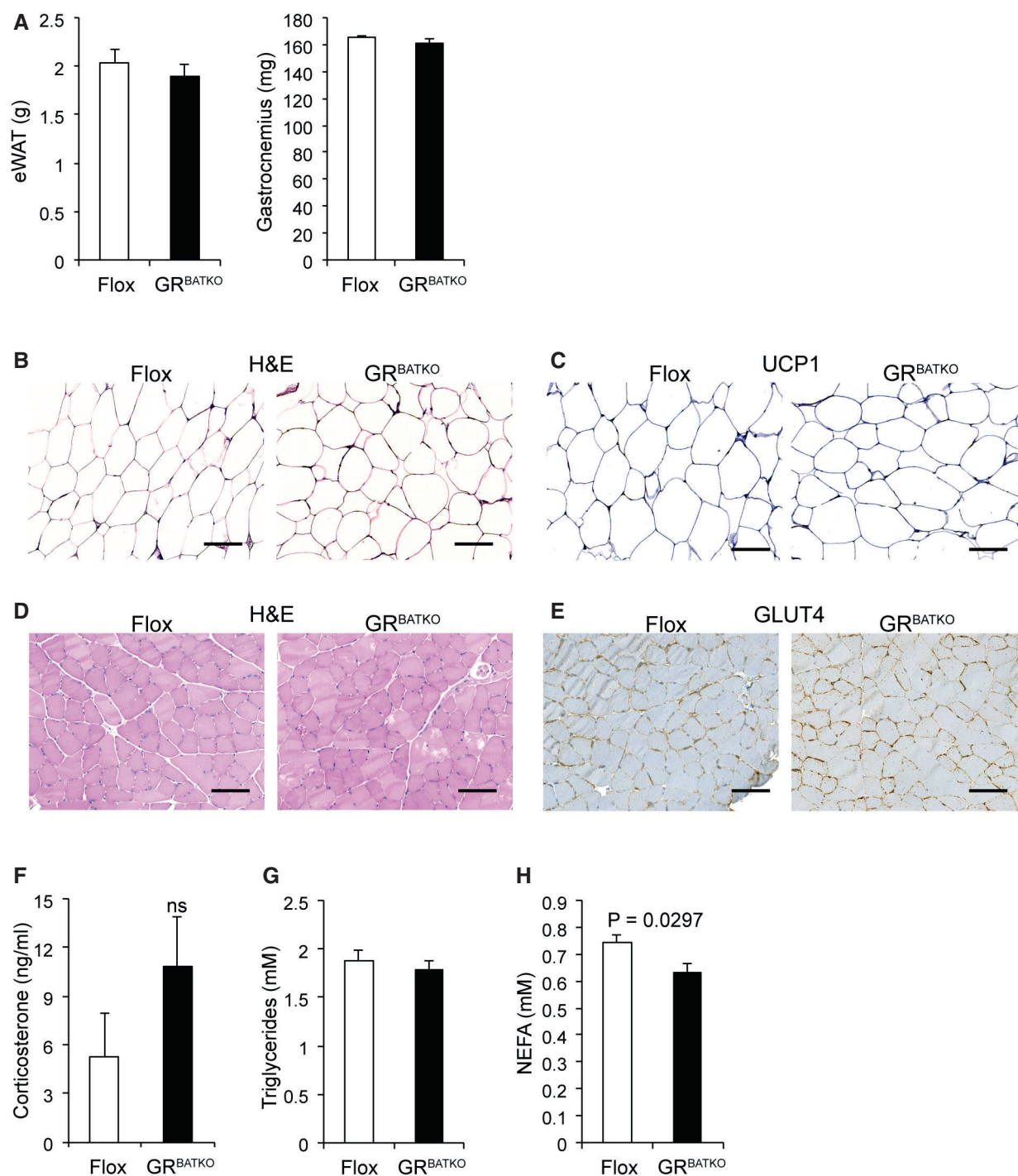


Figure EV5. Tissue weight, morphology, and metabolic parameters on HFD do not differ between GR^{BATKO} mice and Flox controls.

A eWAT and gastrocnemius tissue weights of Flox and GR^{BATKO} mice fed a HFD for 24 weeks ($n = 4-6$ mice per group).
 B Representative H&E staining of iWAT from Flox and GR^{BATKO} mice fed a HFD for 24 weeks ($n = 10-13$ mice per group). Scale bar 100 μ m.
 C Representative immunohistochemistry for UCP1 in BAT ($n = 10-13$ mice per group). Scale bar 100 μ m.
 D Representative H&E staining of gastrocnemius muscle from Flox and GR^{BATKO} mice fed HFD for 24 weeks ($n = 10-13$ mice per group). Scale bar 100 μ m.
 E Representative immunohistochemistry for GLUT4 in gastrocnemius muscle ($n = 10-13$ mice per group). Scale bar 100 μ m.
 F-H Serum corticosterone, triglyceride, and NEFA levels in Flox and GR^{BATKO} animals at the end of the HFD study ($n = 10-13$ animals per group).

Data information: Data were analyzed with two-tailed Student's *t*-test. Error bars represent SEM.