

Supplemental figures

Fig. S1. SPRET/Ei mice are very resistant to LPS lethality and show impaired LPS-induced gene expression. (A) Survival of C57BL/6, SEG/Pas, and SPRET/Ei mice after i.p. injection of 500 µg of LPS. Mortality was monitored for 36 h (no further deaths occurred). ■, C57BL/6 mice (n=6); ▲, SEG/Pas mice (n=5); ○, SPRET/Ei mice (n=4). (B) LPS-induced gene expression in liver shows reduced levels of GR-repressed genes in SPRET/Ei mice compared to control SEG/Pas and C57BL/6 mice. C57BL/6 (n=4, black bars), SEG/Pas (n=4, grey bars) and SPRET/Ei mice (n=4, white bars) were injected with 100 µg LPS *i.p.* and mRNA was isolated 0 and 6 h after injection. qPCR was used to measure mRNA levels of a set of GR-repressed genes encoding IL6, IL1β, IFNγ and CXCL10. Significance was calculated for difference from SPRET/Ei.

Fig. S2. SPRET/Ei mice show enhanced GR mRNA levels. qPCR analysis of GR mRNA expression in various tissues of C57BL/6 (black bars; n=5), SEG/Pas (grey bars; n=4) and SPRET/Ei (white bars; n=5). ***, significance levels for difference between C57BL/6 or SEG/Pas and SPRET/Ei; +++, significance levels for difference between C57BL/6 and SEG/Pas.

Fig. S3. SPRET/Ei mice do not show corticotrophic adenoma's in their anterior pituitary gland. Pituitary sections of non-stressed C57BL/6 and SPRET/Ei animals were stained with an anti-ACTH antibody (red-stained cells). Representative pictures are shown here; bars, 150 µm (pictures above) and 50 µm (pictures below).

Fig. S4. SPRET/Ei mice exhibit increased HPA axis activity. (A) Circulating corticosterone levels, measured in serum from unstimulated C57BL/6 (black bars; n=24), SEG/Pas (grey bars; n=13) and SPRET/Ei mice (white bars; n=17) and in C57BL/6 (n=6), SEG/Pas (n=4) and SPRET/Ei mice (n=8) after 20 h of fasting. (B) Circulating plasma ACTH levels from unstimulated C57BL/6 (black bars; n=13), SEG/Pas (grey bars; n=10) and SPRET/Ei mice (white bars; n=14) and in C57BL/6 (n=5), SEG/Pas (n=4) and SPRET/Ei mice (n=4) after 20 h of fasting. (C) Relative *Pomc* mRNA levels in pituitary glands from C57BL/6 (n=8), SEG/Pas (n=8) and SPRET/Ei mice (n=7) and in C57BL/6 (n=4), SEG/Pas (n=4) and SPRET/Ei mice (n=4) after 20 h of fasting. (D) Mean adrenal weight of 2-3 month old female and male C57BL/6 (black bars; n=11), SEG/Pas (grey bars; n=11) and SPRET/Ei mice (white bars; n=7). Adrenal weight is expressed as milligrams/g body weight. ***, significance levels calculated for difference from SPRET/Ei (unless otherwise noted in the graph).

Fig. S5. SPRET/Ei mice are glucose intolerant and secrete no insulin after glucose administration. (A) Glucose tolerance test: response of C57BL/6 (■; n=10), SEG/Pas (▲; n=5), SPRET/Ei mice (○; n=9) to i.p. insulin injection. (B) Serum insulin levels determined at several timepoints after glucose injection in C57BL/6 (■; n=6), SEG/Pas (▲; n=5) and SPRET/Ei mice (○; n=5). ***, significance levels for difference between C57BL/6 or SEG/Pas and SPRET/Ei; +++, significance levels for difference between C57BL/6 and SEG/Pas.

Fig. S1

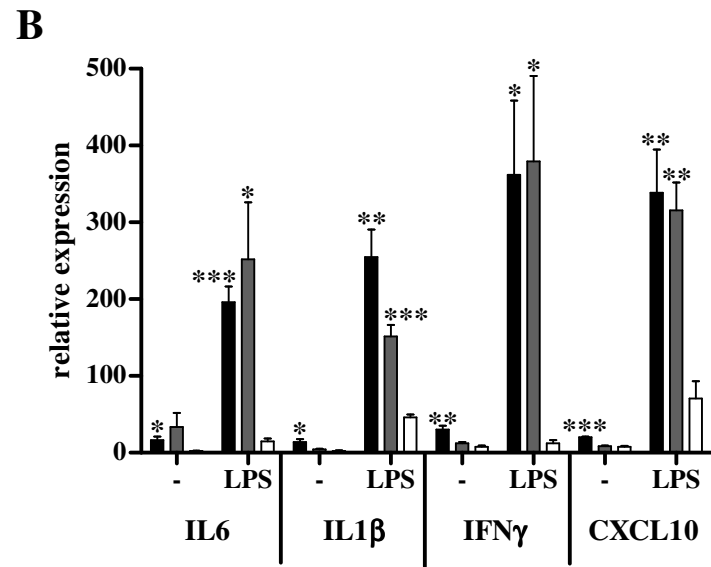
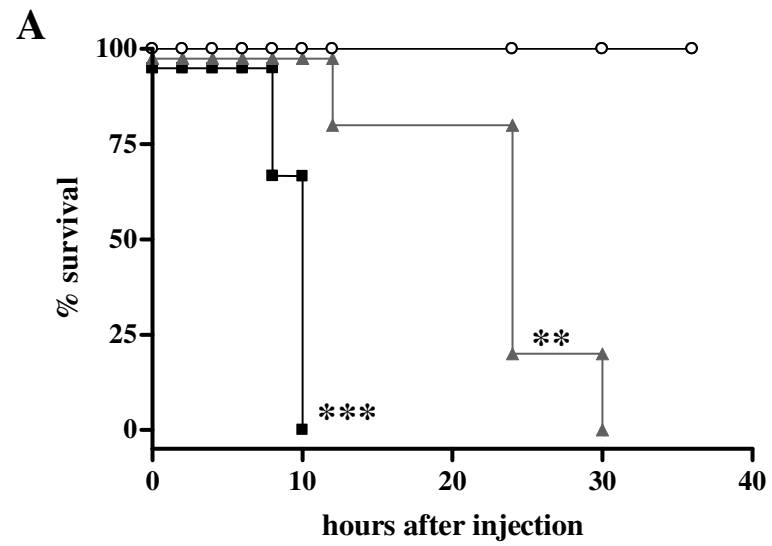


Fig. S2

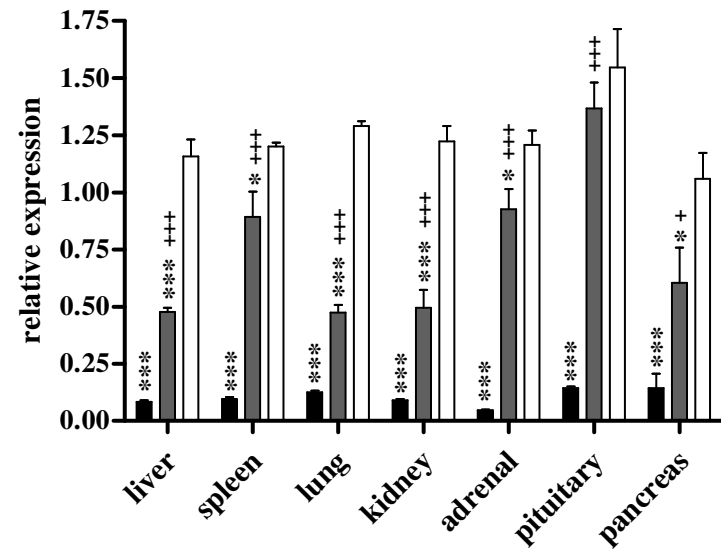
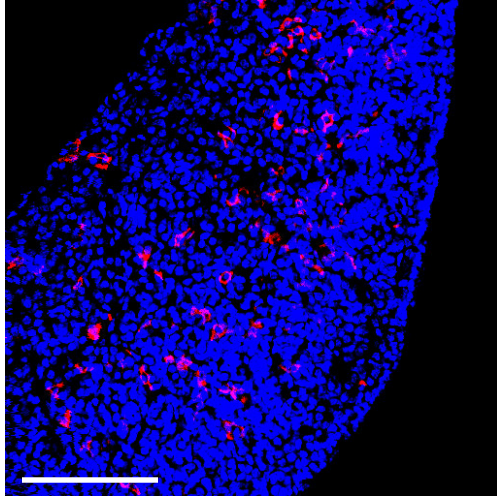


Fig. S3

C57BL/6



SPRET/Ei

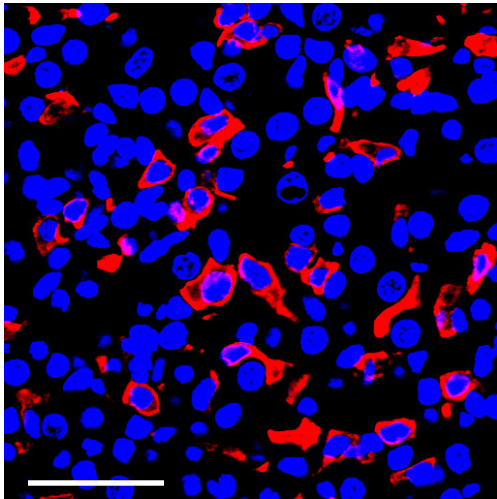
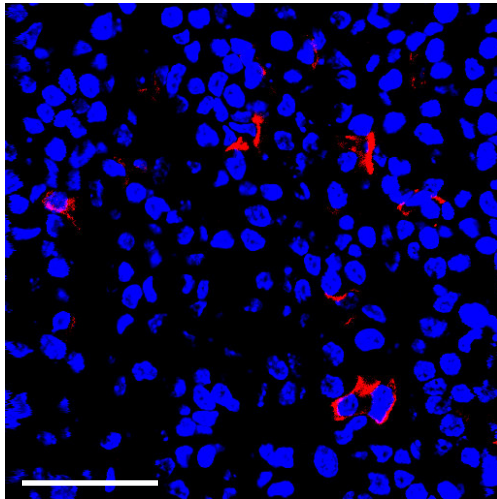
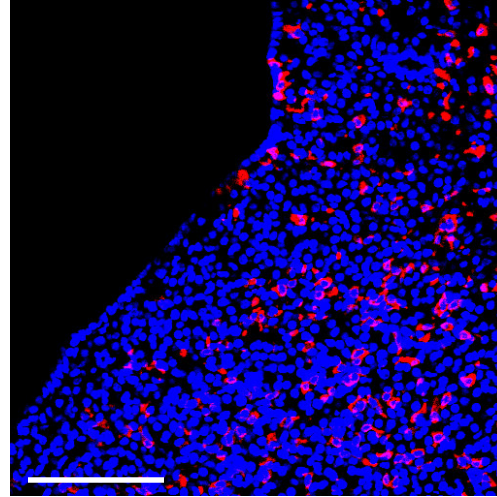
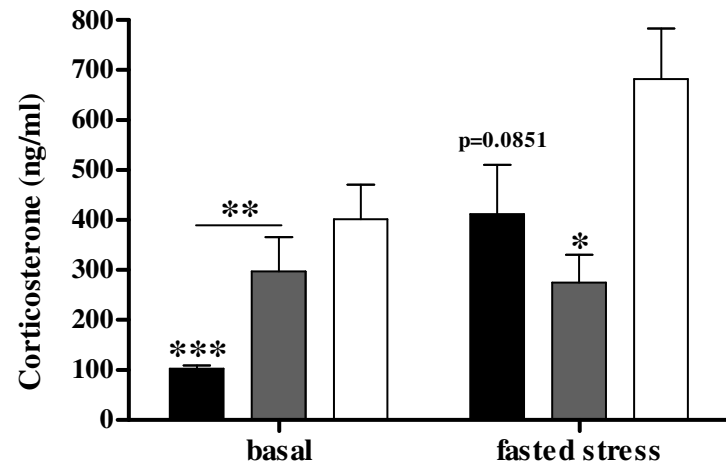
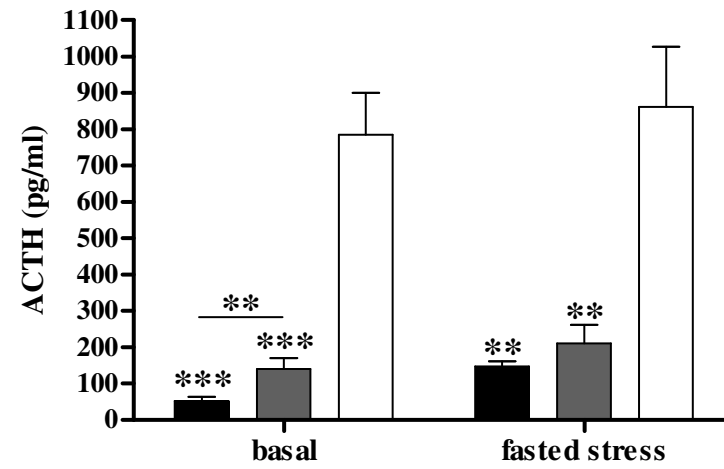


Fig. S4

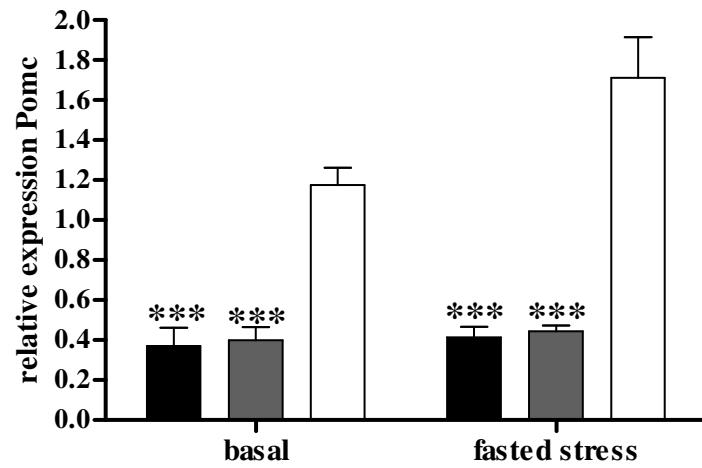
A



B



C



D

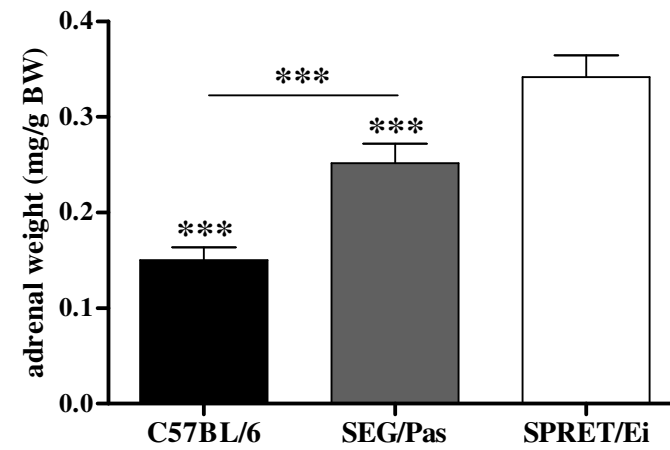
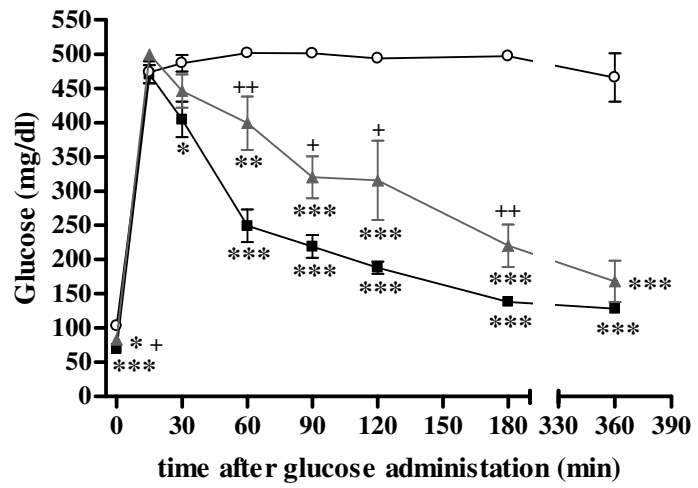


Fig. S5

A



B

