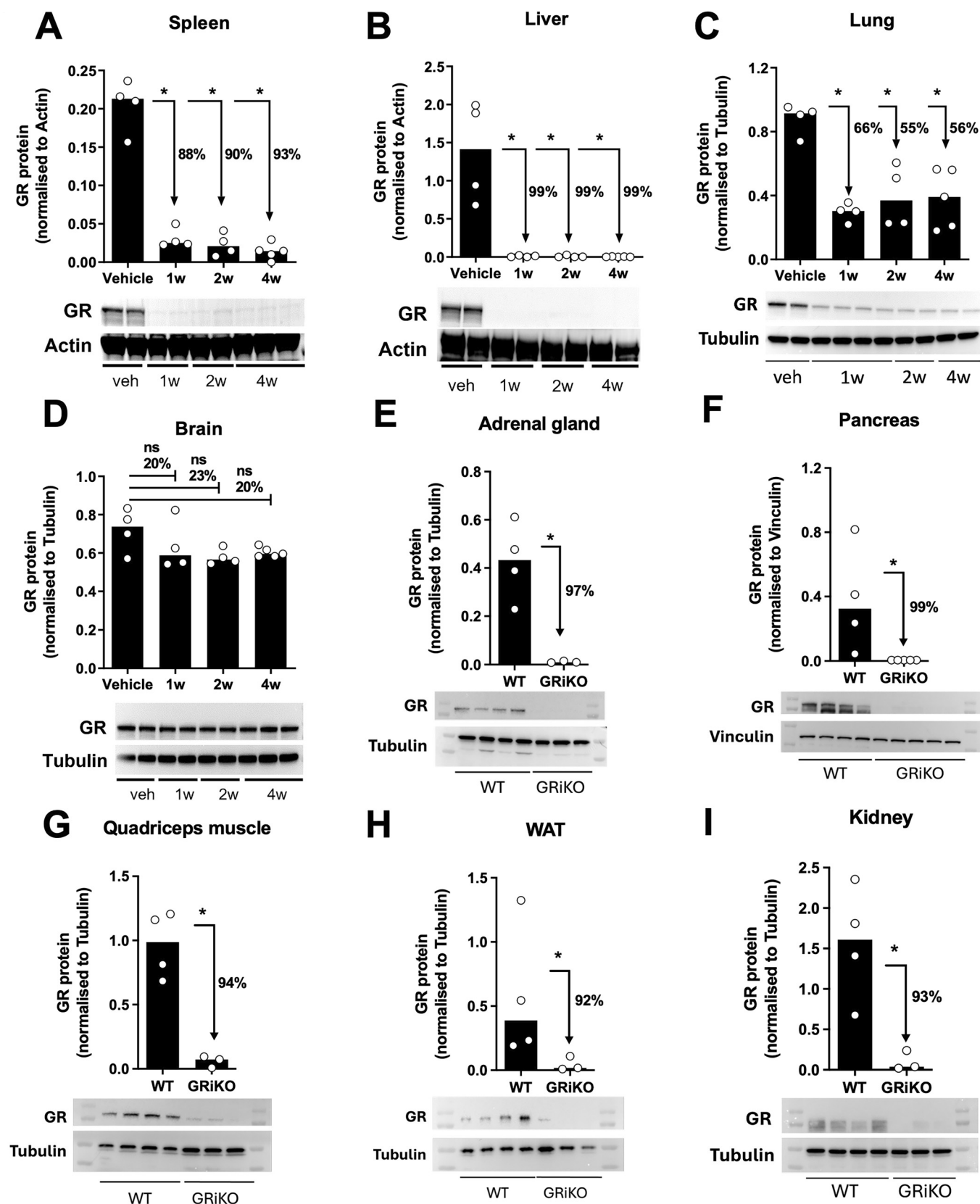


Expanded View Figures

Figure EV1. Validation of tamoxifen treatment for the induction of global GR deletion.

Tamoxifen-inducible WT and GRiKO mice were treated with vehicle or 10 mg/kg tamoxifen for 5 consecutive days. Organs were collected at 1 week, 2 weeks or 4 weeks after the last tamoxifen treatment was given. Protein expression of GR α were determined in (A) spleen, (B) liver, (C) lung, (D) whole brain, (E) adrenal gland, (F) pancreas, (G) quadriceps muscle, (H) white adipose tissue (WAT) and (I) kidney extracts. For (A–D): percentage of reduction in GR α protein expression in tamoxifen-treated GRiKO group relative to vehicle-treated GRiKO group. For (E–I): percentage of reduction in GR α protein expression in tamoxifen-treated GRiKO group relative to tamoxifen-treated WT group is shown. Representative blots are shown together with the semiquantitative determination of band intensities. Each datapoint represents an individual mouse. Data from one or two independent experiments. Bar graph represent median per group. Statistical differences were calculated with the Mann-Whitney *U* test. ns: $P > 0.05$. * $P < 0.05$. Source data are available online for this figure.



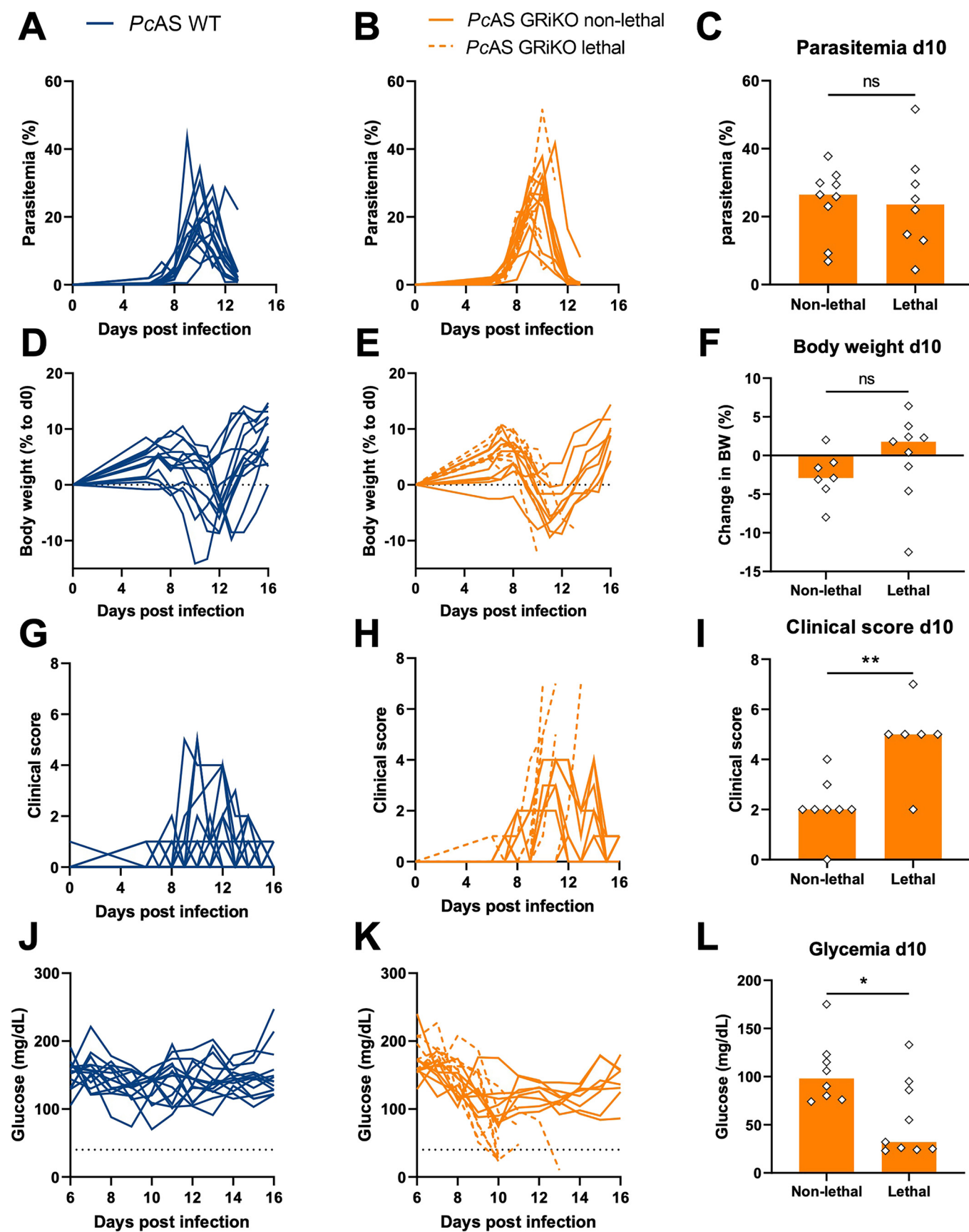




Figure EV2. The observed lethality in infected GRiKO mice is related to clinical score and glycemia, and not to parasitemia or body weight.

WT and GRiKO mice were infected with *PcAS* parasites. (A–C) Parasitemia levels, (D–F) body weight, (G–I) clinical score and (J–L) glycemia were determined each day, from 6 dpi onwards. For each parameter, longitudinal data is represented. A statistical comparison was made for all four parameters (measured at 10 dpi) between lethal and non-lethal infected GRiKO mice (data from the same experiments as in Fig. 1C–E, I–J and Appendix Fig. S1C–E). Statistical differences were calculated with the Mann–Whitney *U* test. Each datapoint or line represents an individual mouse. Solid lines: non-lethal mice, and striped lines: lethal mice. Data from three independent experiments. Bar graph represent median per group. ns: $P > 0.05$, * $P < 0.05$, ** $P < 0.01$.

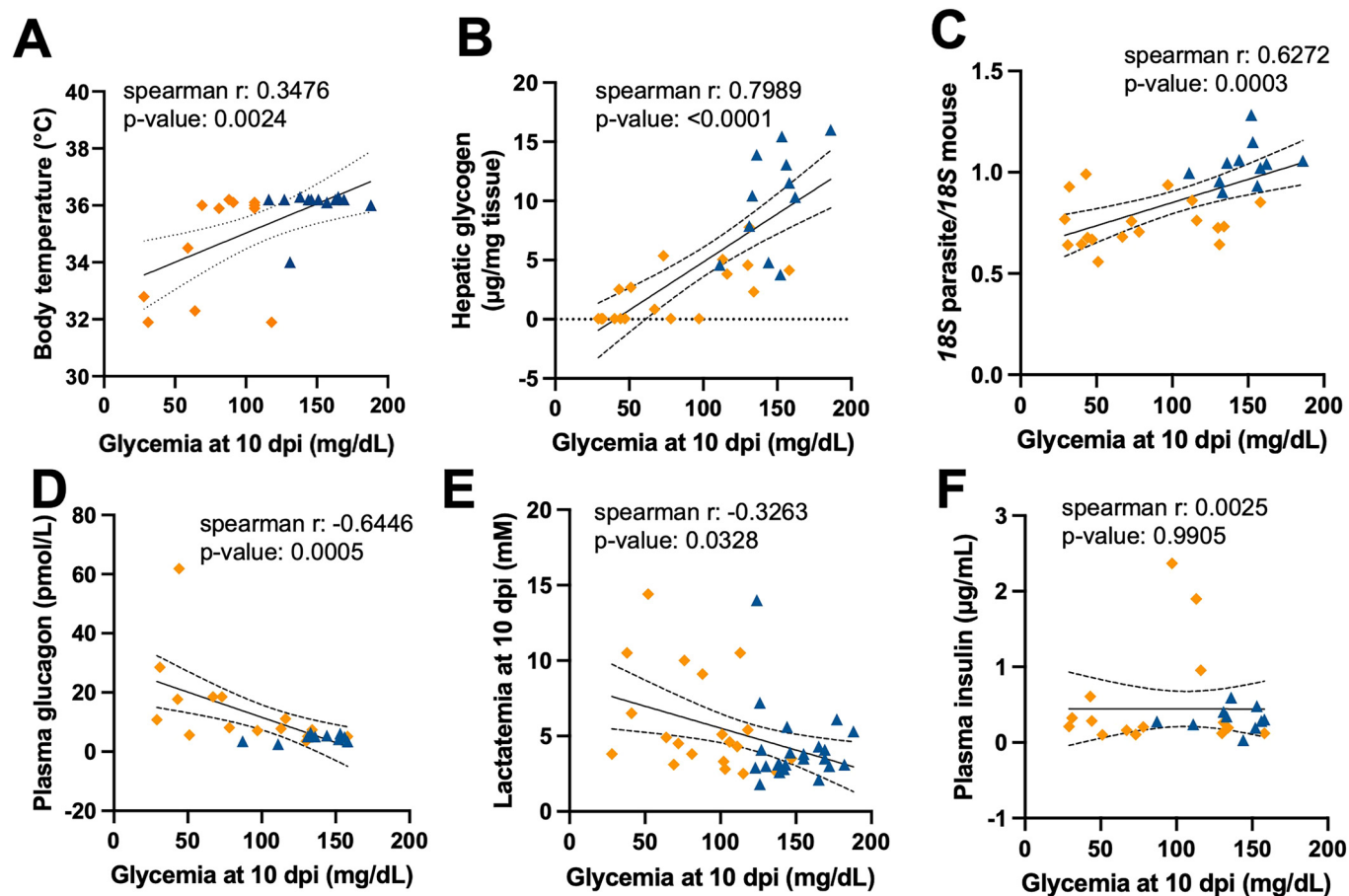
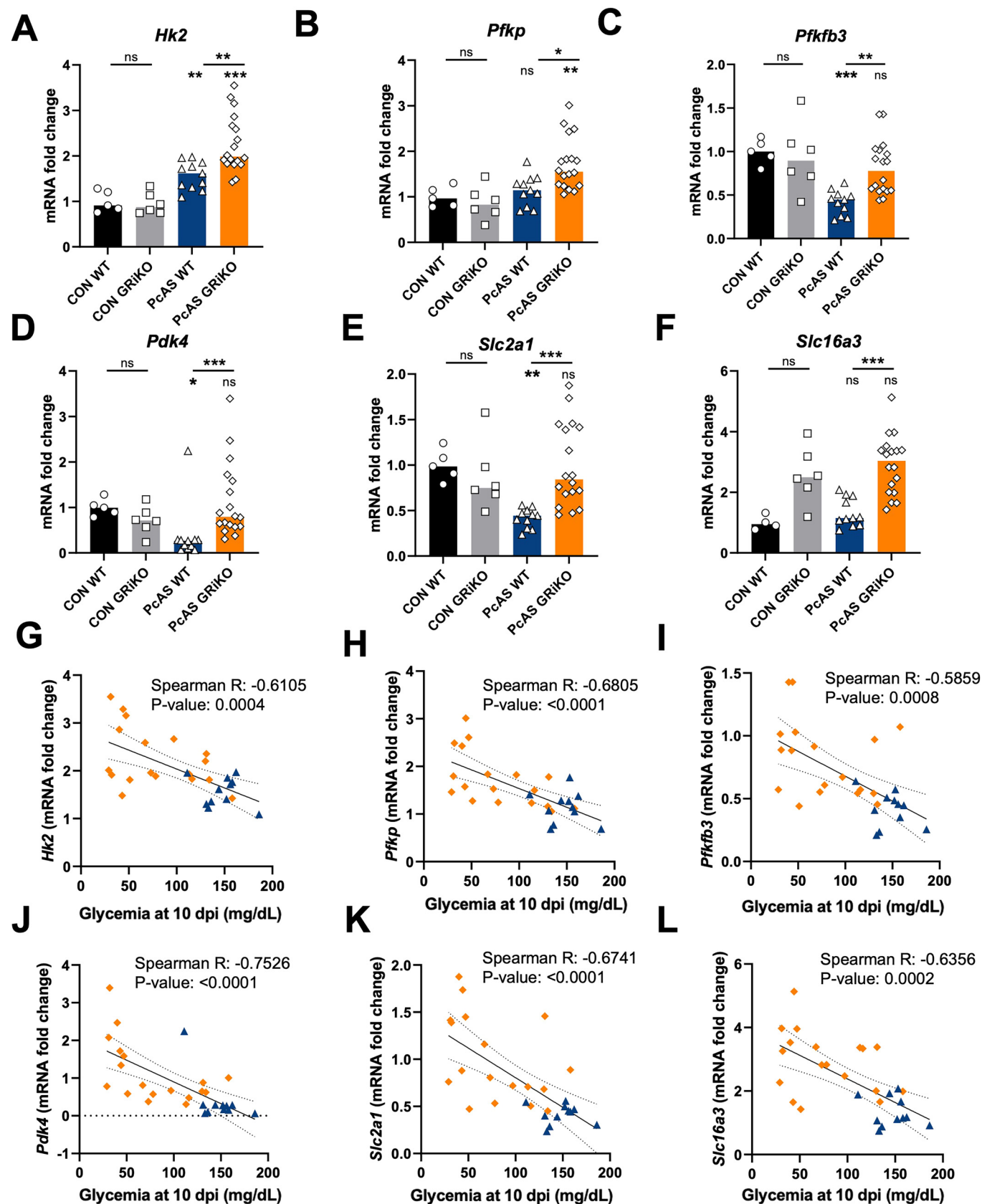


Figure EV3. Body temperature, hepatic glycogen, plasma glucagon, lactatemia and hepatic parasite load correlate with glycemia levels.

WT and GRiKO mice were infected with *PcAS* parasites. At 10 dpi, glycemia, body temperature, hepatic glycogen, plasma glucagon levels and lactatemia were determined. Correlations were assessed between glycemia and (A) body temperature, (B) hepatic glycogen, (C) hepatic parasite load, (D) plasma glucagon, (E) lactatemia and (F) plasma insulin with a nonparametric Spearman test. \blacktriangle : infected WT mice and \blacklozenge : infected GRiKO mice. Each symbol represents an individual mouse. Data from two individual experiments.



◀ **Figure EV4. GR signaling inhibits glycolytic gene expression in spleen during infection.**

WT and GRiKO mice were infected with *PcAS* parasites and spleens were collected at 10 dpi. qPCR was performed to determine mRNA expression of (A) *Hk2*, (B) *Pfkfb3*, (C) *Pfkfb3*, (D) *Pdk4*, (E) *Slc2a1* and (F) *Slc16a3*. Data were normalized towards mouse-specific *18S* and the average expression of CON WT mice. Correlation analyses were performed between glycemia and (G) *Hk2*, (H) *Pfkfb3*, (I) *Pfkfb3*, (J) *Pdk4*, (K) *Slc2a1* and (L) *Slc16a3* with the nonparametric Spearman test. Statistical differences were calculated with the Mann-Whitney *U* test with Holm-Bonferroni correction. ns: $P > 0.05$, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Asterisks above data points indicate significant differences between infected and non-infected mice, asterisks above a horizontal line show significant differences between genotype. Each symbol represents an individual mouse and bar graph represent median per group. ▲: infected WT mice and ◆: infected GRiKO mice. Data from two independent experiments.

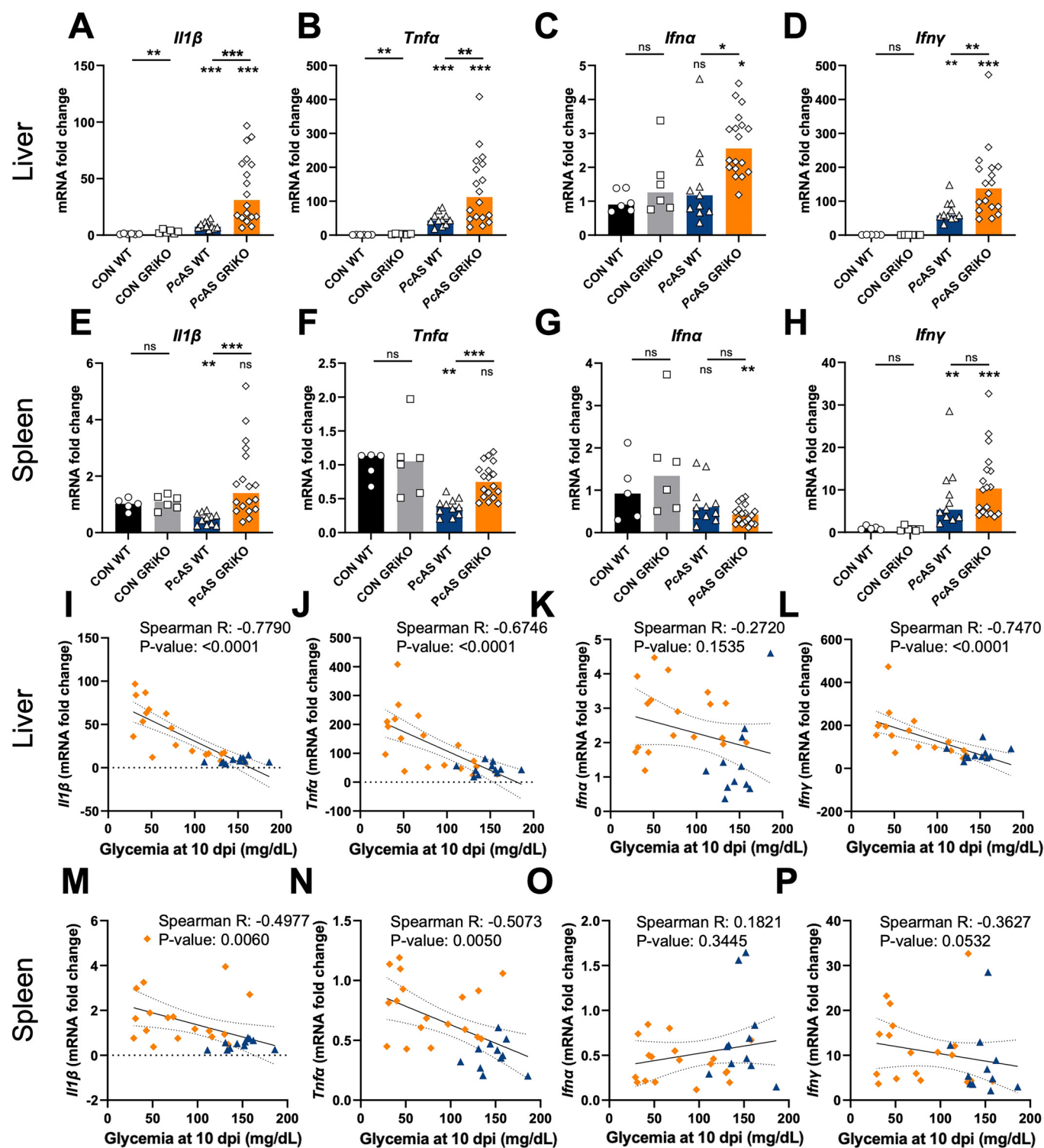


Figure EV5. GR signaling prevents cytokine storm in liver and spleen of PcAS-infected mice.

WT and GRiKO mice were infected with PcAS parasites. At 10 dpi, livers and spleens were collected and expression levels of (A, E) *Il1β* (B, F) *Tnfa*, (C, G) *Ifna* and (D, H) *Ifny* were measured with qPCR. Data were normalized towards mouse-specific 18S and the average expression of CON WT mice. (I–P) Correlations between glycemia levels and the cytokine expressions were assessed with the nonparametric Spearman test. Each symbol represents an individual mouse and bar graph represent median per group. ▲: infected WT mice and ◆: infected GRiKO mice. Statistical differences were calculated with the Mann-Whitney *U* test with Holm-Bonferroni correction. ns: $P > 0.05$, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Asterisks above data points indicate significant differences between infected and non-infected mice, asterisks above a horizontal line show significant differences between genotype. Data from two independent experiments.