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Supplemental Information

Acute *Plasmodium* Infection Promotes Interferon-Gamma-Dependent Resistance to Ebola Virus Infection

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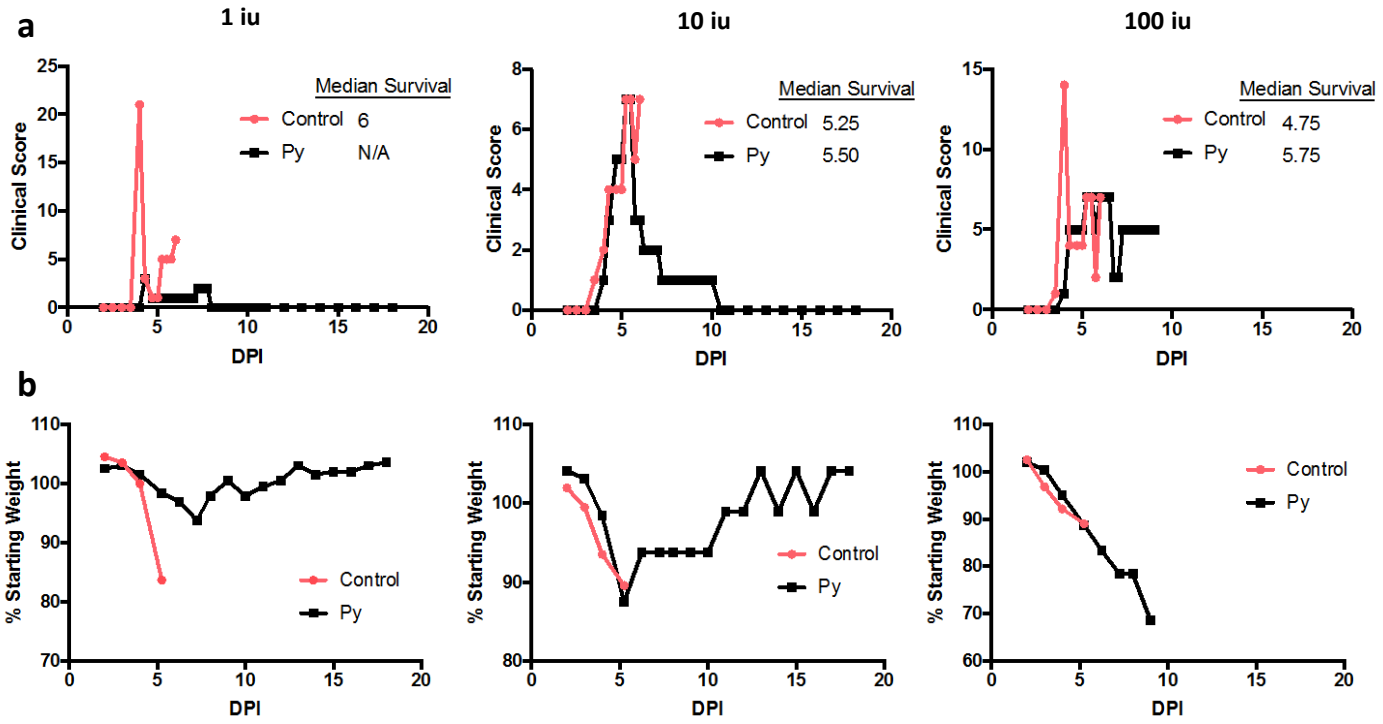

Figure S1: Acute *Plasmodium* infection in mice protects against EBOV challenge, Related to Figure 1. WT BALB/c mice were infected with $1x10^6$ *Plasmodium yoelli* iRBCs and challenged with 1, 10 or 100 iu ma-EBOV (Mayinga) 6 days later. Mice were monitored up to 4 times daily during the critical phase and morbidity was assessed. Shown are clinical scores **(a)** and weight loss **(b)**. Data are expressed as either aggregate clinical scores or average weights compiled from all surviving mice at the time of observation (n=1-7). Statistical analyses were not performed as each point represents an average value of a variable number of mice depending on the number of surviving animals.

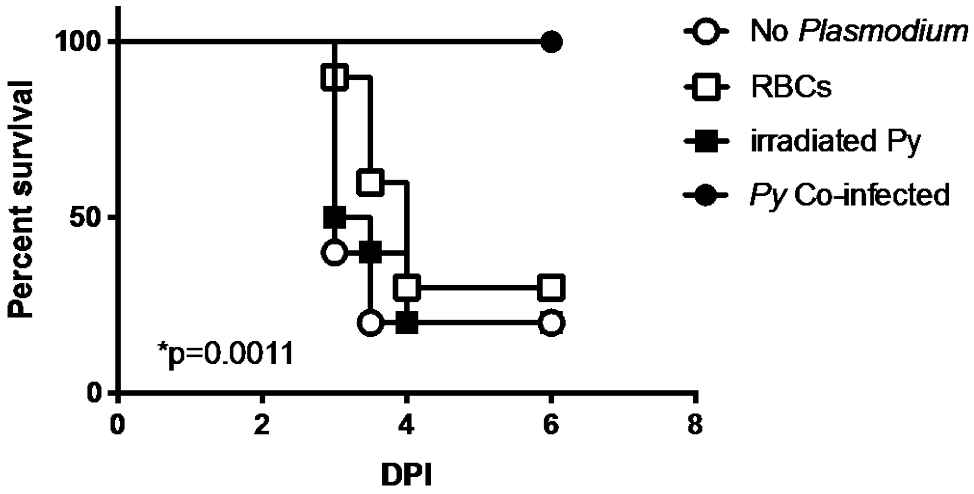

Figure S2: RBCs and irradiated *Py* iRBCs do not protect from rVSV/EBOV GP challenge, Related to Figure 2. C57BL/6 *Ifnar*$^{-/-}$ mice were inoculated i.v. with 10^6 of the indicated RBCs (*Py* infected, uninfected, or irradiated). Mice were challenged with a lethal dose of rVSV/EBOV GP 6 days later. Survival was monitored. n=10 per group.

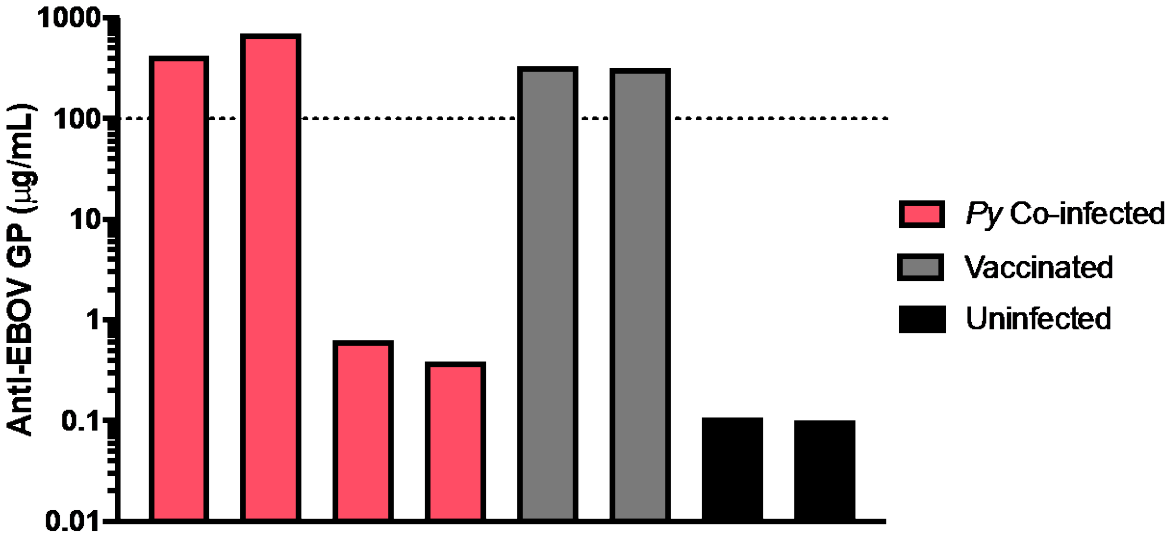

Figure S3: EBOV GP antibody production in *Py* infected mice, Related to Figure 2. C57BL/6 *Ifnar*$^{-/-}$ mice were infected i.v. with 1x10^{6} *Plasmodium yoelli* iRBCs. These mice were challenged with a dose of rVSV/EBOV GP that is lethal to naïve mice (red) or 1e3 EBOV pseudovirions (gray) 6 days later. Anti-GP antibodies in the serum at day 21 were measured by ELISA. Line represents the amount of antibody previously found to be predictive of protection against ma-EBOV challenge. Each bar represents an average of 2 replicates from a single mouse.

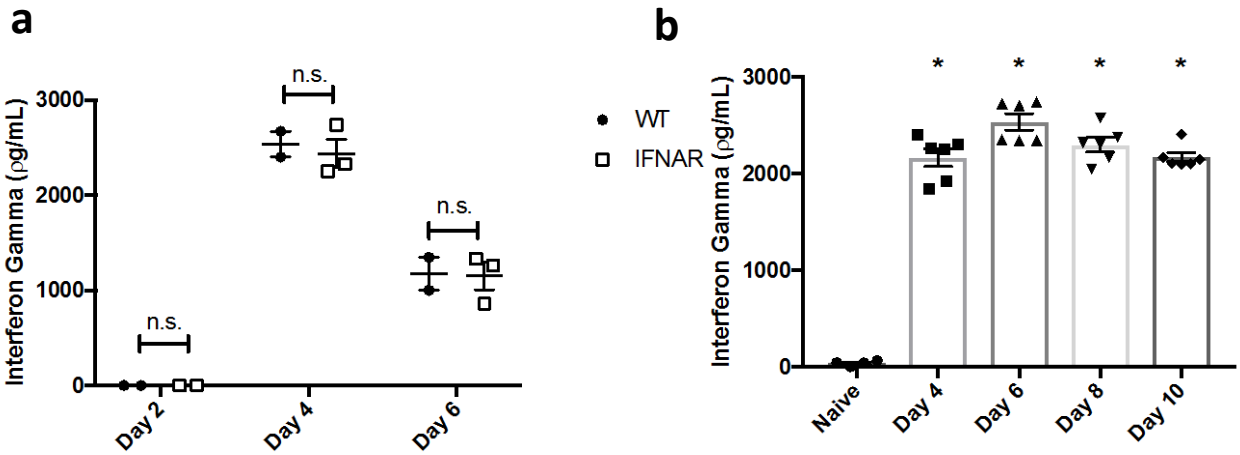

Figure S4: *Plasmodium yoelii* infection robustly stimulates serum IFN-γ levels in WT, *Ifnar*$^{-/-}$ and *Ifnar/Ifngr*$^{-/-}$ mouse strains, Related to Figure 3. a) WT BALB/c (closed squares) or BALB/c *Ifnar*$^{-/-}$ (open squares) mice were infected with 1x10^{6} *Plasmodium yoelli* iRBCs and IFN-γ production was measured by ELISA at the indicated times after infection. **b)** C57BL/6 *Ifnar/Ifngr*$^{-/-}$ mice were infected with 1x10^{6} *Plasmodium yoelli* iRBCs. At the indicated times after infection, serum was harvested and IFN-γ was measured by ELISA. For all experiments, * indicates $p<0.05$.

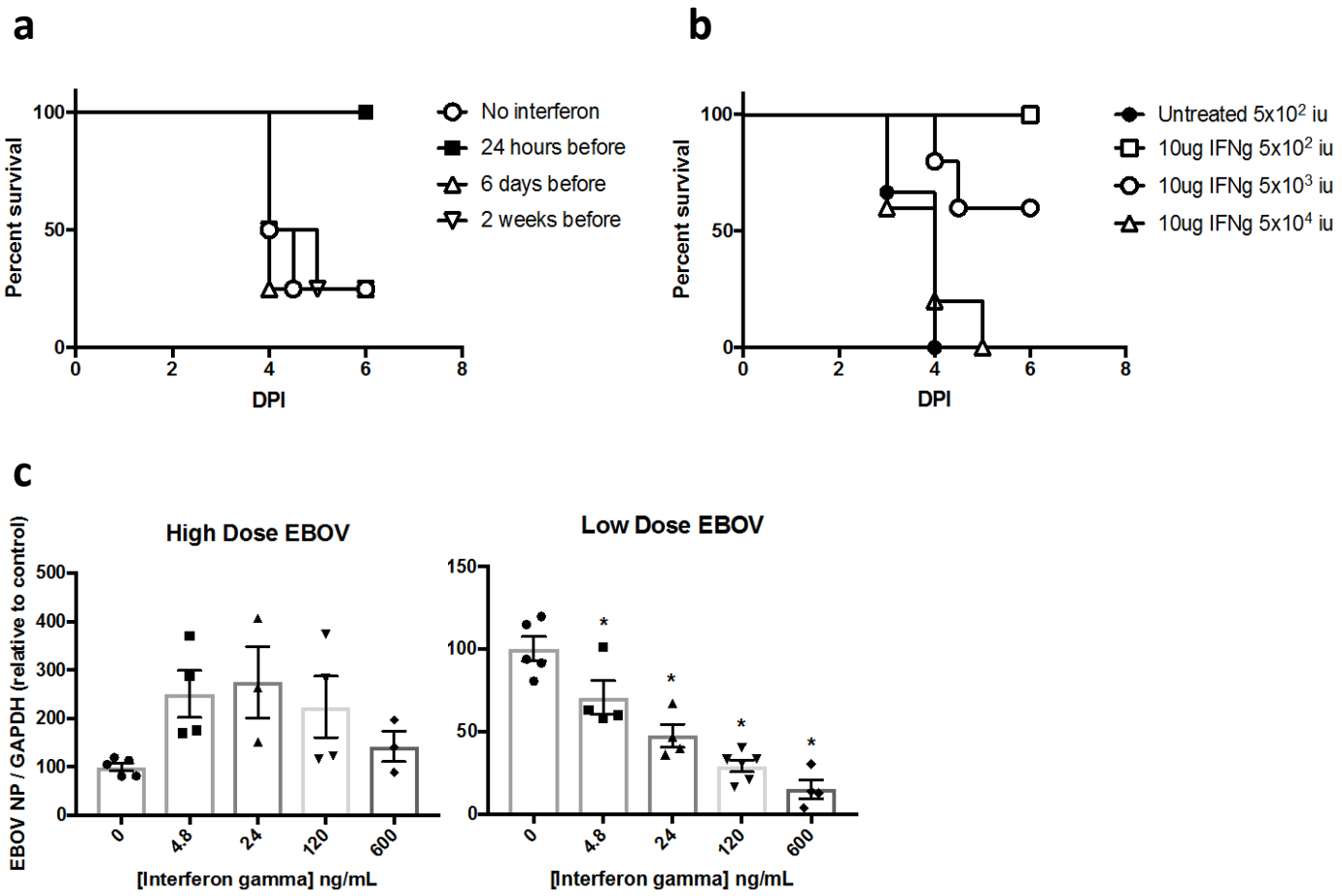

Figure S5: Amount and timing of rVSV/EBOV GP delivered is critical for IFN-γ mediated protection from infection, Related to Figure 5. a) *Ifnar*$^{-/-}$ mice were injected with 5µg IFN-γ at the indicated times prior to challenge with rVSV/EBOV GP. Mice were observed daily (n=4/group). **b)** *Ifnar*$^{-/-}$ mice were injected with 5µg IFN-γ 24 hours prior to challenge with the indicated amount of rVSV/EBOV GP (n=3 untreated, n=5 for each treated group). Mice were observed daily. **c)** *Ifnar*$^{-/-}$ pmacs were treated with varying concentrations of IFN-γ and infected with ma-EBOV under BSL-4 conditions 24 hours later. Cells were infected with either a high dose (2000 pfu) or low dose (200 pfu) of EBOV. RNA was isolated 24 hpi and virus replication was quantified by qRT-PCR for EBOV NP gene expression.