Uptake of *Plasmodium* hemozoin drives Kupffer cell death and fuels superinfections

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Supplementary Fig. 1: Kupffer cell death and cytokine deficient mice. (A) Line graphs correspond to MFI of F4/80^{high} Kupffer cells after overnight culture with natural hemozoin crystals. (B) TNF-\(\alpha\), IFN-\(\gamma\) and IL-10 mRNA expression in isolated liver nonparenchymal cells. (C) Percentage of Kupffer cells from Caspase 1/11\(^{-/-}\), TNF\(\alpha\)R\(^{-/-}\), IFN\(\gamma\)\(^{-/-}\) and RIP3\(^{-/-}\)Casp 8\(^{-/-}\) Gasdermin\(^{-/-}\) mice 7 days post \(P.\ chabaudi\) infection. Data are represented as mean ± SD. Statistical significance comparing infected and non-infected mice. (Student’s t test, **\(p < 0.01\)).
Supplementary Fig. 2: Histopathological scores. (A1) Hydropic degeneration, (A2) Steatosis, (A3) Hyperemia, (A4) Inflammatory infiltrate, (A5) Hemozoin and (A6) Nuclear alterations. Samples: 1) C57BL/6 non-infected. 2) $10^3$ MHV-3. 3) *P. chabaudi* (day 9). 4) *P. chabaudi* (day 9) + $10^3$ MHV-3. 5) $10^3$ MHV-3. 6) *P. chabaudi* (day 32). 7) *P. chabaudi* (day 32) + $10^3$ MHV-3.

Supplementary Video 1: Kupffer cells localization in sinusoids and cytoplasmatic arm-like protrusions. Three-dimensional reconstruction for an intravital microscopy Z-stack showing Kupffer cells (anti-F4/80; green) localization in sinusoids (anti-CD31; blue) and cytoplasmatic arm-like protrusions that can increase their area, allowing a better sampling of molecules and antigens in the circulation. 20x Objective.

Supplementary Video 2: Changes on morphology of Kupffer cells over *P. chabaudi* infection. Three-dimensional reconstruction for an intravital
microscopy Z-stack showing transition of morphology of an Kupffer "star-like" shape cell (anti-F4/80; green) to a round-shape morphology, lacking the classic protrusions. 20x Objective.

**Supplementary Video 3: Catching of E. coli by Kupffer cells of uninfected and infected mice.** Real-time movie showing E. coli (e-GFP; green) free flowing within sinusoids in co-infected group, while they were almost instantaneously arrested by Kupffer cells (anti-F4/80; purple) in mice which are not challenged with Plasmodium. 20x Objective.