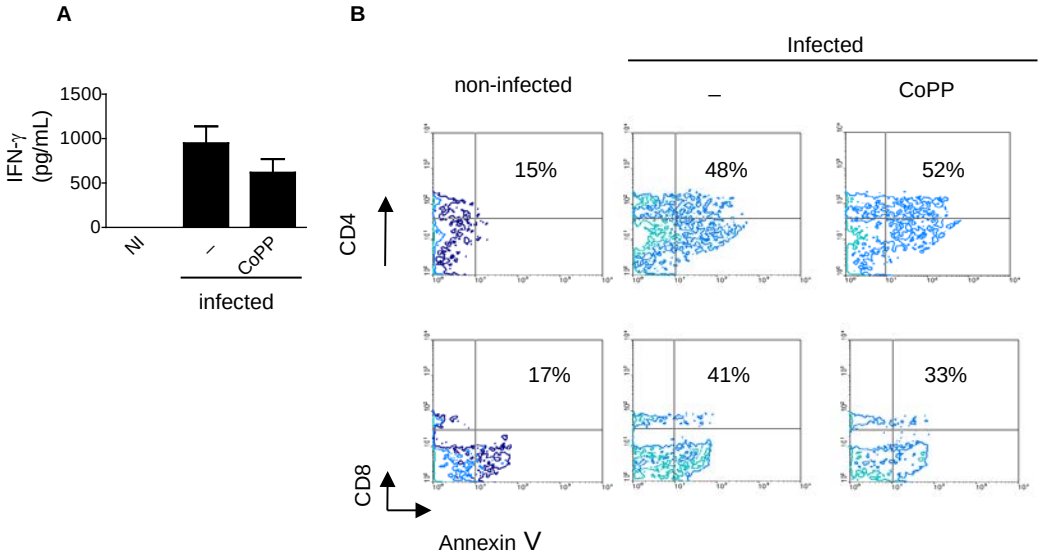
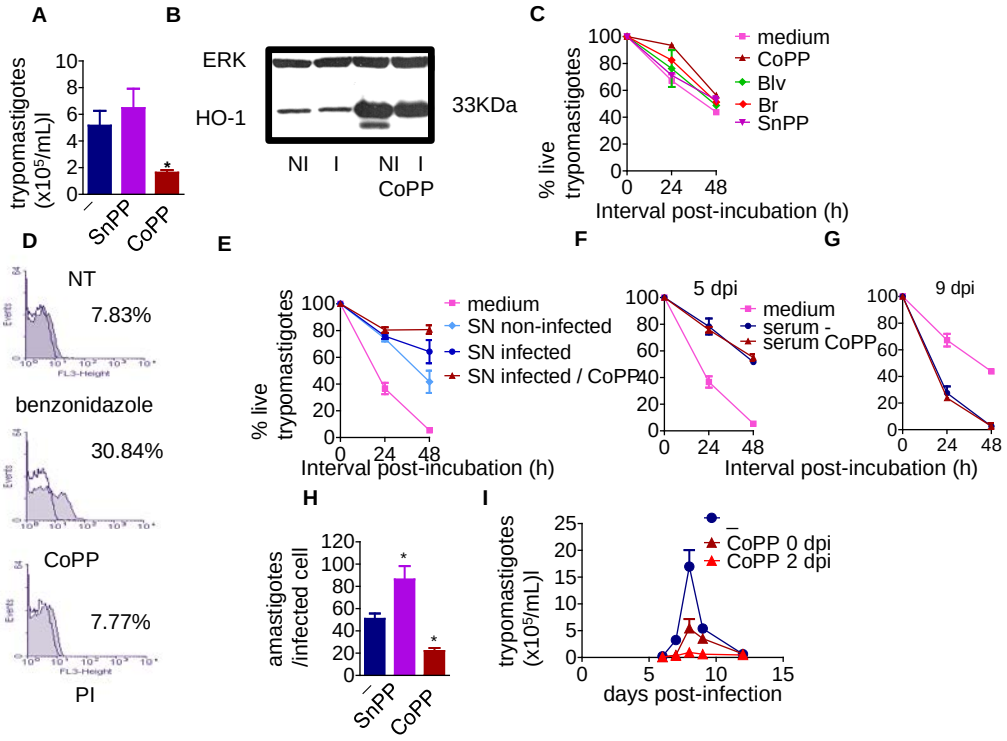
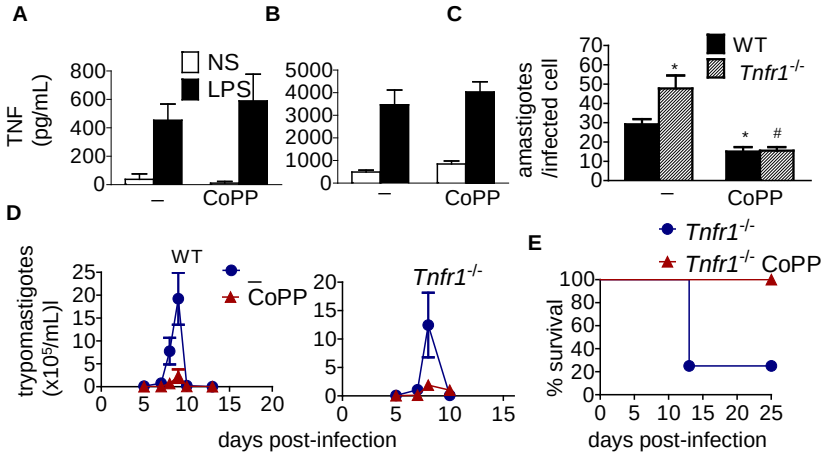


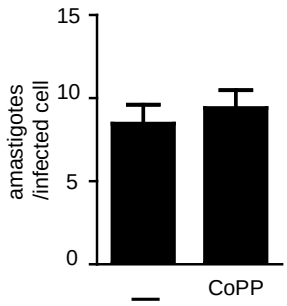
Supplemental Figure 1 – IFN-γ plasma levels and lymphocyte apoptosis in mice treated with metalloporphyrins. (**A**) Effects of treatment with CoPP in vivo on the mean plasma levels of IFNγ at 8 dpi. Samples were taken from 3-8 individual mice and evaluated by ELISA. (**B**) Effects of in vivo treatment with CoPP on the lymphocyte apoptosis, as detected by flow cytometry of splenic lymphocytes for annexin V and CD4 / CD8 at 8 dpi. The percentages inside the contour plots represent annexin V+ cells among the respective T cell subset (CD4 or CD8). Graphs are representative of at least 3 independent samples; each sample was derived from spleens of 3-5 pooled mice. NI= non-infected; - = infected untreated controls.



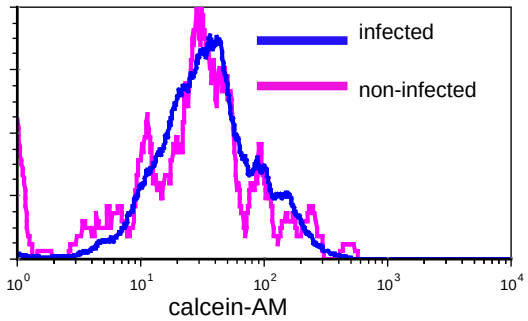
Supplemental Figure 2. CoPP does not directly kill trypomastigotes, interfere with intracellular amastigogenesis or induce secretion of a soluble killing factor. (**A**) Effects of treatment with CoPP and SnPP on the mean trypomastigote number in thioglycollate-elicited macrophages. Trypomastigotes were counted in supernatants after 5 days of cell culture. (**B**) Effects of CoPP and SnPP on the expression of HO-1, as shown by immunoblot. (**C**) Effects of treatment with CoPP, SnPP, biliverdin (Blv), or bilirubin (Bb) on mean trypomastigote survival, as assessed by motility. Three independent wells were counted for each point. (**D**) Effects of treatment with CoPP or benzonidazole (100µM) on the viability of trypomastigotes, assessed by iodide propidium (IP) exclusion (flow cytometry). (**E**) Effects of treatment with supernatants (SN) from derived macrophages as in (A) on trypomastigote survival. Three independent wells were counted for each point. (**F**) Effects of treatment with serum derived from mice treated in vivo with CoPP, SnPP or left untreated, at 5 dpi or (**G**) 9 dpi. (**H**) Effects of treatment with CoPP and SnPP on the mean amastigote number in thioglycollate-elicited macrophages; CoPP was present from 24h after infection on (post-amastigogenesis period). (**I**) Effects of treatment in vivo with CoPP starting 2 days after infection on the mean parasitemia (n=8). Controls treated with CoPP starting 2h after infection (usual regimen) are also shown. NI= non-infected; -=infected non-treated controls. Errors bars represent SEM. All experiments were repeated at least twice with similar results, except for F.



Supplemental Figure 3. TNF is not involved in CoPP-induced reduction of parasitism. (**A**) Effects of treatment in vivo with CoPP or SnPP on the mean TNF production by LPS-stimulated peritoneal macrophages at 8 dpi. Cells were pooled from 3-5 mice / group and results represent 3-4 such pools (ELISA). (**B**) Effects of treatment with CoPP or SnPP on the mean TNF production by LPS-stimulated thioglycollate-elicited macrophages. Results represent 3 independent wells (ELISA). (**C**) Effects of treatment with CoPP or SnPP on mean parasite burden of thioglycollate-elicited peritoneal macrophages derived from wild-types or *Tnfr1*$^{-/-}$ mice. Cells were stained with Giemsa and amastigotes were counted in each cell of a sample of 100 infected cells. (**D**) Effects of treatment in vivo with CoPP or SnPP on the mean parasitemia of wild-types and *Tnfr1*$^{-/-}$ (n=4-6 mice) and (**E**) mortality. NI = non-infected; - = infected untreated controls. Error bars represent SEM.



Supplemental Figure 4. Macrophage parasite burden does not change 6 h after treatment with CoPPi. Effects of treatment with CoPP on mean parasite burden of macrophages. Thioglycollate-elicited macrophages were infected with 10:1 trypomastigotes in vitro for 1 h and treated with CoPP for 6 h. Cells were stained with Giemsa and amastigotes were counted in each cell of a sample of 100 infected cells.



Supplemental Figure 5. Labile iron pool in infected versus non-infected cells. We used the quenching of calcein fluorescence as an indicator of labile iron presence. Thioglycollate-elicited macrophages were infected with 3:1 trypomastigotes in vitro for 12 h or left untreated, then washed and left untreated for additional 6 h. Cells were then scrapped off the plate and loaded with calcein as described in Methods.