Supplementary Figure 1

Disease severity after whole parasite immunization. To determine disease severity after challenge, A/J mice were immunized with decreasing doses i.e., 10^8, 10^3, 10^2 or 0 (adjuvant alone) of (AS) parasitized red blood cells (pRBC) in CpG-ODN or control-ODN. Two weeks after immunization, mice were challenged i.v. with 10^5 homologous (AS) pRBC and disease severity monitored using clinical scores. Scores assessed five parameters including: weight loss (0-2), posture (0-2), activity (0-2), fur texture (0-2) and percent parasitemia (0-2) for a maximal score of 10. Data for individual mice are shown**.** Results are representative of three independent experiments performed.

Supplementary Figure 2

Secretion of cytokines after CpG stimulation. (A) To determine the cell types responsible for the rapid cytokine secretion following by immunization, spleen cells from A/J mice immunized with 10^3 (AS) pRBC in CpG-ODN (grey histograms) or control-ODN (clear histograms) were harvested 48 hours after immunization and stained directly *ex vivo*. T-cells ($CD4^+$), NK cells ($DX5^+$), macrophages ($F4/80^+$), pDC ($CD11c^{dim}B220^+$), cDC ($CD11c^+B220^-$) and B-cells ($CD19^+$) were analyzed for secretion of IFN-γ, TNF-α, IL-12 and IL-10 by intracellular staining. Values indicate mean fluorescence intensity (MFI) on gated populations. **(B)** The profile of cytokine secretion induced was confirmed *in vitro* by culturing spleen cells from naïve A/J mice with 10^3 (AS) pRBC parasites in decreasing doses of CpG or control-ODN (10, 1.0, 0.1 or 0 mM). Two days later, supernatants were collected and levels of IFN-γ, TNF-α, IL-12p70, IL-12p40 and IL10. Results show average ± standard error of the mean. All results are representative of five mice per group and three independent experiments performed. Significant differences compared to no adjuvant controls are shown *$p<0.5$, **$p<0.01$ and ***$p<0.001$.

Supplementary Figure 3

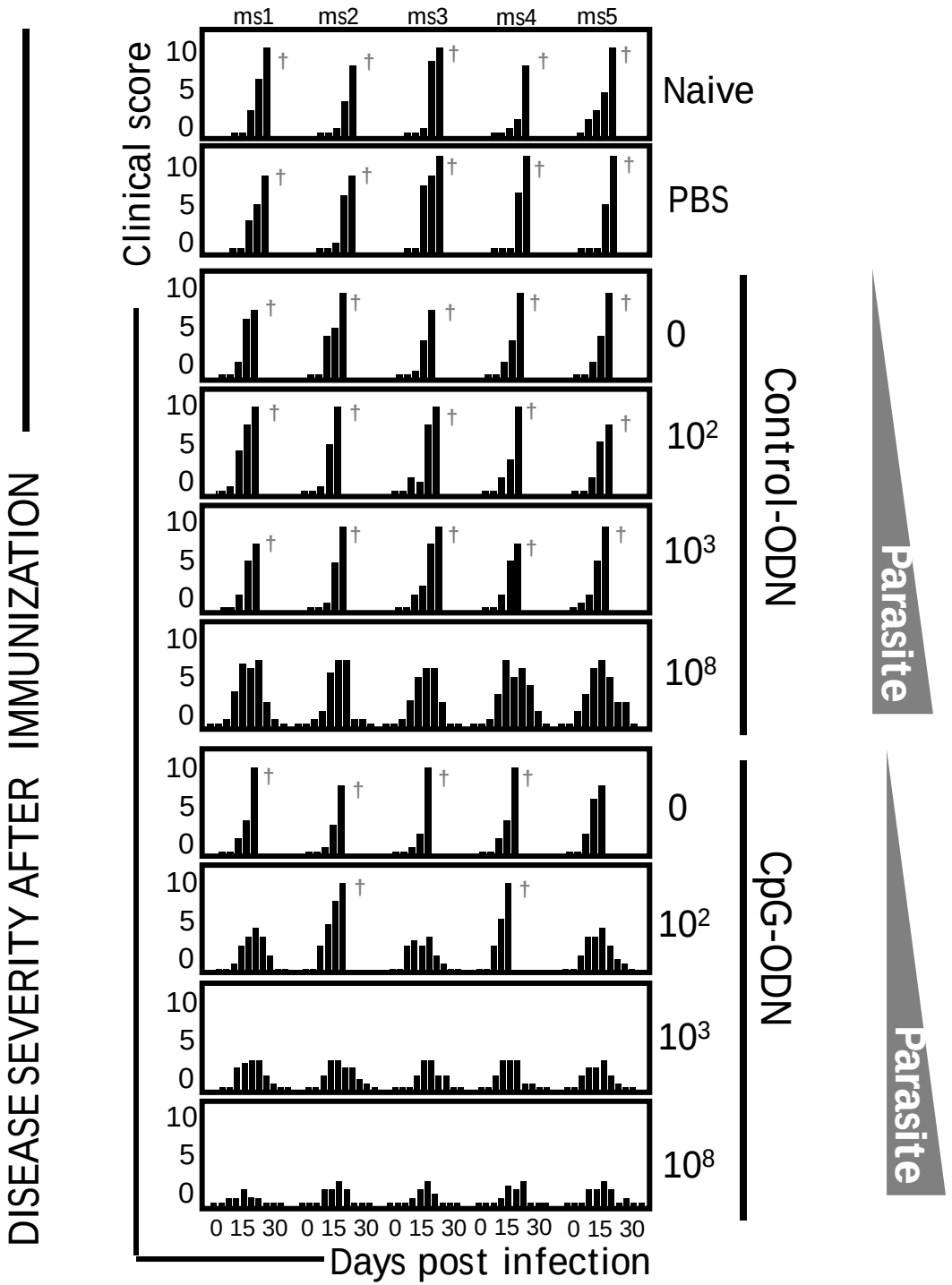
Protection induced by a single low dose immunization. To assess protection elicited by a single low-dose immunization in young mice, 2 week old A/J mice were immunized subcutaneously (s.c.), once with 10^3 (AS) pRBC in CpG-ODN or control-ODN. Two weeks later, mice were challenged i.v. with 10^5 homologous (AS) pRBC and **(A)** parasitemia or **(B)** disease severity monitored. Disease severity was assessed by performing clinical scores as described earlier. Data for individual mice are shown and are representative of three independent experiments performed.

Supplementary Figure 4

Protection induced by low dose intramuscular immunization. To assess protection elicited by immunization using a more human-compatible route, A/J mice were immunized intramuscularly (i.m.) three times, three weeks apart, with 10^3 (AS) pRBC in CpG-ODN or control-ODN. Two weeks later, mice were challenged i.v. with 10^5 homologous (AS) pRBC and **(A)** parasitemia or **(B)** disease severity monitored. Disease severity was assessed by performing clinical scores as described earlier. Data for individual mice are shown and are representative of three independent experiments performed.

Supplementary Table 1

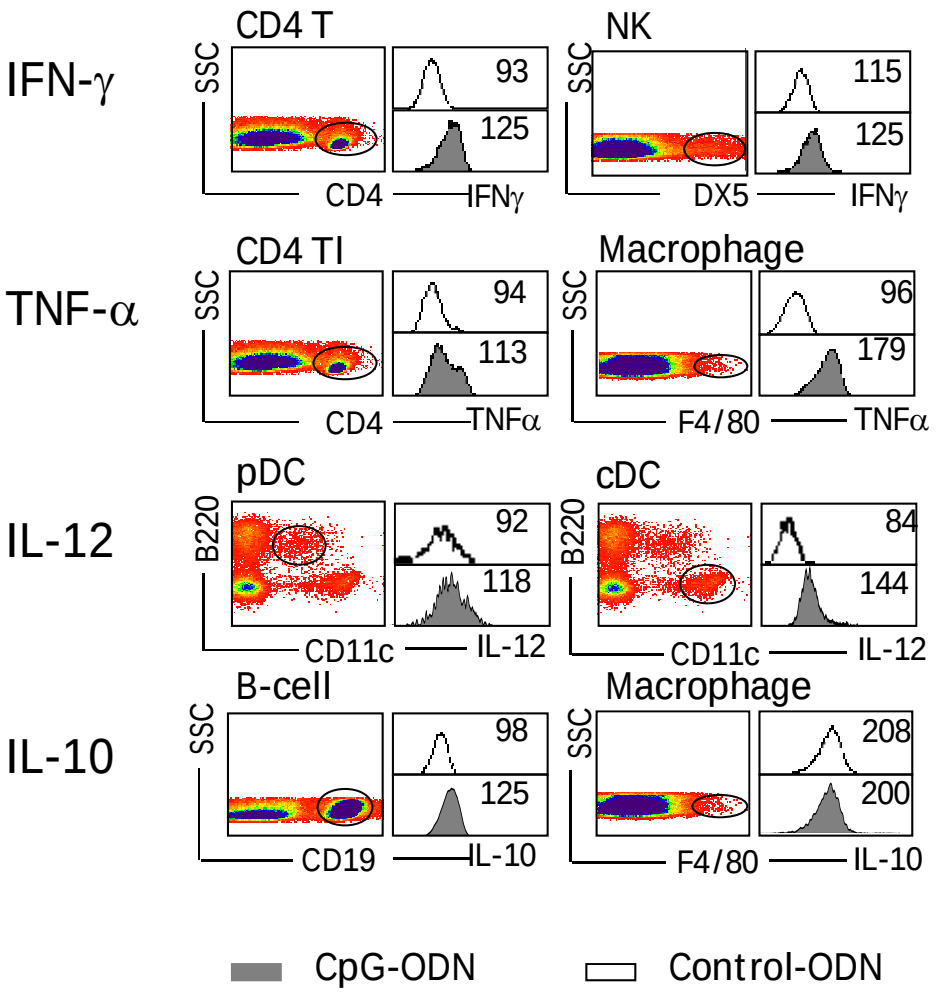
Disease severity assessment. Disease severity was assessed by performing clinical scores monitoring five parameters including: weight loss (0-2), posture (0-2), activity (0-2), fur texture (0-2) and percent parasitemia (0-2) for a maximal score of 10.



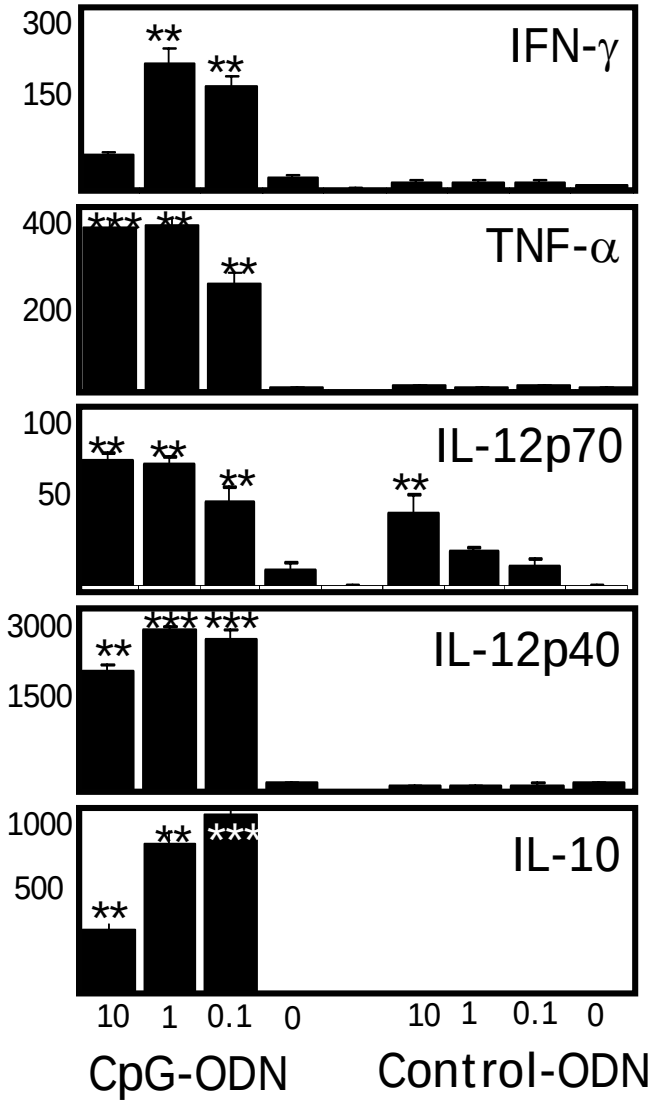
Supplementary figure 1

CYTOKINES AFTER CpG STIMULATION

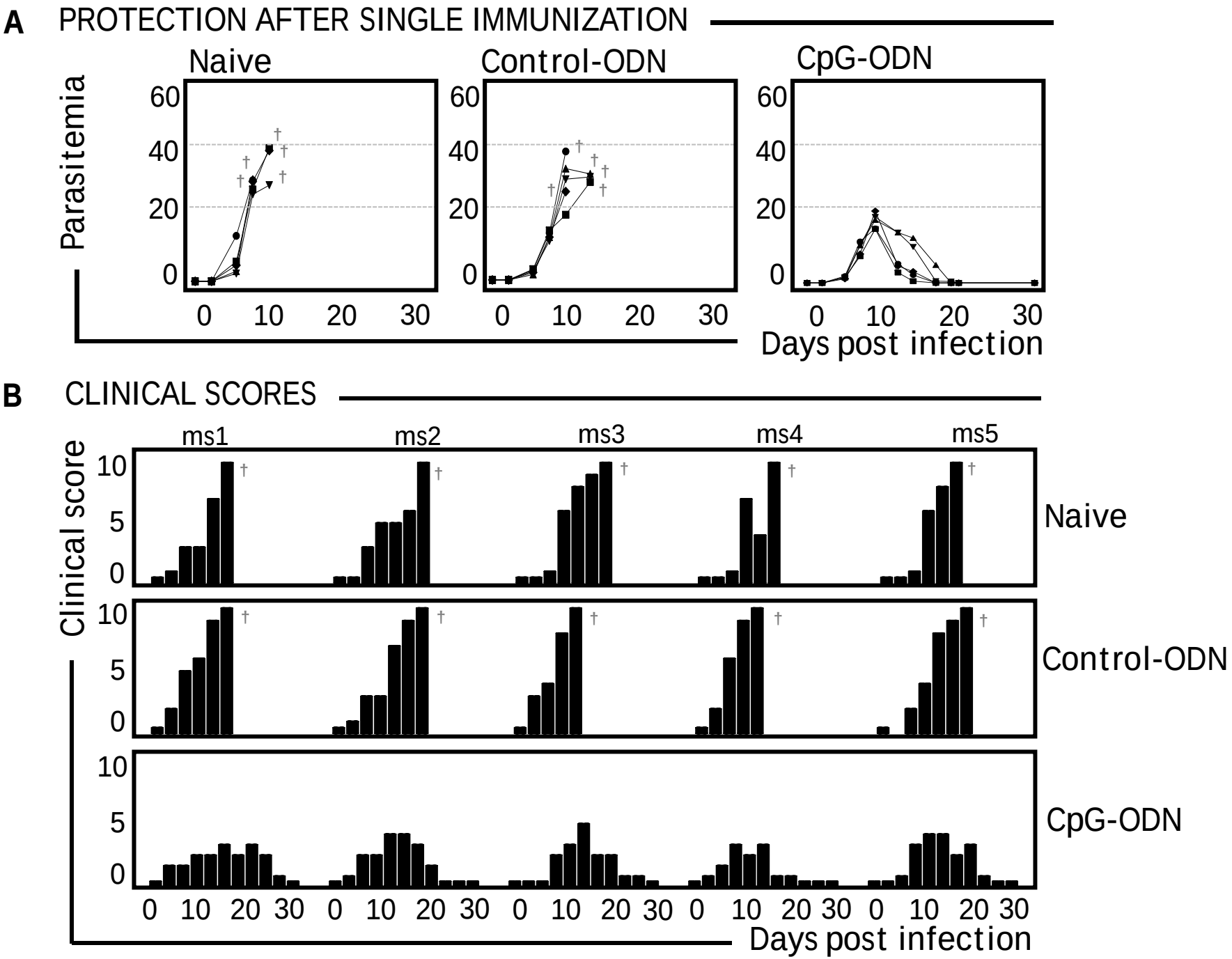
Ex vivo



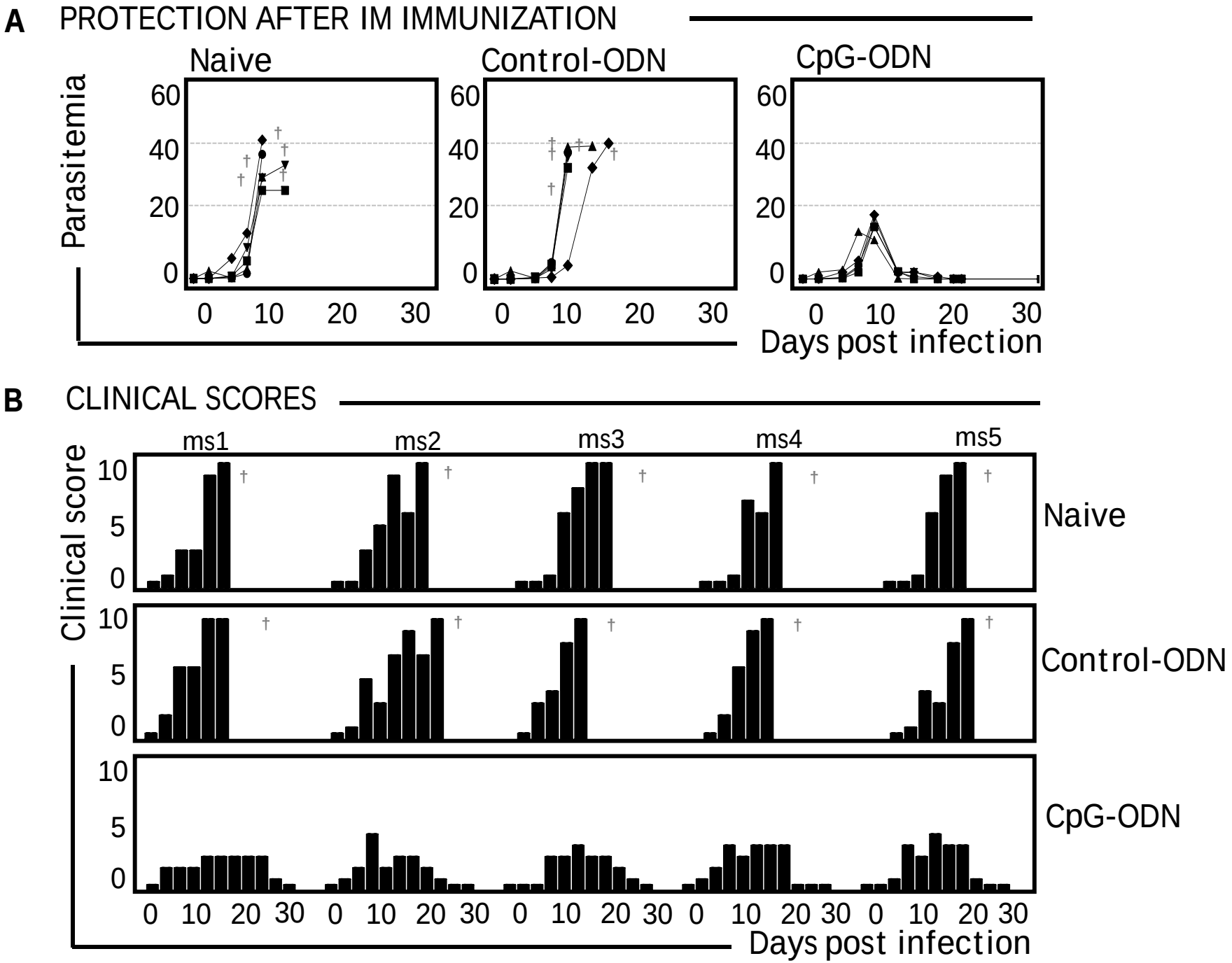
In vitro



Supplementary figure 2



Supplementary figure 3



Supplementary figure 4

CLINICAL PARAMETERS FOR DISEASE SEVERITY

Criteria	Grade 0	Grade 1	Grade 2
Weight loss	<10%	10-25%	>25%
Posture	Normal	Hunching noted only at rest	Severe hunching impairs movement
Activity	Normal	Mild to moderately decreased	Stationary unless stimulated
Fur texture	Normal	Mild to moderate ruffling	Severe ruffling/poor grooming
Parasitemia	<5%	5-20%	>20%

Supplementary table 1