

Supplementary Table 1. Pharyngitis and tonsillitis symptoms scoring system (Skinner et al. Microb Pathog 50:39-47 doi: [10.1016/j.micpath.2010.10.004](https://doi.org/10.1016/j.micpath.2010.10.004)).

Pharyngitis	Tonsillitis	Score
Normal	Normal tonsillar space, & oropharyngeal space	0
Mild erythema with hyperemic blood vessels	Approximate 25% increase in tonsil size; 0-25% occlusion of oropharyngeal space	1
More intense erythema and palatal petechiae	Approximate 50% increase in tonsil size; 25-50% occlusion of oropharyngeal space	2
Intense erythema with palatal petechiae and exudative tonsillitis	Approximate 75% increase in tonsil size; 50-75% occlusion of oropharyngeal space	3

Supplementary Table 2. Colonization, pharyngitis and tonsillitis symptoms in pilot experiments.

	NHP ID	Symptom	Day post-infection								
			0	1	2	3	7	14	21	28	
Pilot 1 (1x10 ⁷ CFU)	RKk15	Colonization**	-	+	+	+	+	+	+	+	+
		Pharyngitis	-	0	0	1	0	1	0	2	
		Tonsillitis	-	0	0	0	1	1	1	2	
	RUj15	Colonization**	-	-	-	-	-	-	-	-	-
		Pharyngitis	-	0	0	0	0	0	1	0	
		Tonsillitis	-	0	0	0	0	0	2	1	
Pilot 2 (5x10 ⁷ CFU)	RQi15	Colonization**	-	+	+	+	+	+	-	-	
		Pharyngitis	0	0	1	NR*	1	1	1	0	
		Tonsillitis	0	0	0	NR*	0	1	1	0	
	Rlp15	Colonization**	-	+	+	+	+	+	+	+	
		Pharyngitis	0	0	1	1	1	1	2	0	
		Tonsillitis	0	0	0	0	1	1	1	1	

*NR - not recorded; ** "+" = β hemolytic colonies detected, "-" = absence

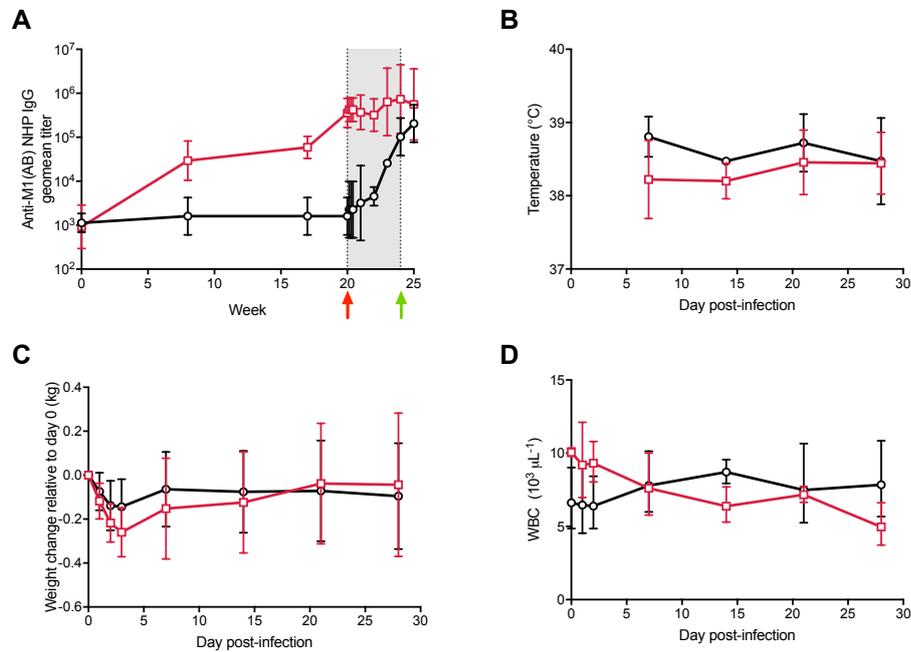


Fig. S1. Antibody response and animal welfare measures following infection of M1

immunized NHPs. (A) Serum samples from M1 (n=5, red line) and PBS (n=2, black line) immunized NHPs were collected before each immunization on weeks 0, 8 and 17 and post-infection on weeks 20 (days 0, 1, 2 and 3 post-infection), 21 (day 7 post-infection), 22 (day 14 post-infection), 23 (day 21 post-infection), 24 (day 28 post-infection) and 25 (one week after antibiotic treatment). Antibody titers at the time of infection (week 20) were significantly higher in M1 immunized NHPs compared to PBS immunized NHPs ($P < 0.0001$). Infection and antibiotic treatment days are marked by red and green arrows respectively. Duration of GAS infection is indicated by the gray shaded area. Values represent the geometric mean titer \pm geometric SD. Welfare of NHPs during the course of infection was monitored by measuring (B) rectal temperature, (C) weight, and (D) white blood cell counts. Symbols represent the mean values \pm SD.

Supplementary Table 3. Colonization scoring system (Dunne EM, et al. BMC Infect Dis 13:312, doi: [10.1186/1471-2334-13-312](https://doi.org/10.1186/1471-2334-13-312))

Colonization	Score
No β -hemolytic colonies	0
<10 β -hemolytic colonies in 1 st quadrant	1
>10 β -hemolytic colonies in 1 st quadrant	2
>10 β -hemolytic colonies in 1 st and 2 nd quadrants	3
>10 β -hemolytic colonies in 1 st , 2 nd and 3 rd quadrants	4
>10 β -hemolytic colonies in 1 st , 2 nd , 3 rd and 4 th quadrants	5

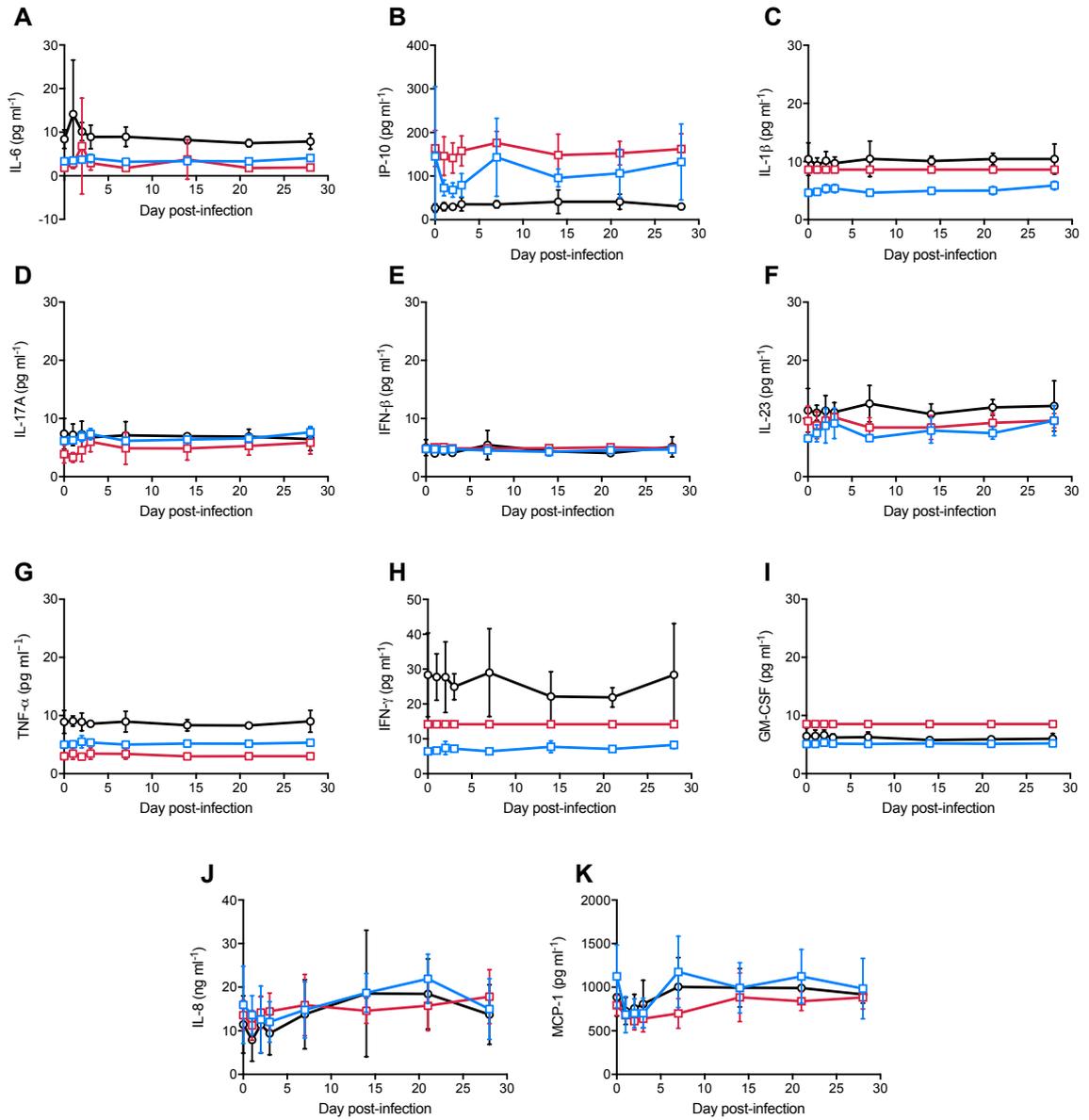


Fig. S2. Inflammation markers during GAS infection. Serum samples from Combo5 (blue line), M1 (red line) and PBS (black line) immunized NHPs collected during GAS infection were used to detect inflammation markers. A multiplex assay was used to detect (A) IL-6, (B) IP-10, (C) IL-1 β , (D) IL-17A, (E) IFN- β , (F) IL-23, (G) TNF- α , (H) IFN- γ , (I) GM-CSF, (J) IL-8 and (K) MCP-1. Samples were analyzed by duplicate, symbols represent the mean values \pm SD.

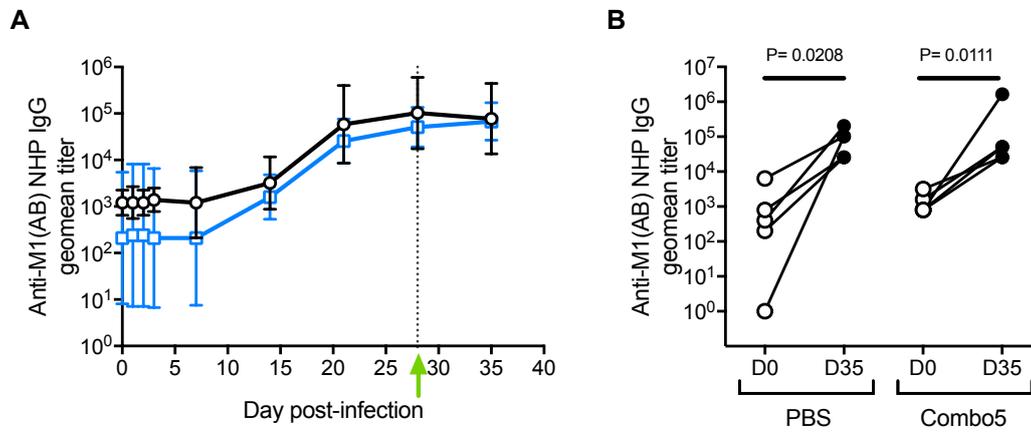


Fig. S3. Development of anti-M1 antibodies in response to infection. (A) Serum samples from PBS (n=5, black line) and Combo5 (n=5, blue line) immunized NHPs were collected at days 0, 1, 2, 3, 7, 14, 21, 28 and 35 post-infection. The green arrow indicates antibiotic treatment. Values represent the geometric mean titer \pm geometric SD. (B) Anti-M1 antibody titers at the end of the experiment (day 35 post-infection) were significantly higher than prior to infection (day 0) for all NHPs in PBS and Combo5 immunized NHPs.

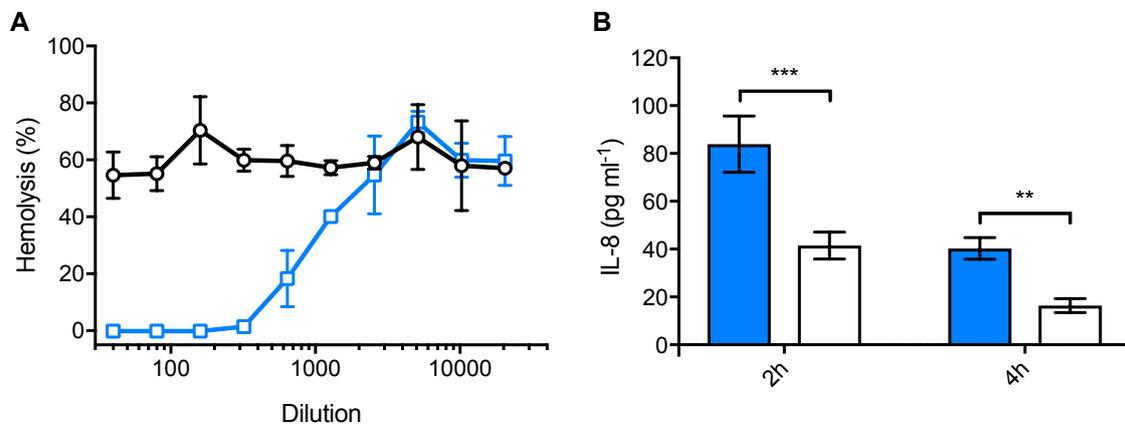


Fig. S4. Effector functions of Combo5 antibodies. (A) Pooled serum from Combo5 (blue line) immunized NHPs was able to inhibit SLO hemolytic activity compared to serum from PBS (black line) immunized NHPs. Hemolytic activity of SLO in the absence of serum was used as 100%. Values represent the mean \pm SD. (B) Serum from Combo5 immunized NHPs (blue bars) significantly inhibited SpyCEP mediated IL-8 degradation compared to serum from PBS immunized NHPs (white bars) after 2 and 4 h co-incubation with live GAS. Bars represent the mean \pm SD. Residual IL-8 concentrations were compared using a two-way ANOVA with Sidak's multiple comparisons test (** $P < 0.005$, *** $P < 0.001$).