

2 **Supplementary Information for**

3 ***Plasmodium* infection induces cross-reactive antibodies to carbohydrate epitopes on the** 4 **SARS-CoV-2 Spike protein**

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16 **This PDF file includes:**

17 Figs. S1 to S2

18 Table S1

Cohort	Country	Region	Malaria exposure status				Male (%)	Mean age, years (min, max)	Dates of collection	# Subjects
			Symptomatic (%)	Asymptomatic (%)	Endemic uninfected (%)	Non-endemic (%)				
CAM	Cameroon	Douala	8 (42.1%)	-	11 (57.9%)	-	11 (52.4%)	26.2 (2, 64)	July-Nov 2018	19
SEN1	Senegal	Kédougou	60 (50%)	-	60 (50%)	-	67 (55.8)	22 (1, 74)	July 2019	120
SEN2	Senegal	Thiès	67 (100%)	-	-	-	67 (100%)	10.9 (5, 16)	2015-2017	67
BUR1	Burkina Faso	Bama	-	13 (14.8%)	75 (85.2%)	-	11 (52.4%)*	2.7 (0.5, 4)	July-Aug 2017	88
GHA	Ghana	Kintampo	-	29 (64.4%)	16 (35.5%)	-	17 (38.6%)**	15.1 (3, 70)**	July 2007 and June 2010	45
BUR2	Burkina Faso	Bama	-	-	25 (100%)	-	14 (60.9%)***	32.6 (21, 43)****	Oct 2016-Feb 2017	25
COL1	Colombia	Urabá	-	-	61 (100%)	-	24 (39.3%)	31 (5, 80)	Nov 2015-Jan 2016	61
COL2	Colombia	Uramita	-	-	-	27 (100%)	6 (22.2%)	38 (5, 70)	Aug-Sept 2016	27
BRA	Brazil	Salvador	-	-	-	80 (100%)	30 (37.5%)	30.6 (5, 71)	Jan-Nov 2010	80
NEP	Nepal	Kavrepalanchok and Dolakha	-	-	-	71 (100%)	31 (44.3%)****	36.2 (4, 80)****	August 2013-June 2016	71
EBV	USA	Illinois	-	-	-	14 (100%)	5 (35.7%)	18.7 (18, 20)	Feb 2015-Oct 2018	14
Total			135 (21.9%)	42 (6.8%)	248 (40.2%)	192 (31.1%)	282 (51.6%)	22.2 (0.5, 80.6)	July 2007-July 2019	617

*In BUR1, data on sex was available for 21 of 88 subjects

**GHA had 1 subject with unknown age and sex

*** BUR2 had unknown sex and age for 2 subjects

****NEP had unknown sex and age for 1 subject.

Table S1. Patient Demographics

A

B

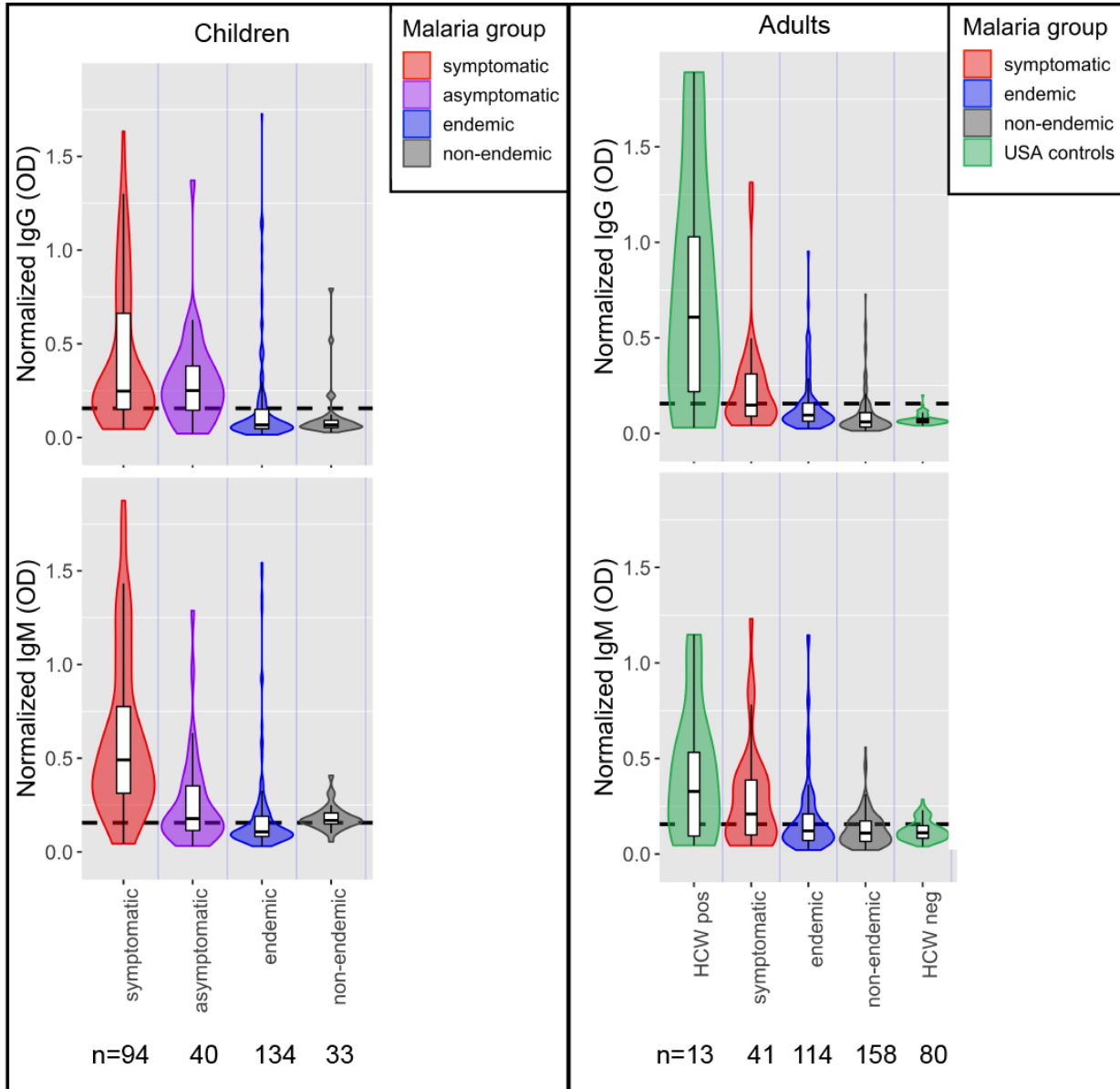


Fig. S1. Acute malaria infection in both adults and children is associated with S1 subunit Spike cross-reactivity.

Violin plots showing normalized IgG and IgM responses among a) children and b) adults with different malaria infection statuses. Children with acute malaria infection had significantly higher normalized IgG and IgM than uninfected children in malaria endemic areas (Welch Two Sample t-tests p-values < 0.0001 and < 0.0001, respectively), and adults with acute infection had significantly higher normalized IgG and IgM than uninfected adults in endemic areas (Welch Two Sample t-tests IgG p-values = 0.037 and IgM p-value = 0.025). Normalized IgG or IgM calculated by IgG or IgM OD divided by IgG or IgM OD of positive control (camelid monoclonal chimeric nanobody VHH72 antibody was IgG control, and pooled convalescent serum from SARS-CoV-2 patients was IgM control). Black dashed lines represent cutoffs for positivity, calculated from normalized IgG and IgM values from 80 healthy US healthcare workers controls without SARS-CoV-2 documented exposure (mean + 3 SDs).

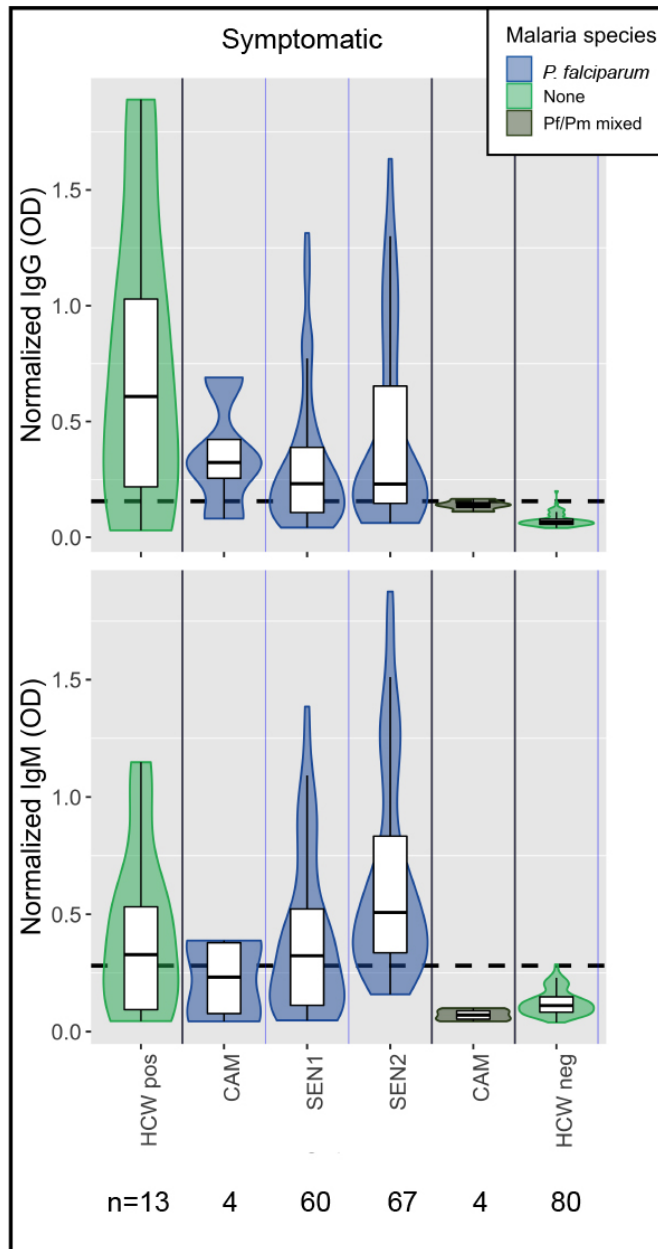
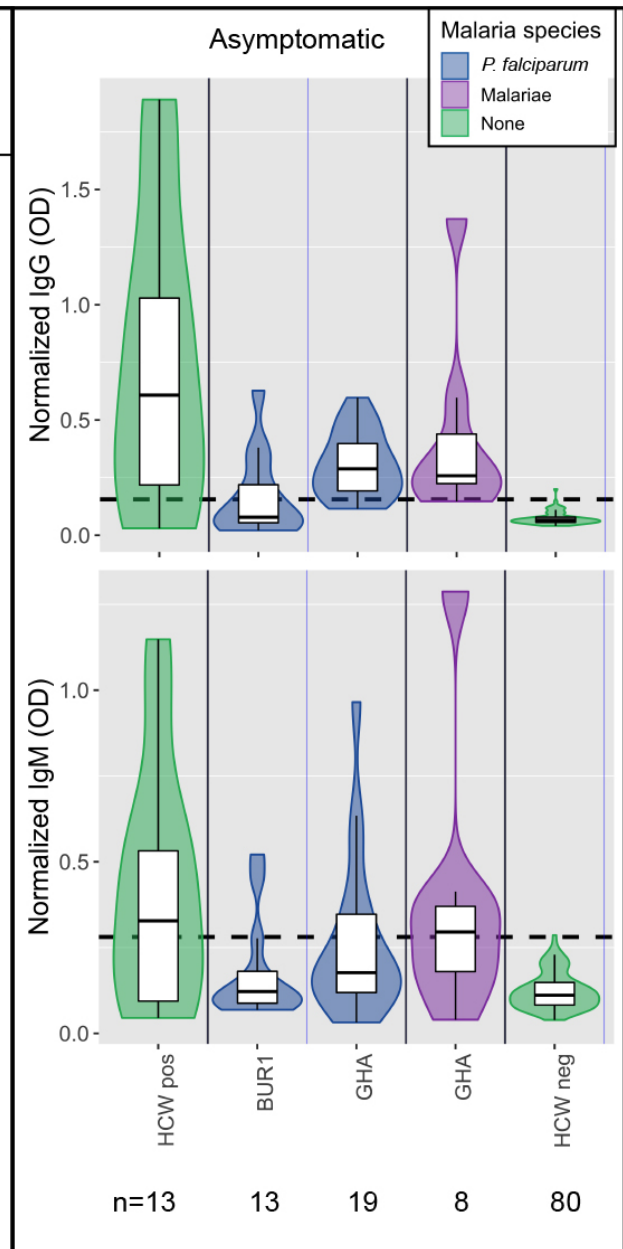
A**B**

Fig. S2. Plasmodium falciparum and P. malariae is associated with S1 subunit Spike cross-reactivity in symptomatic and possibly asymptomatic subjects.

Violin plots showing normalized IgG and IgM responses among a) symptomatic and b) asymptomatic subjects by species of malaria infection. For symptomatic patients, both IgG and IgM was significantly higher among subjects with *P. falciparum* (Welch Two Sample t-tests p-values<0.0001 for both IgG and IgM) and *P. falciparum*/*P. malariae* mixed infection (Welch Two Sample t-tests p-values<0.0001 for both IgG and IgM) than healthy US HCWs controls. For asymptomatic patients, both IgG and IgM was significantly higher among subjects with *P. falciparum* than healthy US HCWs controls (Welch Two Sample t-tests IgG p-value<0.0001 and IgM p-value=0.0063). Asymptomatic patients with *P. malariae* had significantly higher IgG but not IgM than healthy US HCWs controls (Welch Two Sample t-tests IgG p-values=0.044 and IgM p-value=0.106). Normalized IgG or IgM calculated by IgG or IgM OD divided by IgG or IgM of positive control (camelid monoclonal chimeric nanobody VHH72 antibody) was IgG control, and pooled convalescent serum from SARS-CoV-2 patients was IgM control). Black dashed lines represent cutoffs for positivity, calculated from normalized IgG and IgM values from 80 healthy US healthcare workers controls without SARS-CoV-2 documented exposure (mean + 3 SDs).