Supplementary Material

for

Cross-Reactive Immune Responses as Primary Drivers of Malaria Chronicity

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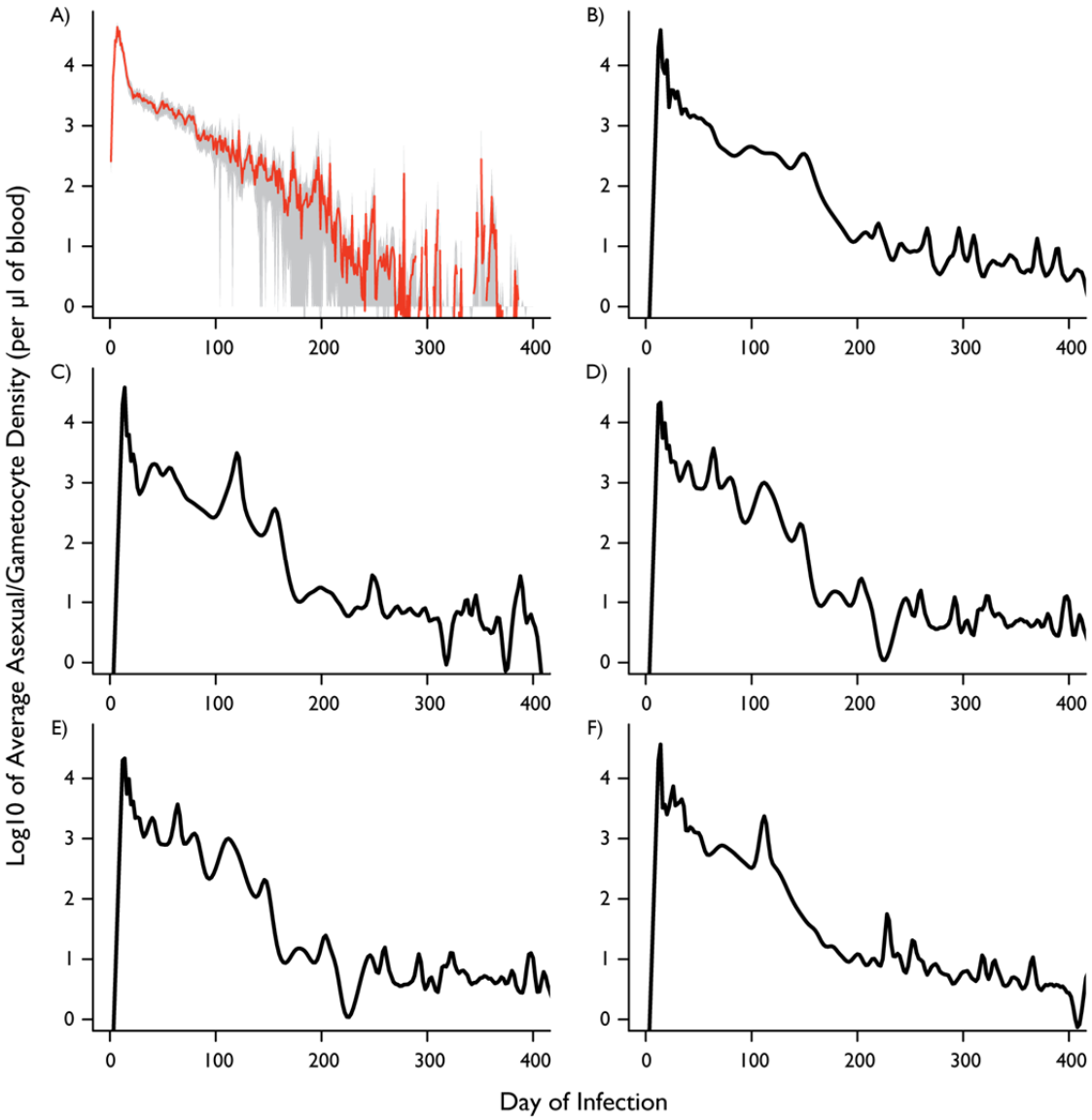
Running Head: Cross-Reactivity Drives Malaria Chronicity

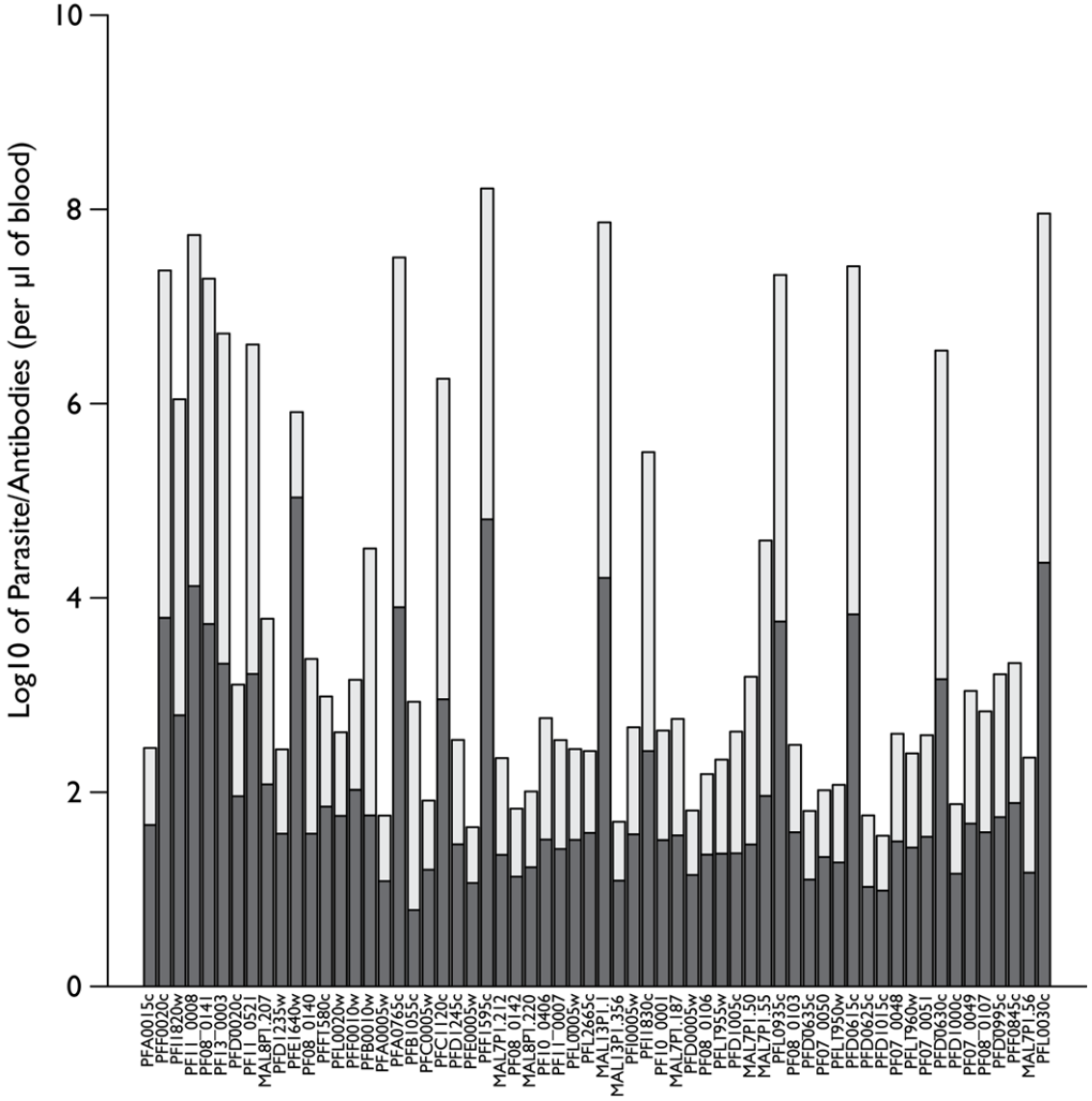
Supplementary Table 1				
	%ID	**Std Dev**	**Min**	**Max**
DBL/CIDR Domain 1				
Group A	29.3	23	6	98
Group B/A	49.3	3.7	6	98
Group B	38.8	5.1	6	98
Group B/C	32.9	11.2	6	63
Group C	37.4	8.4	6	63
DBL/CIDR Domain 2				
Group A	27.1	22.6	8	100
Group B/A	33.7	6	8	100
Group B	35.4	8.5	8	100
Group B/C	37.8	8.3	8	75
Group C	45.2	9.5	8	75
DBL/CIDR Domain 3				
Group A	29.3	23	6	98
Group B/A	49.3	3.7	6	98
Group B	38.8	5.1	6	98
Group B/C	32.9	11.2	6	63
Group C	37.4	8.4	6	63
PfEMP1				
Group A	36.3	14.4	17	91
Group B/A	32.2	7.4	17	91
Group B	46.7	3.4	16	91
Group B/C	42.4	4.3	16	53
Group C	44.9	4.8	16	53

Predicted protein sequences were obtained from PlasmoDB (http://www.plasmodb.org) for all 62 var genes in the 3D7 reference strain. To calculate the similarity of different domains, we obtained domain predictions from the VarDom 1.0 Server (1). Predicted protein sequences of each domain were then aligned and an identity matrix calculated using clustalX2 (2). We then calculated the average identity and standard deviation of each group.



Supplementary Figure 1: Comparison of representative infection dynamics from model with malariatherapy data

Archival data of malariatherapy–the purposeful infection of humans with *P. falciparum* to treat neurosyphilis (3)–were averaged over each day to create a mean daily parasite density (A). This represents the average dynamics of an infection (the grey area is the confidence interval around the average). Panels B-F are representative runs of the model. Source: *Plasmodium falciparum* malaria therapy data of neurosyphilis patients in Georgia and South Carolina (as described in 3). William E. Collins gave us permission to use the data and Klaus Dietz sent us the data.



Supplementary Figure 2: Generation of VSA-specific Immune Effectors
Immune effectors are generated from parasite interactions with undifferentiated as well as primed immune effectors. Cross-immunity is assumed to be due to subdominant epitopes that have a higher binding affinity for other VSAs than for the VSA for which they were initially activated. Through the feedback mechanisms of the immune system, we assume that this results in the generation of new immune effectors that are specific for the new VSA. This chart represents the immune effectors created through VSA-specific interactions (dark) and through cross-immune interactions (light).

References

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