Supplementary Table 1. Age distribution of severe subgroups and uncomplicated malaria.

Clinical presentations	Age, median [IQR] months
Uncomplicated malaria	50 [34-62]
Severe anaemia	37 [26-54]
Hyperparasitaemia	45 [32-59]
Cerebral malaria	47 [40-63]
Acidosis	40 [32-47]

IQR: Interquartile range.

Supplementary Table 2. Number of children with different combinations of severe malaria presentations and percentage out of total children with severe malaria (n=141).

Severe presentations	Count (percentage)
HP+SMA +HL+CM+RD	1 (<1%)
HP+SMA+HL+AC	1 (<1%)
HP+SMA+HL	4 (3%)
HP+SMA+RD	1 (<1%)
HP+SMA	7 (5%)
HP+HL+CM	4 (3%)
HP+HL+AC+RD	1 (<1%)
HP+HL+AC	5 (4%)
HP+HL	5 (4%)
HP+HL+RD	1 (<1%)
HP+CM	3 (2%)
HP+RD	2 (1%)
HP	22 (15%)
HP+AC+HG	1 (<1%)
SMA+HL+CM+AC	1 (<1%)
SMA+HL+AC	1 (<1%)
SMA+HL	1 (<1%)
SMA+RD	1 (<1%)
SMA	16 (11%)
HL+RD	1 (<1%)

HL	2 (1%)
CM+RD	2 (1%)
CM	5 (4%)
AC+RD	1 (<1%)
AC	3 (2%)
RD	3 (2%)
Other	45 (32%)

HP = hyperparasitaemia, SMA = severe malarial anaemia, HL = hyperlactaemia, CM = cerebral malaria, RD = respiratory distress, AC = metabolic acidosis, HG = hyperglycaemia, Other = severe malaria that is not represented by any of the other categories.

Supplementary Table 3. Summary of linear associations between participant group and antibody responses represented in volcano plots. Linear regression was performed between participant group (uncomplicated malaria and severe malaria) and age (as co-variates) with antibody responses, at two timepoints (acute and convalescence). Associations with $p<0.05$ and greater than two-fold difference in geometric mean ratio are summarized.

Recombinant Antigen	Detector/ Assay
Acute uncomplicated > acute severe malaria	
CIDRα1.4	IgG, IgG1, IgG3, FcγRIIIb, FcγRIIIa, c1q
CIDRα1.5	IgG3
CIDRα1.6b	IgG, IgG1, IgG3, FcγRIIIb
CIDRα2.4	IgG, IgG1, IgG2, FcγRIIIb
DBLβ13 (SM25)	IgG3
DBLβ3 (M1)	IgG, IgG3, FcγRIIIb
DBLβ5 (P1014)	IgG3
DBLδ1 (UM2)	IgG
IT4VAR13	ADNP
Acute uncomplicated < acute severe malaria	
DBLβ5 (P1011)	FcγRIIb
Convalescent uncomplicated > convalescent severe malaria	
CIDRα1.4	FcγRIIb, c1q
CIDRα1.5	FcγRIIb, FcγRIIIa, FcγRIIIb
CIDRα1.7	FcγRIIb

CIDRα2.1	FcγRIIb
CIDRα2.4	FcγRIIb
CIDRα3.3	FcγRIIb
CIDRγ12	IgG2, FcγRIIb, FcγRIIIa, FcγRIIIb
DBLβ13	IgG3
DBLβ3 (M1)	FcγRIIIa
DBLβ3 (M6)	FcγRIIIa
DBLβ5 (P1011)	FcγRIIb
DBLβ6 (N32)	FcγRIIb
DBLδ1 (UM2)	c1q
DBLδ1 (SM6)	IgG3, FcγRIIa, FcγRIIb, FcγRIIIa, FcγRIIIb
DBLδ1 (SM9)	FcγRIIb, FcγRIIIb
DBLε9 (SM12)	FcγRIIIa
DBLζ4 (SM15)	IgG2, FcγRIIa, FcγRIIb, FcγRIIIa
DBLε5 (SM22)	IgG, IgG1, FcγRIIa, FcγRIIb, FcγRIIIa, FcγRIIIb
Convalescent uncomplicated < convalescent severe malaria	
DBLβ3 (M6)	c1q
DBLβ5 (P1011)	c1q
CIDRγ12 (SM26)	c1q

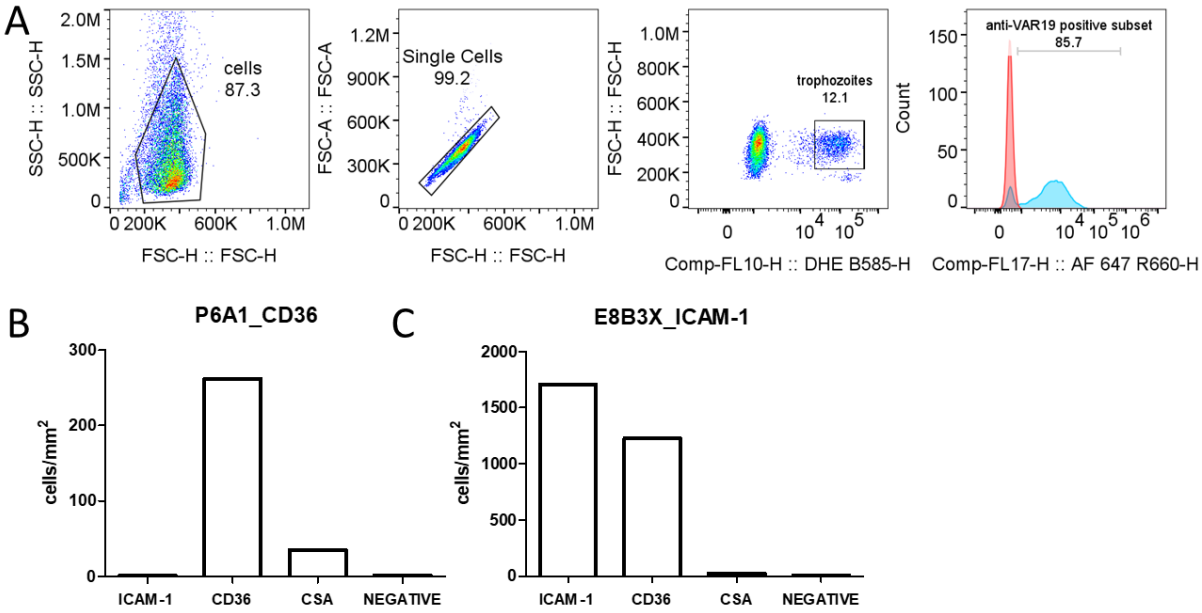
Supplementary Table 4. Summary of linear associations between participant group and antibody responses represented in volcano plots. Linear regression was performed between timepoints (acute and convalescence) and age (as co-variates) with antibody responses, amongst children with severe malaria and uncomplicated malaria. Associations with $p<0.05$ and greater than two-fold difference in geometric mean ratio are summarized.

Recombinant Antigen	Detector/ Assay
Acute uncomplicated < convalescent uncomplicated	
DBLβ7 (N30)	c1q
DBLβ3 (P1021)	c1q
DBLβ5 (P1014)	c1q
CIDRα1.1	c1q
CIDRα1.8a	c1q
CIDRα1.6b	c1q
CIDRα1.7	c1q
CIDRα1.5	c1q
CIDRα2.1	c1q
CIDRα2.2	FcγRIIIa, c1q
CIDRα2.4	IgG2
CIDRα3.3	c1q
DBLβ1 (M9)	c1q
DBLβ3 (N27)	c1q
DBLε5 (SM22)	c1q

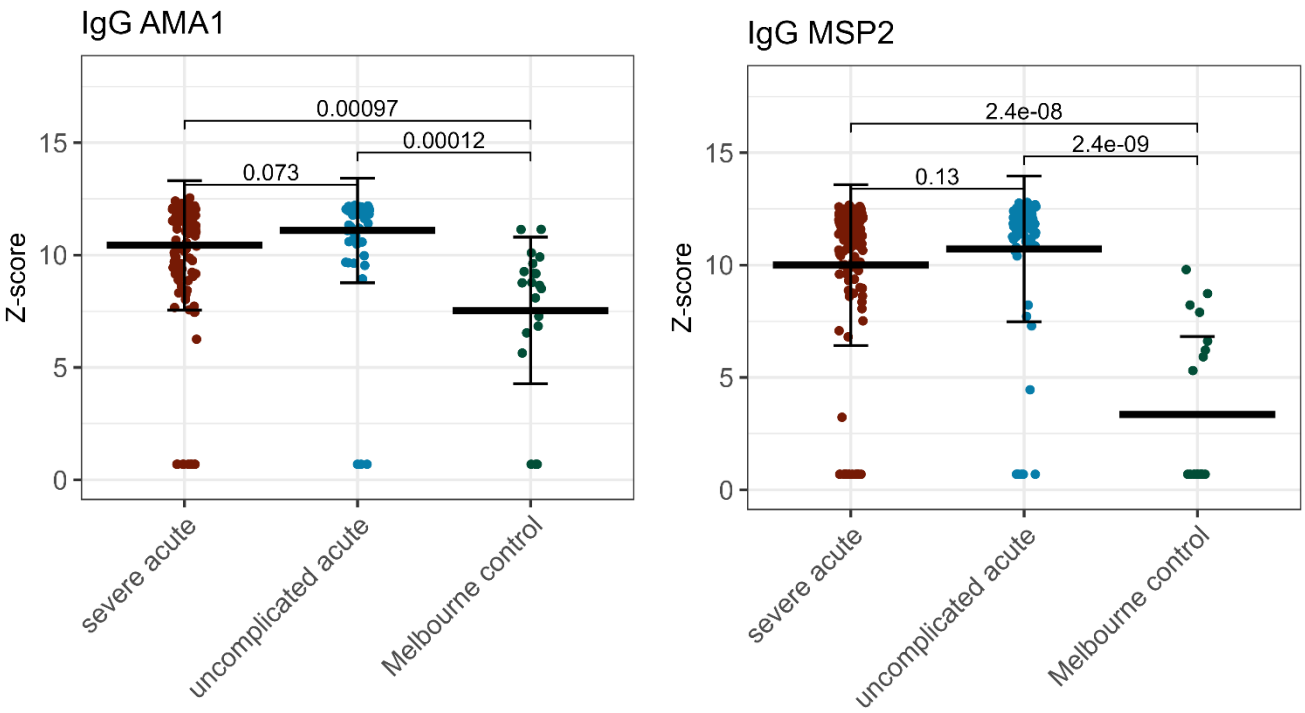
DBLβ13 (SM25)	IgG2, FcγRIIIa c1q
Acute uncomplicated > convalescent uncomplicated	
CIDRα1.6b	FcγRIIIb
CIDRα1.7	FcγRIIIb
CIDRα2.4	FcγRIIIb
DBLβ6 (N32)	FcγRIIIb
DBLβ7 (N30)	FcγRIIIb
DBLβ1 (M9)	IgG3
DBLδ1 (SM6)	FcγRIIIb
DBLδ1 (UM2)	FcγRIIb, FcγRIIIb, c1q
DBLδ1 (SM9)	IgG3, FcγRIIb, FcgRIIIb
DBLε9 (SM12)	FcγRIIIb, FcγRIIb
DBLζ4 (SM15)	FcγRIIb, FcγRIIIb
DBLε5 (SM22)	FcγRIIb, FcγRIIIb
DBLβ13 (SM25)	IgG3, FcγRIIb, FcgRIIIb
CIDRγ12 (SM26)	IgG3, FcγRIIb, FcγRIIIb
3D7VAR04	ADNP
IT4VAR13	ADNP
Acute severe < convalescent severe	
CIDRα1.1	C1q
CIDRα1.4	IgG1
CIDRα1.5	c1q
CIDRα1.6b	IgG1, c1q

CIDRα1.8a	c1q
CIDRα2.1	c1q
CIDRα2.2	c1q
CIDRα2.4	IgG2
CIDRα3.3	c1q
DBLβ3 (M1)	c1q
DBLβ3 (M6)	c1q
DBLβ1 (M9)	c1q
DBLβ3 (P1021)	c1q
DBLβ5 (P1011)	c1q
DBLβ5 (P1014)	c1q
DBLβ3 (N27)	c1q
DBLβ7 (N30)	c1q
DBLε9 (SM12)	IgG2
DBLε5 (SM22)	c1q
DBLβ13 (SM25)	IgG2, c1q
CIDRγ12 (SM26)	c1q
Acute severe > convalescent severe	
CIDRα1.5	FcγRIIIb, FcγRIIb
CIDRα1.6b	FcγRIIb
CIDRα1.7	FcγRIIIb, FcγRIIb
CIDRα1.8	FcγRIIb
CIDRα2.1	FcγRIIb

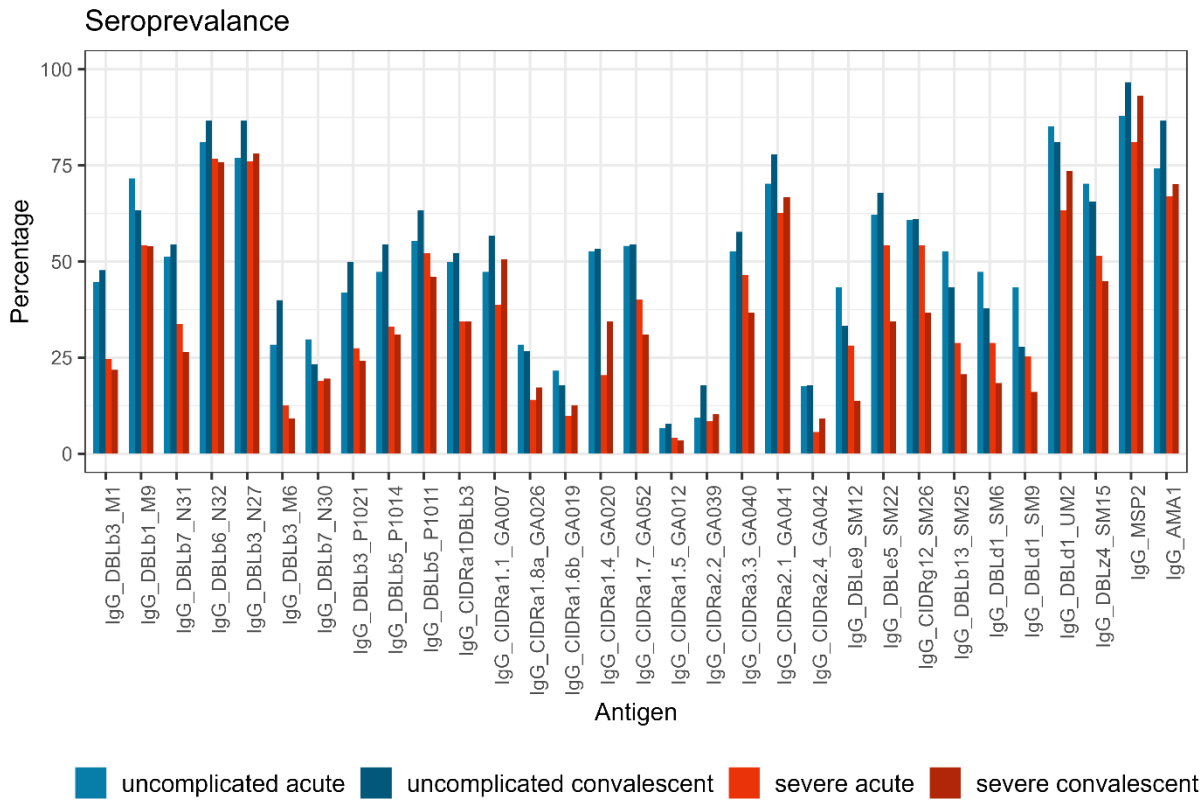
CIDRα2.4	FcγRIIb
CIDRα3.3	FcγRIIIb, FcγRIIb
CIDRα1DBLβ3	FcγRIIb
DBLβ1 (M9)	FcγRIIb
DBLβ6 (N32)	FcγRIIb, FcγRIIIb
DBLβ5 (P1011)	FcγRIIb
DBLδ1(UM2)	FcγRIIb, FcγRIIIb, c1q
DBLδ1 (SM6)	FcγRIIb, FcγRIIIb
DBLδ1 (SM9)	FcγRIIb, FcγRIIIb
DBLε9 (SM12)	FcγRIIb, FcγRIIIb, FcγRIIIa
DBLζ4 (SM15)	FcγRIIb, FcγRIIIb
DBLε5 (SM22)	FcγRIIb, FcγRIIa, FcγRIIIb, FcγRIIIa
DBLβ13 (SM25)	FcγRIIb, FcγRIIIb
CIDRγ12 (SM26)	FcγRIIb, FcγRIIIb



Supplementary Figure 1. A) Representative gating strategy used to determine the phenotype of parasite lines selected for expression of IT4VAR19, IT4VAR13 or PFD1235w. Infected erythrocytes were identified by Forward Scatter (FSC) and Side scatter (SSC) and single cells were identified by FSC Height and Area. IE were identified by dihydroethidium bromide (DHE) labelling. Cells were labelled with the anti-DBL antibody for the respective PfEMP1 variants and a AF647 secondary antibody. The percentage of IE recognized by the relevant anti-PfEMP1 antibodies and AF647 secondary antibody was determined relative to the negative control (DHE and secondary antibody only labelled cells). To confirm the binding phenotypes of B) E8B3X and C) P6A1, the relative binding of IE to recombinant ICAM-1, CD36 and CSA receptors, and no receptor control (negative), was counted by microscopy as cells per mm2.



Supplementary Figure 2. IgG responses to recombinant A) AMA1 protein and B) MSP2 protein, in children with acute severe malaria (red) and uncomplicated malaria (blue) and non-malaria exposed controls from Melbourne, Australia (green). Y-axis represents Z-score of IgG titres measured by multiplex assay, after log10 transformation. Means and one standard deviation from the mean are shown by horizontal bars and associated error bars. Welch's t-test P-values are shown for comparisons between groups.



Supplementary Figure 3. Percentage of children with IgG seropositivity for recombinant proteins, amongst children with uncomplicated malaria (blue) or severe malaria (red), with acute illness or in convalescence. Seropositivity was defined as two-standard deviations above the mean IgG levels of 20 non-malaria exposed control individuals from Melbourne, Australia.