

Extended Data and Tables

Figure 1: 3D7 recAMA1 based pooled phage ELISA against other AMA1 isoforms of *P. falciparum*.

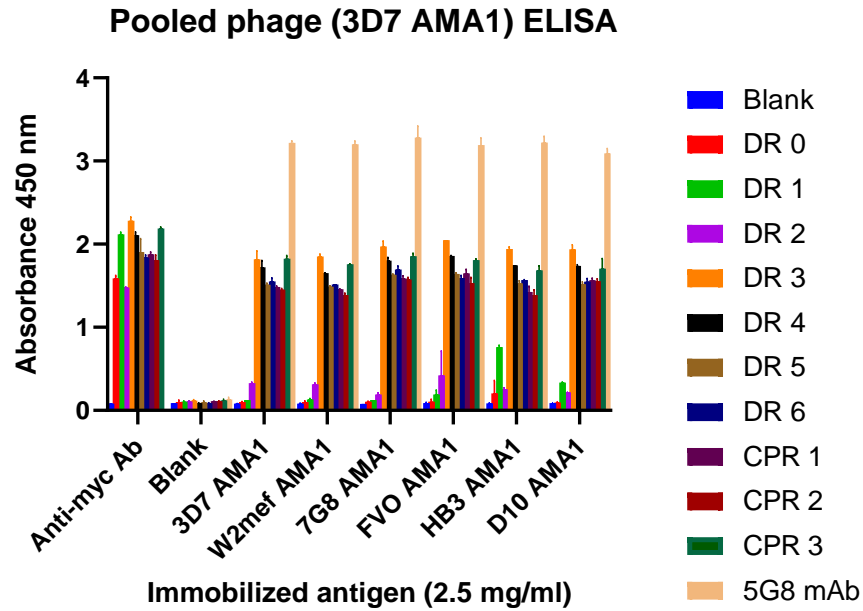


Figure 2: W2mef recAMA1 based pooled phage ELISA against other AMA1 isoforms of *P. falciparum*.

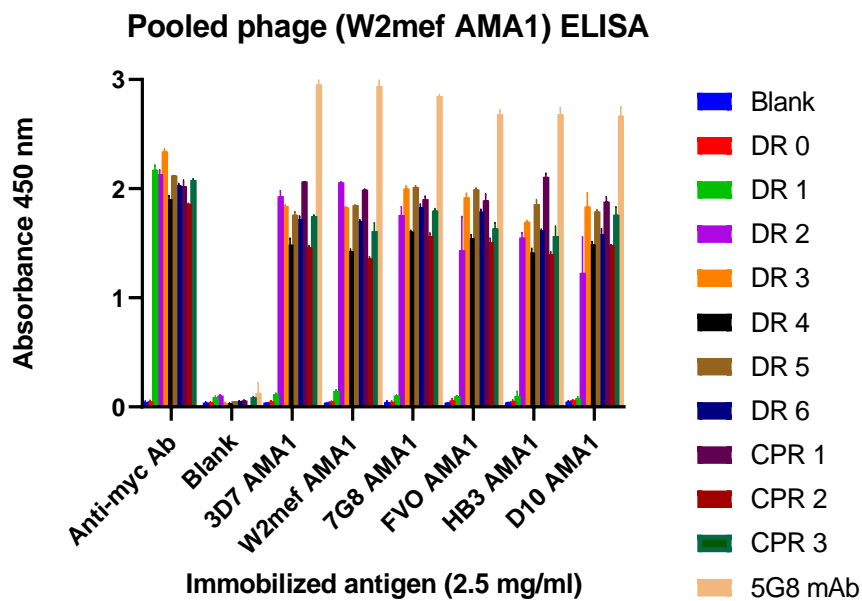


Figure 3: Analysis of the sequence representation of each i-body sequence over each panning campaign.

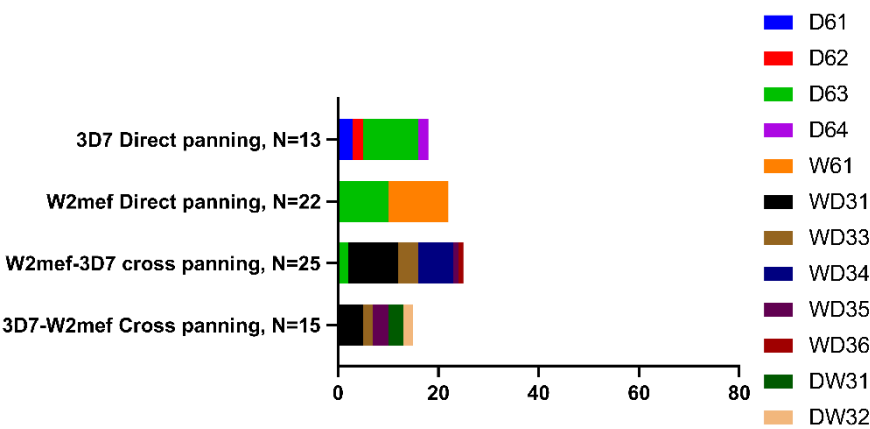


Figure 4: Immunoblotting of saponin lysed late-stage *Pf* schizonts with 1F9 mAb.

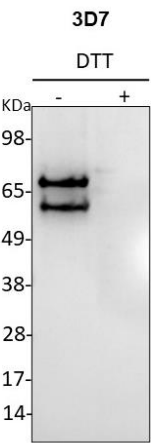


Figure 5: Immunoblotting of saponin lysed late-stage *Pf* schizonts with 4G2 mAb.

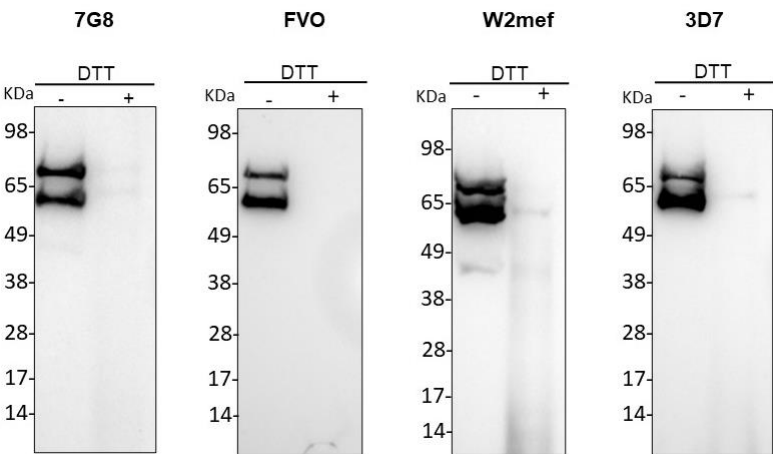


Figure 6: WD34 footprint compared to AMA1-specific IgNAR footprint. The Olive colour represents the IgNAR footprint. The red colour represents the highly polymorphic residues associated with the 1D loop. Purple colour represents the WD34 footprint. Overlapping residues of IgNAR footprint with polymorphic residues in the 1D loop are represented by the orange colour, and the light pink colour represents the shared residues between IgNAR and WD34 footprint.

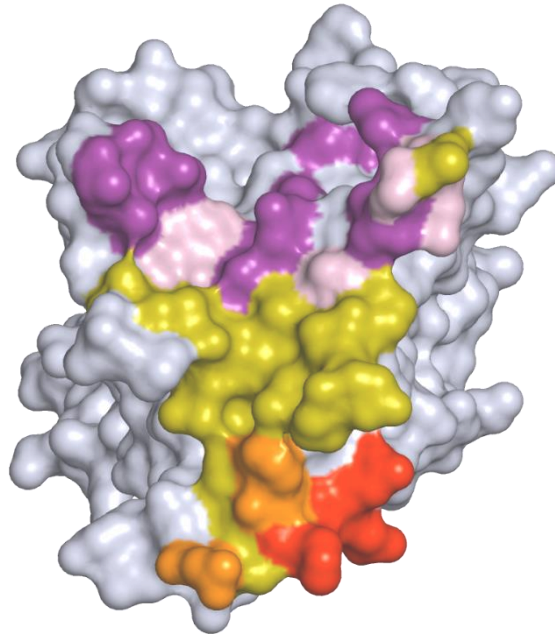


Figure 7: WD34 footprint compared to 1F9 footprint. The pale green colour represents the 1F9 mAb footprint. Purple colour represents the WD34 footprint. Overlapping residues of 1F9 mAb footprint with polymorphic residues in the 1D loop are represented by the salmon colour, and the grey colour represents the shared residues between 1F9 mAb and WD34 footprint.

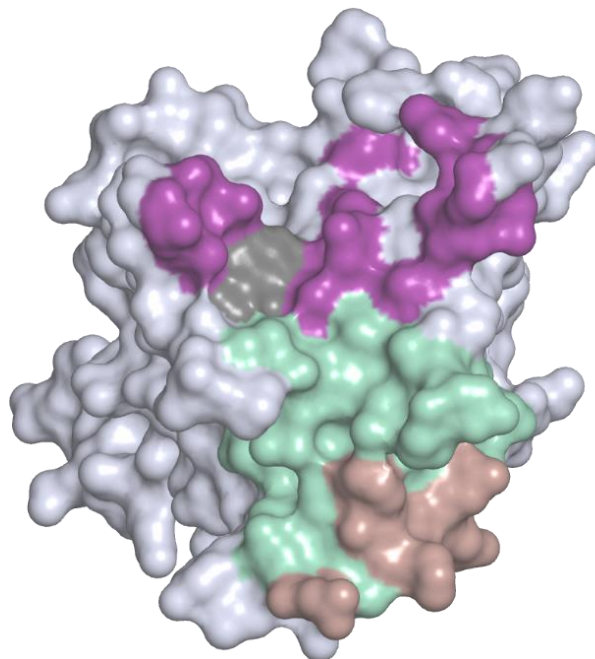


Figure 8: WD34 scaffold involvement in *Pf*AMA1(a) and *Pv*AMA1(b) binding.

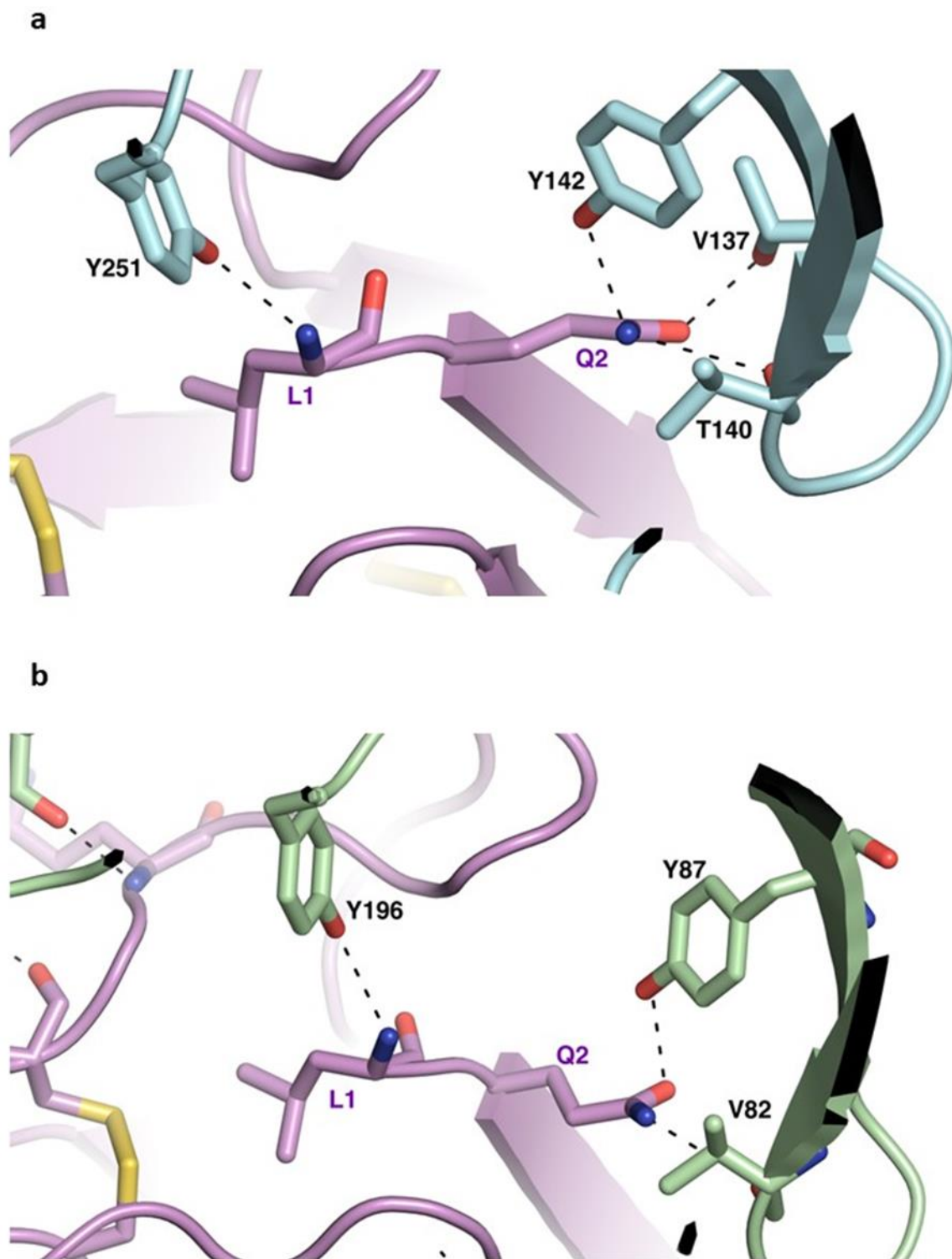


Figure 9: Pi-Pi interaction between Y236^{PfAMA1} and W88^{WD34}.

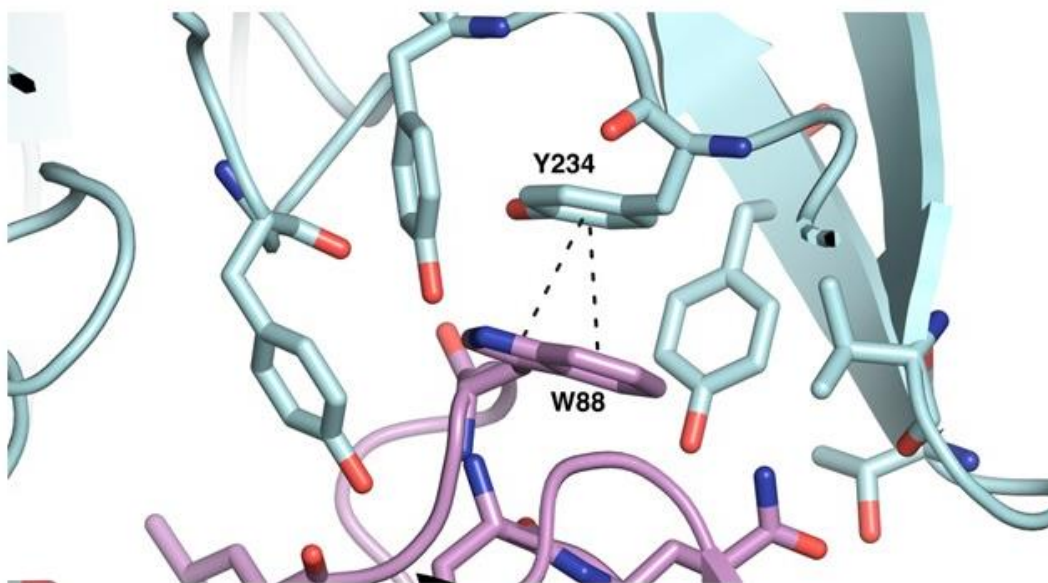


Figure 10: FoldX position scan data.

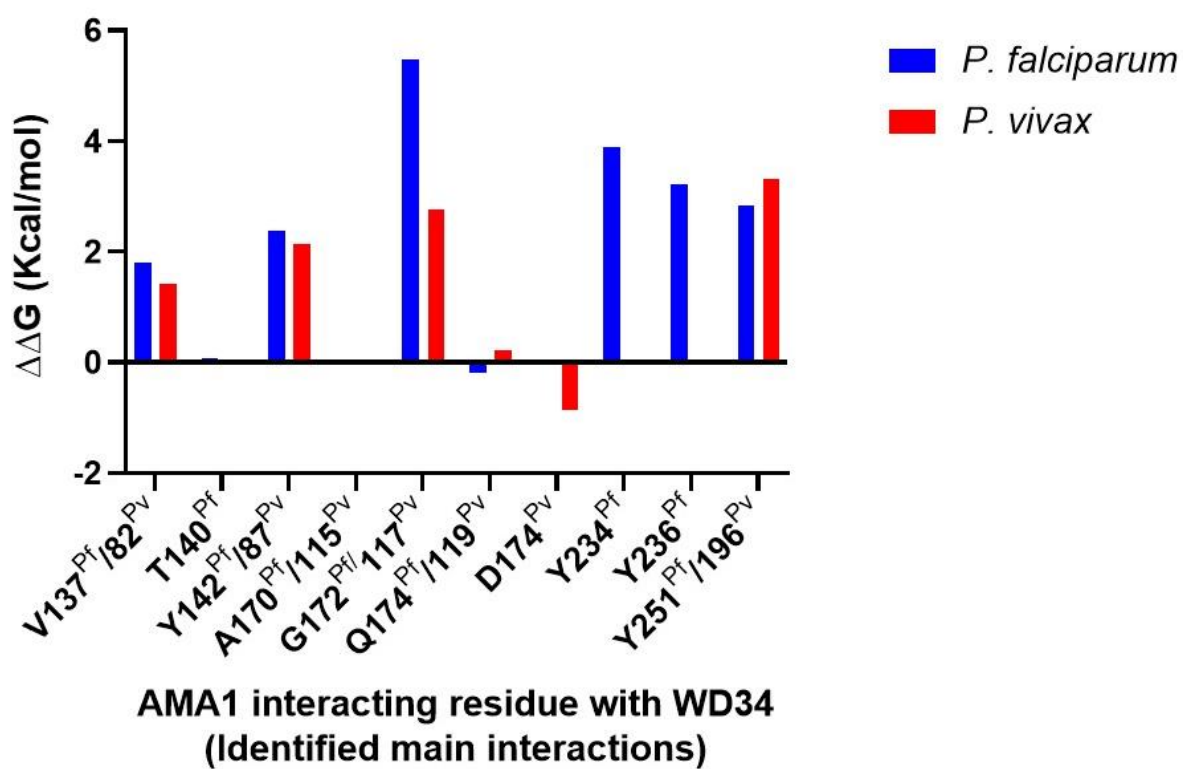


Figure 11: WD34 footprint in relation to hydrophobic groove and surrounding loops in *Pf*AMA1. Stereo view of Hydrophobic groove residues shown in green. Ia, Ib, Ic and Ie loops are shown in blue, and the highly polymorphic Id loop is shown in red. Residues of the WD34 footprint are shown in purple.

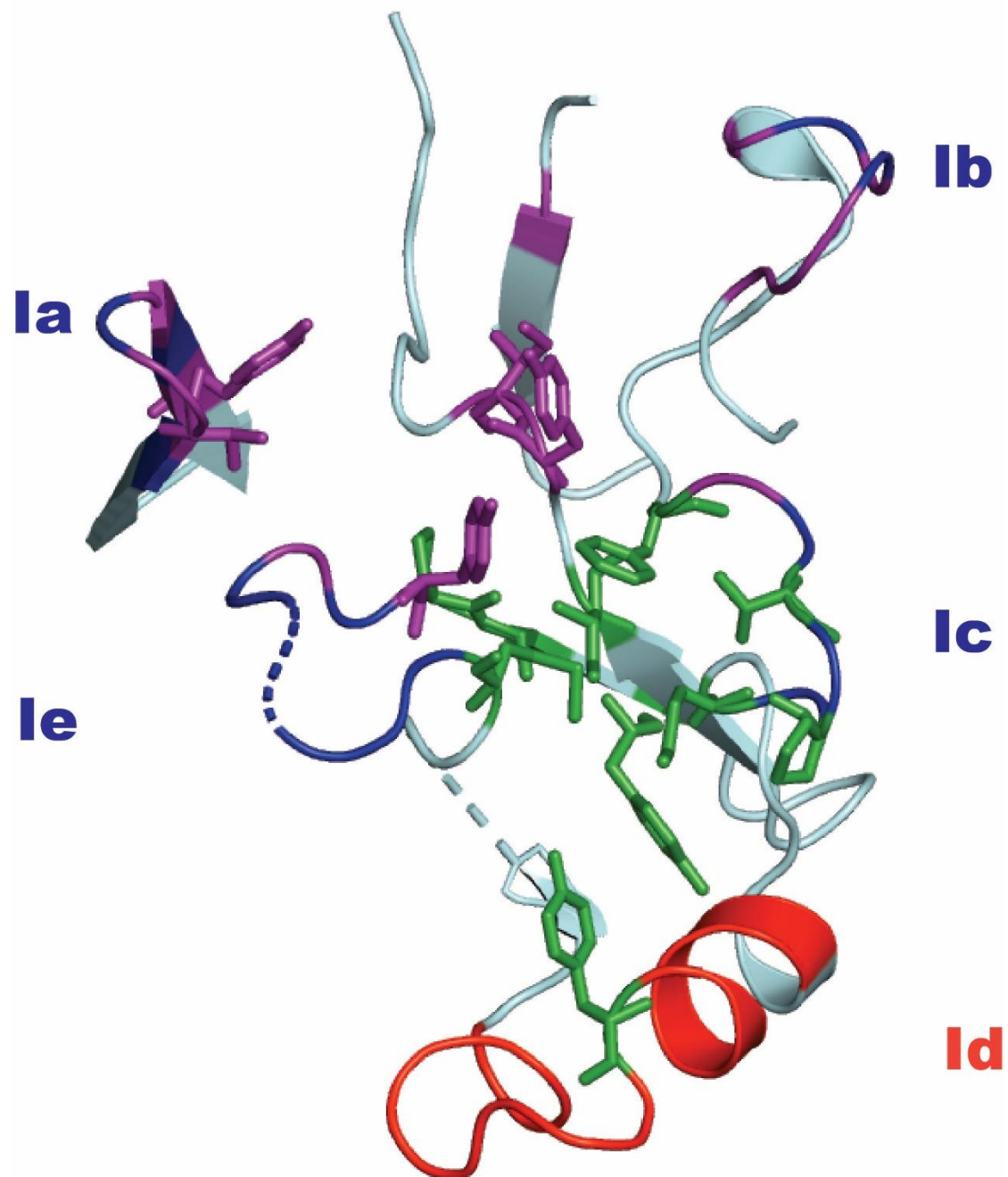


Figure 12: Conservation of AMA1 polar interacting residues among multiple *Plasmodium* species. 1745 *Plasmodium* parasite isolates were analysed. Detailed analysis is presented in the Extended Data sheet 1. Residues greater than 95% coverage are described as being conserved.

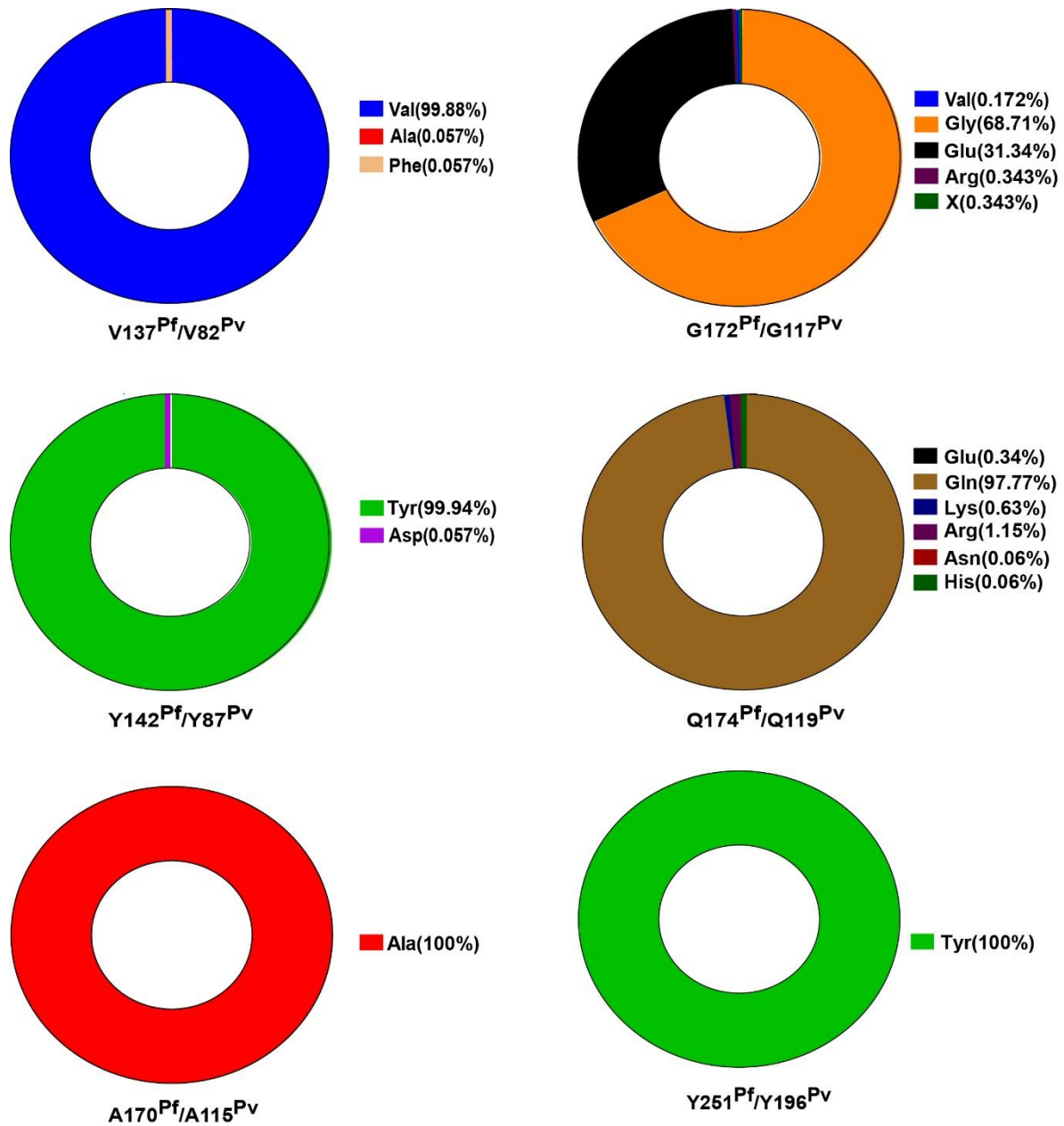


Table 1: Extended SPR Data.

Ligand	Analyte	K_a	K_d	KD	R_{max}
7G8 AMA1	WD34	$5.10 \times 10^5 (\pm 4.88)$	$1.201 \times 10^{-4} (\pm 1.2)$	$1.07 \times 10^{-9} (\pm 0.78)$	68.9 (± 4.38)
HB3 AMA1	WD34	$1.19 \times 10^5 (\pm 0.35)$	$2.22 \times 10^{-3} (\pm 0.33)$	$1.97 \times 10^{-8} (\pm 0.79)$	87.3 (± 22.41)
D10 AMA1	WD34	$3.43 \times 10^5 (\pm 2.31)$	$9.88 \times 10^{-4} (\pm 4.1)$	$3.78 \times 10^{-9} (\pm 2.01)$	85.8 (± 22.35)
FVO AMA1	WD34	$8.79 \times 10^4 (\pm 0.92)$	$1.74 \times 10^{-4} (\pm 0.43)$	$1.96 \times 10^{-9} (\pm 0.30)$	50.6 (± 4.01)
W2mef AMA1	WD34	$1.58 \times 10^6 (\pm 2.194)$	$1.48 \times 10^{-3} (\pm 1.70)$	$4.9 \times 10^{-9} (\pm 5.71)$	99.3 (± 51)
3D7 AMA1	WD34	$8.76 \times 10^4 (\pm 7.04)$	$4.71 \times 10^{-4} (\pm 1.18)$	$7.16 \times 10^{-9} (\pm 3.54)$	83.5 (± 12.98)
Pv AMA1	WD34	$1.54 \times 10^4 (\pm 0.53)$	$1.67 \times 10^{-2} (\pm 0.24)$	$1.19 \times 10^{-7} (\pm 0.37)$	72.1 (± 52.6)
Pc AMA1	WD34	$5.38 \times 10^4 (\pm 1.4)$	$1.14 \times 10^{-3} (\pm 0.13)$	$2.61 \times 10^{-8} (\pm 0.4)$	58.6 (± 4.7)
7G8 AMA1	WD33	$3.35 \times 10^6 (\pm 4.88)$	$7.07 \times 10^{-2} (\pm 0.61)$	$2.13 \times 10^{-8} (\pm 0.18)$	277 (± 27.73)
HB3 AMA1	WD33	$3.47 \times 10^6 (\pm 0.40)$	$6.39 \times 10^{-2} (\pm 0.02)$	$1.86 \times 10^{-8} (\pm 0.22)$	242 (± 6.43)
D10 AMA1	WD33	$3.76 \times 10^6 (\pm 0.56)$	$6.10 \times 10^{-2} (\pm 0.14)$	$1.64 \times 10^{-8} (\pm 0.20)$	273 (± 6.64)
FVO AMA1	WD33	$3.27 \times 10^6 (\pm 0.29)$	$3.72 \times 10^{-2} (\pm 0.05)$	$1.14 \times 10^{-8} (\pm 0.16)$	196 (± 4.3)
W2mef AMA1	WD33	$3.15 \times 10^6 (\pm 0.33)$	$5.26 \times 10^{-2} (\pm 0.02)$	$1.68 \times 10^{-8} (\pm 0.16)$	233 (± 4.65)
3D7 AMA1	WD33	$4.02 \times 10^6 (\pm 0.37)$	$7.74 \times 10^{-2} (\pm 0.53)$	$1.93 \times 10^{-8} (\pm 0.14)$	193 (± 9.6)
7G8 AMA1	RON2 pept	$2.2 \times 10^5 (\pm 0.19)$	$1.13 \times 10^{-3} (\pm 0.04)$	$5.16 \times 10^{-9} (\pm 0.65)$	94.7 (± 4.5)
HB3 AMA1	RON2 pept	$1.89 \times 10^5 (\pm 0.18)$	$1.41 \times 10^{-3} (\pm 0.06)$	$7.54 \times 10^{-9} (\pm 1.07)$	76.2 (± 4.2)
D10 AMA1	RON2 pept	$4.78 \times 10^5 (\pm 0.25)$	$7.59 \times 10^{-3} (\pm 0.23)$	$15.9 \times 10^{-9} (\pm 1.33)$	64.5 (± 2.8)
FVO AMA1	RON2 pept	$1.41 \times 10^5 (\pm 0.53)$	$8.77 \times 10^{-4} (\pm 0.26)$	$6.31 \times 10^{-9} (\pm 0.48)$	60.4 (± 0.20)
W2mef AMA1	RON2 pept	$1.23 \times 10^5 (\pm 0.53)$	$1.46 \times 10^{-3} (\pm 0.41)$	$1.23 \times 10^{-8} (\pm 0.19)$	48.1 (± 4.42)
3D7 AMA1	RON2 pept	$3.83 \times 10^5 (\pm 1.66)$	$8.20 \times 10^{-3} (\pm 2.1)$	$2.23 \times 10^{-8} (\pm 0.39)$	36.6 (± 0.89)

Table 2: IX-ray data collection and refinement statistics for WD34:AMA1^{Pv} and WD34:AMA1^{Pf} complex. Values in parentheses are for the highest resolution shell.

	WD34:AMA1 ^{Pv}	WD34:AMA1 ^{Pf}
Data collection		
Space group	P 21 21 21	I 1 2 1
Cell dimensions		
<i>a</i> , <i>b</i> , <i>c</i> (Å)	44.39 55.27 229.55	71.65 38.46 227.35
α , β , γ (°)	90.00 90.00 90.00	90.00 90.18 90.00
Wavelength (Å)	0.9537	0.9537
Resolution (Å)*	45.90-3.00 (3.18-3.00)	38.45-2.60 (2.72-2.60)
<i>R</i> _{sym} or <i>R</i> _{merge} *	0.130 (0.868)	0.104 (0.401)
<i>I</i> / σ <i>I</i> *	4.6 (1.2)	9.7 (3.0)
CC (1/2)	0.995 (0.829)	0.994 (0.900)
Completeness (%) *	97.8 (99.0)	100.0 (100.0)
Redundancy*	4.4 (4.4)	4.8 (4.9)
Refinement		
Resolution (Å)	44.8-3.001 (3.108-3.001)	38.45-2.6 (2.693-2.6)
No. reflections	11612 (1126)	19608 (1949)
<i>R</i> _{work} / <i>R</i> _{free}	0.2657/ 0.2982	0.2021/0.2323
No. non-hydrogen atoms	3426	3033
Protein	3426	2934
Ligand/ion	-	56
Water	-	74
<i>B</i> -factors		
Protein	87.93	54.20
Ligand/ion	-	53.25
Water	-	34.60
R.m.s. deviations		
Bond lengths (Å)	0.002	0.003
Bond angles (°)	0.43	0.62
Ramachandran plot (%)		
Favored	93.59	95.89
Allowed	6.41	4.11
Disallowed	0.00	0.00

Table 3: Structure-based interactions between AMA1 and WD34.

WD34		AMA1 (<i>falciparum</i>)	AMA1 (<i>vivax</i>)
Res: number	Region		
Vander Waals bonds			
D4	Scaffold	A138, T140	
Q2	Scaffold	V137, A138	A85 (H)
A25	Scaffold		D174
G26	Scaffold		D174
M27	CDR1		M171
L28	CDR1	P184	F128, P129
G80	CDR3	G172	G117
P81	CDR3	T171, G172	T116, G117
Q82	CDR3	T171	T116, P129
C83	CDR3	T171, G172	A115, T116
P84	CDR3	A170, T171, Y251	P129, Y196
R85	CDR3	L176	G117, L121
T87	CDR3	Y251, I252	Y196, L197
W88	CDR3	V137, Y234	Y87, Y179, Y196
S89	CDR3	Y142	
L90	CDR3	I252, F276	L197, A199, N202, F221
Polar Interactions			
L1	Scaffold	Y251(2.86 Å)	Y196(3.14 Å)
Q2	Scaffold	V137(3.36 Å), T140(2.51 Å), Y142(2.71 Å)	V82(3.36 Å), Y87(2.78 Å)
G80	CDR3	G172(3.2 Å)	
C83	CDR3	G172(3.27 Å)	G117(3.26 Å)
R85	CDR3	A170(2.83 Å), Q174(2.66 Å)	A115(2.97 Å), Q119(2.48 Å)
L86	CDR3	Y251(2.67 Å)	Y196(2.51 Å)
W88	CDR3	Y236(2.82 Å)	
G26	Scaffold		D174(3.22 Å)
		One Pi-Pi stack Y234 ^{falci} . W88 ^{WD34} (3.83 Å)	No pi-pi interactions

