

Molecular and functional properties of human *Plasmodium falciparum* CSP

C-terminus antibodies

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P10	RIKPGSANKPKDEL
P11	KPKDEL DYANDIEK
P12	ANDIEK KICKMEKC
P13	CKMEKCSSVFNVVN
P14	MEKCSSVFNVVNSS

Appendix Table S2: Sequenced and cloned antibodies per time-point

	PfCSP Memory B cells				Plasmablasts	
	Sequenced antibodies		Cloned antibodies		Sequenced antibodies	
Donor	III+14	III+35	III+14	III+35	III+14	III+35
M1	67	107	24	23	67	NA
M2	25	35	4	13	53	NA
M3	41	36	13	12	216	196
M4	213	134	26	26	129	136
M5	43	NA	10	-	144	NA
M6	NA	37	-	12	NA	NA
M7	29	14	11	5	177	119
M8	NA	34	-	9	NA	86
M9	22	10	5	1	342	184
M10	24	73	9	15	140	NA
M11	NA	46	-	8	NA	NA
M12	132	50	29	12	147	244

Appendix Table S3: Epitope specificity and 7G8 cross-reactivity pattern of C-CSP specific mAbs

mAbs	Affinity	NF54 C-CSP binding (ELISA AUC) after blocking with the indicated mAbs		7G8 FL-CSP binding
		mAb 1710	mAb 1512	ELISA AUC
3393	5.11E-10	15.48		1
1805	1.41E-09	21.54		1.3
4192	2.77E-09	18.35		0.8
3667	3.49E-09	22.46		1.4
3666	5.50E-09	50.69		2.9
0566	5.70E-09	18.1		0.6
2801	5.74E-09	42.07		0.6
4595	6.40E-09	19.76		10.1
1593	8.00E-09	19.72		0.5
2889	9.28E-09	18.09		0.6
4121	9.81E-09	36.09		12.7
0621	1.02E-08	40.09		1.6
3743	1.04E-08	22.59		0.7
3033	1.09E-08	17.49		13.4
3133	1.21E-08	18.4		0.6
1891	1.25E-08	48.59		0.9
3451	1.26E-08	69.77		0.8
0937	1.34E-08	28.11		1.4
1984	1.50E-08	26.99		1.3
3116	1.74E-08	23.48		0.9
4025	2.31E-08	145.8	28.33	13.2
4164	2.54E-08	25.04		0.5
3268	2.66E-08	41.77		1.8
4118	2.74E-08	149.3	45.37	10.8
2446	2.78E-08	46.61		1.5
2384	2.80E-08	45.21		0.8
3128	2.91E-08	26.48		2.4
4135	3.15E-08	47.63		2.2
2959	3.51E-08	143.9	75.75	13.1
0762	3.70E-08	41.61		0.8
2421	4.10E-08	69.39		1.4
0709	4.11E-08	144.4	27.04	13.1
3616	4.63E-08	49.29		0.6
2599	6.61E-08	31.44		1.1
0335	7.34E-08	51.57		0.5
3694	9.10E-08	155.2	68.04	13.5
3713	9.58E-08	55.03		0.6
3217	9.95E-08	42.57		12

mAb 1710 (Scally <i>et al.</i> , 2017)	7.01E-08	53.74	183.6	0.2
mAb 1512 (Beutler <i>et al.</i> , 2022)	2.85E-10	156.8	21.53	ND

mAbs- monoclonal antibodies; ID- identification number; AUC- area under the curve; ND- not determined

Appendix Table S4: Live sporozoites binding and hepatocyte traversal inhibition

ID	VH	mAbs		Binding affinity K _D (M)	Sporozoite binding (% average)		Traversal inhibition (% average) 100 µg/ml
		VL	Epitope specificity		100 µg/ml	1 µg/ml	
3393	3-21	Vλ3-1	Th2R/Th3R	5.11E-10	0.8		4.1
0566	3-21	Vλ3-21	Th2R/Th3R	5.70E-09	0.4		-3.2
4121	3-30	Vλ1-36	Th2R/Th3R	9.81E-09	0.7		0.7
3743	3-9	Vλ2-23	Th2R/Th3R	1.04E-08	0.6		9.9
4135	3-21	Vλ6-57	Th2R/Th3R	3.15E-08	0.6		-8.3
4025	4-61	Vκ3-20	RII+	2.31E-08	1		3.5
4164	3-7	Vλ3-1	Th2R/Th3R	2.54E-08	0.7		-1.6
4118	3-23	Vλ7-43	RII+	2.74E-08	0.5		5.1
0709	3-48	Vκ3-11	RII+	4.11E-08	0.6		-12.8
2152	3-23	Vκ1-13	ND	1.64E-07	1		2
3764	3-33	Vκ2-30	C-linker	1.72E-07	77	0.9	-12.8
1061	4-59	Vλ1-47	Linear peptide	1.93E-07	0.9		-10.7
0590	1-3	Vλ3-21	ND	2.45E-07	0.6		-13.7
3750	1-3	Vκ1-33	ND	4.17E-07	0.8		16.3
2449	3-9	Vκ1-12	ND	5.04E-07	0.7		3.1

mAbs- monoclonal antibodies; ID- identification number; VH- Variable Ig heavy chain segment; VL- Variable Ig light chain segment; ND- not determined

Appendix Table S5: Statistical analysis for *in vivo* protection of 1961 mAb against mosquito bite challenge infection (Fig 4F).

	1961 (n=8)	317 (n=10)
1710 (n=9)	0.0592	<0.0001
1961 (n=8)	-	0.027

P-values of pair comparisons are indicated, Mantel - Cox log - rank test, N=2.

Appendix Table S6: X-ray crystallography data collection and refinement data

3764 Fab - PfCSP ₂₈₁₋₂₉₄	
Beamline	APS-23-ID-B
Wavelength (Å)	1.033167
Space group	P2 ₁
Cell dimensions	
a, b, c (Å)	92.2, 66.7, 95.5
α, β, γ (°)	90, 113.4, 90
Resolution (Å) ^a	40.0-2.36 (2.46-2.36)
No. molecules in ASU	2
No. observations	303,283 (34,515)
No. unique observations	43,719 (5067)
Multiplicity	6.9 (6.7)
R _{merge} (%) ^b	12.3 (63.4)
R _{pim} (%) ^c	5.0 (26.1)
<I/σ I>	10.9 (1.8)
CC _{1/2}	99.7 (74.9)
Completeness (%)	98.9 (98.6)
Refinement statistics	
Reflections used in refinement	43,695
Reflections used for R _{free}	1995
Non-hydrogen atoms	7007
Macromolecules	6718
Solvent	289
R _{work} ^d /R _{free} ^e	17.5 / 23.7
Rms deviations from ideality	
Bond lengths (Å)	0.007
Bond angle (°)	0.93
Ramachandran plot	
Favored regions (%)	97.6
Allowed regions (%)	2.3
Wilson B-value (Å ²)	43.7
B-factors (Å ²)	
Average	44.5
Macromolecules	44.5
Solvent	44.3

^aValues in parentheses refer to the highest resolution bin.

^b $R_{\text{merge}} = \frac{\sum hkl \sum i |I_{hkl,i} - \langle I_{hkl} \rangle|}{\sum hkl \langle I_{hkl} \rangle}$.

^c $R_{\text{pim}} = \frac{\sum hkl [1/(N-1)]^{1/2} \sum i |I_{hkl,i} - \langle I_{hkl} \rangle|}{\sum hkl \langle I_{hkl} \rangle}$.

^d $R_{\text{work}} = \frac{(\sum | |F_o| - |F_c| |)}{(\sum | |F_o|)}$ for all data except as indicated in footnote ^e.

^e5% of data was used for the R_{free} calculation.