Binding ability prediction of antigen peptides to major histocompatibility complex for development of synthetic peptide vaccine from *Plasmodium falciparum*

Gomase V.S.* and Chitlange N.R.
School of Technology, S.R.T.M. University, Sub-Centre, Latur, 413531, MS, India,
Mobile- 09987770696, Mail- gomase.viren@gmail.com

Abstract- *Plasmodium falciparum* is causative agent of malaria. Peptide fragments of antigen protein can be used to select nonamers for use in rational vaccine design and to increase the understanding of roles of the immune system in infectious diseases. Analysis shows MHC class II binding peptides of antigen protein from *Plasmodium falciparum* are important determinant for protection of host form infection. In this assay, we used PSSM and SVM algorithms for antigen design and predicted the binding affinity of antigen protein having 224 amino acids, which shows 216 nonamers. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from *Plasmodium falciparum*.
Keywords- *antigen protein, epitope, PSSM, SVM, MHC, peptide vaccine*

Abbreviations: Goldman, Engelberg and Steitz, (GES); major histocompatibility complex, (MHC); Position Specific Scoring Matrices, (PSSMs); Support Vector Machine, (SVM)

***Correspondence**: Dr Virendra S. Gomase, School of Technology, S.R.T.M. University, Sub-Centre, Latur, 413531, MS, India, Mobile- 09987770696, Mail- gomase.viren@gmail.com

I. Introduction

Plasmodium falciparum is a protozoan parasite, one of the species of Plasmodium that cause malaria in humans. It is transmitted by the female Anopheles mosquito. *P. falciparum* is the most dangerous of these infections as *P. falciparum* malaria has the highest rates of complications and mortality [1, 2]. *Plasmodium falciparum* bacterial peptides are most suitable for subunit vaccine development because with single epitope, the immune response can be generated in large population. This approach is based on the phenomenon of cross-protection, whereby a host infected with a mild strain of parasite is protected against a more severe strain of the same parasite. The phenotype of the resistant transgenic hosts includes fewer centers of initial parasitic infection, a delay in symptom development, and low accumulation. Antigen protein from *Plasmodium falciparum* is necessary for new paradigm of synthetic vaccine development and target validation [3-5].

II. Methodology

In this research work antigenic epitopes of antigen protein from *Plasmodium falciparum* is determined using the Gomase in 2007, Hopp and Woods, Welling, Parker and Protrusion Index (Thornton) antigenicity [6-8]. The major histocompatibility complex (MHC) peptide binding of antigen protein is predicted using neural networks trained on C terminals of known epitopes. In analysis predicted MHC/peptide binding of antigen protein is a log-transformed value related to the IC50 values in nM units. RankPep predicts peptide binders to MHCI and MHCII molecules from protein sequences or sequence alignments using Position Specific Scoring Matrices (PSSMs). Support Vector Machine (SVM) based method for prediction of promiscuous MHC class II binding peptides. SVM has been trained on the binary input of single amino acid sequence [9-

14]. In addition, we predict those MHC ligands from whose C-terminal end is likely to be the result of proteosomal cleavage [15].

III. Results and Interpretations

We found binding of peptides to a number of different alleles using Position Specific Scoring Matrix. A antigen protein sequence is 224 residues long, having antigenic MHC binding peptides. MHC molecules are cell surface glycoproteins, which take active part in host immune reactions and involvement of MHC class-I and MHC II in response to almost all antigens. PSSM based server predict the peptide binders to MHCI molecules of antigen protein sequence are as 11mer_H2_Db, 10mer_H2_Db, 9mer_H2_Db, 8mer_H2_Db and also peptide binders to MHCII molecules of antigen protein sequence as I_Ab.p, I_Ad.p, analysis found antigenic epitopes region in putative antigen protein (Table 1). We also found the SVM based MHCII-IAb peptide regions; MHCII-IAd peptide regions; MHCII-IAg7 peptide regions and MHCII- RT1.B peptide regions, which represented predicted binders from antigen protein (Table 2). The predicted binding affinity is normalized by the 1% fractil. We describe an improved method for predicting linear epitopes (Table 2). The region of maximal hydrophilicity is likely to be an antigenic site, having hydrophobic characteristics, because terminal regions of parasitic protein is solvent accessible and unstructured, antibodies against those regions are also likely to recognize the native protein (Fig. 1, 2). It was shown that a antigen protein is hydrophobic in nature and contains segments of low complexity and high-predicted flexibility (Fig. 3, 4). Predicted antigenic fragments can bind to MHC molecule is the first bottlenecks in vaccine design.

IV. Conclusion

Antigen protein from *Plasmodium falciparum* peptide nonamers are from a set of aligned peptides known to bind to a given MHC molecule as the predictor of MHC-peptide binding. MHCII molecules bind peptides in similar yet different modes and alignments of MHCII-ligands were obtained to be consistent with the binding mode of the peptides to their MHC class, this means the increase in affinity of MHC binding peptides may result in enhancement of immunogenicity of antigen protein. These predicted of antigen protein antigenic peptides to MHC class molecules are important in vaccine development from *Plasmodium falciparum*.

V. References

[1] W. Trager, J. B. Jensen (1976-08-20). "Human malaria parasites in continuous culture". Science (New York, N.Y.) 193 (4254): 673–5. doi:10.1126/science.781840..

[2] "World Malaria Report 2008". World Health Organisation. 2008. pp. 10. http://apps.who.int/malaria/wmr2008/malaria2008.pdf. Retrieved 2009-08-17.

[3] A. Joshi, J. Tang, M. Kuzma, J. Wagner, B. Mookerjee, J. Filicko, M. Carabasi, N. Flomenberg, P. Flomenberg, "Adenovirus DNA polymerase is recognized by human CD8+ T cells". *J. Gen Virol.*, 90(Pt 1), 84-94, 2009.

[4] D. McDonald, L. Stockwin, T. Matzow, M.E. Blair Zajdel, G.E.Blair, "Coxsackie and adenovirus receptor (CAR)-dependent and major histocompatibility complex (MHC) class I-independent uptake of recombinant adenoviruses into human tumour cells". *Gene Ther.*, 6(9),1512-9, 1999.

[5] V.S.Gomase, K.V. Kale and K. Shyamkumar, "Prediction of MHC Binding Peptides and Epitopes from Groundnut Bud Necrosis Virus (GBNV)". *J. of Proteomics & Bioinformatics*, 1 (4), 188- 205, 2008.

[6] V.S.Gomase, K.V. Kale, N.J.Chikhale, S.S. Changbhale, "Prediction of MHC Binding Peptides and Epitopes from Alfalfa mosaic virus". *Curr. Drug Discov. Technol*., 4(2),117-1215, 2007.
[7] V.S.Gomase and K.V.Kale,"In silico prediction of epitopes: a new approach for fragment based viral peptide vaccines". *Int. J. of Applied Computing*, 1(1), 39-46, 2008.
[8] V.S.Gomase and K.V.Kale, "Approach of proteomics system architecture in plant virus's database". *Int. J. of Applied Computin*g, 1(1), 33-38, 2008.
[9] V.S.Gomase and K.V.Kale, "Bioinformatics based sequence analysis of Nucleoplasmin like viral coat protein". Int. *J. of Information Retrieval*, 1(1), 11-15, 2008.
[10] V.S.Gomase, K.V. Kale, K. Shyamkumar and S. Shankar, "Computer Aided Multi Parameter Antigen Design: Impact of Synthetic Peptide Vaccines from Soybean Mosaic Virus". *ICETET 2008, IEEE Computer Society in IEEE Xplore, Los Alamitos, California*, 629-634, 2008.
[11] V.S.Gomase, J.P.Tandale, S.A.Patil, K.V.Kale, "Automatic modeling of protein 3D structure Nucleoplasmin-like viral coat protein from Cucumber mosaic virus". *14th International Conference on Advance Computing & Communication, Published by IEEE Computer Society in IEEE Xplore USA* 614-615, 2006.
[12] P.A. Reche, J.P. Glutting, E.L. Reinherz, "Prediction of MHC Class I Binding Peptides Using Profile Motifs". *Hum Immun*., 63, 701-709, 2002.
[13] S. Buus, et al., "Sensitive quantitative predictions of peptide-MHC binding by a 'Query by Committee' artificial neural network approach". Tissue Antigens, 62, 378-384, 2003.
[14] M. Nielsen, et al., "Reliable prediction of T-cell epitopes using neural networks with novel sequence representations". *Protein Sci*., 12, 1007-1017, 2003.
[15] M. Bhasin and G.P. Raghava, "Pcleavage: an SVM based method for prediction of constitutive proteasome and immunoproteasome cleavage sites in antigenic sequences". *Nucleic Acids Research*, 33, W202-207, 2005.

Table 1- PSSM based prediction of MHC ligands, from whose C-terminal end are proteosomal cleavage sites

MHC-I	POS.	N	Sequence	C	MW (Da)	Score	% OPT.
8mer_H2_Db	100	ETG	ESKETRIY	EET	1007.12	4.721	8.99 %
8mer_H2_Db	183	ASE	NSEDPKKL	TEQ	912.01	2.981	5.68 %
8mer_H2_Db	137	REG	NKVSGPYE	NSE	874.95	1.685	3.21 %
8mer_H2_Db	175	LGE	NVNDGASE	NSE	786.75	0.574	1.09 %
8mer_H2_Db	110	YEE	TKYNKITS	EFR	936.06	-0.16	-0.30 %
9mer_H2_Db	120	SEF	RETENVKIT	EES	1071.19	2.037	4.04 %
9mer_H2_Db	173	EKL	GENVNDGAS	ENS	843.8	1.65	3.28 %
9mer_H2_Db	146	YEN	SENSNVTSE	SEE	947.91	0.494	0.98 %
9mer_H2_Db	107	TRI	YEETKYNKI	TSE	1169.3	-0.184	-0.37 %
9mer_H2_Db	141	KVS	GPYENSENS	NVT	977.95	-0.745	-1.48 %
10mer_H2_Db	174	KLG	ENVNDGASEN	SED	1029.97	12.924	21.96 %
10mer_H2_Db	149	SEN	SNVTSESEET	KKL	1064.03	9.321	15.84 %
10mer_H2_Db	113	TKY	NKITSEFRET	ENV	1206.32	9.229	15.68 %
10mer_H2_Db	215	ENE	KKADNKKKKK		1197.46	7.955	13.52 %
10mer_H2_Db	146	YEN	SENSNVTSES	EET	1034.99	7.894	13.41 %
11mer_H2_Db	97	ESK	ETGESKETRIY	EET	1294.39	12.302	15.48 %
11mer_H2_Db	162	KKL	AEKEENEGEKL	GEN	1257.33	9.895	12.45 %
11mer_H2_Db	151	NSN	VTSESEETKKL	AEK	1232.35	8.182	10.29 %
11mer_H2_Db	109	IYE	ETKYNKITSEF	RET	1341.48	7.655	9.63 %
11mer_H2_Db	179	VND	GASENSEDPKK	LTE	1143.18	1.42	1.79 %

Table 2- SVM based prediction of promiscuous MHC class II binding peptides from parasitic protein

ALLELE	Sequence	Residue No	Peptide Score
I-Ab	KKLAEKEEN	159	0.825
I-Ab	KITSEFRET	114	0.736
I-Ab	EETKDDKPE	203	0.710
I-Ab	KKLTEQEEN	188	0.691
I-Ad	LAEKEENEG	161	0.550
I-Ad	LGENVNDGA	172	0.415
I-Ad	GESKETGES	3	0.391
I-Ad	GESKETGES	9	0.391
I-Ag7	GESKETRIY	99	1.228
I-Ag7	SGPYENSEN	140	1.172
I-Ag7	ENVNDGASE	174	1.128
I-Ag7	GENVNDGAS	173	1.107
RT1.B	TKESSEETK	198	1.043
RT1.B	TKKLAEKEE	158	0.907
RT1.B	PKKLTEQEE	187	0.611
RT1.B	ETKDDKPEE	204	0.594

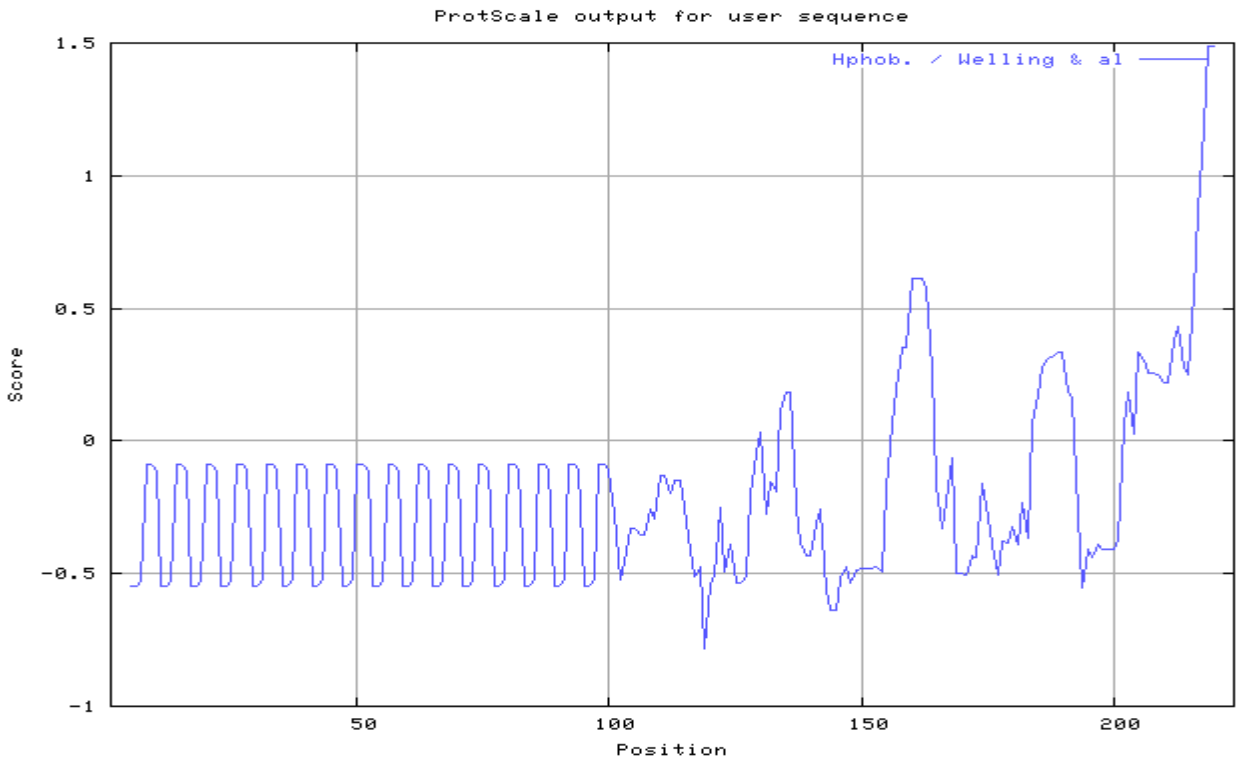

Fig. 1- Antigenicity plot of antigen protein by Welling, et al., scale

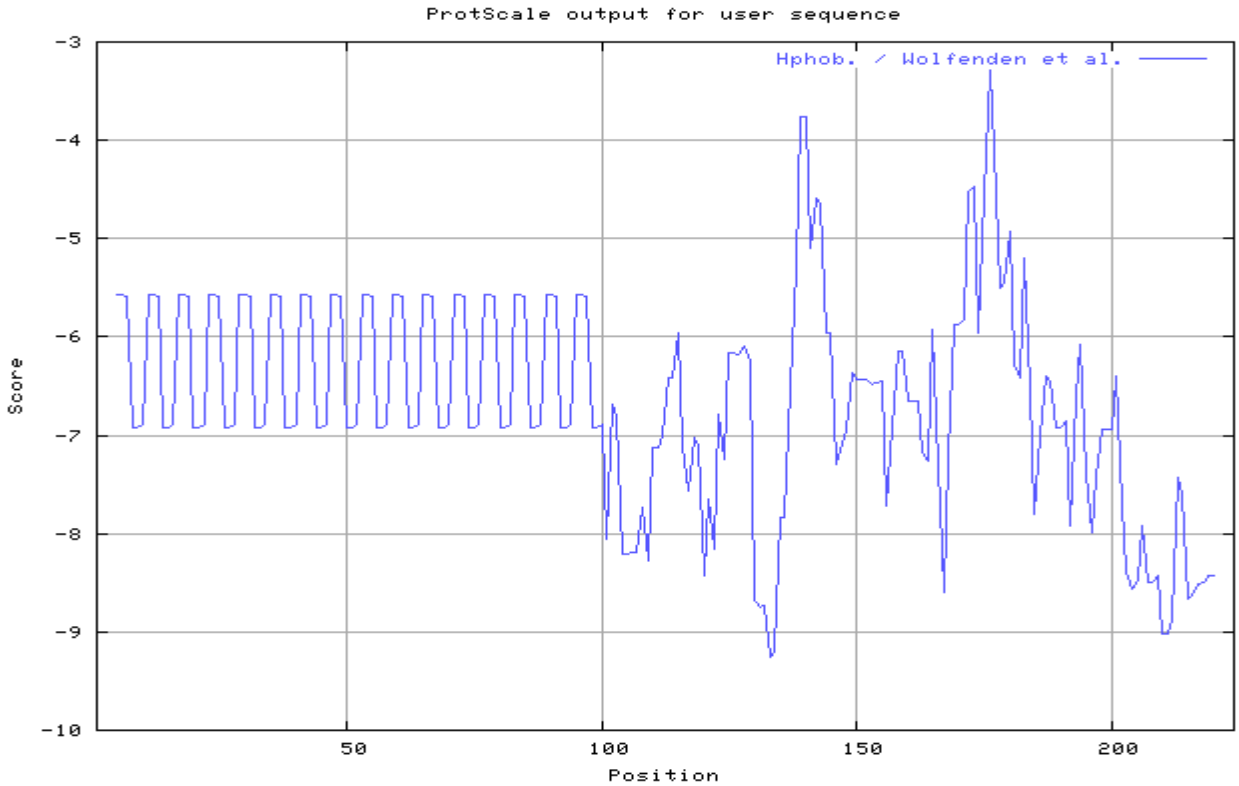

Fig. 2- Antigenicity plot of antigen protein by HPLC / Wolfenden, et al., scale

International Journal of Immunology Research, ISSN:0976-4909 & E-ISSN:0976-4917, Volume 1, Issue 1, 2009

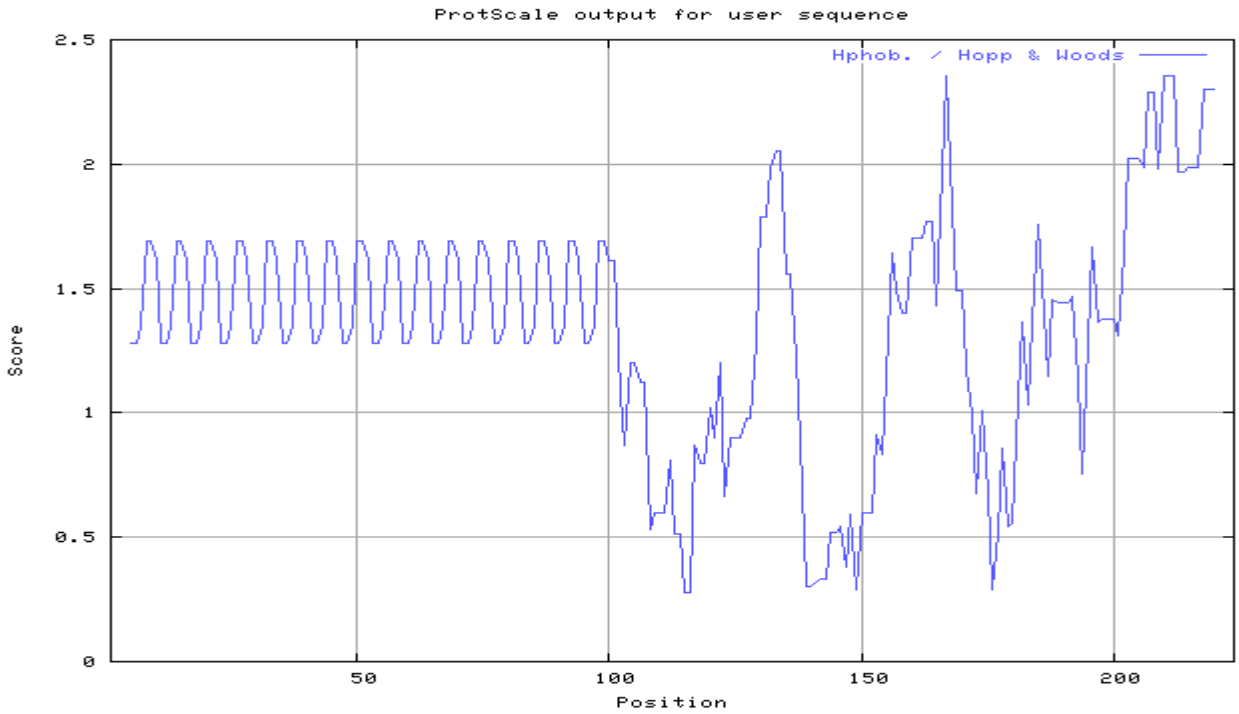

Fig. 3- Hydrophobicity plot of antigen protein by Hopp & Woods, et al., scale

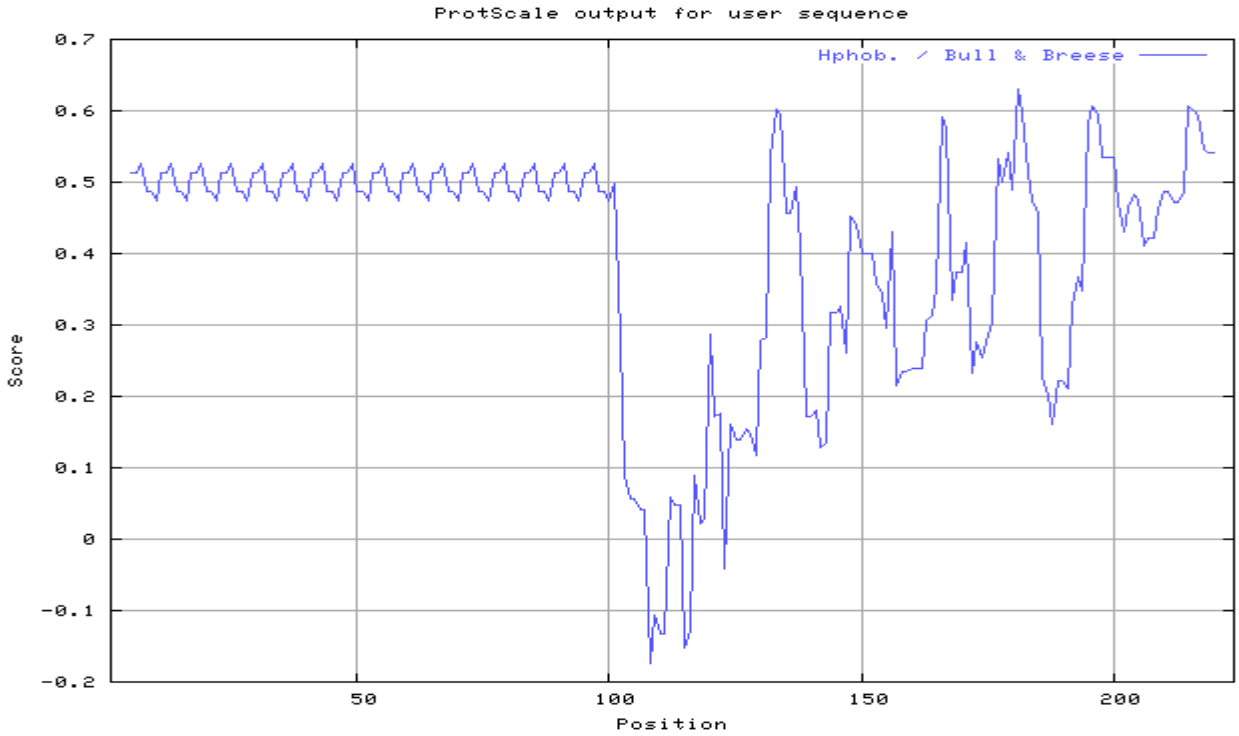

Fig. 4-Hydrophobicity plot of antigen protein by Bull & Breese scale