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ANTIGEN PROTEIN FROM *SCHISTOSOMA MANSONI*: NEW PARADIGM OF SYNTHETIC VACCINE DEVELOPMENT

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ABSTRACT

Schistosoma mansoni causative agent of schistosomiasis. 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 parasitic diseases. Analysis shows MHC class II binding peptides of antigen protein from *Schistosoma mansoni* are important determinant for protection of host form parasitic infection. In this assay, we used PSSM and SVM algorithms for antigen design and predicted the binding affinity of antigen protein having 393 amino acids, which shows 385 nonamers. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from *Schistosoma mansoni*.

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)*

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I. INTRODUCTION

Schistosoma mansoni is a significant parasite of humans, a trematode that is one of the major agents of the disease schistosomiasis. The schistosomiasis caused by *Schistosoma mansoni* is intestinal schistosomiasis. Schistosomes are atypical trematodes in that the adult stages have two sexes and are located in blood vessels of the host. [1,2]. *Schistosoma mansoni* parasite 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 infected host with a mild strain of pathogen is protected against a more severe strain of the same pathogen. The phenotype of the resistant transgenic hosts includes fewer centers of initial pathogenic infection, a delay in symptom development, and low pathogenic accumulation. Antigen protein from *Schistosoma mansoni* 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 *Schistosoma mansoni* 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 393 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 parasitic 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 antigen protein is solvent accessible and unstructured, antibodies against those regions are also likely to recognize the native protein (Fig. 1, 2, 5). 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.

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	271	EYK	GEWTPRRI	DNP	973.14	22.783	43.40 %
8mer_H2_Db	290	WKP	VQIDNPEY	KHD	959.03	18.626	35.48 %
8mer_H2_Db	285	KYK	GEWKPVQI	DNP	915.09	17.965	34.22 %
8mer_H2_Db	262	WER	PQKDNPEY	KGE	972.03	16.295	31.04 %
8mer_H2_Db	101	DKT	VSCGGAYI	KLL	750.87	15.333	29.21 %
8mer_H2_Db	82	SEP	FSNRGKTM	VLQ	922.06	14.809	28.21 %
8mer_H2_Db	67	KTT	QDARFYGI	ARK	951.06	14.6	27.81 %
8mer_H2_Db	65	GLK	TTQDARFY	GIA	983.05	12.679	24.15 %
9mer_H2_Db	290	WKP	VQIDNPEYK	HDP	1087.2	12.514	24.85 %
9mer_H2_Db	174	TLI	VNPNNKYEV	LVD	1058.15	10.951	21.74 %
9mer_H2_Db	146	HVI	FNYKGKNHL	IKK	1102.25	10.802	21.45 %
9mer_H2_Db	100	FDK	TVSCGGAYI	KLL	851.97	10.166	20.18 %
9mer_H2_Db	157	LIK	KEIPCKDDL	KTH	1042.22	9.772	19.40 %
9mer_H2_Db	276	WTP	RRIDNPKYK	GEW	1171.37	7.912	15.71 %
9mer_H2_Db	93	VLQ	FTVKFDKTV	SCG	1066.25	7.785	15.46 %
9mer_H2_Db	175	LIV	NPNNKYEVL	VDN	1072.18	7.626	15.14 %
10mer_H2_Db	174	TLI	VNPNNKYEVL	VDN	1171.31	14.656	24.90 %
10mer_H2_Db	113	LLG	SDIDPKKFHG	ESP	1125.25	13.077	22.22 %
10mer_H2_Db	276	WTP	RRIDNPKYKG	EWK	1228.42	11.738	19.94 %
10mer_H2_Db	99	KFD	KTVSCGGAYI	KLL	980.14	10.666	18.12 %
10mer_H2_Db	53	AGK	SPVDPIEDLG	LKT	1023.12	10.086	17.14 %
10mer_H2_Db	121	KKF	HGESPYKIMF	GPD	1190.39	9.318	15.83 %
10mer_H2_Db	143	KKV	HVIFNYKGKN	HLI	1201.38	8.779	14.92 %
10mer_H2_Db	95	QFT	VKFDKTVSCG	GAY	1065.24	7.248	12.31 %
11mer_H2_Db	35	NWV	QSTYNAEKQGE	FKV	1236.26	14.089	17.72 %
11mer_H2_Db	173	YTL	IVNPNNKYEVL	VDN	1284.47	9.866	12.41 %
11mer_H2_Db	174	TLI	VNPNNKYEVLV	DNA	1270.44	9.104	11.45 %
11mer_H2_Db	135	PDI	CGMATKKVHVI	FNY	1168.46	8.937	11.24 %
11mer_H2_Db	28	FPN	ESIENWVQSTY	NAE	1314.41	7.219	9.08 %
11mer_H2_Db	7	ILL	TLLLSKYALGH	EVW	1197.44	7.099	8.93 %
11mer_H2_Db	303	DPE	LYVLNDIGYVG	FDL	1207.39	6.53	8.21 %
11mer_H2_Db	142	TKK	VHVIFNYKGKN	HLI	1300.51	5.818	7.32 %

Table 2.

SVM based prediction of promiscuous MHC class II binding peptides from antigen protein

ALLELE	Sequence	Residue No	Peptide Score
I-Ab	GKTMVLQFT	86	1.243
I-Ab	IPCKDDLKT	159	1.075
I-Ab	DDLKTHLYT	163	1.026
I-Ab	YVLNDIGYV	304	0.885
I-Ad	DARFYGIAR	68	0.725
I-Ad	DIGYVGFDL	308	0.591
I-Ad	MLSILLTLL	1	0.539
I-Ad	GEFKVEAGK	44	0.532
I-Ag7	RYDAEVAKE	348	1.585
I-Ag7	WDDAMDGEW	251	1.571
I-Ag7	CGGAYIKLL	103	1.545
I-Ag7	SPDFAKEEG	333	1.500
RT1.B	KTTQDARFY	64	1.140
RT1.B	QSTYNAEKQ	35	0.807
RT1.B	WFSETFPNE	20	0.685
RT1.B	DKEEAEETK	363	0.618

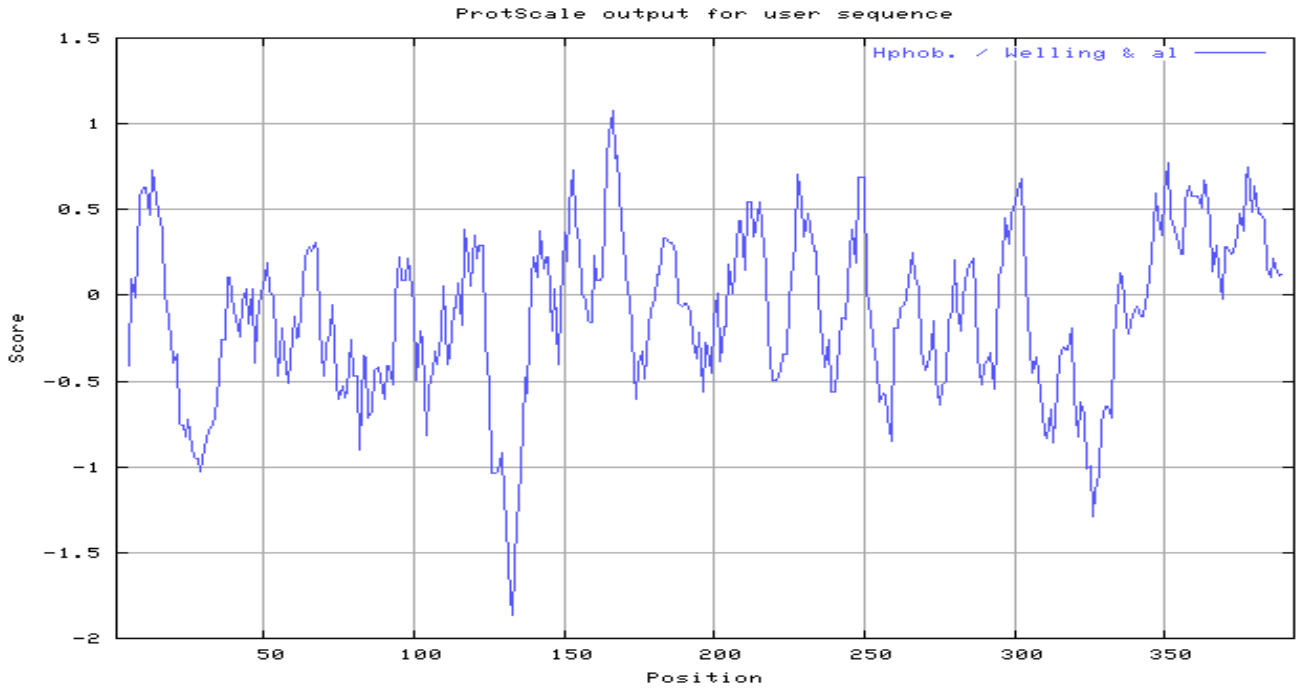

Fig.1

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

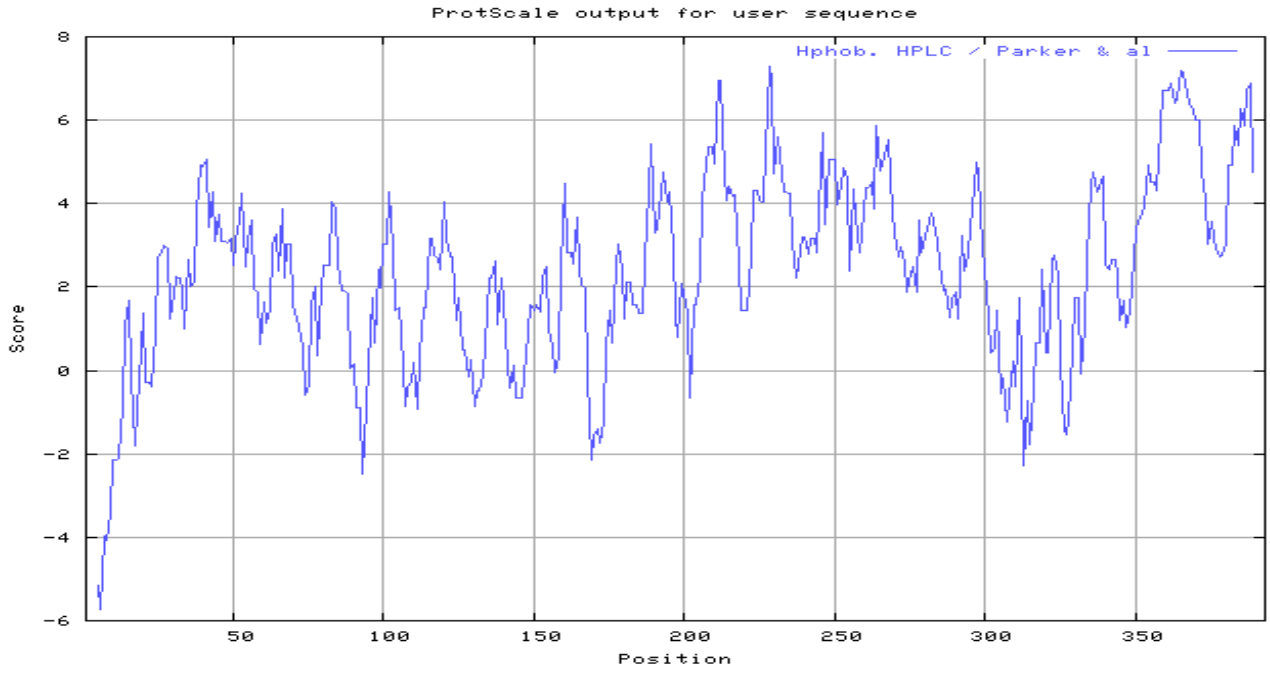

Fig. 2
Antigenicity plot of antigen protein by HPLC / Parker, et al., scale

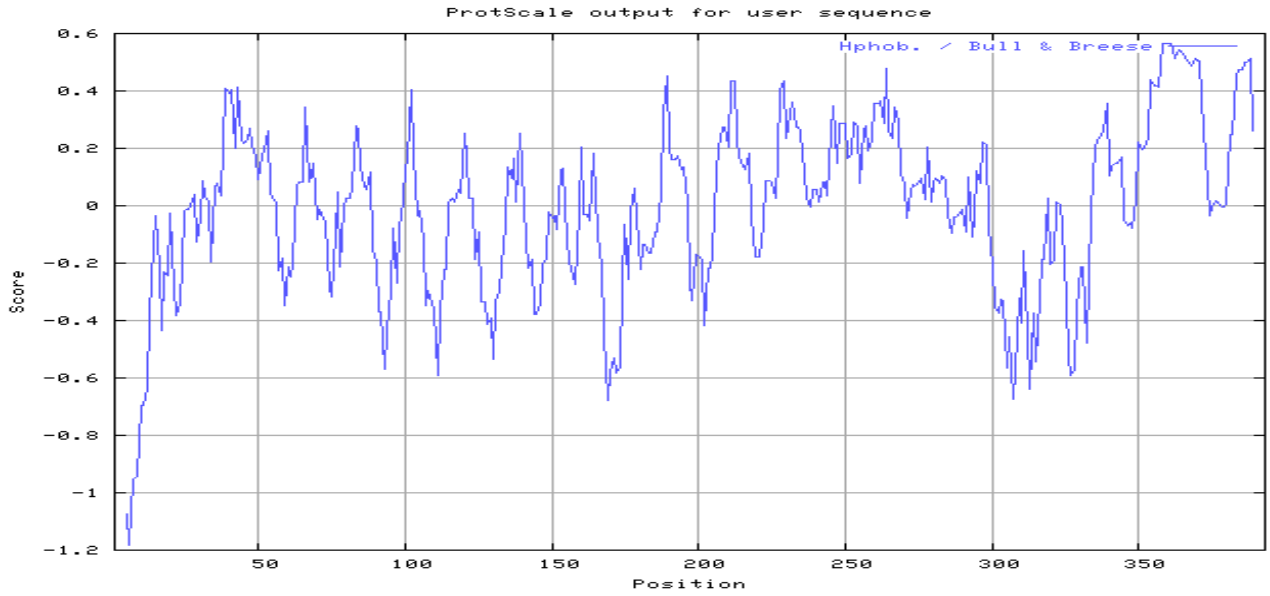

Fig. 3.
Hydrophobicity plot of antigen protein by Bull &Breese, et al., scale

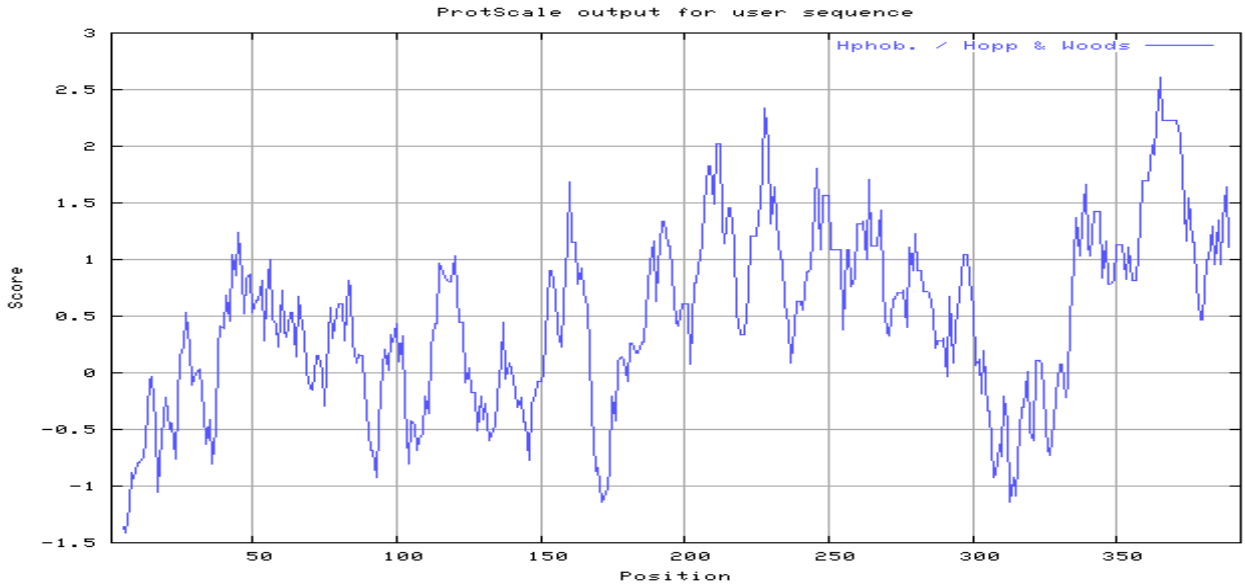

Fig. 4.
Hydrophobicity plot of antigen protein by Hopp & Woods scale

IV. CONCLUSION

Antigen protein from *Schistosoma mansoni* 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 parasitic antigen protein. These predicted of bacterial protein antigenic peptides to MHC class molecules are important in vaccine development from Schistosoma mansoni.

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