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Full Length Research paper

Microbial proteomics approach for synthetic vaccine development from *Taenia solium*

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***Taenia solium*, also called the pork tapeworm causes cysticercosis in humans. 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 *Taenia solium* 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 389 amino acids, which shows 381 nonamers. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from *Taenia solium*.**

Keywords*:* antigen protein, epitope, PSSM, SVM, MHC, peptide vaccine

INTRODUCTION

Taenia solium, also called the pork tapeworm, is a cyclophyllid cestode in the family Taeniidae. It infects pigs and humans. It cause cysticercosis in humans. [Rabiela et al 1989; and Garcia et al 2004]. *Taenia solium* 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 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 *Taenia solium* is necessary for new paradigm of synthetic vaccine development and target validation [Joshi et al 2009 and Gomase et al 2008].

METHODOLOGY

In this research work, antigenic epitopes of antigen protein from *Taenia solium* is determined using the Gomase in 2007, Hopp and Woods, Welling, Parker and Protrusion Index (Thornton) antigenicity [Gomase et al 2007; Gomase and Kale 2008]. 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 [Bhasin and Raghava 2005].

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Abbreviations

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

RESULTS AND INTERPRETATIONS

We found binding of peptides to a number of different alleles using Position Specific Scoring Matrix. A antigen protein sequence is 420 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

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	214	LEY	QEGRATEI	YAK	884.95	13.449	25.62 %
8mer_H2_Db	105	ELE	VNAHFETL	NAL	912.01	13.298	25.33 %
8mer_H2_Db	6	QNG	TPADHPEV	NSV	846.9	12.823	24.43 %
8mer_H2_Db	381	RFL	ADWRDLTL	WIA	948.08	11.061	21.07 %
8mer_H2_Db	1		QPQNGTPA	DHP	793.83	9.169	17.47 %
8mer_H2_Db	73	ENW	IQEKLQTY	SGE	1004.15	8.601	16.38 %
8mer_H2_Db	3	QP	QNGTPADH	PEV	820.81	8.168	15.56 %
8mer_H2_Db	413	AEG	PSRTPQRA		894.01	5.746	10.95 %
8mer_H2_Db	347	TIQ	EKRNTLTM	AWQ	974.13	5.624	10.71 %
9mer_H2_Db	281	DKA	ISWLNEKSI	PLA	1048.24	10.774	21.39 %
9mer_H2_Db	346	DTI	QEKRNTLTM	AWQ	1102.26	8.664	17.20 %
9mer_H2_Db	86	EDY	KDLTNLQSK	KQK	1028.16	6.37	12.65 %
9mer_H2_Db	337	LSE	KHPDSRDTI	QEK	1050.14	6.227	12.36 %
9mer_H2_Db	142	ELH	ALWEKLMAM	FMQ	1051.36	5.496	10.91 %
9mer_H2_Db	124	EMI	SQHHYASEI	IRG	1053.11	5.438	10.80 %
9mer_H2_Db	293	PLA	IEDCGRDLV	SVQ	1001.13	4.851	9.63 %
9mer_H2_Db	104	LEL	EVNAHFETL	NAL	1041.13	4.581	9.10 %
9mer_H2_Db	380	HRF	LADWRDLTL	WIA	1061.24	3.562	7.07 %
10mer_H2_Db	219	GRA	TEIYAKADEL	LKE	1134.26	13.926	23.66 %
10mer_H2_Db	123	EEM	ISQHHYASEI	IRG	1166.27	10.847	18.43 %
10mer_H2_Db	86	EDY	KDLTNLQSKK	QKH	1156.33	10.076	17.12 %
10mer_H2_Db	411	AGA	EGPSRTPQRA		1080.18	9.261	15.73 %
10mer_H2_Db	202	ALQ	KKYDEFMKDL	EYQ	1298.52	7.843	13.33 %
10mer_H2_Db	325	DKV	SQLTTDAEAL	SEK	1030.1	6.591	11.20 %
10mer_H2_Db	288	NEK	SIPLAIEDCG	RDL	999.16	5.217	8.86 %
10mer_H2_Db	77	QEK	LQTYSGEDYK	DLT	1185.26	5.008	8.51 %
10mer_H2_Db	268	YEA	HEIQRFFRET	DKA	1344.51	4.827	8.20 %
11mer_H2_Db	219	GRA	TEIYAKADEL	LKE	1134.26	13.926	23.66 %
11mer_H2_Db	123	EEM	ISQHHYASEI	IRG	1166.27	10.847	18.43 %
11mer_H2_Db	86	EDY	KDLTNLQSKK	QKH	1156.33	10.076	17.12 %
11mer_H2_Db	411	AGA	EGPSRTPQRA		1080.18	9.261	15.73 %
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11mer_H2_Db	268	YEA	HEIQRFFRET	DKA	1344.51	4.827	8.20 %

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

ALLELE	Sequence	Residue No	Peptide Score
I-Ab	GTPADHPEV	5	1.145
I-Ab	YAKADELLK	222	1.142
I-Ab	RYAAFKEAT	38	0.912
I-Ab	REALDRLKE	247	0.904
I-Ad	GILDELHAL	135	0.637
I-Ad	KARLLNLTL	154	0.538
I-Ad	ESFLLHRFL	372	0.514
I-Ad	GEEMISQHH	119	0.495
I-Ag7	EIYAKADEL	220	2.123
I-Ag7	PKDVAGAEG	404	1.779
I-Ag7	LEYQEGRAT	211	1.515
I-Ag7	RYAAFKEAT	38	1.506
RT1.B	YFKRDADEL	61	1.404
RT1.B	QKHQALELE	96	1.240
RT1.B	TTDAEALSE	328	1.145
RT1.B	MFMQKARLL	150	1.140

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 and 2). We also found

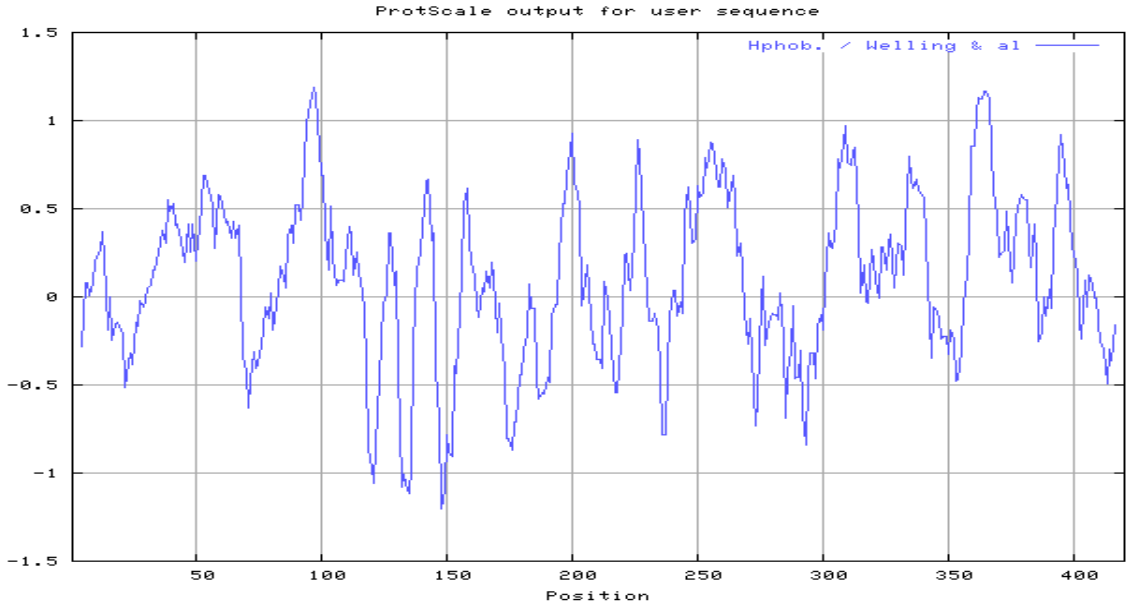

Figure. 1- Antigenicity plot of antigen protein by Welling, et al., scale

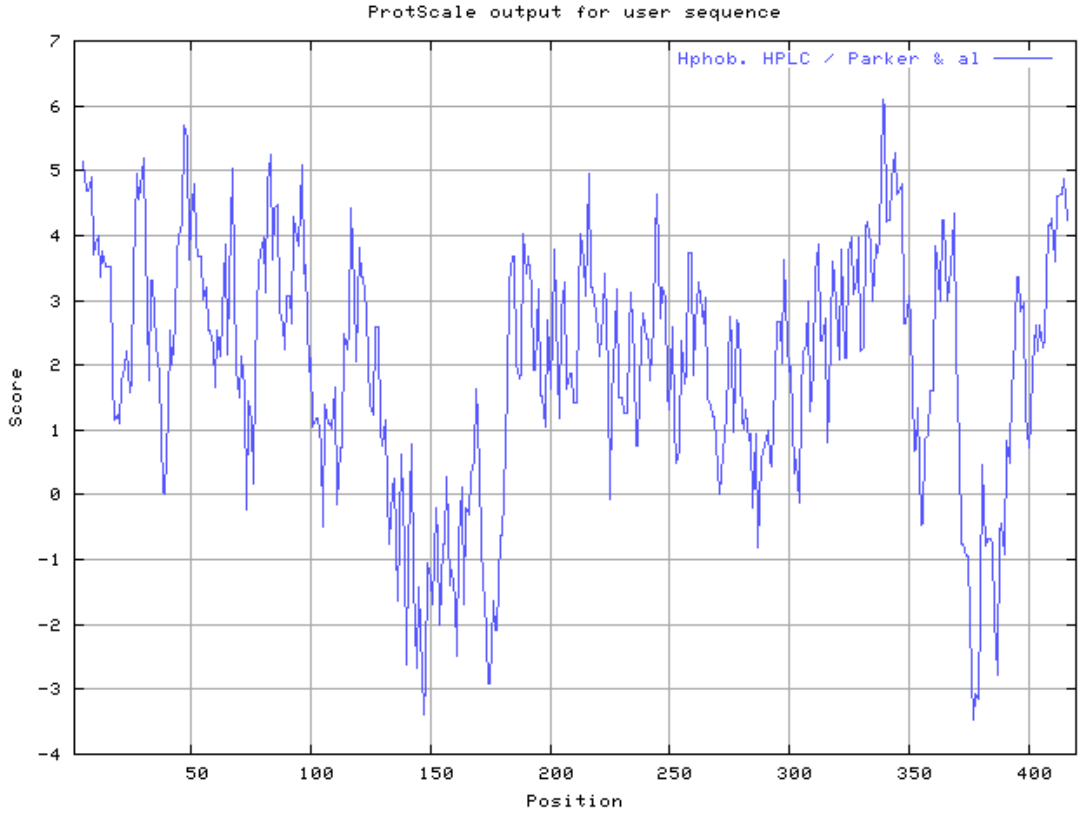

Figure. 2- Antigenicity plot of antigen protein by HPLC / Parker, et al., scale

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

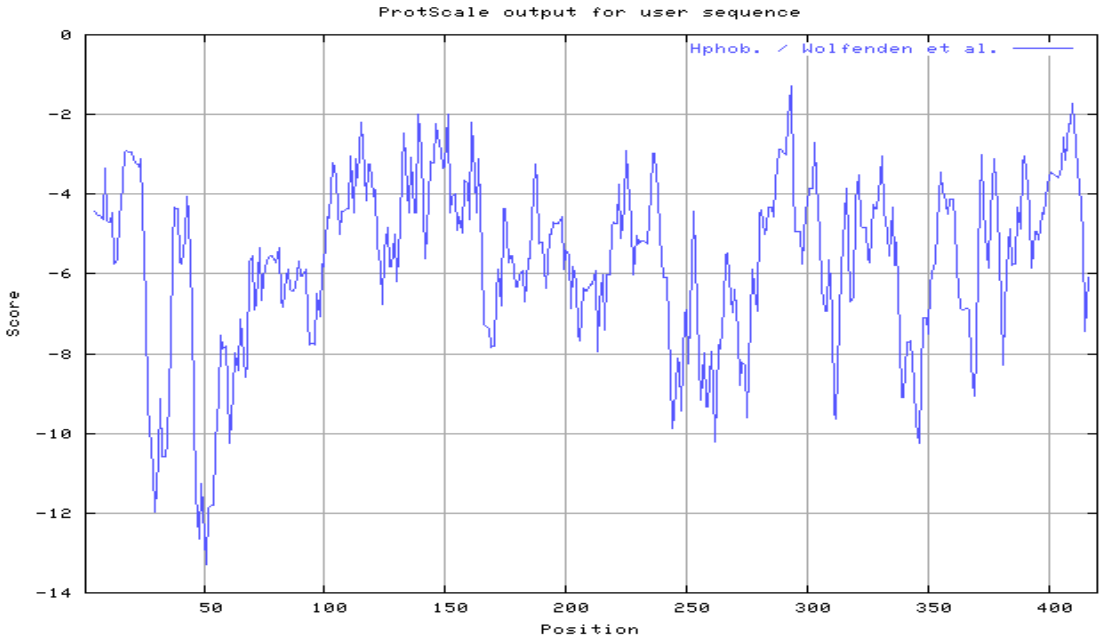

Figure. 3- Hydrophobicity plot of antigen protein by Wolfenden, et al., scale

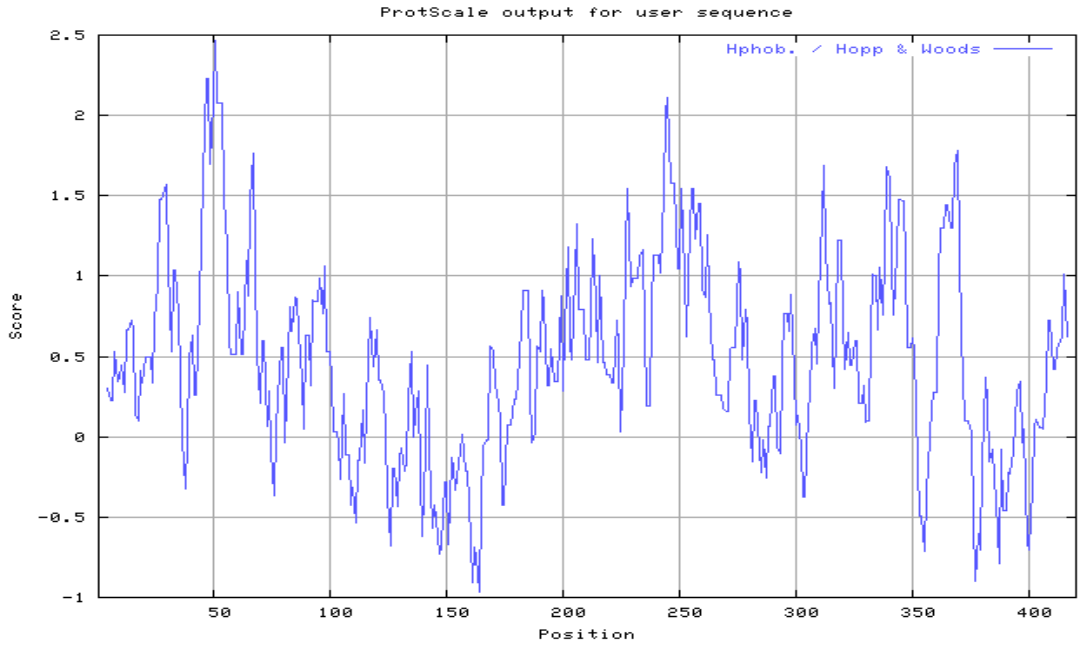

Figure. 4-Hydrophobicity plot of antigen protein by Hopp & Woods scale

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 (Figure. 1, 2, 5). It was shown that a antigen protein is hydrophobic in nature and contains segments of low complexity and high-predicted flexibility (Figure 3, 4). Predicted antigenic fragments can bind to MHC molecule is the first bottlenecks in vaccine design.

CONCLUSION

A antigen protein from *Taenia solium* 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 *Taenia solium*.

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