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PROTEOMICS BASED SENSITIVE QUANTITATIVE PREDICTIONS OF MHC BINDING PEPTIDE FROM *Trichinella spiralis*

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Abstract- *Trichinella spiralis* is a nematode parasite, occurring in rats, pigs, bears and humans and is responsible for the disease trichinosis. 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 *Trichinella spiralis* 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 847 amino acids, which shows 839 nonamers. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from *Trichinella spiralis*.
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)*

I. Introduction

Trichinella species are the smallest nematode parasite of humans, have an unusual life cycle and are one of the most widespread and clinically important parasites in the world [1]. The small adult worms mature in the intestines of an intermediate host such as a pig [2]. *Trichinella spiralis* antigen 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 infected with a mild strain and is protected against a more severe strain of the same. The phenotype of the resistant transgenic hosts includes fewer centers of initial infection, a delay in symptom development, and low accumulation. Antigen protein from *Trichinella spiralis* 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 *Trichinella spiralis* is determined using the Gomase in 2007, Welling, Eisenberg, Parker, Bull & Breese and Deleage & Roux 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. MHC2Pred 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 [15-18].

III. Results and Interpretations

We found binding of peptides to a number of different alleles using Position Specific Scoring Matrix. An antigen protein sequence is 44 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 bacterial 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, 3). It was shown that an antigen protein is hydrophobic in nature and

contains segments of low complexity and high-predicted flexibility (Fig. 4, 5). Predicted antigenic fragments can bind to MHC molecule is the first bottlenecks in vaccine design.

IV. Conclusion

An antigen protein from *Trichinella spiralis* 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 *Trichinella spiralis.*

V. References

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

MHC-I	POS.	N	SEQUENCE	C	MW (Da)	SCORE	% OPT.
8mer_H2_Db	93	PSP	SSWSCSNI	NNS	841.93	22.73	43.30 %
8mer_H2_Db	609	KHV	LNADGKFY	LSL	909.01	18.72	35.66 %
8mer_H2_Db	650	HKK	DSWRVMYL	AVY	1028.23	15.006	28.59 %
8mer_H2_Db	406	VTY	DKQPLFTY	EPY	993.13	14.359	27.35 %
8mer_H2_Db	832	RKY	LENDFCHL	HQC	972.09	13.684	26.07 %
8mer_H2_Db	209	WYV	QQRDQFRI	GSG	1072.2	13.455	25.63 %
8mer_H2_Db	398	REH	DVNCGVTY	DKQ	851.92	13.317	25.37 %
9mer_H2_Db	577	PFD	CVIMNFPHT	GGK	1043.26	18.773	37.27 %
9mer_H2_Db	427	SGP	FCLSGCYFL	CFF	1034.27	16.647	33.05 %
9mer_H2_Db	836	END	FCHLHQCTL	KLR	1083.29	16.353	32.47 %
9mer_H2_Db	137	QTT	VCEHNQLMI	EKI	1068.27	15.776	31.32 %
9mer_H2_Db	233	GYV	VEEYNFQNL	SEN	1137.22	15.503	30.78 %
9mer_H2_Db	779	IFH	PDNNNQLLF	ATT	1056.14	15.409	30.59 %
9mer_H2_Db	777	VEI	FHPDNNNQL	LFA	1080.12	14.944	29.67 %
9mer_H2_Db	102	NIN	NSNSNDNAL	PNG	929.89	14.309	28.41 %
9mer_H2_Db	108	SND	NALPNGEDV	QAE	909.95	12.923	25.66 %
9mer_H2_Db	571	LPR	VSVPFDCVI	MNF	960.16	12.842	25.50 %
10mer_H2_Db	538	FSE	SSNSNIINHL	RNR	1080.16	13.332	22.65 %
10mer_H2_Db	88	EHS	RAPSPSSWSC	SNI	1036.18	12.951	22.00 %
10mer_H2_Db	830	ELR	KYLENDFCHL	HQC	1263.44	12.921	21.95 %
10mer_H2_Db	478	VRM	QSDDPFKQLL	LCK	1172.31	12.214	20.75 %
10mer_H2_Db	351	LKC	CGVKSYTDWL	QSY	1130.31	10.339	17.57 %
11mer_H2_Db	302	MGC	CGALRKSKCLL	IAV	1173.5	25.393	31.94 %
11mer_H2_Db	606	INL	KHVLNADGKFY	LSL	1273.45	17.497	22.01 %
11mer_H2_Db	350	GLK	CCGVKSYTDWL	QSY	1233.45	15.352	19.31 %
11mer_H2_Db	432	LSG	CYFLCFFAAGL	TRR	1236.53	13.95	17.55 %
11mer_H2_Db	185	IIQ	SYVIREEAGML	TSA	1249.46	13.702	17.24 %
11mer_H2_Db	7	EHI	DKQKNKHLQLL	KRK	1346.58	13.485	16.96 %
11mer_H2_Db	376	ELG	VGAGNVGRVPL	SCC	1020.19	12.52	15.75 %
11mer_H2_Db	233	GYV	VEEYNFQNLSE	NVK	1353.42	12.008	15.11 %

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

MHC ALLELE	Rank	Sequence	Residue No.	Peptide Score
DRB1_0101	1	VYILLAVGV	282	3.3000
DRB1_0101	2	VVIFRRVPI	700	2.2800
DRB1_0101	3	FLCFFAAGL	433	1.5800
DRB1_0101	4	LRKSKCLLI	304	1.5000
DRB1_0301	1	VVMSLLGFM	290	5.6000
DRB1_0301	2	IRRGIPPGF	790	5.5000
DRB1_0301	3	VAIDQKHKI	452	4.9000
DRB1_0301	4	LNADGKFYL	608	4.8600
DRB5_0101	1	WRVMYLAVY	651	4.7000
DRB5_0101	2	VPIVVIFRR	697	3.7000
DRB5_0101	3	FRRVPILSM	703	3.7000
DRB5_0101	4	LLFATTIRR	784	3.7000
DRB5_0105	1	WRVMYLAVY	651	4.7000
DRB5_0105	2	VPIVVIFRR	697	3.7000
DRB5_0105	3	FRRVPILSM	703	3.7000
DRB5_0105	4	LLFATTIRR	784	3.7000

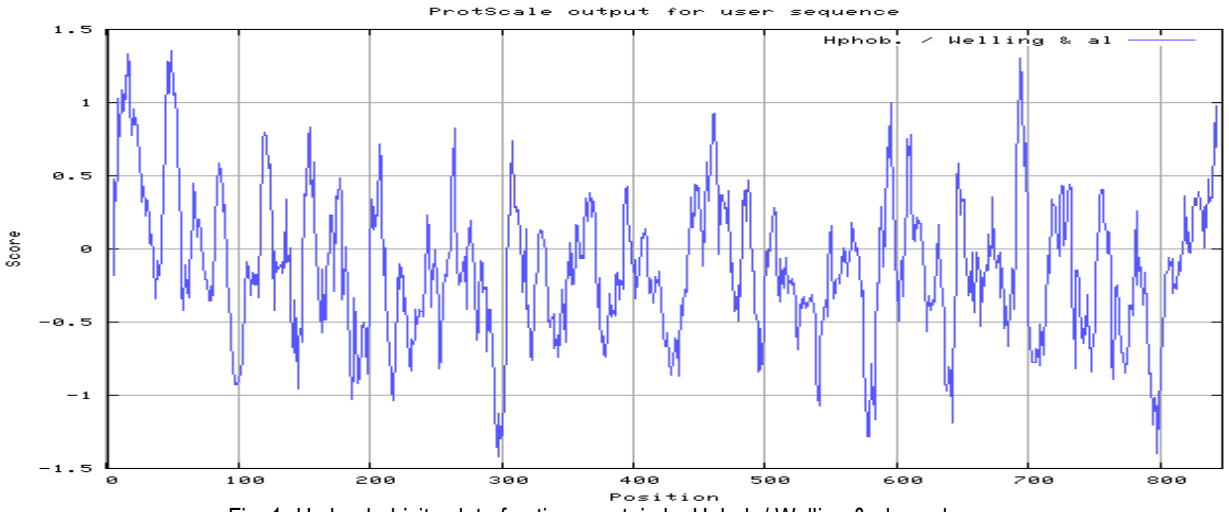

Fig. 1- Hydrophobicity plot of antigen protein by Hphob / Welling & al., scale

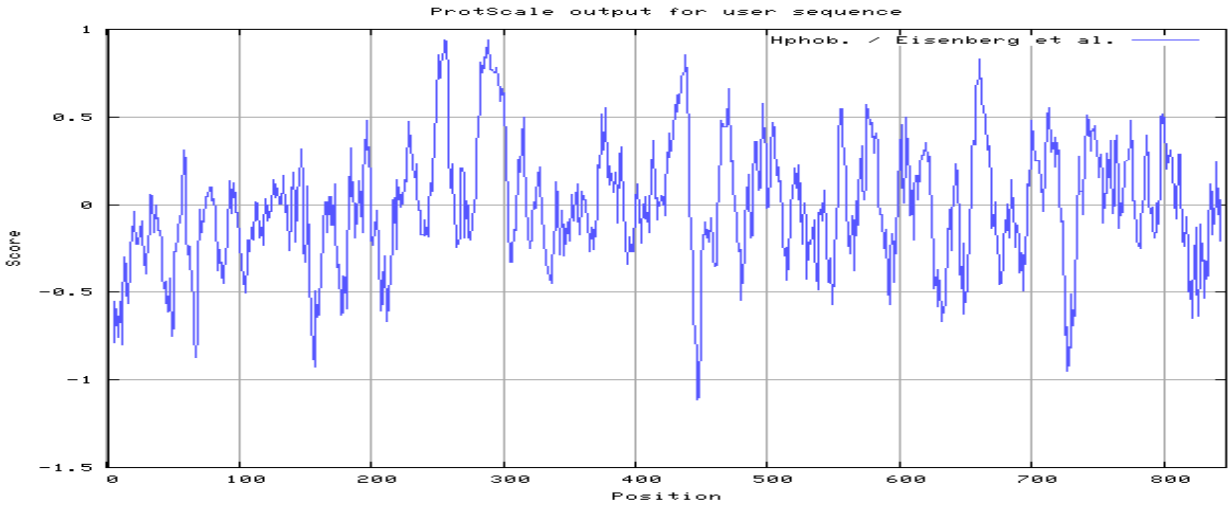

Fig. 2- Hydrophobicity plot of antigen protein by Hphob/ Eisenberg, et al., scale

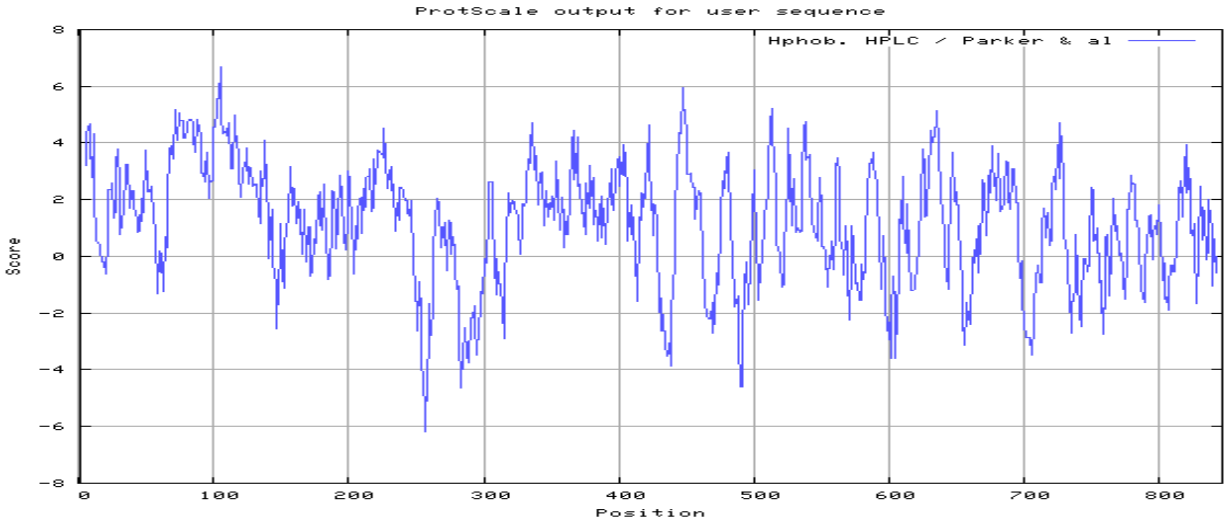

Fig. 3- Hydrophobicity plot of antigen protein by Hphob. HPLC /Parker & et al., scale

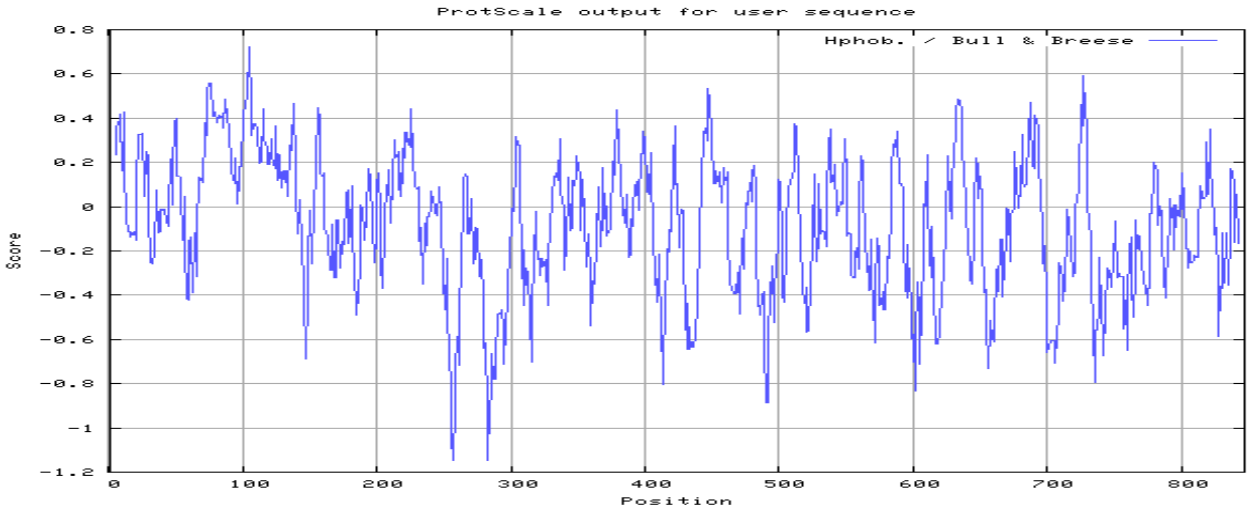

Fig. 4- Antigenicity plot of antigen protein by Hphob. / Bull & Breese, scale

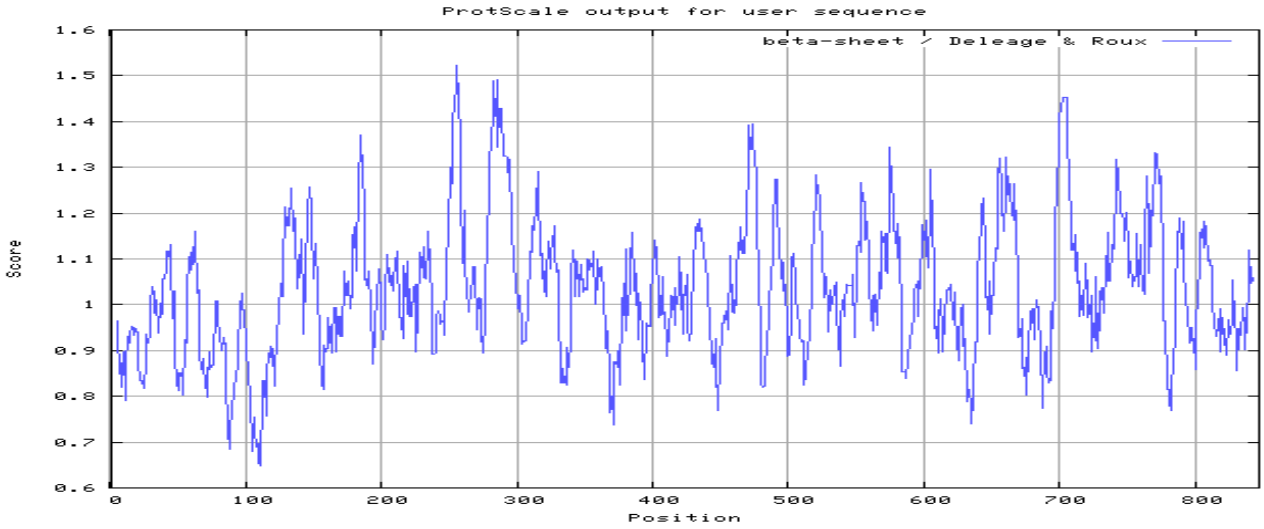

Fig. 5- Antigenicity plot of antigen protein by Beta-Sheet / Deleage & Roux scale