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Sensitive Quantitative Predictions of MHC Binding Peptides and Fragment Based Peptide Vaccines from *Taenia crassiceps*

Gomase VS* and Chitlange NR

Department of Bioinformatics, JJT University, Jhunjhunu Rajasthan, 333001, India

Abstract

Taenia crassiceps is a member of the Taenia genus. It is a tapeworm. It is related to Taenia solium, the pork tapeworm, and to Taenia saginata, the beef tapeworm. Its larvae eat tiny holes in the human retina, eventually detaching it. The life cycle is when an adult lays eggs inside a wild canine. 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 *Taenia crassiceps* 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 72 amino acids, which shows 64 nonamers. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from Taenia crassiceps.

Keywords: Antigen protein; Epitope; PSSM; SVM; MHC; Peptide vaccine

Abbreviations: GES: Goldman; Engelberg and Steitz; MHC: Major Histocompatibility Complex; PSSMs: Position Specific Scoring Matrices; SVM: Support Vector Machine

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 [1,2]. *Taenia crassiceps* 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 *Taenia crassiceps* is necessary for new paradigm of synthetic vaccine development and target validation [3-5].

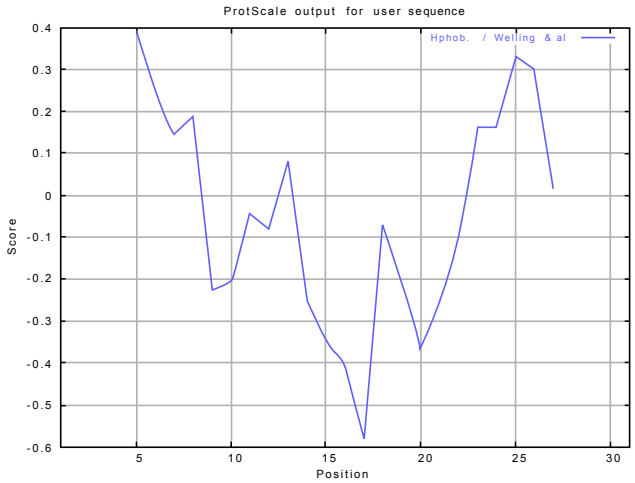

Figure 1: Hydrophobicity plot of antigen protein by Hphob / Welling & al., scale.

Methodology

In this research work antigenic epitopes of antigen protein from *Taenia crassiceps* is determined using the Gomase in 2007; Welling; Eisenberg; Parker and Chou & Fasman and Levitt 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

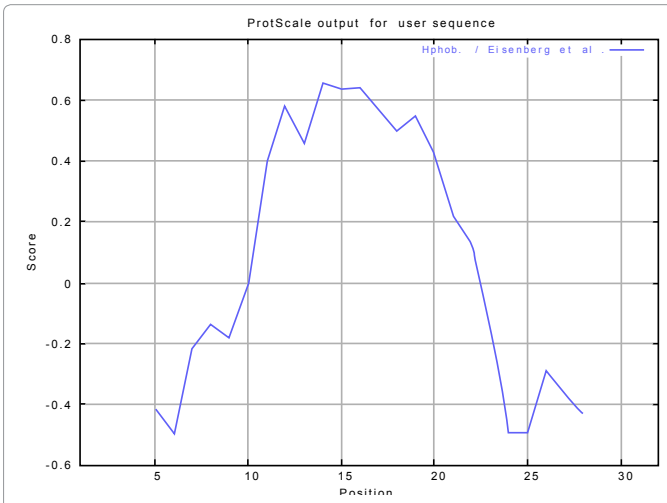

Figure 2: Hydrophobicity plot of antigen protein by Hphob/ Eisenberg, et al., scale.

***Corresponding author:** Gomase VS, Department of Bioinformatics, JJT University, Jhunjhunu Rajasthan, 333001, India; E-mail: gomase.viren@gmail.com

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MHC-I	POS.	N	Sequence	C	MW (Da)	Score	% OPT.
8mer_H2_Db	220	LNE	LEEDFRTI	LSI	1004.12	16.314	31.08 %
8mer_H2_Db	95	RQV	AQYNNFSI	FSK	938.01	13.407	25.54 %
8mer_H2_Db	44	ICQ	FNLRCLEF	LKS	1023.23	9.894	18.85 %
8mer_H2_Db	38	KAV	PSLICQFN	LRC	903.07	9.7	18.48 %
8mer_H2_Db	139	DHL	PINPEVKI	SNG	891.08	8.916	16.98 %
8mer_H2_Db	322	PVS	RKAGPMTY	QML	905.08	8.704	16.58 %
8mer_H2_Db	96	QVA	QYNNFSIF	SKK	1014.11	8.63	16.44 %
9mer_H2_Db	63	EMY	FMLCLIDHI	ISN	1086.38	20.064	39.84 %
9mer_H2_Db	95	RQV	AQYNNFSIF	SKK	1085.19	19.926	39.56 %
9mer_H2_Db	130	MEL	FAHWSKDHL	PIN	1099.25	19.277	38.27 %
9mer_H2_Db	44	ICQ	FNLRCLEFL	KSY	1136.39	15.072	29.93 %
9mer_H2_Db	41	PSL	ICQFNLRCL	EFL	1091.36	13.216	26.24 %
9mer_H2_Db	38	KAV	PSLICQFNL	RCL	1016.23	11.437	22.71 %
9mer_H2_Db	184	GYD	QLIKNAREL	YTE	1066.27	11.399	22.63 %
10mer_H2_Db	306	VSP	SILKPLADYG	ILN	1058.25	22.969	39.02 %
10mer_H2_Db	94	FRQ	VAQYNNFSIF	SKK	1184.32	19.021	32.32 %
10mer_H2_Db	73	HII	SNYEPFRKGF	ATK	1226.37	16.158	27.45 %
10mer_H2_Db	95	RQV	AQYNNFSIFS	KKN	1172.27	16.055	27.28 %
10mer_H2_Db	206	SIF	NGEINEKEKA	ELN	1113.19	15.416	26.19 %
10mer_H2_Db	9	LVK	SAIDNEEVNP	SLH	1069.1	11.88	20.18 %
10mer_H2_Db	70	LID	HIISNYEPFR	KGF	1257.43	11.82	20.08 %
11mer_H2_Db	94	FRQ	VAQYNNFSIFS	KKN	1271.4	13.696	17.23 %
11mer_H2_Db	285	DYS	KTETNYESYPV	QRE	1312.4	10.441	13.13 %
11mer_H2_Db	322	PVS	RKAGPMTYQML	EDD	1277.56	9.568	12.04 %
11mer_H2_Db	57	SYI	SRKEMYFMLCL	IDH	1402.76	9.078	11.42 %
11mer_H2_Db	39	AVP	SLICQFNLRCL	EFL	1291.6	7.777	9.78 %
11mer_H2_Db	8	ELV	KSAIDNEEVNP	SLH	1197.27	6.901	8.68 %
11mer_H2_Db	58	YIS	RKEMYFMLCLI	DHI	1428.84	6.462	8.13 %

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

MHC ALLELE	Rank	Sequence	Residue No.	Peptide Score
I-Ab	1	PSIKDLQRE	39	0.967
I-Ab	2	NTLTNDKRV	61	0.815
I-Ab	3	LTLGVNTLT	56	0.560
I-Ab	4	MLLTLGVNT	54	0.534
I-Ad	1	LSAMLLTLG	51	0.726
I-Ad	2	GAHFCGAMM	3	0.570
I-Ad	3	GIGAHFCGA	1	0.504
I-Ad	4	MAINDINGP	11	0.465
I-Ag7	1	INTAENIAC	23	1.564
I-Ag7	2	EINTAENIA	22	1.461
I-Ag7	3	FCGAMMAIN	6	1.246
I-Ag7	4	GIGAHFCGA	1	1.198
RT1.B	1	TEINTAENI	21	0.660
RT1.B	2	VEALSAMLL	48	0.586
RT1.B	3	TLTNDKRVL	62	0.365
RT1.B	4	TAENIACRA	25	0.250

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

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].

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_

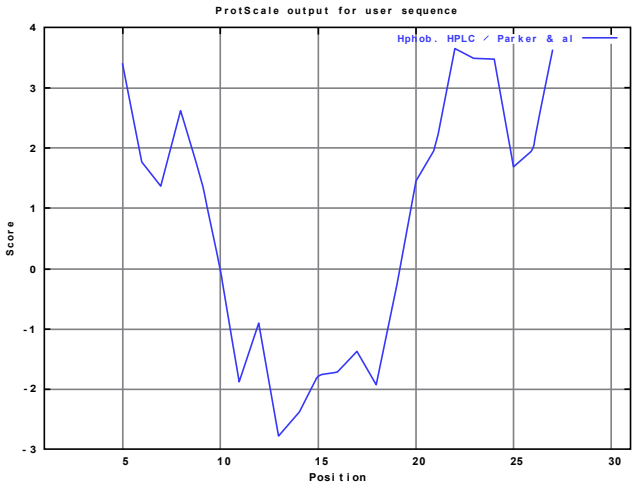

Figure 3: Hydrophobicity plot of antigen protein by Hphob. HPLC /Parker & et al., scale.

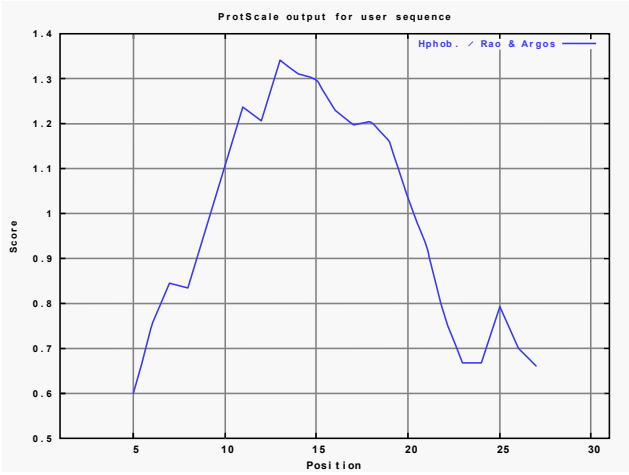

Figure 4: Antigenicity plot of antigen protein by Hphob. / Rao & Argos, scale.

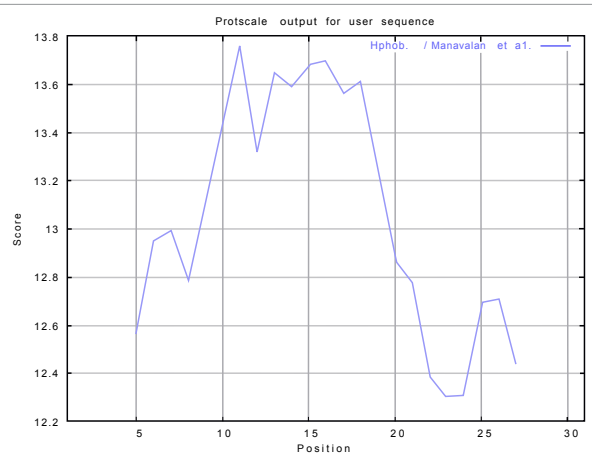

Figure 5: Antigenicity plot of antigen protein by Hphob. / Manavalan et al., scale.

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 a terminal region of antigen protein is solvent accessible and unstructured; antibodies against those regions are also likely to recognize the native protein (Figure 1, 2 and 3). It was shown that an antigen protein is hydrophobic in nature and contains segments of low complexity and high-predicted flexibility (Figure 4 and 5). Predicted antigenic fragments can bind to MHC molecule is the first bottlenecks in vaccine design.

Conclusion

An antigen protein from *Taenia crassiceps* 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 *Taenia crassiceps*.

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