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Prediction of MHC Binding Peptides and Antigenic Peptides from *Ascaris lumbricoides*

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Abstract

The parasitic disease Ascariasis is the major concern because of its morbidity and mortality issue. In this investigation, we predicted the binding peptides of the MHC class I and MHC class II by Position Specific Scoring Matrices (PSSM) and Support Vector Machine (SVM) algorithms. We predicted the binding affinity of Cytochrome c oxidase subunit 2 (mitochondrion) having a 232 amino acids long residue sequence, which shows 224 nonamers. We predicted the peptide binding affinity to MHC I moles are as 8mer_H2_Db(The binding thresholds: 33.04,optimal score:52.494), 9mer_H2_Db(Optimal Score: 50.232, Binding Threshold: 17.96),10mer_H2_Db (The Optimal Score: 58.858, Binding Threshold: 41.32), 11mer_H2_Db(Optimal Score: 79.495, Binding Threshold: 56.96) and MHC- II molecules are as I_Ab.p, I_Ad.p, I_Ag7. We also study integrates prediction of peptide MHC class I binding; proteasomal C terminal cleavage and TAP transport efficiency by using sequence and properties of the amino acids. We also found the binding of peptides to different alleles by using Position Specific Scoring Matrix. PSSM based server will predict the peptide binders of Cytochrome c oxidase subunit 2 from *Ascaris lumbricoides* sequence to, which are found antigenic epitopes region in protein.

Keywords: Ascariasis; *Ascaris lumbricoides*; Epitopes; Antigenic peptides; MHC-Binders; TapPred; PSSM; SVM; Nonamers; cytochrome c oxidase subunit 2 (mitochondrion)

Abbreviations

STH: soil-transmitted helminth; SAC: School-Age Children; MDA: Mass Drug Administration; MHC I: Major Histocompatibility Complex-Class I; MHC I: Major Histocompatibility Complex-Class II; PSSM: Position Specific Scoring Matrices; SVM: Support Vector Machine; GWD: Guinea Worm Disease; UniProt: The Universal Protein Resource; NCBI: National Center for Biotechnology Information; TAP: Transporter Associated with Antigen Processing; HPLC: High Performance Liquid Chromatography.

Introduction

Ascaris lumbricoides is the causative agent of "Ascariasis" in human and other mammals by intestinal roundworm of the genus 'Ascaris'. This parasite is the one of the largest nematode and, the measures of the adult worm measures upto 15-35 cm long and are white or yellow in color. the incubation period of the parasite is 10-24 months in the jejunum and middle ileum of the intestine(of host). Study suggest that, te infected individual sheds the different percentages of the eggs (fertilized egg: 45%, fertilized and unfertilized eggs shedding: 40% and unfertilized eggs: 20%. The fertilized eggs becomes infectious with period of 5-10 days and remain vible for upto 17 months after gets released in the favorable soil [1]. The spreading of the infection is due to soil contamination of hands or food, ingestion, and the subsequent hatching of eggs in the small intestine. The occurrence of this parasite was observed as a zoonotic infection which usually associated with pigs and use of hog manure [2] but, in most endemic areas, it is most likely transmitted from person to person [3].

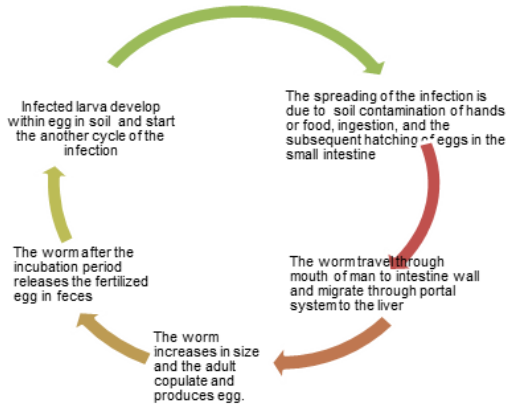

Figure 1: Lifecycle of the *Ascaris lumbricoides*.

The infected individuals, experience the symptoms of pneumonitis including wheezing, dyspnea, nonproductive cough, hemoptysis, and fever, and eosinophilia. The larvae incubation timing in the jejunum expected as 65 days and feeds on digestion of the host. The infected children with a marginal diet found to be susceptible to protein, caloric, or

suffer from Vitamin A deficiency, which stood up in growth retardation and increases the susceptibility to malaria infection [4] and sometime in overexposed situation, it causes relative immunodeficiency [5]. In the higher infection load of this worm causes severe complication whereas, at minimal level it remains asymptomatic. The occurrence of this disease is worldwide but predominantly found in that geographical area with warm and moist climates especially common in tropical and subtropical areas where there is poor practice of the sanitation and hygiene. The estimated worldwide preponderance of this disease is 25% (0.8-1.22 billion people) [6]. Children's of tropical and arising countries are more prone to this infection, where they are carried on by contamination of soil by human feces or use of untreated feces as fertilizer [7]. Symptomatic ascariasis may manifest as growth retardation, pneumonitis, intestinal obstruction, or hepatobiliary and pancreatic injury but, in most endemic areas, it is most likely transmitted from person to person [3]. The differential diagnoses are acute pancreatitis , biliary colic and community-acquired pneumonia. The vulnerable group for soil-transmitted helminth (STH) infections are children and as well as the impact of this infections directly on their health, nutritious status and cognitive ability [8]. The current strategy to control the STH infection is preventive chemotherapy with albendazole or mebendazole [9]. In the other study conducted by researcher in Chencha district where mass drug administration (MDA) to the most risky population including school-age children (SAC) is used as the central strategy to control soil-transmitted helminth (STH) infection [10]. In this study cytochrome c oxidase subunit II (mitochondrion) protein has been used to investigate its role in antigenicity. Cytochrome c oxidase subunit 2, also known as cytochrome c oxidase polypeptide II which is an oligomeric enzyme, an important component of the respiratory chain which involves in the transfer of electrons from cytochrome c to oxygen. This enzyme complex is found located in the mitochondrial inner membrane in eukaryotes. Cytochrome c oxidase subunit 2 contains two adjacent transmembrane regions in its N-terminus. The considerable part of the protein is generally exposed to the periplasmic or to the mitochondrial intermembrane space. The N-terminal domain of cytochrome C oxidase contains two transmembrane alpha-helices. Cytochrome oxidase deficiency and abnormality has been seen in the Leigh's disease. Investigation shows that any alterations in the catalytic genes of cytochrome c oxidase subunits I and II (COI and COII) have an adverse impact on prognosis in patients with acute myeloid leukaemia (AML) [11]. A "mitochondrial hypothesis" of late onset Alzheimer's disease (AD) has been proposed. The in depth biochemical studies propose that there is a significant decrease in cytochrome oxidase (CO) activity as well as perturbed CO I and CO III mRNA levels in platelets and brain tissue from Alzheimer's patients. The phenotypic expression study of the CO mutation is the major reason for reduced CO activity and compromised mitochondrial function [12]. Antigen protein prediction from Ascaris l umbricoides is necessary for few paradigms of synthetic vaccine development and target validation. Antigenicity prediction of the protein from *Ascaris lumbricoides* can play an important role in prototype synthetic vaccine development and as well as for target validation.

Methodology

Retrieval of protein data from database

The protein amino acid sequence of cytochrome c oxidase subunit 2 (mitochondrion)from *Ascaris lumbricoides* parasite was retrieved from www.ncbi.nlm.nih.gov, UniProt databases [13-15].

Protein antigenicity prediction

Prediction of antigenicity Cytochrome c oxidase subunit 2 (mitochondrion) proteins were performed and obtained the peptide segments of protein that are likely to be antigenic and capable of eliciting an antibody response. The methods were used to analyze the antigenic peptide region of Cytochrome c oxidase subunit 2 (mitochondrion) are Hopp and Woods, Welling, Parker, Bepipred ,Kolaskar and Tongaonkar antigenicity methods[16-28].

MHC binding peptide prediction

The major histocompatibility complex (MHC) peptide binding of Ascarislumbricoidespredicted using neural networks trained on C terminals of known epitopes. Rankpep predicting tool predicts peptide binders to MHC-I ligands using PSSMs, whose C-terminal end is likely to be the result of proteosomal cleavage. The sequence similarity is observed to the peptides that bind to a given MHC molecule. Traditionally, the sequence patterns used for the prediction of peptides binding to MHC molecules. Such sequence patterns, however, have proven to be too simple, as the complexity of the binding motif cannot be precisely represented by the few residues present in the pattern [29]. RANKPEP uses "Position Specific Scoring Matrices (PSSMs) or profiles" from set of aligned peptides known to bind to a given MHC molecule as the predictor of MHC-peptide binding and overcome the complexity of the binding motif limitation. RANKPEP web server is a variability masking feature to focus on the prediction of conserved epitopes, which could thus help to avoid immune evasion resulting from mutation. Support Vector Machine (SVM) based method for prediction of promiscuous MHC class II binding peptides from protein sequence; SVM has been trained on the binary input of single amino acid sequence [30-33].

Prediction of antigenic peptides by cascade SVM based TAPPred method

In the present study, we predicted the cascade SVM based several TAP binders which was based on the sequence and the features of amino acids [34]. We found the MHCI binding regions (Table 3), the binding affinity of *Ascaris lumbricoides*.

Solvent accessible regions

We also analyzed the solvent accessible regions of proteins having highest probability that a given protein region lies on the surface of a protein Surface Accessibility, backbone or chain flexibility by Emini et al [35] and Karplus and Schulz [36]. The different scaleswere used to predict the hydrophobic and hydrophilic characteristics of amino acids which is rich in charged and polar residues. The methods used are Sweet et al., Kyte and Doolittle, Abraham and Leo, Bull and Breese, Guy, Miyazawa, et al, Roseman, Wolfenden et al., Wilson et al., Cowan, Chothia [37-46].

Results

Retrieved protein information

The *Ascaris lumbricoides* antigenCytochrome c oxidase subunit 2 (mitochondrion)[gi|319656158|gb|ADV58572.1|], contain a long residue of 232 amino acids with 224 nonamers.

>gi|319656161|gb|ADV58575.1| cytochrome c oxidase subunit 2 (mitochondrion) [Ascarislumbricoides]

MNNFFQDFSLLFSSSLFSSYMDWFYNFNCSLLFGVLSFVSTMFVYL
LLSSFYFKSKKIEYQFGELLCSVFPTLILVMQMVPSLSLLYYYGLMNLDSS
LTVKVTGHQWYWSYEFSDIPGLEFDSYMKSLDQLELGEPRLLEVDNR
CVVPCDVNIRFCITSGDVIHSWALPSMSIKLDAMSGILSTLSYSFPVVG
VFYGQCSEICGANHSFMPVALEVTLLDNFKSWCMGLLND

Antigenic peptides result data through antigenic prediction method

In this prediction, we investigated the area of greatest local Hydrophilicity through antigenic determinants . In the Hopp-Woods scale Hydrophilicity Prediction Result Data found high in Position: 133 Score: 0.956 (max) (130-QLELGEP -136) in a protein, assuming that the antigenic determinants would be exposed on the surface of the protein and thus would be located in hydrophilic regions (Figure 2). Welling et al. antigenicity plot provides value as the log of the quotient between percentage in average proteins and percentage in a sample of known antigenic regions. The prediction result found highest in Position: 98, Score: 0.331 (max) 95-DSSLTVK-101 (Figure 3). We also study Hydrophobicity plot of HPLC / Parker Hydrophilicity Prediction Result Data found in Position:143 (Residue:N) i.e. 140- EVDNRCV-146 with highest score:3.286 (Figure 4), BepiPred predicts the location of linear B-cell epitopes Result found in Position:114(Residue:S) with highest score :0.510 (111-YEFSDIP-117) (Figure 5), Kolaskar and Tongaonkar antigenicity methods (Figures 6a and 6b) Predicted peptides result found

6-QDFSLLFSSSLFS-18,25-YNFNCSLLFGVLSFVSTMFVYLLLSSFYFK-54,61-QFGELLCSVFPTLILVMQMVPSLSLLYYYGL-91,95-DSSLTVKVTG-104, 115-DIPGLEF-121,124-YMKSLDQ-130,132 ELGEPRLLEVDNRCVVPCDVNIRFCITSGDVIHSWALPSMSIKL-175,177 AMSGILSTLSYSFPVVGVFYGQCSEICGA-205, 208-SFMPVALEVTLLD-220 and the predicted antigenic fragments can bind to MHC molecule is the first bottlenecks in vaccine design.

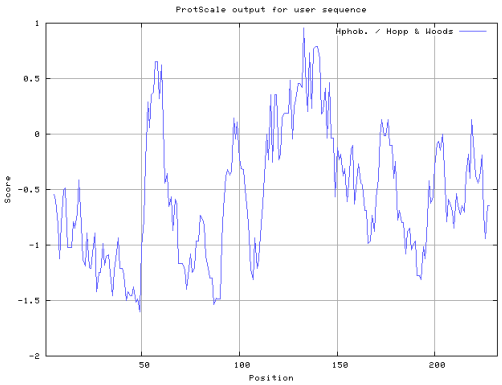

Figure 2: Hydrophobicity plot of Hopp and Woods.

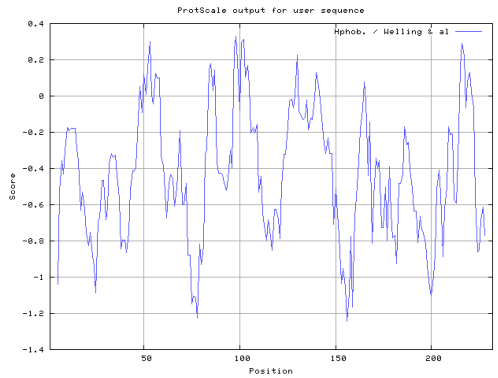

Figure 3: Hydrophobicity plot of Welling et al.

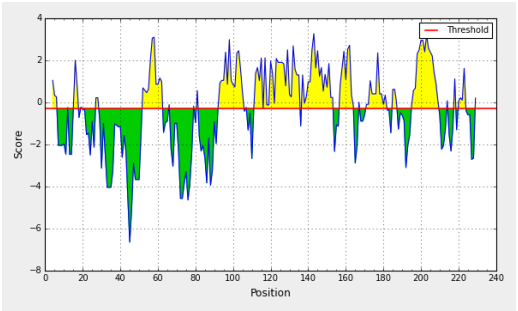

Figure 4: Hydrophobicity plot of HPLC / Parker et al.

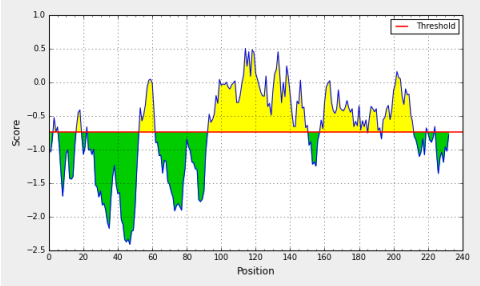

Figure 5: Bepipred Linear Epitope Prediction plot.

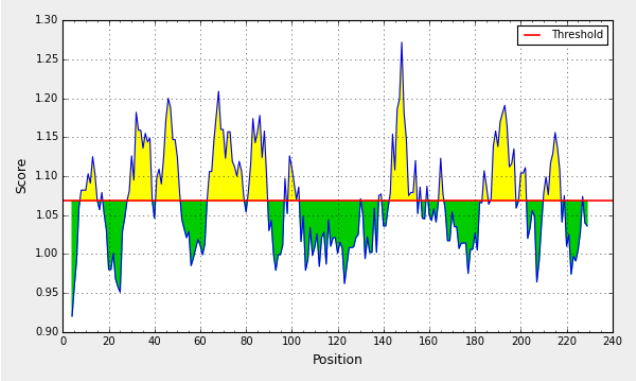

Figure 6: Kolaskar and Tongaonkar antigenicity plot.

Your sequence is 232 residues long

Average antigenic propensity for this protein is 1.0645

Antigenic plot for sequence

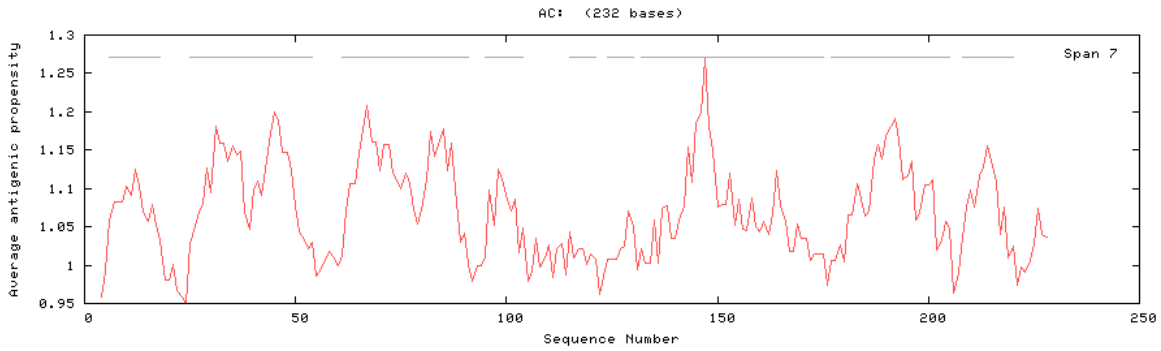

Figure 6a: Kolaskar and Tongaonkar antigenicity plot, the average antigenic propensity for protein is 1.0645.

There are 9 antigenic determinants in your sequence:

n	Start Position	Sequence	End Position
1	6	QDFSLLFSSSLFS	18
2	25	YNFNCSLLFGVLSFVSTMFVYLLLSSFYFK	54
3	61	QFGELLCSVFPTLILVMQMVPSLSLLYYYGL	91
4	95	DSSLTVKVTG	104
5	115	DIPGLEF	121
6	124	YMKSLDQ	130
7	132	ELGEPRLLEVDNRCVVPCDVNIRFCITSGDVIHSWALPSMSIKL	175
8	177	AMSGILSTLSYSFPVVGVFYGQCSEICGA	205
9	208	SFMPVALEVTLLD	220

Figure 6b: The 9 antigenic determinants of Cytochrome c oxidase subunit 2 (mitochondrion) protein.

The predicted peptide of MHC class I & II

We found the binding of peptides to a number of different alleles using Position Specific Scoring Matrix. cytochrome c oxidase subunit 2 (mitochondrion) of *Ascaris lumbricoides* antigen, with sequence 232 amino acid residues long, having 224nonamers. MHC molecules are cell surface proteins, which actively participate in host immune reactions and involvement of MHC-I and MHC-II in response to almost all antigens. We have predicted MHC-I peptide binders of cytochrome c oxidase subunit 2 (mitochondrion) from *Ascaris lumbricoides*. We found predicted MHC-I peptide binders of protein for Matrix: 8mer_H2_Db.p.mtx, Consensus: QNWNCCTI, Optimal Score: 52.494, Binding Threshold: 33.04; Matrix: 9mer_H2_Db.p.mtx, Consensus: FCIHNCDYM, Optimal Score: 50.232, Binding Threshold: 17.96; Matrix: 10mer_H2_Db.p.mtx, Consensus: SGYYNFFWCL, Optimal Score: 58.858, Binding Threshold: 41.32;Matrix: 11mer_H2_Db.p.mtx,Consensus: CGVYNFYYCCY, Optimal Score: 79.495, Binding Threshold: 56.96 (Table 1) and MHC-II peptide binders for Matrix: I_Ab.p.mtx, Consensus: YYAPWCNNA, Optimal Score: 35.632, Binding Threshold: 9.52; Matrix: I_Ad.p.mtx, Consensus: QMVHAAHAE, Optimal Score: 53.145, Binding Threshold: 7.10; Matrix: I_Ag7.p.mtx, Consensus: WYAHAFKYV, Optimal Score: 40.873,Binding Threshold:7.54 for MHC II allele (Table 2) was tested. In this

test, we found the MHCI and MHCII binding regions. T cell immune responses are derived by antigenic epitopes hence their identification is important for design synthetic peptide vaccine. T cell epitopes are recognized by MHCI molecules producing a strong defensive immune response against *Ascaris lumbricoides* antigen cytochrome c oxidase subunit 2. Therefore, the prediction of peptide binding to MHCI molecules by appropriate processing of antigen peptides occurs by their binding to the relevant MHC molecules. Because, the C-terminus of MHCI-restricted epitopes results from cleavage by the proteasome and thus, proteasome specificity is important for determining T-cell epitopes. Consequently, RANKPEP also focus on the prediction of conserved epitopes. C-terminus of MHCI-restricted peptides is generated by the proteasome, and thus RANKPEP also determines whether the C-terminus of the predicted MHCI-peptide binders is the result of proteasomal cleavage. Moreover, these sequences are highlighted in purple in the output results. Proteasomal cleavage predictions are carried out using three optional models obtained applying statistical language models to a set of known epitopes restricted by human MHCI molecules as indicated as I_Ab.p, I_Ad.p,I_Ag7.p,I_Ak.p alleles, which is highlighted in red represent predicted binders. Peptides whose score is above the binding threshold will appear highlighted in red and peptides produced by the cleavage prediction model are highlighted in violet. We also use a cascade SVM based TAPPred method which found 72 High affinity TAP Transporter peptide regions (Table 3) which represents predicted TAP binders residues which occur at N and C termini from *Ascaris lumbricoides* cytochrome c oxidase subunit 2.

Table 1: Promiscuous MHC ligands, having C-terminal ends are proteosomal cleavage sites of *Ascaris lumbricoides*. The antigenic peptide to the MHC-1 Allele i.e. 8mer_H2_Db(The binding thresholds: 33.04,optimal score: 52.494), 9mer_H2_Db(Optimal Score: 50.232, Binding Threshold: 17.96), 10mer_H2_Db(The Optimal Score: 58.858,BindingThreshold: 41.32), 11mer_H2_Db (Optimal Score: 79.495, Binding Threshold: 56.96). (All rows highlighted in red represent predicted binders & A peptide highlighted in violet has a C-teminus predicted by the cleavage model used).

MHC-I Allele	RANK	POS.	N	SEQUENCE	C	MW (Da)	SCORE	% OPT.
8mer_H2_Db	1	151	PCD	VNIRFCIT	SGD	947.16	18.097	34.47%
8mer_H2_Db	2	114	YEF	SDIPGLEF	DSY	858.96	11.881	22.63%
8mer_H2_Db	3	81	QMV	PSLSLLYY	YGL	937.12	9.399	17.90%
8mer_H2_Db	4	140	RLL	EVDNRCVV	PCD	915.03	8.385	15.97%
8mer_H2_Db	5	39	LSF	VSTMFVYL	LLS	941.15	8.221	15.66%
9mer_H2_Db	1	24	MDW	FYNFNCSLL	FGV	1102.28	23.546	46.75%
9mer_H2_Db	2	202	CSE	ICGANHSFM	PVA	961.12	21.224	42.40%
9mer_H2_Db	3	155	NIR	FCITSGDVI	HSW	936.09	20.262	40.23%
9mer_H2_Db	4	145	DNR	CVVPCDVNI	RFC	943.14	18.155	36.05%
9mer_H2_Db	5	222	LDN	FKSWCMGLL	ND	1043.34	17.041	33.84%
10mer_H2_Db	1	217	LEV	TLLDNFKSWC	MGL	1185.39	20.603	35.00%
10mer_H2_Db	2	37	GVL	SFVSTMFVYL	LLS	1175.41	15.765	26.78%
10mer_H2_Db	3	89	LYY	YGLMNLDSSL	TVK	1094.25	12.727	21.62%
10mer_H2_Db	4	179	DAM	SGILSTLSYS	FPV	1009.13	11.842	20.12%
10mer_H2_Db	5	22	SYM	DWFYNFNCSL	LFG	1267.42	9.333	15.86%
11mer_H2_Db	1	217	LEV	TLLDNFKSWCM	GLL	1316.58	15.277	19.22%
11mer_H2_Db	2	33	SLL	FGVLSFVSTMF	VYL	1216.46	11.657	14.66%
11mer_H2_Db	3	190	YSF	PVVGVFYGQCS	EIC	1137.32	11.369	14.30%
11mer_H2_Db	4	22	SYM	DWFYNFNCSLL	FGV	1380.58	10.926	13.74%
11mer_H2_Db	5	81	QMV	PSLSLLYYYGL	MNL	1270.51	9.556	12.02%

Table 2: Prediction of MHCII ligands all rows highlighted in red represent predicted binders to the MHC-II Allele i.e. MHC-II I_Ab, MHC-II I_Ad,MHC-II I_Ag7. (All rows highlighted in red represent predicted binders).

MHC-II Allele	RANK	POS.	N	SEQUENCE	C	MW (Da)	SCORE	% OPT.
MHC-II I_Ab	1	24	MDW	FYNFNCSLL	FGV	1102.28	15.46	43.39%
MHC-II I_Ab	2	146	NRC	VVPCDVNIR	FCI	996.19	11.457	32.15%
MHC-II I_Ab	3	166	IHS	WALPSMSIK	LDA	991.25	9.113	25.58%
MHC-II I_Ab	4	86	LSL	LYYYGLMNL	DSS	1131.36	8.789	24.67%
MHC-II I_Ab	5	66	GEL	LCSVFPTLI	LVM	974.23	8.484	23.81%
MHC-II I_Ad	1	179	DAM	SGILSTLSY	SFP	922.05	11.052	20.80%
MHC-II I_Ad	2	6	NFF	QDFSLLFSS	SLF	1025.14	10.975	20.65%
MHC-II I_Ad	3	56	FKS	KKIEYQFGE	LLC	1123.28	10.568	19.89%
MHC-II I_Ad	4	198	FYG	QCSEICGAN	HSF	906	9.117	17.15%
MHC-II I_Ad	5	33	SLL	FGVLSFVST	MFV	938.09	7.251	13.64%
MHC-II Ag7	1	114	YEF	SDIPGLEFD	SYM	974.05	7.637	18.68%
MHC-II Ag7	2	214	PVA	LEVTLLDNF	KSW	1045.2	6.26	15.32%
MHC-II Ag7	3	190	YSF	PVVGVFYGQ	CSE	947.1	5.899	14.43%
MHC-II Ag7	4	78	LVM	QMVPSLSLL	YYY	969.21	4.86	11.89%
MHC-II Ag7	5	81	QMV	PSLSLLYYY	GLM	1100.3	4.423	10.82%

Table 3: Cascade SVM based High affinity TAP Binders of *Ascaris lumbricoides*.

Peptide Rank	Start Position	Sequence	Score	Predicted Affinity
1	94	LDSSLTVKV	8.645	High
2	34	GVLSFVSTM	8.641	High
3	6	QDFSLLFSS	8.64	High
4	163	IHSWALPSM	8.639	High
5	55	SKKIEYQFG	8.637	High
6	13	SSSLFSSYM	8.635	High
7	147	VPCDVNIRF	8.63	High
8	82	SLSLLYYYG	8.627	High
9	215	EVTLLDNFK	8.627	High
10	185	LSYSFPVVG	8.619	High

Prediction of solvent accessible regions of protein

We also predict solvent accessible regions in proteins; different measurement was performed for the prediction of antigenic activity, surface region of peptides. Emini et al., (Figure 7) predicts the highest probability in position:54 (Residue: K) i.e., 52-YFKSKK-57 with maximum score:5.745, that a given protein region lies on the surface of a protein and are used to identify antigenic determinants on the surface of proteins. Karplus and Schulz (Figure 8) High score is found i.e. found in position:56 (Residue:K) 53-FKSKKIE-59 with maximum score: 1.071. The hydrophobicity and hydrophilic characteristics of amino acids is determined by several other scales i.e. Sweet et al. hydrophobicity prediction result data found high in position in Position:49 with maximum Score: 1.082 (max)(46-LLLSSFY-52) (Figure 9), Kyte & Doolittle result high in position:35, Score:2.689 (max)(32-LFGVLSF-38) (Figure 10), Abraham and Leo result high Position:73, Score:1.707 (max)(70-FPTLILV-76) (Figure 11), Bull and Breese use surface tension to measure in Position: 202, Score:0.387 (max)(199-CSEICGA-205) (Figure 12), Miyazawa result high in Position:73 Score:7.486 (max)(70-FPTLILV-76 (Figure 13), Guy result high in Position:133 Score:0.444 (max)(130-QLELGEP-136) (Figure 14), Wolfenden result high in Position:35, Score:0.737 (max)(32-LFGVLSF-38) (Figure 15), Roseman result high in Position: 35,Score:1.262 (max)(32-LFGVLSF-38) (Figure 16), Wilson et al. Position:87, Score:5.367 (max)(84-SLLYYYG-90) (Figure 17), Cowan Position: 73, Score: 1.270 (max)(70-FPTLILV-76) (Figure18), ChothiaPosition: 35, Score: 0.446 (max)(32-LFGVLSF-38) (Figure 19).

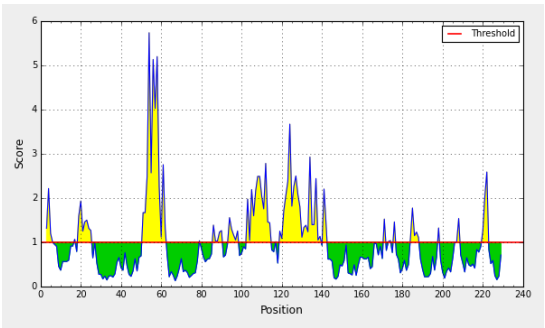

Figure 7: Emini Surface Accessibility Prediction plot.

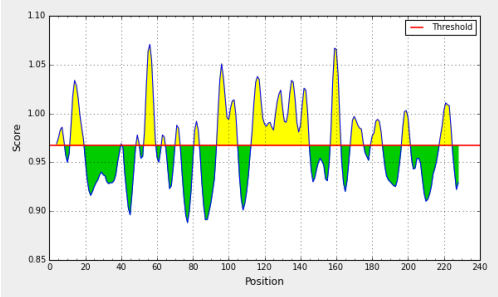

Figure 8: Karplus and Schulz Flexibility Prediction.

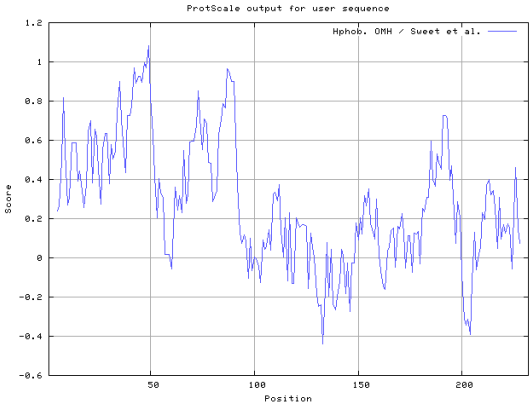

Figure 9: Hydrophobicity plot of Sweet et al.

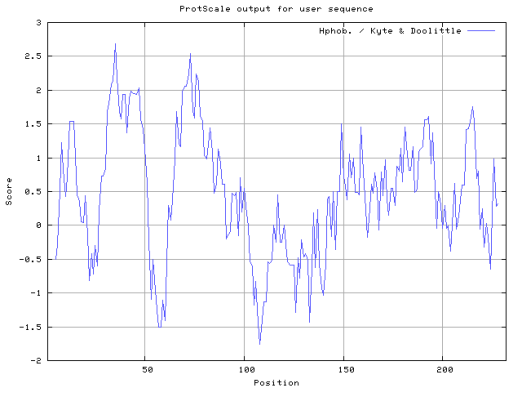

Figure 10: Kyte and Doolittle hydrophobicity plot.

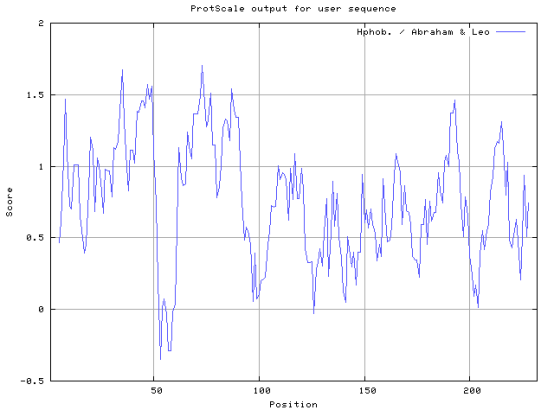

Figure 11: Abraham and Leo hydrophobicity plot.

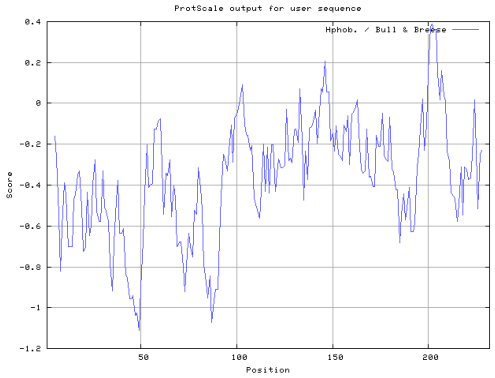

Figure 12: Bull and Breese use surface tension to measure hydrophobicity and also uses negative values to describe the hydrophobicity of antigen Cytochrome c oxidase subunit 2 (mitochondrion).

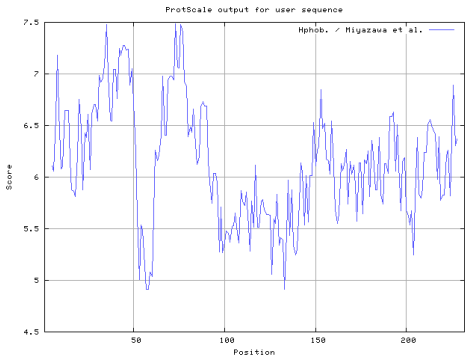

Figure 13: Hydrophobicity plot of Miyazawa et al.

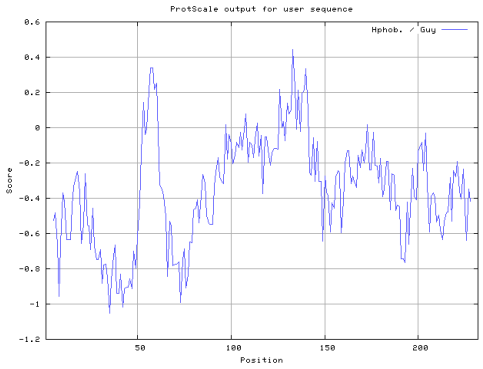

Fig. 14- Hydrophobicity plot of Guy.

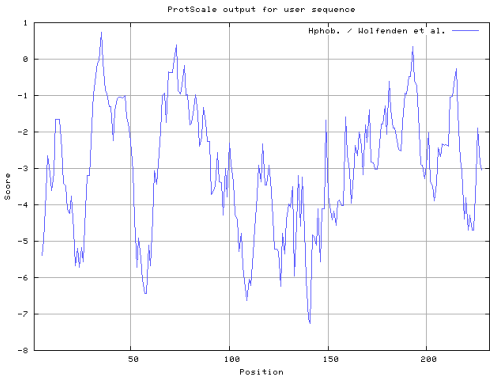

Figure 15: Hydrophobicity plot of Wolfenden et al.

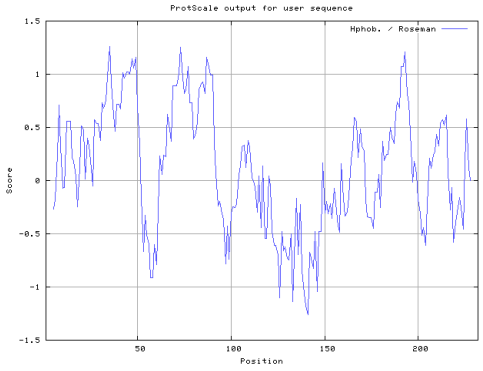

Figure 16: Hydrophobicity plot of Roseman MA [42].

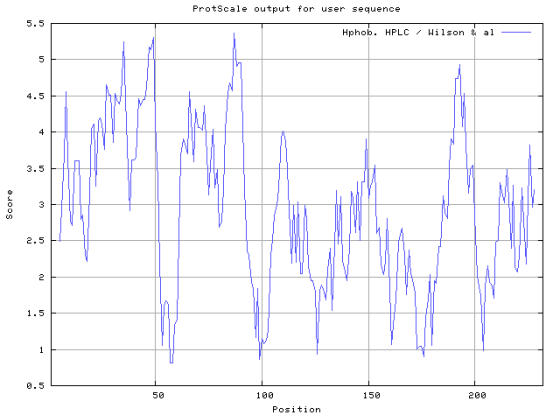

Figure 17: Hydrophobicity/HPLC plot of Wilson et al.

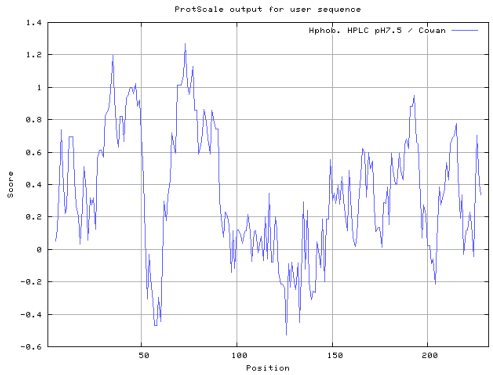

Figure 18: Hydrophobicity/HPLC pH 3.4/ plot of Cowan.

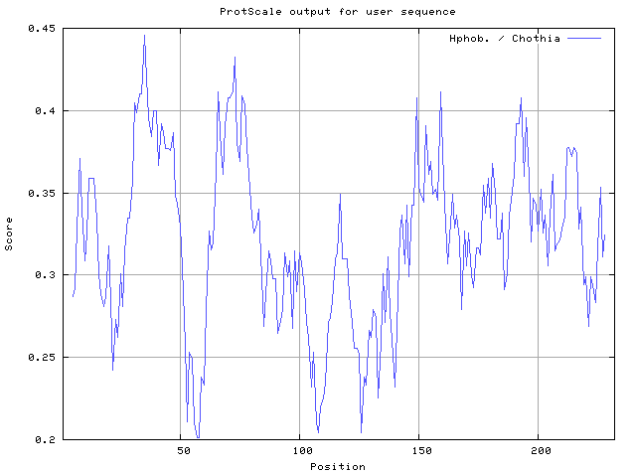

Figure 19: Hydrophobicity plot of Chothia.

Conclusion

MHC molecules are the cell surface proteins, which actively take part in the host immune responses against infection (pathogens) and reason of its involvement in the response to

almost all antigens and it gives effects on specific sites. This knowledge of the immune responses to an antigen protein (cytochrome c oxidase subunit 2 from *Ascaris lumbricoides*) clear that the whole protein is not necessary for raising the immune response, but a small fragment of antigen can induce immune response against whole antigen. This means the increase in affinity of MHC binding peptides may result in enhancement of immunogenicity of cytochrome c oxidase subunit 2 from *Ascaris lumbricoides*, hence are helpful *in silico* to design and develop highly predictive computational tools for the identification of T-cell epitopes. Finally, accurate prediction remains vital for the future to design synthetic peptide vaccine. The Overall conducted study and opted results are encouraging. Both the 'sites of action' and 'physiological functions' can be predicted with very high accuracies which is helping to minimize the number of validation experiments. The future perspectives of this method will be useful in cellular immunology, vaccine design, immunodiagnostics, immunotherapeutic and molecular understanding of autoimmune susceptibility.

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