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Application computational intelligence for development of synthetic peptide vaccine from *Mycobacterium avium*

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Abstract- *Mycobacterium avium* causes MAC diseases. Symptoms of MAC diseases are reminiscent of tuberculosis; they include fever, fatigue, and weight loss. 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 *Mycobacterium avium* are important determinant for protection of host form bacterial infection. In this assay, we used PSSM and SVM algorithms for antigen design and predicted the binding affinity of antigen protein having 195 amino acids, which shows 187 nonamers. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from *Mycobacterium avium*.
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

Mycobacterium avium causes MAC diseases. Symptoms of MAC diseases are reminiscent of tuberculosis; they include fever, fatigue, and weight loss [1, 2]. *Mycobacterium avium* 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 a infected 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 *Mycobacterium avium* 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 *Mycobacterium avium* is determined using the Gomase in 2007, Welling, Parker, Wolfenden, Chou & Fasman and Deleage & Roux [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].

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 195 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 a 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 *Mycobacterium avium* 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 bacterial antigen protein. These predicted of antigen protein antigenic peptides to MHC class molecules are important in vaccine development from *Mycobacterium avium*.

V. References

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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	30	DAK	QPGDYFTT	ITS	909.95	18.618	35.47 %
8mer_H2_Db	140	IVD	PNNEIQFV	SVT	942.04	16.936	32.26 %
8mer_H2_Db	45	DHA	GKWRVVFF	WPK	997.24	15.133	28.83 %
8mer_H2_Db	85	VLG	VSIDSEFV	HFN	876.97	14.226	27.10 %
9mer_H2_Db	138	TFI	VDPNNEIQF	VSV	1057.13	14.168	28.13 %
9mer_H2_Db	91	DSE	FVHFNWRAQ	HED	1163.34	11.984	23.79 %
9mer_H2_Db	51	RVV	FFWPKDFTF	VCP	1193.41	11.092	22.02 %
9mer_H2_Db	153	TAG	SVGRNVEEV	LRV	970.05	10.943	21.73 %
10mer_H2_Db	29	VDA	KQPGDYFTTI	TSE	1151.28	21.893	37.20 %
10mer_H2_Db	128	LNA	DGVADRATFI	VDP	1046.15	14.989	25.47 %
10mer_H2_Db	138	TFI	VDPNNEIQFV	SVT	1156.26	13.55	23.02 %
10mer_H2_Db	40	TIT	SEDHAGKWRV	VFF	1143.26	5.694	9.67 %
11mer_H2_Db	122	SLA	TGVLNADGVAD	RAT	1013.06	8.616	10.84 %
11mer_H2_Db	137	ATF	IVDPNNEIQFV	SVT	1269.42	7.307	9.19 %
11mer_H2_Db	128	LNA	DGVADRATFIV	DPN	1145.28	7.165	9.01 %
11mer_H2_Db	5	PLL	TIGDQFPAYEL	TAL	1235.37	7.048	8.87 %

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

MHC ALLELE	Rank	Sequence	Residue No.	Peptide Score
I-Ab	1	RAQHEDLKN	97	1.015
I-Ab	2	PMLSDIKRE	109	1.007
I-Ab	3	PGDYFTTIT	31	0.909
I-Ab	4	DLSKVDAKQ	22	0.850
I-Ad	1	LATGVLNAD	120	0.809
I-Ad	2	IQFVSVTAG	144	0.588
I-Ad	3	GSVGRNVEE	152	0.494
I-Ad	4	SIDSEFVHF	86	0.490
I-Ag7	1	GDQFPAYEL	7	1.437
I-Ag7	2	EFVHFNWRA	90	1.370
I-Ag7	3	SKVDAKQPG	24	1.333
I-Ag7	4	DPTLNATEL	182	1.273
RT1.B	1	TTITSEDHA	36	1.084
RT1.B	2	TLNATELLK	184	0.658
RT1.B	3	FEDRDAQVL	75	0.640
RT1.B	4	DEFEDRDAQ	73	0.638

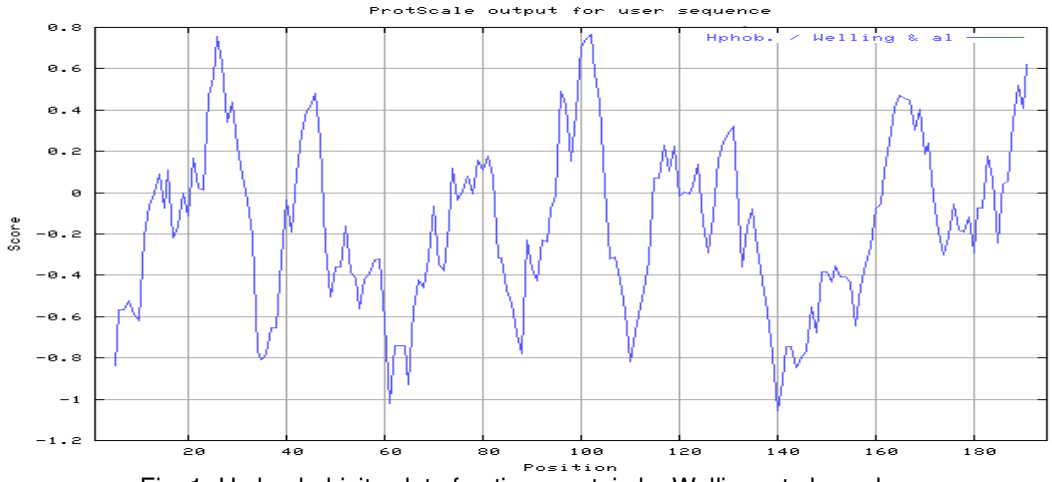

Fig. 1- Hydrophobicity plot of antigen protein by Welling, et al., scale

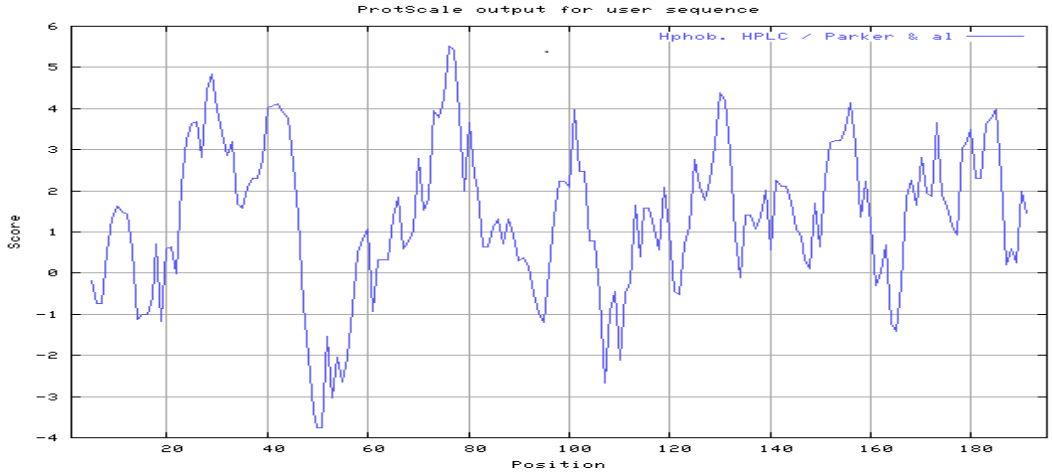

Fig. 2- Hydrophobicity plot of antigen protein by HPLC / Parker, et al., scale

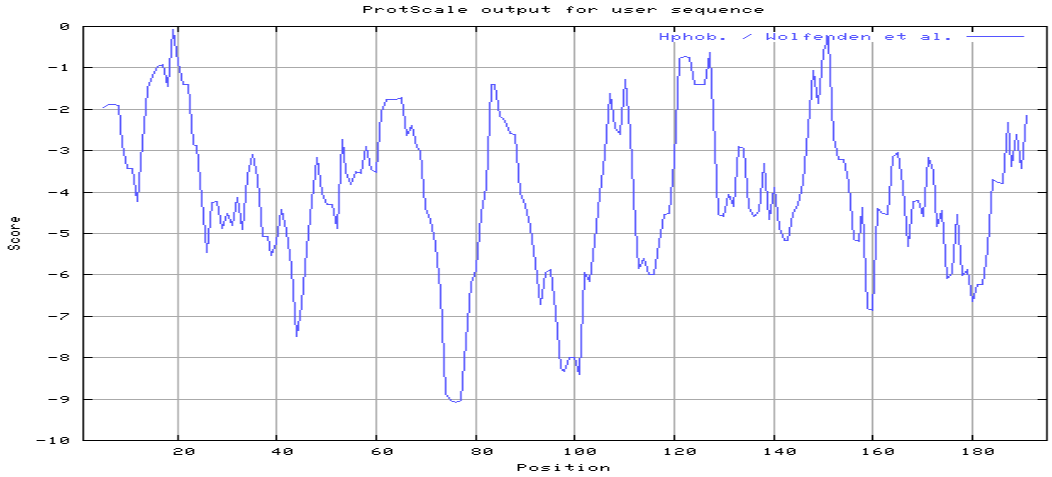

Fig. 3- Hydrophobicity plot of antigen protein by Wolfenden, et al., scale

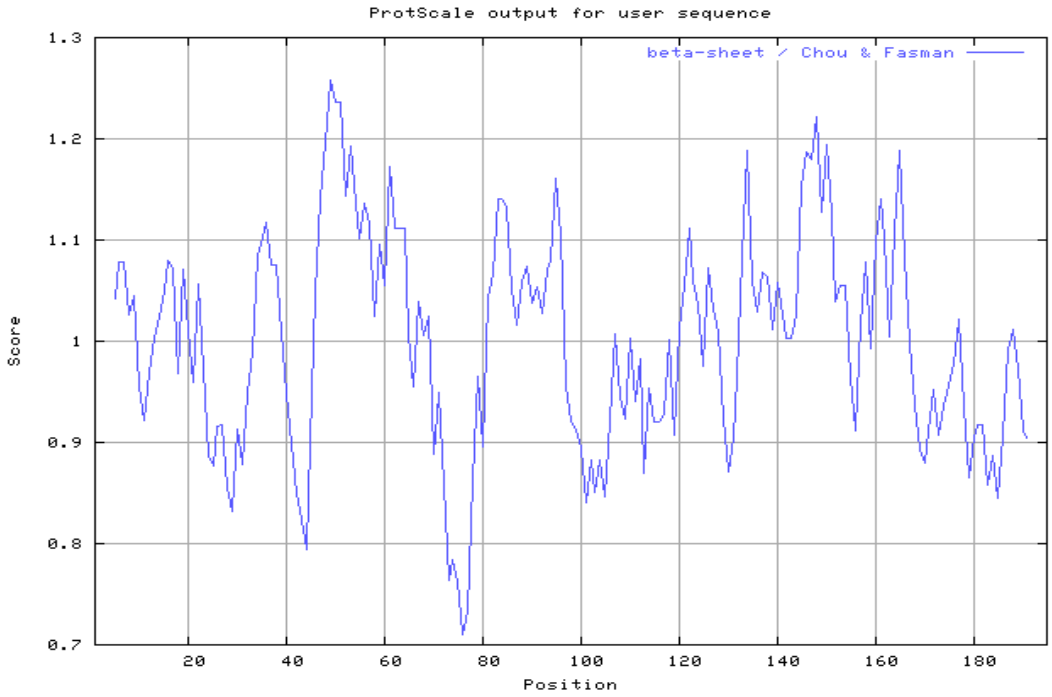

Fig. 4-Antigenicity plot of antigen protein by Beta-Sheet / Chou & Fasman scale

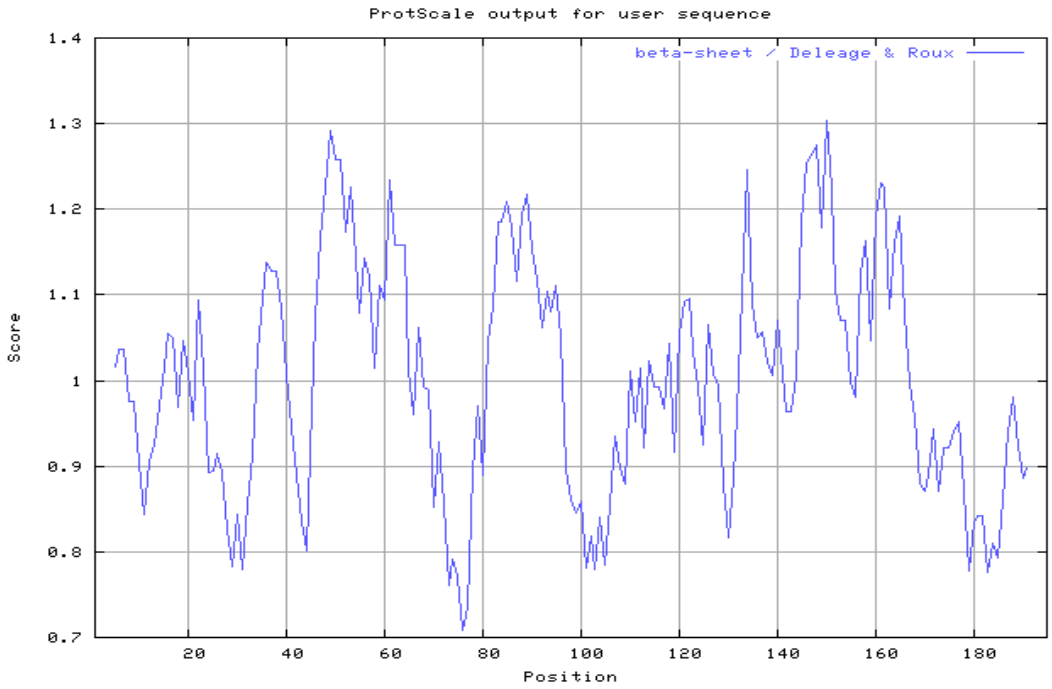

Fig. 5- Antigenicity plot of antigen protein by Deleage & Roux scale