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IMMUNOINFORMATICS STUDY OF PHYSICAL PROPERTIES OF SCORPION NEUROTOXIN BMK-M8 FROM *MESOBUTHUS MARTENSII*

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ABSTRACT

Neurotoxin can cause body paralysis or even death due to respiratory failure. Neurotoxin Bmk-M8 from Scorpio *Mesobuthus martensii* is used to find out potential binding peptides. In this assay, we used PSSM and SVM algorithms to determine antigenic epitopes and predicted the binding affinity of toxin protein having 64 residues, which shows 56 nonamers. In addition we have predicted the hydrophobic secondary structure and solvent accessible structure of *M. martensii* Bmk-M8. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from *Mesobuthus martensii* Bmk-M8.

KEYWORDS: Neurotoxin, Epitope, Nonamers, PSSM, SVM, MHC.

INTRODUCTION

Scorpion neurotoxins have different physiological and pharmacological activities. *Mesobuthus martensii* is one of the toxic scorpions having toxic activity against various mammals including human. Scorpion toxin contains of numerous hydrophobic polypeptides, several polypeptides inhibits activity of ion channels and disturb their functional properties.[1,2] *Mesobuthus martensii* Bmk-M8 peptides found potential for subunit vaccine design because immune response can be generated even with single epitope. This approach is based on the cross-protection phenomenon, whereby an individual with mild toxic effects have strong immunity against severe effects of the same. *Mesobuthus martensii* Bmk-M8 is necessary for new paradigm of synthetic vaccine development and target validation.[3-5]

METHODOLOGY

In this research work antigenic epitopes of *Mesobuthus martensii* Bmk-M8 are determined using the Gomase in 2007, Emini Surface Accessibility, Welling, Bull & Breeze hydrophobicity Scale.[6-11] The MHC peptide binding of toxin protein is predicted using neural networks trained on C terminals of known epitopes. In analysis predicted MHC/peptide binding of toxin protein is a log-transformed value related to the IC50 values in nM units. PSSM based algorithm is used to predicts peptide binders to MHC-I and MHC-II molecules from protein sequences or sequence. Support Vector Machine (SVM) based method for prediction of promiscuous MHC-II binding peptides. SVM has been trained on the binary input of single amino acid sequence.[12-16] In addition, we also predicted the hydrophobic secondary structure and Solvent accessible of Bmk-M8 Neurotoxin [Fig. 1-2].

RESULTS AND INTERPRETATIONS

We found binding of peptides to a number of different alleles using Position Specific Scoring Matrix. An antigen protein sequence is 64 amino acids long, having antigenic binding peptides. MHC molecules are cell surface glycoproteins, which take active part in host immune reactions and involvement of MHC-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 [Table-1]. We also found the SVM based MHCII-IAb, MHCII-IA and MHCII-IAg7 peptide regions, which represented predicted

binders from antigen protein [Table-2]. The predicted binding affinity is normalized by the 1% fractil.

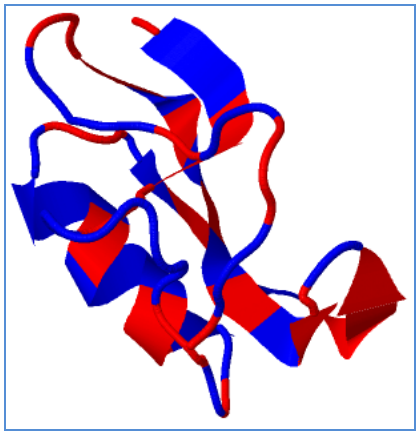

Fig. 1: The NMR Solution Structure of hydrophobicity *Mesobuthus martensii* Bmk-M8.

Table 1: PSSM based prediction of MHC ligands having C-terminal proteosomal cleavage sites.

MHC-I Allele	POS.	N	SEQUENCE	C	MW (Da)	SCORE	% OPT.
8mer_H2_Db	8	YIA	DSENCTYF	CGS	959.99	14.255	27.16 %
8mer_H2_Db	42	AGR	YGNACYCI	DLP	888.03	6.634	12.64 %
8mer_H2_Db	21	SNP	YCNDVCTE	NGA	928.0	5.817	11.08 %
8mer_H2_Db	18	FCG	SNPYCNDV	CTE	892.94	2.639	5.03 %
9mer_H2_Db	7	AYI	ADSENCTYF	CGS	1031.07	17.338	34.42 %
9mer_H2_Db	41	WAG	RYGNACYCI	DLP	1044.22	11.211	22.26 %
9mer_H2_Db	17	YFC	GSNPYCNDV	CTE	949.99	0.469	0.93 %
10mer_H2_Db	40	QWA	GRYGNACYCI	DLP	1101.27	12.044	20.46 %
10mer_H2_Db	16	TYF	CGSNPYCNDV	CTE	1053.13	6.559	11.14 %
10mer_H2_Db	33	GAK	SGYCQWAGRY	GNA	1149.29	2.599	4.42 %
10mer_H2_Db	19	CGS	NPYCNDVCTE	NGA	1139.22	0.466	0.79 %
11mer_H2_Db	39	CQW	AGRYGNACYCI	DLP	1172.35	25.598	32.20 %
11mer_H2_Db	25	CND	VCTENGAKSGY	CQW	1110.2	15.763	19.83 %
11mer_H2_Db	32	NGA	KSGYCQWAGRY	GNA	1277.46	9.137	11.49 %
11mer_H2_Db	28	VCT	ENGAKSGYCQW	AGR	1201.31	7.288	9.17 %
11mer_H2_Db	37	GYC	QWAGRYGNACY	CID	1247.39	2.593	3.26 %

Table 2: Promiscuous MHC class II binding peptides from *M. martensii* Bmk-M8.

MHC-II Allele	POS.	N	SEQUENCE	C	MW (Da)	SCORE	% OPT.
1-Ab	46	GNA	CYCIDLPAS	ERI	966.15	14.216	39.90 %
1-Ab	12	SEN	CTYFCGSNP	YCN	973.09	11.853	33.27 %

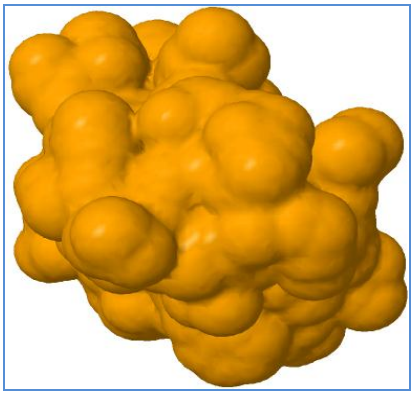

Fig. 2: The Solvent Accessible Structure of hydrophobicity *Mesobuthus martensii* Bmk-M8

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. It was shown that an antigen protein is hydrophobic in nature and contains segments of low complexity and high-predicted flexibility [Fig. 3-5]. Predicted antigenic fragments can bind to MHC molecule is the first bottleneck of subunit vaccine design.

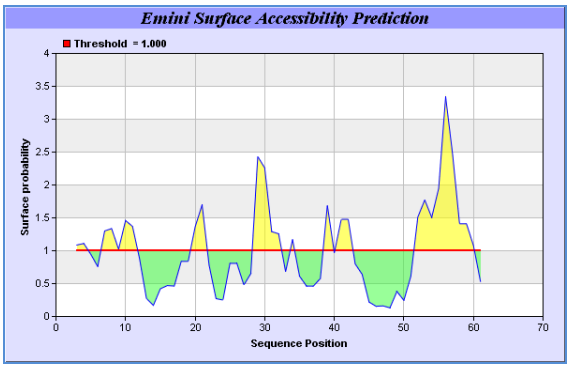

Fig. 3: Emini Surface Accessibily plot of *Mesobuthus martensii* Bmk-M8.

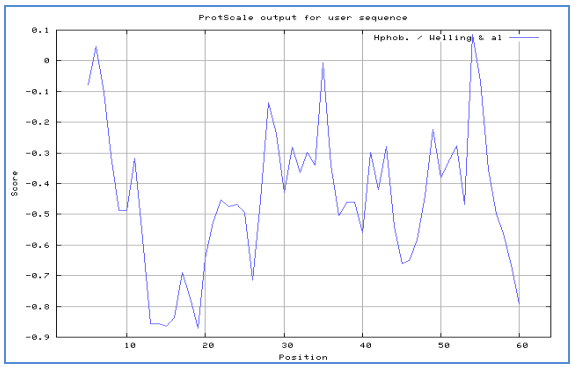

Fig. 4: Welling, et al hydrophobicity plot of *Mesobuthus martensii* Bmk-M8.

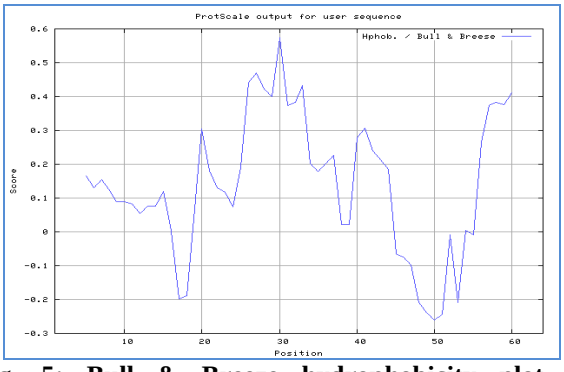

Fig. 5: Bull & Breeze hydrophobicity plot of *Mesobuthus martensii* Bmk-M8.

CONCLUSION

Mesobuthus martensii Bmk-M8 peptides are from a set of aligned peptides known to bind to a given MHC molecule as the predictor of MHC-peptide binding. MHC-II molecules bind peptides in similar yet different modes and alignments of MHC-II 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 *Mesobuthus martensii* Bmk-M8.

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