International Journal of Biotechnology Applications, ISSN: 0975–2943, Volume 1, Issue 1, 2009, pp-01-03

Proteomics approach for prediction of immunogenic site *from Foot-and-mouth disease virus*

Gomase V.S., Phadnis A. C. and Tripathi A.K.

*Proteomics Unit, Department of Bioinformatics, Padmashree Dr. D. Y. Patil University, Plot No-50, Sector-15, CBD Belapur, Navi Mumbai, 400614, MS, India, Mobile- +91-9987770696, Mail-virusgene1@yahoo.co.in

Abstract- Foot-and-mouth disease is caused by FMDV, an Aphthovirus of the viral family Picornaviridae. Peptide fragments of *Foot-and-mouth disease virus* 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 protein from *Foot-and-mouth disease virus* are important determinant for protection of host form viral infection. In this assay we predicted the binding affinity of protein having 213 amino acids, which shows nonamers. These peptides 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 protein nonamers. Binding ability prediction of antigen peptides to major histocompatibility complex (MHC) class I & II molecules is important in vaccine development from *Foot-and-mouth disease virus*.

Key words: Antigen, 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

Foot-and-mouth disease is caused by *Foot-and-mouth disease virus*, which is an Aphthovirus of the viral family Picornaviridae. The viral members of this family are small (25-30 nm), nonenveloped icosahedral viruses that contain single-stranded RNA (ribonucleic acid, the viral genetic material). These viruses come in contact with a host cell, bind to a receptor site and trigger a folding-in of the cell membrane. After the viral entry into inside the host cell, its protein coat dissolves. New viral RNA and components of the protein coat are then synthesized in large quantities and assembled to form new viruses. After assembly, the host cell lyses (bursts) and releases the new viruses. The “O-Strain” of the virus has been taken in this particular analysis [1]. Prediction of peptide fragments from *Foot-and-mouth disease virus* involved multiple antigenic components to direct and empower the immune system to protect the host from infection. MHC molecules are cell surface proteins, which take active part in host immune reactions and involvement of MHC class-I & II in response to almost all antigens. The predicted binding affinity is normalized by the 1% fractil. The MHC peptide binding is predicted using neural networks trained on C terminals of known epitopes. In analysis predicted MHC/peptide binding is a log transformed value related to the IC50 values in nM units [2, 3].

II. Methodology

In this research work antigenic epitopes of major immunogenic site protein from *Foot-and-mouth disease virus* is determined using the Gomase, Hopp and Woods, Welling, Parker and Protrusion Index (Thornton) antigenicity [4-6]. The major histocompatibility complex (MHC) peptide binding of major immunogenic site protein is predicted using neural networks trained on C terminals of known epitopes. In analysis predicted MHC/peptide binding of major immunogenic site 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 [6-11]. In addition, we predict those MHC ligands from whose C-terminal end is likely to be the result of proteosomal cleavage [12].

III. Results and Interpretations

We found binding of peptides to a number of different alleles using Position Specific Scoring Matrix. A major immunogenic site protein sequence is 213 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 major immunogenic site protein sequence are as 11mer_H2_Db, 10mer_H2_Db, 9mer_H2_Db, 8mer_H2_Db and also peptide binders to MHCII molecules of major immunogenic site protein sequence as I_Ab.p, I_Ad.p, analysis found antigenic epitopes region in putative major immunogenic site 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 viral major immunogenic site 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 major immunogenic site protein is solvent accessible and unstructured, antibodies against those regions are also likely to recognize the native protein. It was shown that a major immunogenic site protein is hydrophobic in nature and contains segments of low complexity and high-predicted flexibility. Predicted antigenic fragments can bind to MHC molecule is the first bottlenecks in vaccine design.

IV. Conclusion

A major immunogenic site protein from *Foot-and-mouth disease virus* 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 viral major immunogenic site protein. These predicted of major immunogenic site protein antigenic peptides to MHC class molecules are important in vaccine development from *Foot-and-mouth disease virus.*

References

[1]. Jinding C., Mingqiu Z., Hui, K.H., Leung F.C. (2006) *Virus Genes*. 32(2):139-43.

[1]. López-Revilla R., Pineda M.A., Ortiz-Valdez J., Sánchez-Garza M., Riego L. (2009) *Infect Agent Cancer* 4, 3.

[2]. Mohabatkar H. (2007) *Asian Pac J Cancer Prev*. 8(4), 602-6.

[3]. Gomase V.S. and Kale K.V. (**2007**) *National Symposium on Genomics, Proteomics and Bioinformatics, Osmanabad, India*.

[4]. Gomase V.S., Kale K.V., Jyotiraj A. and Vasanthi R. (**2007**) *Medicinal Chemistry Research*, 15(1/6), 160.

[5]. Gomase V.S., Kale K.V., Shyamkumar K. and Shankar S. (**2008**) *ICETET 2008, IEEE Computer Society in IEEE Xplore, Los Alamitos, California*, 629-634.

[6]. Reche P.A., Glutting J.P. and Reinherz E.L. (**2002**) *Hum Immunol*., 63(9), 701-709.

[7]. Buus S., Lauemøller S.L., Worning P., Kesmir C., Frimurer T., Corbet S., Fomsgaard A., Hilden J., Holm A., Brunak S. (**2003**) *Tissue Antigens,* 62 (5), 378-384.

[8]. Nielsen M., Lundegaard C., Worning P., Lauemøller S.L., Lamberth K., Buus S., Brunak S., Lund O. (**2003**) *Protein Sci.,* 12 (5), 1007-1017.

[9]. Bhasin M. and Raghava G.P. (**2005**) *Nucleic Acids Res*., 33, W202-207.

[10]. Gomase V. S., Tandale J.P., Patil S. A. and Kale K.V. (**2006**) *14th International Conference on Advance Computing & Communication, ADCOM06, Published by IEEE Computer Society in IEEE Xplore USA*, 614-615.

[11]. Gomase V.S., Kale K.V., Chikhale N.J., Changbhale S.S. (**2007**) *Curr. Drug Discov. Technol.,* 4(2), 117-1215.

[12]. Gomase V.S., Waghmare S.B., Jadhav B.V., Kale K.V. (**2009**) *Gene Therapy and Molecular Biology*, 13, 11-15.

TABLE 1- MHC ligands from whose C-terminal end are proteosomal cleavage sites

MHC-I	POS.	N	Sequence	C	MW (Da)	Score	% OPT.
8mer_H2_Db	28	QRR	QHTDVSFI	MDR	928.01	10.529	20.06 %
8mer_H2_Db	64	LVG	GLLRASTY	YFS	862.0	6.251	11.91 %
9mer_H2_Dd	160	RTL	PTSFNYGAI	KAT	951.05	7.477	14.85 %
9mer_H2_Dd	54	LDL	MQVPSHTLV	GGL	993.18	6.795	13.49 %
10mer_H2_Dd	139	YSR	NAVPNLRGDL	QVL	1050.18	19.842	33.71 %
10mer_H2_Kb	204	HKQ	KIVAPVKQTL		1078.35	17.566	29.84 %
10mer_H2_Kb	87	GDL	TWVPNGAPEK	ALD	1057.2	14.234	24.18 %
11mer_H2_Kd	126	HRV	LATVYNGECRY	SRN	1270.43	15.9	20.00 %
11mer_H2_Kd	68	LLR	ASTYYFSDLEI	AVK	1290.41	6.094	7.67 %

TABLE 2- MHC class II binding peptide nonamers from protein

MHC ALLELE	Rank	Sequence	Residue No.	Peptide Score
I-Ab	1	GESADPVTT	5	1.424
I-Ab	2	PYTAPHRVL	118	1.243
I-Ab	3	PLLAIHPTE	190	1.196
I-Ab	4	PEKALDNTT	94	1.125
I-Ad	1	TSFNYGAIK	161	0.708
I-Ad	2	LAQKVARTL	151	0.611
I-Ad	3	LEIAVKHEG	76	0.478
I-Ad	4	SHTLVGGLL	58	0.431
I-Ag7	1	PYTAPHRVL	118	1.744
I-Ag7	2	YSRNAVPNL	136	1.682
I-Ag7	3	WVPNGAPEK	88	1.672
I-Ag7	4	MKRAETYCP	180	1.487
RT1.B	1	TAYHKAPLT	105	1.190
RT1.B	2	TTNPTAYHK	101	1.024
RT1.B	3	STYYFSDLE	69	0.965
RT1.B	4	TTSAGESAD	1	0.646