An Immuninformatics Approach to Design Synthetic Peptide Vaccine from *Dendroaspis polylepis polylepis* Dendrotoxin-K(DTX-K)

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**Abstract**

*Dendroaspis polylepis polylepis* is the most toxic snake commonly known as black mamba, the black mamba venom contains Dendrotoxin-K which is highly specific and virulently toxic protein. Antigenic peptides of Dendrotoxin K toxic protein are most suitable for peptide vaccine development because with single epitope, the immune response can be generated in large population. Analysis shows MHC class II binding peptides of antigenic protein from *Dendroaspis polylepis polylepis* DTX-K are important determinant for protection against several venom toxins. In this assay we predicted the binding affinity of *Dendroaspis polylepis polylepis* DTX-K protein having 79 amino acids, which shows 71 nonamers. In this analysis, we found the High affinity TAP Transporter peptide regions as, 37-KRKIPSFY (score-9.559), 45-YKWAKQCL (Score-8.581) 36-OKRKIPSFY (Score-7.685), 24-AKYCKLPLR (Score-7.669), 42-SFYWKWAK (Score-6.859), 31-LRIGPKCKR (Score-6.848) 65-NRFKTEEC (Score-6.698), 25-KYCKLPLR (Score-6.632), 49-AQKQCLPTF (Score-6.576), 66-RFKTTEECR (Score-6.464), 47-WKAKQCLPF (Score-6.197), 23-AKYCKLPL (Score-6.166). We also found the SVM based MHC-I-Ab peptide regions, 61-GGNANRFKT, 12-TLWAELTPV, 41-PSFYKYKWA, 25-KYCKLPLR (optimal score is 0.946); MHC-I-Ia peptide regions, 2-GHLLLLGL, 57-SGCCGNAN, 3-GLLLLLGL, 1-SGCCGNAN, (optimal score is 0.488); MHC-I-Ia peptide regions 60-CCGNANRFK, 21-SGAAKYCKL, 61-GGNANRFKT, 20-VSGAAKYCK (optimal score is 1.488); and MHC-II-B peptide regions 46-KWKAKQCLP, 24-AKYCKLPLR, 10-LTLWAELT, 45-YKAKQCLQCL (optimal score is 0.569) which represented predicted binders from dendrotoxin. The method integrates prediction of peptide MHC class I binding; proteasomal C terminal cleavage and TAP transport efficiency of the whole antigen. Antigenic peptides are most suitable for subunit vaccine development because with single epitope, the immune response can be generated in large population. Antigenic peptides are most suitable for subunit vaccine development because with single epitope, the immune response can be generated in large population. MHC peptide complexes will be

**Keywords:** *Dendroaspis polylepis polylepis*, Dendrotoxin-K, Antigenic peptides; MHC-Binders; SVM; Nonamers

**Introduction**

*Dendroaspis polylepis polylepis* commonly known as black mamba is the aggressive and highly venomous land snake; *Dendroaspis polylepis* venom contains Dendrotoxin-K (DTX-K), which has ability to kill a mouse within 5 minutes after bite. The dendrotoxin is highly specific and virulently toxic protein of low molecular weight that can spread very rapidly within the bitten tissue, so black mamba venom is the most rapid-acting of all snake venoms. Dendrotoxin inhibits the exogenous process of muscle contraction by means of the sodium potassium pump. Dendrotoxin-K is a selective blocker of voltage-gated potassium channels [1,2].

**Strategy**

The phenotype of the resistant transgenic plants includes fewer centers of initial virus infection, a delay in symptom development, and low bacterial accumulation. Protoplasts from disease resistant centers of initial virus infection, a delay in symptom development, and low bacterial accumulation. Protoplasts from disease resistant transgenic plants are also resistant, suggesting that the protection is largely operational at the cellular level. Transgenic plants expressing nucleocapsid protein are protected against infection by bacteria but are susceptible to bacterial DNA, indicating that the protection may be the result of the phenomenon of cross-protection [3], hereby a plant infected with a mild strain of bacteria is protected against a more severe strain of the same bacteria. Plant Proteins are necessary for its production in or on all food commodities. An exemption from the requirement of a tolerance is established for residues of the biological plant pesticide.

**MHC class binding peptides**

The new paradigm in vaccine design is emerging, following essential discoveries in immunology and development of new MHC Class-I binding peptides prediction tools [4-7]. MHC molecules are cell surface glycoproteins, which take active part in host immune reactions. The involvement of MHC class-I in response to almost all antigens and the variable length of interacting peptides make the study of MHC Class-I molecules very interesting. MHC molecules have been well characterized in terms of their role in immune reactions. They bind to some of the peptide fragments generated after proteolytic cleavage of antigen [8]. This binding acts like red flags for antigen specific and to generate immune response against the parent antigen. So a small fragment of antigen can induce immune response against whole antigen. Antigenic peptides are most suitable for subunit vaccine development because with single epitope, the immune response can be generated in large population. MHC peptide complexes will be

**Keywords:** MHC class binding peptides

**References**

[1] Changbhale S.S, Chitlange N.R, Gomase V.S, Kale K.V (2012) An Immuninformatics Approach to Design Synthetic Peptide Vaccine from *Dendroaspis polylepis polylepis* Dendrotoxin-K(DTX-K). J Environ Anal Toxicol 2:157. doi:10.4172/2161-0525.1000157

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translocated on the surface of antigen presenting cells (APCs). This theme is implemented in designing subunit and synthetic peptide vaccines [9]. One of the important problems in subunit vaccine design is to search antigenic regions in an antigen [10] that can stimulate T cells called T-cell epitopes. In literature, fortunately, a large amount of data about such peptides is available. Pastly and presently, a number of databases have been developed to provide comprehensive information related to T-cell epitopes [11-14].

Materials and Methods

Protein sequence analysis

The antigenic protein sequence of Dendroaspis polylepis polylepis DTX-K was analyzed to study the antigenicity [15], solvent accessible regions and MHC class peptide binding, which allows potential drug targets to identify active sites against plant diseases.

Prediction of antigenicity

Prediction of antigenicity program predicts those segments from within bacterial pathogenicity protein that are likely to be antigenic by eliciting an antibody response. Antigenic epitopes are determined using the Gomase [9], Hopp and Woods, Welling, Parker, B-EpiPred Server and Kolaskar and Tongaonkar antigenicity methods [14,16-20].

Prediction of protein secondary structure

The important concepts in secondary structure prediction are identified as: residue conformational propensities, sequence edge effects, moments of hydrophobicity, position of insertions and Deletions in aligned homologous sequence, moments of conservation, auto-correlation, residue ratios, secondary structure feedback effects, and filtering [21,22].

Finding the location in solvent accessible regions

Finding the location in solvent accessible regions in protein, type of plot determines the hydrophobic and hydrophilic scales and it is utilized for prediction. This may be useful in predicting membrane-spanning domains, potential antigenic sites and regions that are likely exposed on the protein surface [1,2,23-42].

Prediction of MHC binding peptide

The MHC peptide binding is predicted using neural network strained 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. MHC2Pred predicts peptide binders to MHC I and MHC II 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. The average accuracy of SVM based method for 42 alleles is ~80%. For development of MHC binder, an elegant machine learning technique SVM has been used. SVM has been trained on the binary input of single amino acid sequence. In addition, we predicts those MHC I ligands whose C-terminal end is likely to be the result of proteosomal cleavage [43-45].

Result and Interpretation

A antigenic sequence is 79 residues long as-GEDGYIADGDNCT YICTFNNYCHALCTDKKGDSGACDWWVPYGVVWCEDLPTP VPIRGSGKCR

Prediction of antigenic peptides

In these methods we found the antigenic determinants by finding the area of greatest local hydrophilicity. The Hopp-Woods scale was designed to predict the locations of antigenic determinants 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 1). Its values are derived from the transfer-free energies for amino acid side chains between ethanol and water. Welling antigenicity plot gives value as the log of the quotient between percentage in a sample of known antigenic regions and percentage in average proteins (Figure 2). We also study B-EpiPred Server, Parker, Kolaskar and Tongaonkar antigenicity methods and the predicted antigenic fragments can bind to MHC molecule is the first bottlenecks in vaccine design (Figure 3-6).

Secondary alignment

The Robson and Garnier method predicted the secondary structure of the Dendroaspis polylepis polylepis DTX-K. Each residue is assigned values for alpha helix, beta sheet, turns and coils using a window of 7 residues (Figure 7). Using these information parameters, the likelihood of a given residue assuming each of the four possible conformations alpha, beta, reverse turn, or coils calculated, and the conformation with the largest likelihood is assigned to the residue.
Solvent accessible regions

Solvent accessible scales for delineating hydrophobic and hydrophilic characteristics of amino acids and scales are developed for predicting potential antigenic sites of globular proteins, which are likely to be rich in charged and polar residues. It was shown that a *Dendroaspis polylepis polylepis* DTX-K is hydrophobic in nature and contains segments.

Prediction of MHC binding peptides

These MHC binding peptides are sufficient for eliciting the desired immune response. The prediction is based on cascade support vector machine, using sequence and properties of the amino acids. The correlation coefficient of 0.88 was obtained by using jack-knife validation test. In this test, we found the MHC-I and MHC-II binding regions (Tables 1 and 2). 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. In this assay we predicted the binding affinity of *Dendroaspis polylepis polylepis* DTX-K having 79 amino acids, which shows different nonamers (Tables 1 and 2). For development of MHC binder prediction method, an elegant machine learning technique support vector machine (SVM) has been used. SVM has been trained on the binary input of single amino acid sequence. In this assay we predicted the binding affinity of *Dendroaspis polylepis polylepis* DTX-K sequence (Ist) having 79 amino acids, which shows 71 nonamers. Small peptide regions found as High affinity TAP Transporter peptide regions as, 37-KRKIPSFY (Score-9.550), 45-YKWKAKQCL (Score-8.581), 36-CRKIPSFY (Score-7.685), 24-AKYCKLPLR (Score-7.669), 42-SFYYKWKAK (Score-6.859), 31-LRIGPCKRK (Score-6.848), 65-NRFKTIEEC (Score-6.695), 25-KYCKLPLRI (Score-6.632), 49-AKQCLPFDY.
Table 1: TAP peptide binders of Dendroaspis polylepis polylepis DTX-K.

| Peptide Rank | Start Position | Sequence       | Score   | Predicted Affinity |
|--------------|----------------|----------------|---------|--------------------|
| 1            | 37             | KRKIPSFYY       | 9.550   | High               |
| 2            | 45             | YKWAKAQCL      | 6.581   | High               |
| 3            | 36             | CKRKIPSFY      | 7.685   | High               |
| 4            | 24             | AKYCKLPLR      | 7.669   | High               |
| 5            | 42             | SFYKYKKWAK     | 6.859   | High               |
| 6            | 31             | LRIGPCXRK      | 6.848   | High               |
| 7            | 65             | NRFKYTEEC      | 6.698   | High               |
| 8            | 25             | KYCKLPLRL      | 6.632   | High               |
| 9            | 49             | AKGCLPFY       | 6.576   | High               |
| 10           | 66             | RFKTIEECR      | 6.484   | High               |
| 11           | 47             | WKAQCLPFL      | 6.197   | High               |
| 12           | 23             | AAXYCKLPL      | 6.166   | High               |

*Optimal Score for given MHC binder in Mouse

Table 2: Peptide binders to MHCII molecules of Dendroaspis polylepis polylepis DTX-K.

( score-6.576), 66-RFKTIEECR (Score-6.464), 47-WKAQCLPFL (Score-6.197), 23-AAKYCKLPL (Score-6.166). We also found the SVM based MHCII-IAb peptide regions, 61-GGNNANRFKT, 12-TLWAELTPV, 41-PSFYKYKWKA, 25-KYCKLPLRL (optimal score is 0.946); MHCII-IAd peptide regions, 2-GHLLLGG, 57-SGCCGND, 3-HLLLLLLG, 1-SGCCGLL (optimal score is 0.488); MHCII-IAg7 peptide regions 60-CCGNANRFK, 21-SGAAKYCKL, 61-GGNNANRFKT, 20-VSGAAKYCK (optimal score is 1.468); and MHCII-RT1.B peptide regions 46-KWAKAQCLP, 24-AKYCKLPLR, 10-LTLWAELT, 45-YKWAKAQCL (optimal score is 0.569) which represented predicted binders from Dendroaspis polylepis polylepis DTX-K. 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. These MHC binding peptides are sufficient for eliciting the desired immune response. Predicted MHC binding regions in an antigen sequence and there are directly associated with immune reactions, in analysis we found the MHCI and MHCII binding region.

Discussion and Conclusion

Gomase method [9], B-EpiPred Server, Hopp and Woods, Welling, Parker, Kolaskar and Tongaonkar antigenicity scales were designed to predict the locations of antigenic determinants in Dendroaspis polylepis polylepis DTX-K. Nucleocapsid shows beta sheets regions, which are high antigenic response than helical region of this peptide and shows highly antigenicity (Figure 1-5). We also found the Sweet hydrophobicity, Kyte & Doolittle hydrophobicity, Abraham & Leo, Bull & Breese hydrophobicity, Guy, Miyazawa hydrophobicity, Roseman hydrophobicity, Cowan HPLC pH 7.5 hydrophobicity, Rose hydrophobicity, Eisenberg hydrophobicity, Manavalan hydrophobicity, Black hydrophobicity, Fauchere hydrophobicity, Jain hydrophobicity, Rao & Argos hydrophobicity, Wolfenden hydrophobicity, Wilson HPLC hydrophobicity, Cowan HPLC pH 3.4, Tanford hydrophobicity, RF mobility hydrophobicity and Chothia hydrophobicity scales. Theses scales are essentially a hydrophilic index, with a polar residues assigned negative values (Figures 7-28).

In this assay we predicted the binding affinity of Dendroaspis polylepis polylepis DTX-K having 79 amino acids, which shows 71nonamers. Small peptide regions found as, 37-KRKIPSFYY (score-9.550), 45-YKWAKAQCL (Score-8.581) 36-CKRKIPSFY (Score-7.685), 24-AKYCKLPLR (Score-8.581) 36-CKRKIPSFY (Score-7.685), 24-AKYCKLPLR

Figure 8: Hydrophobicity Sweet plot of Kyte for the Dendroaspis polylepis polylepis DTX-K. Nucleocapsid shows beta sheets regions, which are high antigenic response than helical region of this peptide and shows highly antigenicity (Figure 1-5). We also found the Sweet hydrophobicity, Kyte & Doolittle hydrophobicity, Abraham & Leo, Bull & Breese hydrophobicity, Guy, Miyazawa hydrophobicity, Roseman hydrophobicity, Cowan HPLC pH 7.5 hydrophobicity, Rose hydrophobicity, Eisenberg hydrophobicity, Manavalan hydrophobicity, Black hydrophobicity, Fauchere hydrophobicity, Jain hydrophobicity, Rao & Argos hydrophobicity, Wolfenden hydrophobicity, Wilson HPLC hydrophobicity, Cowan HPLC pH 3.4, Tanford hydrophobicity, RF mobility hydrophobicity and Chothia hydrophobicity scales. Theses scales are essentially a hydrophilic index, with a polar residues assigned negative values (Figures 7-28).

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Figure 9: Hydrophobicity plot of Kyte and Doolittle (1982) for the Dendroaspis polylepis polylepis DTX-K.
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**Figure 10:** Hydrophobicity plot of Abraham and Leo (1987) for the *Dendroaspis polylepis polylepis* DTX-K.

**Figure 11:** Hydrophobicity plot of Bull and Breese (1974) for the *Dendroaspis polylepis polylepis* DTX-K.

**Figure 12:** Hydrophobicity plot of Guy (1985) for the *Dendroaspis polylepis polylepis* DTX-K.

**Figure 13:** Hydrophobicity plot of Miyazawa, et al (1985) for the *Dendroaspis polylepis polylepis* DTX-K.

**Figure 14:** Hydrophobicity plot of Roseman (1988) for the *Dendroaspis polylepis polylepis* DTX-K.

**Figure 15:** Hydrophobicity plot of Wolfenden et al. (1981) for the *Dendroaspis polylepis polylepis* DTX-K.
Figure 16: Hydrophobicity Wilson et al. (1981) plot of HPLC for the Dendroaspis polylepis polylepis DTX-K.

Figure 17: Hydrophobicity Cowan (1990) plot of HPLC pH3.4 for the Dendroaspis polylepis polylepis DTX-K.

Figure 18: Hydrophobicity plot of Rf mobility for the Dendroaspis polylepis polylepis DTX-K.

Figure 19: Hydrophobicity plot of Chothia (1976) for the Dendroaspis polylepis polylepis DTX-K.

Figure 20: Hydrophobicity plot of Eisenberg et al. (1984) for the Dendroaspis polylepis polylepis DTX-K.

Figure 21: Hydrophobicity plot of Manavalan, et al (1978) for the Dendroaspis polylepis polylepis DTX-K.
Figure 22: Hydrophobicity plot of Black (1991) for the *Dendroaspis polylepis polylepis* DTX-K.

Figure 23: Hydrophobicity plot of Fauchere, et al (1983) for the *Dendroaspis polylepis polylepis* DTX-K.

Figure 24: Hydrophobicity plot of Janin (1979) for the Dendrotoxin-K.

Figure 25: Hydrophobicity plot of Rao and Argos (1986) for the *Dendroaspis polylepis polylepis* DTX-K.

Figure 26: Hydrophobicity plot of Tanford (1962) for the *Dendroaspis polylepis polylepis* DTX-K.

Figure 27: Hydrophobicity Cowan (1990) plot of HPLC pH7.5 for the *Dendroaspis polylepis polylepis* DTX-K.
class in response to almost all antigens and it gives effects on specific

take active part in host immune reactions and involvement of MHC
glycoproteins, which take active part in host immune reactions and
involvement of MHC class-I and MHC II in response to almost all
antigens (Table 2). Kolaskar and Tongaonkar antigenicity are the sites
of molecules that are recognized by antibodies of the immune system
for the Dendroaspis polylepis polylepis DTX-K, analysis shows epitopes
present in the Dendroaspis polylepis polylepis DTX-K the desired
immune response. The region of maximal hydrophilicity is likely
to be an antigenic site, having hydrophobic characteristics, because
C-terminal regions of Dendroaspis polylepis polylepis DTX-K is solvent
accessible and unstructured, antibodies against those regions are also
likely to recognize the native protein. For the prediction of antigenic
determinant sites of Dendroaspis polylepis polylepis DTX-K, we got
eighteen antigenic determinant sites in the sequence. The SVM based
MHC-Iab peptide regions, 61-GGNANRFK, 12-TLWAELTPV,
57-SGCGGNAN, 3-HLLLLLGLL, 61-GGNANRFKT, 12-TLWAELTPV,
MHCII-IAb peptide regions, 61-GGNANRFKT, 12-TLWAELTPV,
MHCII-IAd peptide regions, 2-GHLLLLLGL, 57-SGCGGNAN, 3-HLLLLLGLL,
61-GGNANRFKT, 12-TLWAELTPV, the desired
immunogenic regions important in cross-protection between strains of a poivus. Mol Plant
Microbe Interact 16: 683-692.

Bhasin M, Singh H, Raghava GP (2003) MHCDB: a comprehensive database
of MHC binding and non-binding peptides. Bioinformatics 19: 665-666.

Singh H, Raghava GP (2001) PredP: prediction of HLA-DR binding sites.
Bioinformatics 17: 1236-1237.

Cui J, Han LY, Lin HH, Tang ZQ, Jiang L, et al. (2006) MHC-BPS: MHC-binder
prediction server for identifying peptides of flexible lengths from sequence-derived
physicochemical properties. Immunogenetics 58: 607-613.

Beaver JE, Bourne PE, Ponomarenko JV (2007) Epitope Viewer: a Java
application for the visualization and analysis of immune epitopes in the Immune
Epitope Database and Analysis Resource (IEDB). Immune Res 3: 3.

Kumar M, Gromiya MM, Raghava GP (2007) Identification of DNA-binding
proteins using support vector machines and evolutionary profiles. BMC
Bioinformatics 8: 463.

Gomase VS, Kale KV, Chihkale NJ, Changbhale SS (2007) Prediction of MHC
Binding Peptides and Epitopes from Alfalfa mosaic virus. Curr Drug Discov
Technol 4: 117-215.

Schirle M, Weinschenk T, Stevanovic S (2001) Combining computer algorithms
with experimental approaches permits the rapid and accurate identification of T
cell epitopes from defined antigens. J Immunol Methods 257: 1-16.

Rammensee H, Bachmann J, Emmerich NP, Bachor OA, Stevanovic S (1999)
SYFPETHI: database for MHC ligands and peptide motifs. Immunogenetics
50: 213-219.

Blythe MJ, Doychitina IA, Flower DR (2002) JenPep: a database of quantitative
functional peptide data for immunology. Bioinformatics 18: 434-439.

Schonbach C, Koh JL, Flower DR, Wong L, Brusic V (2002) FIMM, a database
of functional molecular immunology: update 2002. Nucleic Acids Res 30: 226-
229.

Kolaskar AS, Tongaonkar PC (1990) A semi-empirical method for prediction
of antigenic determinants on protein antigens. FEBS Lett 257: 1-16.

Santhia RK, Jain RK (2007) Nucleotide sequence of the S and M RNA segments
of Dengue virus. J Gen Virol 88: 507-515.

Gomase VS (2006) Prediction of Antigenic Epitopes of Neuraminidase
from Neisseria meningitidis. Curr Drug Discov Technol 3: 225-229.

Hopp TP, Woods KR (1981) Prediction of Protein Antigenic Determinants from
Amino Acid Sequences. Proc Natl Acad Sci USA 78: 3294-3296.

Wellendorf GW, Weyers WJ, van der Zee R, Welling-Wester S (1985) Prediction
of sequential antigenic regions in proteins. FEBS Lett 188: 215-218.

Larsen JE, Lund O, Nielsen M (2006) Improved method for predicting linear
B-cell epitopes. Immunome Res 2: 2.

Parker JM, Guo O, Hodges RS (1986) New Hydrophobicity Scale Derived from
High-Performamnce Liquid Chromatography Peptide Retention Data: Correlation
of Predicted Surface Residues with Antigenicity and X-ray-Derived Accessible
Sites. Biochemistry 25: 5425-5432.
J Environ Anal Toxicol
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21. Garnier J, Osguthorpe DJ, Robson B (1978) Analysis of the accuracy and implications of simple methods for predicting the secondary structure of globular proteins. J Mol Biol 120: 97-120.

22. Robson B, Garnier J (1993) Protein structure prediction. Nature 361: 506.

23. Sweet RM, Eisenberg D (1983) Correlation of sequence hydrophobicities measures similarity in three-dimensional protein structure. J Mol Biol 171: 479-488.

24. Kyte J, Doolittle RF (1982) A Simple Method for Displaying the Hydrophatic Character of a Protein. J Mol Biol 157: 105-132.

25. Bull HB, Breese K (1974) Surface tension of amino acid solutions: A hydrophobicity scale of the amino acid residues. Arch Biochem Biophys 161: 665-670.

26. Guy HR (1985) Amino acid side chain partition energies and distributions of residues in soluble proteins. Biophys J 47: 61-70.

27. Miyazawa S, Jemigien RL (1985) Estimation of Effective Interresidue Contact Energies from Protein Crystal Structures: Quasi-Chemical Approximation. Macromolecules 18: 534-552.

28. Roseman MA (1988) Hydrophobicity of polar amino acid side-chains is markedly reduced by flanking peptide bonds. J Mol Biol 200: 513-522.

29. Wolfenden R, Andersson L, Cullis PM, Southgate CC (1981) Affinities of amino-acid side-chains for solvent water. Biochemistry 20: 849-855.

30. Wilson KJ, Honegger A, Stotzel RP, Hughes GJ (1981) The behaviour of peptides on reverse-phase supports during high-pressure liquid chromatography. Biochem J199: 31-41.

31. Chothia C (1976) The nature of accessible and buried surfaces in proteins. J Mol Biol 105: 1-12.

32. Eisenberg D, Schwarz E, Komaromy M, Wall R (1984) Analysis of membrane and surface protein sequences with the hydrophobic moment plot. J Mol Biol 179: 125-142.

33. Manavalan P, Ponnumwamy PK (1978) Hydrophobic character of amino acid residues in globular proteins. Nature 275: 673-674.

34. Black SD, Mould DR (1991) Development of Hydrophobicity Parameters to Analyze Proteins Which Bear Post- or Cotranslational Modifications. Anal Biochem193: 72-82.

35. Fauchere JL, Pilaika V (1983) Hydrophobic parameters of amino-acid side-chains from the partitioning of N-acetyl-amino-acid amide. Eur J Med Chem 18: 369-375.

36. Janin J (1979) Surface and inside volumes in globular proteins. Nature 277: 491-492.

37. Rao MKJ, Argos P (1986) A conformational preference parameter to predict helices in integral membrane proteins. Biochim Biophys Acta 869: 197-214.

38. Tanford C (1962) Hydrophobicity scale (Comparison of hydrophobic interactions to the stability of the globular conformation of proteins. J Am Chem Soc 84: 4240-4274.

39. Cowan R, Whittaker RG (1990) Hydrophobicity indices at pH 3.4 determined by HPLC. Pept Res 3: 75-80.

40. Rose GD, Geselowitz AR, Lesser GJ, Lee RH, Zehfus MH (1985) Hydrophobicity of amino acid residues in globular proteins. Science 229: 834-838.

41. Wilkins MR, Gasteiger E, Bairoch A, Sanchez JC, Williams KL, et al. (1999) Protein identification and analysis tools in the ExPASy server. Methods Mol Biol 112: 531-552.

42. Eisenberg D, Weiss RM, Terwilliger TC (1984) The hydrophobic moment detects periodicity in protein hydrophobicity. Proc Natl Acad Sci USA 81: 140-144.

43. Brusic V, Rudy G, Honeymau G, Hammmer J, Harrison L (1998) Prediction of MHC class II-binding peptides using an evolutionary algorithm and artificial neural network. Bioinformatics 14: 121-130.

44. Bhasin M, Raghava GP (2005) P cleavage: an SVM based method for prediction of constitutive proteasome and immunoproteasome cleavage sites in antigenic sequences. Nucleic Acids Res 33: W252-W257.

45. Gomase VS, Changbhale SS, Kale KV (2008) Insilico analysis of Mesobuthustamulus neurotoxin from groundnut ringspot virus. Advancements in Information Technology and Internet Security 370-378.

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