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Immunoinformatic Approaches in Epitope Prediction for Vaccine Designing against Viral infections

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Abstract

Epitope prediction of immunogens using bioinformatic approaches is supposed to bring a revolution in vaccine development. Computer based prediction tools has reduced both the number of validation experiments and time for epitope prediction. A number of epitope prediction tools are now available on the web, and bioinformatics-based prediction of CTL epitopes has gained huge popularity in drug designing. For a vaccine to be successful against the viral infections, it needs to ideally stimulate humoral or cellular immune responses. The *in silico* search mainly focuses for individual immunogenic components that can target different arms of the immune system. Peptide based drug can be designed by targeting the protein, involved in stimulating the host cell immune system. Perspectives in this field are presented in the present review.

Keywords: Epitope; Vaccine Design; Viral Infections

Introduction

Effective method for prevention of viral infections has been vaccination. Conventional methods to design vaccine candidate is a laborious process requiring time and economy. During the last three decades efforts to control of viral diseases through the development of large number of antiretroviral drugs, public awareness and other prevention programs across the globe has led to significant reduction in viral cases yet, constantly evolving and drug resistant mutations are posing a continuous challenge to the therapy. This beckons an urgent need for effective vaccines offering a stable solution to control and eradicate the disease. Epitope based vaccine designing is more promising as the conventional approach lies on the responses induced by the natural immunogen which are not optimal. Epitope based drug designing relies not only on understanding the mechanisms of immunodominance but simultaneously analyzes multiple genomes to select the most appropriate epitope.

Challenges in Conventional Methods of Vaccine Development

Development of vaccines or therapeutic measures often requires prior understanding of the immunological aspects during the natural course of an infection. Conventional vaccines prepared by either attenuated or inactivated whole pathogen has a number of limitations as genetic variations in these pathogens all over the globe may results in reduced efficiency of these vaccines in different parts of the world. Many vaccine trials are currently being conducted worldwide, but they fail to reach in phase III. These facts indicate clearly that there is a big gap between the early phase clinical trials (phase I and II) and efficacy trial (phase III) and the need for

further research to gain more knowledge on minimal components which determine the protective nature of the vaccine candidates against virus is desired [1]. Genetic variation in envelope proteins is one of the main hurdles in designing a vaccine [2]. Experimental assays for identification of conserved regions which maintain their structure and function of glycoprotein is a tedious process. Besides this the pathogens utilized during vaccination may revert to its pathogenic form and cause infection [3].

Vaccine Designing through Immunoinformatics

Immunoinformatics, an emerging field of the present era has addressed the complex biological problem of decrypting the immune response for vaccine designing [4]. An ideal vaccine which initiates humoral or cell mediated immune response is essential to completely eradicate the chance of re-infection. The Cytotoxic T lymphocytes (CTL) and Helper T lymphocytes (HTL) recognizes the foreign antigen as peptides that are presented with Major Histocompatibility Complex (MHC) and is expressed on the surface of all nucleated cells. T cell epitope prediction tools assist in identifying allele-specific peptides, thus reducing the number of potential peptides to be considered as vaccine candidates. A rationally designed epitope based vaccine lies in understanding of antigen recognition by both T and B lymphocytes [5,6]. Conserved regions which maintain its structure and function of envelope glycoprotein are searched. The surface of the mature virus which has a large number of envelope proteins can be one of the initiating points for the systematic search of cavities in order to encounter those compounds which are able to interfere with the protein rearrangements. Besides this the protein responsible for participation in cell recognition, cell entrance are also targeted. *In silico* epitope predictions tools have proved advantageous in determining the potential candidates reducing the number of validation experiments and time [7,8]. Presently, huge numbers of computational tools are available to predict peptides (T and B cell) with necessary properties [8]. Algorithms based on binding motifs, Position Specific Scoring Matrices (PSSM), Artificial Neural Network (ANN) and Support Vector Machine (SVM) are often used to predict potential MHC binders.

Bioinformatic Tools for T cell Epitope Prediction

Cytotoxic and helper T-cell epitopes are MHC bound sequences and attach in linear form. Epitopes are linked to MHC class I and MHC class II through their side chain interactions. Based on this, various tools predicting MHC class I binding Cytotoxic T-cell epitopes are designed like ProPred1, NetCTLpan, nHLAPed, RANKPEP, CTLPred, NetTepi. Tools for Helper T-cell recognizing epitopes bound to MHC class II are Propred, EpiDOCK, EpiTOP, MHC2Pred, HLA-DR4Pred [9]. MHC-II binding epitopes have proven less accurate compared to MHC-I [10].

Bioinformatic Tools for B Cell Epitope Prediction

Identification of B-cell epitopes (antigenic regions that stimulate B cell response) is a prominently forward step to propose a peptide vaccine. B-cell epitopes can be both of continuous or discontinuous type. Continuous B-cell epitope prediction is mainly based on the amino acid properties such as hydrophilicity, charge, exposed surface area and secondary structure. Discontinuous B cell epitope prediction requires 3D structure of the antigen [11-14].

Various tools have been developed using different algorithms for B-cell epitope prediction. ABCpred, bepiPred, LBtope, APCpred tools are used to predict continuous B cell epitopes. Disco Tope 2.0 server, BEPro (PEPITO), SEPPA helps in prediction of discontinuous epitopes. Epitopia, ElliPro, PepSurf servers help in predicting both continuous and discontinuous epitopes. For continuous epitope driven vaccine design tools like ABCpred, bepiPred, LBtope and APCpred are available.

Physicochemical Characterization of Epitopes

ProtParam and SOPMA (self optimized prediction method with alignment) of Expasy server can be used for predicting epitope's physiological and chemical characteristics. ProtParam tool show the isoelectric point (pI), molecular weight, amino acid composition, grand average hydropathicity (GRAVY), estimated half-life, extinction coefficient, instability index and aliphatic index of predicted protein sequence [3,15-17]. Grand average hydropathicity (GRAVY) value of protein sequence shows it's hydrophilic and hydrophobic nature i.e, higher the negative value higher will be its hydrophilicity.

Computational approaches for the prediction of highly immunogenic epitope has been employed for a number of viruses as listed in Table 1.

S. No.	Virus	Targeted Protein	Antigens	References
1.	Avian leukosis virus subgroup J	Surface glycoprotein	Gp85	Wang et al. (2017) [18]
2.	Rabies virus	Glycoprotein with molecular adjuvant used C3d-P28.	G5	Galvez-Romero et al. (2018) [19]
3.	Hantavirus	Surface glycoprotein	pVAX-LAMP/Gc	Jiang et al. (2017) [20]
4.	Human immunodeficieny virus	Envelope glycoprotein	Gp120	Thomas et al. (2014) [21]
5.	Aleutian mink disease virus	Capsid protein	VP2	Lu et al. (2017) [22]
6.	Avian leukosis Virus	Structural protein	P27	Khairy et al. (2017) [23]
7.	Influenza A and B virus.	Surface glycoprotein	Haemagglutinin	Ren H and Zhou P. (2016) [24]
8.	Coronavirus	Spike protein and membrane protein	S and M protein	Wang et al. (2008) [25]
9.	Influenza A virus subtype H9N2	Matrix protein and surface glycoprotein	M2e-HA2	Golchin et al. (2017) [26]
10.	Zika virus	Envelop protein	5IRE	Dey et al. (2017) [27]
11.	Varicella-zoster Virus	Envelop glycoprotein	gE protein	Zhu et al. (2016) [28]
12.	Infectious brusal disease virus (IBDV) and Newcastle disease virus (NDV)	Capsid protein and integral membrane protein (45)	VP2 protein and HN protein	Liu et al. (2015) [29]
13.	Rift valley fever virus	Nucleocapsid and Glycoprotein	N and G protein	Adhikari and Rahman (2017) [30]
14.	Human bocavirus 1	Capsid protein	Vp2	Kalyanaraman N (2018) [31]
15.	Ebola virus	Coat proteins	GP2 and VP24	Srivastava et al. (2016) [32]
16.	Zika virus	Structural and non structural protein.	Capsid 1 protein, membrane protein, E protein, NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5	Dikhit et al. (2016) [33]
17.	Influenza A virus(H1 subtype)	Surface glycoprotein	HA	Guo et al. (2015) [34]
18.	Chikungunya virus	Non structural polyprotein	nsPP	Pratheek et al. (2015) [35]

Table 1: Reports on epitope based peptide vaccine design.

Conclusion

Epitope driven vaccine designing has come as an attractive concept in both clinical and biomedical research and holds huge potential to replace the attenuated pathogen based vaccination. Improvements in *in silico* analysis and experimental evaluation will be critical in finally making it a success.

Conflict of Interest Statement: The authors declare that there is no conflict of interest regarding this study.

References

1. Sundaramurthi JC, Ashokkumar M, Swaminathan S, Hanna LE (2017) HLA based selection of epitopes offers a potential window of opportunity for vaccine design against HIV. Vaccine 35(42): 5568-5575.

2. Murrell S, Wu SC, Butler M (2011) Review of dengue virus and the development of a vaccine. Biotechnol advances 29(2): 239-247.

3. Khan MA, Hossain MU, Rakib-Uz-Zaman SM, Morshed MN (2015) Epitope-based peptide vaccine design and target site depiction against Ebola viruses: an

immunoinformatics study. Scand J Immunol 82(1): 25-34.

4. Korber B, LaBute M, Yusim K (2006) Immunoinformatics comes of age. PLOS Comput Biol 2(6): e71.

5. Patronov A, Doytchinova I (2013) T-cell epitope vaccine design by immunoinformatics. Open biol 3(1): 120139.

6. Testa JS, Philip R (2012) Role of T-cell epitope-based vaccine in prophylactic and therapeutic applications. Future Virol 7(11): 1077-1088.

7. Nielsen M, Lundegaard C, Blicher T, Lamberth K, Harndahl M, et al. (2007) NetMHCpan, a method for quantitative predictions of peptide binding to any HLA-A and-B locus protein of known sequence. PLOS one 2(8): e796.

8. Yang X, Yu X (2009) An introduction to epitope prediction methods and software. Rev Med Virol 19(2): 77-96.

9. Dhanda SK, Usmani SS, Agrawal P, Nagpal G, Gautam A, et al. (2016) Novel *in silico* tools for designing peptide-based subunit vaccines and immunotherapeutics. Brief Bioinform Rev 18(3): 467-478.

10. Lin HH, Zhang GL, Tongchusak S, Reinherz EL, Brusic V (2008) Evaluation of MHC-II peptide binding prediction servers: applications for vaccine research. BMC Bioinformatics 9(12): S22.

11. Soria-Guerra RE, Nieto-Gomez R, Govea-Alonso DO, Rosales-Mendoza S (2015) An overview of bioinformatics tools for epitope prediction: implications on vaccine development. J Biomed Inform Methodological Rev 53: 405-414.

12. Sun P, Ju H, Liu Z, Ning Q, Zhang J, et al. (2013) Bioinformatics resources and tools for conformational B-cell epitope prediction. Computational and mathematical methods in medicine 2013: 11.

13. Greenbaum JA, Andersen PH, Blythe M, Bui HH, Cachau RE, et al. (2007) Towards a consensus on datasets and evaluation metrics for developing B-cell epitope prediction tools. J Mol Recognit Rev 20(2): 75-82.

14. Yao B, Zheng D, Liang S, Zhang C (2013) Conformational B-cell epitope prediction on antigen protein structures: a review of current algorithms and comparison with common binding site prediction methods. PLOS One Rev 8(4): e62249.

15. Gill SC, Von Hippel PH (1989) Calculation of protein extinction coefficients from amino acid sequence data. Anal Biochem 182(2): 319-326.

16. Guruprasad K, Reddy BV, Pandit MW (1990) Correlation between stability of a protein and its dipeptide composition: a novel approach for predicting in vivo stability of a protein from its primary sequence. Protein Eng Des Sel 4(2): 155-161.

17. Ikai A (1980) Thermostability and aliphatic index of globular proteins. J Biochem 88(6): 1895-1898.

18. Wang X, Zhou D, Wang G, Huang L, Zheng Q, et al. (2017) A novel multi-variant epitope ensemble vaccine against avian leukosis virus subgroup J. Vaccine 35(48): 6685-6690.

19. Galvez-Romero G, Salas-Rojas M, Pompa-Mera EN, Chávez-Rueda K, Aguilar-Setién Á (2018) Addition of C3d-P28 adjuvant to a rabies DNA vaccine encoding the G5 linear epitope enhances the humoral immune response and confers protection. Vaccine 36(2): 292-298.

20. Jiang DB, Zhang JP, Cheng LF, Zhang GW, Li Y, et al. (2017) Hantavirus Gc induces long-term immune protection via LAMP-targeting DNA vaccine strategy. Antiviral Res 150: 174-182.

21. Thomas MA, Tuero I, Demberg T, Vargas-Inchaustegui DA, Musich T, et al. (2014) HIV-1 CD4-induced (CD4i) gp120 epitope vaccines promote B and T-cell responses that contribute to reduced viral loads in rhesus macaques. Virology 471-473: 81-92.

22. Lu T, Wang Y, Ge J, Ma Q, Yan W, et al. (2017) Identification and characterization of a novel B-cell epitope on Aleutian Mink Disease Virus capsid protein VP2 using a monoclonal antibody. Virus Res.

23. Khairy WOA, Wang L, Tian X, Ye J, Qian K, et al. (2017) Identification of a novel linear B-cell epitope in the p27 of Avian leucosis virus. Virus Res 238: 253-257.

24. Ren H, Zhou P (2016) Epitope-focused vaccine design against influenza A and B viruses. Curr Opin Immunol 42: 83-90.

25. Wang X, Xu W, Tong D, Ni J, Gao H, et al. (2008) A chimeric multi-epitope DNA vaccine elicited specific antibody response against severe acute respiratory

syndrome-associated coronavirus which attenuated the virulence of SARS-CoV in vitro. Immunol lett 119(1-2): 71-77.

26. Golchin M, Moghadaszadeh M, Tavakkoli H, Ghanbarpour R, Dastmalchi S (2017) Recombinant M2e-HA2 fusion protein induced immunity responses against intranasally administered H9N2 influenza virus. Microbial pathogenesis 115: 183-188.

27. Dey S, Nandy A, Basak SC, Nandy P, Das S (2017) A Bioinformatics approach to designing a Zika virus vaccine. Comput Biol Chem 68: 143-152.

28. Zhu R, Liu J, Chen C, Ye X, Xu L, et al. (2016) A highly conserved epitope-vaccine candidate against varicella-zoster virus induces neutralizing antibodies in mice. Vaccine 34(13): 1589-1596.

29. Liu XL, Shan WJ, Xu SS, Zhang JJ, Xu FZ, et al. (2015) The efficacy of chimeric vaccines constructed with PEP-1 and Ii-Key linking to a hybrid epitope from heterologous viruses. Biologicals 43(5): 377-382.

30. Adhikari UK, Rahman MM (2017) Overlapping CD8+ and CD4+ T-cell epitopes identification for the progression of epitope-based peptide vaccine from nucleocapsid and glycoprotein of emerging Rift Valley fever virus using immunoinformatics approach. Infect Genet Evol 56: 75-91.

31. Kalyanaraman N (2018*) In silico* prediction of potential vaccine candidates on capsid protein of human bocavirus 1. Mol Immunol 93: 193-205.

32. Srivastava PN, Jain R, Dubey SD, Bhatnagar S, Ahmad N (2016) Prediction of epitope-based peptides for vaccine development from coat proteins GP2 and VP24 of Ebola virus using immunoinformatics. Int J Pept Res Ther 22(1): 119-133.

33. Dikhit MR, Ansari MY, Vijaymahantesh, Kalyani, Mansuri R, et al. (2016) Computational prediction and analysis of potential antigenic CTL epitopes in Zika virus: A first step towards vaccine development. Infect Genet Evol 45: 187-197.

34. Guo C, Xie X, Li H, Zhao P, Zhao X, et al. (2015) Prediction of common epitopes on hemagglutinin of the influenza A virus (H1 subtype). Exp Mol Pathol 98(1): 79-84.

35. Pratheek BM, Suryawanshi AR, Chattopadhyay S, Chattopadhyay S (2015) *In silico* analysis of MHC-I restricted epitopes of Chikungunya virus proteins: Implication in understanding anti-CHIKV CD8+ T cell response and advancement of epitope based immunotherapy for CHIKV infection. Infect Genet Evol 31: 118-126.