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Original Article

Predicted binding affinity of candidate HDV epitope: a bioinformatics study

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Abstract

Hepatitis D virus (HDV) is an RNA virus that can cause hepatitis. Development and approval of new vaccines are the hope for control of the possible emerging pandemic of this infection. Recently, the possible epitope as 174 to 195 of HDAg was mentioned. Here, the author reports the preliminary data from the computational analysis to find binding affinity of the candidate HDV epitope using new bioinformatics technique. For L-HDAg, the binding affinity for A0203, A0301, A1101, A6801 and DRB0101 are acceptable. For S-HDAg, the binding affinity for A0203, A0301, A1101, A6801 and DRB6802 are acceptable. The binding affinity for A0203 is the most for both L-HDAg and S-HDAg.

Key words: hepatitis D, S-HDAg, L-HD-Ag, epitope, binding affinity.

Introduction

Hepatitis D virus (HDV) is an RNA virus that can cause hepatitis. At present is a sub-viral agent that is dependent for its life cycle on hepatitis B virus (HBV). The help it obtains from HBV is limited to the sharing of envelope proteins.[1] These proteins are needed to facilitate the assembly of the HDV genome into new virus particles, and in turn, to allow the attachment and entry of HDV into new host cells.[1] The unique characteristics of HDV replication, including autocatalytic self-cleavage and editing of the viral RNA, may influence the disease course and the heterogeneity of HDV genome sequence found in various geographic settings may in part account for the spectrum of disease outcomes by influencing the efficiency of any number of complex interactions.[2] The results of antiviral therapy of hepatitis D patients are not satisfactory.[2] Alpha-interferon (alpha-IFN) in high doses is usually recommended.[2]

In patients with established chronic HBV infection, superinfection with HDV may theoretically be controlled, but not prevented, by immunization to the internal components of HDV which may be the target of a cytotoxic T-cell response to HDV infected hepatocytes.[3] Such a response, by analogy to the effects of immunization to HBcAg, may result in rapid lysis of infected hepatocytes thereby limiting the spread of HDV through the liver [3]. Specific HDV vaccination is required. Development and approval of new vaccines are the hope for control of the possible emerging pandemic of HDV infection.[4,5] Vaccination strategies tested in the woodchuck model induced specific B- and T-cell responses but failed to protect from HDV infection.[6-7]

The development of a woodchuck HDV inoculum derived from a molecular clone has facilitated the analysis of viral genetic changes occurring during acute and chronic infection. This analysis has provided insights into one of the more important aspects of the natural history of HDV infection-whether a superinfection becomes chronic. These results could renew interest in further vaccine development. Based on the advance in bioinformatics, the immunomics becomes a new alternative in vaccine development.[8-9]

For HDV, Huang et al reported the possible epitope as 174 to 195 of HDAg.[10] This epitope is expected to be a candidate HDV DNA vaccine in the future.[9] Prediction of peptide binding to major histocompatibility complex (MHC) molecules is the basis for epitope discovery-driven vaccine development). Current developments in computational vaccinology mainly support the analysis of antigen processing and presentation and the characterization of targets of immune response. Here, the author reports the preliminary data from the computational analysis to find binding affinity of the candidate HDV epitope using new bioinformatics technique.

Materials and methods

Here, the author performed computation analysis of available 174 to 195 of both large HDAg (L-HDAg) sequence (accession number = AAC50290, 214 residues)

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and small HDAg (S-HDAg) sequence (accession number = AAQ09794, 195 residues) to find the binding affinity using bioinformatics tool namely MHCPred (available from the URL: http://www.jenner.ac.uk/MHCPred).[11] The MHCPred tool is a partial least squaresbased multivariate robust statistical approach to the quantitative prediction of peptide binding to major histocompatibility complexes (MHC), the key checkpoint on the antigen presentation pathway within adaptive cellular immunity.[11] MHCPred implements robust statistical models for both Class I alleles (HLA-A*0101, HLAA*0201, HLA-A*0202, HLA-A*0203, HLA-A*0206, HLA-A*0301, HLA-A*1101, HLA-A*3301, HLA-A*6801, HLA-A*6802 and HLA-B*3501) and Class II alleles (HLA-DRB*0401, HLA-DRB*0401 and HLA-DRB*0701).[11] The predicted binding affinity is reported as the IC50 value. Usually, peptides with predicted binding affinities < 500 nM are good binders, whereas those with binding affinities > 5000 nM are considered non binders.[12]

Table I. Predicted binding affinities for each allele for both L-HDAg and S-HDAg.

alleles	IC50 value L-HDAg	S-HDAg
A0101	70.47	57.15
A0201	289.07	190.11
A0202	149.97	127.06
A0203	14.69*	12.33*
A0206	64.27	85.11
A0301	31.77*	28.25*
A1101	32.81*	22.34*
A3101	59.43	59.43
A6801	30.76*	63.53
A6802	139.96	24.43*
B3501	185.35	260.62
DRB0101	28.51*	39.90*
DRB0401	246.60	126.77
DRB0701	62.95	50.23

* acceptable binding affinity

Results

The alleles selected for binding affinity prediction are A0101, A0201, A0202, A0203, A0206, A0301, A1101, A3101, A6801, A6802, B3501, DRB0101, DRB0401 and DRB0701. According to the analysis, the predicted binding affinities for both L-HDAg and S-HDAg are presented in *Table I*. For L-HDAg, the binding affinity for A0203, A0301, A1101, A6801 and DRB0101 are acceptable. For S-HDAg, the binding affinity for A0203, A0301, A1101, A6801 and DRB6802 are acceptable. The binding affinity for A0203 is the most for both L-HDAg and S-HDAg.

Discussion

The T-cell-mediated immune response plays a crucial role in defense against hepatotropic viruses as well as in the pathogenesis of viral chronic hepatitides.[13] However, very little is known about the role of specific T cells during hepatitis delta HDV infection in humans.[13] Identification of epitopes capable of binding multiple HLA types will significantly rationalize the development of epitope-based vaccines. Huang et al noted that HDAg-specific antibodies definitely exist following DNA vaccination in mice model.[10] They also noted that the magnitudes of the humoral immune responses generated by L-HDAg- and S-HDAg-encoding DNA vaccines were different.[10] HDV DNA vaccine can produce Th1 and cytotoxic T-cell immune responses but only a low anti-HDV antibody titer is generated with a L-HDAg construct.[14-15] In contrast, DNA vaccine expressing S-HDAg can generate a high titer of anti-HDV antibodies.[14] However, whether the low humoral immunity of L-HDAg DNA vaccine is due to inadequate dosage or can be ameliorated by other modes of immunization needs further evaluation.[14]

The present study focuses the interest on the reported candidate epitope. The author used a bioinformatics technique to predict the binding affinity of the candidate epitope. One of the key goals of immunoinformatics is the development of computer aided vaccine design or computational vaccinology, and its application to the search for new vaccines.[16] Key to solving this challenge is the prediction of immunogenicity, be that at the level of epitope, subunit vaccine or attenuated pathogen.[16] When the new tools are used to search for epitopes, this search is usually coupled with in vitro screening methods; an approach that has been termed computational immunology or immuno-informatics.[17] Researchers are now implementing these combined methods to scan genomic sequences for vaccine components.[17] This immunomics technique is successful used and validated in some previous reports.[18- 19]

In this work, the author used a computational analysis to determine the binding affinity of L-HDAg- and S-HDAg. The author hereby can demonstrate that the binding affinity is different between L-HDAg and S-HDAg. This can confirm the finding of Haung et al.[10] Also, the author can detect the highest affinity for A0203 for both L-HDAg and S-HDAg. However, some limitations of this study should be mentioned. The results from this study are only predicted results. Further confirmation is required.

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