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A virus-like particle of HBV preS elicits robust immune responses

The preS antigen of hepatitis B virus (HBV) corresponds to the N-terminal polypeptide in the large (L) antigen in addition to the small (S) antigen. The virus like particle of the S antigen is widely used as a vaccine to protect the population from HBV infection. The presence of the S antigen and its antibodies in patient blood has been used as markers to monitor hepatitis B. However, there is very limited knowledge about the preS antigen. Previous studies of preS employed recombinant preS proteins or polypeptides from preS. These molecules do not have the proper folded structure, nor proper post-translational modifications. We generated a virus-like particle (preS VLP) that is formed by a chimeric protein between preS and hemagglutinin (HA), and the matrix protein M1 of influenza virus. preS VLP was produced from 293T cells. The HBV preS antigen is displayed on the surface of preS VLP. Asn112 and Ser98 of preS in VLP were found to be glycosylated and O-glycosylation of Ser98 has not been reported previously. Biochemical characterization confirmed that preS in VLP was properly folded. The preS VLP shows a significantly higher immunogenicity than recombinant preS, eliciting robust anti-preS neutralizing antibodies. In addition, preS VLP is also capable of stimulating strong preS-specific T cell responses in Balb/c mice and HBV transgenic mice. Furthermore, preS VLP immunization provided protection against HBV challenge in mice. The data clearly suggest that this novel preS VLP could recapitulate the immunological properties of the L antigen in HBV particles, and can be potentially developed into prophylactic and therapeutic vaccines.

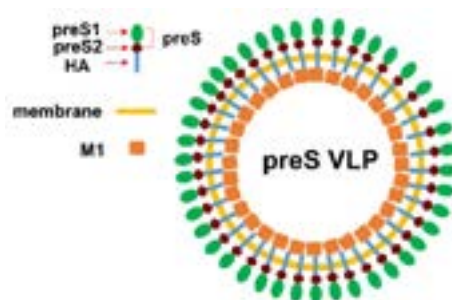


Figure 1: Illustration of HBV preS VLP structure. M1 of influenza virus promotes the release of preS VLP when it was co-expressed with preS-HA chimeric protein.

Biography

Ming Luo works on structures of viruses by employing X-ray crystallography and cryo-EM image reconstruction. His primary studies focus on RNA viruses and HBV. He discovered that the nucleocapsid of negative strand RNA viruses sequestered the genomic RNA by polymerization of a capsid protein. During viral RNA synthesis, the nucleocapsid is used as the template in coordination with the viral polymerase. With his knowledge of virus structure, he has been involved in design of novel antiviral drugs and vaccines. His work resulted in a FDA-approved flu drug. For this study, he combines the proteins from influenza virus and HBV to generate a preS VLP that is highly immunogenic. Further development of preS VLP prophylactic and therapeutic vaccines is in progress.

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