

Cellular proteins that bind the structural proteins of the avian hepatitis B virus.

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The human hepatitis B virus (HBV) is a small and enveloped DNA virus of the prototype of a family of *Hepadnaviridae* that causes acute and chronic liver disease and increases the risk of developing hepatocellular carcinoma. Despite of considerable understanding of the details of hepadnaviral replication and gene expression, little is known about HBV receptors and about the nature of the entry and the release pathways for this virus.

To understand the nature of the uptake and the maturation pathways for the hepadnaviruses, we have begun the search for the host proteins that interacts to structural proteins, envelope and capsid proteins, of the duck hepatitis B virus (DHBV) as a model of these viruses. After our finding of duck gp180, which is now regarded as a host receptor, recent experiments suggest that second host component may be required with gp180 to fully reconstitute viral entry.

By the biochemical-binding assay, we have identified gp180 and additional three host proteins, 64, 66 and 68-kDa proteins that bind the pre-S region of the DHBV envelope L protein (DHBVpre-S). HBVpreS1-preS2 and HHBVpreS can also bind 64 and 68-kDa proteins in every cell examined. Further experiments are in progress to examine the function of these cellular proteins in the life cycle of hepadnaviruses.

We have also identified two host proteins, 33-kDa and 45-kDa proteins (p33 and p45), that bind the DHBV core protein (DHBVc). DHBVc is the component of the nucleocapsid packaging the DHBV genome. The region of DHBVc associated with nucleocapsid assembly lies within the NH₂-terminal half of the protein. The COOH-terminal half of DHBVc contains arginine clusters that appear to be involved in genome packaging and in nucleocapsid traffic from plasma membrane to nucleus. Both p33 and p45 interact with the COOH-terminal region of DHBVc. This fact suggests that these proteins may be involved in genome packaging or traffic. Interestingly, by the binding assay with recombinant DHBVc, p45 cannot bind intact DHBVc, while it binds short COOH-terminal polypeptide of DHBVc. This may be reflected the dynamic topological change of the core protein caused by the phosphorylation of serine residues located in its COOH-terminal region. Functional p33 and p45 are expressed in a wide variety of tissues in susceptible ducks. The HBV core protein (HBc), like DHBc, binds p33 with high affinity indicating that p33 plays an important role in the life cycle of hepadnaviruses.