Hepatitis B virus core proteins associate with host cell protein gC1qR

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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 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 capsid proteins of HBV and the duck hepatitis B virus (DHBV) as a model of these viruses.

We have identified a 33-kDa protein as a DHBV-core binding protein in duck liver extracts using glutathione-S-transferase (GST)-DHBV core-CBD (chitin binding domain) fusion proteins. The same molecular sized protein was also identified with GST-HBV core-CBD fusion protein in HepG2 extracts, so human p33 was subjected to reversed-phase liquid chromatography (LC) coupled with electrospray-tandem mass spectrometry (MS/MS). p33 has turned out to be gC1qR.

To elucidate the function of gC1qR in hepadnavirus life cycle, we examined the binding domain on DHBV and HBV core proteins by constructing the DHBV and HBV core deletion mutants. Our data show 1) the cellular gC1qR protein binds to arginine-rich domain of carboxyl-terminal of core proteins 2) DHBV and HBV has a common binding motif with arginine repeated region, 3) gC1qR binds at least two domains in both DHBV and HBV core proteins (DHBV a.a.213-229, a.a.225-235, HBV a.a.157-169, a.a.164-177), 4) DHBV core proteins substituted two serine residues (a.a.230 and 232) with aspartic acid to mimic the phosphorylated form could not bind to gC1qR. These arginine-rich domains of the hepatitis B virus core protein have been shown to be required for pregenome encapsidation, productive viral DNA synthesis and sorting viral genome to the nuclei. gC1qR may regulate these processes by the interaction with nonphosphorylated core proteins.