Hepatitis B viral polymerase fusion proteins are biologically active and can interact with the hepatitis C virus core protein in vivo

施純明

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摘要.

Abstract

Hepadnaviruses and retroviruses are evolutionarily related families because they both require a process of reverse transcription for genome replication. However, hepadnaviruses produce polymerase (pol) and core proteins separately, while retroviruses synthesize a gag-pol fusion protein that is subsequently cleaved by a virally encoded protease to release a functional polymerase. To test whether an additional sequence at the N-terminus of pol in hepatitis B virus (HBV) interferes with its function, we created two plasmids expressing core-pol fusion proteins, core144-pol and core31-pol. Secreted particles obtained from HuH-7 cells, which were cotransfected with a core-pol fusion protein-expressing plasmid and a core-expressing plasmid, showed a positive signal of HBV DNA by the endogenous polymerase assay, indicating that the core-pol fusion proteins retain DNA priming, polymerization and RNase H activities. The fusion protein was detected in the cytoplasm of transfected cells and in secreted virions by immunoprecipitation. Furthermore, we found by immunofluorescence staining that the HBV core-pol fusion protein colocalized with the hepatitis C virus (HCV) core protein in cytoplasm and in lipid droplets. Immunoprecipitation studies showed that the anti-HCV core complex contained the HBV core-pol fusion protein while the anti-HBV pol complex contained the HCV core protein, which supports the hypothesis that the HCV core protein can form a complex with the HBV core-pol fusion protein.