# Abstract

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Capsid assembly and stability of hepatitis B virus (HBV) core protein (HBc) particles depend on balanced electrostatic interactions between encapsidated nucleic acids and an arginine-rich domain (ARD) of HBc in the capsid interior. Arginine-deficient ARD mutants preferentially encapsidated spliced viral RNA and shorter DNA, which can be fully or partially rescued by reducing the negative charges from acidic residues or serine phosphorylation of HBc, dose-dependently. Similarly, empty capsids without RNA encapsidation can be generated by ARD hyper-phosphorylation in insect, bacteria, and human hepatocytes. De-phosphorylation of empty capsids by phosphatase induced capsid disassembly. Empty capsids can convert into RNA-containing capsids by increasing HBc serine de-phosphorylation. In an HBV replicon system, we observed a reciprocal relationship between viral and non-viral RNA encapsidation, suggesting both non-viral RNA and serine-phosphorylation could serve as a charge balance buffer in maintaining electrostatic homeostasis. In addition, by comparing the biochemistry assay results between a replicon and a non-replicon system, we observed a correlation between HBc de-phosphorylation and viral replication. Balanced electrostatic interactions may be important to other icosahedral particles in nature.

Ref:
Su PY, Yang CJ, Chu TH, Chang CH, Chiang C, Tang FM, Lee CY, **Shih C**. (2016). HBV maintains electrostatic homeostasis by modulating negative charges from phosphoserine and encapsidated nucleic acids. *Scientific Reports* 6: 38959.