Non-Confidential Description - PSU No. 4365
“Hepatitis B Virus Capsid Mutants with Enhanced cccDNA Levels”

**Keywords:**
Hepatitis B Virus, cccDNA, covalently closed circular DNA, virus persistence, capsid protein, core protein, chronic HBV infection, Hepadnavirus family

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**Publications:**
Cui X *et al.*, *J Virol.* 2015, Oct;89(19); PMID: 26202253

**Background**
Hepatitis B virus (HBV) infection is a major health issue worldwide with an estimated 240 million people chronically infected with hepatitis B. More than 780,000 people die every year due to complications of Hepatitis B, including cirrhosis and liver cancer. Hepatitis B infection attacks the liver and can cause both acute and chronic disease. The virus is transmitted through contact with the blood or other body fluids of an infected person. Hepatitis B is an important occupational hazard for health workers. Although it can be prevented by currently available vaccine, there is currently no effective cure for chronic HBV.

**Invention Description**
HBV assembly begins with the packaging into immature nucleocapsids (NCs) of a viral RNA pregenome, which is converted to the DNA genome in mature NCs. Mature NCs are then selected for envelopment and secretion as complete-virion particles or, alternatively, can deliver their DNA to the host cell nucleus to maintain the viral genome as nuclear episomes - covalently-closed circular DNA (cccDNA). cccDNA is the molecular basis of the viral persistence. The present invention addresses the role of the capsid protein in the cccDNA formation of the Hepatitis B virus. Certain HBc (Hepatitis B core protein) mutations were found to alter the integrity of mature nuclear capsid (NC). Those mutations enhanced cccDNA formation and increased the nuclear cccDNA pool. The increased levels of cccDNA formed by these HBc mutants will facilitate efforts to target this critical viral episome for antiviral development. These findings provide the rationale to manipulate the integrity of mature NCs as novel ways to eliminate viral persistence by diminishing levels of viral nuclear episomes. The invention opens the opportunity to designing new antiviral strategies to cure persistent HBV infection.

**Advantages/Applications**
- Screening for capsid-targeted antiviral drugs.
- Diagnostic for HBV cccDNA load as well as effectiveness of the treatment.
- Manipulating levels of viral nuclear episomes (cccDNA).
- Allows identification of host factors regulating HBV capsid assembly.
- Cure for chronic HBV infection.