

New Targets for Antiviral Therapies against Hepatitis B Virus

Pei-Jer Chen

Hepatitis Research Center, National Taiwan University Hospital

Currently the viral reverse transcriptase is the main target for antivirals against hepatitis B virus. Both Entecavir and Tenofovir become the standard of care for chronic hepatitis B patients and achieve effective viral suppression. Despite both drugs can clear the HBV from circulation, they fail reducing the viral DNA, viral gene expression or viral protein levels in the pre-existing infected cells. In order to eliminate HBV from infected cells, new regimens aiming toward reducing intracellular viral protein or DNA are still needed.

The fundamental origin of HBV infection is the intracellular reservoir of viral cccDNA which can persistent for decades. The cccDNA is a very difficult target for drug development. Though recent data suggested the cellular DNA editing enzymes, such as APOBEC, useful in destroying cccDNA; their activities are limited and more potent pathways yet to be discovered. The adoption of CRISP/Cas9 targeting DNA editing system appeared to be a possible alternative, if the efficiency of delivery improved.

To reduce viral gene expression, the HBV X protein is a possible candidate, as it plays the essential viral transcription activator. It is imperative to know how HBV X directing viral transcription, then harnessing the mechanism to down-regulate viral gene expression and viral protein levels.

Finally, the intracellular viral proteins can turn-over, just like cellular proteins. We know very little about the degradation pathways for viral proteins. A better knowledge of viral protein disposal mechanisms may provide new targets for antivirals development.