

## #27: Viral DNA-dependent Induction of Innate Immune Response to Hepatitis B Virus in Immortalized Mouse Hepatocytes

Xiuji Cui, Daniel N. Clark, Kuancheng Liu, and Jianming Hu

Hepatitis B virus (HBV) infects hundreds of millions of people worldwide and causes acute and chronic hepatitis, cirrhosis and hepatocellular carcinoma. HBV is an enveloped virus with a relaxed circular (RC) DNA genome. In the nuclei of infected human hepatocytes, conversion of RC DNA from the incoming virion or cytoplasmic mature nucleocapsid (NC) to the covalently closed circular (CCC) DNA, which serves as the template for producing all viral transcripts, is essential to establish and sustain viral replication. A prerequisite for CCC DNA formation is the uncoating (disassembly) of NCs to expose their RC DNA content for conversion to CCC DNA. We report here that in an immortalized mouse hepatocyte cell line, AML12HBV10, in which NC uncoating is enhanced, the exposed viral DNA could trigger an innate immune response that was able to modulate viral gene expression and replication. When viral gene expression and replication were low, the innate response initially stimulated these processes but subsequently acted to shut off viral gene expression and replication after they reached peak levels. Inhibition of viral DNA synthesis or cellular DNA sensing and innate immune signaling diminished the innate response. These results indicate that HBV DNA, when exposed in the host cell cytoplasm, can function to trigger an innate immune response, which, in turn, modulates viral gene expression and replication.