

HEPATITIS

New mouse model provides novel insights into hepatitis D virus infection and clearance

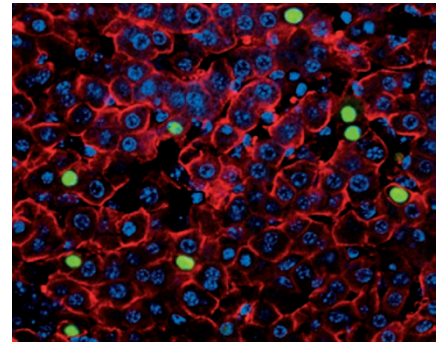
Without the existence of a convenient small animal model, advances in the understanding and treatment of hepatitis D virus (HDV) infection have been slow. Selective expression of the human sodium/bile acid cotransporter (SLC10A1, also known as NTCP) in mouse hepatocytes has led to the development of a new model of HDV infection.

HDV infection occurs in the presence of HBV, as it uses HBV surface proteins to gain entry into host cells. Furthermore, HDV infection results in more severe complications associated with liver failure, progression to cirrhosis and risk of cancer, compared with HBV infection alone. “15 million people are infected by HDV among those 240 million infected by its helper HBV,” says corresponding author Wenhui Li. “There is no specific treatment for HDV and therapeutic options for HBV are limited.”

HDV infection efficiency in 9–10 day old transgenic mice expressing human NTCP

increased proportionally to the amount of virus inoculated, with no infection in wild-type litter-mates. Immunofluorescence staining revealed that 3% of hepatocytes were infected with HDV. Treatment with monoclonal antibodies to the pre-S1 and S domain of the HBV envelope protein could block HDV infection.

The investigators also studied immune-related aspects of HDV clearance. Interferon signalling deficiency is known to impair host defences against HDV; however, mice without IFN- α/β receptor 1 (essential for interferon signalling) were able to clear HDV infection. “Transcriptome analysis of the infected mice revealed that the infection was also associated with upregulation of some novel cellular genes previously unknown for a role in host defence,” explains Li. “This study was the first systemic analysis of HDV–host interaction in animals and unveiled the interaction landscape of HDV and the host.”



HDV infection (green) of mice expressing human NTCP (red). Image courtesy of Wenhui Li.

The investigators hope that future exploration of this model will shed more light on HDV and HBV infection, and serve as a tool for developing new therapeutic strategies.

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