Study finds how the immune system responds to hepatitis A virus

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A surprising finding in a study comparing hepatitis C virus (HCV) with hepatitis A virus (HAV) infections in chimpanzees by a team that includes scientists from the Texas Biomedical Research Institute sheds new light on the nature of the body's immune response to these viruses.

Understanding how hepatitis C becomes chronic is very important because some 200 million people worldwide and 3.2 million people in the U.S. are chronically infected with HCV and are at risk for progression to cirrhosis and liver cancer. Hepatitis C associated liver disease is the most common indication for liver transplantation, while liver cancer due to HCV infection is now the most rapidly increasing cause of cancer death in the U.S.

"Remarkably, we found that HAV was more adept at evading the innate immune response than HCV, the virus that ultimately causes chronic infections," said Robert E. Lanford, Ph.D., a Texas Biomed virologist. The novel findings demonstrate that HAV is the stealthier virus when it comes to evading the innate immune response, despite the lack of persistent infections.

Hepatitis C infections are characterized by a failure of the immune system to combat and eliminate the virus. "We suspect this failure of the immune system shares attributes with other persistent viruses such as HIV and hepatitis B virus," said Lanford. By comparing two similar viruses that infect the liver, one that is always cleared by the immune system, HAV, and one that frequently evades the immune response,

HCV, the team hoped to unravel the mystery of how HCV causes lifelong persistent infections.

The research team involved scientists from Texas Biomed in San Antonio, the University of North Carolina (UNC) at Chapel Hill, and Nationwide Children's Hospital in Columbus, Ohio. The study performed in chimpanzees at Texas Biomed's Southwest National Primate Research Center (SNPRC) and funded by the National Institutes of Health, is published today in Proceedings of the National Academy of Sciences U.S.A.

The new study points out the critical need for more information about how the immune system reacts to HCV. It also reinforces the importance of chimpanzee research in this effort. The chimpanzee, the only animal model susceptible to HCV infection, was critical for probing the molecular differences in gene expression in the liver related to infection by the two viruses.

Examination of the adaptive immune system by co-author Christopher M. Walker, Ph.D., of Nationwide Children's Hospital in Columbus, Ohio, found that the T cell response to HAV was unique as well. "We expected the immune response to kill all HAV infected cells in a short time frame, and yet we could detect the genome of the virus in the liver for up to one year, long after symptoms of the disease were resolved," Lanford explained.

"Hepatitis viruses have co-evolved with humans over a very long period of time and they are good at evading the immune system, but nobody understands how hepatitis C becomes a chronic infection," said co-author Stanley M. Lemon, M.D., of UNC.

"The surprising and exciting results of this research program further highlight the critical value of the chimpanzee model in research on

hepatitis," said John L. VandeBerg, Ph.D., Texas Biomed's chief scientific officer and SNPRC director

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