Hepatitis B: Unusual virus discovered in shrews

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Scientists discovered an unusual Hepatitis B virus in shrews, that offers new opportunities of better understanding the disease. Credit: © Ulrike Rosenfeld

The discovery of an unusual hepatitis B virus from shrews offers new opportunities of better understanding the chronic progression of the disease. International research teams were able to demonstrate that an important protein which is essential for the development of a chronic course of infection is not present in this virus. DZIF scientists at the

Charite—Universitaetsmedizin Berlin and the University of Giessen are leading the research.

Infection with the hepatitis B virus (HBV) is one of the major global health problems. The high number of chronic cases is particularly problematic: More than 240 million people around the world are chronically infected with this virus and over 887,000 of those infected die each year of the long-term consequences such as liver cirrhosis and liver cancer. The chronification of HBV infection that often goes undetected for decades is one of the fundamental characteristics of this virus. "Discovering this unusual HBV in shrews gives us an opportunity to better understand the pathogenesis of this chronic illness," explains lead author of the study Andrea Rasche, scientist at the Charite—University Medicine Berlin and DZIF scholarship holder of the "Maternity Leave" programme.

An important protein that is required for the chronification of the infection is not present in the virus in shrews. "Without this immunomodulator, HBeAg, the disease could not become chronic," emphasises Prof. Dr. Jan Felix Drexler, DZIF scientist at the Charite—University Medicine Berlin and DZIF researcher in the research field "Emerging Infections." And this applies to all known HBVs in mammals. They form this protein during the infection. This immunomodulator suppresses the body's specific immune response to HBV so that the infection cannot heal and becomes chronic—often with very high viral concentrations in the blood. When this viral protein is not present, the body's immune system can successfully fight the infection.

This is not the case with the newly discovered HBV in shrews. The researchers examined almost 700 shrew samples from Europe and Africa and despite the absence of HBeAg, those animals that were infected still showed high concentrations of HBV in the blood. "This indicates a very successful but unusual characteristic of the infection and

the transmission of shrew HBV in its host," explains Prof. Dr. Dieter Glebe, head of the National Reference Centre for Hepatitis B and D viruses at the Justus Liebig University of Giessen (JLU) and DZIF scientist in the research field "Hepatitis." "Since the virus cannot infect human liver cells, it is highly unlikely that the virus can infect people." Therefore, it can be reasonably concluded that there is no risk for humans if they come into contact with shrews infected with HBV.

Another characteristic of the newly discovered virus is that it does not use the liver bile acid transporter to enter the liver cells as is the case with HBV in humans and apes, but takes an unknown path into the cell. "This shows that we still do not know all HBV receptor molecules," explains Prof. Drexler. In addition to these important findings about the HBV infection, the shrew virus gives us new insight into the genealogy of HBV. "Our evolutionary studies show that HBV exists in mammals for millions of years, probably around 80 million years," says Prof. Drexler.

The scientists now want to further examine the unusual infection pattern of shrew HBV that develops without the central immunomodulator HBeAg. Despite intensive international efforts, an effective treatment for chronic hepatitis B has yet to be developed. One reason for this is that there are no suitable animal models that can be used to examine the complex interactions of the virus infection with the host's immune system. "Shrews could be a promising animal model for HBV research. The virus discovered here is particularly suitable for examining the mechanisms of chronic HBV infections," says Prof. Drexler.

More information: Andrea Rasche et al, Highly diversified shrew hepatitis B viruses corroborate ancient origins and divergent infection patterns of mammalian hepadnaviruses, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1908072116

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