

# New therapeutic approach may help to cure chronic hepatitis B infection

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Researchers at Helmholtz Zentrum München, Technical University of Munich (TUM) and the German Center for Infection Research (DZIF) have developed a novel therapeutic approach to cure chronic hepatitis B. The scientists found that the large amount of hepatitis B virus proteins expressed in the liver prevents the body's immune system to defeat the virus, consequently preventing an effective therapy. The researchers were able to show that knocking down the expression of the virus' proteins enables successful vaccination with TherVacB, a novel therapeutic vaccine.

Around 260 million humans, more than three percent of the world's population, are chronically infected by the hepatitis B virus. As a result, every year, 880,000 people worldwide die of liver failure or hepatocellular carcinoma. Currently no curative therapy is available. The therapies available to date inhibit virus replication, but need to be given long-term. As long as infected people cannot form an adequate immune response, the virus will survive. This is precisely where Prof. Ulrike Protzer, head of the Institute of Virology at Helmholtz Zentrum München and TUM, and her team start.

## Novel therapeutic approach

Using a preclinical mouse model, the researchers found that proteins of the hepatitis B virus prevent that certain immune cells of the body, so-called CD8+ T-cells become effective. Based on these finding, the

scientists developed a novel [therapeutic approach](#): first, the expression levels of the virus proteins are knocked down, and then the immune cells are activated by therapeutic vaccination. In contrast to conventional vaccinations, which aim to prevent diseases before outbreak, such a therapeutic vaccination aims to cure already existing [chronic diseases](#).

## **Successful suppression of virus proteins in mice**

Consequently, the researchers first developed a method to suppress the hepatitis B virus proteins. They used siRNAs, small ribonucleic acid molecules that bind to the messenger RNA of the virus' proteins. By labelling the messenger RNA with siRNA, the [infected cell](#) receives the signal that the viral RNA is undesired and removes it. In this way protein expression is knocked down. However, the suppression of protein expression alone was not sufficient to reverse the inhibition of the CD8+ T-cells in chronically infected mice.

## **Infection cured in mice**

The scientists therefore had to go one step further: "We then combined the siRNA method with a therapeutic vaccination developed by us. This enabled us to trigger a strong immune response against the virus. This led to cure of hepatitis B virus infection in two different mouse models," explains Dr. Thomas Michler, physician and one of the two first authors of the study.

## **Novel therapeutic vaccination soon in a clinical trial**

The newly developed vaccine, called TherVacB, will be tested as an immunotherapy in a two-year clinical trial starting in 2021. "The [therapeutic vaccine](#) we have developed is indeed very promising as it induces neutralizing antibodies and T-cell responses," said Dr. Anna

Kosinska, the other first author of the study. The vaccine will be administered in three doses every four weeks. It has been designed to target the majority of all hepatitis B viruses and therefore will be beneficial to most people infected worldwide.

"We are very pleased that for the [clinical trials](#) of TherVacB we are able to cooperate with a consortium of Europe's leading virologists, immunologists and hepatologist, guided by Helmholtz Zentrum München," adds Protzer.

**More information:** Thomas Michler et al. Knockdown of Virus Antigen Expression Increases Therapeutic Vaccine Efficacy in High-titer HBV Carrier Mice, *Gastroenterology* (2020). [DOI: 10.1053/j.gastro.2020.01.032](#)

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