# A Potential Effective And Innovative Therapy For The Treatment of Chronic HBV Infection And Liver Cancer

Hepatitis B is an infectious disease caused by the hepatitis B virus (HBV) that affects the liver, it is a type of viral hepatitis. There are about 300 million people in the world suffer from hepatitis B. Among them, hepatitis B virus (HBV) infections from China account for about one-third, and about one in 16 Chinese people is infected. However, current treatment methods are difficult to cure chronic HBV infection, and many patients will develop liver cirrhosis and liver cancer as a result. Approximately 900,000 people die from liver cirrhosis and hepatocellular carcinoma caused by chronic HBV infection each year.

In a study published in **Nature Communications** on May 14, a research team led by scientists from University College London (UCL) found a new target for the treatment of hepatitis B. The targeted therapy of HBV can not only inhibit the replication of HBV, but also stimulate T cell activity against HBV-infected liver cells. The researchers said that **this target may bring a highly effective and innovative therapy for the treatment of chronic HBV infection and liver cancer.**

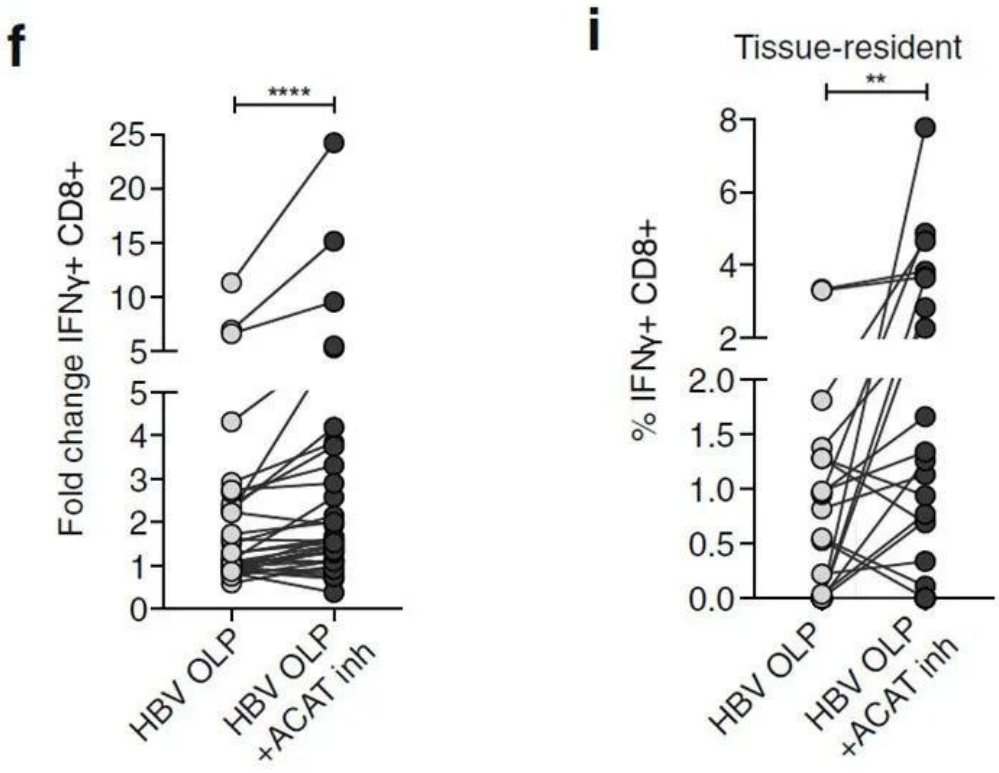

## Two-pronged approach, effective treatment of HBV infection

The reason why HBV infection is difficult to cure is because the virus product has immunosuppressive properties, and the human body's immune system cannot control the virus infection well. Therefore, the functional cure strategy for hepatitis B includes two parts, one is to inhibit the replication of HBV and the level of virus products, and the other

is to activate the body's immune system through immunomodulatory means.

In this study, scientists analyzed blood and liver tissue samples from patients with chronic hepatitis B and found that **CD8-positive T cells, which are specific for HBV and are an important weapon in the body's immune system for recognizing and attacking infected cells or cancer cells**, were not functioning properly. This T cell dysfunction is a common occurrence in patients with chronic hepatitis B.

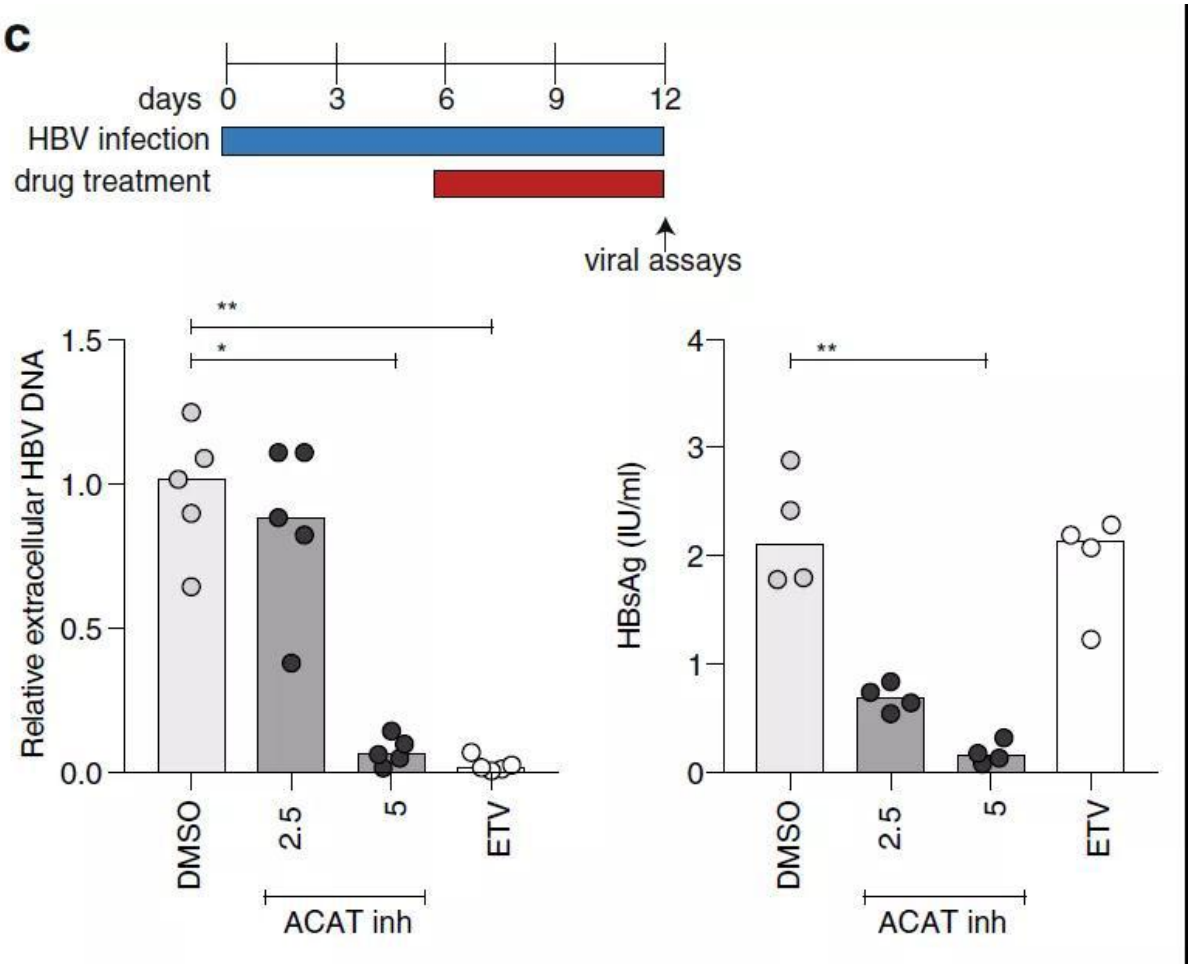
However, when researchers treated these dysfunctional T cells with inhibitors targeting acyl-CoA: cholesterol acyltransferase (ACAT) in in vitro experiments, they found that ACAT inhibitors not only restored the vitality of CD8-positive T cells, but also caused proliferation of these T cells. Moreover, there is a special tissue-resident memory T cell subtype in the liver, and this subtype is expanded in patients with effective HBV control. **ACAT inhibitors significantly enhance the function of this T cell subtype, demonstrating its potential to help enhance long-term virus control.**




▲ACAT inhibitors enhance the function of HBV-specific CD8-positive T cells (left picture) and tissue-resident memory T cells (right picture) (picture source: reference [2])

ACAT is a protease highly expressed in the liver, and it plays an important role in controlling cholesterol metabolism. A metabolite of cholesterol is a component of hepatitis B surface antigen (HBsAg). Therefore, the researchers hypothesized that ACAT inhibitors may affect the production of hepatitis B virus particles and hepatitis B surface antigen by

regulating the metabolism of cholesterol. In vitro cell culture experiments confirmed their hypothesis that **the levels of HBV DNA in cells treated with ACAT inhibitors decreased significantly, and unlike common antiviral therapies, ACAT inhibitors can also effectively reduce HBsAg levels.**




▲ACAT inhibitors significantly reduce HBV DNA levels (left picture) and HBsAg levels (right picture) in vitro (picture source: reference [2])

## Improve the anti-cancer efficacy of anti-PD-1 therapy and T cell therapy

A potentially fatal consequence of chronic HBV infection is the production of hepatocellular carcinoma. Since ACAT inhibitors can activate CD8-positive T cell activity against HBV-infected liver cells, can they further enhance the effectiveness of commonly used cancer immunotherapy? Scientists explored the effect of combining ACAT inhibitors with anti-PD-1 antibodies. They found that **the combination of ACAT inhibitors and anti-PD-1 antibodies can further enhance the immune activity of HBV-specific CD8-positive T cells compared with anti-PD-1 antibody single agents**. Furthermore, further studies have shown that **ACAT inhibitors can also enhance the anti-cancer activity of tumor-infiltrating T cells in patients with hepatocellular carcinoma, as**

**well as the anti-cancer activity of genetically engineered T cell therapy.**

"We have found an innovative target that is highly effective in the treatment of chronic HBV infection and liver cancer." The first author of this study, Dr. Nathalie Schmidt of the UCL Infection and Immunology Department, said: "Drugs that regulate cholesterol are already proved to be safe in humans in clinical trials. We hope that this research can guide the advancement of clinical trials, combine the regulation of cholesterol with other immunotherapies, and provide new possibilities for the treatment of chronic HBV infection and cancer patients."

As a leading API intermediates manufacturer in China, Huateng Pharma has an R&D base of 5,000 square meters and a smart pharmaceutical industrial park of 34,000 square meters. It is dedicated to the R&D and production of high-end biomedical chemical products, such as pharmaceutical intermediates, PEG derivatives, etc. We are able to supply intermediates of Entecavir, which is an antiviral medication used in the treatment of hepatitis B virus (HBV) infection. We can also supply intermediates for other anti-viral drugs, such as oseltamivir intermediates, remdesivir intermediates, favipiravir impurities, Brilacidin intermediates and baloxavir marboxil intermediates, etc.

References:

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