

# New vaccine technology protects mice from hepatitis C virus

EurekAlert

Immunology: Three percent of the world's population is currently infected by hepatitis C. The virus hides in the liver and can cause cirrhosis and liver cancer, and it's the most frequent cause of liver transplants in Denmark. Since the virus mutates strongly, we have no traditional vaccine, but researchers at the University of Copenhagen are now the first to succeed in developing a vaccine, which provides future hope for medical protection from this type of hepatitis.

"The hepatitis C virus (HCV) has the same infection pathways as HIV," says Jan Pravsgaard Christensen, Associate Professor of Infection Immunology at the Faculty of Health Sciences, University of Copenhagen.

"Approximately one newly infected patient in five has an immune system capable of defeating an acute HCV infection in the first six months. But most cases do not present any symptoms at all and the virus becomes a chronic infection of the liver."

Poorly treated donor blood and dirty needles are sinners

Every year three or four million more people become infected and the most frequent path of infection is needle sharing among drug addicts or tattoo artists with poor hygiene, such as tribal tattoo artists in Africa and Asia. Fifteen percent of new infections are sexually transmitted, while ten percent come from unscreened blood transfusions.

According to Allan Randrup Thomsen, Professor of Experimental Virology, "Egypt is one country with a high incidence of HCV. This is particularly due to lack of caution in the past with regards to screening donated blood for the presence of this virus," he says.

China, Brazil, South East Asia and African states south of the Sahara also have a high incidence, while the disease is also spreading through Eastern Europe, especially Romania and Moldova.

HCV mutates too fast for traditional vaccines

The new vaccine technology was developed by Peter J. Holst, a former PhD student now a postdoc with the Experimental Virology group, which also includes Professor Allan Randrup Thomsen and Associate Professor Jan Pravsgaard Christensen.

The technology works by stimulating and accelerating the immune system, and showing the body's defence mechanisms of the parts of the virus that are more conserved and do not mutate as fast and as often, such as the molecules on the

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surface of the HCV.

Basically, traditional vaccines work by showing the immune defences an identikit image of the virus for which protection is desired. Antibodies then patrol all entrances with a copy of this image and are able to respond rapidly if the virus attempts to penetrate. But the influenza virus mutates its surface molecules and in the course of a single season it takes on a new guise so that it no longer resembles the original identikit image and the vaccine loses its efficacy.

Professor Randrup explains, "Mutations of the surface are Darwin at work, so to speak. The virus tries to outwit the immune defences and if it succeeds we get ill, and our response is new vaccines."

Associate Professor Pravsgaard Christensen says, "Viruses like HCV mutate so rapidly that classical vaccine technology hasn't a chance of keeping up. But the molecules inside the virus do not mutate that rapidly, because the survival of the virus does not depend on it."

New vaccine technology gives immune system information about virus' stable parts

According to Professor Randrup, the body's natural defences usually don't see these internal virus molecules until the virus has taken residence in the body.

"Our cells constantly show random samples of their contents to the immune defence patrols, and if there are enough foreign bodies among them, the alarm is triggered," says Professor Randrup.

The cells display fragments of the surface molecules and internal genes from the virus, and if you show the immune defences a kind of X-ray of the inner genes, they will respond. Actually, the response is extremely potent, and one of the things it does is summon the specialised CD8 killer cells.

"We took a dead common cold virus, an adenovirus that is completely harmless and which many of us have met in childhood," Associate Professor Pravsgaard Christensen explains.

"We hid the gene for one of the HCV's internal molecules inside it. At the same time we attached a special molecule on the internal molecule so that when the cells of the mouse body tried to take a sample, they would extract a more extensive section. The immune defences would then be presented with a larger section of the molecule concerned. You may say that the immune defences were given an entire palm print of the internal genes instead of just a single fingerprint."

This strategy resulted in two discoveries from the team. Firstly, the mice were vaccinated for HCV in a way that meant that protection was independent of variations in the surface molecules of the virus. Secondly, the immune defences of the mice saw such an extensive section of the internal molecule that even though some aspects of it changed, there were still a couple of impressions the immune defences could recognise and respond to.

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The new technology to be tested in monkeys

Another virus that mutates its surface molecules with extreme rapidity is HIV. It changes skin in the space of 24 hours, and like HCV, we do not yet have a cure or a vaccine. The researchers think that HIV originally migrated to man from monkeys in the 1930s, when it was the simian Immunodeficiency virus that still circulates among a number of species of wild African monkeys.

"The Danish Medical Research Council (DMRC) has given postdoc Peter Holst a grant to test our technology for a SIV vaccine for macaque monkeys in the US," says Associate Professor Pravsgaard Christensen.

The University of Copenhagen is also currently negotiating the sale of the patent for the process so that the technology can be developed for use in human vaccines.

The discovery of an effective HCV vaccine has just been published in the *Journal of Immunology*.

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