Medical Xpress

Genes show the way to better treatment of hepatitis A

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One of the most common causes of hepatitis A (formerly known as infectious hepatitis) is a hepatitis C virus infection in the liver. The disease can be treated medically, but not all patients are cured by the treatment currently available. New research shows that the response to medical treatment depends on genetic factors.

Our best defence against viral infections is the immune system. However, humans are endowed differently in terms of our immune defence. Recent research has shown how our genetic make-up heavily influences our ability to combat viral infections. Surprisingly, it now turns out that some of the genes that are good for the immune system can at the same time impede medical treatment.

Hepatitis C virus (HCV) infection causes chronic inflammation of the liver, which is slowly broken down and in some cases the disease can progress to liver cancer. It is possible to treat the disease with antiviral medicine, but patients react differently to the treatment and not all of them recover.

An international research group led by scientists at Aarhus University, Denmark, has now found out why some patients respond to the treatment, while others do not. The result of the treatment is determined to a very great extent by the individual patient's genetic heritage (genome). To the great surprise of the researchers, it turns out that variations in our genes for the interferon lambda 4 protein (IFNL4) determine whether we respond well or poorly to treatment.

"Our research shows that genetic mutations that reduce the activity of the interferon lambda 4 protein provide patients with a considerably better chance of recovering from the infection. Or to put it another way, a functional interferon lambda 4 protein is harmful during an infection with HCV. This is paradoxical because IFNL4 is an essential part of our immune defence against viral infections, and should therefore have a positive effect," says Associate Professor Rune Hartmann, Department of Molecular Biology and Genetics, Aarhus University.

Paradox in the laboratory

IFNL4 is a member of the family of proteins called interferons (named after their ability to interfere with viruses), which are an essential part of our immune defence against viral infections. They work by activating a cellular programme that combats viral infections and thereby makes the cells resistant to the virus.

The research group's studies show that IFNL4 has a powerful antiviral activity in the laboratory, and behaves in every way like any other member of the interferon family. Even though IFNL4 is antiviral in the laboratory, the research also clearly shows that it has the opposite effect in patients. This is where the paradox arises. The researchers have a possible explanation of why this happens.

"Our hypothesis is that interferon lambda 4 confuses other parts of the immune system and that HCV is able to exploit this," says PhD student Ewa Terczynska-Dyla, who also took part in the research project.

Possibility of better treatment

The research results from Aarhus University indicate that it is possible to develop new treatments for hepatitis that match the individual patient's

genome. This could be medicine specifically targeting IFNL4, but could also include modifying the normal treatment, depending on whether the patients have fully functional IFNL4 genes, or have a version with either reduced activity or no activity at all.

The latter group of patients is by far the biggest in Denmark, and they do not require anywhere near as long a period of treatment to recover. This is good for both the patients (because they avoid unnecessary treatment) and the public medical expenses (because HCV medicine is very expensive).

The researchers will now carry out further work to understand the fundamental mechanisms that make the interferon lambda genes so important for our ability to combat hepatitis caused by HCV.

The results will be published in the journal *Nature Communications* 23 December 2014.

Provided by Aarhus University