Stress in cells activates hepatitis viruses

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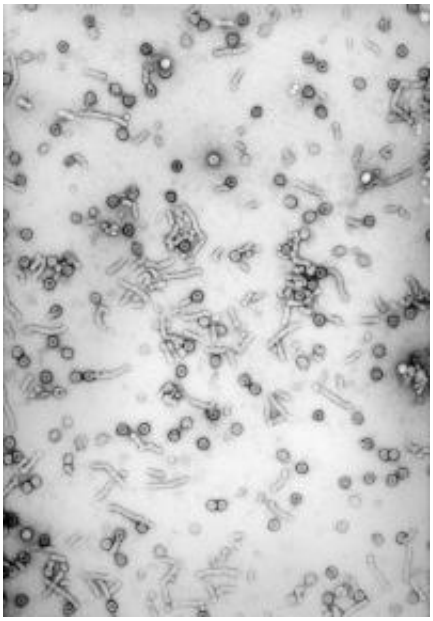

Electron microscopic picture of hepatitis B viruses. Thomas Bock, Hanswalter Zentgraf, German Cancer Research Center.

People who have received a donor organ need lifelong immunosuppressant drugs to keep their immune system from attacking the foreign tissue. However, with a suppressed immune system, many infectious agents turn into a threat. Infections such as with human cytomegalovirus and a certain type of human polyomavirus frequently cause complications in transplant recipients. For these patients it would therefore be particularly beneficial to have substances that suppress the immune system and exert an antiviral activity at the same time – thus killing two birds with one stone.

Jointly with colleges from Heidelberg University Hospital of Internal Medicine, researchers Professors Karin and Felix Hoppe-Seyler of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now tested a number of drugs with such an activity profile. They also tested the substances in liver cells infected with hepatitis B viruses (HBV) in the culture dish. The result: Liver cells that had been treated even produced considerably more viral offspring than untreated ones.

The substances under investigation inhibit the synthesis of nucleotides, which are the basic building blocks of DNA. This is how they exert their immunosuppressive effect: They slow down multiplication of immune cells because these lack building material for duplicating their genetic material. "The lack of DNA building blocks can cause a kind of stress in specific cells, which shows in the activation of a stress protein called p38", says Felix Hoppe-Seyler. "In liver cells, p38 very effectively activates the replication of hepatitis B viruses. "

The findings of the DKFZ researchers are a definite indication that administering these drugs in transplant recipients bears risks. Liver transplants, in particular, often have to be done because the body's own organ has been destroyed by hepatitis B viruses. In such cases, drug-induced activation of remaining HBV in the body may lead to the donor organ being attacked by hepatitis B viruses again.

Felix Hoppe-Seyler suspects that besides the three substances the group has investigated there are other substances which also cause an activation of p38. "In cancer patients being treated by chemotherapy, there is often a reactivation of chronic HBV infections. This has always been put down to their weakened immune system. We will now investigate whether this may also be due to activation of stress protein p38," said the virologist outlining the goals of his further research.

More information: Karin Hoppe-Seyler, Peter Sauer, Claudia Lohrey and Felix Hoppe-Seyler: The Inhibitors of Nucleotide Biosynthesis Leflunomide, FK778, and Mycophenolic Acid Activate Hepatitis B Virus Replication In Vitro. *Hepatology*, 2012, DOI: 10.1002/hep.25602