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Researchers develop first successful laboratory model for studying hepatitis C

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By differentiating monkey stem cells into liver cells and inducing successful infection, researchers from the Icahn School of Medicine at Mount Sinai have shown for the first time that the hepatitis C virus (HCV) can replicate in monkeys, according to research published in the journal *Gastroenterology*. The new findings may lead to the first new animal model and provide new avenues for developing treatments and vaccines for this disease, which impacts more than three million people in the United States.

Scientists have tried for decades to develop animal models to study HCV, but the virus was incapable of infecting any species except for humans and chimpanzees. With a recent National Institutes of Health-imposed moratorium restricting chimpanzee research, the Mount Sinai research team turned to a close relative of chimpanzees and humans—macaques. Led by Matthew Evans, PhD, and Valerie Gouon-Evans, PhD, of Mount Sinai, the research team sought to find out why previous attempts to infect macaques with HCV failed.

Dr. Gouon-Evans, who is Assistant Professor of in the Department of Developmental and Regenerative Biology at Mount Sinai, worked with a team at the Fred Hutchison Cancer Research Center in Seattle to differentiate macaque stem cells into liver cells. Dr. Evans, who is an Assistant Professor in the Department of Microbiology, and his team then attempted to infect these cells with HCV in a petri dish. They found that these differentiated cells were able to support HCV infection and replication, although not as effectively as in human liver cells.

"Now that we know that HCV infection in macaque cells is possible, we wanted to find out why it only worked in liver cells that were derived from stem cells," said Dr. Gouon-Evans. "By identifying where in the viral life cycle the infection is dysfunctional, we can develop an effective animal model of HCV."

Dr. Evans and his team found that HCV was less efficient at entering macaque cells to initiate infection compared to human cells because changes in the macaque form of a certain cell surface receptor rendered it less functional than the human version. This cell entry block could be overcome by expressing the human version of this receptor in macaque cells. Furthermore, HCV infection of normal macaque cells was greatly enhanced by changes to the virus that loosened its requirements for that receptor.

"Our discovery shows that by manipulating either host or viral genetics we can efficiently infect macaque cells," said Dr. Evans. "These findings may open doors for the field of HCV research, lead to new animal models, and hopefully vaccines and therapies."

Next, Dr. Evans plans to take these experiments out of petri dishes by attempting to infect macaques in vivo with the mutant HCV that can use the receptors this animal naturally expresses. If successful, this work would provide a new, much-needed animal model for HCV studies and vaccine development.

Provided by The Mount Sinai Hospital