UC San Diego Health

Improved Culture System for Hepatitis C Virus Infection

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A University of California, San Diego School of Medicine researcher has developed the first tissue culture of normal, human liver cells that can model infection with the Hepatitis C virus (HCV) and provide a realistic environment to evaluate possible treatments. The novel cell line, described in the July 16 issue of *PLoS ONE*, will allow pharmaceutical companies to effectively test new drug candidates or possible vaccines for the HCV infection, which afflicts about 170 million people worldwide. Currently, there is no animal model that is effective for testing such therapies.

Assistant Professor of Medicine Martina Buck, Ph.D., researcher at UC San Diego's Department of Medicine and Moores UCSD Cancer Center developed the novel culture system, which mimics the biology of HCV infection in humans.

"This is the first efficient and consistent model system for HCV to be developed," said Buck, adding that it will now enable researchers not only to conduct mechanistic experiments in culture, such as blocking the virus pathways, but also to more effectively screen possible therapies for HCV. "There is a need for new treatments, and for development of a possible vaccine for HCV. Now we have a model system to support work by investigators in this area."

Currently, there is only a single treatment for HCV, PEG- interferon-α. The drug combination has an average response rate of about 50 percent in HCV cases, but it is much lower than that, closer to 20 percent, in individuals with liver cirrhosis. It can also cause severe flu-like side effects. Approximately 10,000 deaths due to cirrhosis of the liver and several thousand more from liver cancer are attributed to HCV infection in the United States each year.

The HCV life cycle is only partially understood because, until now, it has not been possible to efficiently infect normal human hepatocytes, or liver cells, in culture. According to Buck, the valuable Huh-7 system currently in use to test HCV uses cloned, synthetic HCV RNA expressed from liver tumor cells. These cells cannot be infected with naturally occurring HCV obtained from infected patients.

In contrast, the culture developed by the UCSD scientists allows direct infection with HCV genotypes 1, 2, 3 and 4 from the blood of HCV-infected patients. This system will enable

researchers to study the complete viral lifecycle in its normal host cell, providing novel scientific opportunities. The study reports that the system has been tested using over 30 virus donors as well as multiple donors of hepatocytes, with the production of infectious HCV for all genotypes tested.

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