A Novel Cell Culture System for Hepatitis C Virus (HCV)

This new culture system creates stem cell-derived human hepatocyte-like cells which are Hepatitis C Virus (HCV) infectable. The FSU system establishes a new noncancerous and renewable cell culture system for HCV infection; enables direct infection by patient sera in vitro; identifies a defined transition to HCV permissiveness during hepatocyte differentiation; and demonstrates the feasibility of generating viral-resistant human hepatocyte-like cells in vitro.

Technology

Primary human hepatocytes (PHHs) isolated from patient biopsies represent the most physiologically relevant cell culture model for hepatitis C virus (HCV) infection. However, these primary cells are not readily accessible, display individual variability, and are largely refractory to genetic manipulation.

The FSU-created hepatocyte-like cells derived from stem cells not only overcomes these shortcomings but can also provide an unlimited source of non-cancer cells for both research and cell therapy.

The system, (to be published by Professor Hengli Tang, Department of Biological Science, Florida State University, Tallahassee Fl and others in PLoS Pathogens) reports a novel infection model based upon differentiated human hepatocyte-like cells (DHHs) derived from stem cells, including human embryonic (hESCs) and induced pluripotent stem cells (iPSCs).

Differentiated human hepatocyte-like cells (DHHs) derived from pluripotent stem cells have demonstrated hepatic functions but have not been explored for HCV infection studies as here.

The ability to directly infect cultured cells with HCV patient serum, to study defined stages of viral permissiveness, and to produce genetically modified cells with desired phenotypes all have broad significance for host-pathogen interactions, drug resistance analysis and drug therapy.

Applications

- An HCV platform for drug-resistance analysis
- Infection studies and metabolic studies

Unique Advantages

This system allows a never before demonstrated effect - HCV-infected patient sera leads to robust direct infection in the culture system.
Status

- A Provisional Patent application was filed in late 2011.

Next Steps

FSU will make available the cells and the system for experimentation / evaluation purposes for a preparation fee. A start-up company is seeking partners to develop certain applications. Other applications remain available for direct license from FSU.

The Inventor

Dr. Hengli Tang received his Ph.D. degree in molecular biology and virology with Professor Flossie Wong-Staal at University of California, San Diego in 1998. After several years of post-doctoral and industry experience, Dr. Tang returned to academia in 2004 to take a tenure-tracked position at Florida State University and has recently been awarded tenure and promoted to the rank of associate professor. His group is credited for being the first to report definitive evidence that human cyclophilin A is a critical cofactor for HCV replication and the direct target of derivatives of Cyclosporine, which are being tested in human trials as candidate HCV therapy. He has recently developed a novel genetic selection that will be broadly applicable to diverse RNA viruses and many other cellular cofactors. Dr. Tang is a NIH-supported investigator who actively mentors Ph.D. students and post-doctoral fellows.

Areas of Research

The general area of research interest in my lab is virus-host cell interactions concerning hepatitis C virus (HCV) and human immunodeficiency virus (HIV). Currently, the molecular and cell biology of HCV replication is the main focus of the lab. My lab has characterized in depth the relationship between Cyclophilin A (CyPA), a host factor, and HCV infection in vitro. We obtained definitive evidence that HCV infection of cultured hepatoma cells is critically dependent on CyPA but not several other isoforms of CyPs. We have also demonstrated that the peptidylprolyl isomerase (PPIase) motif of CyPA is essential for the function of the HCV replicase, validating the clinical approach of developing CPIs such as DEB025/Alisporivir as a novel class of anti-HCV drugs. Furthermore, we established that the in vitro resistance to CsA, albeit modest, is directly correlated with a reduced dependence on CyPA; and a functional interaction between CyPA and the HCV replicase exists.

For Licensing Opportunities Contact

Office of IP Development & Commercialization
2010 Levy Avenue, Suite 276-C
Tallahassee, FL 32306-2743
John Fraser / E-mail: jfraser@techtransfer.fsu.edu
Ph: (850) 644-8637 Fax: (850) 644-3675

Published 4/2012