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Pitt Drug Discovery Researchers Receive $5.8 Million Federal Grant to Build 3D Liver Model

PITTSBURGH, Sept. 23, 2014 - With a new $5.8 million, three-year award from the National Institutes of Health (NIH), researchers at the University of Pittsburgh School of Medicine will further develop a state-of-the-art, microfluidic 3D model system that mimics structure and function of the liver to better predict organ physiology, assess drug toxicity and build disease models.

The funding supports the next phase of the NIH’s Tissue Chip for Drug Screening program, which aims to improve ways of predicting drug safety and effectiveness. Researchers from 11 institutions will collaborate over three years to refine existing 3-D human tissue chips and combine them into an integrated system that can mimic the complex functions of the human body.

“We are very enthusiastic about the potential of these microphysiology systems to serve as powerful platforms for studying human diseases and identifying human toxic liabilities,” said the Pitt project’s principal investigator D. Lansing Taylor, Ph.D., Allegheny Foundation Professor of Computational and Systems Biology, Pitt School of Medicine, and director, University of Pittsburgh Drug Discovery Institute.

“The development of tissue chips is a remarkable marriage of biology and engineering, and has the potential to transform preclinical testing of candidate treatments, providing valuable tools for biomedical research,” said NIH Director Francis S. Collins, M.D., Ph.D.

The Pitt research team, along with additional collaborators, is creating models of the functional unit of the liver, called the acinus, using human liver cells and eventually liver cells derived from precursor cells known as induced pluripotent stem cells, as well as three additional cell types. The liver platform includes microfluidic devices, human cells, engineered matrix materials, fluorescence-based biosensors for real-time physiological read-outs, and biochemical and mass spectrometry measurements to determine acute and chronic toxicity effects. They also will build a “microphysiology database” to manage, analyze and model the data collected from the liver constructs.

With such a platform, biomedical scientists will be able to test treatment efficacy in conditions such as non-alcoholic fatty liver disease, liver cancer and breast cancer that has spread to the liver, as well as liver damage including immune-mediated toxicity and fibrosis. Also, a team of institutions and investigators has been assembled to integrate the liver, kidney and gut models to recapitulate the organ system that is central to drug absorption and metabolism.

The integrated platform will involve the creation of a universal medium, the development of the proper “scaling” of the interacting organ constructs, physiologically relevant flow, incorporation of a micro-formulator to add factors from missing organs and micro-analyzers for monitoring parameters such as pH and oxygen.

Fifteen NIH Institutes and Centers are involved in the coordination of the tissue chip program. Current funding is being provided by the National Center for Advancing Translational Sciences, the National Institute for Biomedical
Imaging and Bioengineering, the National Cancer Institute, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institute of Environmental Health Sciences, NIH Common Fund and NIH Office of Research on Women’s Health.

Collaborators include Martin Yarmush, M.D., Ph.D., of Massachusetts General Hospital; John Wikswo, Ph.D., of Vanderbilt University; Jonathan Himmelfarb, M.D., of the University of Washington; Mark Donowitz, M.D., of Johns Hopkins University; and Mary Estes, Ph.D., of Baylor University.

About the University of Pittsburgh School of Medicine
As one of the nation’s leading academic centers for biomedical research, the University of Pittsburgh School of Medicine integrates advanced technology with basic science across a broad range of disciplines in a continuous quest to harness the power of new knowledge and improve the human condition. Driven mainly by the School of Medicine and its affiliates, Pitt has ranked among the top 10 recipients of funding from the National Institutes of Health since 1998. In rankings recently released by the National Science Foundation, Pitt ranked fifth among all American universities in total federal science and engineering research and development support.

Likewise, the School of Medicine is equally committed to advancing the quality and strength of its medical and graduate education programs, for which it is recognized as an innovative leader, and to training highly skilled, compassionate clinicians and creative scientists well-equipped to engage in world-class research. The School of Medicine is the academic partner of UPMC, which has collaborated with the University to raise the standard of medical excellence in Pittsburgh and to position health care as a driving force behind the region’s economy. For more information about the School of Medicine, see www.medschool.pitt.edu.

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