RICHARD AND LOAN HILL DEPARTMENT OF BIOENGINEERING
COLLEGES OF ENGINEERING AND MEDICINE

ANNUAL REPORT 2015-2016









IN THE ISSUE

Microfabricated Tissue Models Lab

- Salman Khetani, PhD

Our Mission

The liver has many functions, such as breakdown of food, detoxification of drugs, and production of proteins that allow proper clotting after a wound. In liver failure, a person can die within hours unless a liver transplant becomes available; however, there is a severe shortage of donor organs. Additionally, liver injury caused by drugs is a major reason behind drug withdrawal from the market, which affects patients' lives and the economy since it takes $13-15B and 12-15 years to develop a single drug. Testing drugs on animals or using animal livers for transplantation is not ideal because of evolutionary differences across species. Therefore, the Microfabricated Tissue Models (MTM) lab at UIC engineers human liver tissues that have utility in: screening toxic drugs in vitro (in a dish) before they reach humans, mimicking liver diseases for developing novel drugs, and cell-based therapies for patients suffering from liver disease. We utilize tools from engineering and biology, and collaborate with researchers from various disciplines to accomplish our goals. Our team is made up of bioengineers with backgrounds in engineering design, life sciences, biomaterials and microfabrication. We are grateful for funding support from the DOD, FDA, NIH and NSF.

Our Impact

We use a micropatterned co-culture (MPCC) platform comprised of micropatterned islands of human liver cells (hepatocytes, Figure 1) surrounded by fibroblasts. Without fibroblasts, hepatocytes quickly die off, but they can survive for 4 weeks in MPCCs, which enables their use in different applications. The micropatterning of cells is accomplished using tools adapted from the semiconductor industry, allowing for a precision (Figure 2) not possible with conventional methods. MPCCs have shown great promise for studying global liver diseases. In particular, when exposed to excessive glucose as in diabetes, the hepatocytes within MPCCs become resistant to insulin's effects on reducing liver glucose output, a hallmark of diabetes. Novel drugs can be discovered using this feature of MPCCs. Additionally, when cultured in MPCCs, hepatocytes derived from induced pluripotent stem cells (iPSCs) from patients can be infected with hepatitis C virus over several weeks, which allows investigations into why some patients respond to treatment while others do not. We continue to improve the physiological relevance of the MPCC system to make it more sensitive for applications. For instance, we have discovered ways to prolong MPCC longevity to 2+ months, which is useful for understanding how taking drugs over a longer time period can cause liver toxicity. Furthermore, we are designing a microfluidic system to allow perfusion of MPCCs with fresh nutrients and removal of waste products, towards mimicking the heart pumping blood through the liver in the body. Beyond MPCCs, we are exploring growing hepatocytes in vitro, building a 3D human liver tissue for implantation, and devising strategies to make iPSCs into more functional hepatocytes.

Our Students

The MTM lab fosters creativity in research and design using state-of-the-art tools in engineering and biology. We teach collaboration, scientific communication, and a passion for making a difference. Below, our graduate students comment on why they chose the MTM lab and the impact they are making through research.

I joined the MTM lab to help solve real-world problems, and because Dr. Khetani's advising style fits what I needed from a mentor. I have worked on several projects towards the goal of engineering complex liver models for screening drugs and studying infectious diseases. Currently, I am developing a model to enable the study of why and how hepatitis C viral (HCV) infection progresses variably in different patients, which has implications for personalized HCV treatment. Our lab also emphasizes collaboration, which has allowed me to draw on the expertise of both academic and industrial groups. The MTM lab has provided me with a deeper understanding of how to design and conduct experiments that will make an impact, and helped me develop the skills I need to be a successful professional. – Christine Lin

I joined the MTM lab because Dr. Khetani and I have a similar passion for progressing medicine and health. The major advantage of working with Dr. Khetani is that he has given me the creative space to develop a new area of research in our lab around understanding diseases associated with obesity such as diabetes. My work has provided the diabetes field with a sensitive new

tool to help understand the detrimental insulin resistance that occurs in the liver, which brings me great pride as much of my family is impacted by this disease. The MTM lab has not only provided me with excellent training through many aspects of biomedical engineering, but it has also allowed me to find my passion by nurturing my interests. – Matthew Davidson

My research at the MTM lab is focused on developing in vitro platforms for better understanding mechanisms of drug-induced liver toxicity using different cell sources such as primary hepatocytes, induced pluripotent stem cell-derived liver cells, mouse liver cells, and liver end-othelial cells. Currently, I am developing a microfluidic platform to perfuse liver cultures with nutrients and remove waste products. What attracted me to the MTM Lab was the interaction between engineering techniques and biological inquiries for meeting real healthcare needs. The training and mentoring I have received from Dr. Khetani will enable me to become a leader in research and science. Most of the experiences I have in the lab, from planning experiments to advising undergraduates to presenting at conferences, are directly translatable to many future career trajectories. – Brenton Ware

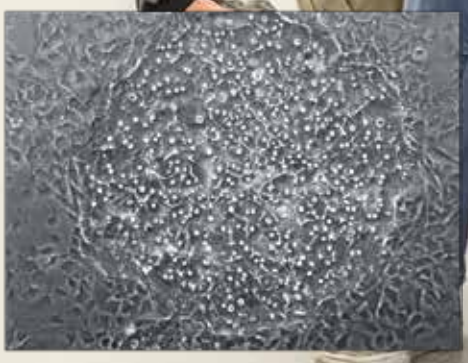

Figure 1: A micropatterned colony of human liver cells surrounded by fibroblasts.

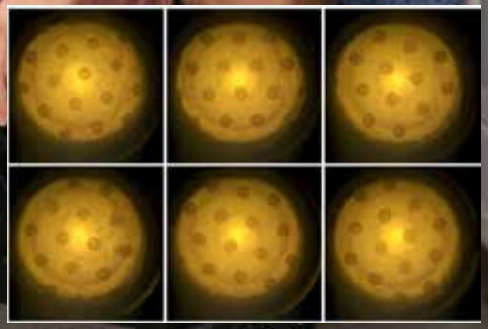

Figure2: Precise micropatterning of cells using tools from semiconductor manufacturing.