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TITLE OF SEMINAR

Microscale Liver Models for Investigating Drug-Induced Liver Injury and Infectious Diseases

ABSTRACT

Drug-induced liver injury (DILI) is the leading cause of acute liver failures while Hepatitis C (HCV) affects approximately 130 million people worldwide. Progress in these fields has been stymied due to the lack of high-fidelity models of human liver tissue that can be: a) used to study the *in vivo*-relevant mechanisms of these diseases, and b) leveraged to build highly parallel and cost-effective platforms for designing and implementing preventative, diagnostic and therapeutic modalities. Primary hepatocytes are critical for progression of DILI and HCV *in vivo*; however, they lose functions *in vitro* which severely restricts their utility in predicting clinical outcomes. The convergence of semiconductor-driven microtechnology tools with the biomedical arena offers the opportunity to fabricate microscale tissue subunits towards improving the phenotypic stability of *in vitro* cultures. As with DNA microarrays, microtechnology also offers the potential to revolutionize biological assays simply through the benefits of miniaturization. We have utilized microtechnology to manipulate, optimize and mechanistically probe the interactions of hepatocytes and stroma towards improving and miniaturizing models of liver physiology and disease. In particular, we developed a liver model with precise microscale cyto-architecture and optimal stromal interactions that displays phenotypic stability for several weeks *in vitro* (micropatterned co-cultures, MPCCs). MPCCs were miniaturized into a high-throughput format and optimized for screening DILI using automated multiplexed imaging. The toxicities and mechanisms of clinical hepato-toxins have been studied in MPCCs under chronic dosing regimens to assess concordance with clinical outcomes. Disease models of MPCCs are under development for molecular investigations and the discovery of therapeutics. For instance, MPCCs have been infected with HCV and can support replication and production of virus for several weeks. In the future, MPCCs may find utility in development of therapeutics, in evaluating the injury potential of chemical pollutants, in mechanistic research, and in personalized medicine for liver disease.

BIOGRAPHY

Salman Khetani received dual BS degrees in Electrical Engineering and Biomedical Engineering from Marquette University, and subsequently obtained MS and PhD degrees in Bioengineering from the University of California at San Diego as a National Science Foundation graduate fellow. Salman was a postdoctoral associate at MIT in the laboratory of Professor Sangeeta Bhatia. Salman and his colleagues have used microtechnology tools to develop highly stable microscale models of human livers for applications in drug development and infectious diseases. His work has been published in journals such as *Hepatology*, *Nature Biotechnology* and recently in the *Proceedings of the National Academy of Sciences*. In 2008, Salman co-founded Hepregen Corporation with Professor Bhatia and Hepregen CEO, Bernadette Fendrock to further develop microscale liver technologies for the broader marketplace. As director of research at Hepregen, Salman led the team conducting research and partnership programs with industrial and government partners. In October of 2011, Salman joined the faculty of Colorado State University as assistant professor of Mechanical and Biomedical Engineering where he is continuing his research on microscale culture models for multiple *in vitro* applications.