



Department of
Biomedical Engineering
UNIVERSITY OF WISCONSIN-MADISON

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Engineering human liver platforms for drug development and disease modeling

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Animal models have been utilized for several decades now for drug development and disease modeling. While these models are an important bridge to human clinical trials, it has become more clear than ever that they do not suffice on their own for preclinical investigations due to significant differences in organ-specific molecular pathways across animals and humans. Therefore, the field of 'tissue engineering' has aimed to create human-relevant tissue culture platforms that can complement and in some cases, replace animal testing altogether. To build such platforms, tissue engineers face common challenges such as sustainable cell sourcing, cell phenotypic stability in vitro, and scaling the constructs for different applications. In this presentation, I will showcase how we have addressed such challenges via state-of-the-art microfabrication tools adapted from the semiconductor industry, biomaterials, stem cell differentiation strategies, and multicellular co-cultures. I will present culture platform development within the context of the liver, which is a difficult organ to engineer in vitro due to its many diverse functions, complex architecture, and multiple types of self- and non-self cellular interactions. Since in vitro culture platforms are only as good as the applications which can be effectively targeted with them, I will next present the utility of our engineered human liver platforms for drug metabolism/toxicity screening and disease modeling (e.g. non-alcoholic fatty liver disease and hepatitis B viral infection); data sets acquired in collaboration with pharmaceutical companies through successful commercial translation will be presented where available. Lastly, I will discuss emerging trends and pending issues that will need to be addressed to fully realize the benefits of the 'organ-on-a-chip' revolution that has garnered substantial attention and funding from the US government. Ultimately, engineered tissues for use in drug development (and regenerative medicine) will most likely be one of the most important contributions of the Biomedical Engineering discipline to 21st-century healthcare.

Salman Khetani received his dual BS degrees in electrical engineering and biomedical engineering from Marquette University, and MS and PhD degrees in bioengineering from UC-San Diego. He was a Jacobs fellow and NSF graduate fellow at UC-San Diego. After postdoctoral research at MIT in the laboratory of Professor Sangeeta Bhatia, Salman co-founded and directed research at Hepregen Corporation to commercialize his bioengineered liver inventions for pharmaceutical drug development. In 2011, Salman returned back to academia, first to Colorado State University and then as associate professor of bioengineering at the University of Illinois at Chicago, where his 'Microfabricated Tissue Models' laboratory (mtm.uic.edu) designs and implements novel engineered tissues for drug screening, investigations of global human diseases, and regenerative medicine. The lab's organs of interests are the liver, heart, and more recently, intestine. Salman's research has been funded by the NIH, NSF, DOD, and the FDA.



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