Synthetic micro/nanoengineering tools for stem cell culture, functional immunophenotyping, and capture of circulating tumor cells

Abstract

Synthetic micro/nanoengineering systems are emerging as powerful high-throughput tools for quantitative analysis of cellular functions at the single-cell level. To approach this opportunity, my research group has recently developed a microscale system comprised of geometrically modulated elastomeric poly-(dimethylsiloxane) (PDMS) micropost arrays that can uncouple changes in matrix rigidity from other properties of the matrix (e.g., adhesive ligand, adhesion area). Using this synthetic cell culture tool, we have implicated matrix rigidity as a critical mechanical signal that can regulate cell adhesion, cytoskeleton contractility, cell spreading, and proliferation. Further, we have found that matrix rigidity can switch differentiation potential of human mesenchymal stem cells (hMSCs) between osteogenic and adipogenic fates. Interestingly, these micromechanical tools help reveal that changes in cytoskeletal contractility can precede differentiation of hMSCs at the single-cell level. More recently, we have extended our research using the PDMS micropost array to investigate mechanoresponsive behaviors of human embryonic stem cells (hESCs), including their self-renewal and differentiation properties. We demonstrate that hESCs are mechanosensitive, and they can increase their cytoskeleton contractility with matrix rigidity. Further, our study suggests that rigid substrates support maintenance of pluripotency of hESCs, and matrix mechanics-mediated cytoskeleton contractility of hESCs is functionally connected to E-cadherin expressions in cell-cell contacts and thus involved in fate decisions of hESCs.

Another area of interest in my group is to develop novel micro/nanoengineering tools for informative functional characterizations of immune cells and circulating tumor cells (CTCs) from blood specimens. As a first step toward these functional goals, we have recently developed a novel PDMS surface micromachining method to generate PDMS microfiltration membranes (PMMs) of large surface areas and high porosity for efficient isolation and enrichment of subpopulations of immune cells from blood specimens. We have developed a microfluidic immunophenotyping assay (MIPA) device incorporating PMMs for isolation and quantitative functional immunophenotyping of subpopulations of immune cells. Our microfluidic immunomonitoring technology allows rapid, accurate, and sensitive cellular functional assays on different types or subpopulations of immune cells, critical for systems-level diagnosis of immune diseases. I will conclude my talk discussing our
recently developed method using nanoroughened glass surfaces for efficient capture of CTCs from blood specimens without using any capture antibody. Our method uniquely utilizes the differential adhesion preference of cancer cells to nanorough surfaces when compared to normal blood cells and thus does not depend on their physical size or surface protein expression, a significant advantage as compared to other existing CTC capture techniques.

Short Biography:

Dr. Jianping Fu has been an assistant professor of Mechanical Engineering and Biomedical Engineering (courtesy appointment) at the University of Michigan (UM), Ann Arbor since 2009. Dr. Fu is also a core faculty member of the UM Center for Organogenesis and Comprehensive Cancer Center. Dr. Fu received a B. E. degree (2000) from the University of Science and Technology of China (USTC) and a M. S. degree (2002) from the University of California at Los Angeles (UCLA), both in Mechanical Engineering. He earned his Ph. D. degree in Mechanical Engineering from the Massachusetts Institute of Technology (MIT) in 2007, with a major of biological engineering and a minor of micro/nanomechanics and engineering. Dr. Fu was an American Heart Association Postdoctoral Fellow in the Department of Bioengineering at the University of Pennsylvania from 2007 to 2009. Dr. Fu’s current research focuses on Bio-Microelectromechanical and Nano-electromechanical Systems (BioMEMS/NEMS), Lab-on-Chip (LOC), mechanobiology, stem cell biology, and applying microfabrication technology to illuminate biological systems at both the molecular and cellular levels.

Dr. Fu is the recipient of the American Heart Association Scientist Development Grant (2012) and the National Science Foundation CAREER Award (2012). Dr. Fu’s research group is currently supported by the National Science Foundation, the National Institute of Health, the American Heart Association, and some other foundations and agencies.

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