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Editorial

# Microfluidic Cell-Based Assays in Stem Cell and Other Rare Cell Type Research

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## What is microfluidics and why is it good for stem cell research?

Microfluidics is a technology defined by the engineered precise manipulation of minute amount of liquids through channels with dimensions in the micron scale. Much of microfluidic devices used for biomedical purposes are produced in the form of so called "lab-on-a-chip" format, where multiple steps of conventional biochemical analyses such as staining, washing, and signal collection are miniaturized and integrated into chips fabricated from polymer or glass [1,2]. Cell-based microfluidic lab-on-a-chip technology provides some obvious advantages: 1) drastically reduced sample and reagent requirement, and 2) separation and detection with improved sensitivity due to fluid properties at the microscale, i.e. laminar flow. Based on these two advantages, the obvious place where microfluidic cell assays will provide the most benefit is wherescientists must gather much information from precious little sample. Stem cells and other precious cell types such as circulating tumor cells (CTCs), and rare immune subsets are the perfect match for microfluidic multiplex assays. The recent demonstration that multiple cellular changes such as surface receptor activation, protein translocation, long and short RNA, and DNA changes can all be extracted from intact single cells [3-6] paves the way to systems level understanding of cellular states during development or disease. With the ability to preserve cell integrity in a microfluidic device during multiplexed analysis, one also preserves the single cell resolution, where information regarding the cell-to-cell heterogeneity during differentiation or response to stimuli is vitally important [7].

Aside from basic research, microfluidic cell analysis systems provide potential use in Point-of-Care (POC) and personalized cell based biomarker research, where precious primary cells are rich for scientific and clinical exploration. To date, there is no commercial cell based POC device that enables the rapid profiling of signaling pathways in live cells taken from a patient. A microfluidic device, along with a set of optimized immunoassays, can be used to profile known pathways that underlie medical conditions, for example the TLR9 pathway defects in the B cells of common variable immune deficiency (CVID) patients, andrapidly provide actionable information that lead to early intervention and improved quality of life for patients. The rapid profiling of cellular events can be performed on a drop of blood generated froma minimally invasivefinger prick, and the automated analysis can performed at the doctor's office, eliminating the need for lengthy pathology laboratory testing. Cell-based POC devices can potentially create new diagnostic or theranostic tests, meanwhile minimizing the cost of these tests and improve the efficiency of diagnosis and patient monitoring.

## Hurdles to technology adoption and the remedy

The biggest hurdle to the adoption of microfluidics instem cell/rare cell research is not technical, but a cultural one. Most microfluidic engineers are chemical or mechanical engineers by training, and the focus in the Engineering disciplines is the design and fabrication of new devices, and not the adaptation and application of existing devices to real-world biological problems. On the other hand, Biologists value data collection above method development, and novel devices and methods without accompanying groundbreaking biological finding do not generate big waves in the biological community. This cultural gap makes adoption of microfluidics technology in Biology as wholea challenge, as technology advancement need to occur incrementally before groundbreaking discoveries can be made. The remedy to this cultural obstacle is to create deep, meaningful collaboration between Biologists/Clinicians and Engineers, and perhaps even more importantly, cross-training both sides with fundamental understanding of the other. For when Biologists understand fundamental engineering concepts, they can best utilize the engineering expertise in their collaborators tomove the research into unprecedented territory. Conversely, having input from Biologists while the microfluidic instruments are being designed and fabricated is crucial in ensuring a smooth technology transition from the engineers table to the biologist's bench/clinic. Certainly, it will be the effective navigation at the interface of Biology and Engineering which will prove the strongest driving force to bring forward breakthroughs in stem cell/rare cell biology.

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