Shannon Stott, PhD

The Stott laboratory is comprised of bioengineers and chemists focused on translating technological advances to relevant applications in clinical medicine. Specifically, we are interested in using microfluidics, biomaterials and imaging technologies to create tools that increase our understanding of cancer biology and of the metastatic process. The Stott laboratory has co-developed innovative microfluidic devices that can isolate extraordinarily rare circulating tumor cells (CTCs) from the blood of cancer patients. New microfluidic technologies are being developed for the isolation of other blood-based biomarkers such as exosomes and microvesicles as well as DNA. Ultimately, we hope that by working in close partnership with the molecular and cell biologists at the Mass General Cancer Center, we can create new tools that directly impact patient care.

Stott Laboratory*

Berent Aldikacti, MD
Cindy Angpraseuth
Sam Au, PhD
Lauren Bookstaver
João Paulo Oliveira-Costa, MD, PhD
Eduardo Reátegui, PhD
Rebecca Sandlin, PhD
Cleo Stannard
Shannon Stott, PhD
Shannon Tessier, PhD
Keith Wong, PhD
Mahnaz Zeinali

*co-directed with Mehmet Toner, PhD

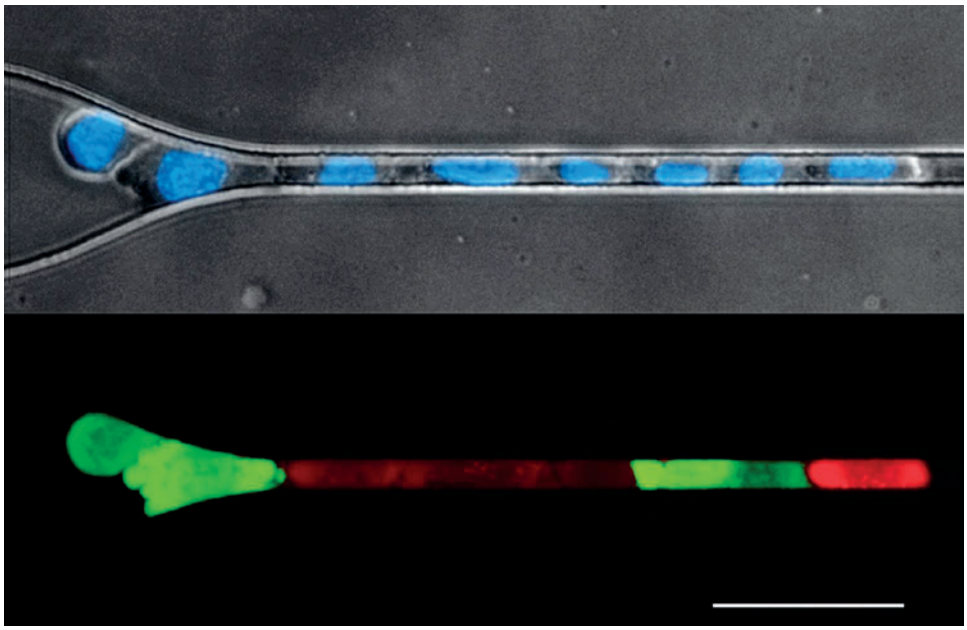
Rapid technological advances in microfluidics, imaging and digital gene-expression profiling are converging to present new capabilities for blood, tissue and single-cell analysis. Our laboratory is interested in taking these advances and creating new technologies to help build understanding of the metastatic process. Our research focus is on 1) the development and application of microfluidic devices and biomaterials for the isolation and characterization of extracellular vesicles, 2) the enrichment and analysis of CTCs using microfluidics, and 3) novel imaging strategies to characterize cancer cells, CTC clusters and extracellular vesicles.

Extracellular Vesicle Isolation and Characterization

Extracellular vesicles (EVs), such as exosomes, microvesicles, and oncosomes, are small particles that bud off of cancer cells, with some cancer cells releasing up to thousands of EVs per day. Researchers have hypothesized that these EVs shed from tumors transport RNA, DNA and proteins that promote tumor growth, and studies have shown that EVs are present in the blood of most cancer patients. Ongoing work in my lab incorporates microfluidics and novel biomaterials to enrich tumor-specific EVs from the plasma of glioblastoma and pancreatic cancer patients, using as little as 1mL of plasma. Once isolated, we are exploring their protein and nucleic acid content to probe their potential as a less invasive biomarker.

Microfluidics for Circulating Tumor Cell Analysis

One of the proposed mechanisms of cancer metastasis is the dissemination of tumor cells from the primary organ into the blood stream. A cellular link between the primary malignant tumor and the peripheral metastases has been established in the form of CTCs in peripheral blood. While extremely rare , these cells provide a potentially accessible source for early detection, characterization and monitoring of cancers that would otherwise require invasive serial biopsies. Working in collaboration with Drs. Mehmet Toner, Shyamala Maheswaran and Daniel Haber, we have designed a high throughput



Micrograph of a microfluidic capillary device, designed to mimic the small constrictions that CTCs must travel through in the body. Shown is cluster of cancer cells as they squeeze and orient themselves so that they can successful passage the capillary. Scale bar is 20um. Image courtesy of Sam Au, Ph.D.

microfluidic device, the CTC-Chip, which allows the isolation and characterization of CTCs from the peripheral blood of cancer patients. Using blood from patients with metastatic and localized cancer, we have demonstrated the ability to isolate, enumerate and molecularly characterize putative CTCs with high sensitivity and specificity. Ongoing projects include translating the technology for early cancer detection, exploring the biophysics of the CTC clusters, and the design of biomaterials for the gentle release of the rare cells from the device surface. We are also developing new strategies for the long term preservation of whole blood such that samples can be shipped around the world for CTC analysis.

High-content and high-throughput imaging of cancer cells

Cancer cells can be highly heterogeneous, with rare metastasis precursors capable of giving rise to a metastatic lesion mixed in with other tumor cells undergoing apoptosis. Thus, due to this heterogeneity, quantitative, robust analysis for individual cells may be critical for determining a particular cancer cells' clinical relevance in different disease contexts. Due to limitations in the number of distinct spectra that can be used in wide-field fluorescence imaging, high throughput characterization of cells and tissue is traditionally done with three to four colors. Our lab is exploring alternative imaging modalities, such as multi-spectral imaging (MSI), to enable quantitative analysis of multiple (8+) markers on a single cell. We are interested in using this technology to interrogate signaling activity in CTCs isolated from the blood of cancer patients. These data will be used to gain an increased understanding in the relationship between pharmacologic measurements and clinical outcomes, ultimately leading to the optimization of patient therapy.

Selected Publications:

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*co-authors, ^Joint corresponding