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Stott Laboratory

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The Stott laboratory is comprised of bioengineers, biologists and chemists focused on translating technological advances to relevant applications in clinical medicine. Specifically, we are interested in using microfluidics, imaging, and biopreservation 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) and extracellular vesicles (EVs) from the blood of cancer patients. New microfluidic tools are being developed to both manipulate and interrogate these cells and vesicles at a single particle level. We also look at tumor specimens using multispectral imaging, hoping that the exploration of the spatial relationships between immune cells and tumor tissue will help us better predict treatment response. Ultimately, we hope that by working in close partnership with the clinicians and cell biologists at the Mass General Cancer Center, we can create new tools that directly impact patient care.

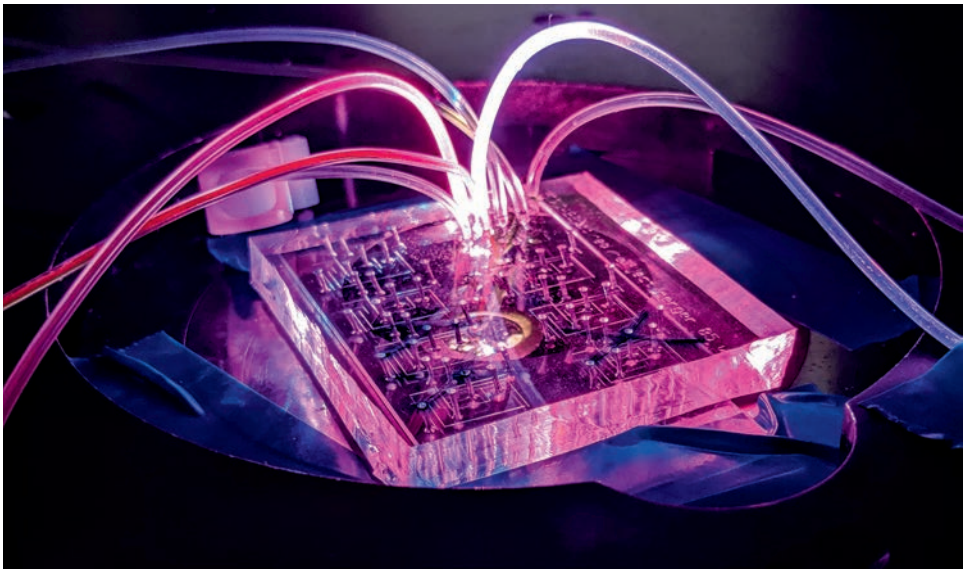
Rapid technological advances in microfluidics, imaging and digital gene-expression profiling are converging to present new capabilities for blood, tissue and single-cell analysis. Our laboratory is interested in taking these advances and creating new technologies to help build understanding of the metastatic 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 at a single cell level, and 3) novel imaging strategies to characterize tumor tissue, cancer cells, 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 cell-specific EVs from 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. Droplet-based microfluidics are being developed to probe the EVs at a single vesicle level.

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.



Droplet based microfluidics for the selective merging of encapsulated cells. Different cell populations can be sorted at a single cell level and then selectively placed into droplets, creating custom culture 'microdrops' for long term culture and monitoring.

Image courtesy of Rohan Thakur

Mehmet Toner, Shyamala Maheswaran and Daniel Haber, we have designed a high throughput 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 Tumor Specimens

Tumors can be highly heterogeneous, and their surrounding stroma even more so. Traditionally, the tumor and surrounding cells are dissociated from the tissue matrix for high throughput analysis of each cell. While this allows for important information to be gained, the spatial architecture of the tissue and corresponding interplay between tumor and immune cells can be lost. The Stott lab is developing quantitative, robust analysis for individual cells within the tumor and neighboring tissue using multispectral imaging. We are using this technology alongside downstream imaging processing algorithms to interrogate signaling activity in cancer cells, immune cell infiltration into to the tumor and pEMT in cancer cells. 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:

Wong KHK, Edd JF, Tessier SN, Moyo WD, Mutlu BR, Bookstaver LD, Miller KL, Herrara S, **Stott SL**†, Toner M†, "Antithrombotic strategies for microfluidic blood processing", *Lab Chip*, 2018; 18(5).

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Park MH*, Reátegui E*, Li W, Jensen AE, Toner M, **Stott SL**†, Hammond PT†. Enhanced Isolation and Release of Circulating Tumor Cells Using Nanoparticle Binding in a Microfluidic Chip Via Place-Exchangeable Ligands. *JACS*. 2017; 139(7).

Au SH, Storey BD, Moore JC, Tang Q, Chen Y-L, Sarioglu AF, Javaid S, Langenau DM, Haber DA, Maheswaran S, **Stott SL**†, Toner M†. Clusters of circulating tumor cells traverse capillary-sized vessels. *PNAS*. 2016; 113 (18).

Reátegui E. Aceto N. Lim EJ, Sullivan JP, Jensen AE, Zeinali M, Martel JM, Aranyosi AJ, Li W, Castleberry S, Bardia A, Sequist L.V, Haber D A, Maheswaran S, Hammond PT, Toner M, **Stott SL**. Nanostructured coating for immunoaffinity capture and selective release of single viable circulating tumor cells". *Advanced Materials*. 2015; 27 (9).

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