Metastasis, the leading cause of cancer related mortality, is a highly orchestrated process involving angiogenesis, invasion, intravasation and survival in the vasculature and extravasation and growth at distal sites. The Maheswaran laboratory is focused on understanding the mechanism of this process using in vitro and in vivo model systems and circulating tumor cells, which are putative metastatic precursors. Epithelial to mesenchymal transition (EMT), an embryonic process reinstated in tumor cells, is a critical modulator of cancer metastasis. EMT is induced by several transcription factors and signaling pathways, and it enhances tumor cell motility and resistance to apoptosis. Using breast cells which are induced to undergo EMT, we intend to gain greater insight into the mechanisms involved in EMT induced tumor progression and identify signaling nodes that render tumor cells susceptible to targeted therapeutic intervention.
HOXB9 overexpressing breast tumors produce growth factors to promote tumor progression.

Influence tumor progression, 2) to identify the pathways that can be targeted either alone or in combination to suppress tumor progression and metastasis in this setting, and 3) to determine whether gain of HOXB9 and/or loss of BTG2 can be used as markers to identify patients who will be responsive/resistant to breast cancer therapies. By modulating HOXB9 and BTG2 expression in breast cancer cells, we intend to identify the molecular mechanisms that will render this subset of aggressive breast cancers susceptible to therapies that target these pathways.

Molecular characterization of circulating tumor cells

In collaboration with Drs. Daniel Haber and Mehmet Toner, I am also interested in the cellular and molecular characterization of circulating tumor cells (CTCs). This interest lies in well with the overall goal of the lab, which is to study cancer metastasis. In cancer patients, a rare population of tumor-derived cells is found in the circulation and is likely the source for distant metastatic disease. Detecting CTCs has far-reaching implications for both clinical care and cancer biology. CTCs are rare, comprising 1 in $10^5$ cells in the blood of patients with metastatic breast cancer. This isolation presents a tremendous technical challenge for existing cell separation technologies. The microfluidic technology developed in Dr. Mehmet Toner’s laboratory enables gentle, efficient and specific isolation of live CTCs in a single step. CTCs isolated from breast, prostate, pancreatic and lung cancer patients using this cutting edge technology will be characterized and standardized to provide a noninvasive tool for early disease detection and for monitoring response/resistance to therapy; viable cells will be cultured to gain insight into the growth, drug resistance and metastatic properties of these epithelial cancers.

Selected Publications:


*Co-corresponding authors