Rewiring Signaling Pathways in Cancer Cells

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Cancer is the second leading cause of death but it has been a difficult disease to effectively understand or treat. The reason relates to the complexity and heterogeneity of the disease. The cause of lethality in most solid tumors such as breast cancer is the metastatic dissemination of tumor cells throughout the body. Metastasis is characterized by many distinct properties that are driven by changing stresses in the tumor microenvironment. Underlying all of these events are subcellular signaling pathways within tumor and environmental cells that are ultimately responsible for driving cells to a tumorigenic state.

The current focus of my laboratory is to understand fundamental signaling mechanisms leading to the generation of tumor cells and their progression to metastatic disease, particularly in triple-negative breast cancer that lacks targeted therapies. We use systems level approaches including activity-based proteomics, RNAseq, ChIPseq, and mass spectrometry as well as computational, molecular, biophysical, cellular and mouse model-based methodologies to identify and characterize key regulators of tumor growth and metastasis. As an additional tool, we have utilized a specific physiological suppressor of metastasis, Raf Kinase Inhibitory Protein (RKIP or PEBP1), and a downstream target of RKIP in cells, BACH1, to identify both molecular and cellular mediators of metastasis.

Our recent studies have shown that regulators of metastasis control multiple processes within the tumor cell microenvironment including metabolism. Correlating omic-generated data from these studies with clinical data from cancer patients led to the identification of novel signaling modules that we used to build gene signatures that predict the metastatic potential of a tumor. More recently, our studies have led us to potential therapeutic treatments based on the concept of targeting key regulators of tumorigenesis, mimicking the action of metastasis suppressors such as RKIP or reprogramming signaling networks in cells to sensitize tumors to therapeutic agents.