

PUBLIC ABSTRACT

Despite numerous advances in chemotherapies and targeted medications over the past few decades, most metastatic breast cancers remain incurable. Dr. Andrei Goga is a physician-scientist at UCSF, who cares for patients with breast cancer and is a co-investigator in multiple clinical trials for metastatic breast cancer. Dr. Goga's basic laboratory efforts seek to identify new therapies for the most aggressive and difficult to treat metastatic breast cancers. As breast cancer cells spread from local growth in the breast to distant sites of metastasis they change and evolve, and the types of genes and signaling pathways that are activated become altered. Thus, metastatic breast cancers acquire new properties when compared to the primary breast cancer from which they originated perhaps years previously. Thus, in order to develop therapies that selectively kill metastatic breast cancers it is important to identify the pathways and genes that are uniquely activated in the metastatic breast tumors compared to the primary cancer. Dr. Goga and colleagues recently discovered that the cancer gene MYC is one of the most highly up-regulated genes when comparing patient-derived tumor metastasis compared to the primary cancer (Lawson, et al., Nature, 2015). Approaches to selectively inhibit cell proliferation selectively kill MYC high cells and resulted in dramatic reduction in metastatic tumor formation and growth. This groundbreaking work revealed that targeting pathways unique to tumor metastasis can lead to important new therapeutics. These studies have led to new clinical studies that are ongoing to determine if improved treatments directed specifically against MYC will lead to improved patient response and benefit. In this proposal, Dr. Goga and colleagues will use two innovative approaches: 1) We will identify new signaling pathways that are unique to metastatic cancer cells. Defining which signaling processes are especially important to metastatic cancers will allow us to identify new and more efficacious treatments for metastatic cancer. 2) We have discovered novel small molecule inhibitors that are predicted to reverse the activity of the MYC cancer gene. We seek to test these new drugs to determine if they can reverse the ability of metastatic tumors with high MYC to grow. If successful, these studies will lead to the development of novel therapies for metastatic breast cancer. Metavivor support will provide the stepping stone to allow us to generate sufficient data to empower transition to clinical trials and the ability to garner additional support from NIH or other sources of research support.