

## "Functional Analysis of Cell-Specific Pharmacology on Tumor Microenvironments"

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**Abstract:** Despite the vast number of patients treated with chemotherapeutics, very little is known about the dynamic response of cancer cells to chemotherapeutic drugs in intact tumors. Understanding the complex interplay between cancer cells and the stromal cells of the microenvironment is a major challenge for the development of effective and safe chemotherapeutic treatments. To address this fundamental issue in cancer therapy, we will bring together the expertise developed in each of our laboratories and evaluate dynamic and cell-specific responses to chemotherapeutic drugs. We will perform dynamic imaging of live mice to study how different tumor microenvironments influence drug effects on cancer and stromal cells using a mouse model of mammary carcinoma (Aim 1). To dissect the effects of drugs on cancer cells versus stromal cells, a genetically-encoded method for cell-specific pharmacology and imaging will be developed, and we will evaluate the cellular responses when chemotherapeutics are targeted either to cancer cells or to the stromal cells of the microenvironment (Aim 2). The combination of molecular imaging and cell-specific pharmacology using mouse tumor models *in vivo* should provide new insight into the dynamic interactions between the cancer and stromal cells and reveal new strategies and protocols for cancer treatment. The development of new technologies for cell-specific imaging and pharmacology should also afford new opportunities to dissect complex multicellular interactions *in vivo*.