



## Scientific Abstract

### SU2C–Breast Cancer Research Foundation Breast Cancer Convergence Research Team: “Ecology of the Tumor Microenvironment in Breast Cancer”



*[This abstract was provided by the scientists when their application was accepted.]*

It is becoming recognized that tumors consist not only of cancer cells, but also stromal and immune cells that constitute the tumor microenvironment (TME). Cancer cells can take on dramatically different properties based on the microenvironment. The clinical impact of the TME is only becoming appreciated in recent years. In many different cancer types, including breast cancer (BC), tumors with higher stromal fractions portend worse clinical outcomes. In contrast, tumors infiltrated by CD8 T cells have better clinical outcomes. Hence, tumors behave differently based on the collective behavior of the microenvironment.

Recent attempts to eliminate stromal cells yielded unintended results sometimes with worse outcomes, highlighting the need for more refined approaches based on mechanistic insights. In this project, we hypothesize that the TME is an important determinant for the efficacy of cancer immunotherapy. The TME is an ecosystem of multiple cell populations, and extracellular matrix (ECM) that they produce, that interact in a complex fashion to yield emergent dynamics. Previous approaches have focused on individual components of the tumor microenvironment (TME) rather than trying to capture the interactions of all the key subpopulations. As such, it is important to apply systems and ecological approaches to study the TME. This will lead to treatment approaches that specifically modulate the TME without damaging normal stroma that is present throughout the body.

In this project, the multidisciplinary team utilizes high dimensional histology, image analysis, culturing cells from primary human breast tumors, next generation and single cell genomics, bioinformatics, ecology modeling, and nanotechnology to study the ecology of the TME in breast cancer, and to develop therapeutic and imaging applications. The City of Hope team has secured human subjects approval to collect patient samples for this study, and have performed extensive tissue and genomics analyses. The Cold Spring Harbor Laboratory team is doing sequencing and bioinformatic analyses on the data. The Rice and UC Irvine teams are doing spatial image analysis and computational modeling. The MIT team is testing several treatment combinations in animal studies.

