



Team Progress Updates

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



Tumors consist not only of cancer cells but also stromal (connective tissue) and immune cells that constitute the tumor microenvironment. Researchers have only recently begun to appreciate the clinical impact of this microenvironment.

In many cancer types, including breast cancer, tumors with a higher proportion of connective tissue are associated with worse clinical outcomes. In contrast, tumors infiltrated by a type of white blood cell that kills cancer (called CD8 T cells) have better clinical outcomes. Therefore, tumors behave differently based on the collective behavior of the microenvironment.

This team hypothesizes that the microenvironment is an important determinant of the effectiveness of cancer immunotherapy treatments. The study brings together expertise in histology, image analysis, cell culturing, bioinformatics, ecology modeling, and nanotechnology to create a three-dimensional model of the tumor microenvironment that incorporates different cell types and genomic information. This will provide insights into the development of new therapeutic and imaging applications.

Researchers are comparing the breast cancer tumor microenvironment with that of normal breast tissue. The goal is to capture the basic way different cell types affect each other and use that knowledge to develop new models with which to test potential therapies.

The team reported the following progress:

April 2019

- The team has shown, using 3-D imaging techniques, that tumors are made up of small, repeated structures. Team members have observed that T cells infiltrating cancer islands showed upregulation of CD103. This could classify them as resident memory T cells, which retain poly-functionality within the tumors and co-localize with cancer cells.
- 3-D analysis of tumor samples has revealed that the spatial distribution of T and B cells within the tumor matters clinically and has prognostic potential. This allows for a separation of patients with positive and negative outcomes based on the distribution of T cells within the tumor biopsy, and B cells show similar spatial dependence.

January 2018

- Progress regarding the ecology of the tumor microenvironment in breast cancer
- Identified genes that are downregulated in cancer associated fibroblasts from primary tumors compared to healthy breast tissue.





Team Progress Updates

- Future studies will be aimed at identifying negative regulators of genes that could serve as targets, or strategies to upregulate these genes or pathways.
- Developed computational methods to process data which allows analysis of the infiltration pattern of many different types of cells.
- Applied concept of entropy to analyze the spatial patterns of cells within the tumor microenvironment.

June 2017

- Progress regarding the structure of the breast cancer tumor microenvironment and the link to clinical outcomes to the distribution of T cells within the tumor and the tumor microenvironment.
- Using RNASeq data to show how patients with higher immune scores do better than patients with lower immune scores.

October 2016

- The team has assembled a set of 30 breast cancer specimens and a number of normal breast specimens. Specific cell populations were identified for epithelial cancer cells and for infiltrating immune cells.
- Multispectral imaging was employed to simultaneously analyze multiple independent markers in a single section.
- Created a model of how cancer associated fibroblasts may form structures or special patterns in the tumor microenvironment based on directed cell motion. Compared with static images of tumor microenvironment.
- Work started on set of triple-negative breast cancer specimens to develop methods to identify prognosis/predict outcome based on multiple features.