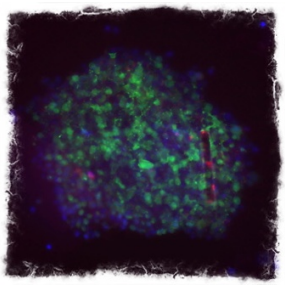

Breast Cancer Biology

The Burow & Collins-Burow Labs: Triple Negative Breast Cancer from Biology to Bedside

Triple Negative Breast Cancer is one of the most rare and aggressive forms of cancer, representing 10-15% of all breast cancer cases. Unlike Estrogen Receptor positive or HER2 overexpressing Breast Cancers, they do not present any obviously targetable, cancer cell-specific treatment options. In **Bridgette Collins-Burow's** oncology practice, they represent approximately 40% of presenting cases. Of these, the vast majority are African-American women that present with abnormally large tumors of 5-7cm (anything over 2 cm is clinically considered 'large'). **Matt Burow** investigates the molecular underpinnings of these aggressive patient cancers. The ready access to this rare, aggressive, and difficult to treat cancer and attendant patient population make these labs unique in the breast cancer field. They are able to study the biology and response to treatment of this rare cancer type in this unique patient population in the clinic and by using a mouse-based Patient-Derived Xenograph (PDX) model.

PDX Modeling: Bridging Tissue Culture & Patient Care

The joint-lab developed PDX model fills the gap between the behavior of cells in culture and an actual tumor behavior in human patients. While cancer cells in culture are valuable for mechanistic studies of key pathways, they fail to accurately represent the complex architecture and heterogeneity of a solid tumor in a patient. For example, cells in culture are 100% cancer cells, while in solid tumors cancer cells are only about 5-10% of the total. The rest are a mix of vasculature, immune cells, and fibroblasts. Additionally, cell lines adapt to being cultured over time, such that their genetics and behavior may no longer accurately reflect what happens in patients. The PDX model involves taking pieces of the patient tumor and growing them in a mouse, preserving the gross architecture and heterogeneity of the tumor in the patient. The labs take triple negative breast cancer samples from patients at Tulane to establish PDX models with them. Eventually, the labs plan to utilize humanized mice for this model, enabling them to study the host immune system interactions with the tumor.

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PDX Modeling: Bridging Tissue Culture & Patient Care

Further, they are establishing unique PDX models that represent patient samples pre- and post-neoadjuvant treatment, allowing the study of patient tumor biology and drug response pre- and post-initial chemotherapy in parallel.

The Tumor Matrix: Breaking Down Breast Cancer

One of the more understudied aspects of solid tumor biology is the role of the tumor extracellular matrix. This matrix provides a support structure and scaffold for the tumor, as well as important signals for cell growth, differentiation, and development. In collaboration with engineering labs at Tulane and LSU, the labs have created a decellularized tumor matrix. When cancer cells are reintroduced to this matrix, they develop a more cancer stem cell-like phenotype. This matrix could be used as a more biologically relevant alternative to Matrigel, enabling study of tumor architecture and biology, as well as aiding in the establishment of additional PDX lines for other difficult to treat cancer types.

Triple Negative Breast Cancer Pathways

In addition to developing and using the PDX model system, both labs study pathways within triple negative breast cancer that contribute to its aggressiveness. The Collins-Burow Lab has identified a novel metastasis-suppressing kinase, for which she is actively pursuing ways to implement an allosteric activator. The Burow Lab has multiple projects currently examining different inhibitors for the MEK5 kinase and various HDACs. Additionally, they are collaborating on the development of an explant assay to examine the transcriptional changes in small pieces of tumor exposed to various drugs in culture. This method could allow for eventual drug screening and dose optimization pre-animal studies, as well as the identification of novel, potentially targetable pathways. All of these projects are in service to the overall goal of the Burow and Collins-Burow labs of studying triple negative breast cancer from its mechanistic origins and progression to its treatment in patients.

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