**BIOINFORMATICS 2018 Spring SEMINAR SERIES**
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http://bioinformatics.udel.edu/Seminars/Current

**MONDAY, February 26, 2018**
**3:30pm**
**DBI Room 102**

# Identifying Key Gene Sets in Metastatic Dormancy; Ontology enrichment in publically available Human Breast Cancer data

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**ABSTRACT:**
For approximately 20% of breast cancer patients, many years pass between initial remission and the emergence of distal metastases. These late recurrences are hypothesized to arise from malignant cells shed from the primary tumor that remain dormant in secondary tissues until resuming metastatic proliferation, where remodeling of the extracellular matrix at the secondary site is thought to play a role in the reactivation of these dormant disseminated tumor cells. A central question is the extent to which the dormancy interval is determined by the initial state of cells in the primary tumor, and whether proliferation resumes as the result of changes in the distal microenvironment. Differential gene expression in primary tumors may provide insight into the processes involved in the maintenance of metastatic dormancy.

Four clinical studies providing microarray profiles were selected based on specific endpoints, and follow-up duration. For each study, two patient groups were assembled based on whether or not they experienced a metastatic event between 5 and 14 years after their initial diagnosis. An automated workflow was implemented to process microarray data, retrieve enriched ontology terms, and evaluate reproducibility of term and pathway enrichment across multiple datasets. Noteworthy overlap between studies was observed at the level of ontological enrichment. Several terms related to microenvironment interaction were detected in enrichments for three or more studies. This is indicated by the detection of terms such as "cell-adhesion", "regulation of cell migration" and "cell proliferation" which represent processes that are involved in the escape from dormancy. On the other hand, there were some concerns with the robustness of differential expression. Some of the challenges, limitations, and opportunities that are present when working with public data resources will be highlighted in this talk, along with relevant findings.

# Probing breast cancer cell activation in response to microenvironment cues in well-defined synthetic extracellular matrices for insights into late recurrence

## April M. Kloxin

### Assistant Professor, Departments of Chemical & Biomolecular Engineering , University of Delaware

## ABSTRACT:

Interactions between breast cancer cells and their microenvironments are essential in tumor growth, metastasis, and recurrence. The tumor stroma undergoes constant structural changes, including degradation, redeposition, and crosslinking of collagens with gradients in matrix stiffness and composition that drive invasion and metastasis. At metastatic sites, similar remodeling events that occur with injury and aging are hypothesized to promote reactivation of dormant tumor cells in late recurrence. Approaches are needed for testing hypotheses about pivotal cell-matrix interactions in the progression of breast cancer for identifying key regulators and improving treatment strategies. In this work, we have designed well-defined materials to mimic key aspects of tumor microenvironments toward studying such complex phenomena in vitro. We have cultured breast cancer cells of different metastatic potential (estrogen receptor positive [ER+, T47Ds] and triple negative [ER-, MDA-MB-231s]) within different matrix densities and compositions and assessed their viability and activation. Toward linking the observations made in this model system to the human disease, we collaboratively are deploying bioinformatics tools to further interrogate cells in these systems and compare observations to those in animal models and clinical data. This talk will highlight the combined tool sets of the controlled 3D culture system and bioinformatics analyses for both fundamental and applied research, with a particular focus on the late recurrence of cancer.