ABSTRACT: Many late breast cancer recurrences are hypothesized to arise from tumor cells within distant metastatic sites that have reactivated in response to extracellular matrix (ECM) remodeling after long periods of dormancy. To study cell-ECM interactions that may play a role in breast cancer recurrence, we are designing a well-defined three-dimensional culture platform to capture critical mechanical and biochemical properties of metastatic tissue sites including the bone marrow, liver, and lungs. Poly(ethylene glycol) (PEG)-based hydrogels have been polymerized via radically-initiated thiol_ene chemistry using PEG-4-thiol and peptides modified with alloxycarbonyl-protected lysine ('ene'). Hydrogels polymerize rapidly after application of cytocompatible doses of light to form matrices with soft moduli (~1 minute, E~0.5-5 kPa). Further, peptides have been added to these PEG matrices to direct cell behavior and interactions within hydrogels. Breast cancer cells encapsulated within hydrogels remain viable after encapsulation and during culture, allowing analysis of cell response to different cues within the synthetic microenvironment. Proteomics techniques are being used to determine how breast cancer and metastatic niche cells (e.g., hMSCs, fibroblasts) respond to and remodel their microenvironment through the deposition of ECM proteins. Additionally, cluster morphology and markers associated with epithelial-mesenchymal transition are being studied to determine how the metastatic microenvironment plays a role in late cancer recurrence. We envision application of these techniques to reveal critical ECM cues driving dormant tumor cell reactivation, allowing improved treatments to prevent cancer recurrence.
BIOGRAPHY: Lisa Sawicki is a Ph.D. candidate in Chemical and Biomolecular Engineering at the University of Delaware. She graduated from the University of Florida in 2011 with a degree in Chemical Engineering. Currently a member of the April Kloxin Lab and an NSF IGERT Fellow, Sawicki’s research is focused on developing biomimetic matrices and tools to study the recurrence of breast cancer. Additionally, Sawicki is a leader in science outreach, including founding a radio talk show “Rise and Science” on WVUD 91.3FM.