3:00-4:00pm, Friday, April 1st, 2022

1221 Patrick F Taylor Hall

Role of collagen fiber morphology and matrix stiffness on ovarian cancer cell biology using multiphoton excited fabricated image-based in vitro models

by Paul Campagnola*

Remodeling of the extracellular matrix (ECM) is an important part in the development and progression of many epithelial cancers. However, the biological significance of collagen alterations in ovarian cancer has not been well established. Here we investigated the role of collagen fiber morphology on cancer cell migration using tissue engineered scaffolds based on high-resolution Second-Harmonic Generation (SHG) images of ovarian tumors. The collagen-based scaffolds are fabricated on a purpose- built microscope via multiphoton excited (MPE) polymerization, which is a freeform 3D method affording submicron resolution feature sizes. This capability allows the replication of the collagen fiber architecture with high fidelity, where we constructed models representing normal stroma, high-risk tissue, benign tumors, and high-grade tumors as shown in the figure. These were seeded with normal and ovarian cancer cell lines to investigate the separate roles of the cell type and matrix morphology on migration dynamics. The primary finding is that key cell–matrix interactions such as motility, cell spreading, f-actin alignment, focal adhesion, and cadherin expression are mainly determined by the collagen fiber morphology to a larger extent than the initial cell type. We also created models with physiological stiffness (~2-10 kPa) and found enhanced motility and cytoskeletal alignment of stiffer substrates, consistent with a durotactic mechanism. These models cannot be synthesized by other conventional fabrication methods, and we suggest this approach will enable a variety of studies in cancer biology. We also present a new approach to optimize scaffold design using the Generative Adversarial Network StyleGAN.

Paul J. Campagnola is the Peter Tong Department Chair of the Biomedical Engineering Department at the University of Wisconsin-Madison and is a Kellett Faculty Fellow. He obtained his PhD in Chemistry from Yale University in 1992 after which he was a postdoctoral associate at the University of Colorado from 1992-1995. He was on the faculty in the Department of Cell Biology, the University of Connecticut Health Center from 1995-2010 and joined the faculty at UW-Madison in 2010. His research is focused on studying structural and functional aspects of the extracellular matrix (ECM), where his lab has developed optical microscopy instrumental and analysis methods to study tissue alterations in diseased states. An integral part of this work is the development of machine learning algorithms customized for classifying normal and diseased tissues. His lab was among the first to use multiphoton excited (MPE) photochemistry for nano/