SMART Biosym Seminar

Imaging and Modeling the Extracellular Matrix in Ovarian Cancer

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Time: Tuesday January 13, 2015, 11:00-12:00
Location: SMART Enterprise Level 5, Perseverance Rooms
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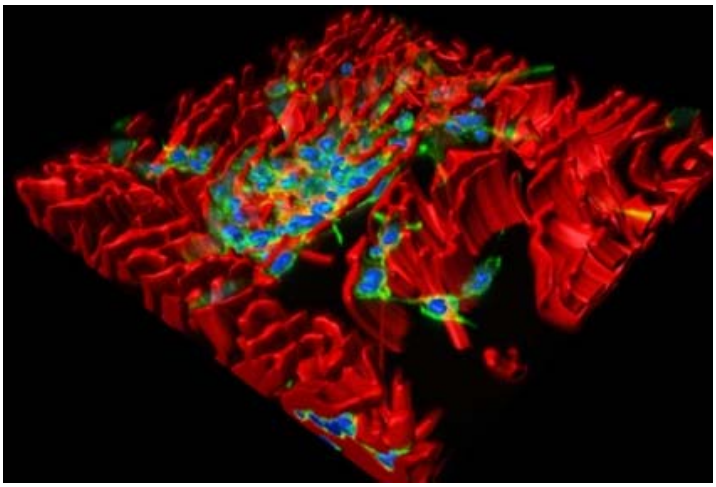

Mouse heart tissue (blue) on gel-MA culture platform (Day 14.5). Structures is 170 x 170 µm.

A profound remodeling of the extracellular matrix (ECM) occurs in human ovarian cancer. We show that Second Harmonic Generation (SHG) imaging microscopy can quantify changes in the architecture in normal and malignant ovaries. We compared the collagen organization using forward-backward (F/B) directional and polarization anisotropy measurements, which are reflective of the fibril and fiber assembly respectively. We found that the stromal collagen in high grade serous tumors is extensively remodeled in the form of new collagen synthesis. We have also used these metrics to compare the collagen structure in normal tissue, benign tumors, and lowgrade tumors and found intermediate behavior between normal and high grade disease. We further investigate the role of the ECM in ovarian cancer by using multiphoton excited (MPE) polymerization to fabricate biomimetic models to investigate operative cell-matrix interactions in invasion/metastasis. First, we create nano/microstructured gradients to study adhesion/migration dynamics of ovarian cancer cells of differing metastatic potential. We find a strong haptotactic response that depends on both contact guidance and ECM binding cues. While we found enhanced migration for more invasive cells, the specifics of alignment and directed migration also depend on cell polarity. We further use MPE fabrication to create scaffolds with complex, 3D submicron morphology directly from collagen and gelatin. The stromal scaffold designs are derived directly from "blueprints" based on SHG images. The models are seeded with different cancer cell lines and this allows decoupling of the roles of cell characteristics (metastatic potential) and ECM structure and composition (normal vs cancer) on adhesion/migration dynamics. We found the malignant stroma structure promotes enhanced migration and cytoskeletal alignment. These models cannot be synthesized by other conventional fabrication methods and we suggest the MPE image-based fabrication method will enable a variety of studies in cancer biology. We further suggest the integrated approach of imaging and modeling has great translational utility.

Paul J. Campagnola is an associate professor in the Departments of Biomedical Engineering and Physics at the University of Wisconsin-Madison. His research focuses on the development of nonlinear optical spectroscopy and microscopy methods, with an emphasis on translational applications. These research efforts are directed at understanding cancer cell-ECM interactions in the tumor microenvironment as well as fabricating scaffolds for tissue regeneration. Among his many accomplishments, he is one of the international leaders in developing second harmonic imaging technologies and one of the inventors of 3D micro-stereolithography based on nonlinear optical excitation. He has published more than 50 peer-reviewed journal articles and several review articles and book chapters, and has delivered more than 70 invited talks. He serves on the editorial board for the Journal of Biomedical Optics and on numerous NIH and NSF review panels.