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High resolution imaging and biological consequences of collagen architecture alterations in ovarian cancer

Many human diseases including all cancers, fibroses, cardiovascular disease and connective tissue disorders are characterized by alterations in the collagen organization relative to normal tissues. We have developed Second Harmonic Generation (SHG) microscope tools to selectively and specifically probe all levels of collagen architecture organization in human ovarian cancer. Using a novel form of 3D machine learning, we successfully classified six types of ovarian tumors based on the observed collagen fiber morphology. We also developed polarization sensitive SHGmethods to extract collagen macro/ supramolecular structural aspects (α-chain pitch and chirality) and found significant differences between normal and malignant ovarian tissues. Collectively, this structural information provides insight into disease etiology and suggests future diagnostic approaches. We have developed an SHG image-based fabrication approach to creating tissue engineered scaffolds of ovarian cancer to study the effects of collagen remodeling on cell-matrix interactions including migration and cytoskeletal dynamics. We found the remodeled matrix drives the cell behavior to a larger extent than the initial cell phenotype. We further created orthogonal models of morphology and stiffness to show how these factors separately and collectively drive cell behavior. We have also developed a machine learning approach using generative adversarial networks (GANSs) to optimize the scaffold design.



Paul Campagnola, Ph.D.



Professor University of Wisconsin-Madison

Paul J. Campagnola obtained his PhD in Chemistry from Yale University in 1992 and was a postdoctoral associate at the University of Colorado from 1992-1995. He was on the faculty in the Department of Cell Biology the Connecticut Health University of Center from 1995-2010. In 2010 became an Associate Professor in Departments of Biomedical Engineering and Medical Physics at the University of Wisconsin-Madison and was promoted to Professor in 2013. He is currently the Tong Biomedical Engineering Department Chair and UW Kellett Faculty Fellow. He is a Fellow of the Optica and American Institute for Medical and Bioengineering and currently a Fellow in the Big 10 Alliance Academic Leadership Program. He has over 100 peer-reviewed journal articles, several review articles and book chapters, co-edited a book "Second Harmonic Generation microscopy" and given over 100 invited talks. He serves on the editorial board for the several journals and serves on numerous NIH and NSF review panels.

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