doi:10.1017/S1431927620018681
Microsc. Microanal. 26 (Suppl 2), 2020

Computational Optics of the Collagen Rich Tumor Microenvironment

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Collagen forms the structural network of the extracellular matrix (ECM) in biological tissues, and is the most abundant protein in vertebrates. The amount, distribution, and structural organization of fibrillar collagen are all important factors underlying the properties of tissues and play an integral role in many diseases. In cancer, we discovered Tumor Associated Collagen Signatures (TACS), where highly aligned collagen fibers are oriented perpendicular to the tumor boundary, was negatively prognostic in human breast cancer. We and other have found similar changes in other cancer types such as ovarian, prostate, pancreas and others.

All these collagen fiber based studies either used specialized imaging approaches, such as specific stains or advanced and costly imaging modalities that are not currently in the clinical workflow. Although pathologists use special staining techniques when fibrosis is of clinical concern, these are not sufficient to fully characterize stromal biomarkers as described in research studies. To facilitate analysis of stromal biomarkers in clinical workflows, it would be ideal to have technical approaches that can characterize fibrillar collagen on standard H&E stained slides produced during routine diagnostic work. In this talk, we present a machine learning- based stromal collagen image synthesis algorithm that can be incorporated into existing H&E- based histopathology workflow. Specifically, this solution applies a convolutional neural network (CNN) directly onto clinically standard H&E bright field images to extract information about collagen fiber arrangement and alignment, without requiring additional specialized imaging stains, systems or equipment. We validated the methods by retrospectively analyzing samples previously used for identifying the negatively prognostic Tumor Associated Collagen Signatures (TACS) biomarker in breast and pancreatic cancers. This proposed solution has great promise to overcome the main technical barriers of transferring collagen image based prognostic stromal biomarkers to clinical practice and research.