Wavelet-Based Gene and Cell Causal Networks Revealed by Spatial Transcriptomics

Tong, Nick (School: Horace Mann School)
Xu, Olivia (School: Horace Mann School)

Understanding disease models and precision medicine require untangling the complexities of spatial-temporal gene and cell interactions. However, inferring causal relationships from spatial transcriptomics data remains difficult. High dimensionality and localized spatial dependencies often hamper these efforts. We present a novel computational framework that combines wavelet-based multi-view decomposition, clustering, and trajectory inference to represent causal relationships using multilayer networks. Using a pancreatic ductal adenocarcinoma (PDAC) Visium dataset (GSE278694), we applied a multi-band discrete wavelet transform in order to obtain multi-scale gene expression representations. These decomposed views enabled refined clustering. We subsequently spatially mapped these clusters to spot-level coordinates for biological interpretation through cluster annotation. We used trajectory inference to assign pseudotime values to each spatial spot so that gene expression data was able to be reorganized into temporally ordered profiles. Next, we estimated directionality via SiCGNet, an ablation-based predictive scheme, to finally construct multilayer causal graphs linking genes and cell types across wavelet scales. Our framework identified previously unrecognized drivers of PDAC, most notably the ANXA10 ? TFH CD4+ T cell link and the C1QTNF3 ? Smooth Muscle ? Acinar cell signaling cascade as potential novel therapeutic targets. This highly efficient and scalable pipeline provides a systematic method to discover directional interactions and prioritize therapeutic targets driving disease progression.

Awards Won:
The Knowledge Society: 1st Place