

Hiding in plain sight: Topological analysis links local expression dynamics with spatial heterogeneity using the GeoMx® DSP Platform

Genomics

Tyler Hether (thether@nanosttring.com), NanoString Technologies, **Jason Reeves**, Nanostring, **Sarah Warren**, Nanostring, **Joseph Beechem**, Nanostring

The GeoMx® Digital Spatial Profiling (DSP) platform enables detection of high-plex protein and RNA expression from user-defined compartments within FFPE tissues. Until now, the tissue architecture within regions of interest (ROIs) used during profiling has only been leveraged to define collection regions, but quantifying the structural variation associated with transcriptomic expression may provide additional insight into biological processes occurring spatially.

We integrated DSP multi-channel immunofluorescent (IF) images and molecular profiling leveraging methods adapted from the field of landscape ecology. We analyzed ROIs from colorectal cancer that had been segmented into tumor and non-tumor segments. Segment-specific RNA expression was collected using the Whole Transcriptome Atlas. Broad patterns of differential expression between tumor and non-tumor segments reveal canonical CRC-associated genes of varying significance.

Beyond traditional analyses, several spatial metrics were computed based on IF staining in each tumor and stroma compartment. These compartment-level metrics include: the “core” area of each compartment within a given ROI, how connected individual patches are to one another in space, and others. We found several examples in which the FFPE spatial composition, tumor/stroma compartment, and their interaction predicted gene expression. For example, the gene CD274 (PDL1), which has previously been shown to be a positive prognostic indicator of CRC, is increased overall in stroma. Expression of PDL1 increases with stomal connectivity while little difference was observed between PDL1 expression and connectiveness in tumor.

Herein, we demonstrate that landscape metrics can drive insight into the of spatial context with transcriptome profiling. As the GeoMx® platform natively registers, measures, and leverages this architecture during collection, we anticipate methods that summarize the tumor’s spatial landscape will provide insight that would be hidden by or are difficult to draw from single-cell or other spatial sequencing approaches.

GeoMx® DSP technology is for Research Use Only and not for use in diagnostic procedures.