Multiple modalities of NanoString GeoMx™ Digital Spatial Profiler allow for spatially-resolved, multiplexed quantification of protein and mRNA distribution and abundance

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Abstract

Characterization of the spatial distribution and abundance of proteins and mRNAs with morphological context within tissue samples is critical in understanding disease mechanisms, guiding clinical decision-making, and studying cellular and molecular biology. However, it has proven difficult to perform such studies in a highly multiplexed manner. To address this current need, we have developed a next generation high throughput based microscopy and tissue-sectioning platform designed to simultaneously analyze hundreds of proteins or mRNAs on a single FFPE slide from different tissue spatial regions (Geometric and Gridded Spatial Profiler, DSP).

Here, we present a series of modalities and associated applications for the GeoMx™ DSP platform and its integrated software. First, geometric profiling can be achieved by drawing automated circles, squares or even manual hand-drawn polygons as regions of interest (ROI) to characterize tissue heterogeneity. Secondly, segmented profiling offers high resolution antibody or tumor profiling by placing a grid on tissue sections and automatically analyzing each square grid element. Third, contour profiling retains the high resolution of segmented profiling, but allows for analysis of regions defined by hand-drawn polygons. Fourth, registration and rare cell profiling exploits fluorophore conjugated antibodies to profile specific cell types. These techniques can be used to discover drug mechanisms at action or tissue architecture, as well as to facilitate prediction of treatment response and disease progression or investigation of specific rare cell populations across profiles.

Using these multiple modalities, we spatially resolve protein and mRNA expression over 30 micron targets in FFPE tissue sections from various organs as well as tumors. We demonstrated multiple detection from discrete regions within a tumor (tumor center and invasive margin), enabling systematic interrogation of gene activity in IBD samples. Finally, we present the utility of each modality under different circumstances.

Geospatial and Geometric Protein and RNA Profiling of a Tonsil Tissue

Segmented and Rare Cell Profiling of CRC and IBD Colon Tissues

Contour Profiling of an Inflammatory Bowel Disease Tissue

References


Conclusions

A key component of DSP is the use of programmable 200 Digital Microtrackers (DMT) - million total events - to perform the spatially-resolved molecular profiling.

The relative choice of tissue fixation and immunoreagents used for guidance in DSP allows for high throughput analysis of rare cell type populations based on location within the tissue.

DSP platform allows a unique range of immunodetection modalities and a unique calibration of proteins and mRNAs in tumors at various magnification levels, which facilitates the understanding of immunology within these segments.

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