Discover Novel Predictive Biomarkers with GeoMx® DSP

Highlights

- Understanding patient, intertumoral, and intratumoral heterogeneity is essential to developing precision therapeutics for patients with cancer
- NanoString® GeoMx® Digital Spatial Profiler (DSP) is designed for oncology research through high-plex spatial profiling of protein or RNA targets
- A recent study employs the GeoMx DSP to investigate novel biomarkers associated with beneficial PD-1 therapy in FFPE samples from patients with NSCLC
- Canopy Biosciences is a Center of Excellence for NanoString services, offering comprehensive experiment and analysis packages to support biomarker discovery

Introduction

Heterogeneity is a term gaining attention which has underlined the importance of precision medicine. We now appreciate that not only do inherent variations between patients mean they respond differently to a specific treatment (patient heterogeneity), but also inherent variations between tumors in the same patient mean the tumors may respond differently (tumor heterogeneity), and the variations within a single tumor mean that each cell responds differently (intratumoral heterogeneity). This poses a problem for oncology researchers and physicians who seek to understand and cure cancer, as heterogeneity at any level may result in varying degrees of efficacy on this treatment strategy (Kravitz et al., 2004). Identifying the right biomarkers that can predict the efficacy of treatment will be crucial to the future of precision medicine.

A significant amount of research to identify predictive biomarkers – which determine the likelihood of response or lack of response of a particular therapy – has already been conducted. Predictive biomarkers help to identify tumors that are most likely to benefit from a specific treatment and spare patients from toxic effects of ineffective therapies. For example, genetic tests that detect BRCA1/2 mutations help identify platinum-sensitive ovarian cancer patients most likely to respond to PARP inhibitors (Ledermann et al., 2012). Both genetic mutations and protein levels in diseased tissues can be examples of predictive biomarkers, yet few platforms enable the simultaneous evaluation of both RNA and protein.

The GeoMx DSP from NanoString offers a solution providing morphological context in spatial transcriptomics and spatial proteomics experiments for immuno-oncology research. The GeoMx DSP platform is ideal for the investigation of novel biomarkers in tissue samples because it offers digital profiling of protein and RNA analytes on the same slide. Canopy Biosciences provides CRO Services including comprehensive experiment and analysis packages for NanoString platforms in a CLIA-Certified laboratory to accelerate your research.

Figure 1. The GeoMx DSP enables spatial analysis of RNA and protein in tissue slides. (Source: NanoString)

Authors: MADISON TYLER, JESSICA RUNYON

CRO Services for Discovering Novel Biomarkers

The GeoMx DSP workflow (Figure 2) is ideal for predictive biomarker studies and maintains morphological context for spatial transcriptomics and spatial proteomics on the same tissue slide. Key features of the GeoMx platform include:

- Digital profiling of 80+ protein analytes and 1000+ RNA analytes on the same tissue slide
- Resolve tissue heterogeneity through ROI selection
- Compatible with FFPE and FF tissue sections, as well as TMAs

NanoString provides morphology markers for ROI segmentation with GeoMx DSP. Canopy Biosciences recently launched an extended catalog of pre-validated morphology markers to supplement NanoString Morphology Marker kits. We run any standard NanoString panel or custom experiment, depending on researcher needs.

A Center of Excellence for NanoString CRO Services

Canopy Biosciences has been named a Center of Excellence for both nCounter® Analysis System and GeoMx® Digital Spatial Profiling services. We offer comprehensive experiment and analysis packages in a CLIA-Certified laboratory to accelerate your research:

- Extensive experience running pre-validated RNA and protein panels from NanoString
- Develop custom panels and ROI Selection Markers
- Custom assay development in a CLIA-Certified lab
- Interactive data review with Canopy analysts
- Generate publication-ready figures in analysis software

In addition to NanoString® services, Canopy Core Laboratory offers a full suite of services to detect and analyze proteins and nucleic acids across a variety of traditional techniques and novel platforms. As a Contract Research Organization (CRO) offering a full suite of services, let Canopy Biosciences help expedite your research to discover novel predictive biomarkers.

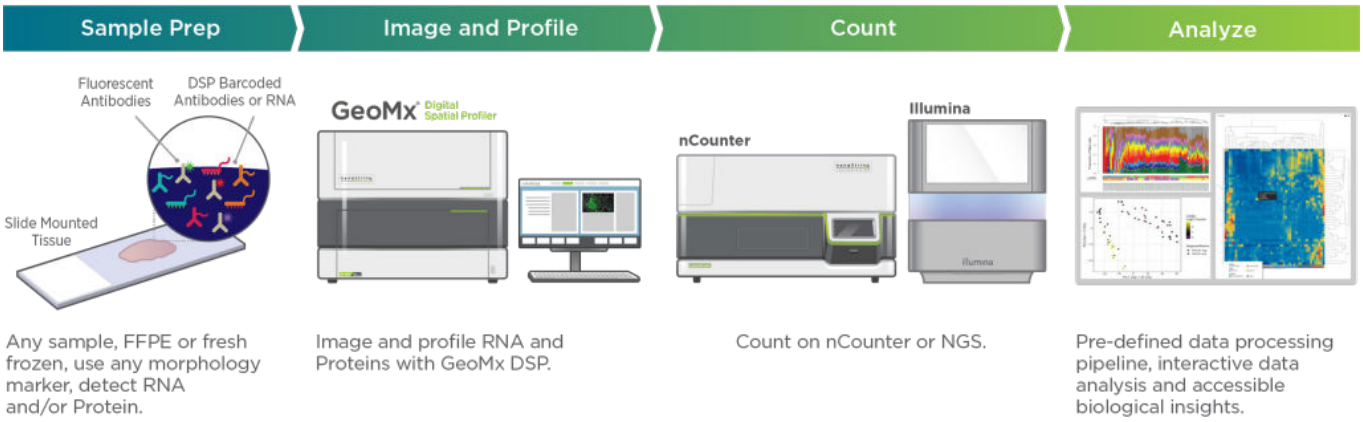

Figure 2. GeoMx DSP Workflow. Step 1: Prepare samples by staining with any morphology marker to identify regions of interest (ROIs). Step 2: Image and profile RNA and proteins with GeoMx DSP. Step 3: Count on nCounter or NGS. Step 4: Interactive data analysis to produce publication-ready figures including heat maps, volcano plots, scatter plots, and bar graphs. (Source: NanoString)

GeoMx DSP Supports Studies to Investigate Novel Biomarkers

Researchers at Yale University and NanoString Technologies used GeoMx DSP to investigate novel biomarkers associated with beneficial PD-1 checkpoint blockade in non-small cell lung cancer (NSCLC) (Zugazagoitia et al., 2020). Researchers collected FFPE tumor specimens represented in a tissue microarray (TMA) from 81 patients with NSCLC treated with PD-1 checkpoint blockade therapy. Figure 3 shows how ROI segmentation antibodies were used to visualize compartments.

The researchers used off-the-shelf panels and a cocktail of 44 unique photocleavable oligonucleotide-labeled antibodies to identify immuno-oncology targets. Using GeoMx DSP, researchers found 12 protein markers associated with benefit from PD-1 checkpoint blockade in patients with NSCLC. This work supports the use of GeoMx DSP to identify more robust predictive biomarkers in patient samples.

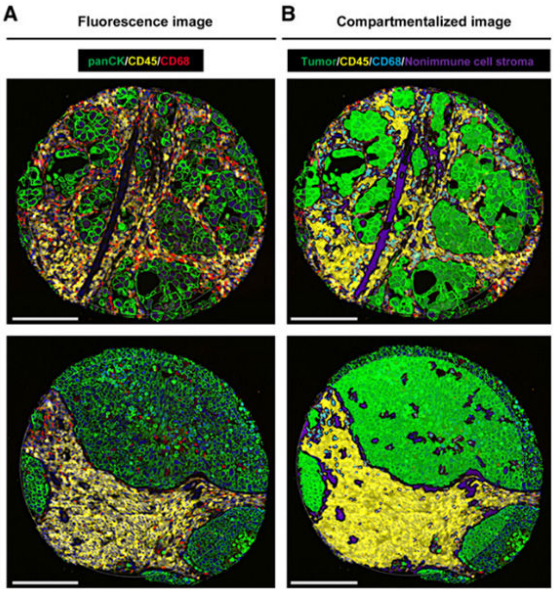

Figure 3. NanoString GeoMx ROI Segmentation. ROI segmentation markers identify tumor (Pan-CK+), immune (CD45+), macrophage (CD68+), and stromal (Pan-CK-/CD45-/CD68-) regions. (Source: Zugazagoitia et al. 2020)

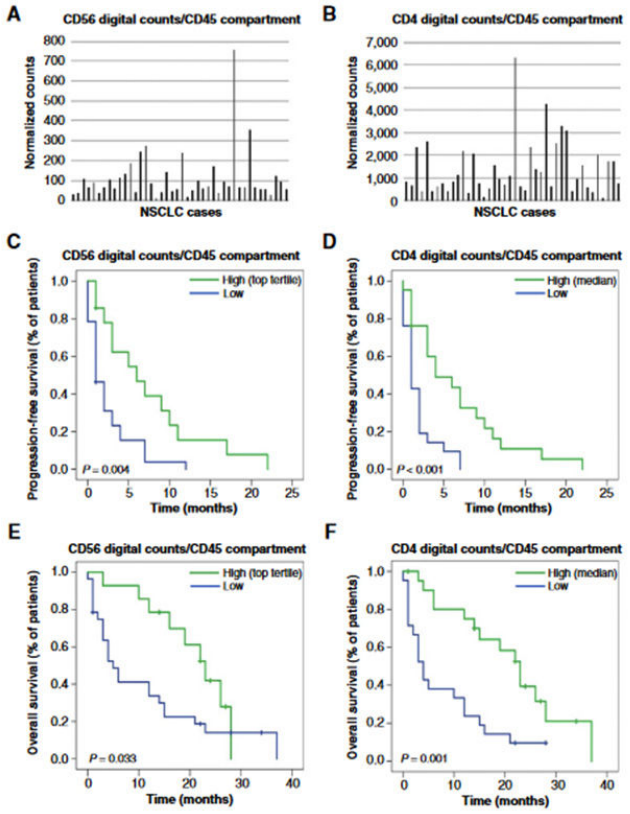

Figure 4. Clinical Outcomes Data Analysis. CD56+ immune cell counts in the stroma were predictive of progression-free survival and overall survival. (Source: Zugazagoitia et al. 2020)

Furthermore, CD56+ immune cell counts in the stroma were predictive of progression-free survival and overall survival (Figure 4). This was confirmed with orthogonal validation of CD56+/Pan-CK- cell counts as assessed by inForm analysis (Akoya) and multiplexed imaging (Vectra Polaris microscope). This data shows the ability of GeoMx DSP assays to produce both clinically relevant and valid data to profile cell counts in tissue compartments.

Taken together, the data in this study demonstrate the utility of GeoMx DSP to identify markers associated with positive clinical outcomes in patients. This is an important feature, given various cell types are likely to play a role in therapeutic efficacy of anti-tumor immune responses following cancer therapy.

Summary

Understanding patient, intertumoral, and intratumoral heterogeneity is essential to developing precision therapeutics for patients with cancer. The GeoMx DSP from NanoString is designed to deeply characterize tumor heterogeneity. Here, we highlight the utility of the GeoMx DSP in a recent study by Zugazagoitia et al. (2020) to investigate novel biomarkers associated with beneficial PD-1 therapy in patients with NSCLC. Using GeoMx DSP, the authors identify more robust predictive biomarkers for NSCLC and additional markers associated with positive clinical outcomes after treatment.

In summary, the GeoMx DSP offers a wealth of data and the ability to profile expression of over 80+ protein analytes and 1000+ RNA analytes on the same tissue slide. With morphological context in spatial transcriptomics and spatial proteomics experiments on the same sample, GeoMx DSP has the power to transform precision medicine as we know it.

References

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