GeoMx™
Digital Spatial Profiler
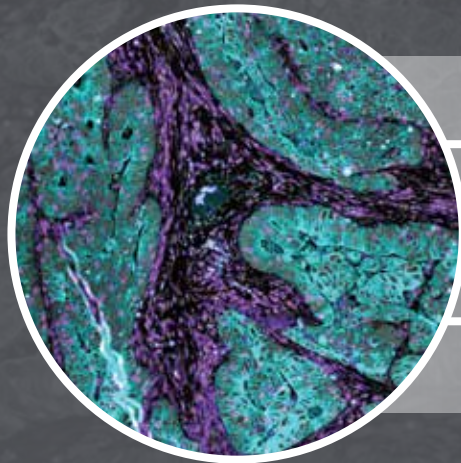
Your GPS for Biology
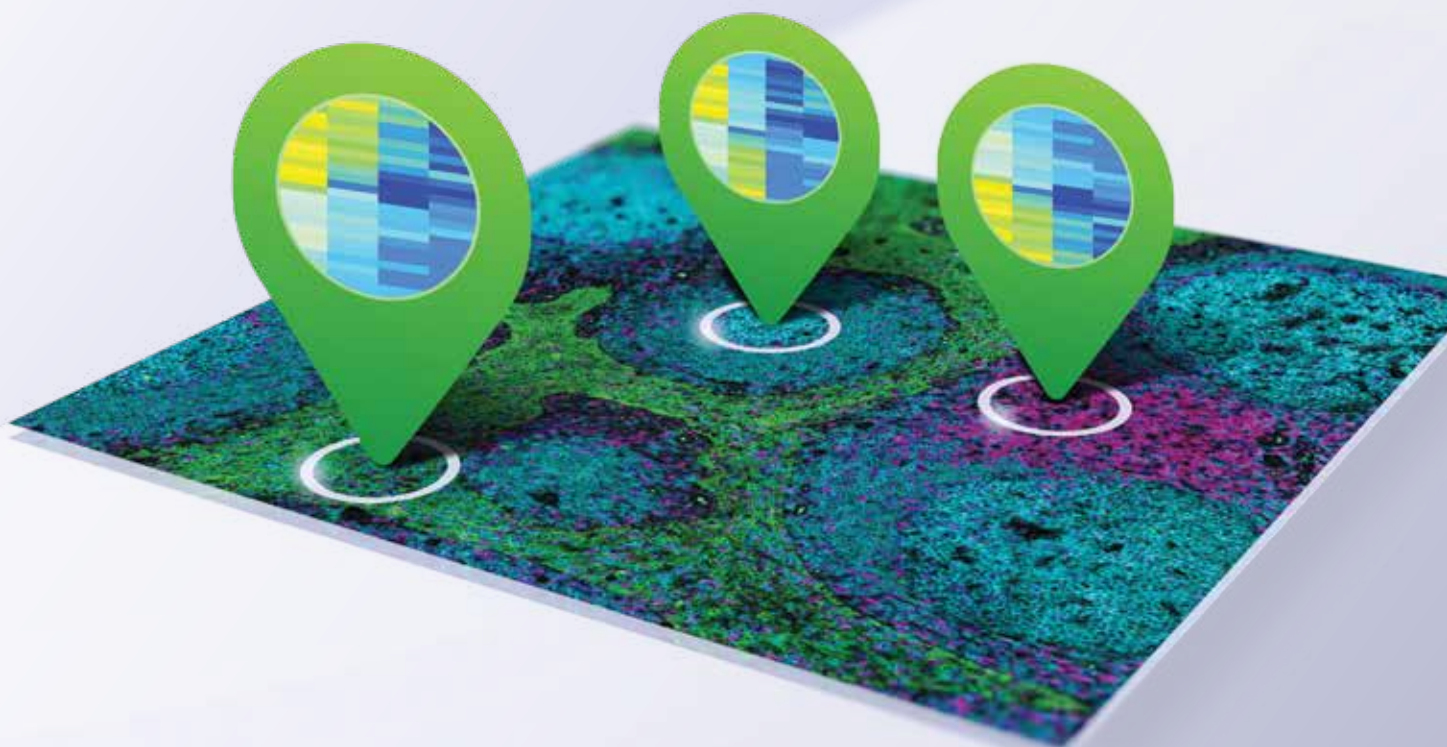
nanoString™

Resolving
Sample Heterogeneity

Spatial information or high-plex: The tradeoff

Understanding tissue heterogeneity is critical to answering key biological questions in translational research. The current tissue analysis paradigm requires a tradeoff between morphological analysis or high plex, sacrificing valuable information or consuming precious samples.

In situ Visualization Technology (FISH/ IHC)

Molecular Profiling Technologies

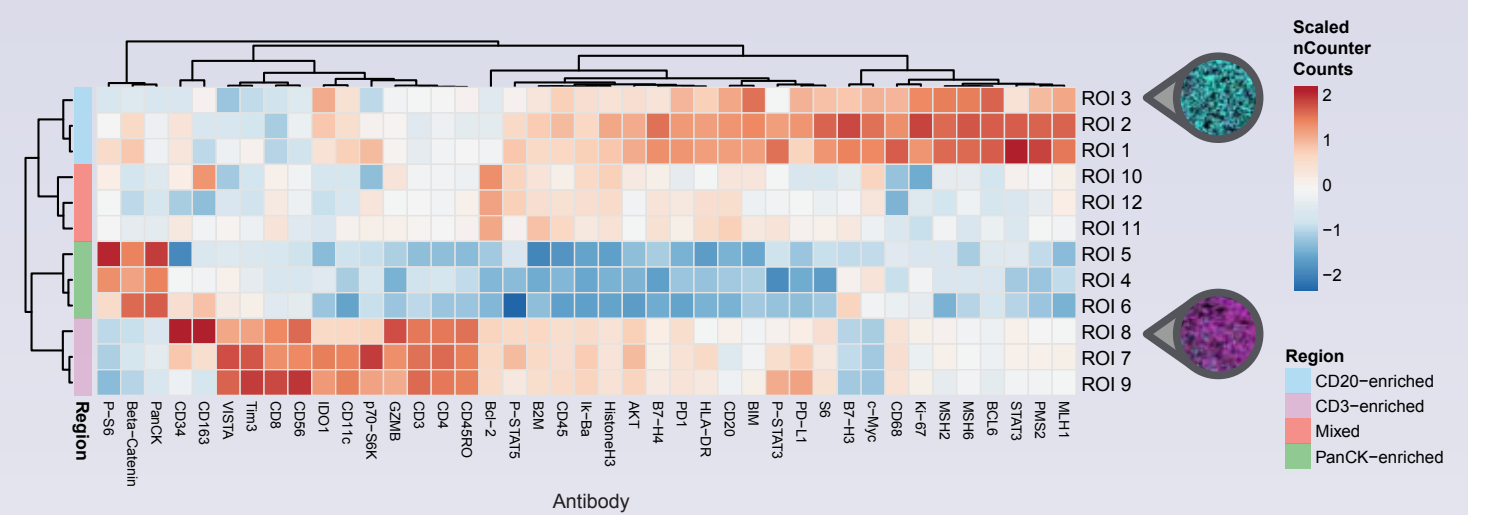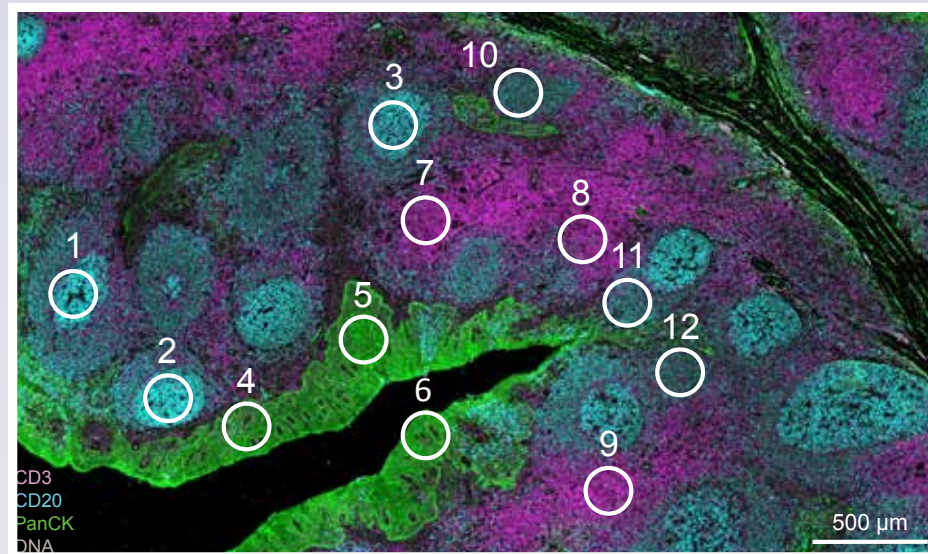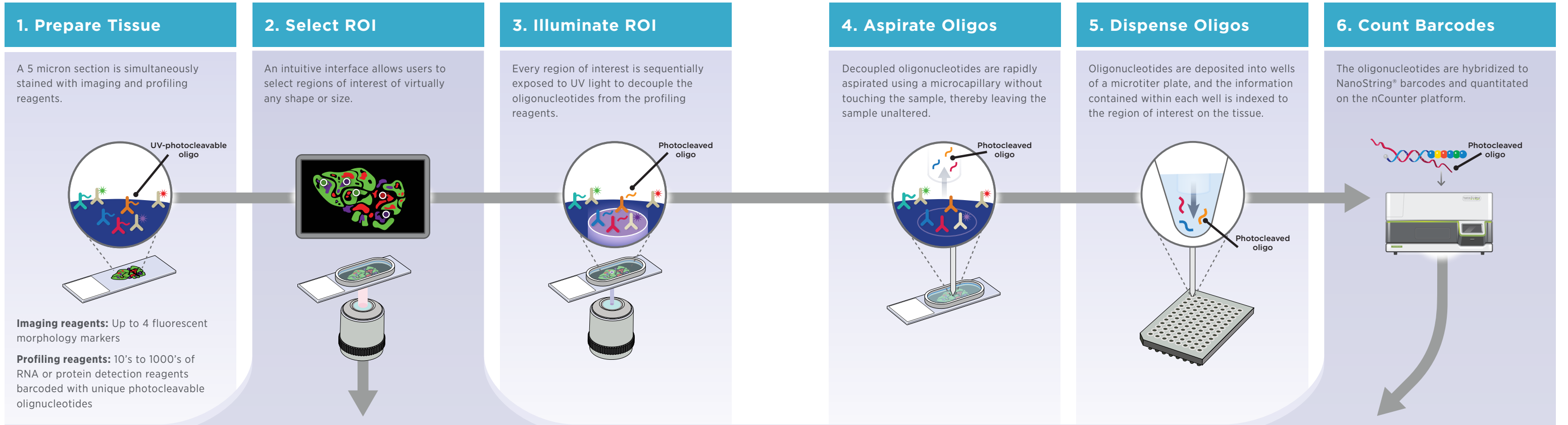|		
+	Spatial	−
−	Plex	+
−	Quantitation	+
−	Precision	+

Introducing
GeoMx™ DSP
Your GPS for biology

NanoString's GeoMx Digital Spatial Profiler (DSP) combines the best of spatial and molecular profiling technologies by generating a whole tissue image at single cell resolution and digital profiling data for 10's-1,000's of RNA or Protein analytes for up to 16-20 tissue slides per day. This unique combination of high-plex, high-throughput spatial profiling enables researchers to rapidly and quantitatively assess the biological implications of the heterogeneity within tissue samples.

HIGH-PLEX · HIGH-THROUGHPUT · MULTI-ANALYTE · QUANTITATIVE · NON-DESTRUCTIVE

The Path is Clear
GeoMx DSP Workflow

1. Prepare Tissue

A 5 micron section is simultaneously stained with imaging and profiling reagents.

Imaging reagents: Up to 4 fluorescent morphology markers

Profiling reagents: 10's to 1000's of RNA or protein detection reagents barcoded with unique photocleavable olignucleotides

UV-photocleavable oligo

2. Select ROI

An intuitive interface allows users to select regions of interest of virtually any shape or size.

3. Illuminate ROI

Every region of interest is sequentially exposed to UV light to decouple the oligonucleotides from the profiling reagents.

Photocleaved oligo

4. Aspirate Oligos

Decoupled oligonucleotides are rapidly aspirated using a microcapillary without touching the sample, thereby leaving the sample unaltered.

Photocleaved oligo

5. Dispense Oligos

Oligonucleotides are deposited into wells of a microtiter plate, and the information contained within each well is indexed to the region of interest on the tissue.

Photocleaved oligo

6. Count Barcodes

The oligonucleotides are hybridized to NanoString® barcodes and quantitated on the nCounter platform.

Photocleaved oligo

CD3
CD20
PanCK
DNA

500 µm

Scaled nCounter Counts
2
1
0
−1
−2

Region
CD20−enriched
CD3−enriched
Mixed
PanCK−enriched

Antibody

Region

ROI 3
ROI 2
ROI 1
ROI 10
ROI 12
ROI 11
ROI 5
ROI 4
ROI 6
ROI 8
ROI 7
ROI 9

P−S6, Beta−Catenin, PanCK, CD34, CD163, VISTA, Tim3, CD8, CD56, IDO1, CD11c, p70−S6K, GZMB, CD3, CD4, CD45RO, Bcl−2, P−STAT5, B2M, CD45, Ik−Ba, HistoneH3, AKT, B7−H4, PD1, HLA−DR, CD20, BIM, P−STAT3, PD−L1, S6, B7−H3, c−Myc, CD68, Ki−67, MSH2, MSH6, BCL6, STAT3, PMS2, MLH1

Locate
Your Regions of Interest

Tunable, light-directed selection enables dynamic profiling modalities
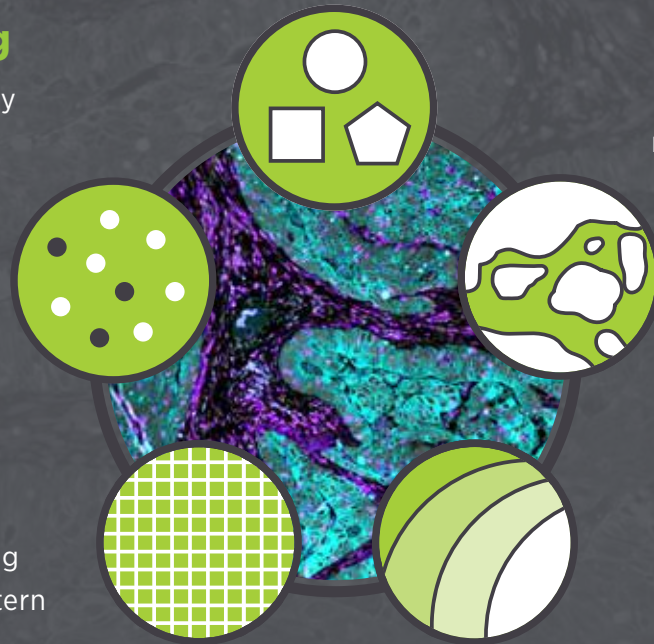
Geometric Profiling
Assess tissue heterogeneity and profile standardized geometric shapes across distinct tissue regions

Rare Cell Profiling
Cell type-specific morphology markers guide profiling, revealing the function of distinct cell populations

Segment Profiling
Maximize cellularity using morphology markers to identify and profile distinct biological compartments within an ROI

Gridded Profiling
Perform deep spatial mapping using a tunable gridding pattern

Contour Profiling
Evaluate how proximity affects biological response and the local microenvironment around a central structure using radiating ROI

Biological questions inform modality selection

Geometric Profiling
How does the expression of tumor and immune markers differ across a sample?

Geometric profiling identifies distinct expression profiles across and within specific regions of the tissue

Segment Profiling
How does the tumor differ from the tumor microenvironment?

Segment profiling reveals unique tumor and tumor microenvironment molecular profiles

Contour Profiling
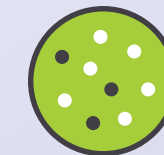*How does proximity to the tumor or an immune cell population alter biological response?*

Radiating ROIs surrounding macrophages show distinct expression profiles based on proximity
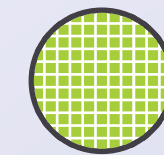
Gridded Profiling
What novel biology is uncovered with deep spatial mapping of the tumor?
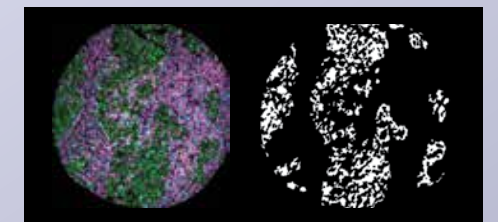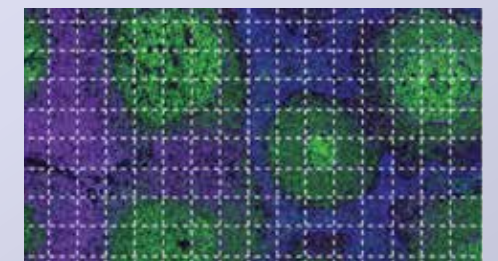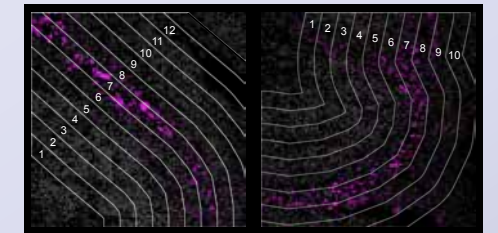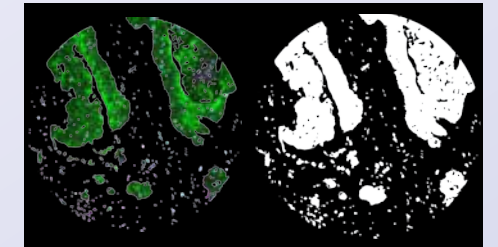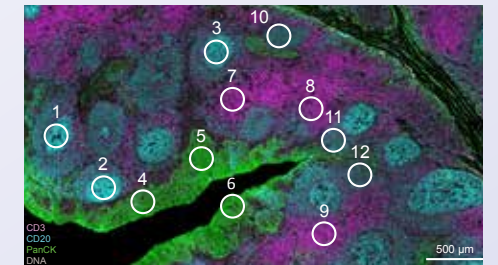
Gridded profiling provides a digital map of the molecular profile of the tumor

Rare Cell Profiling
How do rare immune cells impact tumor biology and therapeutic response?

Isolated immune cell populations show unique expression profiles

Explore
Your Data

GeoMx DSP provides an integrated environment

- **Easy to analyze** - Imaging and profiling data is always connected
- **Easy to integrate** - Open portal to import external data sets such as clinical annotations or sequencing data
- **Easy to collaborate** - Multi-user access to data at the same time

100% traceability from profiling data to tissue image:

When specific profiling data is selected the GeoMx Data Analysis tool will automatically show the tissue image corresponding to a ROI and vice versa.


Image of ROI 4 of 24 *(stroma)*
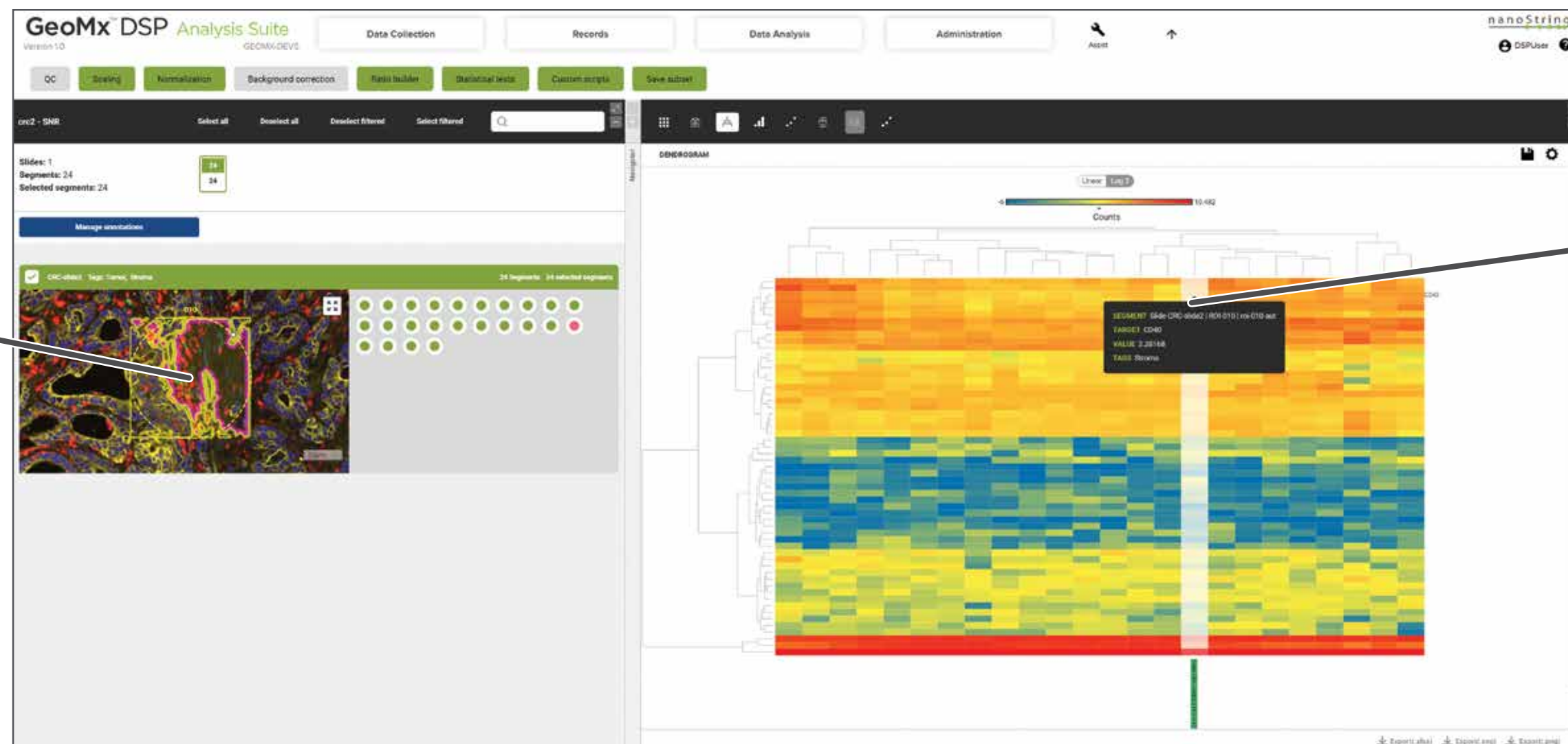
Profiling data from ROI 4 of 24 *(stroma)*

Discover
Your Biomarker

Flexible, pre-verified content to fit a range of research needs

GeoMx assays are modular and optimized for robust performance across samples. Select one core and up to 6 modules to analyze up to 96 targets on a single slide. Available content covers immunology, immuno-oncology, neurodegeneration and neuroinflammation. Additionally, user-defined protein or RNA content can be added using our Protein Barcoding Service and Custom RNA offering.

Module 5 · Module 6 · Custom · Module 1 · Module 2 · Module 3 · Module 4 · **Core**
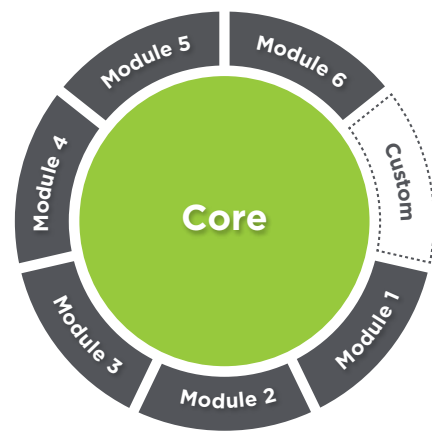
Available content will cover immunology, immuno-oncology, neurodegeneration, and neuroinflammation with a rapidly growing pipeline.

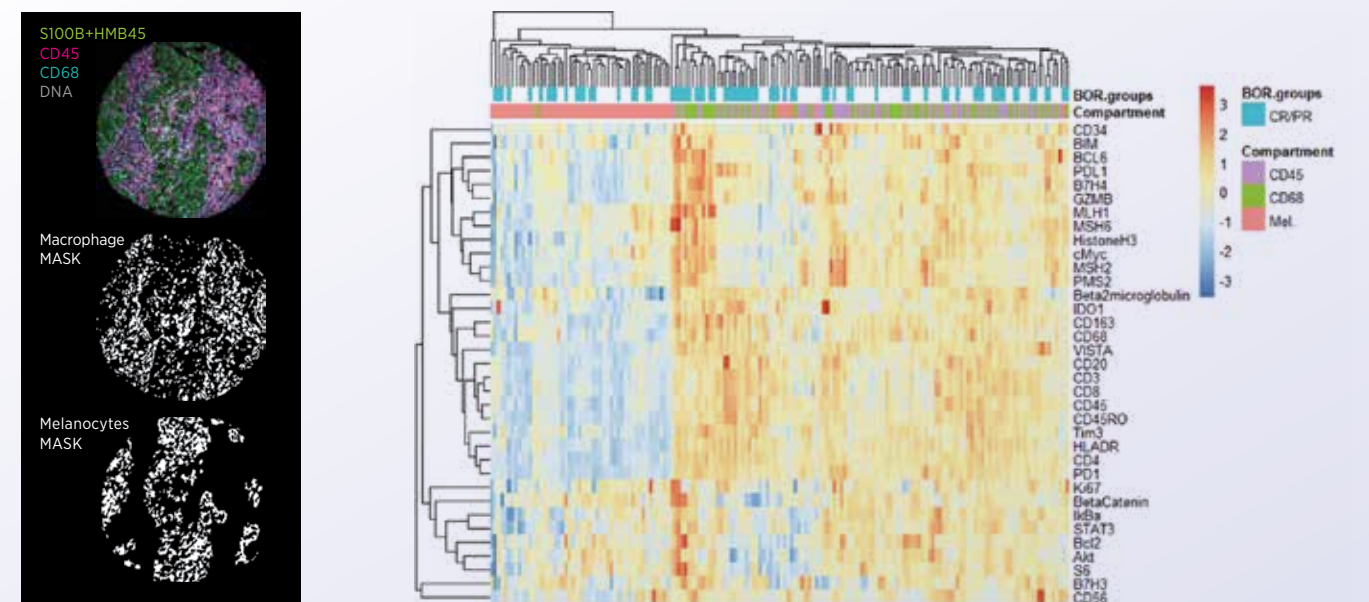|	Immuno-Oncology	Neuroscience
Protein Cores	Immune Cell Profiling ~20-plex Human/Mouse	Neural Cell Profiling ~20-plex Human
Protein Modules	IO Drug Target ~10-plex Human/Mouse	Alzheimer's Pathology ~10-plex Human
	Immune Activation Status ~10-plex Human	Parkinson's Pathology ~10-plex Human
	Immune Cell Typing ~10-plex Human	
	Pan-Tumor ~10-plex Human	
RNA Cores	Immune Pathways ~84-plex Human	N/A
Custom Modules	Available	Available

*Panel concepts and offerings subject to change prior to commercial launch

Case Study: Identification of predictive biomarkers for immune checkpoint in melanoma
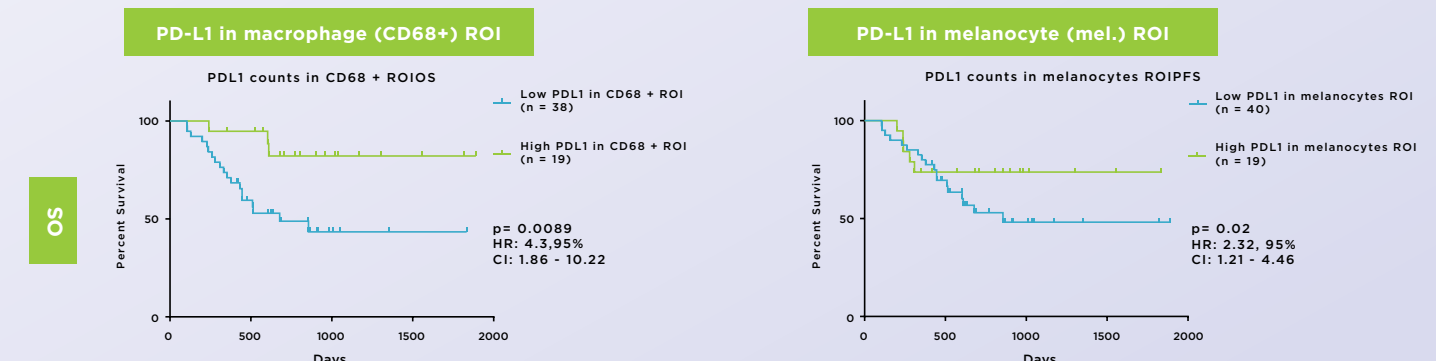
Background: Emerging immuno-therapeutic strategies require predictive biomarkers to select more patients with a positive clinical outcome and reduce toxicity

Experimental design: 44 protein targets spatially profiled across 3 unique compartments (macrophage, leukocytes, and melanocyte) from each melanoma biopsy obtained across 59 immunotherapy-treated patients using rare cell profiling

Results: 5 compartment-specific biomarkers discovered

High PD-L1 expression in macrophages is associated with prolonged survival

PD-L1 in macrophage (CD68+) ROI

PDL1 counts in CD68 + ROIOS

Low PDL1 in CD68 + ROI (n = 38)
High PDL1 in CD68 + ROI (n = 19)

p= 0.0089
HR: 4.3,95%
CI: 1.86 - 10.22

PD-L1 in melanocyte (mel.) ROI

PDL1 counts in melanocytes ROIPFS

Low PDL1 in melanocytes ROI (n = 40)
High PDL1 in melanocytes ROI (n = 19)

p= 0.02
HR: 2.32, 95%
CI: 1.21 - 4.46

Data courtesy of David Rimm, MD, PhD, Yale University