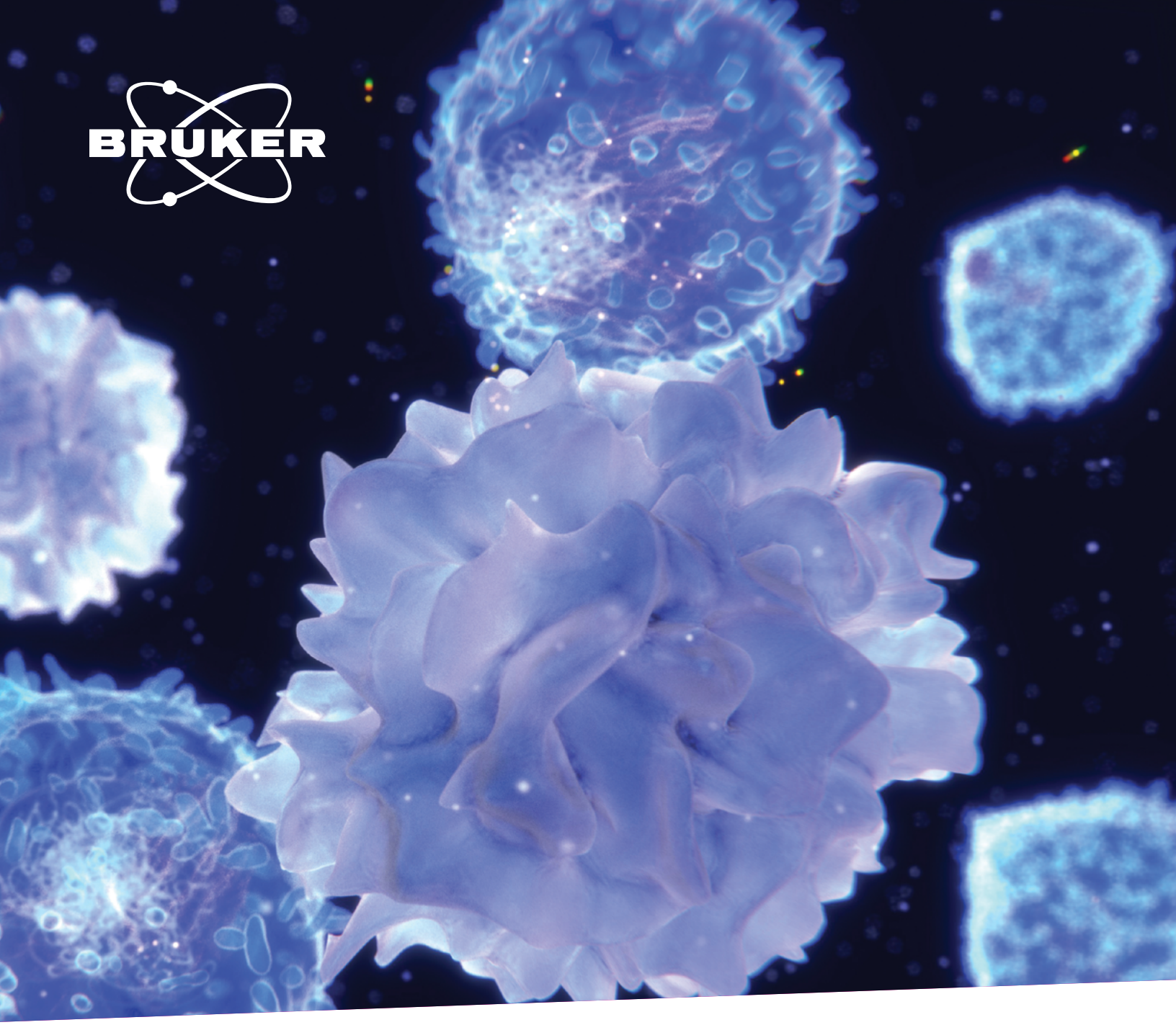
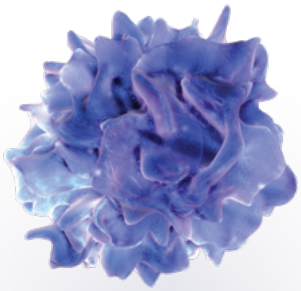


BRUKER SPATIAL BIOLOGY

# Immunology and Infectious Disease Solutions

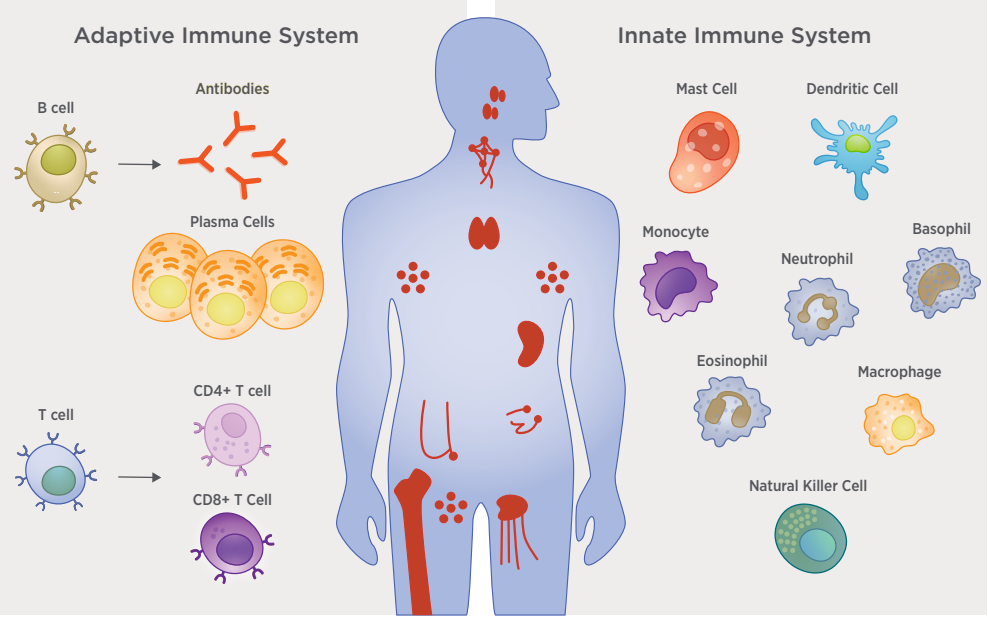


Autoimmune Disease • Organ Transplant
Immuno-Oncology • Infectious Disease

# Creating a Framework

## Supporting Immunology Research

The study of the immune system involves a deep understanding of the fine balance between self and non-self recognition. Nearly all diseases can be characterized by the type of immune response that is involved, whether it is a disease that impacts the normal function of the immune system, a disease that arises as a result of a defect of the immune system, or a disease that is the result of invasion by a foreign pathogen. Recently, much attention has been given to immune checkpoints, receptor-ligand pairs that are involved in the activation or suppression of the immune response, and manipulation of these checkpoints has given rise to the field of immunotherapy. A keen understanding of the different cell types involved in the adaptive and innate immune response is key as is the ability to detect rare cell types and discover new types of immune cells.




Diseases that impact normal function of Immune system

Diseases that arise as a result of defect of the immune system

Diseases that are a result of foreign invaders

Our integrated, multiomic research solutions allow you to study the dynamic and complex nature of the immune response from the level of single cells to multicellular tissue compartments and patient cohorts.

Wherever you are headed with your immunology research, we can get you actionable insights from FFPE, fresh frozen tissue, cell lysates, and biofluids.

- Profile the expression of 800+ genes from a single sample with the nCounter® Analysis System
- Spatially profile the whole transcriptome and hundreds of protein targets within distinct tissue compartments and cell populations with the GeoMx® Digital Spatial Profiler (DSP)
- Profile the immune response at the single cell and subcellular level with the CosMx® Spatial Molecular Imager (SMI)
- Achieve quantitative immuno-phenotyping with high dynamic range and precision optics using the CellScape™ Precise Spatial Proteomics platform

# Creating Novel Solutions

### One Suite of Tools. Unlimited Potential.

The ideal platform for immunology research lets you profile both the systemic and localized immune response and combines expression analysis with tissue imaging to consider the spatial heterogeneity of the immune infiltrate.

Whether you are looking to discover biomarkers using gene expression profiles to understand disease onset, progression, localized immune response or treatment response or characterize tumor heterogeneity at single-cell resolution, Bruker Spatial Biology has you covered.

Uncover the complexities of the immune response with research tools that allow you to profile gene and protein expression in a variety of sample types at the scale and plex that supports your unique research.

## nCounter®

Analysis System

800+ plex pathway-based targeted gene expression profiling in a single tube. Rapid sample to answer workflow.

- Discover predictive and prognostic biomarkers
- Develop signatures associated with inflammation and immune response
- Evaluate mechanisms of treatment response
- Monitor disease biomarkers in clinical trials
- Explore response to infectious disease agents

## CosMx®

Spatial Molecular Imager


High, fidelity spatial exploration of the single-cell whole transcriptome

- Assess heterogeneity of immune cell population and disease progression
- Discover unique cell-cell interactions
- Define cellular neighborhoods
- Discover functionally relevant multi-cellular niches, communities and pathways across any disease state.
- Understand the activities of transmembrane proteins and how they initiate signal transduction pathways

## CellScape™

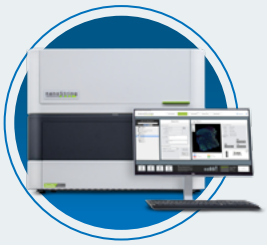
Precise Spatial Proteomics Platform

Highly multiplexed whole-slide immunofluorescence imaging and quantitative spatial phenotyping.

- Characterize immune cell phenotypes and spatial localization
- Map cell–cell interactions in the immune microenvironment
- Track immune infiltration and activation dynamics
- Customize panels to assess immune checkpoints and rare subsets

## GeoMx®

Digital Spatial Profiler

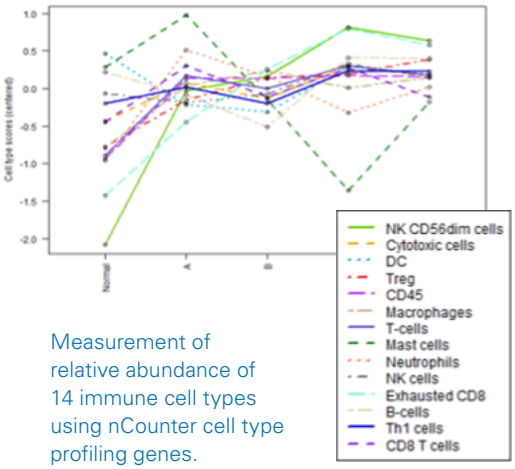


Spatially profile the whole transcriptome and 1000+ protein targets from FFPE and fresh frozen tissue.

- Characterize the immune infiltrate in healthy and diseased tissue
- Profile the cellular makeup of the immune response in tissue
- Study the effect of transplanted tissues on the immune response
- Identify the mechanism of action of drug treatments and vaccinations

# Immune Cell Type Profiling

Select nCounter panels feature genes that provide unique cell profiling data to measure the relative abundance of different immune cell types. To date, 14 different immune cell types have been identified by their gene signatures for inclusion in nCounter panels. The genes were qualified through biostatistical approaches and selected literature in the field of immunology. The panels can be run downstream of flow cytometry to profile specific immune cell populations.




Measurement of relative abundance of 14 immune cell types using nCounter cell type profiling genes.

| Cell Type | Gene(s) | Cell Type | Gene(s)w |
|---|---|---|---|
| B Cells | BLK. CD19, FAM30A, FCRL2, MS4A1, PNOC, SPIB,TCL1A, TNFRSF17 | Mast Cells | CPA3, HDC, MS4A2, TPSAB1/B2 |
| CD45 | PTPRC | NK CD56dim Cells | IL21R, KIR2DL3/4, KIR3DL1/2 |
| CD8T Cells | CD8A, CD8B | NK Cells | NCR1, XCL1/2 |
| Cytotoxic Cells | CTSW, GNLY, GZMA, GZMB, GZMH, KLRB1, KLRD1, KLRK1, NKG7, PRF1 | Neutrophils | CEACAM3, CSF3R, FCAR, FCGR3A/B, FPR1, S100A12, SIGLEC5 |
| Dendritic Cells | CCL13, CD209, HSD11B1 | T Cells | CD3D, CD3E, CD3G, CD6, SH2D1A,TRAT1 |
| Exhausted CD8 | CD244, EOMES, LAG3, PTGER4 | Th1 Cells | TBX21 |
| Macrophages | CD163, CD68, CD84, MS4A4A | Tregs | FoxP3 |

## SPOTLIGHT ON SUCCESS

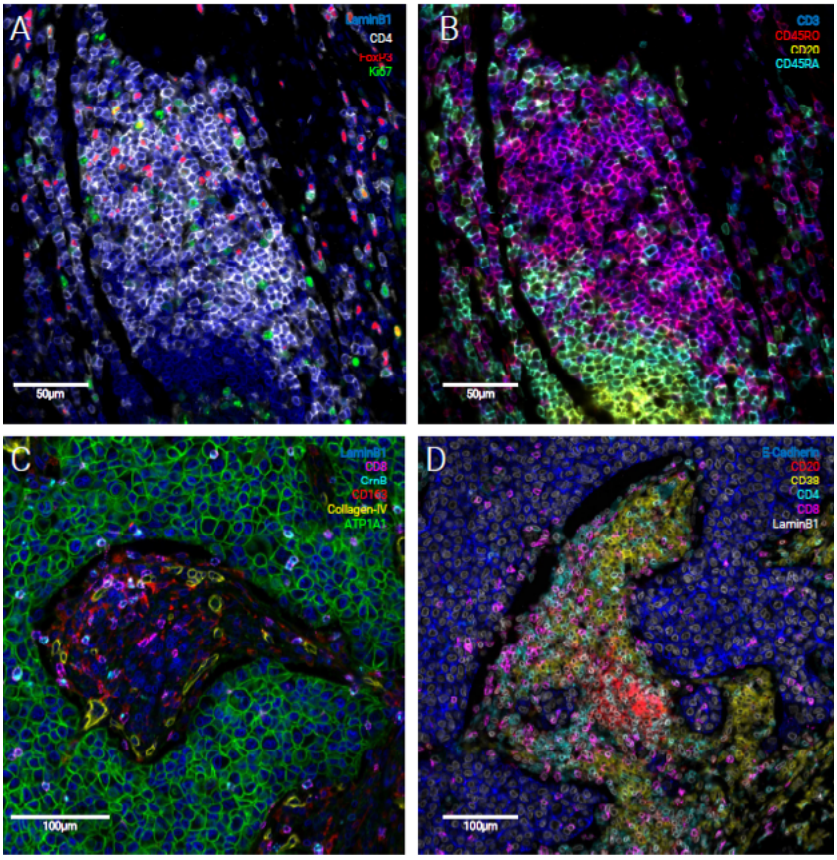
"For the first time ever, we were able to see what is happening immunologically in defined regions of the tissue. This vital data, enabled by Bruker Spatial Biology platforms and an Allo-Xeno gene expression repository, allowed us to understand both the similarities and the novel aspects underpinning organ rejection in xenograft transplantation compared to human organ transplantation. The nCounter and GeoMx instruments harmonized to create a holistic view of the immune response."

**Alex Loupy, MD, Ph.D,**
Paris Institute for Transplantation and Organ Regeneration, INSERM

Immune Cell Type Profiling is also available for GeoMx RNA expression data from the Cancer Transcriptome Atlas or the Human Whole Transcriptome Atlas. The SpatialDecon script can be downloaded through the GeoScript Hub on nanostring.com and estimates the abundance of 18 different immune cell types within an area of interest. The algorithm can quantify immune cell populations defined by single cell sequencing. The immune cell abundance estimates are spatially resolved, granular and paired with highly multiplexed gene expression data.

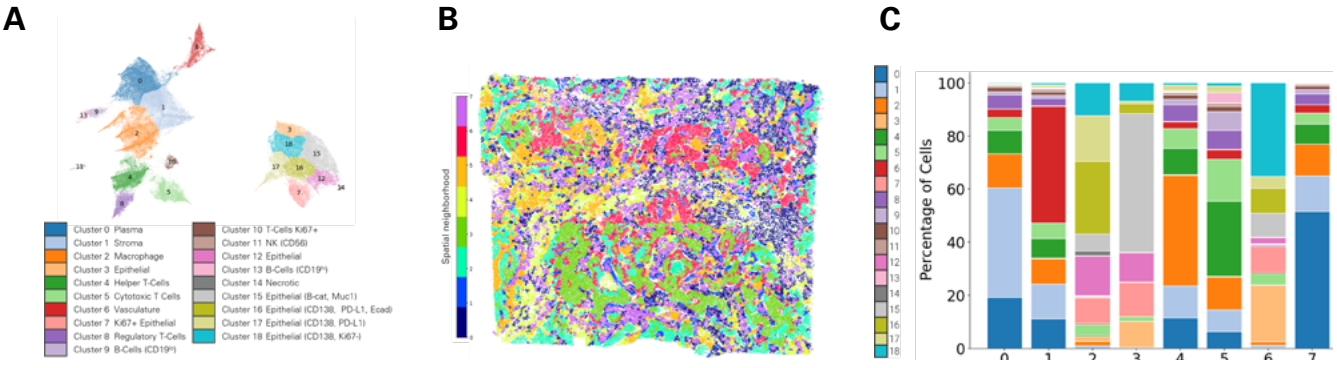
# Spatial Immune Cell Profiling

The CosMx and CellScape platforms both support spatial immune cell profiling–the mapping of immune cell distribution within their native tissue environments. Spatial profiling reveals not only which immune cells are present but also where they reside in relation to other cells and structures in the tissue. Combining biomarker expression with precise segmentation enables accurate cell typing by gating and/or unsupervised clustering as well as more complex neighborhood analyses.




### Spatial Immune Profiling with CellScape

Deep immune profiling using VistaPlex panels for the CellScape platform. The Spatial Immune Profiling kit captures complex CD4+ phenotypes with differential FoxP3 and Ki67 expression **(A)** and differential CD45RA/CD45RO expression in CD3+ and CD20+ cell populations **(B)** in human colorectal cancer. Combining the Spatial Immune Profiling Kit with the Tissue Architecture Kit enables detection of CD8+ T-cell activation by expression of GrnB **(C)** and broad immune infiltrate categorization in breast cancer **(D)**.




### End-to-end analysis

High quality segmentation, phenotyping, and spatial analyses using data generated from the CellScape platform. Precise segmentation enabled accurate phenotyping by unsupervised clustering **(A)**, which allowed for the downstream characterization of spatial neighborhoods **(B)** containing multiple cell types of interest in the context of the surrounding microenvironment **(C)**.

# nCounter
## Analysis System


## Single platform, simple multiomics.

Accelerate your biomarker discovery and development with confidence and peace of mind with the nCounter Analysis System. With robust performance on even the most difficult sample types and unparalleled flexibility in content and throughput, you can rapidly translate discoveries into actionable clinical insights.

### Robust Performance

- Gold standard performance on FFPE
- No technical replicates required
- Five logs of dynamic range
- Broad sample compatibility
- No RT or enzymatic steps

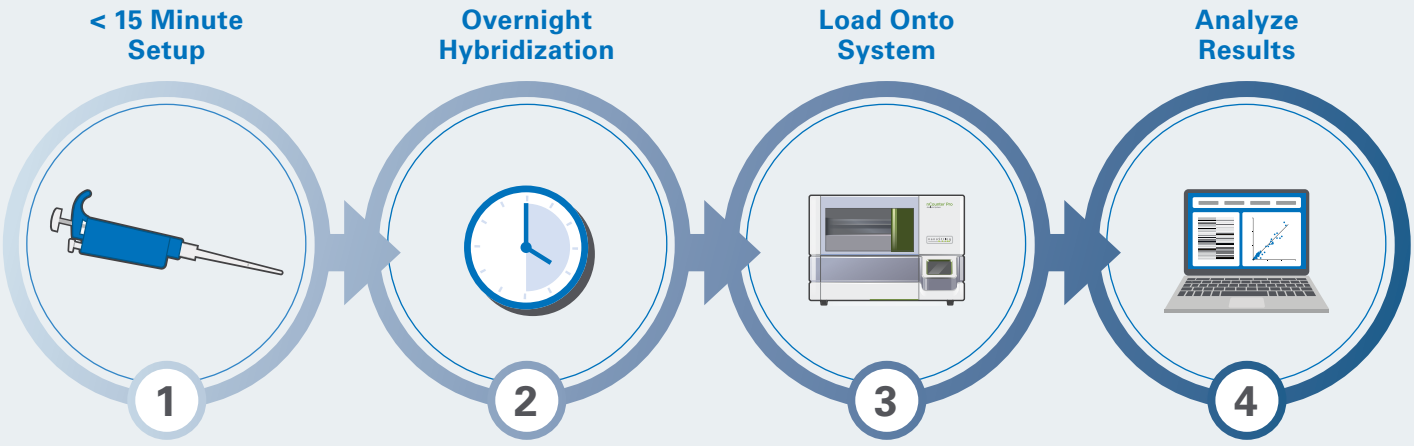
### Flexible Assays

- Extensive ready-to-ship panel menu
- Guided by industry experts and the latest peer-reviewed literature
- Bioinformatics support for custom designs
- Customization of ready-to-ship panels with up to 55 targets

### Efficient Workflow

- Less than 15 minutes hands-on-time
- Go from sample to answer in less than 24 hours
- Highly scalable set-up
- Simplified data analysis
- Minimal data storage required

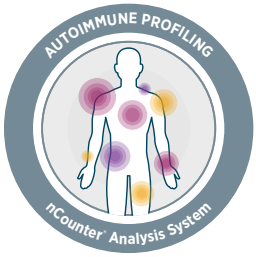
### Four Simple Steps Produce a Huge Amount of Data



# nCounter Immunology Panels

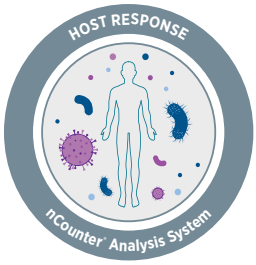
A broad portfolio of expression panels with carefully curated content delivers insights into the role of the immune system in autoimmune disorders, organ transplant rejection, cancer, and infectious disease.

Select nCounter Immunology Panels



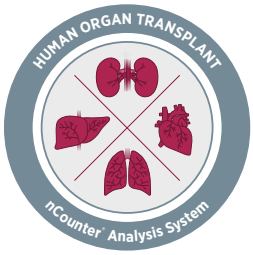

## nCounter Autoimmune Profiling Panel

- Rapidly gain insights into immune dysfunction by profiling 770 human or mouse genes across 35 pathways
- Evaluate the pathways, processes and cell types involved in autoimmune disease, chronic inflammatory disease and immunotherapy-related adverse events
- Cell type profiling feature measures the relative abundance of 14 different immune cell types



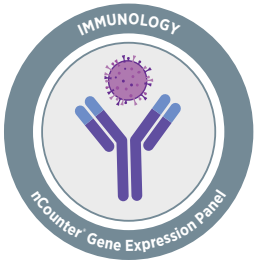

## nCounter Host Response Panel

- Rapidly advance your knowledge of immerging infectious disease by profiling 785 genes in human or mouse samples across 50+ pathways
- Identify and evaluate disease severity biomarkers
- Evaluate the effects of vaccines and therapies
- Cell type profiling feature measures the relative abundance of 14 different immune cell types




## nCounter Human Organ Transplant Panel

- Comprehensively profile 770 genes across 37 pathways involved in immune response to transplanted tissue
- Identify biomarkers for rejection, uncover the mechanisms of tissue damage and study toxicities brought on by immunosuppressive drugs
- Cell type profiling feature measures the relative abundance of 14 different immune cell types




## nCounter Immunology Panel

- Profile over 500 general immunology genes in human or mouse samples
- Includes major classes of cytokines and their receptors, enzymes with specific gene families such as the major chemokine ligands and receptors, interferons and their receptors, the TNF-receptor superfamily, and the KIR family genes
- Includes 84 genes involved with the anti-fungal immune response

## NanoString Signatures

| Tumor Inflammation Signature (TIS) | PAM50 | Lymphoma Subtyping Test (LST) |
|---|---|---|
| An 18-gene signature that measures a pre-existing but suppressed adaptive immune response within the tumor. | An 50 gene signature that distinguishes between breast cancer intrinsic subtypes—Luminal A, Luminal B, HER2-enriched and Basal-like. | An 20 gene signature that determines the Cell-of-Origin (COO) molecular subtypes in diffuse large B-cell lymphomas, activated B-Cells and germinal center B-Cells. |

# GeoMx
## Digital Spatial Profiler

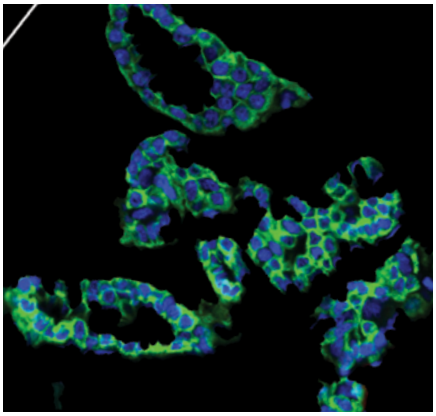
## Confidently advance your multiomic discovery.

### Spatially Profile The Immune Infiltrate With Biology-Driven Segmentation

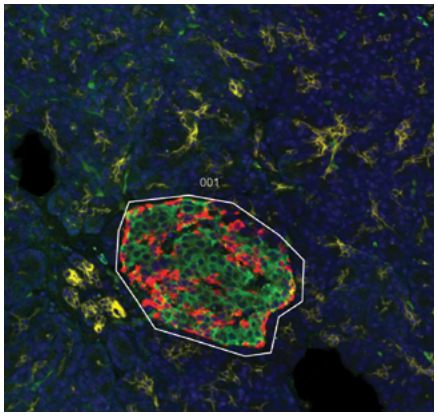
Bridging the gap between tissue imaging and bulk molecular profiling technologies such as RNA-Seq, the GeoMx Digital Spatial Profiler (DSP) allows you to unlock novel biological insights with spatial multiomics in morphologically intact tissue compartments. Detect and add spatial context to biomarkers obscured by bulk expression analysis, spatially profile the immune response to infectious disease, autoimmune disorders, cancer, and transplanted organs, and spatially map the expression patterns and cellular makeup of the immune response in tissue.

### Biology-Driven Profiling

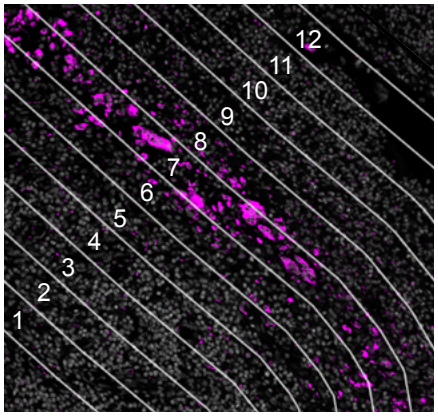
Spatially resolve gene and protein expression from FFPE or fresh frozen tissue sections with flexible profiling strategies that focus on the biology and areas of the tissue that are most relevant to your research questions. Using immunofluorescence staining as a guide to select specific regions and areas of interest, spatially profile the whole human or mouse transcriptome, select RNA and protein targets, or RNA and protein simultaneously.



**Segmentation**




**Geometric Profiling**




**Contour**

# GeoMx Assays for Immunology

## Flexible, Pre-Validated Content For Spatial Profiling

GeoMx RNA and protein assays can be performed separately or together on the same tissue section and include content curated for neuroscience research.

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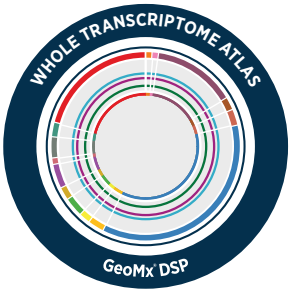
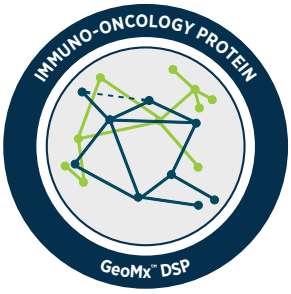



### GeoMx Human and Mouse Whole Transcriptome Atlas

- Comprehensively spatially profile all protein-coding genes from human or mouse samples
- Spike-in up to 400 custom RNA targets including non-coding RNAs, exogenous sequences, and/or viral/bacterial transcripts.
- Superior sensitivity: not reliant on poly-A pulldown
- Uses an Illumina NGS system for readout.


### GeoMx IO Proteome Atlas

- Profile 570+ human proteins involved in the immune response to cancer using virtually all of Abcam's catalog of IHC-compatible antibodies for immuno-oncology research
- Spike-in probes for up to 40 proteins to customize your experiment
- Run as a standalone panel or in conjunction with the GeoMx Human Whole Transcriptome Atlas using our Spatial Proteogenomics workflow




### GeoMx Immuno-Oncology Protein Panels

- Take advantage of curated content that includes up to 96 probes for protein targets involved in immune activation, MAPK signaling, PI3K/AKT signaling, cell death, and the mechanism of action for immuno-oncology drugs.
- Use a universal human or mouse core module and add-on up to 6 modules each containing probes for up to 10 protein targets
- Customize by adding 5-10 targets
- Readout using the nCounter Analysis System (up to 96 plex)


### Coming soon: GeoMx Discovery Proteome Atlas

- Profile over 1000 human proteins with the highest-plex spatially resolved proteomics assay ever developed
- Detect over 100 post-translational modifications
- Pathways targeted include those relevant to oncology, immunology, neuropathology, and neuroinflammation

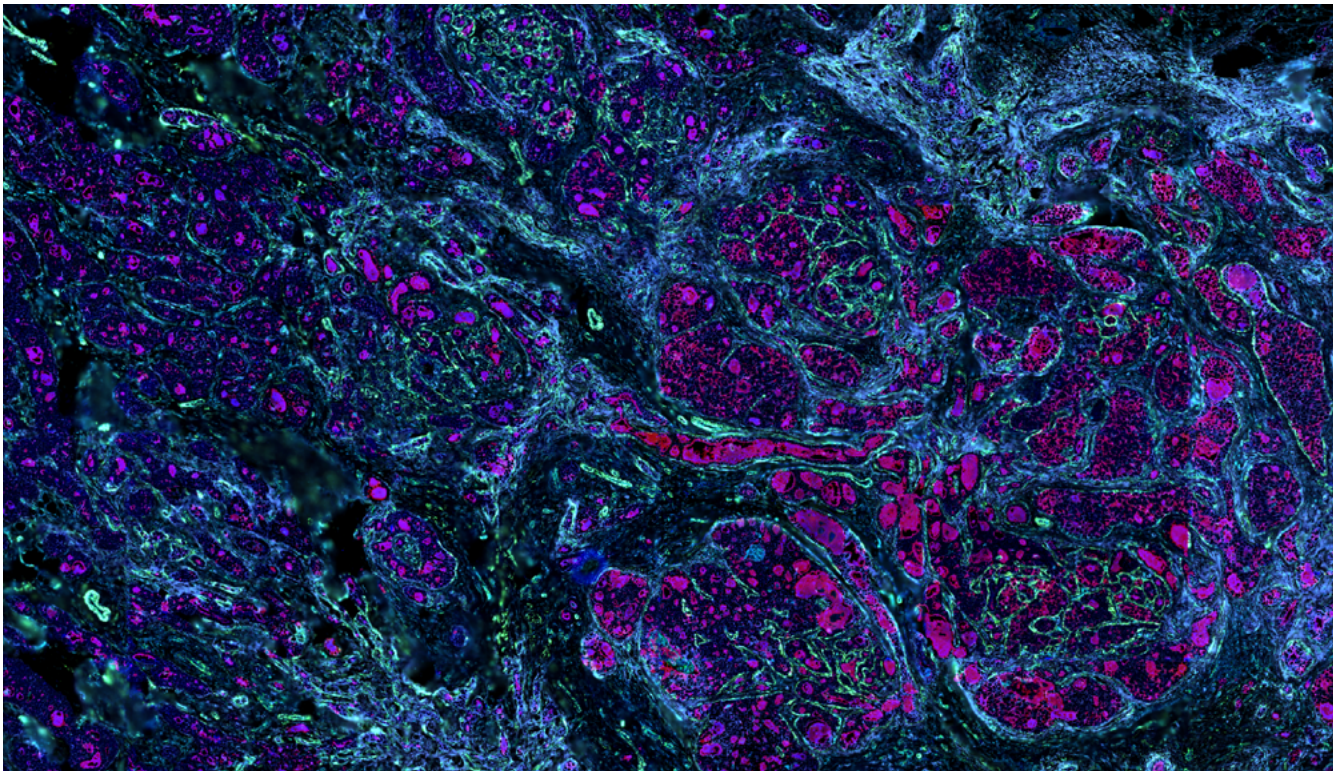
# CellScape

## Precise Spatial Proteomics Platform


## Quantitative, high-resolution imaging of spatial proteomics.

CellScape features high-quality optical performance, integrated fluidics for walk-away automation, and flexibility in assay design. Supported by high dynamic range imaging, the CellScape platform can detect both high- and low-expressing biomarker targets simultaneously.

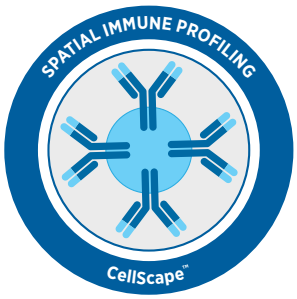
Sample preparation is simple: the CellScape™ Whole-Slide Imaging Chamber converts a standard microscope slide into a microfluidic device for staining, imaging, and safe sample storage. The CellScape staining and imaging technology is compatible with commercially available fluorescently labeled antibodies, circumventing the need for proprietary antibody conjugation and complex assay validation.



**Learn more about CellScape at www.brukerspatialbiology.com/cellscape**

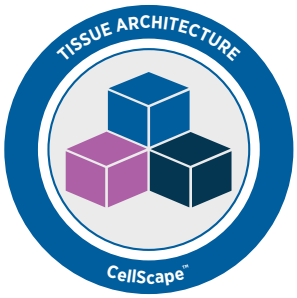
# VistaPlex Assays for Immunology Research

Biomarker detection can be jumpstarted using VistaPlex™ Multiplex Assay Kits: modular antibody panels with optimized protocols. Combine the assay kits together or add your own antibodies to conveniently investigate your sample with the right biomarkers for your immunology research needs. The assay kits are rigorously validated to ensure consistent performance across samples.



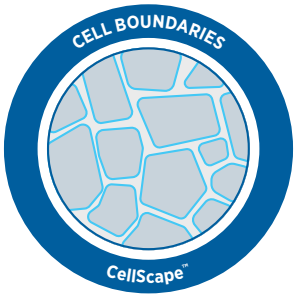

## Spatial Immune Profiling Assay Kit

The Spatial Immune Profiling Kit enables detection of 14 phenotypic biomarkers that define key immune cell populations and subpopulations in human FFPE samples. This panel is optimized for ease of use and throughput in immuno-oncology research. This assay kit consists of antibodies targeting CD20, CD3, CD279, CD274, FoxP3, CD4, CD45, CD19, Granzyme B, CD8, CD45RO, CD38, Ki-67, CD68, CD45RA, PanCK, and CD163.




## Tissue Architecture Assay Kit

Providing a modular building block for identification of key structural features of human FFPE samples, the Tissue Architecture Assay Kit includes a panel of antibodies targeting epithelial, lymphatic, lamina, vasculature and connective tissue biomarkers and can be expanded by pairing with additional VistaPlex assay kits. This panel consists of antibodies targeting CD138, SMA, CD31, Collagen IV, Podoplanin, Beta-catenin, CD34, E-Cadherin, Vimentin, MUC1, CD105 and EpCAM.




## Cell Boundaries Assay Kit

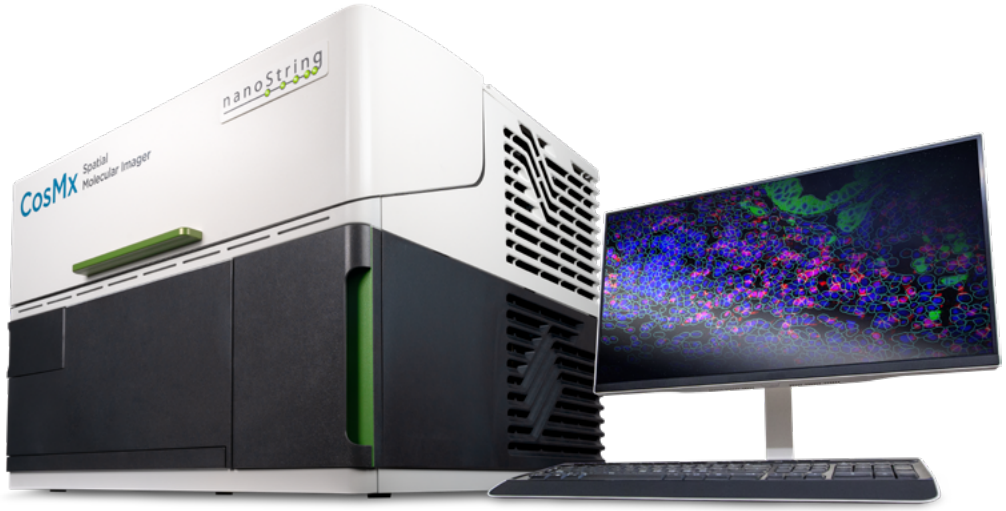
Enable robust delineation of cell boundaries across diverse tissue types and improve accuracy of segmentation and downstream quantitative spatial phenotyping with these markers. This panel includes antibodies against ATP1A1 (plasma membrane), Lamin B1 (nuclear envelope), and B2M (cytoplasm), along with the nuclear dye Sytox™ Orange.


## Fresh Frozen Immune Profiling Assay Kit

Achieve fundamental spatial immunophenotyping of the tumor microenvironment in human fresh frozen tissue sample using the Fresh Frozen Immune Profiling Assay Kit. This panel consists of antibodies targeting HLA-DR, CD56, CD45RA, CD8, CD123, CD14, CD20, CD4, CD27, CD45, Pan-cytokeratin, CD11c, and CD3.

# CosMx

## Spatial Molecular Imager

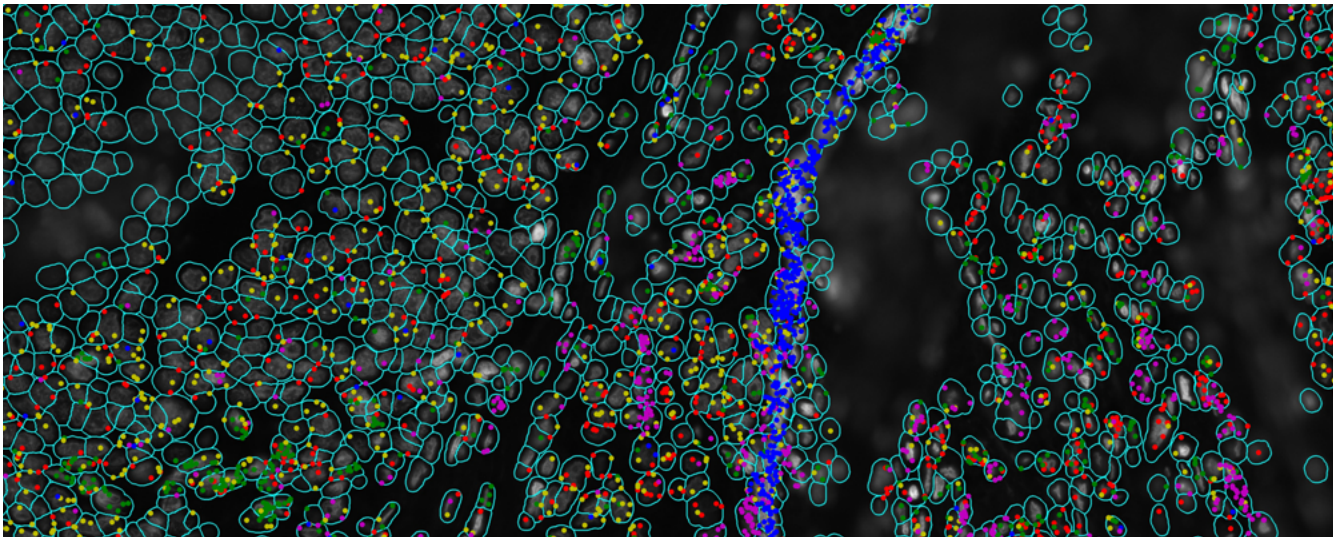



## High-fidelity, single-cell spatial exploration at the highest plex.

Single-cell spatial analysis, facilitated by the CosMx SMI, allows researchers to delve deeper into the function and behavior of individual cells, paving the way for groundbreaking discoveries and new therapies in the field of immunology. The CosMx SMI enables the comprehensive mapping of the expression of 50+ proteins and the whole human transcriptome to individual cells in their native environment, extracting profound biological insights and allowing you to study the cellular and molecular basis for health and disease.

### Uncover Single-cell and Subcellular Insights

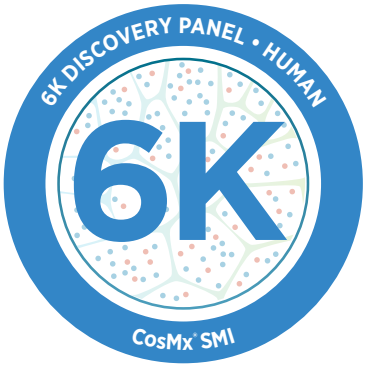
With superior cell segmentation utilizing multi-analyte markers and a machine learning algorithm, the CosMx SMI visualizes immune infiltration and corresponding changes within cells leading to immune evasion. This technology supports cell typing and pathway analysis, resolving cell state, function, ligand-receptor interactions, and cell signaling. Additionally, this technology provides a deeper understanding of the proteomic landscape of tissue samples, identifying new biomarkers and therapeutic targets for numerous disorders.



# CosMx Assays for Immunology Research

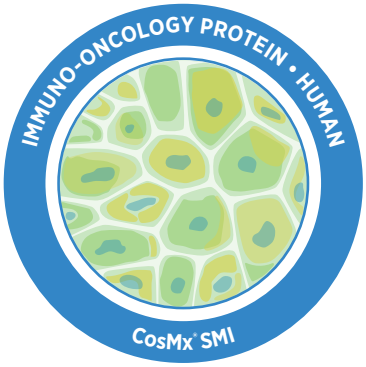

### CosMx Human Universal Cell Characterization Assay

Get robust cell typing data and analyze cell-cell interactions with the CosMx Human Universal Cell Characterization Assay. Spatially profile the expression of 1000 highly curated targets at subcellular resolution and customize with up to 50 custom targets. Identify up to 100 unique ligand-receptor pairs that contribute to all aspects of tumorigenesis.




### CosMx 6K Human Discovery Assay

Accelerate your single cell spatial transcriptomics with this fully validated, 6K plex RNA Assay, with simple sample preparation, an easy-to-use and reliable spatial multiomics platform and streamlined data analysis.




### CosMx Protein Assays

Get a complete picture of the expression changes that occur in cancer with the CosMx Protein Assays and single cell, high-plex analysis of up to 68 proteins from a single FFPE slide. Gain a deeper understanding of the proteomic landscape of tumor biopsies and identify new disease indicators and therapeutic targets.


### CosMx Human Whole Transcriptome Assay (WTX)

Reveal complete biology with subcellular whole transcriptome imaging for uncharted discoveries.  With CosMx WTX, project complete pathway biology in space, map every cell-to-cell interaction at the individual transcript level, and discover the unknown and unexpected—all with best-in-class sensitivity and genomic breadth within a single intact FFPE tissue section.

# Integrating Platforms

## Across the Immunology Research Continuum

By offering a portfolio of complementary solutions that span the entire immunology research continuum, Bruker Spatial Biology provides innovative tools that enable a multiomic, holistic view of immunology. This deeper understanding of both the systemic and local immune response of the innate and adaptive immune response and the impact of different immune cell expression programs can be applied to multiple stages of immunology research, from discovery to pre-clinical models, translational research, and clinical trials.

### Key Applications

| Immune Response to Disease | Translational Research | Clinical Studies | Mechanisms of Infection | Preventing Organ Rejection |
|---|---|---|---|---|
| ▪ Understand innate and adaptive immune cell activation, function and malfunction<br>▪ Understand essential checkpoints involved in immune response<br>▪ Uncover new ways to modulate the immune response<br>▪ Dampen the overactive immune response in autoimmune disorders (T1D, RA, MS, Lupus) and/or allergens | ▪ Define mechanisms of disease and the cell types involved<br>▪ Study signaling pathways involved in disease<br>▪ Develop vaccines<br>▪ Discover targets for therapeutics<br>▪ Explore how to reverse disease<br>▪ Understand the onset of an immunotherapy-induced adverse event | ▪ Monitor clinical samples<br>▪ Stratify patients for clinical trials<br>▪ Evaluate vaccine effectiveness<br>▪ Develop signatures to predict responders to therapies<br>▪ Monitor/mitigate treatment toxicities<br>▪ Assess risk factors | ▪ Understand disease progression and severity<br>▪ Understand mechanisms of infection (e.g., COVID, HIV, EBV)<br>▪ Neutralize and eliminate foreign invaders<br>▪ Develop biomarkers of disease severity<br>▪ Study the effects of co-morbidity<br>▪ Understand disease progression and severity | ▪ Understand mechanisms of organ rejection<br>▪ Understand mechanisms of tissue damage<br>▪ Develop biomarkers and signatures pre- and post- transplant<br>▪ Study immune checkpoints involved in organ rejection<br>▪ Understand the difference between viral infection and organ rejection |

# Data Analysis

## Options for Discovery and Decision Making

Having access to a comprehensive range of analysis tools and services transforms your valuable data to bring test hypotheses, and deliver publication-quality results. Expedite analysis and accelerate discoveries with on-system data analysis tools, secure cloud-based platforms, expert bioinformatics support, and data analysis services.


### ROSALIND

- Cloud-based analysis tool
- Secure platform with flexibility for internal or external collaboration
- T Cell Receptor (TCR) Diversity Analysis

### nSolver Analysis Software

- On-premises analysis tool
- Available at no charge
- Advanced Analysis Module for additional statistics

### GeoMx DSP Data Analysis suite (DSPDA)

- On-instrument
- Data visualization and analysis

### GeoScript Hub Open-Source Software

- Developed by Bruker Spatial Biology R&D
- Supplements capabilities of DSPDA

### A comprehensive cloud platform for single-cell spatial analysis that scales to any plex and throughtput on CosMx SMI.

### Tunable machine-learning cell segmentation tool kit

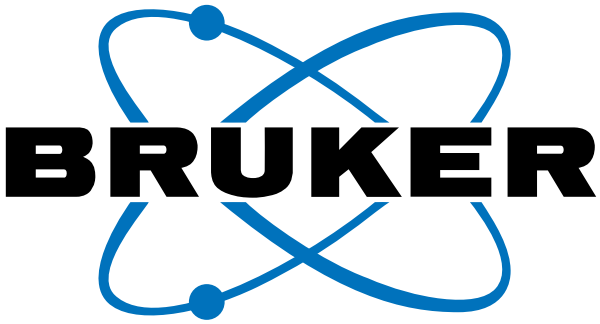
- Multi-sample and iterative analytics suite
- New single-cell spatial algorithms
- Open source portable and flexible data formats

### Data Analysis Service

- nCounter differential gene expression data fully analyzed
- Interpreted by a Bruker scientist inclusive of a consultative reportout.

### Spatial Data Analysis Service (sDAS):

- Work one-on-one with Bruker Spatial Biology computational biologists
- Fully interpreted GeoMx data to answer biological questions.

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