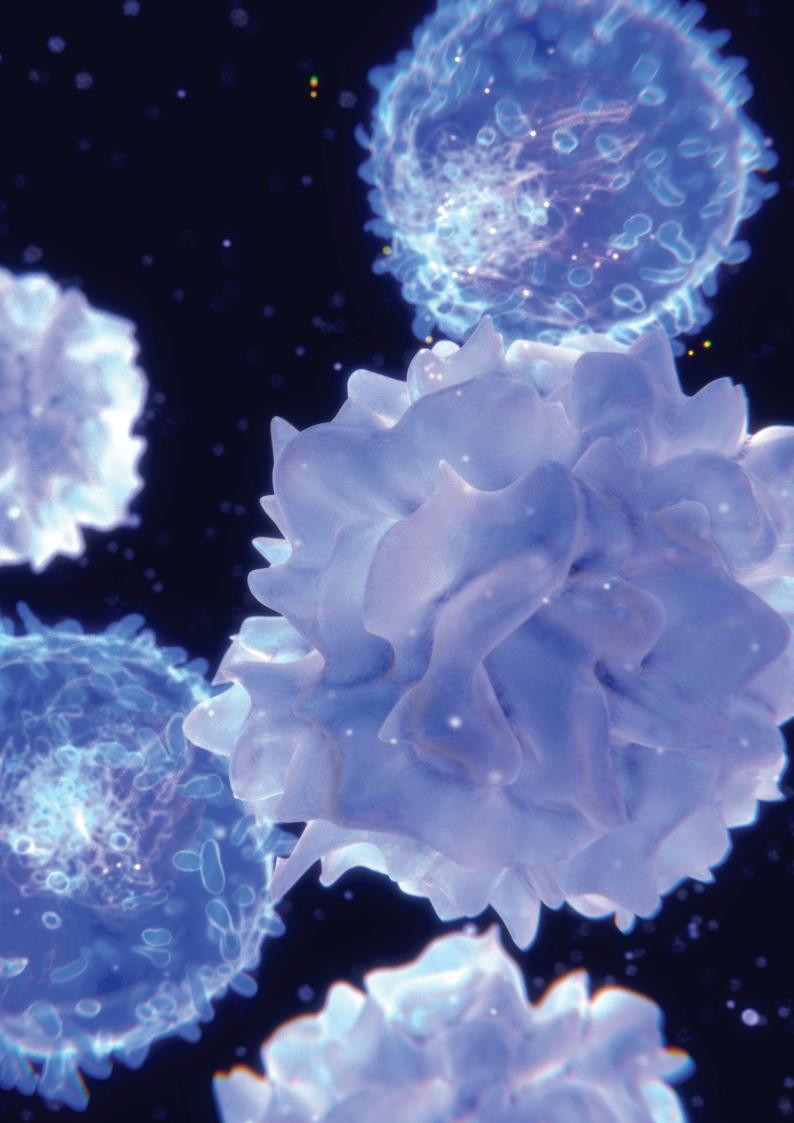
Immunology and Infectious Disease Solutions

Autoimmune Disease • Organ Transplant Immuno-Oncology • Infectious Disease

The CosMx^{IM} SMI and decoder probes are not offered and/or delivered to the Federal Republic of Germany for use in the Federal Republic of Germany for the detection of cellular RNA, messenger RNA, microRNA, ribosomal RNA and any combinations thereof in a method used in fluorescence in situ hybridization for detecting a plurality of analytes in a sample without the consent of the President and Fellows of Harvard College (Harvard Corporation) as owner of the German part of EP 2 794 928 B1. The use for the detection of cellular RNA, messenger RNA, microRNA, ribosomal RNA and any combinations thereof is prohibited without the consent of the President and Fellows of Harvard College (Harvard Corporation).

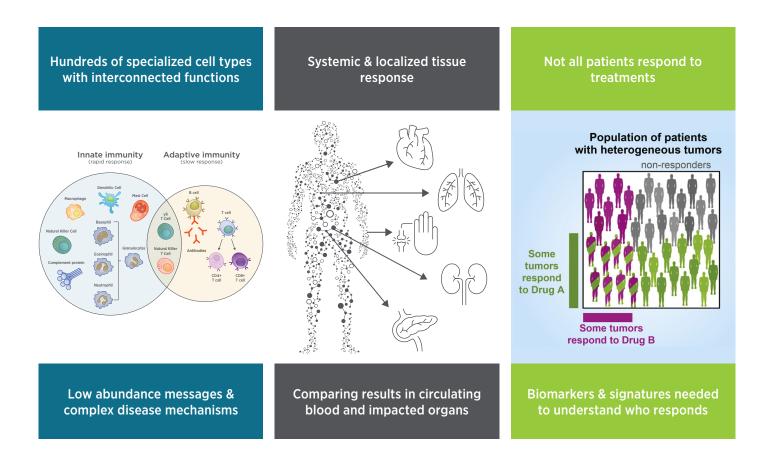


Challenges in Immunology Research

We have only just begun to understand how to harness the power of the immune system to help fight disease.

The immune response plays a role in almost every disorder, and characterizing the complexities of the immune response is key to understanding disease pathogenesis for autoimmunity, organ rejection, cancer, and infectious disease.

Studying the immune system can be challenging due to the sheer number of different cell types involved and the variable response between different individuals. Making meaningful discoveries involves getting a holistic view of both the systemic and localized immune response. Translation of results to the clinic requires reliable preclinical models which don't always correlate to human studies, and better biomarkers are needed that predict treatment response.



NanoString's 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.

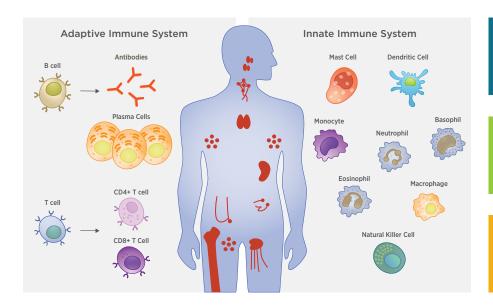
Wherever you are headed with your immunology research, NanoString can get you actionable insights from FFPE, fresh frozen tissue, cell lysates, and biofluids.

- 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)

Creating a Framework

Creating a Framework for 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

A Holistic View of Immunology Across Multiple Dimensions

NanoString's collection of panels and assays across all three of our platforms delivers a family of multiplex gene and protein expression assays for bulk and spatial analysis that support basic and translational studies. Curated content for autoimmune disease, organ transplant, immuno-oncology, and infectious disease enables you to gain a holistic understanding of the function and molecular biology of the systemic and localized innate and adaptive immune response.



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 better understand the role of the immune system in disease onset, progression, and/or treatment response, NanoString has you covered with a trio of platforms.

Unlock the secrets of the immune response with research tools that allow you to profile gene and protein expression in a variety of sample types at different scales from the subcellular to single-cell level and beyond.



nCounter® Analysis System

Pathway-based gene expression profiling of 800+ targets in a single tube. Compatible with a full spectrum of sample types.



GeoMx[®] Digital Spatial Profiler

Spatial profiling of the whole transcriptome and 100s of protein targets from FFPE and fresh frozen tissue



CosMx[™] Spatial Molecular Imager

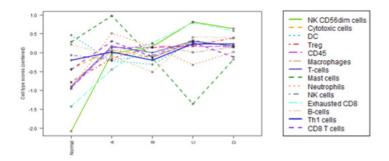
Single-cell profiling of RNA and proteins with subcellular resolution from a single slide.

- 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
- 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
- Study the localized immune response to infectious disease in different organs
- Characterize the mechanism of action of drug treatments and vaccinations
- Discover and validate spatial biomarkers for disease onset, progression, and treatment response

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

Immune Cell Type Profiling

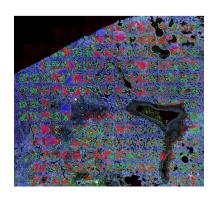
Select nCounter panels feature genes that provide unique cell profiling data to measure the relative abundance of different immune cell types. To date, 14 different immune cell types have been identified by their gene signatures for inclusion in nCounter panels. The genes were qualified through biostatistical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

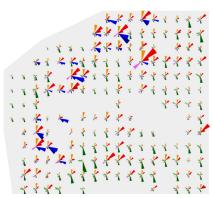


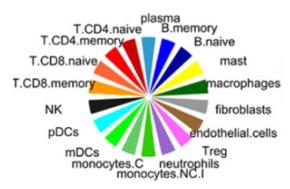
Cell Type	Gene(s)	Cell Type	Gene(s)
B Cells	BLK. CD19, FAM30A, FCRL2, MS4A1, PNOC, SPIB, TCL1A, TNFRSF17	Mast Cells	CPA3, HDC, MS4A2, TPSAB1/B2
CD45	PTPRC	NK CD56dim Cells	IL21R, KIR2DL3/4, KIR3DL1/2
CD8 T Cells	CD8A, CD8B	NK Cells	NCR1, XCL1/2
Cytotoxic Cells	CTSW, GNLY, GZMA, GZMB, GZMH, KLRB1, KLRD1, 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

nCounter Cell Type Profiling Genes Provide Unique Cell Profiling Data to Measure the Relative Abundance of 14 Different Immune Cell Types

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 the NanoString website 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.







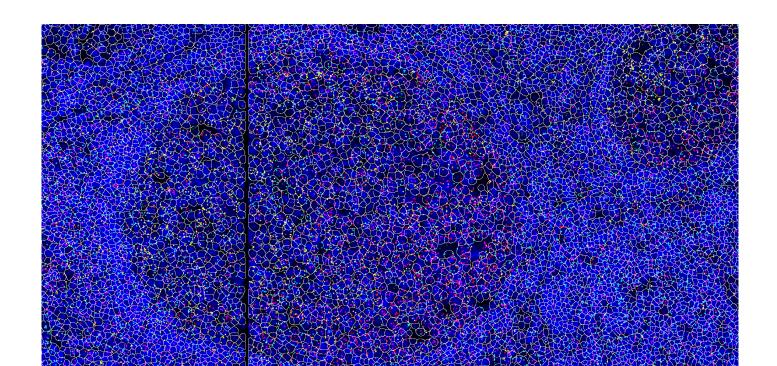
Abundance estimates of 18 different immune cell types within 191 regions of interest in a tumor section made from GeoMx Whole Transcriptome Atlas data using the SpatialDecon script. Cell counts are proportional to the wedge size of each color. Figures reproduced with permission from Danaher et al. Nat Commun 13, 385 (2022) under the Creative Commons License.

SPOTLIGHT ON SUCCESS



"With NanoString we gained vital data and, for the first time ever, we were able to see what is happening immunologically in defined regions of the tissue. This data, enabled by NanoString's 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. NanoString's 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





Gene Expression You Can Count On

Accelerate your immunology research with confidence and peace of mind with the <u>nCounter Analysis System</u>. Confidently profile gene expression in biofluids and tissues to assess the systemic immune response in health and disease. Robustly detect even low expressing immune response genes. Identify biomarkers or develop novel therapeutics using a platform with unparalleled flexibility in both content and throughput. With the nCounter Analysis System you can rapidly translate discoveries into actionable insights that help you better understand the immune system.

Robust Performance

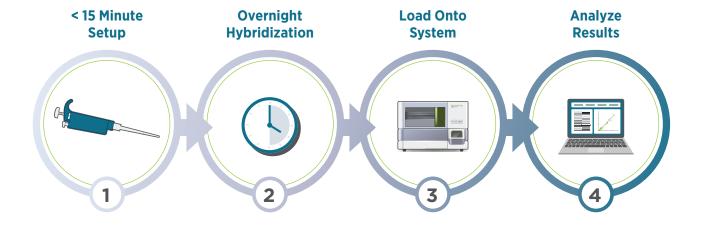
- Gold standard performance even on difficult sample types
- No technical replicates required
- · Five logs of dynamic range
- · Broad sample compatibility
- No RT or enzymatic steps

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
- Compatible as a readout for spatial biology assays

Efficient Workflow

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



nCounter Immunology Panels

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



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



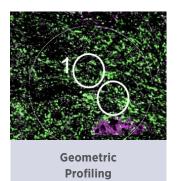
Resolve the Heterogeneity of the Localized Immune Response

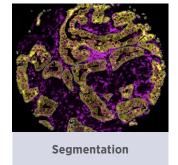
Spatially Profile The Immune Infiltrate With Biology-Driven Segmentation

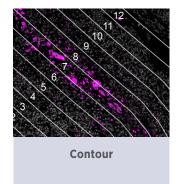
Bridging the gap between tissue imaging and bulk molecular profiling technologies such as RNA-Seq, the <u>GeoMx®</u> <u>Digital Spatial Profiler (DSP)</u> allows you to unlock novel biological insights with spatial multiomics in morphologically intact tissue compartments. Detect and add spatial context 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.







GeoMx Assays for Immunology

Flexible, Pre-Validated Content For Spatial Profiling

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



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 immunooncology 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)



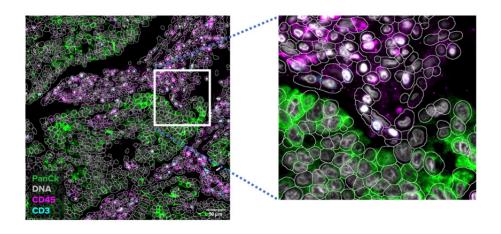
Highest-Plex, Single-Cell And Subcellular Spatial Multiomics

As immunology research progresses, the significance of comprehending the intricacies of individual cells and their interactions becomes increasingly evident, whether you are studying the immune response to infectious disease, autoimmune disorders, transplanted organs, or cancer. 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 over 6000 RNAs 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.

Get More Accurate Cell Segmentation With Dedicated Cell Membrane And Nuclear Markers



CosMx Assays for Immunology Research



CosMx 6K Human Discovery Panel

The CosMx 6K Human Discovery Panel can accelerate single cell spatial transcriptomics research with this fully validated, 6K plex RNA panel, with simple sample preparation, an easy-to-use and reliable spatial platform and streamlined data analysis. Measure 6000 RNA targets with best-in-class cell segmentation and customize with up to 200 additional RNA targets.



CosMx Human Universal Cell Characterization Panel

The CosMx Human Universal Cell Characterization Panel is designed to provide robust cell typing and cell-cell interaction analysis among other applications in a wide range of tissues and disease states. Profile expression of 1000 highly curated targets at subcellular resolution and customize with up to 50 custom targets.



CosMx Human Immuno-Oncology Protein Panel

The Human Immuno-Oncology Protein Panel enables high-plex analysis of up to 68 proteins from a single FFPE slide with spatial context at single-cell resolution, providing a deeper understanding of the proteomic landscape of tissue and identifying new biomarkers and therapeutic targets. The panel offers researchers a unique view of the spatial protein expression for the immune response, enabling cell profiling of immune and non-immune cells, including T cells, B cells, macrophages, NK cells, epithelia and stroma.

Integrating Platforms

Across the Immunology Research Continuum

By offering a portfolio of complementary solutions that span the entire <u>immunology research continuum</u>, NanoString 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.

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



Options for Discovery and Decision Making

Having access to a comprehensive range of analysis tools and services transforms your valuable data to bring insights, 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 NanoString R&D
- Supplements capabilities of DSPDA



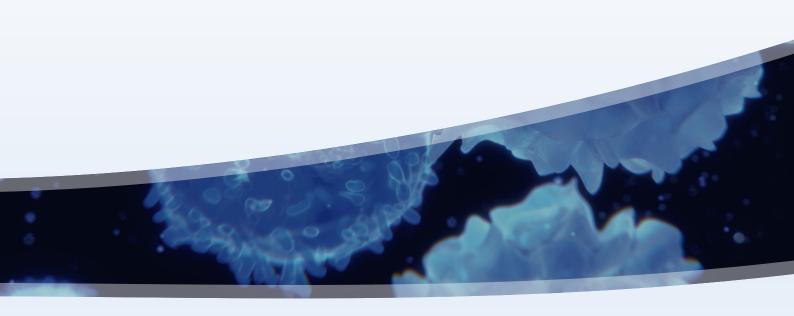
- A cloud-based, integrated informatics platform for spatial biology
- Analyze and visualize, large amounts of spatial multiomics data
- Preset analysis modules and pipelines
- Advanced analytics support global data sharing and collaboration



Spatial Data Analysis Service (sDAS):

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





For more information, please visit nanostring.com/immunology

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