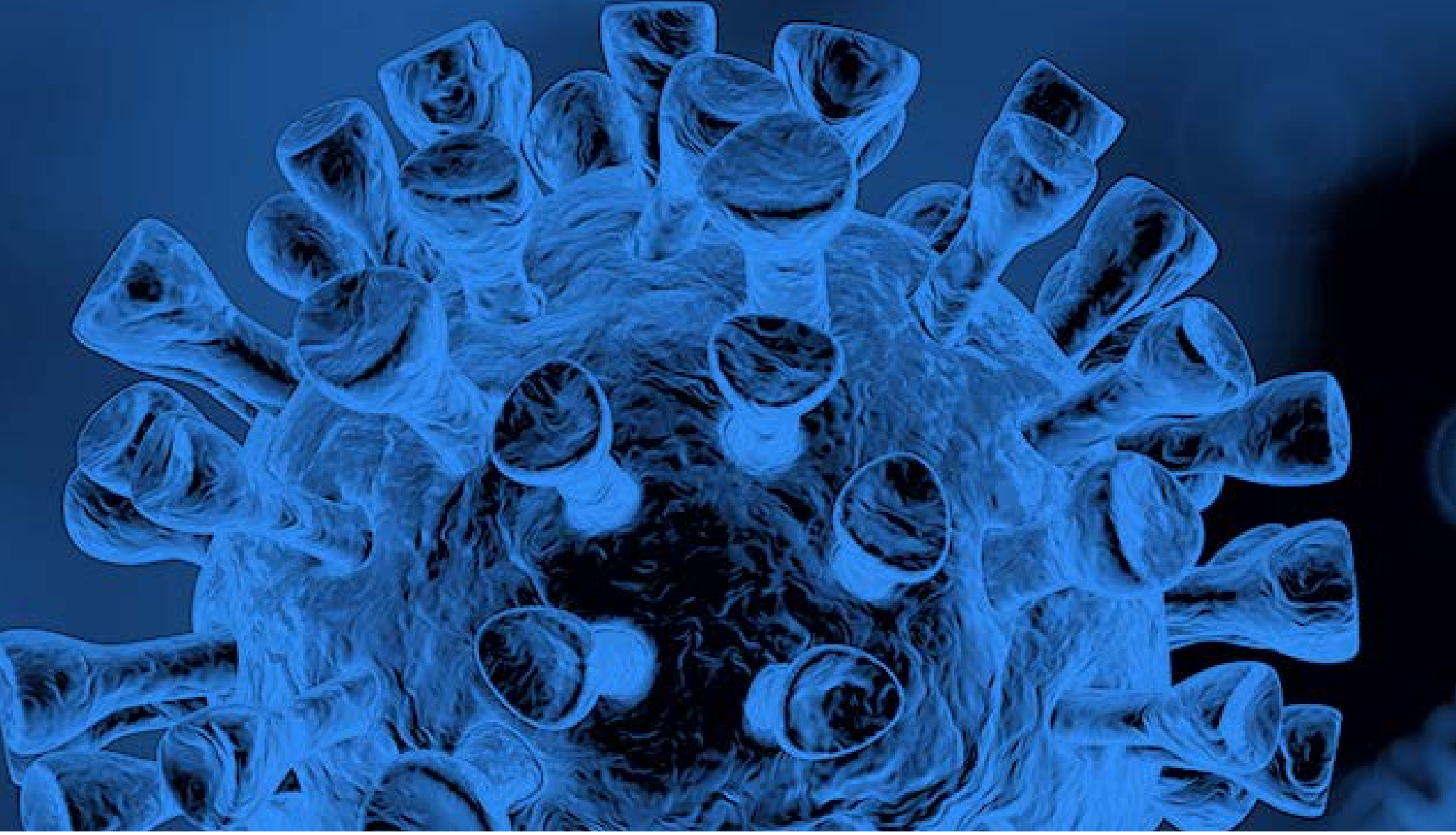
PRODUCT GUIDE

Research Solutions for COVID-19



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nanoString®

Table of Contents

Introduction

nCounter® Gene Expression Assays

a. nCounter Host Response Panel

   i. COVID-19 Tissue Reference Gene List

   ii. Coronavirus Panel Plus

   iii. Human and Mouse Tissue Gene Lists

b. Complete Toolbox of nCounter Gene Expression Panels for Infectious Disease

GeoMx® Digital Spatial Profiling Assays

a. RNA: GeoMx Whole Transcriptome Atlas

b. Protein: GeoMx Immune Cell Profiling Core + 5-antibody custom COVID-19 module

On-Demand COVID-19 Technical Webinars

NanoString COVID-19 Publications

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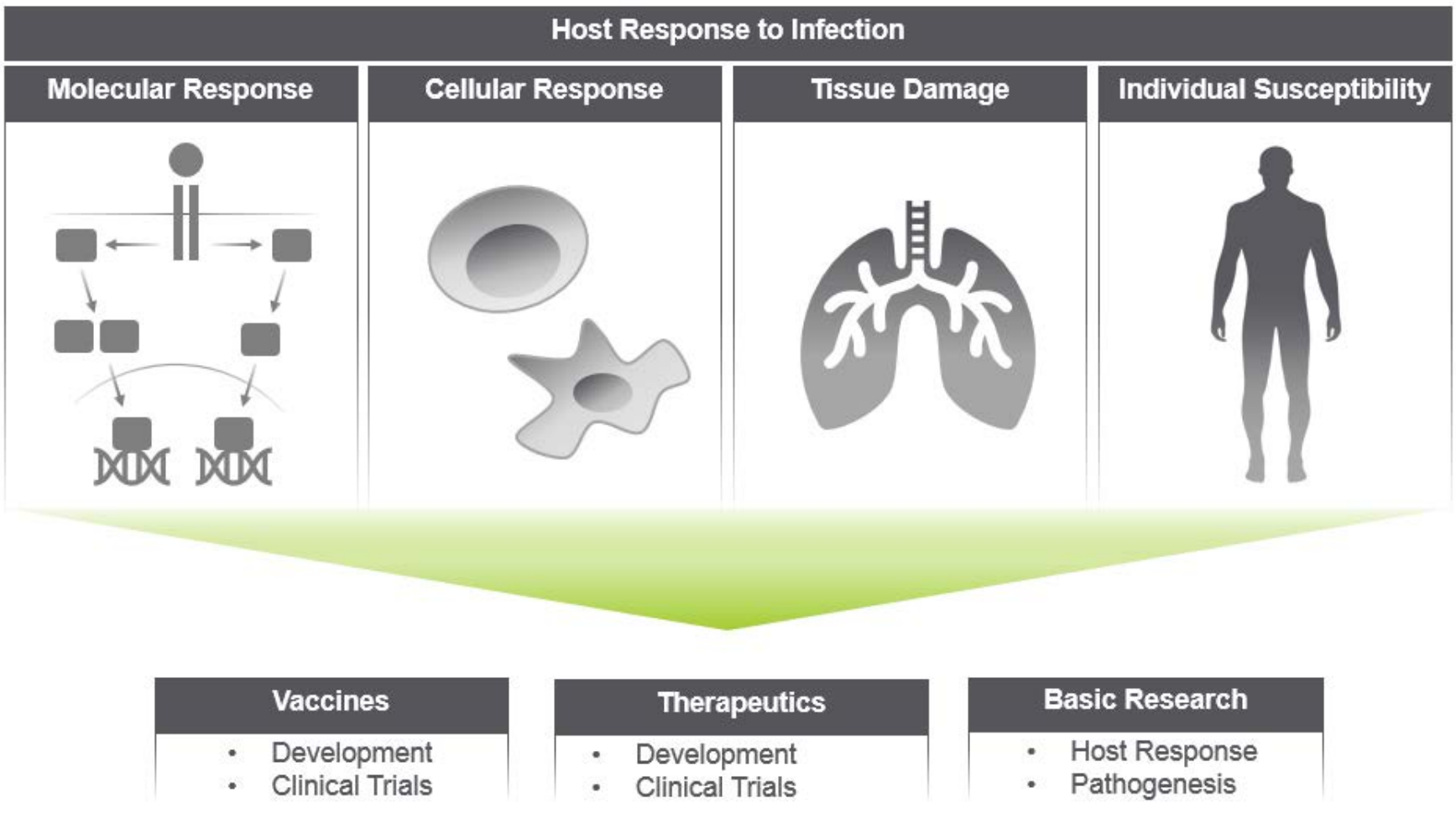
NanoString Technologies Research Solutions for COVID-19

NanoString is committed to advancing scientific understanding of the impact of the coronavirus SARS-CoV-2 on human health worldwide. As many of our customers shift their work to addressing urgent needs around therapeutic & vaccine development, and studying viral pathogenesis, we are joining them in this effort.

NanoString offers a broad range of high-plex gene expression panels enabling research on pathogenesis and the host response. In several recently published studies, nCounter® gene expression assays such as the **Immunology Panel** and **Inflammation Panel** have been used to describe the dynamic and varied host response that shapes the progression of COVID-19. Building on this success, NanoString has created the 785-plex **Human and Mouse nCounter Host Response Panel** as well as a Coronavirus Panel Plus spike-in, enabling measurement of the SARS-CoV-2 virus, additional human coronaviruses, and the human ACE2 receptor RNA in addition to the measurement of host immune response genes. The Coronavirus Panel Plus can be spiked-in to any gene expression panel, expanding the range of biology that can be studied with COVID-19 samples.

The **GeoMx® Digital Spatial Profiler (DSP)** enables simultaneous high-plex spatial analysis of pathogens and the host response with FFPE or fresh frozen tissue. The **GeoMx Whole Transcriptome Atlas** plus custom content facilitates spatial studies of the SARS-CoV-2 virus and host response with >18,000 human RNA targets. The **COVID-19 GeoMx-formatted Antibody Panel** developed in partnership with Abcam is a five-antibody custom spike-in assay that can be run alongside GeoMx protein assays. The panel includes SARS-CoV-2 viral markers and the ACE2 receptor, among other receptors, proteases, cell markers, and viral response markers, and is available through Abcam.



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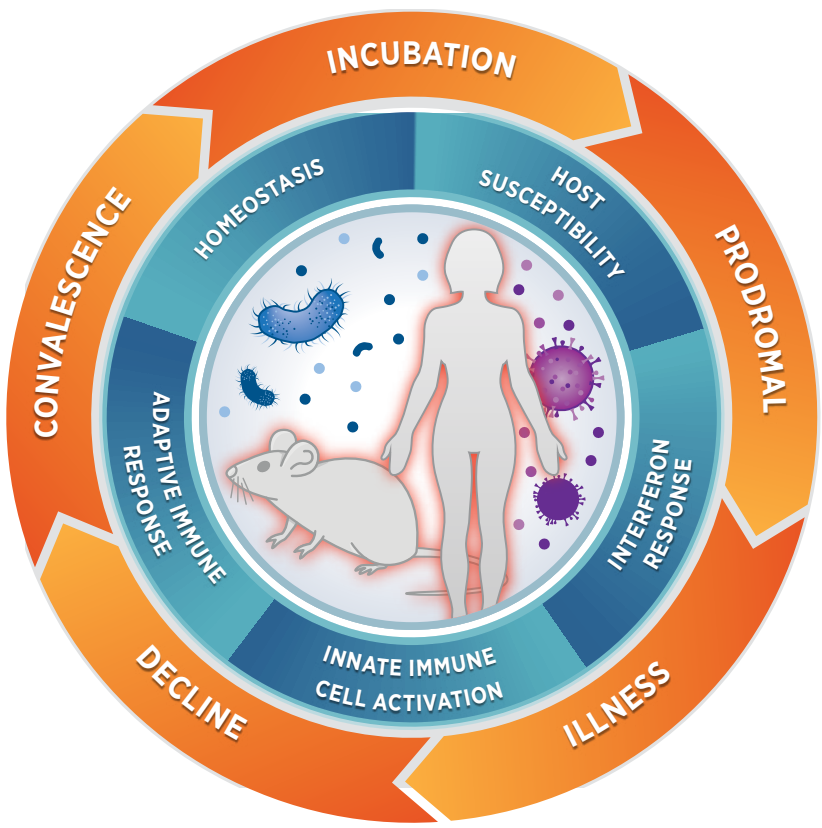
nCounter Host Response Panel

The 785-plex **nCounter Host Response Panel** contains probes for human or mouse genes involved in the host response to pathogens. Best suited for use with blood samples, but compatible with other sample types, the Host Response Panel covers the five stages of infection: incubation, prodromal period, peak illness, decline, and convalescence, with probes for genes involved in the innate and adaptive immune response, interferon signaling, host susceptibility, and homeostasis. The panel includes NanoString's unique immune cell typing signatures for quantifying the relative abundance of 14 different immune cell types, and data from the panel can be easily analyzed in minutes with either **nSolver™ Data Analysis Software** or the cloud-based **ROSALIND® platform**. The panel is ideally suited for use with the Coronavirus Panel Plus to study SARS-CoV-2 but can be used alone or with a user-defined Panel Plus to study different types of pathogens.



Customize the Host Response Panel, or any Gene Expression Panel of your choice:

Customize your research project by adding tissue or pathogen-specific probes to the Host Response Panel with a 55-gene **Panel Plus**. Mix and match transcripts from the pathogen of your choice and additional host tissue markers to study the host response in particular organs.

Add the off-the-shelf 20-gene **Coronavirus Panel Plus** to study SARS-CoV-2 and other coronaviruses or build your own Panel Plus gene list with transcripts specific for different tissue types.

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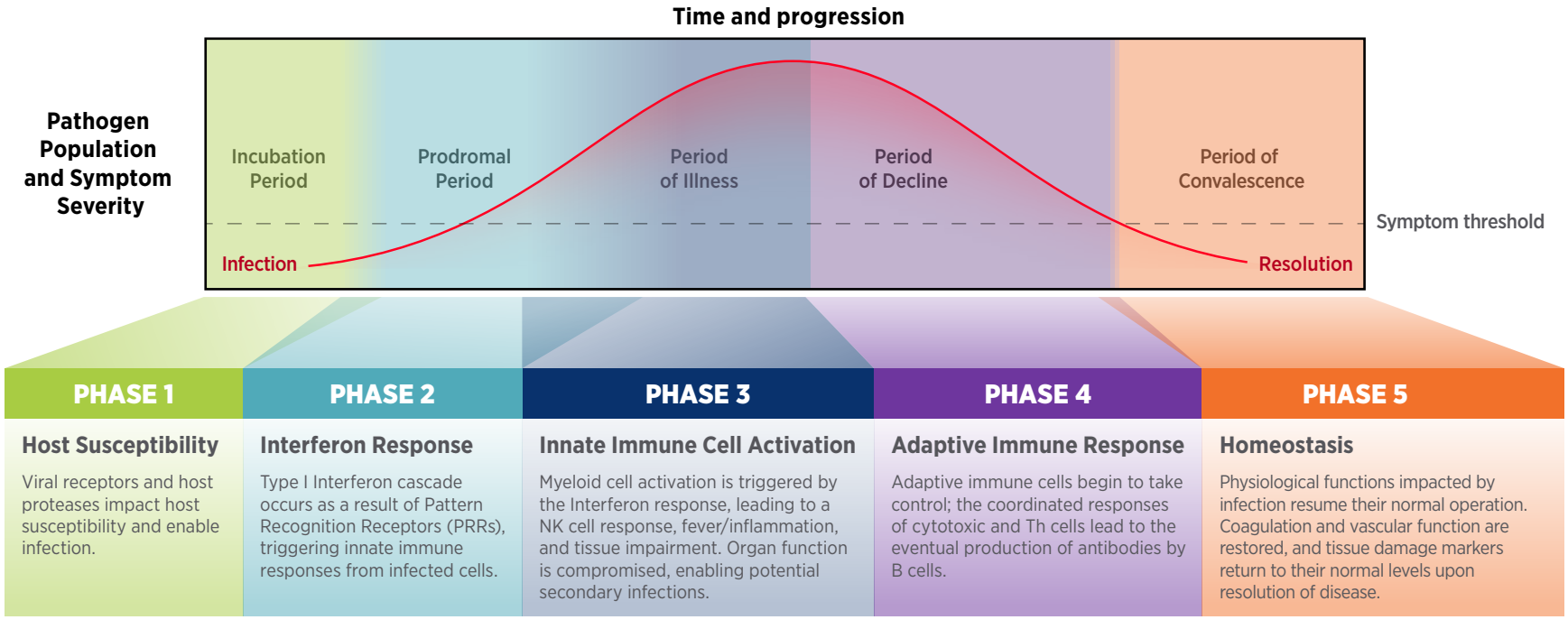
Biological Framework of the Host Response Panel



COVID-19 Tissue Reference Gene List

Add up to 55 tissue relevant genes as a Panel Plus to the Host Response Panel or add custom targets to a GeoMx DSP assay to study organ damage wrought by COVID-19. **Download** the COVID-19 Tissue Reference Gene List to get ideas on which genes to add to study the effect of COVID-19 on the kidney, GI tract, heart, liver, endothelium, lung, and brain. Check back often for updates as the NanoString Bioinformatics team continually adds to and refines these reference gene lists. The content is mined from publications and represents tissue genes associated multiple times in the literature with COVID-19, as well as the top ten genes associated with each tissue. The rationale for each gene's inclusion and its presence or absence in the Host Response Panel is noted. Listed genes can be used alongside any nCounter gene expression panel or GeoMx RNA assay; please contact Bioinformatics for more information on which genes may already be present in a given assay of interest.

Coronavirus Panel Plus

The Coronavirus **Panel Plus** product can be added as a spike-in to nCounter Gene Expression panels and/or **Custom CodeSets**.

The nCounter Coronavirus Panel Plus includes 9 probes targeting the SARS-CoV-2 virus, 1 probe for the human gene encoding the viral receptor ACE2, and probes targeting the N and S ORFs of HCoV-229E, HCoV-HKU1, HCoV-NL63, HCoV-OC43, and SARS-CoV. The probes for the SARS-CoV-2 virus were designed to the reference sequence, Wuhan-Hu-1 (NC_045512), and one probe targets the negative strand of the viral genome.

Download the Coronavirus Panel Plus Gene List.

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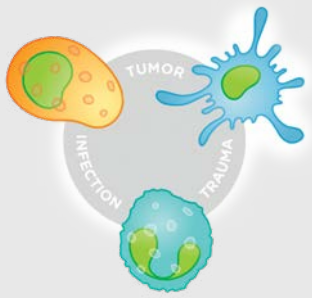
Complete Toolbox of nCounter Gene Expression Panels for Infectious Disease

The **NanoString Panel Pro** panel selection tool can be used to browse our catalog of inventoried and made-to-order panels by name, application area, biologic pathway/process, or gene name(s). Upload your own gene lists to find the panel that best matches your selection or compare gene coverage across multiple panel types.

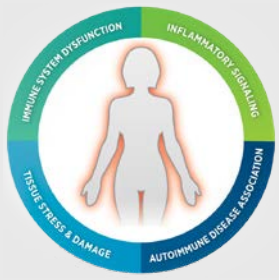
Highlighted panels often utilized in the area of infectious disease research include:

Early Infection



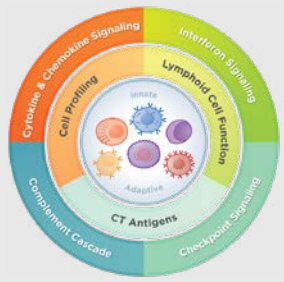
Myeloid Innate Immunity

Late Infection & Vaccine Development



Autoimmune Profiling

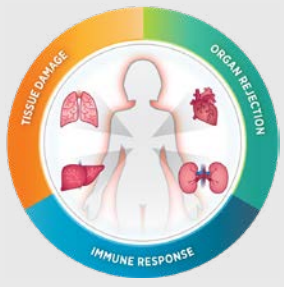
CAR-T Characterization



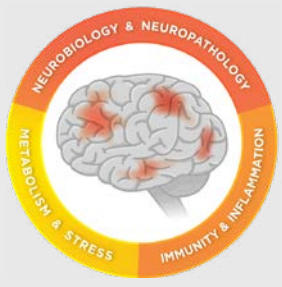
PanCancer Immune Profiling

Tissue Impact & Autopsy Studies

Fibrosis



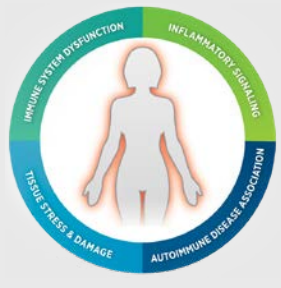
Human Organ Transplant



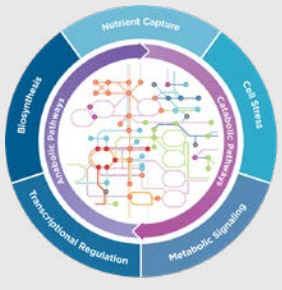
Neuroinflammation

Glial Profiling

Comorbidities & Susceptibility

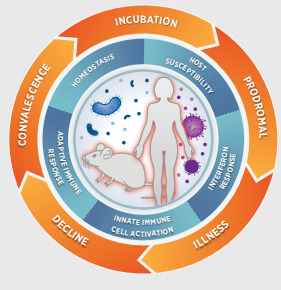


Autoimmune Profiling



Metabolic Pathways

Host Response Panel + Coronavirus Panel Plus



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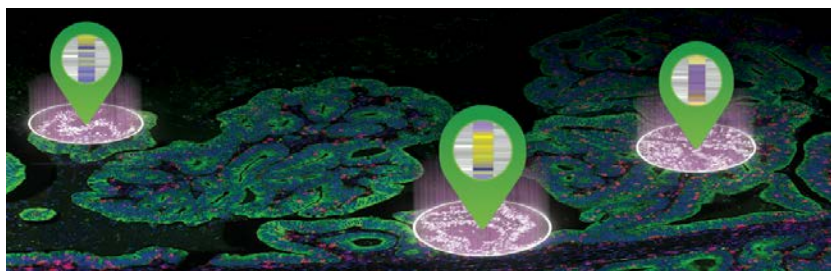
GeoMx® Digital Spatial Profiler Assays

GeoMx Digital Spatial Profiler Assays

Rapidly perform high-plex spatial analyses of the host response in FFPE or fresh frozen tissue using the **GeoMx Digital Spatial Profiler (DSP)**. NanoString's GeoMx DSP platform enables high-plex protein and RNA experiments in key areas of biology such as molecular response, cellular (immune) response, tissue damage, and drivers of individual susceptibility to severe forms of disease.

- Profile over 18,000 RNA targets with the Whole Transcriptome Atlas and spike-in custom probes for SARS-CoV-2 receptors and proteases
- Run the 5-antibody custom COVID-19 GeoMx-Formatted Antibody Panel with the GeoMx Immune Cell Profiling Core and profile up to 96 protein targets simultaneously
- Study rapid autopsy FFPE or fresh frozen tissue samples



RNA: GeoMx Whole Transcriptome Atlas

The **GeoMx Whole Transcriptome Atlas (WTA)** is designed for comprehensive spatial transcriptomics of FFPE and fresh frozen tissue sections with coverage of over 18,000 protein-coding genes in the human transcriptome. Due to its unique design and probe architecture that avoids any poly(A) pulldown, the GeoMx WTA delivers high sensitivity and specificity while at the same time giving you the flexibility to home in on the areas of the tissue and particular cells/structures that matter the most to your research. RNA targets are profiled simultaneously using the GeoMx DSP and an Illumina next-generation sequencer (NGS) is used for the readout. Users can use ACD RNAscope™ probes alongside GeoMx RNA probes to identify phenotypic markers that reveal the most relevant regions of interest.

Use RNAscope™ probes alongside GeoMx RNA probes to identify regions of interest (FIGURE 1).

ACD a biotechne brand

SARS-CoV-2
ACE-2
TMPRSS2
IL-6
TNFα
IFNγ

GeoMx® RNA targets include:

- COVID receptors & proteases
- Pulmonary alveolar type I and II markers
- Lung biology markers
- Viral response markers
- SARS-CoV-2 probes

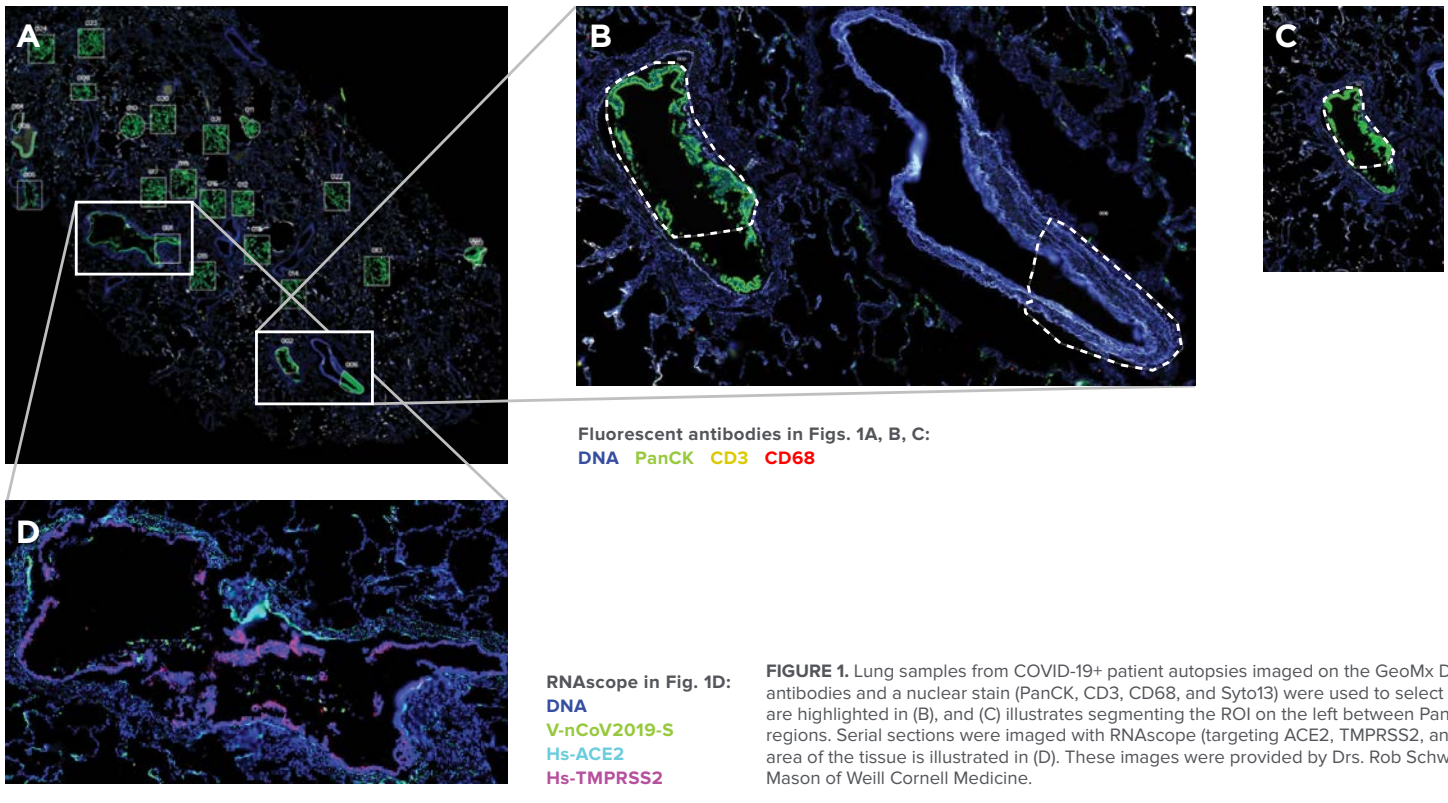


FIGURE 1. Lung samples from COVID-19+ patient autopsies imaged on the GeoMx DSP platform. Three fluorescent antibodies and a nuclear stain (PanCK, CD3, CD68, and Syto13) were used to select regions of interest (A). Two ROIs are highlighted in (B), and (C) illustrates segmenting the ROI on the left between PanCK positive and PanCK negative regions. Serial sections were imaged with RNAscope (targeting ACE2, TMPRSS2, and the viral spike protein), and one area of the tissue is illustrated in (D). These images were provided by Drs. Rob Schwartz, Alain Borczuk, and Chris Mason of Weill Cornell Medicine.

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Protein: GeoMx Immune Cell Profiling Core + 5-antibody custom COVID-19 module

Assess the spatial proteomic profile of SARS-CoV-2 infected samples with up to 96 antibodies including a 5-antibody custom protein module developed in partnership with Abcam. Run the **COVID-19 GeoMx-formatted Antibody Panel** from Abcam with the 20-plex GeoMx Immune Cell Profiling Core (plus controls) and up to six ~10-plex modules, including an Immune Activation Status Module, an Immune Cell Typing Module, and a Cell Death Module.

Immune Cell Profiling Core	Key immune targets and markers of T cells, B cells, macrophages, and more
Immune Activation Status Module	Additional T cell and T cell activation markers
Immune Cell Typing Module	More cell type markers including dendritic cells and Tregs
Cell Death Module	Protein mediators of immunogenic and programmed cell death

COVID-19 GeoMx-formatted Antibody Panel targets:

- ACE2
- TMPRSS2
- Cathepsin L/V/K/H
- DDX5
- SARS-CoV-2 Spike

Available for purchase from Abcam **abcam.com/ab273594**.

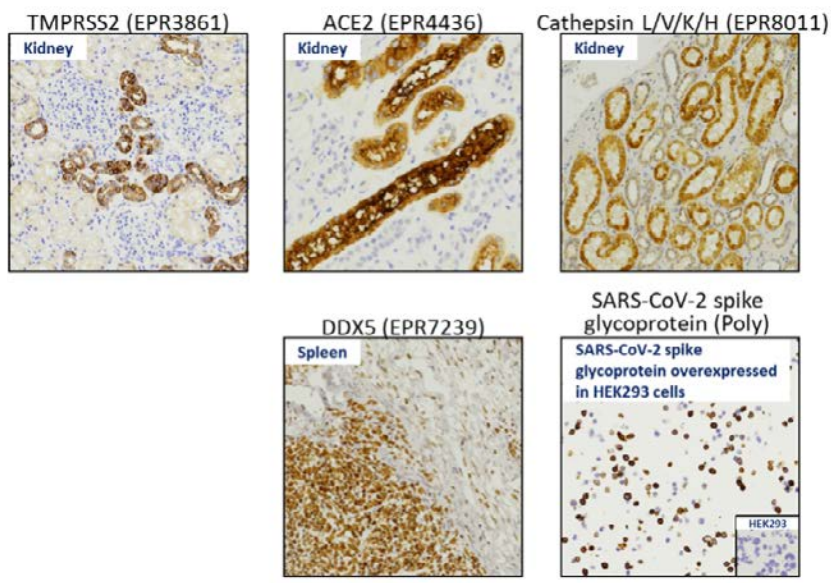

FIGURE 2. Post-conjugation IHC of the 5 antibodies in the COVID-19 custom antibody module developed with Abcam. In addition to a pre- and post-conjugation IHC screen, antibodies were tested in 30+ tissues in a tissue microarray and the SARS-CoV-2 spike antibody was tested in 3 viral overexpressing cell lines.

Use up to 3 fluorescent antibodies plus a nuclear stain to identify regions of interest. NanoString can recommend commercially-available markers for COVID-19 research, including:

- Pneumocyte type II (SFTPC)
- Nasal Epithelium (TNFS10)
- Immune Response Marker (CD38, CXCR3)
- Viral Spike (Figure 3) and Nucleocapsid Protein

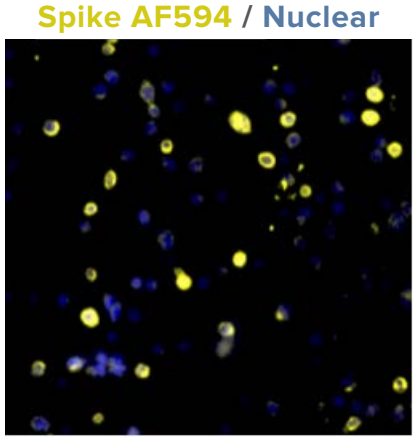

FIGURE 3. SARS-CoV-2 spike protein morphology marker tested in HEK294/SARS-CoV-2 Spike Cells on the GeoMx DSP.

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The Immunology of COVID-19: A dynamic immune signature for prognosis and spatial transcriptomics of lung tissue

VIEW ON-DEMAND

Miguel Muñoz-Ruiz, PhD from the Francis Crick Institute and Arutha Kulasinghe, PhD from Queensland University of Technology discuss the immune context of samples taken from COVID-19 patients with severe disease using, respectively, the nCounter CAR-T Characterization Panel and GeoMx Digital Spatial Profiling.

Investigating the Host Response to SARS-CoV-2

VIEW ON-DEMAND

Joseph Beechem, Ph.D., NanoString Chief Scientific Officer & Senior Vice President, Research and Development, discusses our most recent understanding of how the host immune system responds to SARs-CoV-2 and the myriad ways in which NanoString research tools can be used to study pathogenesis and aid in vaccine & therapy development. James Heath, PhD, of the Institute for Systems Biology presents recent findings in COVID-19 research utilizing the GeoMx Digital Spatial Profiler.

Insights into the Pathogenesis of COVID-19 as Revealed by Spatial Biology

VIEW ON-DEMAND

Joseph Beechem, Ph.D., NanoString Chief Scientific Officer & Senior Vice President, Research and Development, opens by summarizing recent insights into how the host responds to SARs-CoV-2. Christopher E. Mason, Ph.D., Associate Professor Weill Cornell Medicine, and Robert E. Schwartz, PhD, Assistant Professor of Medicine, Weill Medical College of Cornell University, discuss recent investigations into spatial gene expression differences seen in COVID-19 lung tissue vs. non-COVID-19 lung tissue and healthy controls.

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Two-Part Series: The Latest Tools for Assessing Immunity

Part 1: COVID-19 and Immune Profiling VIEW ON-DEMAND

Erin Piazza, Ph.D., NanoString Senior Bioinformatics Scientist, reviews recent research on COVID-19 in relation to immune response, at-risk groups (cardio, transplant, metabolic diseases, diabetes, oncology, autoimmunity), and how NanoString tools can help you in your own research efforts.

Part 2: New COVID-19 Product: Host Immune Response & Tools for Research VIEW ON-DEMAND

Erin Piazza, Ph.D., NanoString Senior Bioinformatics Scientist, discusses the new Host Response gene expression panel development and case studies in several areas of research.

Infectious Disease Research with NanoString

Introduction to Studying Infectious Disease with Multiplexed Direct Digital Detection VIEW ON-DEMAND

Amy Wahba, Ph.D., NanoString Field Applications Scientist, covers an overview of infectious disease research solutions from NanoString.

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Selected COVID-19 NanoString Customer Publications

1 Ackermann M et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med. 2020; 383:120-12.

2 Bastard P et al. Autoantibodies against type I IFNs in patients with life-threatening COVID-19. Science. 2020;370(6515):eabd4585.

3 Butler D et al. Shotgun transcriptome, spatial omics, and isothermal profiling of SARS-CoV-2 infection reveals unique host responses, viral diversification, and drug interactions. Nature Communications. 2021;12:1660.

4 Desai N et al. Temporal and Spatial Heterogeneity of Host Response to SARS-CoV-2 Pulmonary Infection. medRxiv 2020.07.30.20165241, August 02, 2020.

5 Galimberti S et al., The CoV-2 outbreak: how hematologists could help to fight Covid-19. Pharmacol Res. 2020; 157: 104866.

6 Gardinassi LG et al. Immune and Metabolic Signatures of COVID-19 Revealed by Transcriptomics Data Reuse. Front Immunol. 2020; 11: 1636.

7 Hadjadj J et al. Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients. Science. 2020;369(6504):718-724.

8 Laing AG et al. A dynamic COVID-19 immune signature includes associations with poor prognosis. Nat Med. 2020;26(10):1623-1635.

9 Li G et al. Transcriptomic signatures and repurposing drugs for COVID-19 patients: findings of bioinformatics analyses. Comput Struct Biotechnol J. 2021; 19: 1–15.

10 Maremanda KP et al. Age-Dependent Assessment of Genes Involved in Cellular Senescence, Telomere, and Mitochondrial Pathways in Human Lung Tissue of Smokers, COPD, and IPF: Associations With SARS-CoV-2 COVID-19 ACE2-TMPRSS2-Furin-DPP4 Axis. Front Pharmacol. 2020; 11: 584637.

11 Monneret G et al. Immune monitoring of interleukin-7 compassionate use in a critically ill COVID-19 patient. Cell Mol Immunol. 2020: 1–3.

12 Ong EZ et al., A Dynamic Immune Response Shapes COVID-19 Progression. Cell Host Microbe. 2020; 27(6): 879–882.e2.

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COVID-19 NanoString Customer Publications

13 Rendeiro AF et al. The spatial landscape of lung pathology during COVID-19 progression. Nature. 2021 Mar 29. doi: 10.1038/s41586-021-03475-6. Online ahead of print.

14 Rinchai D et al. A modular framework for the development of targeted Covid-19 blood transcript profiling panels. J Transl Med. 2020; 18: 291.

15 Smadja DM et al. Angiopoietin-2 as a marker of endothelial activation is a good predictor factor for intensive care unit admission of COVID-19 patients. Angiogenesis. 2020;27 : 1–10.

16 Sohn KM et al. COVID-19 Patients Upregulate Toll-like Receptor 4-mediated Inflammatory Signaling That Mimics Bacterial Sepsis. J Korean Med Sci. 2020; 35(38): e343.

17 Trouillet-Assant S, et al., COVID HCL Study group Type I IFN immunoprofiling in COVID-19 patients. J Allergy Clin Immunol. 2020;146(1): 206–208.e2.

18 Wang Q et al. E-cigarette-induced pulmonary inflammation and dysregulated repair are mediated by nAChR α7 receptor: role of nAChR α7 in SARS-CoV-2 Covid-19 ACE2 receptor regulation. Respir Res. 2020; 21: 154.

19 Widiasta A et al. Potential role of ACE2-related microRNAs in COVID-19-associated nephropathy. Noncoding RNA Res. 2020; 5(4): 153–166.

20 Woolsey C et al. Establishment of an African green monkey model for COVID-19 and protection against re-infection. Nature Immunology volume 2021;22:86–98.

21 Wu H et al. AKI and Collapsing Glomerulopathy Associated with COVID-19 and APOL1 High-Risk Genotype. J Am Soc Nephrol. 2020;31(8):1688-1695.

NanoString Technologies, Inc.
530 Fairview Avenue North
Seattle, Washington 98109

T (888) 358-6266
F (206) 378-6288

nanostring.com
info@nanostring.com

Sales Contacts
United States us.sales@nanostring.com
EMEA: europe.sales@nanostring.com
Asia Pacific & Japan apac.sales@nanostring.com
Other Regions info@nanostring.com

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