nCounter® Host Response Panel for Infectious Disease Research

Highlights

- Understanding the complexities of the immune response to infection is essential to developing vaccines to treat infections
- The nCounter® Host Response Panel from NanoString® is designed for infectious disease research through targeted gene expression analysis
- A recent study employs the nCounter Host Response Panel to investigate the interferon (IFN) response to infection in samples from patients with COVID-19
- Canopy Biosciences is a Center of Excellence for NanoString services, offering comprehensive experiment and analysis packages to support infectious disease research

Introduction

Understanding the complex relationship between a pathogen and host response is important to developing effective vaccines and therapeutics to fight infectious disease. Secretion of cytokines and chemokines by cells of the innate immune system can activate the T and B cells of the adaptive immune system (Sokol & Luster, 2015). One family of cytokines – interferons – trigger immune system defenses in host cells and interfere with viral replication (Bonjardim et al., 2009). The interferon (IFN) pathway plays a critical role in stimulating the adaptive immune system to promote virus clearance.

New tools support the development of vaccines for infectious diseases – including COVID-19 (O'Callaghan et al., 2020). Gene expression technologies are one such tool that has grown in popularity to profile hundreds of genes at a time. Interpreting gene expression data is critical to understanding biological pathways involved in host response. Differential gene expression (DGE) analysis can help determine the relative abundance of genes in two samples, a useful metric given the wealth of data produced in a single experiment.

Yet, current high-throughput gene expression technologies have significant limitations. Next-generation sequencing techniques have complex workflows and slow turnaround times, especially when target genes include the whole genome. Other techniques for measuring gene expression include traditional qPCR, which involves library preparation and amplification of RNA targets, a principal source of bias in resulting data (van Dijk et al., 2014).

The NanoString nCounter Host Response Panel offers a simple and cost-effective solution for analysis of up to 800 RNA targets for infectious disease reasearch. nCounter assays accelerate research without amplification, cDNA conversion, or library preparation. Partner with our CLIA-certified Canopy Core Laboratory and work with scientists with years of experience in assay performance and DGE analysis.

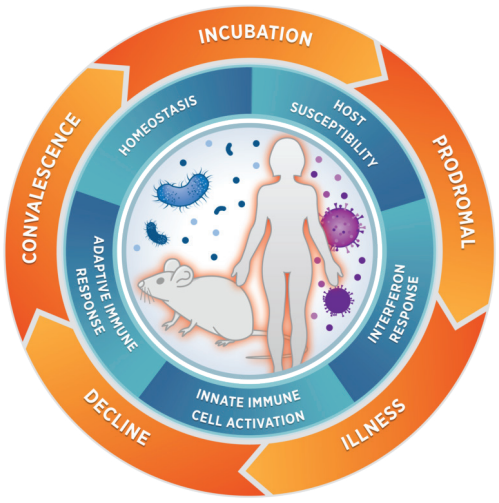

Figure 1. The nCounter Host Response Panel enables researchers to study the immune response to infectious disease. (Source: NanoString)

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CRO Services for nCounter Analysis System

The nCounter platform enables analysis and quantification of RNA and DNA targets by employing color-coded molecular barcodes. Canopy Biosciences' Data Analysis Center makes use of the ROSALIND platform to analyze gene expression data and perform differential gene expression (DGE) analysis. Key features of the nCounter platform include:

- Amplification-free digital counting of RNA
- Compatible with multiple sample types including FFPE, crude cell lysates, and cell lines
- Ideal for degraded RNA from FFPE tissue
- Multiplex 100s of custom targets per sample in a single tube

NanoString has released dozens of panels to target genes of biological relevence to assist researchers with targeted gene expression analysis. Canopy Biosciences has been named a Center of Excellence for NanoString services and offers comprehensive experiment and analysis packages in our CLIA-Certified laboratory.

The Host Response Panel Supports Infectious Disease Research

NanoString recently launched the Host Response Panel, targeting 800 genes in over 50 key immune pathways. The Host Response Panel is ideal for infectious disease research to study disease progression – from infection to resolution. Figure 2 details the key phases of infection including host susceptibility, interferon response, innate immune cell activation, adaptive immune response, and homeostasis.

Studies designed by researchers at the National Center for Scientific Research in Lyon, France used nCounter and the Host Response Panel to investigate the IFN response as an indicator of disease severity and progression in patients with COVID-19 (Lopez et al., 2021). They focused on type I and type III immunity and found that the gene signature correlates with the amount of virus present. They also found that autoantibodies against IFN-I have antiviral effects in the early stages of COVID-19 infection.

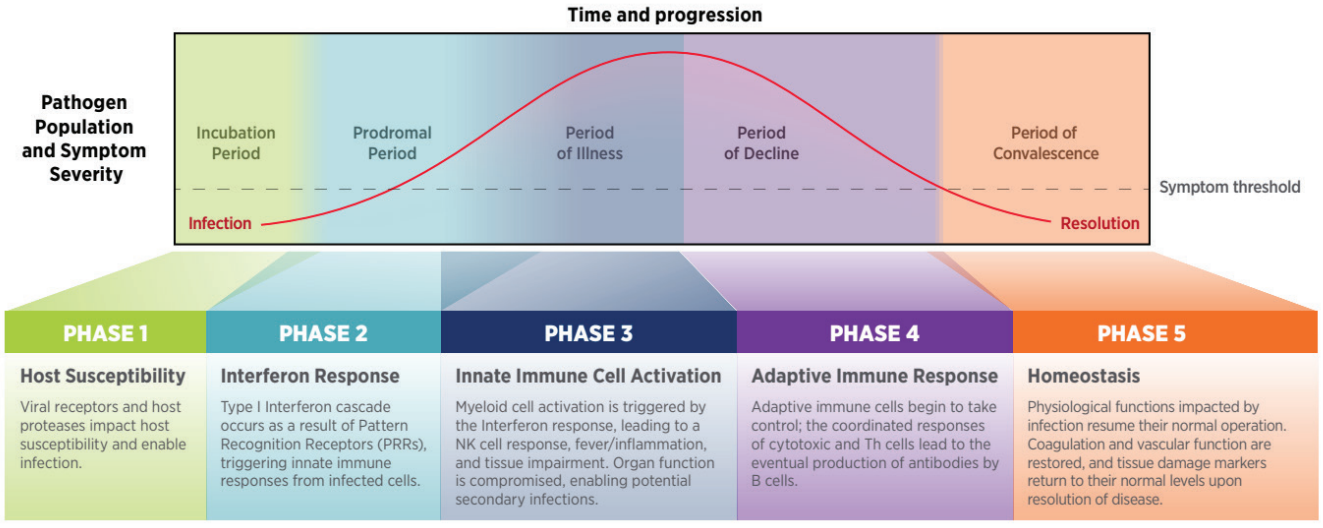

Figure 2. The five phases of the host-response to infectious disease from infection to resolution. (Source: NanoString)

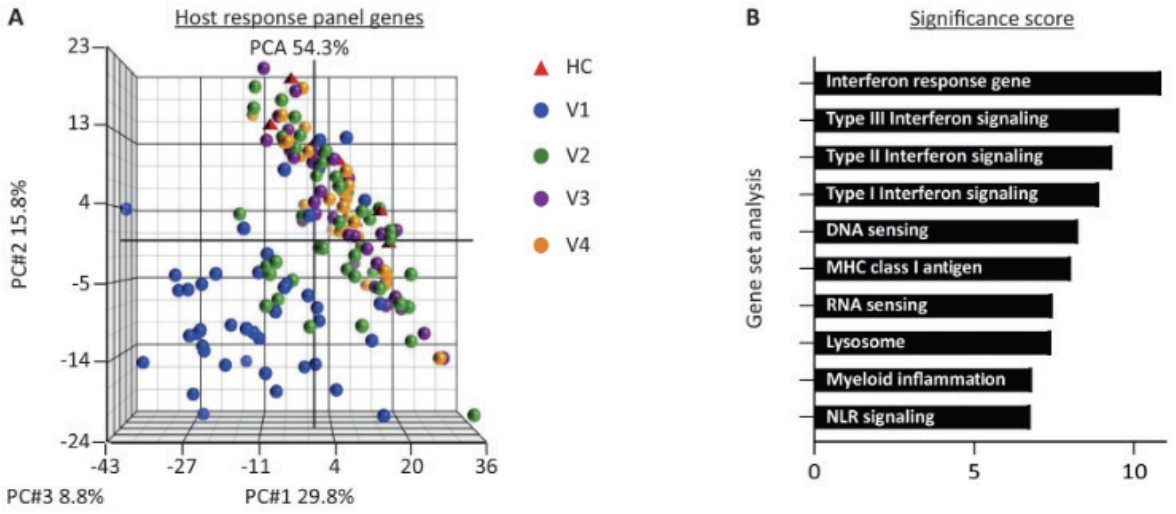

Figure 3. A) PCA of gene expression data from COVID-19 patients (spheres) and healthy controls (red triangles). B) Pathway analysis using NanoString nSolver analysis software. (Source: Lopez et al., 2021)

Differential Gene Expression Analysis Reveals ISG Signature

Whole-blood samples from COVID-19 patients were taken at different timepoints, from diagnosis to recovery. Differential gene expression (DGE) revealed differences in gene expression in patient samples collected at different time points throughout the study. Figure 3 shows the principal component analysis (PCA) of blood from 44 COVID-19 patients. Unsupervised clustering of this data presented as a heatmap shows 17 genes downregulated and 106 genes upregulated at time of infection (timepoint 1) compared to later timepoints (Figure 4). These results elucidate the role of IFN-stimulated genes in response to COVID-19 infection.

Taken together, the data in this study demonstrate the utility of the nCounter, Host Response Panel, and DGE analysis to profile interferon gene signatures as a biomarker for COVID-19 disease severity. The research lays the foundation for the possibly of interferon score with nCounter assay, as previously done (Kim et al., 2018).

Key Questions in Vaccine Development

COVID-19 has highlighted the inherent challenges of vaccine development, a critical goal for infectious disease research. Goodman and colleagues (2020) have posed key questions to be answered, especially in the wake of rapid development. Assays like nCounter provide a wealth of data and are important tools to help answer key questions toward vaccine development:

- How much does a vaccine reduce the risk of disease and its complications?
- How safe is a vaccine candidate and how is it determined?
- Will the vaccine be effective for all patients?
- How is important information made available to the public?
- Is a vaccine licensed or provided under an Emergency Use Authorization?
- Are all vaccines for a disease the same?
- Can vaccinated people stop worrying about the disease?

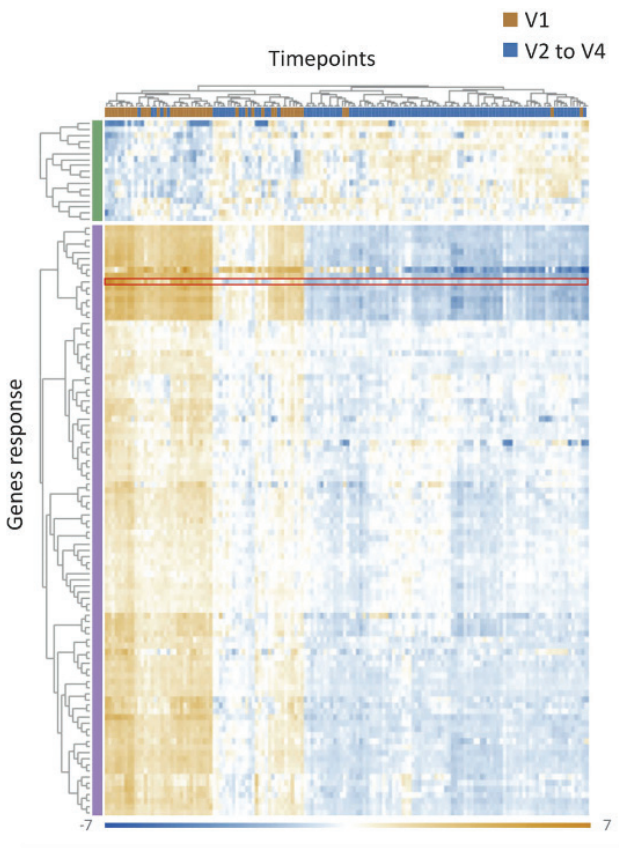

Figure 3. Unsupervised clustering of gene expression data at different timepoints post-infection showing downregulated (green bar) and upregulated genes (purple bar). (Source: Lopez et al., 2021)

Summary

Understanding the complexities of the immune response to infection is essential to developing vaccines and medications to treat infections. The nCounter Host Response Panel from NanoString is designed for infectious disease research – from infection to resolution. Here, we highlight the utility of the Host Response Panel in a recent study by Lopez et al. (2021) to investigate the IFN response to infection and the role of autoantibodies in mitigating that response in patients with COVID-19.

In conclusion, the nCounter Host Response Panel is a simple and cost-effective solution for all phases of infectious disease research – from discovery to translation. The Host Response Panel offers a wealth of data, profiling expression of over 800 key genes in infectious disease research.

References

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