

Viral Immunologist Taps “Incredible Potential” of Immune System

Paul Thomas, PhD, will combine computational and empirical approaches to understand the immune repertoire and turn this knowledge into new diagnostic and therapeutic tools

November 18, 2025 By Fred Hutch News Service and Sabrina Richards

Viral immunologist [Paul Thomas, PhD](#), is working to turn the “incredible potential” of the immune system into real-life diagnostic and therapeutic applications that will improve vaccination strategies and cancer treatments. Thomas, who recently joined Fred Hutch Cancer Center’s [Vaccine and Infectious Disease Division](#), studies how our immune system responds to (and evolves with) the pathogen exposures that leave an imprint in our genes and shape how we will respond to the next infection.

“Quantitative human immunology is a unifying theme of my program,” said Thomas, Bezos Family Distinguished Scholar in Viruses and Vaccines. Thomas comes to Fred Hutch from St. Jude’s Children’s Research Hospital and the University of Tennessee, where he was a member of St. Jude’s Center of Excellence for Influenza Research and Response. “The approach we take is a mix of quantitative methods, computational methods and experimental approaches to try to really understand human immunology.”

Using these methods and cohorts of adult and pediatric patients, Thomas seeks to define important immunological patterns and understand what they mean for our health and susceptibility to disease.

“Paul is an internationally renowned T-cell immunologist and leader in the influenza field,” said VIDD Senior Vice President and Director [Julie McElrath, MD, PhD](#), who holds the Joel D. Meyers Endowed Chair. “He brings new cutting-edge technologies to Fred Hutch for both infectious disease and cancer research, as well as skilled lab team members who are arriving now and over the next few months. We are so excited to have Paul join us in VIDD, and overall, he is a giant win for all of us!”

In particular, Thomas studies critical immune cells called T cells and their T-cell receptors (or TCRs), specialized molecules T cells use to recognize immunological threats. T cells’ duties range from big-picture orchestration of immune responses to boots-on-the-ground elimination of infected cells. TCRs help them zero in on targets by detecting changes in the proteins our cells produce, which may signal infection or cancer. We are constantly churning out new T cells, and each new T

cell carries a one-of-a-kind TCR.

“TCRs have this vast potential diversity,” Thomas said. “And you can see your risk or protection level encoded in your T-cell receptor repertoire.”

“Vast” is an understatement.

Scientists estimate that there are over a [novemdecillion](#) (i.e., more than 10^{60}) potential TCR gene sequences. Your T-cell repertoire (huge, but still a mere sliver of that novemdecillion) is your personal collection of T cells and their TCRs. When we fight off infections, the T cells involved transform into long-lived “memory” T cells that serve as a living record of our immunological history. These memory T cells, plus newly generated “naïve” T cells that have yet to meet a microbe, make up our T-cell repertoire.

We need a diverse range of TCRs to combat microbial diversity. An individual’s unique TCR repertoire influences how well their immune system can protect them against a particular infection and or tumor, as well as their responses to vaccines.

“The potential of the T-cell repertoire, and the immune repertoire more broadly, is incredible in terms of both diagnostic and therapeutic applications,” Thomas said.

Diagnostic and therapeutic potential

Thomas hopes to use the knowledge he gains to improve diagnostic and therapeutic tools. He and collaborators like Fred Hutch computational and structural biologist [Phil Bradley, PhD](#), who holds the Bob and Pat Herbold Computational Biology Endowed Chair, are working to understand the complex relationship between TCR gene sequences, TCR protein structures and their targets.

“If we can learn how that code works between the T cell and its antigens [TCR targets], we can then also use it as this backward-looking lens of everything that’s happened to you immunologically over the course of your life, and a forward-looking lens to your potential response to an infection,” Thomas said.

Accurately interpreting the TCR code could help us design better vaccines, improve [T cell-based immunotherapies](#) and possibly lead to new diagnostic tools for infections or tumors.

Cracking the TCR code

Decoding what TCRs mean for our health is not simple.

A TCR is made up of two molecules, each encoded by a different gene — on separate chromosomes. A full picture only comes into view when scientists can match the two correct genes; identifying one or the other gives only spotty insight. Even though technologies have

improved the picture, there's still much to be done to define TCR signatures and decode their meaning.

Thomas and his collaborators have developed several computational approaches, including [single-cell](#) and bulk-cell methods, to tackle the problem. One of their recent innovations, called [TIRTL-seq](#), uses computational strategies, rather than single-cell technologies, to extract single-cell resolution of the TCR repertoire's gene pairings at high depth. TIRTL-seq provides scientists a low-cost way to glean highly specific information from millions of cells, Thomas said.

His computational work is buttressed by real-life TCR, T-cell and immune data collected from real people. This information is essential to interpreting what a TCR repertoire means for a person's health. With his collaborators, Thomas has assembled multiple cohorts of patients (adult and pediatric) to track their immune responses to influenza infection and vaccination over time.

As part of these efforts, he co-leads the [DIVINCI consortium](#), a flu research collaboration across 12 institutions that draws on a cohort of children enrolled at birth and followed as infants. The cohort is providing insights into how the early immune system develops. Thomas is extending these studies to the immune response against cancer.

"The idea is to use these approaches to both build up our understanding of the human immune repertoire in actual humans, and try to understand empirically what these receptors are and what they target," Thomas said. "And then also to build up enough data to potentially solve this problem synthetically and computationally in collaboration with the structural biologists here."

Synthetic TCRs would be scientist-designed TCRs that, ideally, improve on nature, and enable the development of more selective and effective cancer immunotherapies.

Thomas is looking forward to taking advantage of the scientific milieu of Fred Hutch and Seattle, deepening long-standing collaborations and initiating new connections.

"Fred Hutch is just incredibly well-situated for human immunology. They've been leaders in this for years," he said, pointing to Fred Hutch's leadership role in the HIV Vaccine Trials Network and the computational work from Fred Hutch biostatistician [Peter Gilbert, PhD](#), which has helped define immunological signatures that predict protection for vaccines to a variety of infections, including HIV and COVID-19.

"Fred Hutch is this perfect mix of infectious disease, cancer, computation, and immunology that I think is very unique in the world," Thomas said.

Sabrina Richards, a senior editor and writer at Fred Hutch Cancer Center, has written about scientific research and the environment for The Scientist and OnEarth Magazine. She has a PhD in immunology from the University of Washington, an MA in journalism and an advanced certificate from the Science, Health and Environmental Reporting Program at New York University. Reach her at srichar2@fredhutch.org.

[This article](#) was originally published November 5, 2025, by Fred Hutch News Service. It is republished with permission.

© 2026 Smart + Strong All Rights Reserved.

<http://beta.docker.cancerhealth.com/article/viral-immunologist-taps-incredible-potential-immune-system>