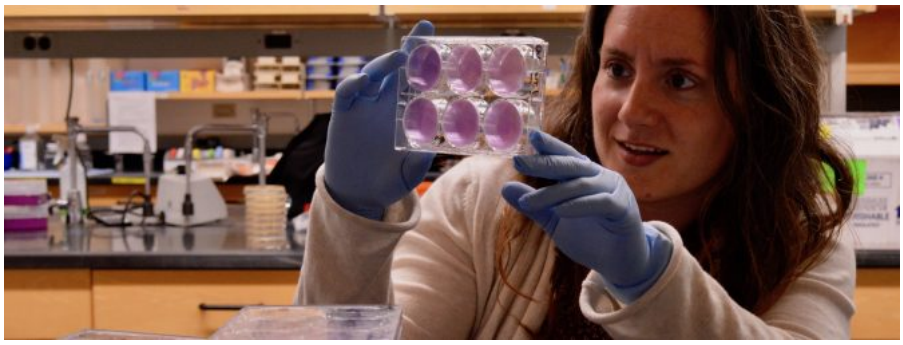
Science@CornellVet
A science blog straight from the students and trainees of Cornell Vet



Age: is it really just a number for T-cells?

It's a widely accepted idea that we are a product of our environments. This idea is also relevant for the cells in our bodies.

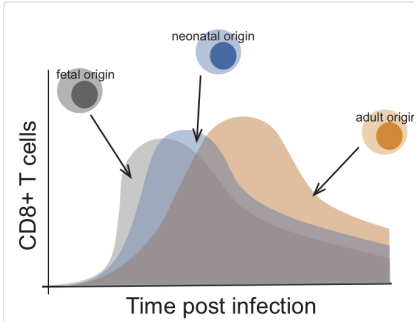
In order for the immune system to properly protect an individual, the T-cell population needs to be composed of various subsets, each specialized to react to different types and stages of infections. Dr. Brian Rudd, an Assistant Professor of Immunology at the Cornell School of Veterinary Medicine, focuses on understanding the cell intrinsic differences within the T-cell repertoire of neonates versus their adult counterparts. Rudd seeks to answer the question: what makes a T-cell behave like a T-cell and understand why these two populations behave differently from one another.

Currently, Dr. Norah Smith, a Research Associate in the Rudd lab, is working on a project affectionately known as the "Timestamp project." The Timestamp project aims to understand how the host environment can impact a T-cell's behavior, specifically, how the age of a T-cell can change its ability to respond to different microbial insults. Smith hopes her work will contribute to designing more effective childhood vaccination strategies and understanding why individuals at various developmental stages are more susceptible to illness.

Stage of development determines T-cell behavior

"A T-cell isn't *just* a T-cell. Its function depends on when it was made and what was happening in the individual when it was made," Smith explains, "it's necessary to address sources of these differences in order to understand variation within the population."

The Timestamp project focuses on understanding behavioral and phenotypic differences within the T-cell population made at birth, during childhood, and in adulthood, and how/if these T-cells respond differently to challenges such as infections. The central idea of this project revolves around the need to understand how T-cells that are made early in life persist until adulthood and differentially contribute to mounting an immune response.



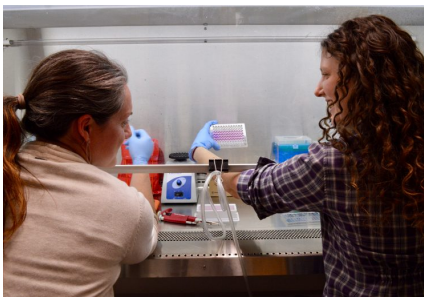
Schematic of the developmental layering of T-cells b
Smith

Members of the Rudd lab gather around Smith as she explains her results.

Previous work done in the Rudd lab by Smith, Jocelyn Wang, Ph.D. candidate, and Dr. Neva Watson showed different stem cell precursor populations give rise to various populations of CD8+ T-cells—these are T-cells which have distinct behavior following infection, which led Smith to hypothesize that there are developmentally-related differences within T-cell populations. Additionally, Smith made the exciting discovery that neonatal T-cells are more responsive towards infections compared to their adult counterparts. Therefore, Smith realized focusing on the developmental origins of T-cells is necessary in order to fully understand why populations behave differently.

Smith realized many T-cells are long-lived, therefore, she wanted to develop a way to track the various populations made at different developmental time points and understand how the age of the T-cell impacts its function.

The unique approach



The heart and soul of the Timestamp Project lies within the mouse model, which was developed by Smith. In this model, T-cells have been engineered to express a red fluorescent protein when activated by the compound tamoxifen. By introducing tamoxifen to the model at different developmental stages, Smith can preferentially mark T-cells produced at specific developmental time points, such as at birth, seven days old, and adulthood and track them from then on. By using this model, Smith is able to "fatemap" T-cells, i.e., determine when in the animal's life a specific T-cell was made and elucidate how different-aged T-cells behave in response to stimuli throughout an animal's lifetime, thus further understand how differences in effector function arise.

Smith's ultimate goal is to discover the function of these different 'aged' T-cells, and if age is a relevant factor for T-cell function. So far, the dat point to yes.

-Cybelle Tabilas, Ph.D. student in Immunology and Infectious Diseases

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