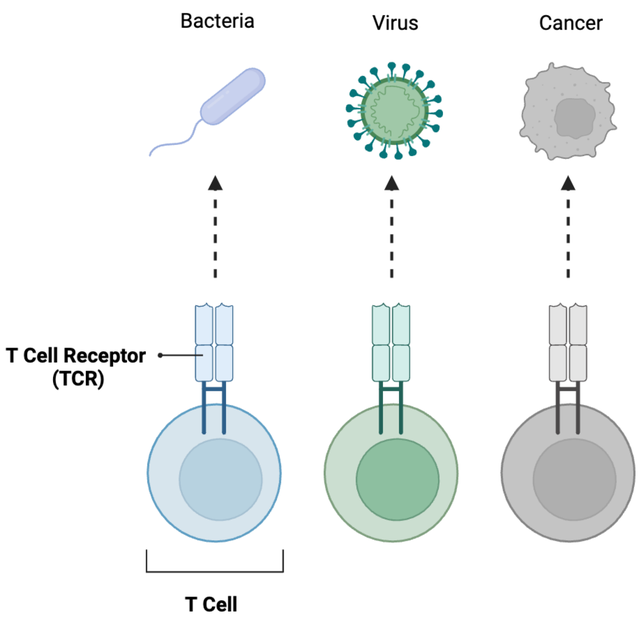
The role of pre-TCR signaling beyond β-selection

Andrew Dayton[1,2], Sébastien This[1,2], Ève Mallet Gauthier[2,3], and Heather Melichar[1,2]

[1]Department of Microbiology & Immunology, McGill University, Montréal, Québec, Canada [2]Rosalind & Morris Goodman Cancer Institute, McGill University, Montréal, Québec, Canada [3]Department of Microbiology, Infectious Diseases, and Immunology, Université de Montréal, Montréal, Québec, Canada

T Cells: Targeted Killers



T cells are the immune system's targeted killer cells which keep us alive.

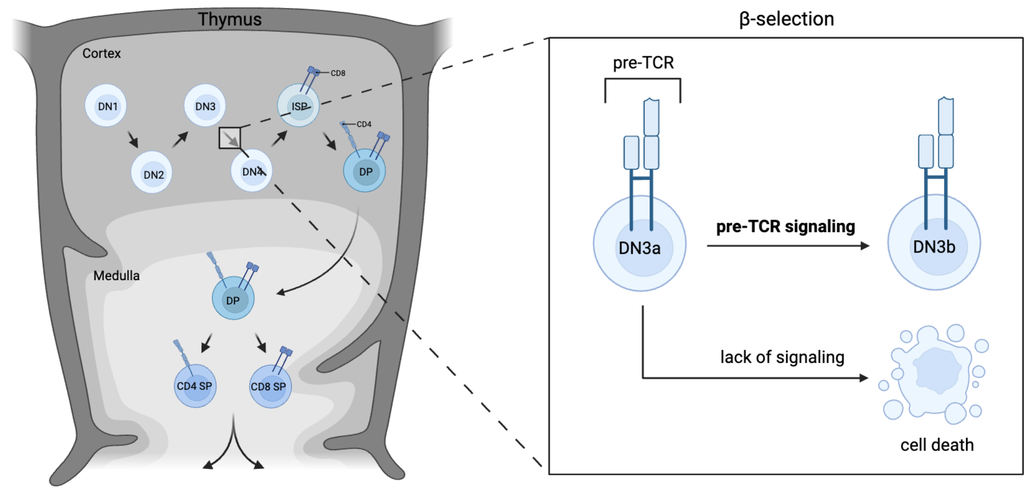
Each T cell has a unique **T cell receptor (TCR)** which enables it to recognize, bind, and kill a specific target. These targets can be bacteria, viruses, cancer cells, or anything else which poses a threat.

To ensure the best defense, our immune system generates a T cell repertoire composed of a staggering ~10^{20} TCRs.[1]

This means, in theory, we are protected against 100,000,000,000,000,000,000 enemies.

…but not all TCRs are functional

The 'Murder University' of the Thymus



T cells develop in the **thymus**, an organ which subjects developing T cells, called **thymocytes**, to a gauntlet of tests which ensure a safe and effective T cell repertoire.

The first test is called **β-selection**, which tests whether each thymocyte's **pre-TCR** is functional.[2,3] If it is, the cell will receive **pre-TCR signaling** and will continue to develop.[2,3] However, the role of pre-TCR signaling beyond β-selection (DN3a – DN3b transition) is unknown.

Question

What is the role of pre-TCR signaling, if any, beyond β-selection?

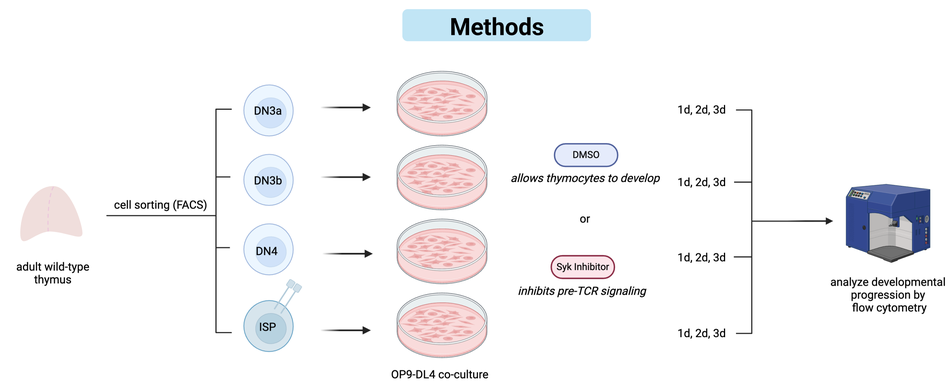
Aim

To assess how thymocyte survival and differentiation are affected by blocking pre-TCR signaling after β-selection.

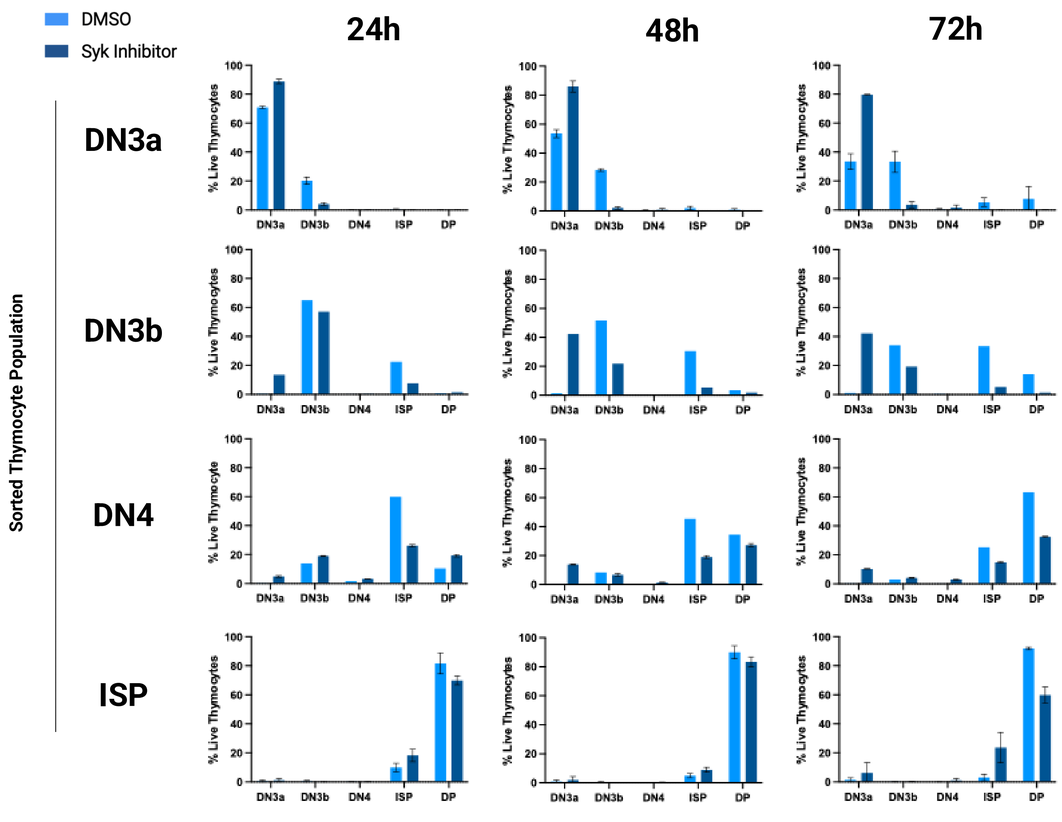
Hypothesis

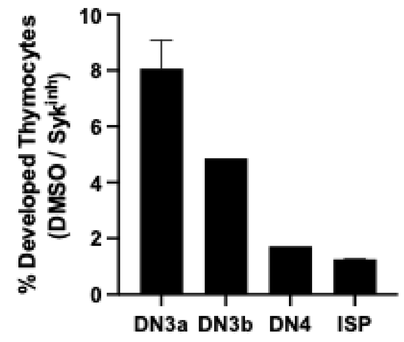
We hypothesize that pre-TCR signaling is required for both efficient thymocyte survival and differentiation beyond β-selection.

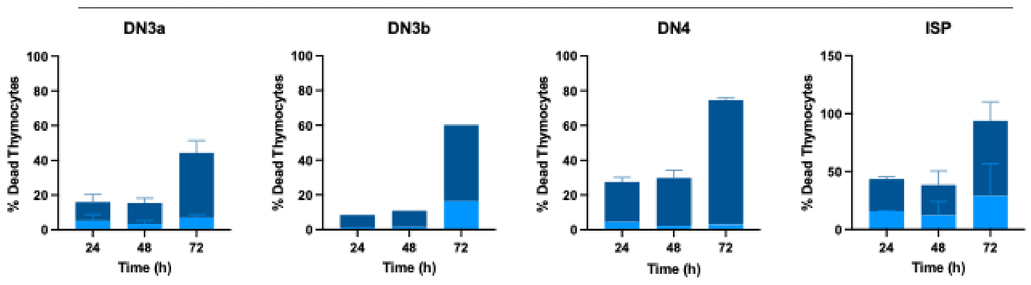
Methods



pre-TCR signals are required beyond β-selection



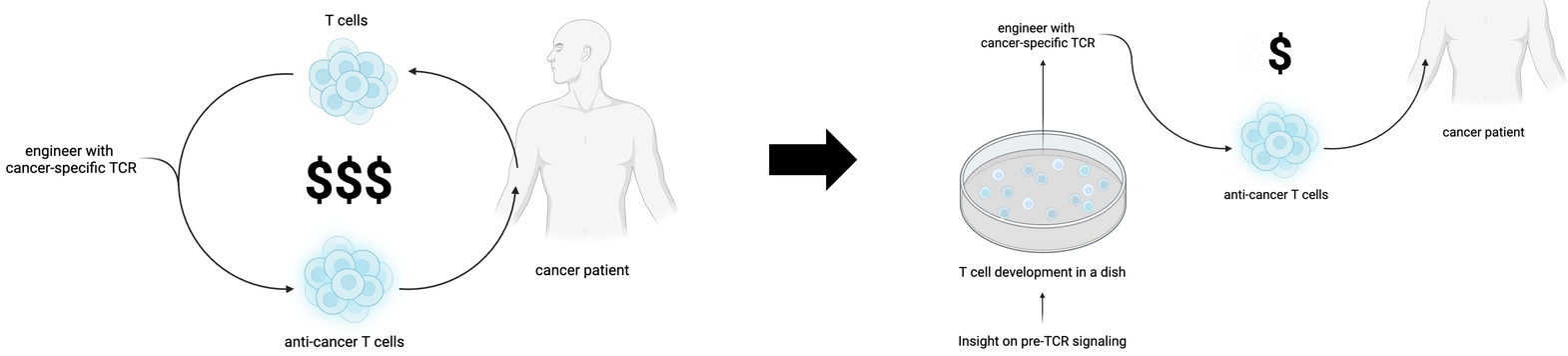




pre-TCR signals are important for cell survival and differentiation beyond β-selection.
However, the dependency on these signals decreases across developmental stages.

Insight on pre-TCR signaling can help develop T cells in a dish

Adoptive T Cell Therapy is a highly effective pipeline for cancer immunotherapy, but its reliance on patient-derived cells makes it extremely expensive, time-consuming, and inaccessible.[4]



If we understand the requirements and characteristics of pre-TCR signals, we can attempt to replicate them *in vitro* to **develop T cells in a dish.**

This approach could vastly improve the accessibility of these life-saving therapeutics.

Institut du cancer Rosalind & Morris Goodman Cancer Institute.

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Questions? andrew.dayton@mail.mcgill.ca

References: