

Penn researchers describe key molecule that keeps immune cell development on track

August 8 2011

In the latest issue of *Nature*, researchers at the Perelman School of Medicine at the University of Pennsylvania clarify the role of two proteins key to T-cell development. They found that one well-known protein called Notch passes off much of its role during T-cell maturation to another protein called TCF-1. T cells are required for many aspects of immunity, and understanding how these proteins influence the production of infection-fighting cells could improve treatments for immune-suppressed patients.

The research group, led by senior author Avinash Bhandoola, MBBS, PhD, associate professor of Pathology and Laboratory Medicine, found an important role in early T-cell [development](#) for T-cell factor 1 (TCF-1), which is turned on by Notch signals.

"Notch triggers the process of T-cell development, and turns on expression of TCF-1, but Notch itself doesn't stick around; it's more of a kiss-and-run molecule," says Bhandoola. In contrast, once induced by Notch, TCF-1 is faithfully expressed throughout T-cell maturation.

T cells are made in the thymus, a small organ situated under the [breastbone](#) near the heart. However, T cells, like all blood-cell types, originate from blood-producing [stem cells](#) in the [bone marrow](#). Immature T-cell progenitors leave the bone marrow, settle within the thymus, and eventually give rise to T cells.

Notch regulates cell-fate decisions in many cell types in addition to

[immune cells](#). Past work at Penn helped demonstrate that Notch is active in early T-cell progenitors in the [thymus](#) of mice, and drives the differentiation of these progenitors down the T cell pathway.

Delegating Work

Co-first authors, Anthony Wei-Shin Chi, MD, PhD, and Brittany Nicole Weber, BS, were graduate students together in the Bhandoola lab. They used retroviruses to express TCF-1 in immature blood progenitor cells. "If you expose progenitor cells to Notch signals in culture, we know that they will express TCF-1 and take on other features of T cells," says Chi.

However, when they forced expression of TCF-1 in cells using retroviruses, Weber noticed expression of T-cell proteins on the surface of cells -- even when Notch signals were absent. The team further characterized these new T-lineage cells by looking at gene expression on microarrays and found they expressed many T-cell specific genes. They concluded that Notch normally turns on TCF-1 early in development, and that TCF-1 then does the job of turning on T-cell genes and keeps T-cell maturation on the right track.

"The data are telling us that Notch delegates much of its work during T-cell development to TCF-1," says Bhandoola, "But we now have many questions about what comes next."

Adds Weber, "Some of the new questions are: How is TCF-1 regulated after Notch steps off stage? What keeps it on? What is TCF-1 doing? And how is it doing it?"

In many clinical settings, early T-cell [progenitors](#) are likely to be deficient, especially in patients undergoing bone marrow or blood-cell-producing stem cell transplantation - situations in which new T cells fail to be produced for long periods of time. In some patients, especially

elderly ones, there is never true recovery of T [cells](#), and this non-recovery can be associated with infection.

"To improve the outcome of transplant patients, the process of T-cell development needs to be better understood," says Chi. This may also be important in cancer patients who get profound immunosuppression from treatments and in AIDS patients when [T cells](#) are not made at a rate sufficient to replenish the T-cell pool.

"It's possible that one day we will use molecules like TCF-1 to improve T-cell development for people," says Weber.

Provided by University of Pennsylvania School of Medicine

Citation: Penn researchers describe key molecule that keeps immune cell development on track (2011, August 8) retrieved 21 November 2023 from <https://medicalxpress.com/news/2011-08-penn-key-molecule-immune-cell.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.