Switch to make 'killer' T cells identified by La Jolla Institute researchers

By Bradley J. Fikes 10:04 A.M. JAN. 20, 2013

Hilde Cheroutre, Division Head and Professor, La Jolla Institute for Allergy & Immunology

LA JOLLA — *Here's my take on a scientific paper of potentially great significance. The language gets technical at times, so I've added links to scientific terms that you can follow to learn about them.*

A molecular call to arms that turns white blood cells called 'helper' T cells into pathogen-destroying 'killer' T cells has been identified by a team led by researchers at the La Jolla Institute for Allergy & Immunology.

The discovery could be of use in goading the immune system to make more of the CD4+ killer cells, which target bacteria, viruses, malignant and other damaged cells.

A paper on the discovery was published Sunday in Nature Immunology. It is titled: *"Transcriptional reprogramming of mature CD4 helper T cells generates distinct MHC class II-restricted cytotoxic T lymphocytes."*

(CD4+ refers to a kind of molecule found on the surface of these cells, used to identify them. For example, the drug Rituxan works by binding to another molecule called CD20, found on the surface of B cells, another type of white blood cells.).

Earlier research has shown that helper T cells can become killer cells in some instances. However, the precise molecular mechanism for that transformation hasn't been identified until now.

"We have identified the molecular switch that enables CD4 T cells to override their programming as helper cells and transform into cytolytic (killer) cells," said La Jolla Institute scientist and study co-leader Hilde Cheroutre, in a study press release. "Our team also showed that these transformed helper T cells represent a separate and distinct population of cells. They are not a subset of TH-1 helper cells as previously thought."

In the study, the researchers found that a certain transcription factor prevents helper T cells from turning into killer T cells. Working in mice, the researchers found that turning off this transcription factor, called ThPOK, enabled helper cells in the blood, spleen and intestines to become killer T cells.

"While our work focused on the intestines, we found that helper T cells in all tissues of the body have the potential to become killer cells in response to recognition of viral, tumor or other antigens in the context of cytokines such as IL-15," Cheroutre said in the press release.

Moreover, this transformation into killer cells takes place naturally. Cheroutre said such a transformation could explain why some HIV+ people don't develop AIDS -- their boosted immune-fighting power might be enough to keep the virus in check.

HIV becomes AIDS after another kind of T cell called CD8 becomes exhausted. The fresh supply from helper T cells could make the difference, she said.

"It's like the helper cells can come in as reinforcements to keep the virus under control," she said. "If we can develop ways to artificially trigger that process, we may be able to significantly help people with HIV and other chronic infections."

Cheroutre is the paper's senior author. First authors on the paper are: Mohammad Mushtaq Husain, of the La Jolla Institute; Daniel Mucida, Ph.D., formerly of the La Jolla Institute, now at Rockefeller University; Femke van Wijk, formerly of the La Jolla Institute, now at the University Medical Center Utrecht, The Netherlands, and Sawako Muroi, of the Riken Institute in Japan.

The more scientists study the immune system, the more refinements they discover about the roles of the various white blood cells in identifying invaders and responding to them. This knowledge can be applied to modulating the immune system so it can recognize threats from inside the body, such as cancer; or in convincing it not to attack the body, as in autoimmune diseases.

Alternatively, molecules produced by the immune system can be used for these purposes in a passive therapy. Rituxan, for example, was originally approved to treat B-cell non-Hodgkin's lymphoma, by killing B-cells. It's also used in autoimmune disorders like rheumatoid arthritis, which results in B-cell dysfunction.