MedicalXpress

T-cell discovery holds promise for organ transplant and immunodeficiency treatment

August 23 2011

University of British Columbia researchers have solved a long-standing mystery surrounding the activation of T-cells, white blood cells that find and kill viruses and bacteria but also participate in the rejection of transplanted organs.

By identifying the mechanism that leads T-cells to spring into action and proliferate, the research, published online this month by the journal *Immunity*, provides a new target for future or existing drugs that could bolster the immune systems of people with HIV or cancer, according to lead researcher Wilfred Jefferies, professor in the Michael Smith Laboratories. Such drugs could also be used for the opposite effect – to stop the rejection of transplanted organs, or inhibit the immune system from attacking normal tissues, as happens in auto-immune disease such as arthritis or diabetes.

T-cells, so named because they mature in the thymus organ, located just above the heart, are one of the "scouts" of the immune system, traveling through the bloodstream searching for foreign substances. Once they find a target, they activate and directly attack it, and also proliferate to assist in finding and killing other similar foreign targets.

T-cells are regulated through a receptor on their surface that binds with complementary receptors on infected cells that act as a "flag" that infection has occurred. The interaction triggers a signaling pathway that includes a flow of calcium ions in the T-cell, ultimately leading it to become an effector T-cell, which kills the infected cell. The signaling

also allows the T-cell to replicate in sufficient numbers to destroy other similarly infected cells.

Such "calcium channels" play a role in the contraction of muscle cells or transmission of signals in neurons, but it wasn't clear until now what mediates the flow of calcium ions into T-cells. Jefferies' team identified the specific channel and demonstrated the unique qualities that enable it to be activated by the T-cell receptor.

The researchers also found that, compared to normal mice, mice lacking the gene for this specific calcium channel have significantly compromised immune systems. Further analysis demonstrated that in T-cells missing the specific calcium channel gene, immune activation through engagement of the T-cell receptor was severely impaired.

"Other types of calcium channels expressed in neurons have been used as effective targets for the identification of new drugs that manage pain, so it's not much of a leap at this point to target this particular channel for a different purpose – to either enhance or inhibit a person's T-cell response," says Jefferies, who holds appointments in the departments of microbiology and immunology, medical genetics and zoology, and also is a member of the Biomedical Research Centre and the Centre for Blood Research.

Provided by University of British Columbia