SOUTHWESTERN NEWS

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Two molecules work together to aid transport of immune cells, UT Southwestern researchers find

DALLAS – April 20, 2004 – New research findings about T-cell transport shed light on how the normal immune system functions and could have implications in fighting autoimmune and inflammatory diseases, say researchers at UT Southwestern Medical Center at Dallas.

Two molecules on the surfaces of T-cells – a type of immune cell – must work in tandem to help the T-cells cross from the bloodstream into infected tissues, where the T-cells initiate an immune or inflammatory response, researchers at UT Southwestern have discovered.

The research, which was done in mice, appears in the April 21 issue of the journal *Immunity*.

In order to fight certain infections, T-cells must migrate from the bloodstream and into infected tissue. T-cells also cross blood vessel walls to initiate inflammatory or autoimmune responses in diseases such as rheumatoid arthritis, type 1 diabetes, lupus, asthma, Crohn's disease and colitis.

Scientists know that two specific molecules, or receptors, on passing T-cells in the bloodstream interact with receptors on the walls of blood vessels. One T-cell receptor, called CD44, is responsible for getting the T-cells to "roll" along the blood vessel wall.

"CD44 governs the rolling behavior of the T-cell, where it touches and then lifts off the vascular wall," said Dr. Mark Siegelman, associate professor of pathology at UT Southwestern and senior author of the study.

A second receptor, VLA-4, stops the T-cells from rolling. This step in the process is called firm adhesion.

"You need both of these steps in order to get the T-cells out of the blood vessel and into tissue," Dr. Siegelman said. "Only by completing the second step, firm adhesion, has the T-cell committed to sticking and getting out."

In the new research, UT Southwestern scientists found that in order to get the T-cells to stick

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firmly to the vascular wall, the CD44 and VLA-4 receptors on the T-cell had to be physically linked. If they do not form what's called a bimolecular complex, firm adhesion does not occur.

"Our findings define a relationship between CD44 and VLA-4 that results in a cooperative system," Dr. Siegelman said. "If they aren't linked, the T-cells exhibit rolling behavior, but not firm adhesion, and, therefore, they don't move through the blood vessel wall to initiate immune or inflammatory responses."

The researchers also found that if part of the CD44 receptor is missing, the bimolecular complex does not form, inhibiting the T-cells from moving out of the bloodstream.

The research results may aid in future development of treatments for rheumatoid arthritis, for example, a condition in which T-cells travel from the bloodstream and into the space between joints, causing painful inflammation.

"One strategy for drug development might be to target CD44 or this bimolecular complex in order to prevent T-cells from getting in there and starting an inflammatory response," Dr. Siegelman said.

Other UT Southwestern researchers involved with the study are Dr. Animesh Nandi, research scientist in biochemistry, and Dr. Pila Estess, assistant professor of pathology.

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