

SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS DISCOVER STAGES USED BY IMMUNE SYSTEM CELLS TO ELIMINATE VIRAL INFECTIONS, CANCER CELLS

DALLAS – June 9, 2003 – Researchers at UT Southwestern Medical Center at Dallas have partially uncovered the stages in the elimination of viral infections and cancer cells by the human immune system, a finding that may lead to better treatments for certain cancers.

Their work appears in an upcoming issue of the *Proceedings of the National Academy of Sciences* and is currently available online.

“We have been applying new technology to an old problem: How do cells of the immune system recognize and deal with infected cells and other cells, such as tumor cells, that would be harmful to the well-being of the organism?” said Dr. John Schatzle, assistant professor of pathology and senior author of the study.

The immune system uses natural killer (NK) cells and cytotoxic T cells to help eliminate viral infections and cancer cells, said Dr. Christoph Wuelfing, assistant professor in the Center for Immunology and the study’s lead author.

UT Southwestern researchers used three-dimensional microscopy in real-time to visualize the subcellular localization of components of NK cells during the in vitro killing of tumor target cells. By learning that cellular organization has to go through a defined series of steps to kill a target cell, researchers now can study how these cells function, said Dr. Wuelfing.

Specifically, the researchers examined the NK cell cytoskeleton (the part of each cell primarily responsible for the spatial organization of its components) during target cell killing in comparison to that of cytotoxic T cells. Both of these immune system cells release toxic molecules through a highly regulated process controlled by receptors attached to them.

The cells, however, differ in their roles and the types of receptors they use to recognize cells to be eliminated, Dr. Schatzle said. The NK cells represent effectors of the innate immune response and constitute a first line of defense against infection and tumors. The cytotoxic T cells represent the acquired arm of the immune system, providing a more thorough second line of

(MORE)

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defense and “memory” by responding vigorously if the same infected cell or tumor returns to the organism.

In their study, the UT Southwestern researchers learned while both cell types kill targets using the same mechanisms, there are significant differences in how they achieve the same goal.

“Up to now, it has not been appreciated that cytoskeletal organization is an important element in the regulation of NK cell activity,” Dr. Wuelfing said. “Establishing this in our study will allow further research to better understand NK cell activation and possibly the development of tools to regulate NK cell behavior in combating cancer cells.”

The next step is to find out how the cytoskeleton of the natural killer cells is regulated and what signaling molecules and receptors are involved in the process. That eventually could allow the manufacturing of more efficient NK cells.

This could be significant in combating cancer, Dr. Wuelfing said, as the reactivity of NK cells – in particular against leukemia – is currently mediocre. Leukemia is a cancer of the bone marrow and blood characterized by the uncontrolled accumulation of blood cells.

“Our ability to regulate the function of these cells could allow us to manipulate the immune system in new ways to combat infections and cancer,” Dr. Schatzle said. “Our discovery that these cells regulate their ability to release the toxins that kill their targets in very different ways was surprising and has now led us to the point where we can begin to define the molecules that specifically control that process.”

Other UT Southwestern contributors to the *PNAS* study were Bozidar Purtic, Center for Immunology student research assistant, and Dr. Jennifer Klem, recent graduate of the Southwestern Graduate School of Biomedical Sciences.

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