Researchers find chemical signals that initiate the body's immune response

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(Medical Xpress) -- University of Florida researchers have identified two key steps required to activate the body's innate immune system, its first line of defense against infection.

The discoveries offer insight into why some trauma patients survive their initial injuries but die from seemingly less serious causes soon afterward.

"We're able to bring them through the trauma with an 80 percent or higher success rate, and then after a few weeks in the hospital they succumb to secondary infections, like pneumonia and urinary tract infections," said Dr. Matthew Delano, a UF surgical resident.

Researchers, including Delano and Lyle Moldawer, a professor and vice chairman of research in UF's department of surgery, say understanding the chemical signals that help direct immunity may lead to improved therapies for patients with suppressed immune systems, such as those with critical injuries, HIV and cancer, who need extra help fighting infections.

In an article published in the July issue of the *Journal of Experimental Medicine*, the scientists describe how B cells, a specific type of white blood cell, release a chemical called CXCL10 to trigger inflammation and the deployment of cells designed to fight any pathogens or foreign matter.

Previously, B cells were thought to be involved only in the body's

adaptive immune response, which recognizes invaders, proliferates and responds more effectively to subsequent encounters. The innate immune response is more generic and wasn't thought to convey any long-lasting immunity to specific threats.

"What we showed, which is actually quite revolutionary, is that B cells modulate the early innate immune response," Moldawer said.

A review of the paper appeared in the August issue of Nature Reviews Immunology.

In a separate study published in the July 15 issue of the Journal of Immunology, researchers identified a protein called stromal cell-derived factor 1, known as SDF-1, that directs the release of neutrophils, another type of white blood cell, from the bone marrow to the site of infection. Neutrophils will attack any pathogen and are one of the body's first weapons used to fight infection.

Bone marrow usually makes SDF-1, but stops production when an infection begins. Tissues at the infection site start making the protein instead, and neutrophils migrate to the areas with the highest concentrations of SDF-1. Once there, they battle the invading pathogens.

"If we block this increase (in SDF-1 in the infected area), then we don't see a mobilization," Moldawer said. "The neutrophils are not recruited to the site of infection and the infection can't be controlled."

Moldawer said SDF-1 also speeds neutrophils' development from stem cells and increases their "bacteria-killing properties."

The identification of SDF-1 and of CXCL10 in activating the body's innate immune response could pave the way for medicines that stimulate innate immunity in immune-suppressed patients.

Scientists from the University of California,-Los Angeles, Yale University, Duke University Medical Center, Osaka University, Merck Research Laboratories and the University of Virginia also helped with the studies.

“The next step is to ask whether giving SDF-1 can improve outcomes in patients that have reduced numbers of inflammatory cells due to chemotherapy, malnutrition, etc.,” Moldawer said.

The researchers will ask the same question about CXCL10.

Dr. Richard Hotchkiss, a professor at Washington University School of Medicine in St. Louis, applauded the researchers’ efforts to find new approaches to fighting infection and preventing and battling sepsis. Sepsis is a serious complication of infection in which the immune system becomes overactive and disrupts normal blood flow. The condition can lead to organ failure. Hotchkiss was not involved in the research.

“Using drugs which can up- or down-regulate host immunity would be a nice accompanying approach to sepsis,” he said. “Rather than just focusing on antibiotics, we should be focusing on drugs which can improve patient immunity and their ability to fight off new, secondary infections.”

Provided by University of Florida