MedicalXpress

Regulatory B cells exist -- and pack a punch

May 27 2008

Researchers at Duke University Medical Center have uncovered definitive evidence that a small but potent subset of immune system B cells is able to regulate inflammation.

Using a new set of scientific tools to identify and count these cells, the team showed that these B cells can block contact hypersensitivity, the type of skin reactions that many people have when they brush against poison ivy.

The findings may have large implications for scientists and physicians who develop vaccines and study immune-linked diseases, including cancer. Once the cells that regulate inflammatory responses are identified, scientists may have a better way to develop treatments for many diseases, particularly autoimmune diseases such as arthritis, type 1 diabetes and multiple sclerosis.

“While the study of regulatory T cells is a hot area with obvious clinical applications, everyone has been pretty skeptical about whether regulatory B cells exist,” said Thomas F. Tedder, Ph.D., chairman of the Immunology Department and lead author of the study published in the May issue of Immunity. “I am converted. They do exist.”

Koichi Yanaba and Jean-David Bouaziz identified this unique subset of small white blood cells, which they call B10 cells, in the Tedder laboratory.

The researchers found that B10 cells produce a potent cytokine, called

IL-10 (interleukin-10), a protein that can inhibit immune responses. The B10 cells also can affect the function of T cells, which are immune system cells that generally boost immune responses by producing cytokines. T cells also attack tumors and virus-infected cells.

The study was supported by grants from the NIH, the Association pour la Recherche contre le Cancer (ARC), Foundation Rene Touraine, and the Philippe Foundation.

Depleting B10 cells may enhance some immune responses, Tedder said. Enhancing B10 cell function may inhibit inflammation and immune responses in other diseases, like contact hypersensitivity.

“Now that we have been able to identify this regulatory B cell subset, we have already developed treatments that deplete these cells in mice. We are moving to translate these findings to benefit people,” he said.

“The discovery of the ability to identify this potent regulatory cell type should provide important clues to how the immune system regulates itself in response to vaccines as well as infectious agents,” says Barton F. Haynes, M.D., leader of the international Center for HIV/AIDS Vaccine Immunology (CHAVI), a consortium of universities and academic medical centers, and director of the Duke Human Vaccine Institute. “This information should enable researchers to design ways to help the immune system control infections more effectively, and could be a useful advance as we refine approaches to preventing HIV infection.”

There’s a huge initiative underway to look at regulatory T cells in autoimmune disease, HIV infection, and cancer therapy,” Tedder said. “What we have also shown is that it is not only regulatory T cells, but also regulatory B cells that could prevent a person from making effective immune responses in HIV and many other diseases, particularly cancer.”

The Duke researchers developed a way to mark the B10 cells so that they could see that just these cells were producing IL-10. Previously, scientists could only purify a population of B cells and see whether IL-10 could be produced by some of these cells in the population.

In this study, they found that the B10 cells represented only 1-2 percent of all of the B cells in the spleen of a normal mouse. Before this, no one had definitively identified this B cell subset or such regulatory B cells in normal mice, although B cell regulatory function had been described in some genetically altered mice with chronic inflammation.

“In this study, we could directly look at the B cells that were producing IL-10, and figure out what their cell surface molecules looked like, so that we could isolate them. This allowed us to show that this rare subset of B cells controlled immune responses by producing IL-10, which inhibits T cell inflammatory responses,” Tedder said.

The scientists studied a special mouse (CD19-deficient) with altered genes that give them an increased contact hypersensitivity reaction. As it turned out, these mice lacked B10 cells, which resulted in exaggerated inflammation reaction. “This allowed us to show that giving CD19-deficient mice a few B10 cells had a big effect on reducing inflammation,” Tedder said.

They found that depleting all B cells in the mice also resulted in worse inflammation. Since total B cell depletion therapies are now being used to treat people with B cell cancers and autoimmune disease, these findings help to further explain how these therapies treat disease. They also open the door to creating new therapies that take advantage of the power of B10 cells.

This is the first of several papers that will describe cases in which regulatory B10 cells help control immune responses, Tedder said.

Source: Duke University