The Right B Cells at the Right Time Fight Nerve Disease

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(PhysOrg.com) -- Duke University Medical Center scientists have figured out which type of B cells act -- and at what time -- to keep a multiple-sclerosis (MS)-like disease under control, knowledge that will help to create better therapies.

Thomas Tedder, Ph.D., chair of the Duke Department of Immunology, and colleagues have identified a regulatory B cell subset, called B10 cells, that does more than just create antibodies. They appear to control the action of other lymphocytes.

"In the case of MS-like symptoms, these rare B10 cells are so potent, they are amazing," Tedder said. "This special B-cell subset is needed early in the disease to reduce symptoms and tissue destruction. After that, depleting other B cells is helpful, because B cells can go on to amplify responses by other cells that produce detrimental effects once the disease is established."

In lab experiments, the researchers showed that these B10 cells strongly blocked contact hypersensitivity responses in mice, the type of skin reactions that poison ivy causes.

The Duke team's work is timely because the U.S. Food and Drug Administration is close to approving a form of B-cell depletion therapy to treat MS.

But depleting these regulatory B cells along with other B cells may not be

good for people predisposed to some autoimmune diseases, in which wayward antibodies and lymphocytes attack the body's own cells, Tedder said. "Data with mice show that caution is needed as you could accelerate disease in some people, although this may be very rare based on the drugs currently in clinical trials. However, these studies are exciting in that we can now learn how to use B10 cells to reduce or delay autoimmune disease onset or accelerate immune responses to cancers."

Tedder noted, "Until recently, we didn't think of these autoimmune diseases as conditions in which B cells play an active role, other than producing autoantibodies, but they do play a role. It is remarkable how much they contribute to inhibiting and exacerbating these diseases."

The conclusion is that if you can create a drug that preserves the B10 subset and depletes other B cells at the right time, that would be the best therapy, Tedder said. The study was published in the Journal of Clinical Investigation. "Alternatively, selective B10 cell depletion may be advantageous in the case of cancers," he said.

The scientists brought their knowledge of B10 power to the autoimmune disease known as EAE, the rodent equivalent of multiple sclerosis.

When they depleted B cells, including the B10 cells, a week before they induced EAE in the study mice, the mice developed severe symptoms of the disease. When the scientists gave B10 cells before they induced the disease, the B-cell depleted mice had normal disease symptoms.

Then they looked at what happened after the disease had begun. Fourteen days after the disease was induced, the scientists showed that depleting B cells during the EAE disease progression dramatically suppressed MS-like symptoms, something that is also being observed in ongoing clinical trials.

A three-page commentary on the study, also in the Journal of Clinical Investigation, noted that "it will be very important to determine the involvement of ... regulatory B cells in each autoimmune disease and, if there is any, to determine when this subset participates during disease initiation and progression.... This new study definitely provides important insight for developing the best regimen of anti-B cell therapy for autoimmune diseases."

Provided by Duke University