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Cell-signaling protein holds key to understanding autoantibody formation in lupus patients

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A signaling molecule called interferon gamma could hold the key to understanding how harmful autoantibodies form in lupus patients. The finding could lead to new treatments for the chronic autoimmune disease, said researchers at Penn State College of Medicine.

Systemic lupus erythematosus (SLE) is the most common form of lupus. In patients with SLE, the immune system forms autoantibodies that attack the body's own cells, causing inflammation and tissue damage. How these rogue antibodies form is an important area of interest for lupus researchers.

When a pathogen like a virus invades the body, immune cells called B lymphocytes multiply to fight the foreigner. These groups of B lymphocytes produce antibodies specially designed to fight the specific invader or turn into antibody-secreting cells and memory B cells that give long-term protection and help protect the next time the same pathogen is encountered.

In both humans and mice with lupus, groups of B lymphocytes (B cells) spontaneously arise in the absence of a pathogenic infection. Instead of producing antibodies to fight an infection, these groups pump out specialized autoantibodies that efficiently attack healthy tissue. These attacks on the body's own cells are the hallmark of autoimmune disorders like lupus.

Autoantibody-secreting B cells and memory B cells that continuously generate autoantibodies are also created, setting the body up for ongoing attacks, chronic inflammation and—over time—organ damage.

But what factors drive the development of groups of B cells, called autoreactive B cells, that produce autoantibodies in lupus?

Dr. Ziaur S.M. Rahman, assistant professor of microbiology and immunology, is working to answer what factors drive the development of B lymphocyte groups without the presence of a pathogen.

Penn State College of Medicine researchers homed in on the role of a particular cytokine—a cell-signaling protein—called interferon gamma, that is involved in the immune system. Researchers published their results today in the Journal of Experimental Medicine.

People with SLE tend to have higher levels of interferon gamma production, and lupus mice that are deficient in it have reduced autoantibody production and less severe renal disease, a major lupus complication.

To find out if interferon gamma is behind the formation of spontaneously developed B lymphocyte groups, the researchers looked at lupus mice whose interferon gamma receptors in B cells had been removed.

These mice did not form the groups, while mice that had intact interferon gamma receptors did. These mice also had lower levels of autoantibodies involved in lupus compared to the normal mice.

"This suggests that interferon gamma signaling in B cells is critical for the formation of spontaneously-developed B lymphocyte groups and autoimmunity," Rahman said. "If you could target this interferon gamma signaling pathway in B cells, you could potentially treat lupus."

Moreover, the researchers also discovered that the formation of normal B lymphocyte groups that produce antibodies to fight real infections is not dependent on interferon gamma signaling.

The current treatment options for SLE are limited to the use of immunosuppressive agents that make patients susceptible to infection. This novel intervention could be an improvement for lupus patients, as targeting interferon gamma signaling would eliminate spontaneously developed groups of B cells that produce autoantibodies and keep normal B cell responses intact to fight against infection, Rahman said.

Source:
Penn State Milton S. Hershey Medical Center
