

Researchers find new clue in lupus autoantibody production

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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 specifically designed to fight the invader or turn into antibody-secreting cells and memory B cells that will 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 attack healthy tissue. These attacks on the body's own cells are the hallmark of an autoimmune disorder.

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 those B cells, called autoreactive B cells that produce autoantibodies?

In work led by Ziaur S.M. Rahman, assistant professor of microbiology and immunology, a team

at Penn State College of Medicine found that a cytokine—a cell-signaling protein—called interferon gamma may play a role. The research was published online April 11 in the *Journal of Experimental Medicine*.

Interferon gamma stimulates [immune cells](#) as part of the normal immune response to infection. Earlier studies showed that people with SLE tend to have higher levels of interferon gamma, 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 B lymphocyte groups that produce autoantibodies, the researchers looked at lupus mice whose interferon gamma receptors on B cells had been removed.

These mice did not form the damaging B cell groups, while lupus mice that still had intact interferon gamma receptors did. The mice without interferon gamma receptors also had lower levels of autoantibodies involved in lupus compared to the lupus mice with normal numbers of receptors.

"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](#)."

The researchers also discovered that normal B lymphocyte groups could produce antibodies to fight real infections even in the absence of interferon gamma signaling.

The current treatment options for SLE are limited to the use of immunosuppressive agents that reduce immune function in general and make patients susceptible to infection. An intervention targeting the [interferon gamma](#) pathway could be an

improvement for [lupus patients](#), as it would eliminate spontaneously developed groups of B [cells](#) that produce autoantibodies and keep normal B cell responses intact to fight against infection, Rahman said.

Provided by Pennsylvania State University

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