Commonly used drugs may not be effective against autoimmune illness

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Credit: Patrick Lynch

(Medical Xpress)—Drugs for autoimmune diseases like lupus that block only one of the two principal signaling pathways can activate an overabundance of one potentially disease-causing type of immune cell population over another, a Yale study has found. The findings about T lymphocytes, white blood cells that regulate the immune response, have implications for the development of new vaccination strategies and therapies for autoimmune diseases. The study appears in the Cell Press journal *Immunity*.

The researchers studied this process in a model of viral infection that is similar to human influenza and certain autoimmune diseases like systemic lupus erythematosus (SLE). They uncovered opposing roles for signaling pathways STAT3 and type I interferon (IFN) in differentiating the T helper cells that regulate immune cell response to viruses. Blockade of one resulted in an increase of T helper cells in the other that could lead to an immune system overreaction, and, ultimately, in lupus, exacerbation of the autoimmune disease.

Patients with autoimmune diseases like lupus contain both populations of T lymphocytes examined in this study. Previous strategies have been focused on treating patients by blocking one principal pathway or the other. Based on findings in the Yale work, such a strategy could boomerang, promoting activation of the opposing pathway, and lack of therapeutic efficacy. By contrast, the work suggests that more effective therapies should block both pathways.

"This suggests that both pathways would have to be blocked in human SLE in order not to risk exacerbation of one or the other," said senior author Dr. Joseph Craft, the Paul B. Beeson Professor of Rheumatology, professor of immunobiology, and director of the investigative medicine program at Yale School of Medicine.

Standard treatments for SLE and other autoimmune illnesses involve steroids and immunosuppressive drugs, as well as newer, cutting-edge biologics, but Craft says these are not as beneficial as the scientific community had hoped. "Our lab and others are working now on combining therapies to block pathways for both inflammation and antibody production," he said.

Provided by Yale University