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B cells can act alone in autoimmune disease

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B cells, the source of damaging autoantibodies, have long been thought to depend upon T cells for their activation and were not considered important in the initiation of autoimmune diseases like lupus or rheumatoid arthritis.

In the Aug. 7 online issue of the journal of *Immunity*, Yale University researchers turn this paradigm on its head by showing that in systemic autoimmune diseases B cells can be activated the absence of T cells.

The study suggests new ways to intervene in the immune system's chronic attacks on the body's own tissue.

The findings were surprising because many scientists believed that B cells remain quiet in autoimmune diseases unless they are stimulated first by T cells, said Mark Shlomchik, MD, professor of laboratory medicine and immunobiology at the Yale School of Medicine and senior author of the study.

"It became a chicken or egg problem. If cooperation between T and B cells is needed to create an autoimmune disease, who falls off the fence first, and why?" Shlomchik said.

Recently this same Yale group along with collaborators at Boston University discovered an unexpected role in autoimmunity of Toll-like receptors, previously thought to be stimulated by molecules expressed on microbial pathogens. Shlomchik and his colleagues showed that they can also recognize and react to "self" molecules, in particular mammalian

DNA and RNA. When this occurs, these receptors help activate B cells that make the classical autoantibodies of lupus.

The new Yale study now shows that these signals substitute for T cells in starting the autoimmune process in B cells. The researchers propose that once B cells are activated via Toll-like receptors, they can subsequently recruit T cells and that this can lead to a "vicious cycle" of chronic autoimmune disease in which the two types of cell activate each other.

The findings might explain why treatments that target T cells in autoimmune diseases have fared relatively poorly, while newer treatments aimed at B cells have shown great promise, he said.

The current study is a direct outgrowth of groundbreaking work conducted at Yale over the last 15 years that showed that elements of the innate, or non-specific immune system such as Toll-like receptors, needed to be triggered before more sophisticated adaptive immune system of humans and other animals could hone in on specific pathogens.

Source: Yale University