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Researchers find potential new antibody treatment for autoimmune diseases

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Scientists at UCSF have discovered an abnormality in a patient's immune system that may lead to safer therapies for autoimmune diseases such as rheumatoid arthritis and colitis, as well as potential new ways to treat transplant rejection.

The research identified antibodies from a woman's immune system that prevent infection-fighting T cells from moving through her blood stream and entering her body's organs to attack invaders such as bacteria or viruses. Findings appear in the current online edition of the *FASEB Journal*, the official journal of the Federation of American Societies for Experimental Biology.

Based on studies in which the woman's antibodies were transferred into mice, researchers hope these antibodies can be used to treat patients with autoimmunity or transplant recipients whose immune systems attack a transplanted organ or tissue.

Autoimmunity occurs when the body perceives its own cells or tissue as foreign organisms and creates an immune response to itself. Autoimmune diseases affect approximately five to eight percent of Americans and their prevalence is increasing, according to the National Institute of Allergy and Infectious Diseases. The majority of people with autoimmune diseases are women.

"This is the first selective antibody of its type discovered in a patient," said lead study author Edward J. Goetzl, MD, UCSF professor of

medicine and immunology. "Antibodies that react more generally against blood cells, such as T cells, previously have been identified. However, this is the first to block a specific aspect of T-cell function. Our study offers a potential new approach to developing safer, more targeted therapies based on human antibodies."

Therapies using proper doses of these newly discovered antibodies may carry less risk of infections or tumors than current treatments, since the antibodies target T cells' specific patrolling activities, rather than their overall function.

Goetzl's team evaluated a woman with a low number of blood T cells and frequent infections in the ears, urinary tract and lungs. The infection of several organs suggested a defect in the patient's immune system similar to Acquired Immune Deficiency Syndrome (AIDS), but the patient tested negative for human immunodeficiency virus (HIV).

Further studies revealed that the patient's CD4 T cells did not move out of her lymph nodes as they would in a normal immune system because her body created antibodies to one type of sphingosine 1-phosphate (S1P) receptor. S1P is critical to appropriate immune responses since it regulates T- and B-cell movement throughout the body by interacting with its receptor. The patient's antibodies blocked the signaling that triggers T-cell movement from the thymus and lymph nodes into blood and then into many organs.

Researchers then explored whether the woman's antibodies effectively could inhibit an autoimmune response in mice. Antibodies against the S1P receptor, created from the patient's antibody-producing cells, were injected into mice that were induced to develop colitis. The result was a significant reduction in severity of their diseases, including colitis-associated weight loss, in those mice compared to mice that did not receive the antibodies.

"These results have broad biological implications, since the cells that carry out our immune responses are present in every organ," said Goetzl, director of UCSF Allergy and Immunology Research, which focuses on developing new diagnostic approaches and treatments for allergic and immunological diseases.

Source: University of California - San Francisco