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Immune Cell Plays Unexpected Role in Autoimmune Disease

A new study provides fascinating insight into the underlying pathology associated with the autoimmune disease, Systemic Lupus Erythematosus (SLE). The research, published by Cell Press in the December issue of the journal Immunity, reveals an unexpected role for a key type of immune cell and provides a potential new therapeutic strategy for SLE and, potentially, other autoimmune diseases.

SLE is a chronic systemic disease that can affect many regions of the body and, as a result, presents with diverse clinical symptoms. As is characteristic of other autoimmune disease, in SLE the immune system attacks and damages the body's own cells and tissues. Previous research had shown that SLE is associated with activation of the two main parts of the adaptive immune system, B cells and T cells.

"We were interested in examining the contribution of another type of immune cell, the dendritic cell (DC), to SLE pathology," explains senior study author Dr. Mark J. Shlomchik from Yale University School of Medicine in New Haven, Connecticut. "DCs initiate and control the adaptive immune response to infection and have the potential to influence SLE in many different ways."

Dr. Shlomchik and colleagues deleted DCs in a mouse model of SLE and observed that although DCs contributed to the expansion and differentiation of T cells, they were surprisingly not required for the initial activation of T cells. These findings were unexpected because it is well established that DC cells initiate the T and B cell immune response to pathogens. Alternatively, DCs were very important for the invasion of target organs by inflammatory

cells, including T cells. SLE-prone mice lacking DCs had markedly reduced kidney and skin disease. DCs also markedly affected the quantity and quality of the classic autoantibody response associated with lupus.

Taken together, the observations indicate that the way DC cells function in autoimmune disease is quite different from their role in the immune response to pathogens. "Our findings reveal that DCs operate not to initiate but rather to amplify disease in a mouse model of lupus which is in contrast to how they are thought to work in response to infection," concludes Dr. Shlomchik. "Although there is much more work to do in defining the roles of DCs in autoimmunity our current data validate DCs as a potential new therapeutic target in autoimmunity as well as point to future studies to determine how DCs promote local tissue inflammation and to test if depleting DCs will be therapeutic during disease."

Lino L. Teichmann, Michelle L. Ols, Michael Kashgarian, Boris Reizis, Daniel H. Kaplan, Mark J. Shlomchik. Dendritic Cells in Lupus Are Not Required for Activation of T and B Cells but Promote Their Expansion, Resulting in Tissue Damage. *Immunity*, 16 December 2010 DOI: 10.1016/j.immuni.2010.11.025