Follicular dendritic cells are essential for maintenance of autoreactive B cells

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Follicular dendritic cells (FDC) are essential for directing and sustaining a protective and long-lasting antibody response to infection in lymphoid tissues. This important function is mediated by their unique ability to retain antigen for extensive periods and to provide essential cytokine signals for lymphocytes. Whether they play a similar role in maintenance of autoreactive B cells and self-antigen specific germinal centers is not known. Recently, we identified a novel pathway by which FDC endocytose and cycle foreign antigen via complement receptor CD21 and periodically present it to cognate B cells (Heesters et al, *Immunity, 2013*). To test whether this pathway is required for maintenance of autoreactive B cells, FDC were characterized in lupus-prone mice.

We found that FDC in the autoimmune strains take-up and cycle immune complexes containing self-antigen similar to that observed with foreign antigen. Strikingly, FDC internalization of nucleolar antigens via CD21 triggers endosomal Toll-like-receptors, leading to induction of IFNα secretion. Blockade *in vivo* of this pathway leads to a marked reduction in circulating autoreactive B cells and autoantibody titers.

In summary, we propose that FDC "survey" internalized immune complexes for the presence of danger via intersection of the CD21 receptor containing endosome with the TLR compartment. These findings have implications for not only autoimmunity but could be exploited in vaccine development.