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Development of a novel way to treat autoimmune disease by regulating humoral immune systems

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Abstract

Memory antibody response is characterized by its rapidness and robustness, which are regulated by memory B cell intrinsic and extrinsic mechanisms. We have previously demonstrated that CD4 T cells were found to reside close to memory B cells and that depletion of CD4 T cells abolished secondary antibody response. However, the identity of these CD4 T cells was not clear. Here, we show that memory B cells are preferentially activated by antigen-specific memory CD4 T cells. Follicular helper T effector cells could give rise to long-lived memory T cells and majority of those memory T cells were $CXCR5^{+}CD62L^{lo}$, which resided at T-B border or follicles and exhibited potent helper activity for memory B cell activation. Those memory T cells expressed Bcl6 promptly after re-stimulation in vivo and Bcl6 expression in memory T cells were required for their ability to activate memory B cells. Antigen-specific memory B cells appeared to be primary antigen-presenting cells for memory T cell activation, since memory B cells presented antigenic peptide efficiently in vivo and depletion of $CD11c^{+}$ cells did not compromise memory T cell activation. Thus, our results suggest that new compartment of memory T cells is retained at the site of primary immune responses with antigen-specific memory B cells, which accelerate antigen-recall ability.