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## HOW AUTOACTIVE B CELLS ARE ACTIVATED

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How autoreactive B cell responses initiate has been unclear. We have used the AM14 Rheumatoid Factor (RF) system to investigate the site and types of initial autoreactive B cell responses, which occurs spontaneously only in autoimmune-prone mice. The autoimmune response is characterized by a predominantly extrafollicular B cell reaction that generates short-lived plasmablasts, without GCs. Investigating the factors that control the extrafollicular response, and why it differs from the GC response, we have discovered that the introduction of IgG2a anti-chromatin Abs (but not other types of ICs) triggers a response that highly resembles the spontaneous one in MRL/lpr mice. We have used this system to test the requirements for T cells and TLRs in RF B cell activation and somatic hypermutation. We have also studied a number of other factors that could impact on the response, including BlyS, APRIL, IL-21, and DCs. I will present data from some of these new studies, which together better define the nature of the autoreactive extrafollicular B cell immune response. Overall, our results indicate that autoreactive B cell activation can occur first, prior to and without concurrent T cell activation. However, B-T interaction does occur physiologically, suggesting that once B cell tolerance is broken, activated B cells can break T cell tolerance. DCs may also amplify activation of certain types of B cells and promote some aspects of disease, but they most likely function downstream of initial activation of B and then T cells.

### References:

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