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Paying the price: Protection against intracellular bacterial infection but at what cost?

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Humoral immunity was originally believed to have a limited role in the immune response to intracellular bacteria, and that cell-mediated immunity was the principle mechanism of host defense. However, a number of studies have demonstrated a role for B cells and antibodies, even though T cells are required for optimal function. We have previously demonstrated that infection with *Ehrlichia muris*, a gram-negative intracellular bacterium, elicits CD4 T cell-independent protection against fatal ehrlichia challenge. *E. muris* infection induces a robust expansion of a novel splenic CD11c^{lo} plasmablast population at peak infection. These cells secrete nearly all of the IgM, which dominates the acute humoral response against the bacterium and is responsible for the generation of long-term immunity against secondary challenge with fatal ehrlichia. Even though long-term immunity is achieved, the massive IgM response impairs the generation of high-affinity, isotype-switched antibodies. It is not until day 15 post-infection that we are able to detect an IgG titer in the sera of *E. muris*-infected mice. Furthermore, we demonstrate that the IgG-secreting cells are not produced in the spleen but are generated only in the lymph nodes of infected mice. Lymphotoxin-deficient chimeric mice, which lack lymph nodes, mount a comparable IgM response, however, these mice have no detectable antigen-specific IgG titers. These results are further supported by the studies examining the kinetics of germinal center formation. As early as day 13, GC B cells can be detected in the lymph nodes of infected mice. It is not until day 28 post-infection, that germinal center B cells can be detected in the spleen, however, it is minimal compared to the response generated in lymph nodes. Furthermore, *E. muris*-infected mice challenged with a T cell-dependent antigen, NP-CGG, exhibited an impaired IgG response. At day 19 post-infection, NP-specific IgG titers were 100-fold lower compared to controls. The results from our studies first demonstrate that the IgM secreted by the novel CD11c^{lo} plasmablasts populations generates immunity against fatal ehrlichia challenge. Even though long-term protection is generated, *E. muris* also induces immunosuppression since there is an attenuated IgG response upon secondary challenge with a T cell dependent antigen.