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**B lymphocytes in health and disease:** The Waldschmidt laboratory is focused on the studying the function of B cells, one of the key lymphocyte subsets within the adaptive immune system. B cells produce antibodies, an essential weapon used by the body to eliminate extracellular pathogens like bacteria and fungi. Antibodies induced by vaccines are also crucial to protect against infection with viruses such as influenza. Work in the laboratory is focused on three facets of B cell biology: The first is to understand the development and activation of this lymphocyte subset under normal conditions. The second is to fully explore the role of B cell-mediated immunity invoked after influenza infection. The third is to reveal the means by which chronic abuse of alcohol leads to compromised B lymphocyte function and poor antibody responses in alcoholic patients.

**B cell maturation and germinal center reactions:** It is understood that B cells mature in the bone marrow and undergo a well-defined developmental sequence. This process leads to a variety of mature B cell subsets in the peripheral lymphoid organs (spleen and lymph nodes) including follicular B cells, marginal zone B cells and B1 B cells. The Waldschmidt laboratory has participated in a number of studies to not only
help clarify the various stages of B cell development, but the factors necessary for maturation. Additional work has focused on defining B cell subsets in the periphery as well as their role in antibody-based immunity. Equally important, the laboratory is interested in revealing key signals necessary for activation and differentiation of mature B cells, especially those leading to germinal centers (GCs), a key response that generates high affinity plasma cells and memory B cells. These cell types produce antibodies crucial for clearing the offending pathogen and protecting the host upon secondary infection. Research is focused on understanding the complex cellular and molecular events that occur within GCs, as well as the role T regulatory cells play in governing this reaction.

**B cell responses to infection with influenza virus:** After primary infection with influenza virus (e.g. H1N1), cytotoxic CD8+ T cells play a central role in clearing the infection. However, B cells are also activated and GCs induced in order to generate plasma and memory cells that can produce anti-influenza antibodies. These antibodies are crucial to prevent infection upon subsequent exposure to the same virus, and can offer cross-protection to related viruses. The induction of GCs and generation of antibodies is also the goal of influenza vaccines, and the primary reason why these vaccines are effective. The Waldschmidt laboratory is investigating the means by which GCs are induced and regulated after influenza infection, not only in the secondary lymphoid organs, but in the lungs as well. These studies include exploring the role of both innate immunity and T follicular helper cells in the induction and maintenance of influenza-specific GCs.

**Immune deficiency induced by chronic alcohol exposure:** Chronic alcohol consumption severely compromises the immune system leading to a marked increase in infectious diseases. In collaboration with a number of investigators within the Department, a mouse model of long-term ethanol intake was established which recapitulates the immune deficiency observed in humans. Using this model, the Waldschmidt laboratory is focused on documenting lesions within the B cell compartment, and the ethanol-induced events which lead to these defects. Recent efforts have also led to the development of a fetal alcohol exposure model, with offspring likewise exhibiting profound immune deficiency.

*(See complete publications list at PubMed)*