OVERVIEW/ABSTRACT

Persistent and chronic infections pose a major, worldwide public health problem. They generally involve a complex balance between protective immunity and immunopathology. New insights into mechanisms that control this balance are needed to better combat persistent and chronic infections. A number of bacterial pathogens can cause persistent or chronic infections. Examples of bacterial pathogens that can cause persistent or chronic infections in humans include *Brucella abortus*, *Borrelia burgdorferi*, *Helicobacter pylori*, *Mycobacterium tuberculosis*, and *Salmonella enterica*. Histologically, persistent, or chronic infections with some of these pathogens (*i.e.*, *Brucella abortus*, *Mycobacterium tuberculosis*, and *Salmonella enterica*) have been associated with granulomas in peripheral tissues. Granulomas are composed primarily of macrophages (histiocytes) mixed with lymphocytes and fewer plasma cells and neutrophils. They are sites of chronic inflammation, presumably triggered by pathogen persistence. The role of granulomas in disease containment or progression is poorly understood. Recent studies have indicated that the granuloma is more complex than previously thought, highlighting the need to gain new insights into this important, yet understudied structural feature of persistent and chronic infections caused by these and other intracellular bacterial pathogens. Using a murine model of persistent salmonellosis, we recently published that inflammatory monocytes promote granuloma-mediated control of persistent *Salmonella enterica* infection. To determine the generalizability of our findings and their relevance to other types of granulomatous diseases, we will evaluate the role of inflammatory monocytes in the granulomatous response to *Mycobacterium tuberculosis*, the world's leading infectious killer. It is our expectation that the conceptual advances resulting from the proposed research will provide new insights into the role of inflammatory monocytes in immunity and host defense. Successful completion of the proposed research will provide the robust preliminary data needed to submit within the award period a new R01 grant application to the National Institutes of Health aimed at advancing fundamental knowledge of tuberculosis by characterizing tuberculosis disease, a stated strategic priority of the National Institute of Allergy and Infectious Diseases.