Abstract

Babesiosis is caused by the intraerythrocytic parasite *Babesia microti (Bm)* and is an emerging vector borne infection transmitted by the *Ixodes scapularis* tick in the U.S. with significant morbidity and mortality in elderly and immunocompromised hosts. Babesiosis incidence continues to rise, correlating with climate change and seasonal expansion of tick activity in endemic regions like Long Island. While antibiotic treatment is successful in many cases, a subset of patients present with severe parasitemia with progressive anemia and despite best measures available, 1.6% will die of refractory infection. While adaptive *Babesia* immunity has been studied in mouse models, immunity during acute human exposure is not well understood. To generate effective host-directed therapies such as vaccines, it is necessary to elucidate the immune mechanisms that control parasitemia in humans. To fill this gap, we propose to study the immunology of acute human babesiosis through recruitment of a longitudinal cohort of adult and pediatric patients with symptomatic *Bm* infection admitted to Stony Brook University Hospital who are subsequently followed as outpatients for six months after acute infection. Patients complete clinical questionnaires to assess symptoms and donate blood for our immunology and parasitology studies. As controls, we recruit age- and sex-matched source community donors without tick exposure or history of symptomatic *Bm* infection. This proposal will define the immune correlates of acute babesiosis focusing on innate lymphocytes hypothesized to be critical during the acute phases of infection, specifically mucosal-associated invariant T (MAIT) cells and Natural Killer (NK) cells that our laboratory has identified as responsive to acute *Bm* infection in unpublished data accompanying the application. Our technical approaches include clinical cohort recruitment, flow cytometry, scRNASeq, in vitro functional studies, and computational modeling. Our results will advance the fields of basic innate lymphocyte biology and *Bm* innate immunology, informing babesiosis immunotherapy or preventive vaccines.