The Warawa laboratory COBRE project focuses on understanding the interaction between a biodefense pathogen, *Burkholderia pseudomallei*, and its preferred replicative niche, the mammalian lung. We have previously developed a lung-specific model of melioidosis in mice which allows us to study a disease process which progresses into a lethal septicemia, mimicking the moribund endpoint of human melioidosis. It is in this clinically-relevant model that we have begun to develop an immunomodulatory therapeutic which provides complete protection against a lethal *B. pseudomallei* challenge, and treated mice protected from the initial challenge achieve a memory immunity which protects them from rechallenge with no additional treatment. These preliminary findings provide a tantalizing novel modality therapy for *B. pseudomallei* which is resistant to numerous classes of antibiotics. Our studies will characterize the mechanism for the immunomodulation challenge by characterizing the native and treatment-based host response to infection. Furthermore, *B. pseudomallei* is a facultative intracellular pathogen which can grow within cultured phagocytes, but whose *in vivo* replicative niche has not been identified. We will characterize which cells facilitate the intracellular growth cycle of *B. pseudomallei* to identify how these host-pathogen interactions are affected by immunomodulatory therapeutic, and we will also begin to characterize how *B. pseudomallei* manipulates the host response away from an effective Th1 response in favor of a less effective Th17 response.