Dana May of the Beirne B. Carter Center for Immunology Research Awarded $141,141 R35 Diversity Supplement Grant to Study Brain Endothelial Dysfunction in Cachexia

Dana May, M.Sc., Neuroscience PhD Candidate in the Sarah Ewald Lab

Cachexia, or the inflammatory loss of lean body mass, is a leading predictor of morbidity across chronic diseases. A disease of complex etiology, cachexia has proven difficult to model in animals. Little is known regarding the molecular mechanisms controlling cachexia onset, persistence, and pathology; and widely efficacious interventions to reverse cachexia are lacking. We have recently shown that *Toxoplasma gondii* infection in mice is a novel animal model to study sustained cachexia. The longevity of this model has led to the discovery that a major driver of cachexia is persistent central nervous system (CNS) inflammation driven by IL-1R signaling. To understand the mechanism of CNS infection and inflammation, Dana generated a barcoded library of parasites which led to the unexpected discovery that the blood-brain barrier is highly permissive to parasite entry. Endothelial cells are integral to the blood-brain barrier but can also support *T. gondii* growth and transfer into the brain parenchyma, Dana will test the role that the IL-1R signaling axis plays in regulating parasite growth in endothelial cells. Using barcoded parasite libraries, Dana also aims to determine the mechanism of parasite entry into the brain and test the hypothesis that regional differences in parasite load are associated with local susceptibility to infection and/or spatial regulation of immune reactivity. Using *T. gondii* as a model, understanding the role of the IL-1 axis in cachexia will improve the life span and comfort of patients suffering from a wide range of debilitating chronic diseases.