Project Title: Molecular Biomarkers for Identification of Disease Stage in Lyme Borreliosis

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Project Period: 8/15/2012 to 2/28/14

Project Summary/Abstract:

Lyme disease is a multisystem infection, caused by bacteria of the *Borrelia burgdorferi* species complex and transmitted by *Ixodes* ticks. Currently a two-tier protocol is recommended to detect the presence of antibodies to *B. burgdorferi.* Seropositivity requires both a positive first-tier ELISA and a positive second-tier IgM or IgG immunoblot. While this strategy has improved the specificity of serologic testing, it lacks sensitivity in patients with erythema migrans and has several other significant drawbacks including: 1) subjectivity in the interpretation of immunoblot bands, 2) lack of specific correlation with stage or particular clinical presentation of Lyme disease such as neurologic Lyme disease, and 3) inability to identify patients with, or at risk of developing, post-Lyme disease syndrome (PLDS). Our recently published studies demonstrate the presence of significant differences in the antigen and epitope specificity of the antibody response between PLDS patients and post-Lyme healthy individuals. The central hypothesis of this proposal is that the molecular specificity of the antibody response to *B. burgdorferi* changes substantively depending on the stage of the infection, which can be exploited for development of advanced assays for Lyme disease that would effectively overcome the above shortcomings of the current system. The specific aim of this project is to characterize the antigenic specificity of the immune response to the entire proteome and glycolipids of *B. burgdorferi* in patients with different stages and clinical manifestations of Lyme disease, using an innovative microarray antibody profiling approach. It is expected that the generated data will provide the necessary information and rationale to move forward with further development of a new generation of serologic assays to aid in determining the phase and clinical phenotype of Lyme disease and in identifying patients with, or at risk of developing, PLDS.