

Lyme Disease



The Embers Lab

With over 300,000 estimated cases annually, Lyme disease (LD) is the most common tick-borne illness in North America. The causative agent, *Borrelia burgdorferi*, is a spirochete that can chronically infect humans, causing rash, arthritis, carditis, myalgia, extreme fatigue and neurological dysfunction. Despite generally effective treatment with antibiotics, a proportion of Lyme disease patients continue to experience symptoms after antibiotic treatment, a phenomenon that is known as Post-Treatment Lyme Disease Syndrome (PTLDS). Early and accurate diagnosis of LD leads to a better treatment outcome. Studies from Lab of **Monica Embers** have demonstrated an inability of currently used antibiotic treatment protocols to eliminate the pathogen. The laboratory aims to improve diagnosis and treatment of LD through the use of appropriate animal models.

The utilization of natural (tick-mediated) infection of rhesus macaques most closely represents human infection and is a key resource of the labs research program.

Lyme Diagnostic Test Discovery and Development

Reliable testing for Lyme disease demands an assay that can: (1) detect infection early (within 2 weeks of tick bite); (2) detect infection with multiple *B. burgdorferi* genospecies; (3) detect late, disseminated infection; and (4) distinguish infection from clinical cure. The bacterial dissemination patterns, pathogen burden, and immune responses generated after infection in humans are mimicked much more closely in nonhuman primates (NHP) than in rodents. Controlled infections of NHP have been used by the lab to discover antigen targets for early detection and to develop a serological test based upon knowledge of antigen-dependent changes in antibody responses over the course of infection.

Evaluation of Therapeutics Against Persistent *B. burgdorferi* Infection

The question of the effectiveness of antibiotic treatment for Lyme disease has been contentious among physicians and researchers for some time. Among the challenges to determining if antimicrobial therapy is curative is the absence of reliable measures to determine that infection has been cleared from Lyme disease patients and the vague, non-specific symptoms with which patients present in PTLDS. The Embers Lab has shown, using the technique of xenodiagnosis (feeding uninfected ticks on test subjects) that in NHP, morphologically intact spirochetes can persist following antibiotic treatment. They house a colony of *Ixodes scapularis* ticks on site and routinely use xenodiagnosis among other detection methods (molecular, immunostaining, culture systems) to evaluate the efficacy of therapeutic regimens in animals. Specifically, The Embers Lab has developed a pipeline of drug testing using acute and disseminated infection in mice, followed by testing top candidates in NHP. This model system that utilizes controlled tick-transmitted infection may also be used for preclinical evaluation of vaccine safety, immunogenicity and efficacy in both mice and NHP.

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