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Research Foundation for Tick-Borne Diseases to Fund Four Pilot Studies

The National Research Fund for Tick-Borne Diseases (NRFTD) today announced grant awards totaling \$240,000 to four investigators to study key aspects of Lyme disease and Rocky Mountain spotted fever. The NRFTD is the nation's only non-profit organization dedicated primarily to funding scientific research in the rapidly expanding field of tick-borne infections.

"We are immensely grateful to our donors for providing the resources to fund these studies," said Carl Brenner, a member of the NRFTD's Research Board. "Our hope is that these innovative projects will produce findings that quickly translate into benefits for patients. The NRFTD's projects are selected not only for the immediate scientific value they offer, but also for their potential to lead to further work that will enable researchers and clinicians to find answers to these serious tick-borne illnesses."

Grant winners were selected following a rigorous peer-review process by the NRFTD's distinguished five-member Scientific Advisory Board using guidelines akin to those established by the National Institutes of Health. Four ad hoc reviewers from prestigious national academic institutions provided additional expertise in the review of the applications.

Dr. Stephen Barthold of the Center of Comparative Medicine at the University of California in Davis has been awarded an NRFTD grant to continue his investigations into the ability of the Lyme disease bacterium, *Borrelia burgdorferi*, to survive antibiotic treatment in a mouse model. Previous work by Dr. Barthold's laboratory has shown that *B. burgdorferi* can persist in an infectious but non-cultivable state in mice for at least 90 days after the animals have been treated with ceftriaxone, a powerful antimicrobial often used to treat Lyme disease in humans. These bacteria can then be acquired by ticks and subsequently transmitted to other mice. In his NRFTD project, Dr. Barthold will attempt to verify these findings with additional strains of the Lyme bacterium and investigate the long-term fate of these organisms. Special fluorescence techniques will be employed to discern the morphology and location of the spirochetes and, hopefully, lay the groundwork for determining definitively whether these bacteria are capable of causing persistent disease. It is possible that the findings from this study could have a profound impact on current conceptualizations and treatment paradigms for human Lyme disease.

Also studying the fate of *B. burgdorferi* in mice after antibiotic treatment is Dr. Linda Bockenstedt of Yale University's Department of Internal Medicine. Dr. Bockenstedt's study will employ multiphoton microscopy, a cutting-edge form of imaging that permits the visualization of cells and bacteria in tissues of living laboratory animals. Using this technique, Dr. Bockenstedt will be able to study the behavior of *B. burgdorferi* spirochetes in live anesthetized mice and examine in real-time the effects of antibiotics on spirochete populations within the infected animals. These studies will provide insight into how the Lyme bacteria move between the tick and the mammal, and may yield important information with implications for the treatment of Lyme disease in humans.

The third NRFTD grant has been awarded to Dr. Melissa Caimano of the Department of Medicine at the University of Connecticut Health Center. Dr. Caimano's project will investigate in detail how *B. burgdorferi* transits from ticks to mammalian hosts during tick feeding. Recent work by Dr. Caimano and others has shown that the migration of the bacteria out of the ticks' midgut is considerably more complex than previously recognized: During tick feeding, spirochetes undergo a burst of replication, forming non-motile networks that adhere to differentiating tick midgut epithelial cells and only later in the feeding process become individually motile forms. Dr. Caimano will investigate the interplay between *B. burgdorferi* and the tick midgut epithelium; this work will likely further the long-term objective of identifying bacterial and tick gene products and regulatory pathways that enable dissemination of the Lyme spirochete within both ticks and mammals. It is possible that this work could ultimately lead to novel vaccine strategies that block the exit of spirochetes from the tick midgut during feeding.

The fourth NRFTD grant has been awarded to Dr. Gustavo Valbuena of the University of Texas Medical Branch, who will develop and test a novel animal model of Rocky Mountain spotted fever, the most common fatal tick-borne infection in the United States. Dr. Valbuena's objective is to create a "humanized" mouse model by transplanting human immunological cells into laboratory mice. This will make it possible to then transplant human skin into the mice, expose them to *Rickettsia rickettsii*, the causative agent of spotted fever in the United States, and study the pathogenesis of the disease. Because little is known about the specific processes that determine disease outcome and severity in Rocky Mountain spotted fever, the development of a viable animal model that mimics human disease is crucial for increasing understanding of these mechanisms. An additional complication in studying spotted fever is that endothelial cells, the main targets of *Rickettsia* bacteria, are different in culture than they are *in vivo* (i.e., in animals themselves). Dr. Valbuena's model will ensure that these cells will remain in their natural state as the pathogenic processes are investigated.

All four NRFTD projects are expected to begin in May of 2009 and to be completed in one year.

About the National Research Fund for Tick-Borne Diseases, Inc.

The NRFTD is a nonprofit, tax-exempt organization devoted strictly to raising funds in support of scientific research on tick-borne diseases. It aims to advance scientific understanding of these complicated infections by sponsoring innovative research at premier institutions throughout the world.

The NRFTD was founded in 1999 to address the complex and critical research questions raised by thousands of patients afflicted with emerging tick-borne diseases, including Lyme disease, relapsing fever, babesiosis, ehrlichiosis and anaplasmosis. The need for answers has grown markedly as Lyme disease continues to spread throughout the country and as other tick-borne infections have been recognized as public health threats.

For more information about the NRFTD, or to make a tax-deductible donation, please visit www.nrftd.org.