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Research Foundation for Tick-Borne Diseases to Fund Studies of Neurological and Immunological Mechanisms in Lyme Disease

The National Research Fund for Tick-Borne Diseases, Inc. (NRFTD), the nation's only non-profit organization dedicated primarily to funding scientific research in the rapidly expanding field of tick-borne infections, has announced the award of four grants totaling $344,000 for basic and translational research in Lyme disease. The two largest projects will focus on the pathogenesis of the illness. “Our goal this year was to fund research with maximum translational value to patients,” said Carl Brenner of the NRFTD’s Research Board. “Special emphasis was placed on proposals that showed particular promise for accelerating the transfer of findings to clinical application.”

Grant winners were selected following a rigorous peer-review process by the NRFTD’s distinguished Scientific Advisory Board using guidelines akin to those established by the National Institutes of Health. In addition to selecting projects that adhere to the highest standards of quality, the likelihood that a project’s results will lead to additional long term funding by the National Institutes of Health, National Science Foundation or other scientific or biomedical agencies is factored strongly into the NRFTD proposal evaluation process.

Leo J. Shea, III, Ph.D., Chairman of the NRFTD Board of Directors said, “We take pride in knowing that our organization has funded more research grants at prestigious scientific institutions than any other non-government organization in the field of Lyme and other tick-borne diseases. The world-wide scientific community and our contributors have recognized the NRFTD’s unparalleled contributions to the field of scientific research and the goal of finding a cure for these dreaded diseases.”

Dr. Mark Wooten of the University of Toledo in Ohio has been awarded a two year NRFTD grant to examine the interactions between *Borrelia burgdorferi*, the causative agent of Lyme disease, and mouse skin cells. Dr. Wooten’s laboratory has developed a technique to directly assess these interactions *in vivo* – that is, in live mice. Because the *B. burgdorferi* bacterium is adapted to specific host organisms, studies performed in “test tubes” do not accurately reflect the true nature of this pathogen’s interplay with host immune cells. The studies will use novel fluorescent mouse strains, fluorescent bacteria and powerful microscopic techniques to visualize how *B. burgdorferi* interacts with immunological cells directly within the skin tissues of living mice and in real time. This innovative approach should help identify the critical events that allow the bacteria to escape immune clearance, thus providing a potential target for curative treatments.

Among the most devastating manifestations of Lyme disease are its neurologic complications. When invading the central nervous system (CNS), *B. burgdorferi* must first cross the blood-brain barrier, a specialized group of capillaries that act as the body’s first line of defense against CNS invasion. The barrier is comprised of specialized blood vessel cells called “brain microvascular endothelial cells,” or BMECs. Dr. Dennis Grab of Johns Hopkins University in Maryland has been awarded an NRFTD grant to study the mechanisms by which the pathogen evades these defenses. Dr. Grab and colleagues have evidence that *B. burgdorferi* causes BMECs to release enzymes that break down the connections holding the endothelial cells together, thus allowing the blood-brain barrier to be breached. This grant will allow Dr. Grab to discover which enzymes are released and the role they play in helping the bacterium cross capillaries and enter the brain. Armed with this knowledge, researchers may then be able to design therapies that prevent CNS invasion by the Lyme bacterium, thus significantly reducing the morbidity associated with Lyme disease.

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Also receiving an NRFTD grant award is Dr. Linden Hu of Tufts-New England Medical Center, who will study the way *B. burgdorferi* responds and adapts to challenges posed by its different host environments. In nature, the Lyme organism is transmitted primarily between ticks and small mammals, and over millions of years has evolved to survive successfully in both. However, the mechanisms by which *B. burgdorferi* recognizes its environment and prepares for transition between the two types of hosts have not been well understood. Although it is known that the microbe shifts its outer surface proteins in response to changes in its environment, it has not been clear what signals the organism uses to trigger this change in protein expression. Dr. Hu has identified specific host hormones that appear to have a key role in this process, and will perform studies to elucidate the precise mechanisms that enable it. Understanding the elements critical to host adaptation may lead to new strategies for disrupting the ability of the organism to survive in its natural hosts, thus reducing transmission to humans.

NRFTD has funded an additional project focused on potentially reducing *B. Burgdorferi* infection in the wild. There are several types of animals, including different rodents, shrews, and birds, that are reservoirs for *B. burgdorferi*. Dr. Alan Barbour of the University of California at Irvine has been awarded a grant by NRFTD to develop techniques for precisely identifying the sources of tick infection with *B. burgdorferi* in nature. Dr. Barbour is presently compiling a database of proteins associated with specific host species, and the NRFTD grant will help him determine the most informative and sensitive targets for further development of specific assays. Researchers will then be able to detect blood components in the tick and determine where they came from – that is, identify what animals a tick fed on months earlier. Once this is accomplished, disease prevention efforts that focus on natural reservoirs of infection can be initiated.

In addition to providing funds for these four projects, NRFTD also donated $3000 in support of the 2008 Gordon Conference on the Biology of Spirochetes, held in Venice, California on January 20-25, 2008. The Biology of Spirochetes conferences, which are held every two years, bring together international scientists from diverse research disciplines to exchange information, present findings and foster future collaborations in the study of spirochetal bacteria, which include the causative agents of Lyme disease and relapsing fever. Special emphasis is placed on new techniques for genetic manipulation that aid in studies of the physiology, structure, pathogenesis and immunobiology of these microbes. NRFTD funds were used to support the attendance of several conference participants from remote locales. Regarding the Gordon Conference participation, Dr. Shea said, “It is especially gratifying to know that the NRFTD was selected from among all Lyme organizations and asked to participate in Gordon Conference. Our selection is de facto evidence that scientists from around the world recognize the singular contribution the NRFTD is making in the field of Lyme and other tick-borne diseases."

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, anaplasmosis, babesiosis, and ehrlichiosis. 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.