



National Research
Fund for Tick-Borne
Diseases, Inc.

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Research Foundation for Tick-Borne Infections Fights Lyme Disease, Babesiosis and Encephalitis with Pilot Studies

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

"We continue to receive remarkably innovative applications," said Carl Brenner of the NRFTD Research Board. "It is always difficult for our reviewers to choose among them, but we feel that the ones selected for support in this cycle were particularly noteworthy. We are fortunate that our donors were generous enough this year to allow us to fund four projects – projects that we hope will eventually translate into tangible benefits for patients."

The four \$60,000 grant winners were selected following a rigorous peer-review process by the NRFTD's distinguished Scientific Advisory Board, using guidelines similar to those established by the National Institutes of Health. Three ad hoc reviewers from leading national academic institutions provided additional expertise in the review of the applications.

Dr. Brian Stevenson, a Professor at the University of Kentucky's Department of Microbiology, Immunology and Molecular Genetics, has been awarded a grant to study the influence of a newly-discovered protein, called EbfC, on gene expression in *Borrelia burgdorferi*, the causative agent of Lyme disease. Vector-borne pathogens like *B. burgdorferi* are transmitted back and forth between hosts and need to sense and respond to their environment by upregulating expression of certain proteins while suppressing others, depending on their current host environment, in order to enhance their chance for survival. Dr. Stevenson has discovered that EbfC, a site-specific DNA-binding protein, regulates expression of over 50 genes in *B. burgdorferi* – or more than 5% of its entire genome. Many of these genes are differentially expressed depending on the host environment and are likely critical to the pathogen's ability to maintain infectivity in both ticks and mammals. By studying the effects of EbfC on different phases of the tick-mammal infectious cycle, Dr. Stevenson hopes to decipher the specific details of its regulatory role. Further, because regulatory pathways are attractive targets for the development of novel preventative and curative therapies, and because many other bacterial pathogens contain genes similar to EbfC, this work has the potential to improve prevention and treatment not only of Lyme disease, but of other significant human diseases as well.

A second Lyme disease-related grant has been awarded to Dr. Mollie Jewett of the University of Central Florida. Like Dr. Stevenson, Dr. Jewett will be examining gene regulation in *B. burgdorferi*, but her focus will be on small regulatory RNAs (sRNAs). The role of sRNAs in *B. burgdorferi* is still unclear, but they have been definitively shown to control the pathogenic properties of other bacterial species. Preliminary work in Dr. Jewett's lab has led to the identification of presumed novel sRNAs that are expressed by *B. burgdorferi* during mammalian infection, and the NRFTD award will

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help her characterize this regulatory molecule, increase understanding of the genetic mechanisms employed by *B. burgdorferi* to survive throughout its infection cycle, and possibly lead to novel ways to treat patients with Lyme disease.

NRFTD has also awarded a grant to Dr. Edouard Vannier of the Tufts Medical Center's Division of Geographic Medicine and Infectious Diseases. Dr. Vannier will be studying host resistance to infection by *Babesia microti*, the malaria-like causative agent of human babesiosis. Babesiosis is a potentially serious tick-transmitted disease characterized by fever, chills, fatigue and anemia, and can be spread by blood transfusion as well as by ticks. In certain patient populations, such as the elderly or patients who are immunocompromised, it can be severe and potentially fatal. However, the severity of illness is variable even in these groups, and Dr. Vannier hopes to characterize the host genetic factors that influence the course and severity of disease. Dr. Vannier has already identified a group of genes in mice that appear to determine host infectivity and will use his NRFTD award to create mice that lack the gene coding for this host factor in order to assess their resistance to infection. An additional aim of this work is to characterize the specific mechanisms by which these genes affect host susceptibility; once this is understood, Dr. Vannier proposes to screen libraries of small molecules that might inhibit the activity of the specific genes involved, possibly leading to novel treatments for severe babesiosis.

Powassan encephalitis is a serious, emerging tick-borne disease that is fatal in about 10% of its victims. Recent evidence suggests that its incidence is increasing in eastern North America, and no vaccine for the disease currently exists. NRFTD has awarded a grant to Dr. Saravanan Thangamani, an Assistant Professor in the Department of Pathology at the University of Texas Medical Branch in Galveston, to study tick-virus-host interactions during transmission of the Powassan virus (POWV). Specifically, Dr. Thangamani will investigate the cutaneous immune responses of mice to tick-transmitted POWV in order to determine if and how tick saliva compromises the ability of the mice to fight off infection with the virus. Tick salivary glands produce a complex mixture of bioactive molecules that frequently have an effect on transmission efficiency, pathogen establishment and disease pathogenesis. Dr. Thangamani hopes to elucidate the specific factors that determine the course of Powassan virus infection, which could aid in future vaccine development not just for this tick-transmitted disease, but others as well.

All four NRFTD projects are expected to begin in early 2013 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.