

TICK-BORNE DISEASE RESEARCH PROGRAM



WHAT IS THE PROGRAM'S CONGRESSIONAL INTENT?

Established in 2016, the Tick-Borne Disease Research Program (TBD RP) supports innovative and impactful research that addresses fundamental issues and gaps in tick-borne diseases.



FY22 Congressional Appropriations	
\$7M	
FY22 Research Investment	
Idea Development Award.....	\$2,494,008
Therapeutic/Diagnostic Research Award.....	\$3,694,274
Total:	\$6,188,282
FY22 Withholds and Management Costs	
USAMRDC	\$135,320
SBIR/STTR	\$234,000
Mgt Costs (6.67%)	\$442,398
Total:	\$811,718

WHY IS THERE A NEED FOR TICK-BORNE DISEASE RESEARCH?

In the U.S., **>50,000** cases of tick-borne diseases occur each year¹

Over a 14-year period, **~6,000** Service Members and nearly **56,000** beneficiaries received a diagnosis of a reportable tick-borne disease,² and of these...

Lyme disease accounted for **~80%** of these diagnoses

- Reported cases of tick-borne diseases likely underrepresent the total number of infections, as the number of people treated for Lyme disease is **~476,000** annually based on insurance records in the U.S.³
- At least **20** known conditions can result from tick bites, including **13** illnesses caused by at least **18** tick-borne infectious pathogens⁴
- Tick populations are increasing and geographically expanding; as a result, new tick-borne diseases will emerge and disease incidence will rise⁵



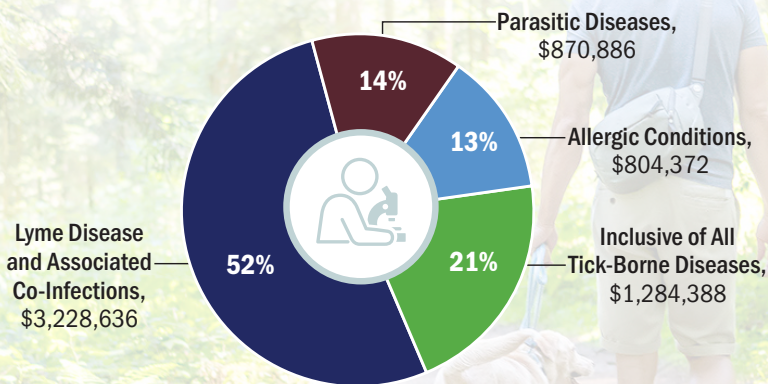
"I'm incredibly grateful for the innovative and cutting-edge research CDMRP enables.

This critical research provides hope and ultimately solutions for DOD members and their families as they face medical challenges comparable to combat."

U.S. Air Force Maj. Anders Karlsen, Center for Lyme Action, Consumer Peer Reviewer, FY21-FY23

HOW IS THE PROGRAM ADVANCING TICK-BORNE DISEASE RESEARCH?

In FY22, the TBD RP directed investments into four disease categories.



¹ Centers for Disease Control and Prevention. 2021. https://www.cdc.gov/ticks/resources/Reported-Tickborne-Disease-Cases-by-County-of-Residence_2016-2019.xlsx. | ² Data from the Armed Forces Health Surveillance Division for the years 2006-2020. | ³ Kugeler, KJ, Schwartz, AM, et al. 2021. Estimating the Frequency of Lyme Disease Diagnoses, United States, 2010-2018. *Emerging Infectious Diseases* DOI: 10.3201/eid2702.202731. | ⁴ Tick-Borne Disease Working Group. 2018. U.S. Department of Health and Human Services. <https://www.hhs.gov/sites/default/files/tbdwg-report-to-congress-2018.pdf>. | ⁵ Beard CB, Eisen L, and Eisen RJ. 2021. The Rise of Ticks and Tickborne Diseases in the United States - Introduction. *Journal of Medical Entomology* 58:1487-1489. <https://doi.org/10.1093/jme/tjab064>.



PROGRAM MISSION: *To understand the pathogenesis of Lyme disease and other tick-borne illnesses and conditions, and to deliver innovative solutions to prevent, diagnose, and treat their manifestations for the benefit of U.S. Service Members and the American public*

HOW IS THE PROGRAM MAKING AN IMPACT?

Vaccine

Development of a Live Attenuated Powassan Virus Vaccine

Margaret MacDonald, M.D., Ph.D., Rockefeller University

Dr. MacDonald and her team worked to advance the **development of a vaccine for Powassan virus, which can infect the brain and cause neurological issues**. Recent results published in the journal *Vaccines*⁶ demonstrated increased survival for mice administered the team's vaccine with **100% survival** observed for animals receiving a **prime-boost vaccination regimen** and **70% survival** for animals receiving a **two-dose vaccination regimen**. The prime-boost strategy included an initial vaccination to stimulate the immune system (prime) and a second vaccination containing a protein associated with Powassan virus infection to further stimulate the protective effects of the immune system. This work establishes a **novel vaccination strategy that lays the groundwork for further development of a potential Powassan virus prophylactic in humans**.

Babesiosis Pathology

Analysis of the Peripheral Blood Transcriptome to Identify Clinical Correlates of Pathology in People Living with Babesiosis

Dana Mordue, Ph.D., New York Medical College

Mordue and team enrolled people who presented with **babesiosis, a disease caused by parasites that infect red blood cells**, in a study to correlate host RNA signatures and disease symptom severity. Analysis of participant blood samples published in *Open Forum Infectious Diseases* showed a distinct difference in RNA profiles from uninfected participants and those with babesiosis. In people with babesiosis, blood profiles indicate **increased red blood cells** and transcriptional pathways associated with **damage to the heart, liver, and kidneys**. Additionally, surveys reported **decreased cognition and deteriorated quality of life** even after receiving treatment. These results provide **insight into babesiosis pathology** and suggest **further studies should focus on long-term impacts on quality of life**.

Diagnostic Test

Development of a Highly Sensitive and Specific Acute Diagnostic Test for Tick-Borne Rickettsioses

Rong Fang, M.D., Ph.D., University of Texas Medical Branch, Galveston

Currently, there is no timely diagnostic lab test for **tick-borne rickettsioses**, a group of diseases caused by various species of Rickettsia bacteria, resulting in fatal cases and significant morbidity due to delays in administering antibiotic. Dr. Fang made substantial progress in developing a **rapid and easy-to-perform test to detect a rickettsial diagnostic marker** at the early stage of rickettsioses using experimental animal models. The team is collaborating with scientists from the Centers for Disease Control and Prevention, Brazil, and other locations to validate the test using patient samples. This test will enable **timely and differential diagnosis of rickettsioses from a group of infections with similar symptoms, thereby reducing misdiagnoses and ensuring effective treatment**.

Immune Response

A Longitudinal Systems-Level Analysis of the Human Immune Response During Lyme Disease

Naeha Subramanian, Ph.D., Institute for Systems Biology

In people with Lyme disease, 10-20% will develop **post-treatment Lyme disease syndrome**, characterized by persistent symptoms for six or more months after antibiotic treatment, though the cause remains unclear. Subramanian characterized the **acute immune response to Lyme disease** and is exploring whether and how **immune dysregulation** may contribute to syndrome development. Using blood samples from patient cohorts tracked over time, the team analyzed distinct immune cell populations and assessed differential immune system activity in Lyme disease patients over time. This research will contribute to **improved host-based diagnostic biomarkers of Lyme disease to accurately diagnose infection earlier** and the development of new **treatments that are milder than broad spectrum antibiotics like doxycycline**, which can contribute to antibiotic resistance if overused or misused.

⁶ Cheung AM, Yip EZ, et al. 2023. Characterization of Live-Attenuated Powassan Virus Vaccine Candidates Identifies an Efficacious Prime-Boost Strategy for Mitigating Powassan Virus Disease in a Murine Model. *Vaccines* (Basel) 8;11(3):612. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10058527/>. | ⁷ Marcos LA, Lamba P, et al. 2022. Peripheral Blood RNA Signatures Associated with Human Babesiosis, Quality of Life, and Neurological Symptoms. *Open Forum Infectious Diseases* Vol. 9, No. <https://doi.org/10.1093/ofid/ofac492.563>. Supplement: https://academic.oup.com/ofid/article/9/Supplement_2/ofac492.563/6902911.

