LDA Research Funding Results Summary

The Lyme Disease Association (LDA) has been funding research nationwide over its 31 year history, awarding 123 research grants to date Click here for list of grants. To date, 60 journal publications have resulted from LDA funding/support Publications LDA-Funded research. Additionally, researchers have presented their LDA-funded work at many conferences Conference Presentations Resulting from LDA-Funding. For the research to move the field forward, optimally, the researcher should publish the study in peer-review and/or make conference presentations or otherwise share the findings. Several sample projects are summarized below.

Some early LDA-funded research began with a 1994 grant to Mario Phillip, Tulane, which led to a collaboration with Patricia Coyle at Stony Brook, and further led to incorporation of a neurotropic strain of *B. burgdorferi* from the CSF of a patient into the then new rhesus monkey studies. Work performed in Philadelphia at Fox Chase Cancer Center, by Drs. Manfred and Margret Bayer under an LDA grant, resulted in "*Borrelia burgdorferi DNA in the Urine of Treated Patients with Chronic Lyme Disease Symptom: A PCR Study of 97 Cases*" published in the journal, *Infection,* in 1996. The study, using then very new PCR technology, found that some participants had positive PCRs after intensive antibiotic treatment.

Another LDA-funded research project has been published in peer-review "Regional Cerebral Blood Flow & Cognitive Deficits in Chronic Lyme Disease," summer 2003 issue of *The Journal of Neuropsychiatry and Clinical Neurosciences,* Fallon, et al. The LDA funded a pilot project which produced the data used by Dr. Brian Fallon to apply for the NIH grant of $4.7 million received by him for the long-term treatment study published in 2008 *Neurology*. Subsequently, LDA partnered to endow the research center for chronic Lyme disease at Columbia University in 2007, the only center in the world devoted to chronic Lyme, and also gave a grant creating a tissue bank there to store samples for Lyme disease research. Another ongoing Columbia project has co-principal investigators Drs. Brian Fallon and Madeleine Cunningham, University of Oklahoma, looking at biomarkers for Lyme disease. A research/education project ongoing out of Columbia is educating physicians about different kinds of EM rashes, and posters were recently distributed at the 15th LDA/Columbia University conference. Physician surveys will also be developed.

LDA jointly funded a project at Stony Brook with Dr. Benjamin Luft in 2008 on the development of proteins arrays which could potentially lead to vaccines or diagnostic tools. In 2010, LDA funded Dr Steven Schutzer, UMDNJ (now Rutgers) for a project which involved isolating *B. burgdorferi* and Powassan virus from individual ticks resulting in a publication in *Journal of Medical Entomology*

LDA-funded research published in *PLOS One* in 2012 by noted researchers from diverse institutions and backgrounds including Drs. Emmanuel Mongodin, Sherwood Casjens, Steve Schutzer, Ben Luft, Claire Fraser et al, in *"Genome Stability of Lyme Disease Spirochetes: Comparative Genomics of Borrelia burgdorferi [Bb] Plasmids"* uses very new techniques to present a comparative analysis of several strains of *Bb* to help us understand the genetic diversity and evolution of the Lyme disease organism.

The publication in *Proceedings of the National Academy of Science*, September 2004, on the rapid exchange of genetic material by *Borrelia,* presents a finding which can have a significant impact on the diagnosis, treatment, and prevention of Lyme disease. The researchers concluded that *B. burgdorferi* undergoes genome-wide genetic exchange, including plasmid transfers. This work, initially funded by LDA through Steven Schutzer, MD, UMDNJ, has shown that different strains of the Borrelia bacteria have the ability to exchange genetic material among strains, a trait greatly benefiting their survival and probably confounding the body's ability to eradicate the organism.

LDA-initiated funding of genome mapping with Dr. Schutzer and a team of researchers across the country helped to lead to 17 strains being mapped. LDA also has a long-term research project with the team which has been examining ticks from across the country using new cutting-edge lab testing to analyze what disease agents are found in ticks—they can discover known and unknown organisms. Next, they will examine whether those agents are also being found in people. They are typing strains which can lead to better diagnostics but also can eventually lead to treatments specific to those strains. Currently, LDA is funding a study in Virginia looking at genetics in Lyme patients. The LDA has funded work with Dr. Eva Sapi, the University of New Haven (CT), examining biofilms, a method Lyme bacteria may be using to outwit the immune system and treatment. More research needs to be done in that area. A 2014 study publication with co-author Sapi has demonstrated that infection rates of filarial nematode in Ixodes ticks collected in Connecticut is relatively high(about 22% and 30% in nymphal and adult Ixodes ticks, respectively). The next step would be to determine if this is a tick-borne co-infection which could be causing patients

with tick-borne diseases to have a chronic condition.

LDA has also funded tick studies with Dr. Kerry Clark, University of North FL, which demonstrated that several *B. burgdorferi sensu lato* species may be associated with Lyme disease-like signs and symptoms in southern states. Based on the findings of this study, he suggested that human Lyme borreliosis occurs in Florida and Georgia, and that some cases of Lyme-like illness referred to as southern tick associated rash illness (STARI) in the southern U.S. may be attributable to previously undetected B. burgdorferi sensu lato infections (2013 *International Journal of Medical Sciences*). The LDA also funded Dr. David Fulford, Edinboro University of Pennsylvania, a study which showed 10% of mice captured on Presque Isle State Park in Erie, PA, had evidence of Borrelia infection. As a result of the funding, one graduate student completed a thesis, two undergraduates completed independent study projects about the biology of *Borrelia*. LDA also funded Alan Giese, PhD, Lyndon State College, Vermont, who published results showing ~ 9% infection rate with Bb in adult *Ixodes scapularis* (deer ticks) in Vermont in the journal *NE Naturalist*, 2013.

In 2016, LDA reached a milestone in its Lyme research support – the 40th journal article was published containing research supported by the LDA. The 39th and the 40th articles were research by Ying Zhang, MD, PhD, et al, both published in *Frontiers in Microbiology*. The 40th journal article, *Ceftriaxone Pulse Dosing Fails to Eradicate Biofilm-like Microcolony B. burgdorferi Persisters Which Are Sterilized by Daptomycin/Doxycycline/Cefuroxime Drug Combination without Pulse Dosing* is also work Dr. Zhang discussed at the recent LDA/Columbia University CME Lyme conference in St. Paul, MN, on October 16, days before his journal publication appeared. The research demonstrates the results of specific drug treatment for B. burgdorferi persisters, including single drug pulse dosing, combination drug pulse dosing; and which approaches are more effective at killing resistant biofilm-like microcolonies of persisters. It is a first step to identifying drug combinations for therapies to successfully treat chronic Lyme patients. The LDA recently provided a gift grant to Dr. Zhang to purchase a microscope. The LDA provides seed money funding to researchers to enable them to garner data to be used to apply for further funding from government

or large foundations. Dr. Zhang’s data was compelling as he just received a $2.5 million grant from the Steven & Alexandra Cohen Foundation to continue his study focusing on developing effective oral drug combination regiments that will be tested in vitro then in mice and then in monkeys. Dr. John Aucott, Johns Hopkins, who also presented at the recent LDA/Columbia conference, just received a $6 million grant from the Cohen Foundation for his work on Lyme. Seed grants in prior years to Drs. Brian Fallon, Columbia University, and Steven Schutzer, Rutgers, resulted in significant NIH funding for each and a treatment trial and extensive genome sequencing project respectively.

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