Conference Presentations from LDA Funding

The LDA has a long history of funding/supporting research projects. Below is a sample list of conference presentations that were made by researchers who received LDA funding for the work that was presented. The authors shown in green were the researchers who were provided the funding for the work that was presented, although multiple researchers on the article may have shared in the award.

11. Presented at the 2019 LDA/Columbia CME Lyme Conference – Lyme & Other Tick-Borne Diseases

*From Bench to Bedside: Anti-Neuronal Autoantibodies in Lyme Disease and Beyond*

Published on January 7, 2020

Anti-lysoganglioside and other anti-neuronal autoantibodies in post-treatment Lyme Disease and Erythema Migrans after repeat infection


Brian A. Fallon, Barbara Strobino, SeanReim, JulieStoner, Madeleine W. Cunningham

Abstract: **Background:** Molecular mimicry targeting neural tissue has been reported after Borrelia burgdorferi(Bb) infection. Herein, we investigate whether antineuronal autoantibodies are increased and whether antibody-mediated signaling of neuronal cells is elevated in a cohort of symptomatic adults with a history of Lyme Disease (LD).

**Methods:** Participants (n = 179) included 24 with recent Erythema Migrans (EM) without prior LD, 8 with recent EM and prior LD (EM + prior LD), 119 with persistent post-treatment LD symptoms (PTLS), and 28 seronegative endemic controls with
no prior LD history. Antineuronal immunoglobulin G (IgG) titers were measured by standard ELISA and compared with mean titers of normal age-matched sera against lysoganglioside, tubulin, and dopamine receptors (D1R and D2R). Antibody-mediated signaling of calcium calmodulin dependent protein kinase II (CaMKII) activity in a human neuronal cell line (SK-N-SH) was identified in serum. Results: EM + prior LD cases had higher antibody titers than controls for anti-lysoganglioside GM1 (p = 0.002), anti-tubulin (p = 0.03), and anti-D1R (p = 0.02), as well as higher expression in the functional antibody-mediated CaMKII Assay (p = 0.03). The EM cases with no prior history showed no significant differences on any measures. The PTLS cases demonstrated significantly higher titers (p = 0.01) than controls on anti-lysoganglioside GM1, but not for the other measures. Conclusion: The finding of elevated anti-neuronal autoantibodies in our small sample of those with a prior history of Lyme disease but not in those without prior Lyme disease, if replicated in a larger sample, suggests an immune priming effect of repeated infection; the CaMKII activation suggests that antineuronal antibodies have functional significance. The elevation of anti-lysoganglioside antibodies among those with PTLS is of particular interest given the established role of anti-ganglioside antibodies in peripheral and central neurologic diseases. Future prospective studies can determine whether these autoantibodies emerge after Bb infection and whether their emergence coincides with persistent neurologic or neuropsychiatric symptoms.


The possible association between the human ABCB1 gene and Post Treatment Lyme Disease Syndrome

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Genetic Variation in the ABCB1 Gene Associated with Post Treatment Lyme Disease Syndrome Status


Joanna Lyon, Hyunuk Seung

Abstract: Post Treatment Lyme Disease Syndrome (PTLDS) poses a difficult to understand health issue. This multi-centered, randomized control trial studied the possible correlation between ABCB1 (MDR1) gene variants and the incidence of PTLDS in affected patients. Genomic DNA was isolated and analyzed for four ABCB1 gene SNPs (rs1128503, rs1045642, rs2235067, and rs4148740). Significant findings include the association of rs1128503 TC variant with PTLDS status. Additionally, the rs1128503+ rs1045642+ rs2235067 SNP combination increased rs1128503 genotype TC significance to 3.83 times the rs1128503 genotype CC. The TT variant of rs4148740 in conjunction with rs1128503 reduced the odds ratio and appeared to convey a PTLDS protective status to the rs1128503 TC variant.


Host-Specific Antiviral Responses to the Tick-Borne Flaviviruses: Powassan and TBEV

Published June 26, 2017

Interferon signaling in Peromyscus leucopus confers a potent and specific restriction to vector-borne flaviviruses

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5484488/

Adaeze O. Izuogu, Kristin L. McNally, Stephen E. Harris, Brian H. Youseff, John B. Presloid, Christopher Burlak, Jason Munshi-South, Sonja M. Best, and R. Travis Taylor

ABSTRACT: Tick-borne flaviviruses (TBFVs), including Powassan virus and tick-borne encephalitis virus cause encephalitis or
hemorrhagic fevers in humans with case-fatality rates ranging from 1–30%. Despite severe disease in humans, TBFV infection of natural rodent hosts has little noticeable effect. Currently, the basis for resistance to disease is not known. We hypothesize that the coevolution of flaviviruses with their respective hosts has shaped the evolution of potent antiviral factors that suppress virus replication and protect the host from lethal infection. In the current study, we compared virus infection between reservoir host cells and related susceptible species. Infection of primary fibroblasts from the white-footed mouse (*Peromyscus leucopus*, a representative host) with a panel of vector-borne flaviviruses showed up to a 10,000-fold reduction in virus titer compared to control *Mus musculus* cells. Replication of vesicular stomatitis virus was equivalent in *P. leucopus* and *M. musculus* cells suggesting that restriction was flavivirus-specific. Step-wise comparison of the virus infection cycle revealed a significant block to viral RNA replication, but not virus entry, in *P. leucopus* cells. To understand the role of the type I interferon (IFN) response in virus restriction, we knocked down signal transducer and activator of transcription 1 (STAT1) or the type I IFN receptor (IFNAR1) by RNA interference. Loss of IFNAR1 or STAT1 significantly relieved the block in virus replication in *P. leucopus* cells. The major IFN antagonist encoded by TBFV, nonstructural protein 5, was functional in *P. leucopus* cells, thus ruling out ineffective viral antagonism of the host IFN response. Collectively, this work demonstrates that the IFN response of *P. leucopus* imparts a strong and virus-specific barrier to flavivirus replication. Future identification of the IFN-stimulated genes responsible for virus restriction specifically in *P. leucopus* will yield mechanistic insight into efficient control of virus replication and may inform the development of antiviral therapeutics.

Eradication of Borrelia Persisters for More Effective Treatment of Lyme Disease

(Published 3 days later, as Ceftriaxone Pulse Dosing Fails to Eradicate Biofilm-like Microcolony B. burgdorferi Persisters Which Are Sterilized by Daptomycin/Doxycycline/Cefuroxime Drug Combination without Pulse Dosing)

Jie Feng, Shuo Zhang, Wanliang Shi, Ying Zhang


Abstract: Although the majority of Lyme disease patients can be cured, at least 10-20% of the patients continue to suffer from persisting symptoms such as fatigue, muscular and joint pain, and neurologic impairment after standard 2-4 week antibiotic treatment. While the causes for this post-treatment Lyme disease symptoms are unclear, one possibility is due to B. burgdorferi persisters that are not effectively killed by current antibiotics such as doxycycline or amoxicillin used to treat Lyme disease. A previous study showed that four rounds of ceftriaxone pulse dosing treatment eradicated B. burgdorferi persisters in vitro using a relatively young late log phase culture (5 day old). In this study, we investigated if ceftriaxone pulse dosing could also eradicate B. burgdorferi persisters in older stationary phase cultures (10 day old) enriched with more resistant microcolony form of persisters. We found that ceftriaxone pulse dosing could only eradicate planktonic log phase B. burgdorferi spirochetal forms and round body forms but not more resistant aggregated biofilm-like microcolony persisters enriched in stationary phase cultures. Moreover, we found that not all drugs are suitable for pulse dosing, with bactericidal drugs ceftriaxone and cefuroxime being more appropriate for pulse dosing than bacteriostatic drug doxycycline and persister drug daptomycin. We also showed that drug combination pulse dosing treatment was more effective than single drug pulse dosing. Importantly, we demonstrate that pulse dosing treatment impaired the activity of the persister drug daptomycin and its drug combination against B. burgdorferi persisters and that the most effective way to kill the more resistant biofilm-like microcolonies is the daptomycin/doxycycline/ceftriaxone triple drug combination without pulse dosing. Our findings indicate pulse dosing may not always work as a general principle but rather depends on the specific drugs used, with cidal drugs being more appropriate for pulse dosing than static or persister drugs, and that drug combination approach with persister drugs is more effective at killing the more resistant microcolony form of persisters than pulse dosing. These observations may have implications for more effective treatment of Lyme disease. Future studies are required to validate these findings in animal models of B. burgdorferi persistence.

7. Northeast Natural History Conference, Syracuse, NY 2012

A Survey of Tick Populations Along the Connecticut River in Vermont

A.C. Serra, A.R. Giese Lyndon State College, VT

ABSTRACT: Ixodes scapularis (Black-legged Tick) has expanded its range in recent decades. To establish baseline data on the abundance of the Black-legged Tick and
Borrelia burgdorferi (the causative agent of Lyme disease) at the edge of a putative range expansion, we collected 1398 ticks from five locations along the Connecticut River in Vermont. Collection locations were approximately evenly distributed between the villages of Ascutney and Guildhall. Relative abundance and distribution by species varied across sites. Black-legged Ticks dominated our collections (n = 1348, 96%), followed by Haemaphysalis leporispalustris (Rabbit Tick; n = 45, 3%), and Dermacentor variabilis (American Dog Tick; n = 5, <1%). Black-legged Tick abundance ranged from 6198 ticks per survey hectare (all life stages combined) at the Thetford site to zero at the Guildhall site. There was little to no overlap of tick species across sites. Phenology of Black-legged Ticks matched published information from other regions of the northeastern USA. Prevalence of B. burgdorferi in adult Black-legged Ticks was 8.9% (n = 112).


Investigations of Human Borreliosis in the Southern US

Kerry Clark, PHD University of N. Florida

ABSTRACT: This study address the hypothesis that lone star ticks (Amblyomma americanum), in addition to blacklegged ticks (Ixodes scapularis), serve as vectors of Bbsl to humans. The study results are expected to confirm a previously unrecognized genetic group of Bbsl as the cause of a significant portion of LB cases in the U.S., to estimate the rate of infection in ticks biting humans in the southern U.S., to provide evidence of the tick species responsible for transmitting Lyme Borrelia to humans in southern states, and to provide improved methods for DNA testing and identification of Lyme Borrelia in human patient samples.

History: Dr. Clark’s research is focused on the ecology and epidemiology of Lyme disease and other tick-borne diseases in the southern U.S. He collaborated with investigators at Georgia Southern University in several studies, including those leading to the first isolations and characterizations of B. burgdorferi in South Carolina. Dr. Clark and colleagues have documented the presence of several Lyme Borrelia species infecting small mammals, ticks, and lizards in Florida and South Carolina. He was the first to ever report finding Lyme disease spirochetes infecting
wild reptiles. More recently, he has focused his investigative efforts on the cause of Lyme-like illness in humans in the southern U.S.

Objectives: The primary objectives of his research and service activities are the following: (1) to learn more about the ecology and epidemiology of Lyme and other tick-borne diseases affecting humans in the U.S.; (2) to improve early detection and diagnosis by developing better diagnostic tests; and (3) to educate clinicians, public health personnel and the general public about the presence, identification, and prevention of tick-borne infections.

5. Presented at LDA Columbia University Lyme & Other Tick-Borne Diseases: Solutions through Cutting Edge Science 2008

Profiling the humoral response to Borrelia burgdorferi infection with protein microarrays

New Insights from the Borrelia Genome

Benjamin J Luft PhD Stony Brook University, NY

ABSTRACT: Dr. Luft spoke about studies including studies of different strains of Bb to identify virulence markers, which have investigated gene expression in B. Burgdorferi. He reported that under laboratory conditions around half of the potential 1400 Borrelia proteins are expressed. Conditions such as pH and temperature can be varied and the effects on gene expression can be studied.


Lyme Disease Association and Columbia University, conference co-sponsors.

Results from Lyme Disease Clinical Treatment Trial

Daniel Cameron, MD Private practice, NY

ABSTRACT: Methods: Data were obtained from a randomized, double-blind placebo-controlled study of patients with recurrent Lyme disease. Patients received either amoxicillin 500mg. 3 times/day or placebo for 3 months. The Short Form-36 Health
Survey, administered at baseline and at the conclusion, provided a Mental Component Summary (MCS) and a Physical Component Summary (PCS) for HRQOL. Baseline HRQOL scores were compared with the general US and chronically-ill populations. Patients with Lyme disease were divided into the lowest, moderate, and higher initial quality of life as measured by SF-36.

Results: The quality of life of Lyme disease was significantly lower than the US norm and chronically-ill patients on all SF-36 scales. Compared with patients who received placebo, patients treated with amoxicillin showed greater improvement on SF-36 physical function, general health perception, vitality, social function, and emotional health. Lyme disease patient presenting with the best initial quality of life had the highest success rate.

Conclusion: Recurrent Lyme disease severely impairs quality of life. Retreatment is effective.


Recovery of Lyme Spirochetes in Semen Samples of Previously Diagnosed Patients

(2) Dr. Bach also presented results of the study at the American Psychiatric Association meeting in November 2000. The presentation was mentioned in Alternative Medicine, May 2001.

Gregory Bach, DO, PC Private practice, PA

ABSTRACT: The findings were that 43% of the males tested carried evidence of the Lyme disease bacterium in semen by PCR DNA testing.


Preliminary in Vitro and in Vivo Findings of Hyperbaric Oxygen Treatment in Experimental Bb Infection.

Charles Pavia, PhD NY Medical College School of Medicine, NYCOM Microbiology and Immunodiagnostics Laboratory of NYIT.

ABSTRACT: In these studies, we evaluated repeated HBOT for its ability to kill Bb in vitro, and in vivo, in a murine model of Lyme disease. Several North American tick-derived and recently obtained patient isolates were studied separately in our assay systems. To test for in vitro susceptibility, one-half to one million Bb were cultured in a small volume (0.1 – 0.2 ml) of BSK media using small snap-cap test tubes. With the caps removed, these cultures were then exposed, for one hour (twice daily for 2 consecutive days), to pure, filtered oxygen pressurized to 2-3 times normal atmospheric conditions. This was achieved using a specially constructed, miniaturized cylindrical chamber (length = 12 inches; diameter = 8 inches), equipped to accept any pressurized gas mixture through its portal opening. After the final HBOT, all cultures received an additional 0.5 ml of BSK media (making the final volume now 0.6 – 0.7 ml), and their caps were snapped shut. Matching control cultures received no HBOT. All cultures were incubated at 33° C for 2-3 days and were examined microscopically for live Bb. Our results showed that 14 of 17 strains of Bb had their growth inhibited by 33-94%, while there was little or no inhibition of 3 Bb strains. For the in vivo studies, separate groups of C3H or CO1 mice were infected intradermally with 100,000 Bb. Two to 4 weeks later, one group of infected mice received two, 1.0-1.5 hour HBO exposures, for two consecutive or alternating days. The treated mice were sacrificed one day after the last treatment, and extract cultures of their urinary bladders were prepared in BSK media. It was found that no Bb grew out of 80% of these extract cultures, whereas live Bb organisms were recoverable from 90% of extract cultures prepared from matched, infected control mice not treated with HBO. These data suggest that HBOT may be considered as a clinically useful form of adjunct therapy in the treatment of Lyme disease.

* CONFERENCE PRESENTATION

PCR Evidence for Borrelia Burgdorferi DNA in Synovium in Absence of Positive Serology.

ABSTRACT: Although Borrelia burgdorferi have been identified in synovium by several groups using immunohistochemistry, EM Steiner stains and PCR, there is controversy about whether they can infect joints without inducing a serologic response and whether they can persist after antibiotic treatment. We have performed PCR for Borrelia on a series of 185 synovial biopsies and synovial fluid regardless of clinical diagnosis. There were no cases included with known clinical Lyme disease or with positive Lyme ELISA serology. A positive control was from an erythema migrans lesion with known Lyme disease. PCR primers used identified Borrelia burgdorferi Osp A DNA. In 6 PCR positive cases synovium was also studied by Steiner stain and 4 had transmission EM to search for evidence of organisms.

Ten of the 185 cases studied (5, 3%) and the positive control were positive for the Osp A gene of Borrelia burgdorferi. Steiner stains were negative in all 6 studied. EM in no cases revealed any classic organisms but did show several features (including a variety of unusual membranous arrays) that have been reported before in known Lyme disease and other infections. Clinical patterns were reviewed on the Borrelia PCR positive patients. Clinical diagnoses were RA in 4, Adult Onset Stills Disease or JRA in 2, reactive arthritis in 2, psoriatic 1, and unclassified oligoarthritis 1. Four had received extensive antibiotics before the biopsy with improvement in 2.

PCR evidence for Borrelia has been identified in synovial biopsies of patients with clinical pictures that had not initially suggested Lyme disease. All patients were negative for antibodies to Borrelia and some were PCR positive in synovium despite previous treatment with antibiotics.

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