Accreditation Statement 2018 Columbia/LDA CME Lyme Conference

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Target Audience: The target population is physicians from all specialties, nurses, psychologists, scientists, public health workers. It is also open to the public, and Lyme disease educators generally attend. The geographic area being reached is national. No special background is required for effective participation, although those whose practices contain a high proportion of Lyme disease patients and those whose research concentrates on Borrelia burgdorferi will receive the most benefit.

Learning Objectives: Practitioners should be better able to discuss with patients the role of inflammation in chronic symptoms; Practitioners should be able to outline some new diagnostic test developments; Practitioners should not only learn about new findings and be able to describe them but also be able to share these findings and clinical recommendations with patients; Practitioners should be better able to describe novel strategies for vector control; Practitioners should be able to explain to patients the risks associated with alpha-gal meat allergy & prevention measures.
With this in mind, we set out to identify antimicrobials that efficiently kill Many common-sense measures have been proposed over the years for the prevention of Lyme disease, though often without much evidence of efficacy. Several levels of prevention have evolved to have a larger body of the most recognizable early sign/symptom of the illness: the EM rash. The consequences of missed and delayed diagnosis and treatment of Lyme disease are significant. All of these elements make continue to be evaluated. Early diagnosis and treatment have been shown to be effective in many cases. But not every case is recognized early. Of the cases confirmed by CDC over a 15 year period, 30% did not have The increasing number of cases of Lyme disease as well as the spread of Lyme disease into previously non-endemic areas have been well documented. Environmental and other factors that contribute to this expansion any experiments were conducted in the lab. Mice Against Ticks will be guided by public feedback as we aim to provide a long-lasting, safe and eco-friendly solution to this growing public health challenge. mouse population by breeding with the local mice, deplete the local disease reservoir and dramatically reduce the population of infected ticks. Mainland mouse populations within individual towns could be similarly immunized pathogens.

A Combination of Perseverance, Luck and the Joy of Tick Collecting

In large areas of the United States, the lone star tick Amblyomma americanum has increased dramatically because of the increase in the deer population which is the primary breeding host for this tick. The lone stars are Thomas A. E. Platts-Mills, PhD, FRS

Borrelia burgdorferi, Borrelia miyamotoi, Ehrlichia chaffeensis, Rickettsia rickettsii, Lyme disease. Finally, the importance of defining terms will be highlighted using clinical and research case examples.

Robert K. Naviaux, MD — Metabolic Features of Chronic Illness—Lessons from Gulf War Illness and Chronic Fatigue Syndrome

Metabolomics has emerged as a powerful new tool in systems biology. We have collected data on over 600 natural metabolites in 8 different chronic disease cohorts by broad-spectrum targeted metabolomics using hydrophilic interaction liquid chromatography electrospray ionization tandem mass spectrometry (HILIC-ESI-MS/MS), or LC-MS/MS for short. These studies have included autism spectrum disorder (ASD), post-traumatic stress disorder (PTSD) with and without traumatic brain injury (TBI), Gulf War Illness (GWI), major depressive disorder (MDD), major-epilepsy/myoclonic epilepsy fatigue syndrome (MUFFIES), primary angioedema channeling (PSC), the response to endurance and resistance exercise, and natural aging. In addition, we have studied mouse models and the developmental state known as dauer in the worm, C. elegans. These studies have shown that a diagnostic metabolite signature is present in every chronic illness studied to date, and that strong gender differences are present in each disease. All chronic illnesses that last more than about 6 months were found to express the metabolic features of a universal cellular response called the cell damage response (CDR). The CDR is comprised of a compartmentalized sequence of cellular metabolic transitions that must be completed as part of an evolutionarily conserved healing cycle. Chronic illness results when the healing cycle is blocked at different stages by abnormal metabolic signaling. Metabolites are signaling molecules like A TP, butyrate, succinate, eicosanoids, long chain fatty acids, glutathione, and sphingolipids that are natural products of metabolism inside of cells, but bind to specific G protein-coupled receptors (GPCRs) and ionotropic receptors outside of the cell. The relevance of these findings for post-treatment Lyme disease syndrome (PTLDS) will be discussed.

Claudia R. Molins, PhD — Use of Metabolic Profiles as Diagnostic and Prognostic Biomarkers of Lyme Disease

Laboratory diagnosis of Lyme disease is currently performed using a two-tiered approach that is limited by low sensitivity in early stages of infection, to inability to differentiate active from previous infection and by difficulties in performing and interpreting immunoreactions performed in the second tier. Similarly, there are no objective prognostic or diagnostic methods in place to confidently identify patients that develop Post-Treatment Lyme Disease Symptoms Syndromes (PTLDS), a condition defined by the persistence of subjective symptoms for at least 6 months following antibiotic treatment and resolution of an objective manifestation of Lyme disease, such as arthritis. The goal of our laboratory is to develop novel tools for diagnosis and prognosis of early Lyme disease, including PTLDs. To date we have developed small molecule biosignatures that differentiate with high accuracy between early Lyme disease patients, healthy individuals and patients with diseases that have look-alike symptoms or that are cross-reactive with existing serology-based tests for Lyme diseases, including Southern Tick-Associated Rash Illness (STAR) and infectious mononucleosis. Furthermore, metabolomics biomarkers that differ between non-PTLDS and non-PTLDS patients have been identified. These efforts not only hold potential for new Lyme diagnostic and prognostic tools, but will also provide new information about the biology of Lyme disease.

John Aucott, MD — Updates on Research in Lyme Disease

Chronic Lyme disease is one of the most misunderstood and controversial disorders in modern medicine. This talk will examine the form of this and how it has evolved over time. The relationship of the Lyme disease diagnosis to phenotype, pathogenesis and available diagnostic biomarkers will be examined. The research case definition of post-treatment Lyme disease syndrome will be examined in the context of Chronic Lyme Disease. Finally, the importance of defining terms will be highlighted through clinical and research case examples.

Rafal Tokarz, PhD — Novel Approaches to Serologic Diagnosis of TBD

Tick-borne diseases are the most common zoonotic diseases in the United States, with serology being the primary method of diagnosis. We developed the first multiplex, array-based assay for serodiagnosis of tick-borne diseases called the TBD-Seq. The TBD-Seq was designed to discriminate antibody responses to 8-9 major tick-borne pathogens present in the United States, including Anaplasma phagocytophila, Babesia microti, B. burgdorferi sensu lato, Borrelia mayonii, Borrelia afzelii, Borrelia garinii, Ehrlichia chaffeensis, Haemaphysalis longicornis, and Powassan virus. Each of these pathogens is either the most rampantly spreading or the most severe and difficult to diagnose. We identified a wide range of specific discriminatory epitopes that facilitated accurate diagnosis of each disease. We also identified previously undiagnosed infections. Our results indicate that the TBD-Seq is a promising tool for a diagnostic differential not available with currently employed serodiagnostic assays for TBDs.

Neil Lee Specter, MD — Applying the Lessons From Cancer Research to the Diagnosis and Treatment of TBD

There are striking similarities in the pathogenesis of many cancers and Borrelia infection. The insights that have been made in understanding tumorogenesis and cancer progression and metastatic dissemination have led to paradigm shifts in the development of targeted small-molecule and immunotherapies. Biologic therapies from the historical reliance on antibiotics and small-molecule targeting oncogenic driver mutations and immunotherapies designed to activate antitumor immune responses. The latter targeted therapies have transformed clinical outcomes for many patients with solid tumor and hematological malignancies. In this presentation, I will discuss how the successful lessons learned in cancer biology and targeted immunotherapy drug development may apply to the way we think in terms of new, non-antibiotic therapies for Borrelia and other tick-borne illnesses. I will discuss an ongoing collaborative project in our lab and others to utilize a platform technology that has successfully identified novel small molecule therapies for cancer, metabolic and certain infectious diseases, to identify a new class of molecule targeted therapies for Borrelia.

William Robinson, MD, PhD — Protective and Pathogenic B Cell Responses in Lyme Disease

We are applying immune repertoire sequencing to characterize the B cell and antibody responses following Borrelia burgdorferi infection and in post-treatment Lyme disease syndrome (PTLDS). We show that robust B cell responses producing anti-Borrelia burgdorferi antibodies are associated with return to health following acute infection.

Jon T. Skare, PhD — Pathogenesis-related features of Borrelia burgdorferi

In this presentation, Dr. Jon Skare will present a background of Lyme borreliosis as well as a discussion of some of the limitations and challenges that are currently under investigation from the basic science perspective. He will also present some of the work he is doing in his research group to evaluate how B. burgdorferi carries out its pathogenic potential at the molecular level.

Utupal Pal, PhD — Immune Evasion of Lyme Disease Agents

Borrelia burgdorferi and related spirochetes cause Lyme disease, a prevalent tick-borne zoonosis. The pathogen displays a remarkable evolutionary divergence from other bacteria and thus it is perhaps not surprising that the vast majority of the B. burgdorferi genome encodes proteins of yet unknown functions. To advance our knowledge of microbial pathogenesis, we have characterized a select set of structurally unique B. burgdorferi gene-products that act as novel immunomodulatory agents. Our most recent studies have uncovered a unique innate immune evasion strategy of B. burgdorferi that is orchestrated by one of its cell surface proteins of unknown function, annotated as BBAF7. We show the protein is highly induced during early mammalian infection and supports microbial persistence via evasion of a plethora of host microbial responses. We also discovered a remarkable plasticity in the spirochete immune evasion strategy as even in its absence, B. burgdorferi still able to adapt and establish long-term infection. Understanding the fundamentals of spirochetal immune evasion mechanisms that ensures their host persistence is critical for the development of novel approaches to combat highly prevalent zoonotic infections like Lyme borreliosis.

Thomas A. E. Platts-Mills, PhD, FRS — The Alpha-Gal Syndrome as a Consequence of Bites From The Lone Star Tick

In large areas of the United States, the lone star tick Amblyomma americanum has increased dramatically because of the increase in the deer population which is the primary breeding host for this tick. The lone stars are vectors for several vectors for several diseases, but recently it has been shown that bites from larval or adult ticks can induce sensitization to an important oligosaccharide of the non-primate mammals. This sensitization can be passed from mother to offspring through the placenta. The relevance of these findings for post-treatment Lyme disease syndrome (PTLDS), the response to endurance and resistance exercise, and natural aging. In addition, we have studied mouse models and the developmental state known as dauer in the worm, C. elegans. These studies have shown that abnormal metabokine signaling. Metabokines are signal molecules that carry out their pathogenic potential at the molecular level.

James L. Occi, PhD (Candidate) — The Discovery of the “Asian long-horned tick,” Haemaphysalis longicornis, in New Jersey: A Combination of Perseverance, Luck and the Joy of Tick Collecting

In November 2017 the USDA confirmed an infestation of the longhorned tick (Haemaphysalis longicornis) on a sheep in Hunterdon County, New Jersey. This tick is indigenous to parts of China, Korea and Japan where it typically feeds on cattle. I will summarize the situation on the where the longhorned tick has been found in the US and discuss ongoing research on its ecology, life cycle and possible involvement in transmission of bovine pathogens.

Joanna Buchthal, PhD (Candidate) — Mice Against Ticks: Community Guided Research for Public Health

Few areas are as affected by Lyme as the islands of Martha’s Vineyard and Nantucket, which have some of the highest rates of infection in the nation. Mice Against Ticks is an open, community-guided project which aims to safeguard these islands by reducing the number of disease-carrying ticks. Because most ticks become infected when they bite infected white-tailed mice, scientists are working to create tick-borne disease resistant white-tailed mice by passing the pathogenic bacteria into their genes. One of the largest number of resistant mice were released onto an island like Martha’s Vineyard or Nantucket, they would introduce immunity to the native mouse population by breeding with the local mice, deplete the local disease reservoir and dramatically reduce the population of infected ticks. Mainland mouse populations within individual towns could be similarly immunized using early detection technology being developed. A new version of the lab at MIT. Uniquely, the communities of Martha’s Vineyard and Nantucket have been involved in the project from the outset, providing direction before any experiments were conducted in the lab. Mice Against Ticks will be guided by public feedback as we aim to provide a long-lasting, safe and eco-friendly solution to the growing public health challenge.
Beatrice M. Szantyr, MD, FAA — Lyme Disease – An Ounce of Prevention: Survey of the Evidence for Prevention Strategies in Lyme Disease

The increasing number of cases of Lyme disease as well as the spread of Lyme disease into previously non-endemic areas have been well documented. Environmental and other factors that contribute to this expansion continue to be evaluated. Early diagnosis and treatment have been shown to be effective in many cases. But not every case is recognized early. Of the cases confirmed by CDC over a 15-year period, 30% did not have a history of the most recognizable early symptom of the illness, the EM rash. The consequences of missed and delayed diagnosis and treatment of Lyme disease are significant. All of these elements make prevention an important consideration.

Many common-sense measures have been proposed over the years for the prevention of Lyme disease, though often without much evidence of efficacy. Several levels of prevention have evolved to have a larger body of evidence supporting their use. These measures range from the immediate fallouts of hobbies/tick management strategies to personal protection measures and host and property management, vaccine development for humans and host animals, and wider integrated pest management strategies that combine many of these individual measures in a more comprehensive approach to this important public health issue. This presentation will present a survey of prevention approaches and the evidence supporting their implementation.

Kim Lewis, PhD — Updates on New Treatments for Borrelia Persister

The nature of Post-Treatment Lyme Disease Syndrome (PTLDS) remains unknown, but it is reasonable to assume that minimizing the duration of an acute infection will diminish if not prevent the chronic form of the disease. With this in mind, we seek to identify antimicrobials that efficiently kill Borrelia burgdorferi. This led to the identification of two experimental compounds. One is disulfiram, an FDA approved drug for treating alcoholism that eradicates persisters of B. burgdorferi and acts selectively against the pathogen. We developed a stable formulation of disulfiram that is effective in a mouse model of Lyme disease. If the pathogen is present at the chronic stage, disulfiram is also applied to clear it. The other compound is a natural product selective against B. burgdorferi. An antibiotic microbe is known to contribute to a number of autoimmune diseases, and patients with PTLDS exhibit changes in the microbiome as well. This suggests microbiome restoration, and using antibiotics that do not harm gut symbionts.

Choukri Ben Mamoun, PhD — Targeting the Achilles Heel of Babesia Parasites’ Mode of Survival Within Human Red Blood Cells

Since the completion of the assembly and annotation of the genome of the human pathogen Babesia microti, my laboratory has been involved in the development of novel approaches to detect active babesia infection and discovery of more effective therapies to treat human babesiosis. In this lecture, I will present new data showing that B. microti uses a novel mechanism for delivery of proteins into the host, and how we exploited this information to develop a highly sensitive assay for detection of B. microti active infection in human and mouse blood. Furthermore, I will present our recent discovery of a new combination therapy that targets a critical step in B. microti metabolism during its development within mouse and human red blood cells and results in radical cure of the disease.

Anne Louise Oaklander, MD, PhD — Small-Flower Peripheral Neuropathy: A Pathway for Some Patients

Our research team investigates biological causes of unexplained sensory and other symptoms. We have studied unexplained multimorbidity illnesses that include chronic widespread pain, fatigue, difficulty on standing and rapid heartbeat (POTS), and gastrointestinal symptoms. In some but not all clinical patients and research subjects, we find evidence suggesting that small-fiber polyneuropathy (SFPN) may be part of the problem. The strongest studies so far are for fibromyalgia. Our lab and others around the world have published that about 40% of fibromyalgia patients have skin biopsies and other neurological evidence of SFPN. For them, we recommend the standard blood tests to look for potentially treatable causes or contributors, especially smoking and diabetes, and then medical treatment targeting that own problem. We have helped identify disease-specific treatments for genetic and autoimmune types of SFPN. We provide non-commercial information for the public at https://neuropathycomm.org and in a public lecture at Radcliffe posted at https://www.youtube.com/watch?v=KLQVSZQ2s.

Monika Gulia-Nuss, PhD — Generating Transgenic Ticks for Ticks and Tick-Borne Diseases Management

The sequencing and annotation of a new Babesia genome opened up new avenues for functional characterization of tick genes and tick-pathogen interaction research. However, the large genome size posed its own challenges for assembly and resulted in a fragmented genome. My laboratory has now reassembled the genome using Hi-C genome scaffolding method. This allows us to reassemble the genome and correct existing gene models. We are now applying the gene-editing technique to disrupt the gene functions in order to identify the genes that are important for tick development, survival, or immune response to the pathogens. We expect that gene-editing in ticks will provide new opportunities for identification of targets for vaccine for Lyme disease and other tick-borne diseases. Additionally, it will also lead to carcinoid patients identification. I will present this work at the meeting.

Jaroslav Flegr, Ph.D. — Bartonella, Toxoplasmosis, Psychiatric Effects

Shannon Delaney, MA, MD — Borrelia Miyamotoi Exposure in a Clinical Population

The first recognized cases of Borrelia Miyamotoi disease (BMD) in North America were reported in the northeastern United States in 2013, but much about the clinical features of this disease remains unknown. Our Second Opinion/Evaluation Service at Columbia University Medical Center evaluates patients with persistent symptoms who have a history of treatment for possible or definite Lyme disease. Since the summer of 2017, we assessed 52 patients for B. miyamoti antibodies (using an ELISA based on the recombinant glucosyltransferase phosphotransferase [GtfQ] protein) through a specialty laboratory in Massachusetts. 14 of the 52 (27%) were positive for GtfQ IgG antibodies. In a preliminary exploration to assess whether a history of infection with B. miyamoti alters the clinical profile among persistently ill patients, we compared individuals representing subgroups: a) history of well-documented past Lyme disease (Lyme positive) and MB positive, b) Lyme positive but BM negative, and c) Lyme negative and BM negative. Results confirm that self-report assessments (anxiety, behavioral, functioning) completed by all patients will be contrasted and reported. Additionally, results from comprehensive neuropsychometric testing on a subset of these patients will be reported.

Kavin Patel, MD — First Confirmed Case of Powassan Neuroinvasive Disease in Rhode Island (co-presenting with Dr. Reece)

The Powassan virus is the boreal forest rodent-borne flavivirus responsible for Powassan neuroinvasive disease. The virus was first isolated in 1958 and has been responsible for approximately 100 cases of neuroinvasive disease. Rates of infection have been on the rise over the past decade with numerous states reporting their first confirmed case. New Jersey, New Hampshire, and Connecticut all reported their first case within the last five years. The following presentation reviews the first confirmed case of Powassan neuroinvasive disease in the northeastern United States within a clinical compatible syndrome. The case study provides evidence for the increasing spread of Powassan in neuroinvasive disease and reinforces the importance of requesting focused testing for Powassan Virus in patients from an endemic area with a clinically compatible syndrome.

Rebecca Reece, MD — First Confirmed Case of Powassan Neuroinvasive Disease in Rhode Island (co-presenting with Dr. Patel)

The Powassan Virus is the tick-borne vector responsible for Powassan neuroinvasive disease. The virus was first isolated in 1958 and has been responsible for approximately 100 cases of neuroinvasive disease. Rates of infection have been on the rise over the past decade with numerous states reporting their first confirmed case. New Jersey, New Hampshire and Connecticut all reported their first case within the last five years. The following presentation reviews the first confirmed case of Powassan neuroinvasive disease in the northeastern United States within a clinical compatible syndrome. The case study provides evidence for the increasing spread of Powassan neuroinvasive disease and reinforces the importance of requesting focused testing for Powassan Virus in patients from an endemic area with a clinically compatible syndrome.

Elizabeth L. Maloney, MD — Concurrent Tick-Borne Illnesses: A Case Report and Review of the Literature

The list of known tick-borne diseases has grown in the last several years and cases numbers for several of these infections are on the rise. Many of these infections are transmitted by blacklegged ticks, which are known to simultaneously harbor more than one pathogen. As such, when managing patients with a blacklegged tick-borne disease, clinicians must consider whether these individuals have additional co-infections. This presentation uses a case study as a springboard to a literature review regarding concurrent blacklegged tick-borne diseases.

Brian A. Fallon, MD, MPH — Borrelia and the Brain: Phase 1 of a Post-Mortem Study

This talk consists of three parts. First, the animal and human peer-reviewed literature will be reviewed regarding whether Borrelia has been found in brain tissue as well as the link between Borrelia and dementia. Second, the design of a new study undertaking human brain for evidence of Borrelia burgdorferi will be described. Third, results from the clinical and gross neuropathological assessment of a small sample of donor brains with a history of treated Lyme disease will be presented.