GLOBAL LYME ALLIANCE

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GLA.org

LYME DISEASE RESEARCH

LOOKING BACK,
MOVING FORWARD

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"SO VERY GRATEFUL FOR THE OPPORTUNITY TO WORK WITH GLA. ALL THE PERSISTER WORK AND ALL THIS DEVELOPING THE METHOD FOR A RAPID DRUG SCREEN WAS SUPPORTED THROUGH GLA."

— *Ying Zhang, M.D., Ph.D.*

Ying Zhang, M.D., Ph.D., Professor, Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health. Dr. Zhang's Lyme disease research focuses on the study of persister bacteria. He is a GLA grantee.

"GLA PLAYS A CRITICAL ROLE IN LYME DISEASE RESEARCH. THEY'RE THINKING OUT OF THE BOX. THEY'RE LOOKING FOR INNOVATION, FOR CREATIVITY. THEY'RE FUNDING SCIENTISTS ASKING THE CRITICAL QUESTIONS — AND THIS IS THE ONLY WAY OF FINDING THE BIG PRIZE — THE CURE."

— Benjamin Luft, M.D.

Benjamin Luft, M.D., Director and Principal Investigator, Stony Brook University WTC Wellness Program. Dr. Luft is an internationally recognized expert in the treatment of Lyme disease and AIDS-related conditions. The use of Ceftriaxone for the treatment of neuroborreliosis is based upon Dr. Luft's ground-breaking work. He is a GLA grantee.

INSIGHT

—

A LETTER FROM OUR CEO & CHAIRMAN

MAY 2018

DEAR FRIENDS:

We are pleased and excited to share with you Global Lyme Alliance's inaugural Research Report. As these pages show, Global Lyme Alliance (GLA) has been shifting the paradigm for Lyme disease research ever since we funded our first research initiative in 1998. Through a combination of generous support from donors, a dedicated and professional internal team, and a focused mission—GLA continues to advance critically-needed Lyme and tick-borne disease research, accelerating progress toward reliable diagnostics, better treatments and ultimately a cure.

The biggest driver of our research agenda is patients. More people are suffering from Lyme and other tick-borne diseases today than at any other time. The harrowing truth is that 329,000 new cases of Lyme disease are diagnosed each year in the U.S. alone, according to the Centers for Disease Control and Prevention. Add to that the growing number of ticks and their expanding geographical range and the result is a pandemic.

GLA is at the forefront of discovery and innovation, making us a catalyst for change across the Lyme disease world. Despite all GLA has learned about the complex nature of the Lyme bacterium, the dearth of federal funding makes it challenging to convert promising tests and therapies from the lab to the doctor's office.

Our Scientific Advisory Board reviews all research grants to determine whether they can deliver significant, measurable advances that will be accepted by the medical community. GLA-funded grantees are discovering the underlying molecular biology of the Lyme bacterium; identifying new and better targets for treatment; and exploring drug combinations that successfully attack "persister" cells that evade conventional antibiotics, as well as antibiotic resistant Lyme bacteria.

GLA has been the only 501(c)(3) focused on research with either an M.D. or a Ph.D. at the helm of its science program. GLA's research initiatives are currently led by our in-house Chief Scientific Officer and our Director of Research and Science. Their combined 30 years of experience in Lyme disease research, and track record of building bridges among scientists, clinicians, industry and government, makes GLA the preferred partner for researchers. These partnerships allow GLA to bridge the gap between its research discoveries and their translation into marketable products, a process ensuring that discoveries reach the public in a practical and useful form.

Together with our supporters, we will accelerate Lyme knowledge by funding great minds, innovative ideas, and results-driven efforts for the benefit all Lyme disease patients and their families.

Thank you,

Scott Santarella
CEO

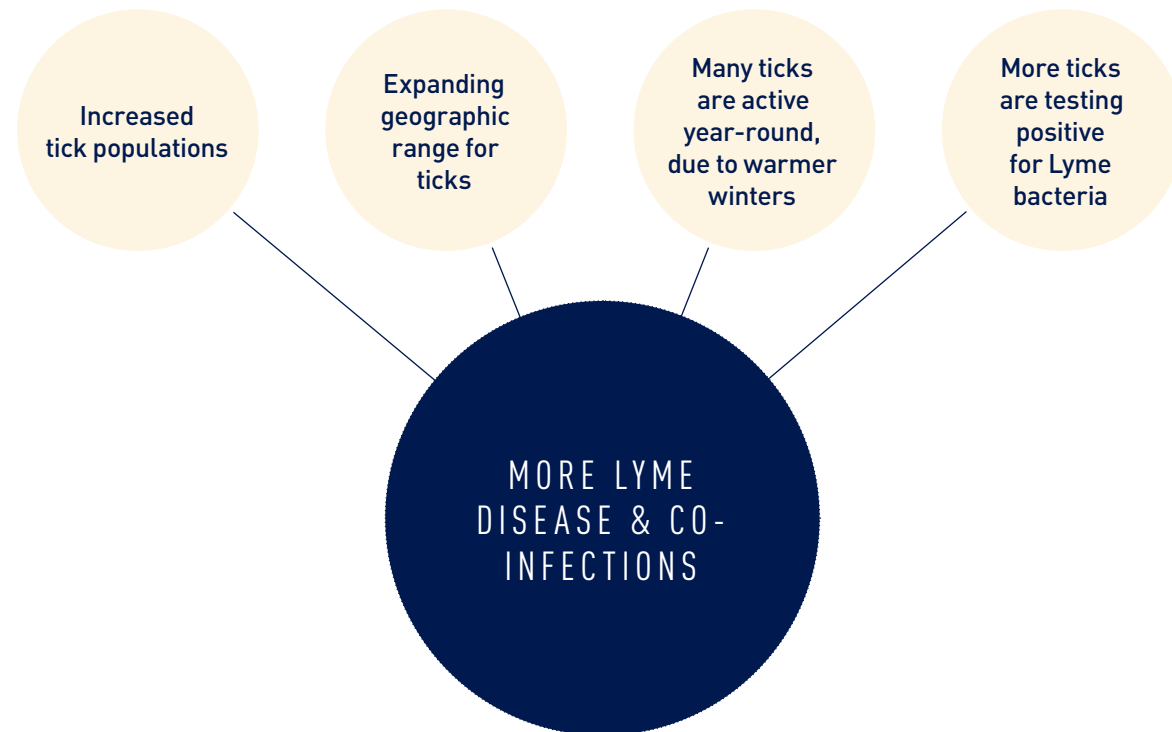**Robert Kobre**
Chairman of the Board

WHY WE ARE FIGHTING SO HARD

ESCALATING INCIDENCE

There are 329,000 new cases of Lyme each year in the U.S. alone. Combine this fact with the escalating number of reported cases worldwide and the result is a global pandemic.

Research indicates that the tick population has exploded in number and geography over the last 15 years, and a greater proportion of deer ticks are infected with *Borrelia burgdorferi,* the Lyme disease bacterium. Due to warmer winters, many ticks are active year-round instead of seasonally.

WHY THE PROBLEM IS WORSENING

Increased tick populations

Expanding geographic range for ticks

Many ticks are active year-round, due to warmer winters

More ticks are testing positive for Lyme bacteria

MORE LYME DISEASE & CO-INFECTIONS

INCIDENCE OF CO-INFECTION

Tick-borne co-infections such as Babesiosis, Bartonella, Anaplasmosis, Ehrlichiosis are increasingly being reported. In one study, 40% of Lyme patients experienced concurrent Babesiosis, according to researchers at Columbia University, Tufts Medical Center, Stony Brook University and Yale School of Medicine.

For a list of co-infections, go to: **GLA.org**

LIMITED GOVERNMENT SUPPORT

Despite the pressing need, Lyme disease research is seriously underfunded at the government level. See chart on page 10 to learn how much Lyme disease received in 2016 from the National Institutes of Health (NIH) compared to some other diseases.

PERSISTENCE

Based on GLA-funded research, it's estimated that 10-20% of acute Lyme disease cases are not cured by immediate antibiotic treatment. This statistic is now used by mainstream medicine and is the direct result of exclusive GLA-funded research at Johns Hopkins.

INJUSTICE

Lyme patients today face an incredible injustice, both from the medical community, insurance companies and their peers. Until an accurate diagnostic test and standard of care is established and accepted by the medical community, this will continue.

DELAYED TREATMENT

The longer a patient goes without treatment of their Lyme or tick-borne infection, the worse the symptoms may become. For some patients, symptoms become life threatening. An early, accurate diagnostic test and improved understanding of tick-borne infections will help patients get more timely and effective treatment.

INCIDENCE AMONG CHILDREN

Children are most at risk. The highest incidence of Lyme disease occurs in children, ages 3—14. More than 200 children contract Lyme disease every day.

STIGMA

Many Lyme patients with persistent symptoms are dismissed by the medical community as hypochondriacs or malingerers, when in fact their symptoms are very real. Patients are also often criticized by friends and family because of the difficulty of diagnosis.

FUNDING CHALLENGE FOR RESEARCHERS

MANY SCIENTISTS HOPE TO MAKE A DIFFERENCE IN THE FIGHT TO PROTECT PEOPLE FROM LYME AND OTHER DEBILITATING TICK-BORNE DISEASES. BUT THEY FACE AN UNPLEASANT REALITY. FEDERAL FUNDING FOR LYME RESEARCH IS MINISCULE, WHICH PUTS THE ONUS INTO THE HANDS OF PRIVATE DONORS WILLING TO FUND SUCH VITAL WORK.

WITHOUT ONGOING FEDERAL FUNDING, THE LYME FIELD RISKS LOSING QUALIFIED RESEARCHERS, WHO EITHER MOVE ON TO BETTER-FUNDED CAUSES OR LEAVE SCIENCE ALTOGETHER. THIS MEANS WE ARE PERPETUALLY AT RISK OF LOSING THE RESEARCHER WHO COULD DISCOVER THE NEXT BIG BREAKTHROUGH.

Research laboratories need to apply for new funds regularly if they are to keep their labs open and running. The universities themselves depend on institutional support funds that are attached to research grants. In general, when labs receive reduced federal funding, research positions are eliminated. According to a recent NPR analysis of National Institutes of Health data, 3,400 scientists lost sustaining grants in fiscal year 2013. Thus, valuable investigations by trained scientists were curtailed.
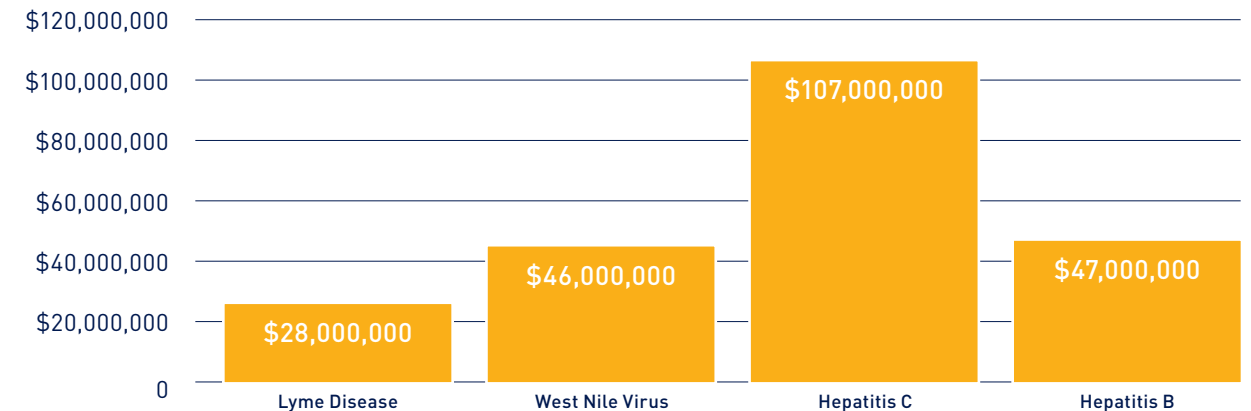
Complicating matters, most NIH grants tend to be awarded to more established Lyme researchers. This in effect cuts out a number of highly qualified young researchers and postdoctoral candidates with fresh perspectives. GLA funds researchers based on the quality of their work and potential for meaningful results regardless of their legacy standing.

The dearth of federal grants, especially when seen in light of the growing threat of Lyme, makes research funding from Global Lyme Alliance more important than ever. Our support of essential research is crucial if pioneering scientists are to undertake necessary investigations. It is only through the generous support of our donors that we can continue to disburse critical research funds that contribute to the future of every family at risk for tick-borne diseases, and those now living with persistent or chronic Lyme.
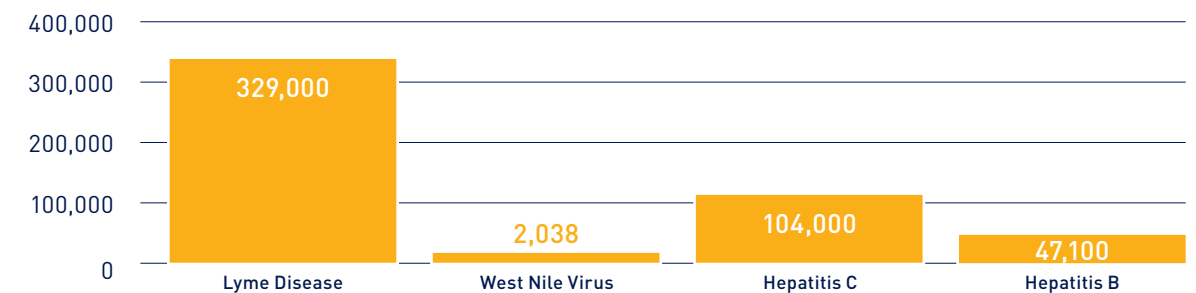
WHERE DOES THE NIH FUNDING GO

Lyme funding awarded by the NIH goes to basic biology research, while relatively little goes to research which seeks to develop new diagnostic tests, therapies, or understand the best tick reduction and prevention strategies.

NIH spending Lyme vs other diseases (2016)

Disease	Spending
Lyme Disease	$28,000,000
West Nile Virus	$46,000,000
Hepatitis C	$107,000,000
Hepatitis B	$47,000,000

Annual new cases of Lyme in U.S. vs. other diseases (CDC)

Disease	New cases
Lyme Disease	329,000
West Nile Virus	2,038
Hepatitis C	104,000
Hepatitis B	47,100

WE'RE HELPING TO FUND YOUNG SCIENTISTS!

GLA recently announced the first cohort of the "Deborah and Mark Blackman Postdoctoral Fellowship in Bacterial Persistence and Host Evasion." The three-year fellowships support five recent Ph.D. graduates with specific interest in understanding whether persistence of the bacteria *Borrelia burgdorferi*, the Lyme disease pathogen, or host evasion mechanisms are responsible for the continued symptoms experienced by patients treated for Lyme disease. Each fellow will receive $75,000 annually. The funding will allow the young scientists to equip themselves to eventually become independent, principal researchers in their own labs. The first five Blackman Postdoctoral Fellows are: George Aranjuez, Ph.D., from the University of Central Florida; Ashley Groshong, Ph.D., University of Connecticut; Matthew Muramatsu, Ph.D., University of Texas-Southwestern; Bijaya Sharma, Ph.D., Tufts University, and Chrysoula Kitsou, Ph.D., University of Maryland.

SCIENCE WE FUND

LYME IS A COMPLEX DISEASE WITH MANY BACTERIAL STRAINS AND CO-INFECTIONS. THE COMPLEXITY OF THE DISEASE COMBINED WITH LACK OF FEDERAL FUNDING MAKES GLOBAL LYME ALLIANCE'S ROLE IN TICK-BORNE DISEASE RESEARCH ESSENTIAL. GLA IS COMMITTED TO UNCOVERING THE KEYS THAT WILL OPEN THE DOOR FOR ACTIONABLE, SCIENCE-BASED ANSWERS THAT WILL IMPACT PATIENTS. GLA'S OBJECTIVE IS TO DEVELOP MORE EFFECTIVE MEANS OF DIAGNOSING AND TREATING THE DISEASE.

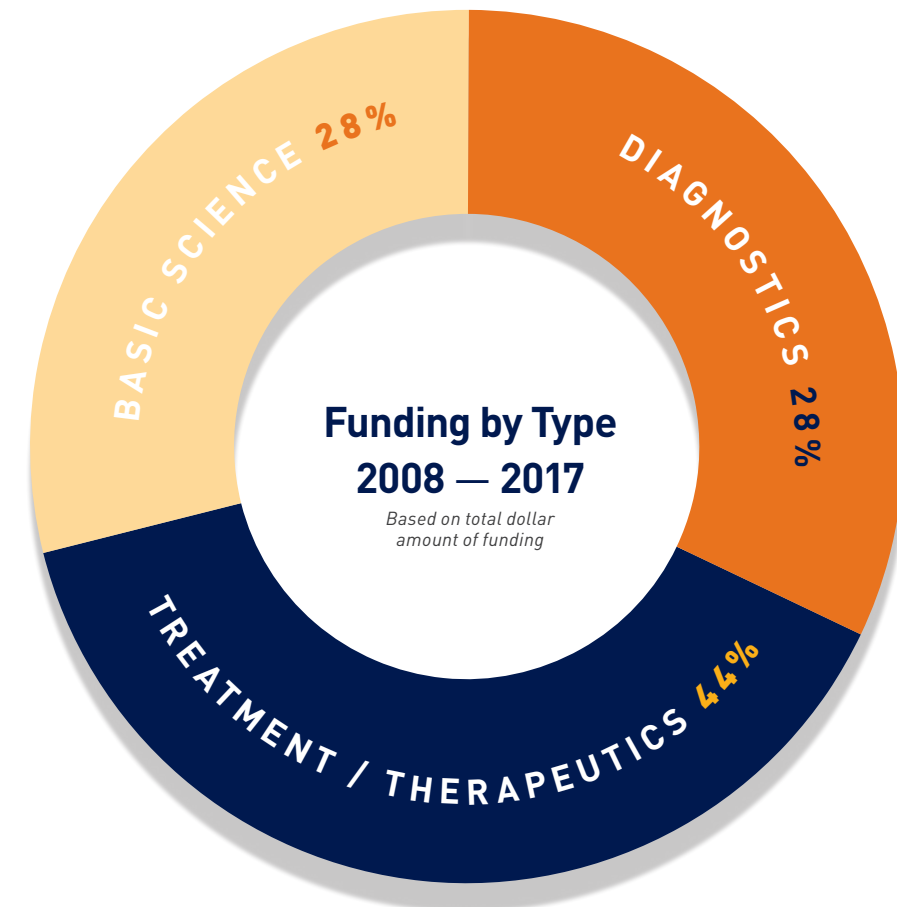## GLA FUNDS RESEARCHERS IN THREE PRIMARY AREAS:

1 DIAGNOSTICS:

There is an urgent need to develop accurate, dependable diagnostic tests, for both Lyme disease, in all stages, and for detecting other tick species and tick-transmitted co-infections. GLA-supported research has been and will continue to be focused on the development of various technologies and methodologies that can lead to reliable diagnostic testing.

2 TREATMENT/THERAPEUTICS:

GLA-funded researchers are identifying new and effective treatments for both early and late-stage Lyme disease. They are also studying optimal treatments and therapies to help the body fight infection with reduced side effects. For example, GLA has funded studies to identify new antibiotics and combinations of antibiotics that may more effectively kill Lyme bacteria. These studies have shown that slow-growing persister forms of *Borrelia* may survive conventional antibiotics.

3 BASIC SCIENCE:

Basic science research focuses on questions about Lyme and tick-borne diseases at the fundamental molecular and cellular level, resulting in a better understanding of the bacteria or immune response. This research is not conducted on people. It is carried out in a laboratory with experiments involving cells, tissue or blood samples *in vitro* (such as test tubes) or *in vivo* (with animals). This vital work is important because scientific findings can be translated into diagnostic, preventive and therapeutic benefits for patients, or lead to entirely new concepts in applied medicine.

**Funding by Type
2008 — 2017**
Based on total dollar amount of funding

BASIC SCIENCE 28%
DIAGNOSTICS 28%
TREATMENT / THERAPEUTICS 44%

"WHEN OUR SON WAS SO SICK WITH LYME MORE THAN 10 YEARS AGO, I VOWED TO BECOME AN ACTIVIST TO HELP FIND A CURE SO THAT OTHER INDIVIDUALS AND FAMILIES WOULD NOT SUFFER AS WE DID. I AM PROUD TO SUPPORT GLOBAL LYME ALLIANCE. IT IS THE RIGHT ORGANIZATION TO FUND THE EDUCATION AND RESEARCH NECESSARY TO COMBAT TICK-BORNE DISEASES."

— Karen Peetz

Karen Peetz is the former President of The Bank of New York Mellon Corporation (BNY Mellon). She is a member of GLA's Board of Directors.

OUR GRANTING PROCESS

GLOBAL LYME ALLIANCE AWARDS RESEARCH GRANTS FOLLOWING A RIGOROUS PEER-REVIEW PROCESS USING GUIDELINES ESTABLISHED BY THE NATIONAL INSTITUTES OF HEALTH (NIH). EACH GRANTEE MUST MEET THE SAME SCIENTIFIC STANDARDS THAT THE NIH APPLIES TO ITS OWN RESEARCH GRANT REVIEW PROCESS.

This thorough process ensures that GLA funds only the most outstanding research projects with the best prospects of advancing knowledge and delivering actionable results.

The grants process starts with a request for proposals (RFP) issued by GLA in the spring of every year. The RFP guidelines are established by GLA's Chief Scientific Officer and Director of Research and Science. The Chairman, CEO, CSO, and key members of the Board of Directors also augment the RFP process by identifying themes to proactively pursue based upon cutting edge science. All applications received undergo a thorough review by members of our Scientific Advisory Board (SAB), comprised of some of the most distinguished researchers and clinical innovators in multidisciplinary fields of Lyme and tick-borne disease. Grants are awarded to projects judged to have exceptional prospects of delivering measurable advances, and that will best fulfill our mission of improving diagnostic testing, uncovering more effective treatment protocols. The Financial Review Sub-Committee of the SAB, composed of business

leaders with extensive strategic, operational and senior management experience, works to bridge the gap between the research community and the marketplace with the goal of transitioning successful research programs into accessible treatments that are readily available to patients. The Sub-Committee also ensures that the aggregate research projects meet with GLA's budget and appropriate benchmarks are set for the phasing of research funding.

To underscore our research commitment, GLA sets itself apartment from other Lyme organizations by having a Board Chair who is immersed in Lyme disease and sits on the SAB, along with a full-time, in-house, fully credentialed Chief Scientific Officer and a Director of Research and Science. GLA's CEO also has extensive disease and research experience.

With a business-minded Board of Directors who demand accountability, we proactively manage our grants, with payments structured on a multiple installment basis that required detailed reporting and accountability at each stage.

The review process—including all deliberations, scores and proposal critiques—remains confidential. Grants for projects selected through the process are then made to academic institutions on behalf of individual investigators.

OVER THE YEARS, GLA HAS SELECTED ITS TALENTED GRANTEES FROM DISTINGUISHED INSTITUTIONS ACROSS THE COUNTRY, INCLUDING:

Boston Children's Hospital	University of California-Irvine
Columbia University	University of California-San Francisco
Cornell University	University of Central Florida
Harvard Medical School	University of Colorado
Institute for Systems Biology	University of Connecticut
Johns Hopkins Bloomberg School of Public Health	University of Illinois-Chicago
Johns Hopkins University School of Medicine	University of Maryland
Massachusetts General Hospital	University of Missouri-St. Louis
Northeastern University	University of New Haven, CT
Rutgers New Jersey Medical School	University of North Dakota
Stanford University	University of Pennsylvania
State University of New York-Stony Brook	University of Texas-San Antonio
Texas A&M	University of Texas-Southwestern
Tufts University	Virginia Commonwealth University
Tulane National Primate Research Center	Washington University in St. Louis
University of California-Davis	

"GLA ADDRESSES A CRITICAL NEED FOR BASIC RESEARCH INTO THE DIAGNOSIS, PROGRESSION AND TREATMENT OF LYME DISEASE. WITH SUBMISSION REQUIREMENTS AS RIGOROUS AS THE NIH, APPLICATIONS ARE EVALUATED BY A FIRST CLASS SCIENTIFIC ADVISORY BOARD. AWARD WINNERS ARE THEN MONITORED FOR COMPLIANCE BY AN EXPERT IN-HOUSE SCIENTIFIC TEAM."

— Mark Blackman

Long-time supporters of GLA research, Mark Blackman and his wife, Deborah, are parents of a child who has not been "easy to cure."

SCIENTIFIC ADVISORY BOARD

GLA'S SCIENTIFIC ADVISORY BOARD (SAB) IS COMPRISED OF WORLD-RENOWNED LYME AND TICK-BORNE DISEASE RESEARCHERS, SCIENTISTS AND CLINICAL INNOVATORS IN THE FIELD. FOR MORE THAN A DECADE, THE SAB HAS PROVIDED STRATEGIC GUIDANCE AND DIRECTION FOR OUR RESEARCH AND SCIENTIFIC PROGRAMS JUDGED TO HAVE THE BEST PROSPECTS OF DELIVERING MEASURABLE RESULTS AND THE GREATEST IMPACT.

In addition, GLA hosts the only annual symposium for Lyme and tick-borne disease researchers, including GLA SAB members and grant recipients, whose purpose is to foster brainstorming of new diagnostic and therapeutic measures, communication of ideas and collaboration. The Financial Review Sub-Committee of the SAB is composed of business leaders with extensive strategic, operational and senior management experience, and provides financial oversight.

Timothy J. Sellati, Ph.D. *Chief Scientific Officer, GLA*
Dr. Sellati has more than 25 years experience in Lyme disease research, extensive disease knowledge and a track record of building bridges among scientists, clinicians, and important figures in industry and government. He joined GLA from the Southern Research Institute in Alabama where he served as a Senior Research Fellow and Chair of the Infectious Diseases Department. Dr. Sellati received his Ph.D. in cellular and developmental biology from the State University of New York at Stony Brook.

Mayla Hsu, Ph.D. *Director of Research and Science, GLA*
Dr. Hsu received a Ph.D. from McGill University, followed by postdoctoral training at Rockefeller University. She has worked in infectious diseases research in the pharmaceutical industry, academia, and a non-governmental organization. Her responsibilities include coordinating the research grant program, scientific writing and clinical assay validation.

Catherine A. Brissette, Ph.D., *Associate Professor of Biomedical Sciences,* University of North Dakota School of Medicine and Health Sciences, Grand Forks, ND. Dr. Brissette's research focuses on bacterial-host interactions, with a particular interest in pathogenic spirochetes.

Charles Chiu, M.D., Ph.D., *Associate Professor of Laboratory Medicine and Medicine,* University of California, San Francisco, and Director of the UCSF–Abbott Viral Diagnostics and Discovery Center. Dr. Chiu is an expert in advanced genomic technologies, pathogen discovery and clinical assay validation.

Allison K. DeLong, M.S., *Biostatistician at the Center for Statistical Studies,* Brown University, Providence, RI. With a M.S. degree in applied mathematics and statistics, she is certified as a professional statistician by the American Statistical Association. Her interests include the quantification of Lyme disease incidence among populations.

Richard Goldstein, D.V.M., *Executive Director and Chief Medical Officer of Diagnostics,* Zoetis, Inc. in New Jersey. Dr. Goldstein is internationally recognized for his expertise in infectious diseases in dogs and cats, especially those common to both animals and humans, most notably Lyme disease and leptospirosis.

Andreas Kogelnik, M.D., Ph.D., *Founder and Director,* of the Open Mind Institute in Mountain View, CA. and a practicing physician. His interests are in the bioinformatics and genomic revolution in medicine.

Richard T. Marconi, Ph.D., *Professor,* School of Medicine, Virginia Commonwealth University in Richmond, VA. Well recognized for his diverse research accomplishments, he is focused on the development of vaccines for tick-borne diseases for both human and veterinary applications.

Scott J. Mellis, M.D., Ph.D., *Vice President,* Early Clinical Development and Experimental Sciences, Rare Diseases, at Regeneron Pharmaceuticals Inc. in Tarrytown, NY. Dr. Mellis is a rheumatologist, currently leading the effort to optimize Regeneron's development of new medications for patients with rare diseases.

Richard S. Ostfeld, Ph.D., *Senior Scientist and Disease Ecologist,* Cary Institute of Ecosystem Studies, Millbrook, NY. Dr. Ostfeld is a pioneer in developing our understanding of the ecology of infectious diseases, especially those carried by ticks in the northeastern U.S.

Utpal Pal, Ph.D., *Professor,* Department of Veterinary Medicine and Director of the Veterinary Medical Sciences Graduate Program at the University of Maryland, College Park, MD. Dr. Pal is an expert on pathogenic spirochete biology, with several research interests related to *Borrelia* and *Leptospira* species.
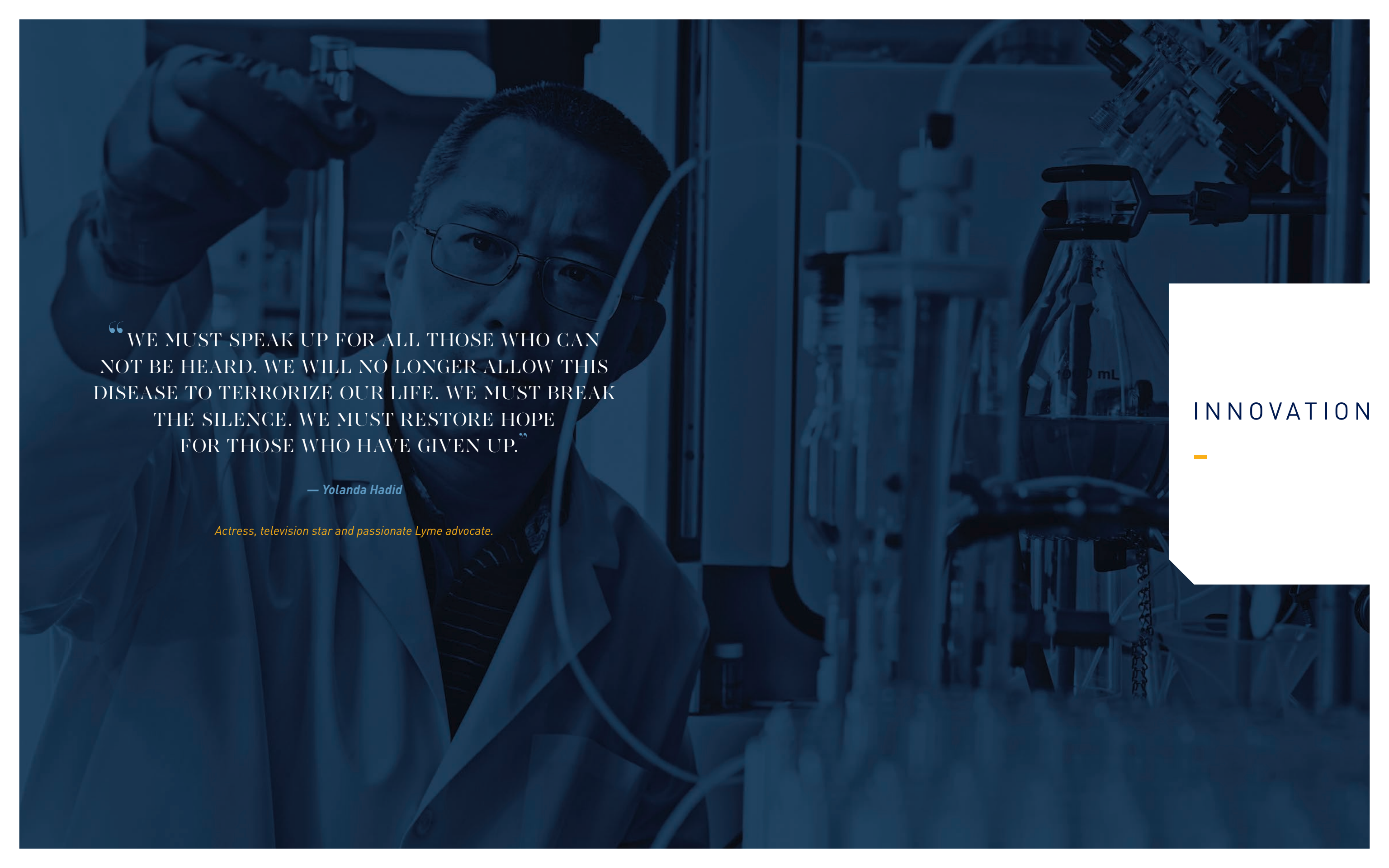
Mark J. Soloski, Ph.D., *Professor of Medicine,* Pathology, Molecular Biology & Genetics and Molecular Microbiology and Immunology at Johns Hopkins University School of Medicine, Baltimore, MD. He is a co-principal investigator with Dr. John Aucott on the landmark SLICE (Study of Lyme disease Immunology and Clinical Events) trial.

FINANCIAL REVIEW COMMITTEE

Robert Kobre, *C.P.A., M.B.A., Vice Chairman,* Investment Banking at Credit Suisse. Kobre has analyzed and helped construct over 200 business plans and financial forecasts. He specializes in IPOs, leveraged loans, high yield bonds and M&A. With over 20 years of financial and health care industry experience, he has advised GLA over the past six years on research objective protocols and grant-making strategy.

Scott Santarella, *GLA's CEO,* brings more than 25 years experience as a senior executive with a proven track record in strategic planning, innovative marketing, and fundraising. He has run businesses with annual revenues ranging from $5 million to $30 million.

Brian Scanlan *is the President of Mount Hope Capital,* a family firm based in Greenwich, CT. Scanlan was also the founder of Caminus Corporation (formerly ZaiNet Software, Inc), a NASDAQ-listed energy software company based in New York.

"WE MUST SPEAK UP FOR ALL THOSE WHO CAN NOT BE HEARD. WE WILL NO LONGER ALLOW THIS DISEASE TO TERRORIZE OUR LIFE. WE MUST BREAK THE SILENCE. WE MUST RESTORE HOPE FOR THOSE WHO HAVE GIVEN UP."

— Yolanda Hadid

Actress, television star and passionate Lyme advocate.

INNOVATION

RESEARCH FIRSTS

GLOBAL LYME ALLIANCE HAS PIONEERED MANY KEY ADVANCEMENTS IN LYME AND TICK-BORNE DISEASE RESEARCH, AND IS CHARTING THE PATH FOR THE NEXT BIG FINDINGS.

GLA, IN COLLABORATION WITH OUR FUNDED SCIENTISTS, IS THE ORGANIZATION RESPONSIBLE FOR MANY EVIDENCE-BASED FIRSTS ABOUT LYME DISEASE, INCLUDING:

- Identified that 10-20% of Lyme patients do not react to early antibiotic therapy – now widely accepted

- Definitively proved that Lyme patients with neurological issues are in fact ill, and have a unique set of proteins in their spinal fluid that healthy and chronic fatigue syndrome patients do not have

- Came up with the idea that the Lyme bacteria could go dormant when exposed to antibiotics and then start growing once antibiotics were stopped – and then proved this to be the case *in vitro* at two major medical institutions

- Mapped the genome of strains of *Borrelia burgdorferi*

- Came up with two drug cocktails to potentially stop growing of persister Lyme cells

- Showed Lyme is the only bacteria that does not require iron but rather manganese

- Developed a test kit for chronic Lyme

- Developed the most accurate Lyme blood test (not yet commercially available)

- Hosted a scientific, researcher only, symposium to facilitate sharing of ideas and funding at Banbury Medical Conference (and in Greenwich, CT)

- Coordinated and funded the Banbury paper, of leading Lyme in authorities from academic and the federal government, questioning the utility of the current 2-tier system diagnostic testing and encouraging better techniques.

- Hired an M.D. as Chief Scientific Officer, a Ph.D. as Director of Research and Science, and a Ph.D. with 25 years' Lyme research experience as full-time Chief Scientific Officer

- Created a world class Scientific Advisory Board

- Established and implemented an NIH-based, peer reviewed system to evaluate grants

- Found *Borrelia burgdorferi* in the tissue of a human being post antibiotic treatment

- Found that *Borrelia burgdorferi* invades the lymph nodes of Lyme patients

- Discovered that Lyme camps out in the meninges of the brain

- The first organization to fund research for an amplified-PCR diagnostic blood test

- Created the first research Centers at any university dedicated to Lyme disease – at Columbia University.

ACCELERATING RESEARCH

GLOBAL LYME ALLIANCE HAS GAINED NATIONAL PROMINENCE FOR ITS COMMITMENT TO CHANGING THE COURSE OF TICK-BORNE DISEASE BY FUNDING INNOVATIVE, GROUND-BREAKING, EVIDENCE-BASED RESEARCH. OUR RESEARCH PROGRAM IS ONGOING AND IS RESPONSIBLE FOR MAJOR ACCOMPLISHMENTS.

SOME GLA RESEARCH ACCOMPLISHMENTS INCLUDE:

- The GLA thesis of persister cells in Lyme disease, as proven *in vitro*
- First to show Lyme disease behavior in the brain
- Developed a diagnostic test for chronic Lyme infection
- Developed a diagnostic test more sensitive and accurate than any currently available
- Two independent GLA-funded researchers showed the survival of persisting Lyme bacteria antibiotic treatment, which suggests the existence of chronic Lyme disease

- Mapped the genome of the bacterium that causes Lyme
- Showed ongoing and evolving antibody response to *Borrelia* bacteria in patients with persisting Lyme disease symptoms
- Uncovered the unique metal properties of Lyme bacteria
- 100% of GLA-funded research projects have been published in peer-reviewed scientific journals such as *Emerging Microbes & Infections, Journal of Immunology, PLoS ONE, Frontiers in Microbiology*, and *Clinical Infectious Diseases*

Our researchers are on the threshold of devising new diagnostic tests and GLA has partnered with Ionica Sciences and Cornell to accelerate the development of a very promising new, advanced science Lyme disease diagnostic. In addition, our investigators are uncovering the molecular biology of the Lyme bacterium; exploring how the disease can survive antibiotic therapy; identifying new and better targets for treatment, and analyzing how and why a large percentage of individuals continue to experience persistent, debilitating symptoms after their initial treatment.

YOUR RESEARCH DOLLARS AT WORK

Thanks to the generosity of our donors, research dollars have helped support:

50+ RESEARCH GRANTS

MORE THAN $10,000,000 IN RESEARCH AWARDS

RESEARCHERS AT 35 LEADING UNIVERSITIES & INSTITUTIONS

FIRST TO IDENTIFY AND FUND POSTDOCTORAL FELLOWS WORKING ON CHRONIC LYME DISEASE

RESEARCH

1998 **2002** **2006** **2007** **2008** **2009** **2011** **2012** **2013** **2014** **2015** **2016** **2016** **2017** **2018**

{ GLOBAL LYME ALLIANCE HAS A LONG HISTORY OF LEADING THE CHARGE INTO LYME & TICK-BORNE DISEASE RESEARCH. WE CONTINUE TO LEAD THE WAY. }

1998
Global Lyme Alliance (GLA) is founded. *(See GLA History).*
—
GLA presents Columbia University with the first installment of a $2 million endowment to create the nation's first Lyme and Tick-Borne Diseases Research Center at Columbia University Medical Center.

2002
GLA awards funds to Joseph Burrascano, M.D. to develop a Lyme and associated diseases database.

2006
Neurologist Harriet Kotsoris, M.D., accepts the role of GLA's Chief Scientific Officer. She recruits successful researchers and creates an annual scientific symposium.

2007
The Columbia University Lyme and Tick-Borne Diseases Center officially opens, led by Director, Brian Fallon, M.D.
—
GLA awards Karen Newell-Rogers, Ph.D., University of Colorado, a grant to test a peptide that plays a key role in inflammation and immune responses.

2008
GLA creates a Scientific Advisory Board composed of experts, modeled after NIH guidelines.
—
John Aucott, M.D., of Johns Hopkins University School of Medicine, is awarded his first research grant by GLA to launch SLICE, the first prospective study examining the impact of acute Lyme disease on long-term health outcomes and immune function.
—
Grant awarded by GLA to Eva Sapi, Ph.D., University of New Haven, and Alan MacDonald, M.D., to study the role of *B. burgdorferi* biofilms in Lyme disease.

2009
The Columbia Center clarifies the brain blood flow and metabolic profile of patients with chronic unexplained symptoms (altered cognition, pain, fatigue) after Lyme disease.
—
Cheryl Koopman, Ph.D., Stanford University, receives funding from GLA to identify diverse manifestations of Lyme disease to help explain the complexity of the illness.

2011
The Columbia Center, with collaborators, demonstrates that patients with chronic symptoms have an altered spinal fluid proteome and elevated inflammatory cytokine expression in the blood.
—
GLA grantee Steven Schutzer, M.D., of the University of Medicine and Dentistry of New Jersey, publishes findings that for the first time identify post-treatment Lyme disease based on unique proteins found in cerebrospinal fluid. His findings make the "100 Top Stories of 2011" list in *Discover* magazine.
—
Grant awarded by GLA to Karen Newell-Rogers, Ph.D., at Texas A&M University to examine the genetics of chronic inflammation.
—
Based on a 2009 GLA grant, Armin Alaedini, Ph.D., Columbia University, and colleagues publish findings showing that patients diagnosed with post-treatment Lyme disease syndrome have anti-*Borrelia* antibodies that change over time, suggesting an ongoing and evolving immune response.

2012
The Columbia Center highlights the role of the central nervous system as a potential key player in the chronic pain associated with Post-Treatment Lyme Disease Syndrome.
—
A GLA-funded team led by Karen Newell-Rogers, Ph.D., announce a FDA preliminary filing to begin clinical trials for a new drug targeting the autoimmune mechanism triggered by Lyme disease. This is the first novel drug candidate to ever be proposed for study in the treatment of chronic Lyme disease.
—
GLA funds the first Banbury Conference for Lyme disease research; the Conference brings together major scientists and institutions, including the CDC.

2013
The Centers for Disease Control and Prevention announces a recalculation of estimated annual Lyme disease incidence, from 33,000 to 329,000.
—
With a GLA grant, Valeria Culotta, Ph.D., of Johns Hopkins University, discovers the unique roles of manganese and iron in the metabolism of the Lyme disease bacterium. The results enabled Dr. Culotta to secure NIH funding.
—
GLA grantee Dr. Letitia Gutierrez, D.V.M., then a Ph.D. candidate at the University of Missouri, in collaboration with Dr. Robert E. Ricklefs, is awarded a grant for the first comprehensive study on biodiversity and tick-borne disease in the upper Midwest.
—
GLA recruits Kim Lewis, Ph.D., of Northeastern University, to focus on Lyme disease with a multi-year GLA grant to test the best possible antibiotic driven drug cocktails *in vitro*, for killing Lyme persister bacteria, which survive antibiotic treatment, as well as microbiome analysis.
—
GLA grantee Ying Zhang, M.D., Ph.D. of the Johns Hopkins Bloomberg School of Public Health, demonstrates that pyrazinamide (PZA) is uniquely effective against tuberculosis bacteria that have transitioned to a persister state. He tests compounds singly, and in combination with PZA, to find an optimal combination to kill persister *B.burgdorferi.*

2014
Charles Chiu, M.D., Ph.D., of the University of California, San Francisco, uses a GLA award to develop the TickChip diagnostic test to directly detect RNA of *Borrelia* and other tick-borne pathogens.
—
The Columbia Center reveals the unreliability across labs of current diagnostic testing for Lyme disease.
—
GLA grantee A.T. Charlie Johnson, Ph.D. and his University of Pennsylvania team work to develop a diagnostic test by focusing on a technique that uses nanotubes—tiny threads of carbon — to create synthetic antibodies that can locate tiny levels of the Lyme bacteria in blood.

2015
Kim Lewis, Ph.D. reports in *Antimicrobial Agents and Chemotherapy*, and confirms GLA/Johns Hopkins original findings, that the bacterium that causes Lyme disease forms dormant persister cells, which are known to survive antibiotics. He also presents two methods for eliminating persister bacteria — one using an anti-cancer agent called Mitomycin C, and another via pulse-dosing of antibiotic.
—
GLA grantee Alla Landa, Ph.D., of Columbia University, focuses on mechanisms in the brain responsible for cognitive deficits and chronic pain in post-treatment Lyme disease patients.
—
From a large collection of FDA approved drugs Dr. Ying Zhang determines the optimal drug combinations that eradicates *B. burgdorferi* persisters in vitro and then tests them in infected mice.
—
With GLA funds, Benjamin Luft, M.D. of SUNY-Stony Brook continues his work on a highly dependable Lyme disease diagnostic test using synthesized *B. burgdorferi* proteins. Dr. Eva Sapi publishes findings suggesting that *B. burgdorferi* has the ability to form biofilm-like structures under *in vitro* culture conditions.
—
In another step differentiating GLA's scientific platform from other Lyme organizations, GLA hires a full-time, in-house Ph.D. credentialed science officer to support strategic initiatives related to research and scientific priorities.

2016
GLA receives the most grant applications in its history—$4.3 million in funding requests.
—
A group led by Dr. Ying Zhang tests sulfa drugs against *B. burgdorferi* (Bb) persisters. They show that alone, they are ineffective, but their activity increases when combined with antibiotics such as doxycycline and daptomycin. They also show that *B. burgdorferi* biofilm forms of Bb persisters can be killed by daptomycin, doxycycline and cefuroxime in combination.
—
A multi-year GLA grant leads Dr. Armin Alaedini's team at Columbia University to find evidence that C-reactive protein (CRP), a marker of inflammation, is elevated in patients with PTLDS compared to those who have recovered. They also show antibodies targeting VlsE, a protein on the surface of Bb, persists and evolves in patients with symptoms of later-stage Lyme disease. These results are suggestive of an ongoing immune response, and the basis for a diagnostic suite of tests.

2016
A GLA-funded study by Dr. John Aucott finds that sustained and elevated CCL19, a chemokine made by humans after infection, is associated with persisting symptoms event after antibiotic treatment for Lyme disease.
—
A team led by Dr. Charles Chiu, using a GLA grant, shows that PTLDS patients have some similar gene expression patterns with those suffering chronic immune system dysfunctions.

2017
GLA announces its first venture philanthropy initiative, partnering with Ionica Sciences and Cornell University to accelerate the development of a highly sensitive, reliable Lyme diagnostic test.
—
With GLA backing and encouragement, Dr. Ying Zhang publishes an article identifying that essential oils from oregano, cinnamon bark and clove bud have a very strong capability to kill anti-persister forms of *B. burgdorferi (in vitro). In vivo* studies are commencing.
—
GLA adds to its research strength by hiring a full-time, in-house Chief Science Officer with more than 25 years experience in Lyme research.
—
GLA awards its first-ever fellowships to five young postdoctoral scientists whose work is focused on chronic Lyme.

2018
GLA awards 10 new research grants.

GLA HISTORY

Greenwich Lyme Disease Task Force (GLDTF) was created in 1998 by Diane Blanchard, Debbie Siciliano, Fran Herzog and other Greenwich, Connecticut residents. In 2005 GLDTF changed its name to Time for Lyme (TFL). In 2012 TFL changes its name to Lyme Research Alliance (LRA).

Turn the Corner Foundation (TTC) was founded in 2002 by Staci and Rich Grodin. In 2012 TTC joins forces with the Tick-Borne Disease Initiative and changes its name to Tick-Borne Disease Alliance (TBDA).

Global Lyme Alliance is officially created from the merger of LRA and TBDA. The merger creates a national footprint and expands GLA's ability to keep pace with the high level of funding needed to accelerate ground-breaking research.

—

PEOPLE FUEL PROGRESS
ACTIVE GRANTEES & PROJECTS

GLA AWARDED 26 GRANTS IN 2017 AND 2018. EACH GRANT HAS POTENTIAL FOR GROUNDBREAKING RESEARCH.

MILESTONES

Armin Alaedini, Ph.D., *Columbia University*
Dr. Alaedini's research has shown that individuals suffering from chronic Lyme have specific antibodies that bind to a protein called VlsE, which is found on the surface of *B. burgdorferi*, the bacterium that causes Lyme disease. He found that chronic Lyme patients have a greater variety of VlsE antibodies than patients who were successfully treated. He will determine whether these antibodies are also in patients who are infected with different strains of *Borrelia burgdorferi*, in order to develop a more comprehensive test.
STUDY (2017): *"VlsE antibodies against different Bb strains"*

John Aucott, M.D., *Johns Hopkins University*
At GLA's recommendation and funding, Dr. Aucott agreed to study a cohort of chronic Lyme patients, called SLICE (Study of Lyme Immunological and Clinical Events). The study has identified important biological differences in patients who suffer post-treatment Lyme disease compared to those who recover completely. He seeks to determine whether neurological dysfunctions in the former are due to abnormal antibody production against the patient's own proteins, which could lead to immune therapy treatment.
STUDY (2017): *"Anti-brain antibodies in PTLDS"*

Alan Barbour, M.D., *University of California-Irvine*
Dr. Barbour is focused on the wildlife that are reservoirs of Lyme and other tick-borne diseases. Wild mice, despite high levels of *B. burgdorferi* infection, do not get sick. Dr. Barbour is studying such mice and is comparing the infected vs. uninfected to determine what genes are expressed. This will help us to understand how wild mice tolerate infection and to see if the human immune system can be supplemented.
STUDY (2017): *"Why don't wild mice get Lyme disease?"*

Nicole Baumgarth, D.V.M, Ph.D., *University of California-Davis*
An abnormal immune response to *B. burgdorferi* may be one reason why we become sick from Lyme disease and in some cases, continue to be ill after antibiotic treatment. Using the mouse model of Lyme disease, Dr. Baumgarth studies the role of helper CD4+ T cells, which may fail to respond appropriately, and cause antibodies to remain high on Western Blots.
STUDY (2017): *"Immune cell dysfunction in mouse model of Lyme disease"*

Antibodies, made by the immune system, are important in controlling infections. The carbohydrates attached to them may affect how well they function. Dr. Baumgarth will study how *B. burgdorferi* infection in mice promotes changes in the composition of these sugars, which may be another tactic used by the bacteria to cause immune dysfunction.
STUDY (2018): *"Defining protective antibody-mediated immunity to Borrelia burgdorferi"*

Catherine Brissette, Ph.D., *University of North Dakota*
Dr. Brissette has identified *Borrelia* adhesion proteins which promote bacterial infection, penetration and persistence. She is studying epigenetic changes in human cells that are exposed to *B. burgdorferi* to determine whether inflammatory changes are due to differences in gene expression.
STUDY (2017): *"Control of Bb DNA expression"*

Dr. Brissette will study the effect of maternal Lyme disease on the offspring of infected mice, and will determine the timing of transplacental (from mother to fetus) infection.
STUDY (2018): *"Adverse outcomes in gestation as a consequence of immune responses to B. burgdorferi infection during pregnancy"*

Charles Chiu, M.D., Ph.D., *University of California-San Francisco*
Ticks are responsible for the transmission of a growing list of diseases, including both bacteria and viruses. Dr. Chiu is applying comprehensive deep DNA sequencing techniques to identify new pathogens in Pacific Coast and Lone Star ticks, a first step toward being able to treat tick-borne diseases more efficiently. The Lone Star tick which carries STARI (southern tick-associated rash illness) has recently been found in New York State.
STUDY (2017): *"Tick chip: identify pathogen cause of STARI"*

Thomas Divers, D.V.M., *Cornell University*
Pastured beef cattle are exposed to tick bites and may acquire *Borrelia* infection in Lyme-endemic areas, but do not exhibit Lyme symptoms. Dr. Divers is analyzing blood samples from these animals to determine whether they have antibodies that recognize the bacteria. These results can help identify antibody mechanisms that could be applied to humans.
STUDY (2017): *"Do cattle get Lyme disease?"*

Monica Embers, Ph.D., *Tulane National Primate Research Center*
Dr. Embers has shown that *B. burgdorferi* persists in animal models after antibiotic treatment. She will determine if certain antibiotics alter the genes of Lyme bacteria by comparing antibiotic treated animals vs. those that are untreated.
STUDY (2017): *"Bb genetic changes with antibiotic treatment, in rats"*

Henry Hampton, Ph.D., *Institute for Systems Biology*
It is not clear why some people with Lyme disease develop persistent symptoms after antibiotic therapy while others do not. Dr. Hampton is analyzing blood from infected individuals and studying immune cells at multiple time points. He studies how gene expression and immune proteins vary during disease progression.
STUDY (2017): *"Gene transcription in PTLDS patients: postdoc training"*

Genetics, particularly the expression of different genes in response to Lyme disease, may determine whether a patient recovers or continues to suffer symptoms. Dr. Hampton's work will address gene expression changes in patients at various stages of Lyme disease.
STUDY (2018): *"A longitudinal systems-level dissection of the immune response during Lyme disease"*

Chris Janson, M.D., *University of Chicago*
Dr. Janson, a neurologist, is interested in the neurological effects of Lyme by determining how *B. burgdorferi* penetrates and persists, using an *in vitro* model of the blood brain barrier.
STUDY (2017): *"Bb persistence in BBB model"*

A.T. Charlie Johnson, Ph.D., *University of Pennsylvania*
Dr. Johnson is working to develop a fast, accurate, affordable Lyme diagnostic test to detect *B. burgdorferi* antigens and antibodies. Dr. Johnson is focusing on a technique that uses single-layered molecular graphene sheets attached to antibodies that react with specific proteins carried by the bacteria responsible for Lyme disease.
STUDY (2017): *"High tech Bb antibody and antigen detection"*

Kim Lewis, Ph.D, *Northeastern University*
Dr. Lewis has found novel drugs that are effective against persister forms of *B. burgdorferi* in the test tube, and will extend this work to the mouse model of Lyme disease. His work will identify new potential targets for antimicrobial therapy, and illuminate the role of the host response in clearing infection.
STUDY (2017): *"Discovery of new antibiotics and combos"*

Dr. Lewis continues his study to identify drugs and combinations of drugs that may be useful for treating Lyme disease more effectively than current therapies.
STUDY (2018): *"Treatment of Lyme disease"*

Benjamin Luft, M.D., *State University of New York-Stony Brook*
It is not understood why some Lyme disease patients experience neurological symptoms even after antibiotic treatment. Dr. Luft is conducting the first microquad PET scan Lyme study to examine the Post-Treatment Lyme Disease Syndrome patient.
STUDY (2017): *"PET scans neuroborreliosis"*

Richard Marconi, Ph.D. *Virginia Commonwealth University*
Therapeutic vaccines are designed to elicit beneficial immune responses after infection, and may be important new tools in the treatment of Lyme disease. This study will identify critical *B. burgdorferi* targets and design a vaccine to enhance bacterial killing.
STUDY (2018): *"Therapeutic vaccine for Lyme disease"*

Lise Nigrovic, M.D., *Harvard Medical School*
This project will establish a systematic collection of patient information and samples from six clinical sites, for detection of *B. burgdorferi* and tick-borne co-infections in children living in Lyme-endemic areas.
STUDY (2018): *"A pediatric multi-center Lyme disease research network with biosample collection"*

Janakiram Seshu, Ph.D., *University of Texas-San Antonio*
Dr. Seshu studies fatty acid metabolism by *B. burgdorferi*, which varies in different hosts. His aim is to understand how these key pathways can be exploited to identify new targets for antimicrobial therapy. These mechanisms may also influence the efficacy of the immune response in different hosts.
STUDY (2017): *"Bb fatty acid metabolism; do statins kill Bb?"*

Mark Soloski, Ph.D., *Johns Hopkins University*
T cells command multiple arms of the immune response, yet their activity during *B. burgdorferi* infection is not well understood. This study will identify T cell subsets that are active during infection and determine what portions of the bacteria are recognized by them. This may help to explain immune dysfunctions that cause many patients to suffer continued symptoms after initial treatment.
STUDY (2018): *"T cell immunity in human Lyme borreliosis"*

Klemen Strle, Ph.D., *Harvard Medical School*
Patient genetics are important in determining the immune response to infections evoked by *Borrelia burgdorferi*. This study will identify specific genes whose polymorphisms may promote immune dysfunction and more severe acute and post-acute disease.
STUDY (2018): *"Host genetic factors in the pathogenesis of Lyme disease and its post-Lyme syndromes"*

Edouard Vannier, Ph.D., *Tufts University*
Babesia is a tick-borne pathogen that often co-infects alongside Lyme disease. Dr. Vannier's study centers on identifying neutralizing antibodies that may promote clearance of the parasite from infected mice.
STUDY (2018): *"Antibody-based therapy for severe babesiosis"*

Ying Zhang, M.D., Ph.D, *Johns Hopkins University Bloomberg School of Public Health*
Dr. Zhang has found effective antibiotic combinations that kill persister *B. burgdorferi* in the test tube. He will determine whether antibodies that recognize persister bacteria exist in patients with Post-Treatment Lyme Disease Syndrome. This could lead to a diagnostic test for dormant Lyme bacteria.
**STUDY (2017):** *"Persister antibodies in PTLDS patients?"*

Dr. Zhang will continue his work of identifying and defining how certain essential oils harbor antibacterial effects on persister forms of *B. burgdorferi*.
STUDY (2018): *"High activity of selective essential oils against Borrelia persisters"*

2017 MARKED OUR FIRST VENTURE PHILANTHROPY INITIATIVE: IONICA SCIENCES. THE DEVELOPMENT OF A RELIABLE AND SENSITIVE LYME DISEASE DIAGNOSTIC TEST IS BEING PURSUED BY THIS BIOTECHNOLOGY EFFORT, LED BY DR. JOEL TABB AND DR. OMAR GREEN.

WHERE GLA SCIENTISTS ARE FROM
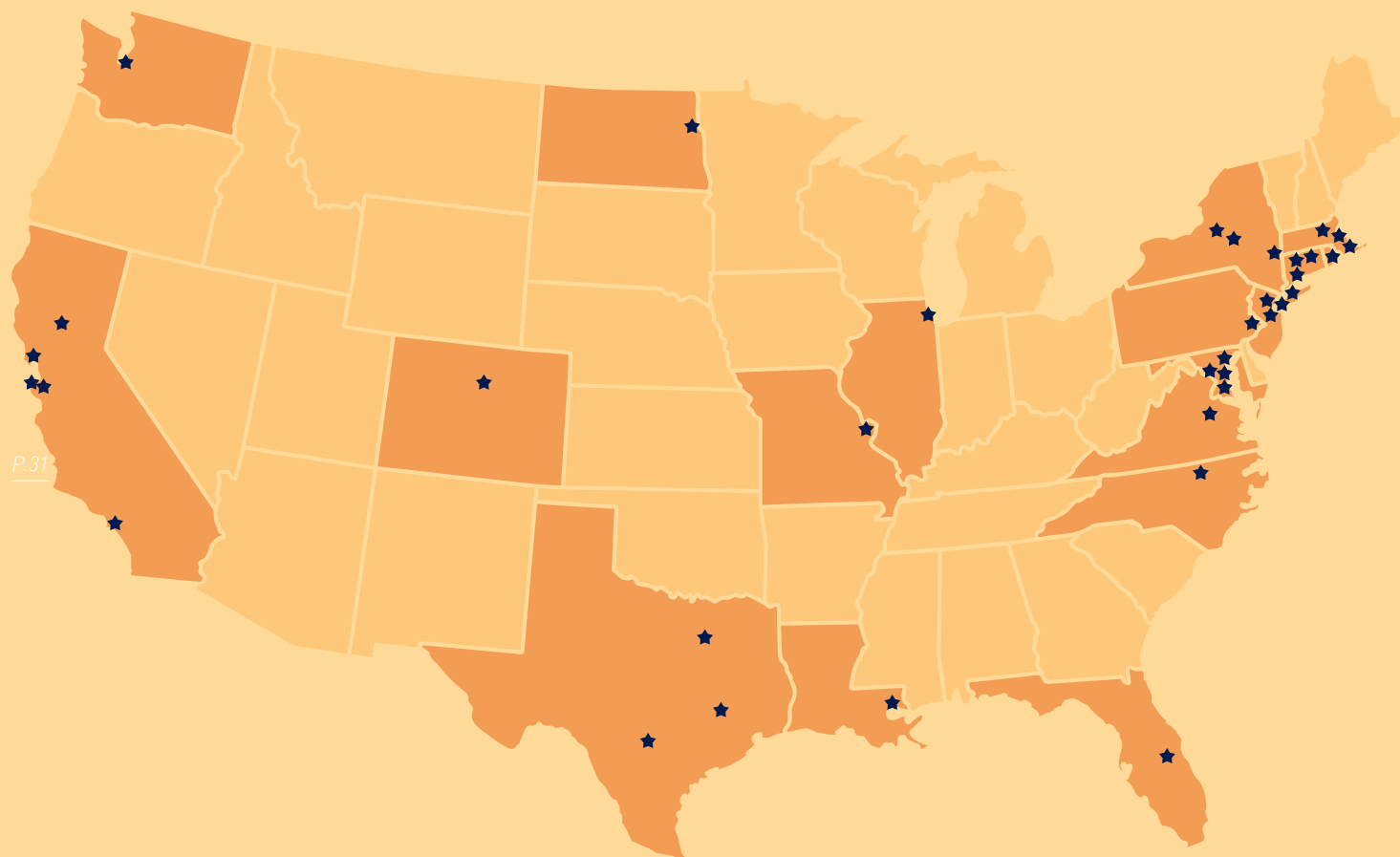
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{ GLA PARTNERS WITH THE MOST TALENTED LYME AND TICK-BORNE DISEASE RESEARCHERS AT TOP INSTITUTIONS ACROSS THE COUNTRY. }

CALIFORNIA
Open Medical Institute, Stanford
Stanford University, Stanford
University of California-Davis
University of California-Irvine
University of California-San Francisco

CONNECTICUT
University of Connecticut, Storrs
University of New Haven
Yale University, New Haven

COLORADO
University of Colorado, Colorado Springs

FLORIDA
University of Central Florida, Orlando

ILLINOIS
University of Chicago

LOUISIANA
Tulane National Primate
Research Center, New Orleans

MARYLAND
Johns Hopkins University, Baltimore
Johns Hopkins University Bloomberg
School of Public Health, Baltimore
University of Maryland, College Park

MASSACHUSETTS
Harvard Medical School, Cambridge
Northeastern University, Boston
Tufts University, Medford

MISSOURI
University of Missouri, St. Louis

NEW JERSEY
Rutgers New Jersey Medical School, Newark
University of Medicine and Dentistry
of New Jersey, Newark

NEW YORK
Cary Institute, Millbrook
Columbia University, New York
Cornell University, Ithaca
Ionica Sciences, Ithaca
State University of New York-Stony Brook

NORTH CAROLINA
Duke University, Durham

NORTH DAKOTA
University of North Dakota, Grand Forks

PENNSYLVANIA
University of Pennsylvania, Philadelphia

RHODE ISLAND
Brown University, Providence

TEXAS
Texas A&M University, College Station
University of Texas-San Antonio
University of Texas-Southwestern, Dallas

VIRGINIA
Virginia Commonwealth University, Richmond

WASHINGTON
Institute for Systems Biology, Seattle

WHAT WE FUND: A LOOK BACK AT FIVE YEARS OF FUNDING

2015—2016

Armin Alaedini, Ph.D. "Immunologic Mechanisms and Biomarkers of Post-Treatment Lyme Disease Syndrome."

Nicole Baumgarth, D.V.M., Ph.D. "Host Response to *Borrelia burgdorferi (Bb)* Infection."

Alla Landa, Ph.D. "Uncovering Neural and Immune Mechanisms Underlying Chronic Pain and Central Sensitization in Post-Treatment Lyme Syndrome."

Christopher Janson, M.D. "Generation and Characterization of Brain Lymphatic Co-culture System."

Kim Lewis, Ph.D. "Treatment of Lyme Disease."

Benjamin Luft, M.D. "Multiprotein Recombinant Assay for the Diagnosis of Lyme Disease."

Karen Newell-Rogers, Ph.D. "Effects of TLR-2 Activation or Bb Infection on Blood Brain Barrier, Immune Trafficking and Neuropathology."

Eva Sapi, Ph.D. "Characterization of *Borrelia* and Other Pathogenic Species in Autopsy Tissues of an Antibiotic-refractory Lyme Disease Case."

Ying Zhang, M.D., Ph.D. "Optimal Drug Combinations Targeting Bb Persisters for Improved Treatment of Lyme Disease."

2014—2015

Armin Alaedini, Ph.D. "Novel Antibody Biomarkers of Post-Treatment Lyme Disease Syndrome."

John Aucott, M.D. "Anti-*Borrelia* Antibodies in a Cohort of Well-Characterized Patients with PTLDS/CLD."

Nicole Baumgarth, D.V.M., Ph.D. "Host Defense Against Bb Infection."

Charles Chiu, M.D., Ph.D. "Pathogen Characterization and Discovery by Deep Sequencing of Two Major Vectors Associated with Lyme Disease and Other Tick-Borne Infections."

A.T. Charlie Johnson, Ph.D. "Effective Lyme Disease Diagnostic."

Kim Lewis, Ph.D. "Formation of Persisters in Bb and their Elimination"

Steven Schutzer, M.D. with Claire Fraser, Ph.D. "CNS-Associated *Borrelia* and Other Microbes in LD Patients with Persistent Neurocognitive and Fatigue Features."

2013—2014

Leticia Gutierrez, D.V.M, Ph.D. "The Effects of Complex Mammalian Trophic Structure on Emerging Tick and Rodent-Borne Diseases."

Kim Lewis, Ph.D. "Persister Cells and Antibiotic Tolerance in Bb."

Ying Zhang, M.D., Ph.D. "Targeting Dormant Bb Persisters for Improved Treatment of Chronic and Persistent Lyme."

2012—2013

Armin Alaedini, Ph.D. "Novel Antibody Biomarkers of Post-Treatment Lyme Disease Syndrome."

John Aucott, M.D. "Clinical Evaluation of Patients with Early Lyme Disease and Direct Detection of Bb in Whole Blood and Skin Using Nested Isothermal Amplification Prior to Multilocus Broad Range PCR and Mass Spectroscopy."

Valeria Culotta, Ph.D. "The Role of Manganese and Iron in Growth Control of Bb."

Benjamin Luft, M.D. "New Diagnostics for Lyme Disease."

Steven Schutzer, M.D. "Proteomic Investigation of Lyme Disease."

2011—2012

Karen Newell-Rogers, Ph.D. "Correlation Between Immune Response Genes, B cell Activation, and Susceptibility to Chronic Lyme Disease."

Karen Newell-Rogers, Ph.D. "A New Model of Intervention for Lyme Disease by Targeting Chronic Inflammation and Selective Aspects of Immune Activation."

Karen Newell-Rogers, Ph.D. "Lyme Disease: Preventing and/or Controlling Chronic Hyperimmune Activation with Targeted Peptide Therapy."

Steven Schutzer., M.D. "Diagnostic Biomarkers for Persisting Brain and Nervous System Symptoms in Lyme Disease."

Robert, E. Thach, Ph.D. "Vertebrate Reservoirs for Tick-Borne Diseases in the Central United States."

Ying Zhang, M.D. "Identified *Borrelia burgdorferi* L-form specific Proteins (ie: Persisters) for Development of New Diagnostics, Vaccines and Also Drugs Targeting L-Form *Borrelia*."

"IT'S AN HONOR TO BE A PART OF THIS AMAZING ALLIANCE THAT IS FIGHTING TIRELESSLY TO GIVE US A VOICE AND HELP FIND A CURE. SO THAT OTHERS WON'T EVER HAVE TO SUFFER THIS WAY AGAIN."

— *Marisol Thomas*

Marisol Thomas, philanthropist and animal rights activist, is the wife of GRAMMY Award-winning singer/songwriter Rob Thomas.

IMPACT

FROM SEED FUNDING TO NIH SUPPORT

GLOBAL LYME ALLIANCE'S COMMITMENT TO FUND INNOVATIVE AND PROMISING LYME DISEASE RESEARCH IS UNRIVALED. A VITAL COMPONENT OF GLA'S RESEARCH INITIATIVE INCLUDES EARLY-STAGE FUNDING, TO ASSIST RESEARCHERS AT A CRITICAL STAGE IN THEIR CAREERS AND THEIR RESEARCH. **GLA'S EARLY-STAGE FUNDING HAS HAD A SIGNIFICANT IMPACT ON THE LYME LANDSCAPE.**

Here are profiles of four individuals who advanced from GLA seed funding to significant support from the NIH and other research institutions.

Armin Alaedini, Ph.D. *Columbia University Medical Center*

Why do Lyme disease symptoms linger in some individuals, but not others? With a 2009 GLA grant, Dr. Armin Alaedini, then at Weill Medical College of Cornell University, analyzed blood and spinal fluid of patients whose symptoms persisted after antibiotic treatment. Dr. Alaedini and his colleagues demonstrated that the infection can trigger an ongoing abnormally activated immune response in some patients, suggesting some immunologic distinction between patients who responded favorably to treatment and those who did not.

As a result of this GLA-funded work, in 2011 Dr. Alaedini was awarded a one-year $360,000 grant from NIH/ National Institute of Allergy and Infectious Diseases, followed by a two-year grant of more than $373,000. He has since demonstrated that individuals who experience chronic Lyme disease have specific antibodies to parts of the *B.burgdorferi* surface protein, VlsE. His work continues to help us better understand immunologic mechanisms and biomarkers of post-treatment Lyme patients.

John Aucott, M.D. *Johns Hopkins University*

Dr. Aucott is Principal Investigator of the landmark SLICE project, the first prospective controlled study in the U.S. to examine the impact of Lyme disease on patients' immune systems and their long-term health.It seeks to understand why some patients suffer from Post Treatment Lyme Disease Syndrome (PTLDS), while others do not. The study has helped to advance research, including biomarker discovery, for improved diagnostics and optimal therapies.

When he was honored by GLA at our Greenwich Gala in 2015, Dr. Aucott spoke about the early days with his team and GLA: "We started eight years ago," he said, "without any funding until GLA (then called Time for Lyme) took a chance on us," he said. In 2014, Dr. Aucott received a two-year grant from GLA to recruit larger numbers of patients with medically documented chronic Lyme. In 2016, he and colleague Mark Soloski, Ph.D., also a GLA grantee, received a five-year $6 million grant from a national foundation to support the continuation of the SLICE study.

Valeria Culotta, Ph.D. *Johns Hopkins Bloomberg School of Public Health*

In 2013, GLA awarded a grant to Valeria Culotta, Ph.D. to further study the role of manganese and iron in the cellular workings of the Lyme bacterium. Dr. Culotta's research group, working in collaboration with Woods Hole Oceanographic Institute, had discovered that *B.burgdorferi* uses manganese instead of iron to survive. Iron, which is crucial to the survival of all other bacteria *in vivo*, is in fact toxic to *B. burgdorferi*.

With her findings, Dr. Culotta was well-positioned to apply for additional funding from the NIH. The results obtained from her GLA-supported study led to a two-year $162,000 NIH grant to focus on "metal trafficking" in living organisms, or how bacteria and individual cells obtain and use metals in their biological processes.

Kim Lewis, Ph.D., *Northeastern University*

In 2013, Kim Lewis, Ph.D., took aim at the *B.burgdorferi* bacterium, the chief cause of Lyme disease and PTLDS. In a landmark paper published two years later, he pointed to persisters—cells that evolve a way for bacterial species to escape being destroyed by the immune system—as the cause of persistent Lyme. Persisters play dead and then reawaken once treatment is completed. "They start multiplying again," Dr. Lewis said, "and you get this relapsing, chronic infection."

Thanks to early support from GLA, including an initial 2013-14 grant, Dr. Lewis identified not only *B.burgdorferi* persisters but also a regimen for eradicating chronic bacterial infections. Last year, Dr. Lewis received nearly $3 million in new awards from a national foundation, GLA and an anonymous source. "The terrific thing about America is private philanthropy," said Lewis, who grew up in Russia.

RESEARCHERS WE HAVE HONORED

EACH YEAR, THE LAUREN F. BROOKS HOPE AWARD IS GIVEN BY GLOBAL LYME ALLIANCE TO RENOWNED SCIENTISTS WHO ARE MAKING SIGNIFICANT STRIDES IN RESEARCH AND TREATMENT IN PURSUIT OF A LYME DISEASE CURE. HERE ARE SIX SCIENTISTS GLA HAS HONORED IN RECENT YEARS.

Drs. Monica Embers, Brian Fallon and Henry Hampton at 2017 GLA Research Symposium

John Aucott, M.D., *2015 Lauren F. Brooks Hope Award recipient*

See Dr. Aucott's bio page 38.

Brian A. Fallon, M.D., M.P.H. *2016 Lauren F. Brooks Hope Award recipient.*

Dr. Fallon is director of the Lyme and Tick-Borne Diseases Research Center at Columbia University Medical Center, which was founded and endowed jointly by GLA and the Lyme Disease Association in 2007. He is one of the world's leading researchers of tick-borne diseases. A Professor of Clinical Psychiatry at Columbia University Medical Center, he has served on expert panels for the NIH and has received over $9 million to support his research. His primary focus is on persistent cognitive impairment, fatigue and pain in patients with Post-Treatment Lyme Disease Syndrome (PTLDS) as well as the efficacy of repeated antibiotic therapy. Dr. Fallon's most recent book, "Conquering Lyme Disease: Science Bridges the Great Divide" was published in December 2017.

Kim Lewis, Ph.D. and Ying Zhang, M.D., Ph.D. *2014 Lauren F. Brooks Hope Award recipients.*

Two distinguished Lyme disease researchers both GLA grantees—Kim Lewis, Ph.D. of Northeastern University and Ying Zhang, M.D., Ph.D., of Johns Hopkins Bloomberg School of Public Health— were honored by GLA in 2014 for their work with persisters, cells that manage to survive antibiotic assault. Dr. Lewis, distinguished professor and director of Northeastern's Antimicrobial Discovery Center, has since continued his work with *B. burgdorferi* persisters and has tested pulse-dosing antibiotics to target persistent infection. Dr. Zhang, professor of molecular microbiology and immunology at Johns Hopkins is testing compounds to find an optimal treatment regimen for patients with chronic Lyme disease.

Steven Schutzer, M.D. and Mark Eshoo, Ph.D. *2013 Lauren F. Brooks Hope Award recipients.*

The importance of furthering research to ultimately find a cure for Lyme was emphasized in 2013 when GLA grantees Dr. Steven Schutzer of the University of Medicine and Dentistry of New Jersey and Mark Eshoo, Ph.D., director, New Technology Department, Abbott Laboratories received the Hope Award. Dr. Schutzer was honored for his ongoing work in the identification of distinct protein biomarkers. His work was cited for providing hope for furthering understanding the persistent symptoms of Lyme and, ultimately, for more effective diagnosis and treatment of the disease. Dr. Eshoo was recognized for working to improve the sensitivity of diagnostic tests and continues to make progress in the detection of Lyme disease during the initial stages of infection, when diagnosis and treatment are most effective. Together, utilizing state-of- the-art technology to identify Lyme and other tick-borne diseases in a speck of body fluid, Drs. Eshoo and Schutzer were honored for revolutionizing the field of diagnostics.

THE FUTURE

Despite a host of advances in twenty-first century medicine and technology, Lyme patients today continue to receive virtually the same treatment options they were offered decades ago. There is still a serious lack of Lyme awareness among the general public, not to mention unreliable diagnostics and limited treatment options—all of which is unacceptable.

That said, we at Global Lyme Alliance believe we are in a period of incipient change in Lyme diagnosis and treatment. Today, GLA-funded scientists and others in medical research are ever more confident of their growing understanding of the many forms and causes of Lyme and its co-infections. Researchers have made strides in understanding the genetics of the Lyme bacterium; new light has been shed on the role the immune system plays in the illness; and researchers are closer than ever to knowing why some individuals have a greater risk of persistent Lyme when treatment ends than others.

Healthcare technology is also changing the future of Lyme. A wide variety of technologies, as well as emerging scientific approaches, are advancing exponentially, all of which could have a profound impact on the lives of Lyme patients. We have entered a new era in medicine with a growing wave of progress in diseases employing immunotherapies, genetic

testing and precision medicines. Moreover, GLA is establishing relationships and collaborating with other disease organizations as a means of translating their life-changing findings to benefit Lyme patients.

Our CEO, Scott Santarella, has more than 25 years of research experience and leadership in the oncology field. He has seen the advances that have come about in the cancer world as a result of interdisciplinary collaborations, and he envisions a similar interdisciplinary approach changing the face of Lyme research soon.

The good news is that the future looks brighter than ever for Lyme patients. But government research funding is trending downward. Therefore, the onus on GLA to advance scientific knowledge is greater than ever before. There is much work to be done—and we have the team to do it. We hope you'll continue to support us in our efforts to accelerate research, identify new treatments and advance the opportunities for Lyme sufferers to live better lives.

Special thanks for the generous gifts from those who share our passion. **With your support, we can do much more. Please make a tax-deductible donation to support Lyme research at GLA.org/donate or call 203.969.1333.**

> "GLA IS THE LEADER IN LYME RESEARCH THAT OTHER GROUPS FOLLOW AND SEEK TO EMULATE."
>
> — *Robert Kobre*
> *Chairman, Global Lyme Alliance*