

Fisher FOCUS

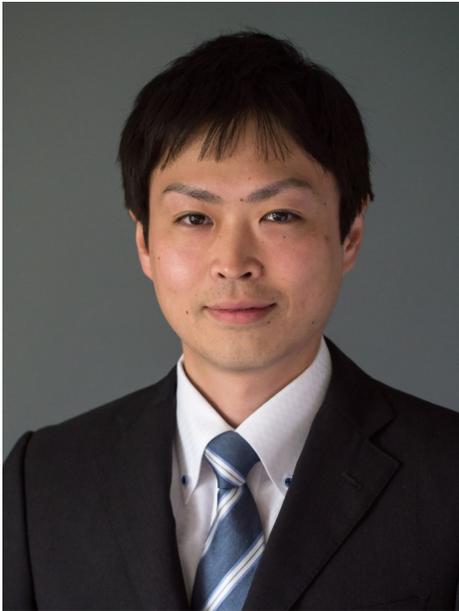


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News from the Sherrilyn and Ken Fisher Center for Environmental Infectious Diseases

Kobayashi Completes Fisher Research Fellowship



Takaaki Kobayashi, MD, a citizen of Yamanashi, Japan, recently completed a ten month research fellowship with the Fisher Center. Dr. Kobayashi graduated from the Juntendo University School of Medicine in Tokyo, Japan in 2008. After completion of medical school he served as a junior resident at the Juntendo University Hospital and senior resident at the Kameda Medical Center in Kamogawa, Japan. He received board certification from the

Japanese Society of Internal Medicine in 2011.

Dr. Kobayashi's interest in evidence-based medicine as practiced in the United States led him to serve an internship with the United States Naval Hospital Yokosuka in Kanagawa, Japan from 2013-2014. While there he developed his interest in infectious disease and clinical research. His mentor at the US Naval Hospital, Sybil Tasker, MD, suggested he contact Dr. Paul Auwaerter regarding a fellowship with the Fisher Center.

Beginning in June 2014, Dr. Kobayashi served as a post-doctoral research fellow in Infectious Diseases at Johns Hopkins and was quite instrumental in completing over 1200 chart abstractions and data analysis for the project *Lyme Disease Consultations at Johns Hopkins 2000-2013*. He presented preliminary data in poster format at the Mid-Atlantic Tick Summit IV, in February 2015 and again at the Department of Medicine Research Retreat, Johns Hopkins University School of Medicine, in March 2015. Project data is currently under consideration for additional meetings. He also completed work on the Lyme Carditis chapter of the Infectious Disease Clinics of North America

volume: *Lyme Disease and Other Infections Transmitted by Ixodes scapularis*, to be published June 2015. In July 2015 Dr. Kobayashi will begin an internal medicine residency after a highly competitive process at Mount Sinai Beth Israel Hospital in New York, NY.

On a personal note, tradition dictated that Dr. Kobayashi was to have been a Buddhist priest. His father is the 35th (not a typo) generation to serve as a Buddhist priest in his hometown near Tokyo. As the eldest son, Takaaki was to have succeeded his father. He credits his father's assistance to grieving families as informing his choice to help others by entering medicine. Realizing that medicine was Takaaki's calling, his younger brother agreed to accept the post as Buddhist priest, thus the family tradition continues. Takaaki's choice of medicine has proven to be quite suitable for him personally and his family is very proud of his dedication to the medical profession. Takaaki married his wife, Nao, in 2014. She will accompany him to New York later this year.

The faculty and staff of the Fisher Center grew quite fond of Dr. Kobayashi over the past year and wish for him a successful residency and sojourn in Manhattan.

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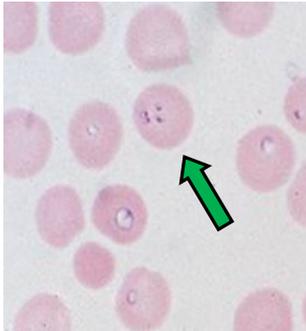
The Sherrilyn and Ken Fisher Center for Environmental Infectious Diseases is dedicated to the clinical research of environmental pathogens which improves the diagnosis and treatment of these infections.



A word from our Director Paul Auwaerter, M.D., M.B.A.

Clinical Director, Division of Infectious Diseases

Babesiosis: less known but likely to have higher profile soon



Arrow: classic *Babesia tetrad* parasite within human red blood cell

Babesiosis can be a life threatening infection with a malaria-like parasite that thrives in red blood cells. In the United States, this is most commonly acquired through the bite of the *Ixodes scapularis* tick, commonly known as the black-legged deer tick, which is more famous for being the same vector that causes Lyme disease. Due usually to the species *Babesia microti*, this infection remains most common in coastal New England, Mid-Atlantic and upper Midwest states, but is slowly spreading beyond historic

ranges (as Lyme disease also advances) into newly described locations including Maryland, Pennsylvania, Maine and Canada. The infection is most severe in people with existing health problems such as the elderly or people who lack spleens. Babesia is not a nationally reported infection, but there has been a growing number of recognized cases with 1762 described in 2014 from the 27 states the perform surveillance. Despite treatment, parasites can persist for a period of months even in people without active symptoms.

A fact little known, Babesiosis is the most common infection acquired from blood transfusions in the United States. From 2004-2008 an estimated 63 cases were described as resulting from receiving blood or blood products, but this is likely an under-representation. Acknowledging a growing problem, especially in older patients, U.S. Food

and Drug Administration convened a panel in May of this year. This panel advocated national screening of blood donors for presence of antibodies to Babesia as well as molecular testing for the parasite in donors from high risk states. This will certainly help improve the safety of the blood supply since some people who are feeling perfectly well when they donate blood may harbor the infection. However, Babesia serology has some significant rates of false positive results, especially if performed in states where the infection is not known to exist. Blood donors may be receiving reports that they can no longer donate blood, and may be seeking opinion from their physicians whether they need antimicrobial therapy. Routine testing by blood banks will certainly raise the profile of this important but less well known tick pathogen.

Thank you to those who contributed so generously to Environmental Infectious Disease research this past year. Such gifts help facilitate innovative research, especially targeted to younger investigators.

In particular we would like to acknowledge:

- The Scott Sherman and Julie Rothman Charitable Gift Fund
- Jewish Philanthropies (Robert Bank)
- Walt and Nancy Tilley

Fisher Center Early Career Support for Faculty

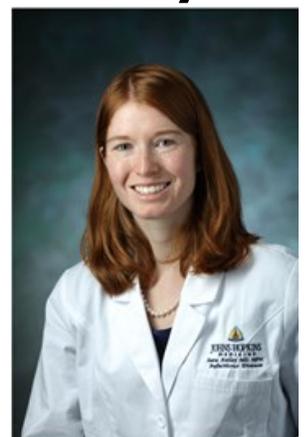
Since the 1970s, many patients needing long-term intravenous therapies, like antibiotics for complicated infections or total parenteral nutrition, have been able to get these therapies at home with assistance from home infusion nurses and pharmacists. Most of these patients have central venous catheters like PICC lines and tunneled catheters.

Research focusing on inpatients has shown over the last 20 years that bloodstream infections from central venous catheters lead to significant morbidity and mortality. Therefore, researchers have developed ways to safely care for these catheters in inpatients, and rates of central venous

catheter-related bloodstream infections in inpatients have started to decrease. However, we know little about these bloodstream infections in patients discharged home with central venous catheters, although patients may be exposed to environmental pathogens once they go home. Patients at home may have pets, perform gardening or yardwork, do recreational activities in the water, or prepare food. These patients are responsible for caring for their own catheters, and we don't know how well they care for the catheters. We also don't know much about other side effects of central venous catheters in the home (like clots) or about side effects of outpatient parenteral

antimicrobial therapy (OPAT).

Under the direction of Dr. Trish Perl and Dr. Sara Cosgrove, and with support from the Fisher Center Discovery Program as well as the Johns Hopkins Home Care Group, **Sara Keller, MD, MPH, MSHP**, is performing a (continued page 3)



Tackling the Issue of Bacterial Persisters

Ying Zhang, MD, PhD, Professor in the Department of Molecular Microbiology and Immunology in the Bloomberg School of Public Health, has joined with the Fisher Center to research Lyme disease. Having received his MD from Taishan Medical College in China and his PhD from Birmingham University (England) in 1991, Dr. Zhang has researched drug resistance, bacterial persistence, diagnostic tool development and vaccine development since joining the Johns Hopkins faculty in 1995.

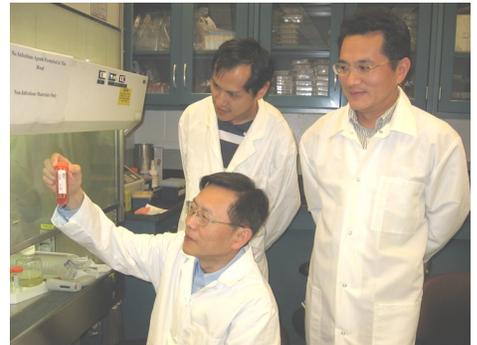
Dr. Zhang has held a long-term interest focused on Mycobacterium, which causes tuberculosis (TB) and other non-TB infections in the human population. In particular, Dr. Zhang studied TB drug resistance mechanisms and mycobacterial persisters. Persisters are bacteria that remain in the human

body after the initial infection, often in a different form, and may be described as bacteria in a dormant state.

His work with TB led him to study the medication pyrazinamide (PZA) which is effective against persistent TB. This prompted him to consider PZA in the fight against *Borrelia burgdorferi* (Bb), the bacteria that causes Lyme disease. With support from Global Lyme Alliance (formerly Lyme Research Alliance), the LymeDisease.org (formerly CALDA) and the Fisher Center, Dr. Zhang, has been studying the persistence of *Borrelia burgdorferi* and identified FDA-approved drug candidates with good activity against *B. burgdorferi* persisters in an effort to discern if persistent Bb bacteria play a part in human disease. Collaborators on the Bb persister research include Jie Feng, PhD, Wanliang Shi, PhD, Shuo

Zhang, PhD, David Sullivan, MD, and Paul Auwaerter, MD.

Dr. Zhang is the recipient of numerous grants and awards. In April 2014 he received the Lauren F. Brooks Hope Award at Lyme Research Alliance's "Time for Lyme" Gala, held in Old Greenwich, CT.



Examining *Borrelia* cultures in the lab: Ying Zhang, Jie Feng, and Wanliang Shi

Relevant Zhang Lab Publications in Collaboration with the Fisher Center

Identification of novel activity against Borrelia burgdorferi persisters using an FDA approved drug library. Feng J, Wang T, Shi W, Zhang S, Sullivan D, Auwaerter PG, Zhang Y. Emerg Microbes Infect. 2014 Jul;3(7):e49. doi: 10.1038/emi.2014.53. Epub 2014 Jul 2. PMID: 26038747. Summary: A minority of patients who have been adequately treated for Lyme disease continue to have persistent symptoms such as joint pains, fatigue, and neurocognitive difficulties. It is unclear what causes Post Treatment Lyme Disease Syndrome (PTLDS). This study focused on identifying the presence of a persistent stage of Bb and drug combinations that may be useful against it. Researchers identified 165 agents approved for use in other disease conditions that had more activity than doxycycline and amoxicillin against *B. burgdorferi* persisters. This may have implications for the development of a more effective treatment for Lyme disease and for the relief of PTLDS.

Drug combinations against Borrelia burgdorferi persisters in vitro: eradication achieved by using daptomycin, cefoperazone and doxycycline. Feng J, Auwaerter PG, Zhang Y. PLoS One. 2015 Mar 25;10(3):e0117207. doi: 10.1371/journal.pone.0117207. eCollection 2015. PMID: 25806811. Summary: Building on the previous research described above, the research team found daptomycin-containing drug combinations were the most effective against persistent forms of Bb in vitro. These findings may have implications for improved treatment of Lyme disease, if persistent organisms or detritus are responsible for PTLDS symptoms. Further studies are needed to validate whether such combination antimicrobial approaches are useful in animal models and human infection.

Keller, MD (continued from page 2) cohort study of patients discharged with central venous catheters to understand risks of complications, and will soon be undertaking conversational, semi-structured interviews to learn more about how patients care for their catheters and what environmental exposures they might have. She plans on using her findings to develop and test a quality improvement intervention to reduce the risks of complications in patients discharged home on OPAT or central venous catheters.

Dr. Keller received a Master's degree

in Public Health in epidemiology from the University of North Carolina, Chapel Hill and then her MD from Duke University School of Medicine. She completed her internal medicine residency training at the Johns Hopkins University School of Medicine and her infectious diseases fellowship at the University of Pennsylvania. She was also a fellow in the Center for Healthcare Improvement and Patient Safety receiving a Master's of Health Policy Research from the University of Pennsylvania. Dr. Keller joined the Division of Infectious Diseases as a

Clinical Associate in 2013, and she is now an Assistant Professor of Medicine on the full-time faculty. Her research interests include OPAT, health services research, and quality improvement research. She is also using Fisher Center resources to study outcomes in orthopedic hardware infections, under the mentorship of **Dr. Paul Auwaerter**. She was awarded a National Institutes of Health (NIH) KL2 Mentored Career Development grant that will begin in July 2015 to further her time and training for clinical investigation.

Funding Our Future

Thanks to all of you that believe in the mission of environmental infectious disease research. As always, we are extremely grateful to those who have contributed. To donate, please consider the following options:

Online: To make a gift or pledge online, please complete our secure online giving form, <https://secure.jhu.edu/form/infdis>

Phone: To speak to someone directly about making a gift, please call 410-550-9893

Presentations

Antimicrobial Shortages? There's an App for That. **Paul G. Auwaerter, MD.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/845037>. May 26, 2015

Generics Tested for Skin and Soft Tissue Infections. **Paul G. Auwaerter, MD.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/842956>. April 15, 2015

Lyme Disease Consultations at Johns Hopkins 2000-2013. Poster. **Takaaki Kobayashi, MD, Yvonne Higgins, PA, MAS, MS/ITS, Michael Melia, MD, Paul G. Auwaerter, MD.** 2015 Department of Medicine Research Retreat, Johns Hopkins University School of Medicine, Tuner Auditorium and Concourse, March 10, 2015.

Managing Systemic Exertion Intolerance Disease (SEID): A New Name for Chronic Fatigue Syndrome. **Paul G. Auwaerter, MD.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/840635> March 03, 2015

Lyme Disease Consultations at Johns Hopkins 2000-2013. Poster. **Takaaki Kobayashi, MD, Yvonne Higgins, PA, MAS, MS/ITS, Michael Melia, MD, Paul G. Auwaerter, MD.** Mid-Atlantic Tick Summit IV, Maryland Department of Health and Mental Hygiene, Center for Zoonotic and Vector-borne Diseases, National Wildlife Visitor Center at Patuxent Research Refuge, Laurel, MD. February 25, 2015

A New Virus in the Midwest – The Bourbon Virus. **Paul G. Auwaerter, MD.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/838479>. January 28, 2015

Injectable Peramivir for Influenza: Will It Aid In-Hospital Care? **Paul G. Auwaerter, MD.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/836702>. December 22, 2014

Fisher Focus

Johns Hopkins University, School of Medicine
Department of Medicine, Division of Infectious Diseases
The Fisher Center for Environmental Infectious Diseases
Pre-Clinical Teaching Building, Suite 211
725 N. Wolfe St.
Baltimore, MD 21205

For questions or comments, contact:
Yvonne Higgins, PA, MAS, MS/ITS
fishercenter@jhmi.edu or 443-287-4840

Recent Publications

Lyme Disease and Other Infections Transmitted by Ixodes scapularis. **Paul G. Auwaerter, MD,** Editor. Infectious Disease Clinics of North America volume 29, issue 2, June 2015. June 2015 ISSN 0891-5520, ISBN-13: 978-0-323-38892-4doi:10.1016/S0891-5520(15)00034-3. Elsevier <http://www.theclinics.com>

Lyme disease: knowing good evidence to help inform practice. **Auwaerter PG.** Infect Dis Clin North Am. 2015 Jun;29(2):xi-xvi. doi: 10.1016/j.idc.2015.03.001. No abstract available. PMID: 25999231

Lyme Carditis. **Robinson ML, Kobayashi T, Higgins Y, Calkins H, Melia MT.** Infect Dis Clin North Am. 2015 Jun;29(2):255-268. doi: 10.1016/j.idc.2015.02.003. Review. PMID: 25999222

Unorthodox alternative therapies marketed to treat lyme disease. Lantos PM, Shapiro ED, **Auwaerter PG,** Baker PJ, Halperin JJ, McSweegan E, Wormser GP. Clin Infect Dis. 2015 Jun 15;60(12):1776-82. doi: 10.1093/cid/civ186. PMID: 25852124

Life After Lyme Disease. **Auwaerter PG.** Clin Infect Dis. 2015 Apr 17. pii: civ279. [Epub ahead of print] No abstract available. PMID: 25888673

Drug combinations against Borrelia burgdorferi persists in vitro: eradication achieved by using daptomycin, cefoperazone and doxycycline. **Feng J, Auwaerter PG, Zhang Y.** PLoS One. 2015 Mar 25;10(3):e0117207. doi: 10.1371/journal.pone.0117207. eCollection 2015. PMID: 25806811

Staphylococcus aureus colonization is associated with wheeze and asthma among US children and young adults. **Davis MF,** Peng RD, McCormack MC, **Matsui EC.** J Allergy Clin Immunol. 2015 Mar;135(3):811-3.e5. doi: 10.1016/j.jaci.2014.10.052. No abstract available. PMID: 25533526

Low prevalence of mupirocin resistance among hospital-acquired methicillin-resistant Staphylococcus aureus isolates in a neonatal intensive care unit with an active surveillance cultures and decolonization program. Suwantarant N, **Carroll KC,** Tekle T, Ross T, Popoola VO, **Milestone AM.** Infect Control Hosp Epidemiol. 2015 Feb;36(2):232-4. doi: 10.1017/ice.2014.17. No abstract available. PMID: 25633010

Laboratory testing for lyme neuroborreliosis—reply. **Melia MT,** Lantos PM, **Auwaerter PG.** JAMA Neurol. 2015 Jan;72(1):126. doi: 10.1001/jamaneurol.2014.3555. No abstract available. PMID: 25581866

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