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.
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.
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.

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)

Keller, MD, Clinical Associate 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.
Focus

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Presentations


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.


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