

◀ *P. falciparum* sporozoite in a mosquito midgut



Infectious Diseases

Washington University in St. Louis
SCHOOL OF MEDICINE

DIVISION NEWSLETTER

March 31, 2015 • Volume 11, Issue 1

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Calendar Highlights

Global Health & Infectious Disease Events Next Week

Annual Conference: Shrinking the Cure and Prevention Divide that Separates Populations from Life-Saving Drugs and Vaccines

Friday, April 15 | 8:30 am to 5:30 pm | Check-in at 8 am
Eric P. Newman Education Center, Medical Campus
Free and open to all.
More details | Registration

Forum for International Health & Tropical Medicine 18th Annual Global Health Symposium: Health Without Borders

Saturday, April 16 | 9:30 am to 2 pm | Check-in at 8:45
Farrell Learning and Teaching Center
Eric P. Newman Education Center, Medical Campus
More details | Registration

We are interested in your achievements, clinical and/or research activities, and other personal news since leaving Washington University School of Medicine. Please contact Dr. Gerald Medoff at gmedoff@wustl.edu with any information you would like to share.

All division newsletters can be found at:
ID Division Newsletters

Teaching Uninsured Patients to Self - Administer IV Antibiotics at Home



Kavita P. Bhavan, M.D., MHS and son, Ajay Bhavan

Former WUSM ID Fellow, Kavita P. Bhavan, M.D., MHS, Assistant Professor of Medicine at the University of Texas – Southwestern, and her colleagues have shown that providing uninsured patients with low-literacy levels the training and independence to manage their own care, can actually improve outcomes while significantly saving hospital health care costs.

Outpatient parenteral antimicrobial therapy (OPAT) is accepted as safe and effective for medically stable patients to complete intravenous (IV) antibiotics in an outpatient setting. Uninsured patients typically cannot access standard of care OPAT services and may, therefore, remain in the hospital purely to infuse antibiotics. This often results in a disproportionate burden on safety net hospitals utilizing beds that could be used for other patients requiring more intensive services, while posing an additional burden on the individual patient delaying their ability to return to work and activities of daily living while completing their treatment course in the safety and comfort of their own home.

OPAT is generally delivered in the community in one of four settings: infusion centers, nursing homes, at home with skilled nursing assistance, or at home with self-administered therapy. The first three— termed healthcare-administered OPAT (H-OPAT)—are most commonly used in the United States by patients with insurance coverage. The fourth—self-administered OPAT (S-OPAT) is relatively uncommon.

Dr. Bhavan led a research effort at UT Southwestern and Parkland Hospital, a safety-net hospital serving Dallas County, Texas, enrolling uninsured patients who administered their own IV antibiotics. They established an S-OPAT clinic in 2009 to shift care of selected uninsured patients safely to self-administration of their IV antibiotics at home. They undertook this study to determine whether the low-income, mostly non-English-speaking patients in their S-OPAT program could administer their own IV antimicrobials at home with outcomes as good as, or better than, those receiving H-OPAT.

continued

FEATURED COLLEAGUE



Somnuek Sungkanuparph, MD
“Cruising the fjord of Milford Sound,
South Island, New Zealand”
March 2015

It's been ten years since I left Washington University and returned to my native Thailand. Upon completing my ID fellowship training at Wash U, I rejoined the attending staff in the Division of Infectious Diseases, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, in Bangkok. My research in the fields of HIV/AIDS, tuberculosis, cryptococcosis, and other opportunistic infections has been mainly focused on solving problems in Thailand and other resource-limited settings.

I attained the position of Associate Professor in 2006 and then advanced to Professor of Medicine in 2009. Since then I have devoted more time for teaching about infectious diseases and medical research to the medical students, residents of internal medicine, and ID fellows in my institute. Witnessing the success of our young doctors and having my research cited in national and international guidelines are very important to me and it inspires me to continue what I have been doing. I have been honoured with the “Most Favorite Attending Staff Award” in the Department of Medicine for four consecutive years, 2011-2015 and I also received the “Thailand Innovation Award” in 2011.

continued next column

teaching s-opat continued

Between 2009 and 2013, of the 1,168 patients discharged to receive OPAT, 944 (81%) were managed in the S- OPAT program and 224 (19%) by H-OPAT services. Uninsured patients meeting criteria (fig 1 Patient Assessment for OPAT Program) were enrolled in S-OPAT, while insured patients were discharged to H-OPAT settings. The S-OPAT patients were trained through multilingual instruction to self-administer IV antimicrobials by gravity, tested for competency before discharge, and provided 24-hour hotline support. After discharge, they were followed at designated intervals in the S- OPAT outpatient clinic for IV access care, laboratory monitoring, and physician follow-up.

Some well-educated, insured patients have been taking self-administered antibiotics for decades, but this population was different. Many were far below the poverty line, with very little education, and faced language barriers.

To teach patients, a group of nurses, doctors, and social care workers distilled the education to a fourth grade literacy level; they did bedside training with a photo-packed manual and used technology. A QR code was added to every bag of antibiotics that links to a YouTube video in English and Spanish.

This study has proven that if patients are adequately taught and are engaged in their own care, they can do it. “Not only do they do it well, but they’ve done it better in our study, when we looked at the controls who went home with some home health services,” says Bhavan, who is also Medical Director of the Infectious Diseases Parenteral Antibiotic Therapy Clinic at Parkland.

By letting patients go home and care for themselves, Parkland estimates in 2015 alone, the program helped it save more than seven million dollars — it also freed up 6,000 hospital bed days — for patients requiring more intensive services

S-OPAT was associated with similar or better clinical outcomes than H-OPAT. S-OPAT may be an acceptable model of treatment for uninsured, medically stable patients to complete extended courses of IV antimicrobials at home. The four year study, recently published in PLOS Medicine, challenges traditional ideas about what patients are capable of.

“We aimed to reduce health care disparities for uninsured patients . . . by enabling them to complete therapy at home. We sought to improve their outcomes, lower their hospital-based risks, increase their sense of self-efficacy, and reduce costs.”

continued on page 6

Somnuek Sungkanuparph, MD continued

I still enjoy photography and back-pack travel around the world during my limited free time. My experiences in 47 countries, on 6 continents have helped me to see the world with a greater perspective, and having my photographs tell the stories from around the world are one of my greatest joys. The Wash U ID reunions that occur at IDSA/ID Week every year are always a wonderful opportunity to see everyone and refresh my fond memories of my tenure at Wash U ID. I quite often reflect on my time at Wash U and St. Louis and hope that I get the chance to return there for a visit some time.

awards & announcements

RECENT AWARDS		
PRINCIPAL INVESTIGATOR(S)	AWARD	PROJECT TITLE
Thomas Bailey, MD	Institute of Clinical and Translational Sciences/Barnes Jewish Hospital Foundation	Fitbits to monitor outpatient heart rate, activity, and sleep deprivation/quality in patients at risk of hospital readmission.
Jennie H. Kwon, DO	Institute of Clinical and Translational Sciences/Barnes Jewish Hospital Foundation	The Fecal Microbiome and Resistome of Patients with Multidrug-Resistant UTIs
Robyn Klein, MD, PhD	National Institute of Neurological Disorders and Stroke	Neuroprotection and repair during West Nile Virus Encephalitis
Robyn Klein, MD, PhD	National Institute of Neurological Disorders and Stroke	Mechanisms of sex differences in blood-brain barrier biology
Robyn Klein, MD, PhD	National Multiple Sclerosis Society	Targeting S1PR2 to prevent disease progression in females with CNS autoimmunity

special recognition



Jeffrey Henderson, MD, PhD, Assistant Professor of Medicine and Molecular Microbiology was elected to membership in the American Society of Clinical Investigation (ASCI) and will travel to the annual meeting of the Association of American Physicians, the ASCI, and the American Physician-Scientists Association on April 15 2016 in Chicago for the ceremony. The American Society for Clinical Investigation (ASCI), established in 1908, is one of the nation's oldest and most respected medical honor societies. The ASCI represents active physician-scientists who are at the bedside, at the research bench, and at the blackboard.

David Clifford, MD, principal investigator of the AIDS Clinical Trials Unit, received the Samuel R. Goldstein Leadership Award in Medical Student Education. Nominated by their peers, School of Medicine faculty are honored for their dedication, talent and wide-ranging activities. The annual awards are among the highest honors that School of Medicine teachers can achieve.



farewell... *Best wishes to Dr. Diana Nurutdinova, MD*

I want to take a moment to let you know that I am leaving my positions at Washington University School of Medicine and the VA Medical Center St. Louis. I will be moving to New York City to join the Infectious Diseases Faculty at Mount Sinai St. Luke's, Icahn School of Medicine at Mount Sinai.

Although my move to St. Louis after my residency training was unplanned, the years I lived in St. Louis have proven to be the most formative for me. When I first came to visit St Louis I was instantly charmed by the city, the people, and the heartwarming environment in the ID division. Everyone's generosity and kindness made me instantly feel that I was a part of a family.

The Infectious Disease fellowship training made me the physician I am now. I will take with me many wonderful memories and impressions of my time in St. Louis. I am now very excited to pursue a dream job in a dream city and I am looking forward to starting a new chapter in my life in New York City! ~Diana



faculty news bites



Society for Healthcare Epidemiology of America (SHEA)

Hilary Babcock, MD, MPH, was elected to the Board of Trustees of SHEA. SHEA's accomplishments are grounded in outstanding leadership from the Board of Trustees, committee chairs and members, and additional volunteers. The Board of Trustees sets SHEA's strategic direction and holds responsibility for the actions and policies recommended by SHEA committees.

Hilary Babcock, MD, MPH



SHEA Publications Committee

Jennie H. Kwon, DO, was selected for a three-year term on the SHEA Publications Committee. The committee oversees and makes policy recommendations to the SHEA Board concerning all formal SHEA contracts with the journal editor, publishers, publications and the journals. It is also tasked with the peer review of SHEA white papers for publication in ICHE.

Jennie H. Kwon, DO

Additionally, **Jennie** received a Burroughs Wellcome Fund Travel Award to attend Translational Science 2016, April 13-15 in Washington, D. C. Translational Science 2016 is jointly hosted by the Association for Clinical and Translational Science (ACTS), American Federation for Medical Research (AFMR) and Clinical Research Forum (CR Forum).



Indian Council of Medical Research

Rupa Patel, MD, MPH, BTM&H, Instructor in Medicine, Director, Global Health Scholars in Medicine Program is invited by the Indian Council of Medical Research to participate in the National Council on "Expanding research on implementation of oral pre-exposure prophylaxis for HIV prevention", which will be held April 18, 2016 in Chennai, India. Rupa's commitment, rich experience and expertise in the field will allow for expert input during this meeting.

Rupa Patel, MD, MPH, BTM&H

2016 Anne Maurer-Cecchini Award



Gary J. Weil, MD

The research work of Gary J. Weil, M.D., Professor of Medicine and Molecular Microbiology and Ramakrishna U. Rao, PhD, Associate Professor of Medicine, has been selected to receive the 2016 Anne Maurer-Cecchini Award, officially given during the closing ceremony on April 21st of the Geneva Health Forum, an international congress on global health organized by the University of Geneva and the Geneva University Hospitals.



Ramakrishna U. Rao, PhD

The Anne Maurer-Cecchini Foundation was created in memory of Anne Maurer-Cecchini, a young Swiss researcher who had chosen to devote herself to research on neglected tropical diseases (NTD) that mainly or exclusively affect poor populations living in tropical areas. The purpose of the award is to support research on neglected tropical diseases by rewarding a clinical or epidemiological research project carried out on these diseases, in order to enable its continuation. This award will help Dr. Rao and his colleagues at the Sri Lankan Ministry of Health to refine post-Mass Drug Administration surveillance methods in ways that will benefit both Sri Lanka and the global Lymphatic Filariasis elimination effort. Dr. Weil emphasizes "The award is meaningful in the NTD research world (the only award that I know of for this type of work) and large enough to have an impact for our colleagues in Sri Lanka."

Recently Invited Guest Speakers of National & International Symposia



Keith F. Woeltje, MD, PhD

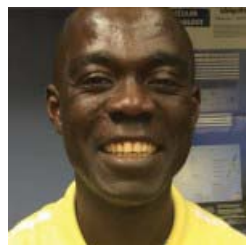
Keith F. Woeltje, MD, PhD, Professor of Medicine and Vice President, Chief Medical Information Officer (CMIO) at BJC Healthcare, recently presented, “Reconciling Abstracted to Electronic Quality Measures” at the March 2016 Healthcare Information and Management Systems Society (HIMSS). The HIMSS Annual Conference & Exhibition is the industry’s largest health IT educational program and exhibition center.

Makedonka Mitreva, PhD, Associate Professor of Medicine and Assistant Director, The Genome Institute, was invited to present at the Anthelmintics: From Discovery to Resistance II, San Diego, California. She had chaired a keynote lecture and session and held a workshop on “Helminth genomics - looking for biology in tera-bases of sequence data.”



Makedonka Mitreva, PhD

Dr. Mitreva also co-chaired with Ilan Youngster, MD, Boston Children’s Hospital, the symposium “Intestinal Microbiota in Health Disease at the 17th International Congress on Infectious Diseases, Hyderabad, India. Makedonka presented at the Scientific Program on “The Healthy Human Antibiotic Resistome: a multi- body habitat analysis.”



George B. Kyei, MBChB, PhD

George B. Kyei, MBChB, PhD, Assistant Professor of Medicine, received The American Society for Clinical Investigation (ASCI) “2016 Young Physician-Scientist Award” and will be recognized at the 2016 AAP/ASCI/APSA Joint Meeting and present his work on April 16, 2016, along with other awardees. Both Dr. Kyei and Dr. Dan Goldberg are invited to attend the ASCI President’s Reception on Friday, April 15. Dr. Kyei will receive a \$500 honorarium at the Joint Meeting, in addition to complementary registration.

SHEA 2016 Annual Spring Conference

Kevin Hsueh, MD, Instructor of Medicine, will be presenting at an oral abstract session at the annual spring conference for the The Society for Healthcare Epidemiology of America (SHEA), “Science Guiding Prevention,” in Atlanta, GA. Oral Abstract Session: Antibiotic and Test Stewardship, Talk Title: Effective Antibiotic Conservation by Emergency Antimicrobial Stewardship During a Drug Shortage, Session Date: Saturday, May 21, 2016 Session Time: 8:00 AM - 9:30 AM

Immunology of Infectious Diseases Journal Club

The Immunology of Infectious Diseases Journal Club (JC) is an exciting new forum to stimulate discussions on cutting-edge scientific papers on the topic with guest faculty participant and trainee involvement. Sessions are once each week throughout March and April. Although ending in April, there was overwhelming support for this program resulting in discussions for more clinically oriented JC in the fall and the basic science JC in the spring.

fellows’ corner

In December, Andrej Spec, MD, 3rd year fellow, attended the first “Histoplasmosis in the Americas and the Caribbean Meeting” in Paramaribo Suriname. Andrej is working to increase collaboration for a histoplasmosis study throughout South America and the Caribbean. The meeting objectives included equipping 80% of laboratories in the Americas and the Caribbean with the ability to rapidly diagnose Histoplasmosis by 2020 and to make antifungal medications available to all patients who need them.



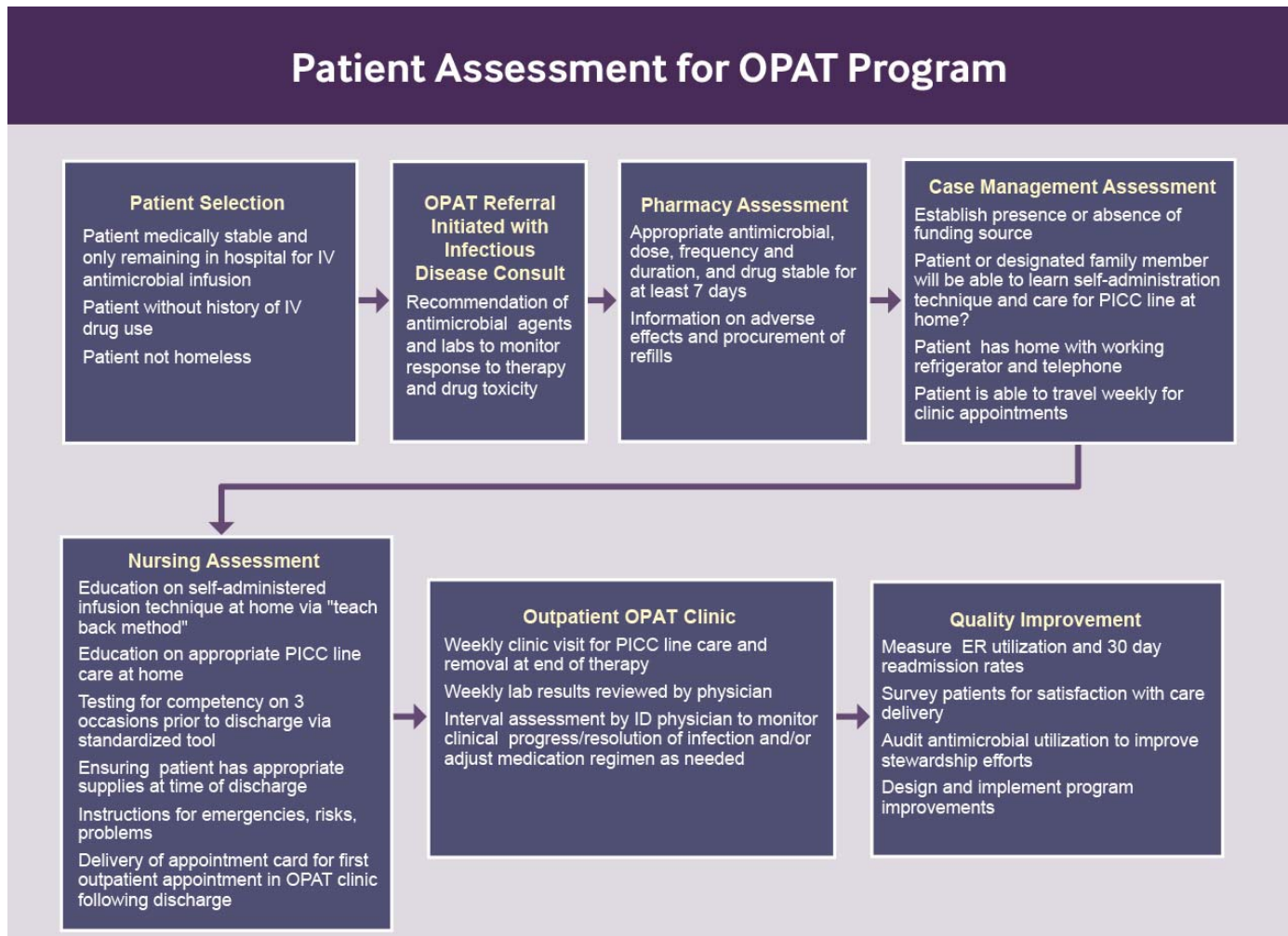
Andrej Spec, MD



Caline Matter, M.D., 2nd year fellow has just returned from a 2-month Global Health Policy elective at the World Health Organization headquarters in Geneva, Switzerland. Her work at the WHO primarily focused on the implementation of the “Global Action Plan on Antimicrobial Resistance”. More specifically, Caline is involved in the education and behavior change aspect to increase awareness of the healthcare workforce on the importance of antimicrobial resistance, and how it affects patient care day-to-day.

Caline Matter, MD

Fig 1



Adapted from Bhavan KP et al. (2015) Self-Administered Outpatient Antimicrobial Infusion by Uninsured Patients Discharged from a Safety-Net Hospital: A Propensity-Score-Balanced Retrospective Cohort Study. *PLOS Medicine*. Dec 15, 2015. DOI: 10.1371/journal.pmed.1001922



The full implementation of S-OPAT at Parkland saved over 27,000 hospital bed days in the first four years leading to \$40,000,000 savings for the hospital while freeing beds for acutely ill patients who need them. (Cerise, F (2015) Safety-Net Providers Can Be Leaders in Health Care Innovation. Organizational Structure. Harvard Business Review. Boston, MA: Harvard Business School Publishing).

Dr. Bhavan completed her Infectious Diseases Fellowship Training at Washington University School of Medicine in 2009.

*Kavita P. Bhavan, MD
Assistant Professor of Medicine
University of Texas - Southwestern
Dallas TX*

recent publications

MITREVA LAB

My research uses next-generation genomic and computational approaches to study neglected tropical diseases, ~ 85% of which are caused by helminthic infections that are highly endemic in the developing world.

Due to an increasing problem of drug resistance among almost all parasites species ranging from protists to worms, there is an urgent need to explore new drug targets and their inhibitors to provide new and effective parasitic therapeutics. We use 'omics' data (genome, transcriptome, proteome, interactome, etc.) to identify new targets and drugs that act differently from currently available anti-parasitic drugs. Building on our previous success (PMID: 23459584; PMID: 23935495), we recently explored known drug leads of human epigenetic enzymes as potential starting points to develop novel treatments for parasitic diseases, by screening hydroxamate- or benzamide-based small molecules KDAC inhibitors, against a range of parasitic species, including the pathogen of malaria, kinetoplastids and roundworms. The compounds showed nanomolar to sub-nanomolar potency against various parasites, and some selectivity was observed and will be explored for determining potential parasite-versus-host selectivity (PMID: 26402733).

We also study the nematode intestine functions as good anthelmintic targets since the intestine is continuous with the outside environment, making it easily accessible to anthelmintics for parasite control. However the development of new therapeutics is impeded by limited knowledge of nematode intestinal cell biology, therefore we developed a body of knowledge about the *Ascaris suum* genes constitutively or differentially expressed among tissues and between sexes (PMID: 24516681), directed determination of proteins located in intestinal lumen and apical intestinal membrane compartments (PMID: 25569475), derived molecular determinants archetypical to the nematode intestine (PMID: 2560983), and elucidate essential intestinal functions with potential for a broad control (PMID: 26501106).

We continue to provide important tools (e.g. PMID: 26000881; PMID: 25392426) and resources for future comparative genomic and molecular biological investigations as well as for biotechnological research toward new anthelmintics (e.g. PMID: 26026709), vaccines and diagnostic tests (e.g. PMID: 26472727). The common theme of the projects/publications outlined above is that we are attempting, through applied genomics, to translate basic into practical knowledge that may help to control or eliminate infectious diseases.



Associates of the Mitreva Lab

FELLOWS' RECENT PUBLICATIONS

George IA, Santos CA, Olsen MA, Bailey TC. (2016). Epidemiology and Outcomes of Nontuberculous Mycobacterial Infections in Solid Organ Transplant Recipients at a Midwestern Center. *Transplantation*. 2016 Mar 4 PMID: 26950719

Janowski AB, Michaels MG, Martin JM, Green MD. Piperacillin-Tazobactam Usage at a Tertiary Pediatric Hospital: An Antimicrobial Stewardship Review. *J Pediatric Infect Dis Soc*. 2015 Jul 13. pii: piv036.

Orvedahl A, Padhye A, Barton K, O' Bryan K, Baty J, Gruchala N, Niesen A, Margoni A, Srinivasan. (2016). Clinical Characterization of Children Presenting to the Hospital with Enterovirus D68 Infection During the 2014 Outbreak in St. Louis. *M. Pediatr Infect Dis J*. 2016 Jan 14 PMID: 26771663

Non L, Jeroudi A, Smith BT, Parsaei S. (2015). Bull's eye maculopathy in an HIV-positive patient receiving ritonavir. *Antivir Ther*. 2015 Nov 11. doi: 10.3851/IMP3007.

Rosen DA, Hilliard JK, Tiemann KM, Todd EM, Morley SC, Hunstad DA. 2016. *Klebsiella pneumoniae* FimK Promotes Virulence in Murine Pneumonia. *J. Infect. Dis*. 213: 649-658. PMC4721909

Spec A, Shindo Y, Burnham CA, Wilson S, Ablordeppey EA, Beiter ER, Chang K, Drewry AM, Hotchkiss RS. (2016). T cells from patients with *Candida* sepsis display a suppressive immunophenotype. *Crit Care*. 20(1):15.

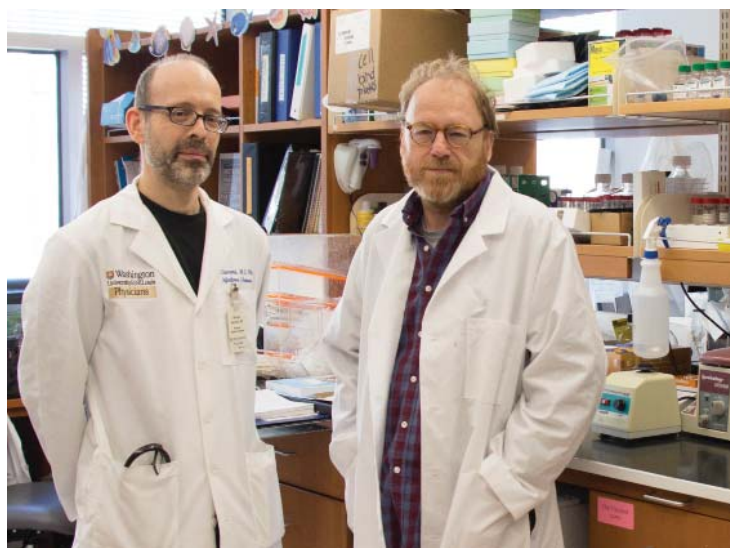
Spec A, Raval K, Powderly WG. End-Stage Liver Disease Is a Strong Predictor of Early Mortality in Cryptococcosis. (2015). *Open Forum Infect Dis*. 2015 Dec 15; 3(1)

Wylie KM, Blanco-Guzman M, Lawrence SJ, DiPersio JF, Storch GA. (2016). High-throughput sequencing of cerebrospinal fluid for diagnosis of chronic propionibacterium acnes meningitis in a patient with chronic myelogenous leukemia. *Transplant Infectious Diseases*. 18(1) 31 MAR 2016 doi: 10.1111/tid.12512

Scientists team up to fight Zika

Over the past seven months, two collaborating teams of scientists at Washington University School of Medicine – both focused on emerging infectious diseases – have redirected their efforts to concentrate on Zika virus. An outbreak of the mosquito-borne virus in the Americas has been linked to a startling surge of babies born with abnormally small heads and underdeveloped brains, a condition known as microcephaly, prompting new research aimed at answering critical questions about the virus.

The Washington University teams have logged countless hours in the laboratory – probing the Zika virus, and generating antibodies and viral proteins – laying the groundwork for the development of a precise diagnostic test for Zika as well as therapeutics and an eventual vaccine.



E. HOLLAND DURANDO

Washington University School of Medicine researchers Michael Diamond, MD, PhD, and David Fremont, PhD

“Our progress gives us good reason to believe that the work we put into studying related viruses has value and that we can pivot to an emerging infectious disease in a very rapid fashion,” said David Fremont, PhD, a professor of pathology and immunology, who is leading one of the teams. “It’s heartbreaking for the families who are adversely affected by Zika, but we’re hoping to help in this outbreak – that’s our major interest.”

Fremont has teamed again with collaborator Michael Diamond, MD, PhD, professor of medicine and leader of the other research team. Their enduring scientific collaboration – they’ve published nearly 40 papers together on other similar viruses – puts them out front in the fight against Zika.

Diamond first learned in late June 2015 that a Zika virus outbreak in South America might be linked to microcephaly. At the time, he was attending a scientific conference at the National Institutes of Health (NIH) focused on another infectious disease – chikungunya – that was moving through South America and the Caribbean. Between scientific sessions, Diamond’s colleagues from South America told of unusual complications that

appeared to be related to Zika, and in addition to microcephaly, Brazilian researchers at the conference also noted an increase in cases of Guillian-Barré.

Armed with that unsettling information, Diamond returned to Washington University and quickly mobilized his laboratory, shifting multiple researchers to work on Zika. “We’ve got a lot of students and postdoctoral fellows working right now to try to understand Zika virus infection and its potential complications,” said Diamond, whose earlier research on West Nile led to an investigational antibody therapy for that disease. The situation is particularly urgent because there’s no conclusive test, no treatment and no vaccine for Zika.

That’s where Diamond and Fremont hope to make pivotal contributions. They are experts in flaviviruses – a large family of viruses that includes West Nile, dengue, yellow fever and Zika. Together, their laboratories are working to understand how Zika is recognized and neutralized by the immune system – an endeavor critical to developing diagnostics for Zika, as well as therapeutics and a vaccine.

For starters, Diamond has created monoclonal antibodies – an engineered version of antibodies produced naturally by the immune system – that could be used to develop a specific diagnostic test for Zika. Because the virus is so similar to dengue and yellow fever, current diagnostic tests generate too many false positive results because they often pick up any of those infections, rather than just Zika.



E. HOLLAND DURANDO

Haiyan Zhao, PhD, a postdoctoral researcher in David Fremont’s laboratory, purifies the Zika surface protein that allows the virus to enter and infect cells of the body.

For his part, Fremont is generating multiple Zika proteins to understand exactly how antibodies bind to the virus to shut down infection. This information also is key to developing vaccines and treatments. One goal of Fremont's laboratory is deciphering the three-dimensional structure of Zika's protein-antibody complexes, using X-ray crystallography – an exercise that could offer clues to why the virus appears to be behaving differently in the current outbreak.

"We've made good progress in a short amount of time and are enthusiastic about where we can go from here with the tools that our groups are developing," Fremont said. Both Diamond and Fremont have applied for supplemental NIH funding for their Zika research and are planning to submit grants to support additional work. "It's very clear that the National Institute of Allergy and Infectious Diseases has prioritized Zika research and reached out to flavivirus experts to devote attention to the current outbreak," Fremont added.

This week, Diamond also will ship his monoclonal antibodies, developed from mice infected with Zika, to the NIH and the Centers for Disease Control and Prevention, where scientists will use those tools to study the virus. Fremont and Diamond also are working on identifying human monoclonal antibodies with their long-term collaborator, James Crowe Jr. at Vanderbilt University, and those, too, eventually will be shared with other researchers. In addition, Washington University's Office of Technology Management is licensing the mouse antibodies and recombinant proteins to companies interested in developing diagnostics and therapeutics.

Another avenue of research involves creating mouse models of Zika. "These are important for understanding disease pathogenesis and also for vaccines and therapeutics," said Diamond, director of the Division of Infectious Diseases and Vaccine Development in the Center for Human Immunology and Immunotherapy Programs. "We're very interested in therapeutics and are testing our antibodies now to see if any of them have therapeutic capacity."

In one model, Diamond developed mice that have slightly compromised immune systems. When sickened with Zika, the mice develop lethal disease, making them good models for evaluating vaccines and therapeutics. He's also working on another mouse model to test the theory that transmission of the virus from mother to baby causes microcephaly.

"We're very much interested in finding out whether the virus is crossing the placenta," Diamond said. Another theory Diamond and Fremont want to explore is whether pre-existing immunity to dengue in South America may make Zika infections more severe and account for birth defects and other complications. It's possible that antibodies against dengue can cross-react with Zika and make Zika infections worse, although there's no data yet to support this idea.

However, it is known that a prior infection with dengue puts people at risk of more severe disease if they are infected a second time with a slightly different subtype of the virus. "In dengue, if you're infected with one serotype of the virus and later you're infected with another serotype, you can get worse disease because there is cross-reactivity – something we call antibody-dependent enhancement," Diamond explained. "The question is, for people infected with dengue, can their antibodies cross-react and make Zika worse? And alternatively, does Zika make dengue worse? This is not the major issue now, but as the epidemic spreads, Zika could impact dengue. We don't know yet, but these are fundamental basic questions that we want to answer."

Dengue is estimated to be responsible for 390 million infections annually across the globe, according to the World Health Organization. In South America, 90 percent of people are infected with dengue by age 12, compared with a much smaller percentage of people in Africa, where dengue infections are more sporadic. Researchers have not seen similar complications from Zika infections in Africa. The researchers also acknowledge that microcephaly and Guillian-Barré may not be related to Zika virus at all. But the mouse models and other tools they have developed provide an opportunity to explore critical questions about the virus.

Diamond and Fremont said they are optimistic about their research and recognize that contributions from many scientists worldwide will be needed to make progress against Zika.

"The more people we have working on Zika, the more likely we'll be able to gain traction against the virus," Diamond said.



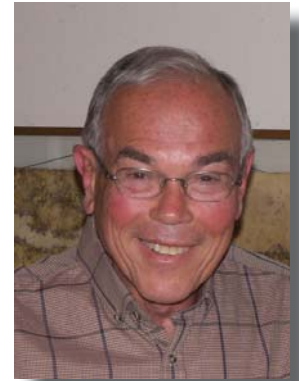
E. HOLLAND DURANDO

This flask holds Zika virus proteins that are being purified. Scientists at the School of Medicine are generating multiple Zika proteins to understand exactly how antibodies bind to the virus to shut down infection.

Adapted with permission, Caroline Arbanas, "Washington University Record",
February 4, 2016

LEADING *Together*

Our mission is to provide outstanding clinical care, conduct ground-breaking research, and train the next generation of leaders in academic medicine and infectious diseases. Dr. Gerald Medoff has been among the most influential leaders in the School of Medicine in the past half century, and the contributions of Dr. Medoff to the field of medicine are clearly reflected in the quality of the School and in the extraordinary individuals he has mentored. It is therefore only appropriate that we honor him by creating a fund that will provide support for young trainees and junior faculty in the Division, helping them transition their independent careers. Additionally, we rely heavily on outside donations to continue to recruit, train, and retain high quality staff to support the research, education, and clinical mission of the division.



Gerald Medoff, M.D.
Emeritus Professor of Medicine

We believe that you share our sense of pride in what we have been able to build, much of which is due to the leadership of Dr. Medoff. To make a gift online please visit our “LEADING *Together*” page to direct your gift to honor Dr. Medoff to the Division of Infectious Disease Fund (90991).

Thank you to our recent donors

Dr. Ernie Paul Barrette & Dr. Keiko Hirose
Dr. Alex Granok

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To make a gift to the Infectious Diseases Division, please contact Dan Korte, Division Administrator, Infectious Diseases Division, or mail your contribution. Checks can be made payable to :

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Please be sure to designate the School of Medicine and Infectious Diseases.