The parasite that causes river blindness infects about 37 million people in parts of Africa and Latin America, causing blindness and other major eye and skin diseases in about 5 million of them. A study from Washington University School of Medicine in St. Louis sheds light on the genetic makeup of the parasite, a step toward the goal of eradication.

The study appears Nov. 21 in the journal Nature Microbiology, along with a companion paper also focused on the genetics of the parasite.

“In West Africa, there are two separate strains of this parasite based on geographic areas — the savanna strain and the forest strain,” said senior author Makedonka Mitreva, an associate professor of medicine. “The severity of the disease caused by each strain is very different. The savanna strains are much more virulent and have been associated with higher rates of blindness. The forest strains cause a mild skin disease. That’s why we wanted to see how they differ genetically.”

The parasite is a roundworm called Onchocerca volvulus and is carried by black flies that thrive near rivers and streams. Large-scale efforts to control the disease have been underway for decades, with mass drug-administration programs beginning in the 1970’s in West Africa and in Central Africa and Central and South America in the early 1990’s. The drug ivermectin remains the first-line treatment to target the parasite. The drug’s discoverers were honored with the Nobel Prize in Physiology of Medicine just last year.

With this treatment success combined with insect-control programs to reduce black fly populations, the World Health Organization (WHO) has set a goal of eliminating the river blindness parasite by 2025. But after several decades of exposure to ivermectin, these parasites are beginning to show resistance. “We want to understand the origin of this resistance,” said Mitreva, who also is an associate professor of medicine and an assistant director of The McDonnell Genome Institute at Washington University. “Are these parasites evolving to survive the treatment, or are the surviving worms actually new strains that have been introduced due to migration of the black flies or of the parasite itself?”

To find out, Mitreva and her colleagues studied samples of the roundworms that have been stored since the early 1990’s, before large-scale ivermectin treatment programs began. They also are...
sequencing present-day strains for comparison. The current study reports data only from the historical samples.

“We worked hard to find samples of the parasite that had not been exposed to the drug because we needed to establish an ancestral baseline,” Mitreva said. “The current worm populations and their genomes have been strongly shaped by 30 years of massive drug-administration programs. So you can’t just collect worm samples from these parts of the world today and sequence them. We had to look back in time.”

The new study included 27 roundworm samples taken in the early 1990’s from four distinct regions — West African forest, West African savanna, Uganda and Ecuador. According to Mitreva, the Uganda strains, collected in central Africa, could not be classified as either the forest or savanna strain. Similarly, the strains from Ecuador, in South America, were also very different from the African strains. Mitreva and her colleagues showed gene movement between the savanna and forest strains, but only in one direction. Genes from the savanna strain have flowed into the forest strain but not vice versa. This is due to differences in climate and the versatility of the black flies that carry the parasite.

“Black flies in the savanna region are known to survive in the forest region,” Mitreva said. “They can fly longer distances and live in the forest environment. But the forest black flies can’t survive in the savanna.”

The new study also included the complete genome sequence of a type of bacteria living in the parasite that the worm relies on for survival. Past evidence suggested that the more bacteria living in the parasites, the more severe the infection. But Mitreva said the current study may provide clues to how the worm has become resistant to drug therapies. (Image: Thomas Unnasch)
## Awards & Announcements

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**Announcement...**

*The Infectious Diseases Division has a new website!*

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**Parasite - river blindness continued**

The current study does not support that observation. The investigators also are sequencing the same bacteria from present-day strains to see what, if anything, may have changed about them over the past three decades.

In general, Mitreva said, large-scale control efforts — including mass treatment with ivermectin and the use of insecticides to reduce black fly populations — have been very effective over the past 30 years. But since pockets of drug resistance are showing up, she said studies such as this one are important if the WHO’s goal of eliminating the parasite by 2025 is to be met.

*Story Source: Washington University in St. Louis. Original written by Julia Evangelou Strait.*
Jeffrey Henderson, received the Outstanding Faculty Mentor Award.

Several Department of Medicine faculty members recently were honored with Distinguished Faculty Awards for their wide-ranging achievements, dedication and talent. This year’s winners of the Samuel R. Goldstein Leadership Awards in Medical Student Education were also honored.

Thomas C. Bailey, MD, professor of medicine, was recently honored with a Distinguished Clinician Award for his wide-ranging achievements, dedication and talent. Dr. Bailey was nominated by his peers to recognize achievements in clinical care, community service, research and teaching.

Steven J. Lawrence, MD, associate professor of medicine, was honored with the Samuel R. Goldstein Leadership Award in Medical Student Education. The Goldstein awards recognize outstanding teaching and commitment to medical education. Recipients were selected by a committee of faculty members.

Jeffrey Henderson, MD, PhD, was among the faculty who received an Outstanding Faculty Mentor Award. This prestigious award is offered to only seven faculty mentors, with nominations received from departments across both campuses at Washington University.

“This is an opportunity for faculty and staff from all departments across both the Danforth and Medical Campus to come together in order to celebrate and highlight something we have in common, despite the differences in each of our disciplines: outstanding mentorship and support,” says Roger Wong, who is the Graduate Student Senate and Outstanding Faculty and Staff Awards committee chair and PhD student in public health sciences.

The awards ceremony is not only a time to celebrate those involved in mentoring and service, but it’s also a time for graduate students to learn more about mentors across campus that are outside their disciplines. “We typically don’t get the chance to hear about the contributions of faculty and staff members outside our departments,” Wong adds. “Through the awards ceremony, graduate students are able to formally express their gratitude to faculty and staff members who have significantly impacted their graduate experiences.
Diamond Named Gasser Professor of Medicine

Michael Diamond, MD, PhD, recognized internationally for his research involving Zika and related viruses, has been named the Herbert S. Gasser Professor of Medicine at Washington University School of Medicine in St. Louis.

A professor of medicine, of molecular microbiology, and of pathology and immunology, Diamond studies viruses — such as West Nile, Zika, dengue and chikungunya — that are growing in importance because they are causing more cases of disease or spreading to new parts of the world. He seeks to understand how they cause illness and interact with and evade the immune system.

“Mike is a world-renowned scientist working on the frontlines of emerging infectious diseases, especially mosquito-borne viruses,” said Victoria J. Fraser, MD, the Adolphus Busch Professor of Medicine and head of the Department of Medicine. “His work in the laboratory is aimed at understanding how these viruses lead to disease so that effective treatments can be developed.”

Diamond is known for leading some of the ground-breaking initial studies into Zika virus, including why and how it causes devastating neurological damage to the developing fetus. With colleagues, Diamond developed the first animal model of Zika infection during pregnancy, showed that the virus can infect the eye, identified protective antibodies against the virus, showed that Zika infection reduces the fertility of male mice and developed a Zika vaccine that is now in clinical trials. “Mike was one of the first to realize how important Zika was going to be,” said Herbert W. “Skip” Virgin IV, MD, PhD, the Mallinckrodt Professor and head of the Department of Pathology and Immunology. “His lab was able to quickly apply techniques and knowledge the team had developed studying other viruses, and in the process became one of the global leaders in Zika research.”

Diamond earned his bachelor’s degree in political science from Columbia University in 1985, followed by his medical and doctorate degrees from Harvard in 1994. After completing a research fellowship in molecular and cell biology at the University of California, Berkeley, Diamond moved across the bay to the University of California, San Francisco, where he completed his residency in internal medicine and a clinical fellowship in infectious disease. He returned to Berkeley to complete another research fellowship in infectious diseases in 2001, before joining the Washington University School of Medicine that year as a junior faculty member.

The Gasser Professorship is one of four chairs endowed by John F. McDonnell, vice chairman of the Board of Trustees, and the JSM Charitable Trust Foundation as part of the university’s BioMed 21 initiative launched in 2006. BioMed 21 aims to promote the translation of basic science discoveries into real-world clinical solutions. The chair was named for Herbert Gasser, a former head of the pharmacology department at the School of Medicine. Gasser won the Nobel Prize in physiology or medicine in 1944 jointly with his mentor Joseph Erlanger, a former head of the physiology department at the School of Medicine. Gasser and Erlanger studied the different functions of single nerve fibers. Their work led to advances in our knowledge of the mechanism of pain and of reflex action. Gasser used his prize money to fund further research into the subject.

Clay Semenkovich, MD, was the inaugural Gasser Professor. He is now the Irene E. and Michael M. Karl Professor of Endocrinology and Metabolism in Medicine.
Klein Elected Co-chair Gordon Research Conference

Robyn Klein, MD, PhD, professor of medicine, was elected co-chair of the next Gordon Research Conference on Neuro-Immune Interactions. The field of neuroimmunology is in a phase of rapid growth. The meeting will reflect the breadth of the field by hosting speakers and attendees with an interest in understanding neuro-immune interactions that maintain a healthy CNS during development and in adulthood as well as ones that participate in different pathophysiological conditions, such as autoimmune disease, stroke, neurodegenerative disorders, infection, brain/spinal cord injury, etc. These meetings aim to attract the top researchers in the field and promote dynamic discussions as well as a sustainable forum for members of the community to interact in the future.

Mitreva Serves as Symposium Co-chair of Scientific Committee

Makedonka Mitreva, PhD, MD, associate professor, was elected and recently served as co-chair of the scientific committee of the “Molecuraly Helminthology: An Integrated Approach” symposium which took place on the Cape Cod peninsula at the southern tip of Massachusetts March 19-22, 2017. The conference was designed not just to present the recent findings in the field of molecular helminthology but also to take advantage of the remarkable advances anticipated and occurring in the field.

Hilary E. Reno, MD, PhD in the News

Hilary Reno, MD, PhD has been interviewed by the media on several occasions recently about the increasing prevalence of syphilis in the St. Louis region and the alarming number of babies born with the sexually transmitted disease. The numbers are prompting city and county health officials to recommend that all pregnant women get screened for the disease late in pregnancy and at delivery.

The results are devastating, explained Dr. Hilary Reno, infectious disease expert at Washington University School of Medicine. Nearly 40 percent of exposed babies are stillborn, and other outcomes include blindness, deafness and bone deformities.

“The number is small, but the consequences of congenital syphilis are so severe, and the test is readily available and easy,” Reno said. “Any case of congenital syphilis should have been prevented.” Missouri law already requires syphilis testing with a blood test for all pregnant women in the first trimester. Because women who remain sexually active during pregnancy can still contract the disease, local health officials are recommending testing again during the third trimester and at delivery. Dr. Reno serves as medical consultants to the Division of STD Prevention at the CDC.

Original written by Michele Munz, health reporter for the St. Louis Post-Dispatch. Note: Content may be edited for style and length.
Mati Hlatshwayo, MD, 2nd year fellow, presented a poster entitled “Risks for COPD in HIV-infected Individuals Using Symptom-Based Scores and Spirometry” at the Pulmonary Research Day on March 9, 2017 hosted by Washington University School of Medicine Division of Pulmonary and Critical Care Medicine.

Pulmonary Research Day is a half-day conference developed to showcase and promote pulmonary and critical care research at Washington University and to foster collaboration, communication, and mentorship between the faculty and trainees from multiple departments and divisions on campus. The conference includes a keynote presentation by alumnus from the training program and shorter talks and a poster sessions to highlight current basic and clinical research activities.

Mati also had two abstracts accepted for presentation at the International AIDS Society (IAS) conference in Paris, France from July 23-26. They are: “Perceptions on Co-morbidities and Research Participation in HIV-positive Individuals” and “Risks for COPD in HIV-infected Individuals Using Symptom-based Scores and Spirometry”.

Jason P. Burnham, MD, 2nd year fellow, was among the finalists selected for the 2017 Society for Healthcare Epidemiology of America (SHEA) Epi Project Competition. The SHEA Epi Project Competition identifies bright and dedicated early investigators with a MPH, PhD or MD degree within 5 years of completion of training in the field of healthcare epidemiology research and are selected by a panel of reviewers from a highly competitive field of submissions prior to the SHEA conference. Jason delivered an oral presentation of “Readmissions and Mortality after Multidrug Resistant Infections: the impact of various definitions of multidrug resistance on outcomes” at the conference on March 30.

Congratulations to Jason for being among only five finalists selected by a panel of reviewers from a highly competitive field of submissions prior to the conference!

Jason received a Jonathan Freeman Scholarship at SHEA, and the abstract he presented won a top abstract award. It was titled “Readmissions with Multidrug Resistant Infections in Patients with Prior Multidrug Resistant Infection.”
Anucha Apisarnthanarak, MD, former ID fellow, is inducted in Hall of Fame, Royal College of Physicians in Thailand

Former ID fellow, 2001-2003, Anucha Apisarnthanarak, MD, was inducted into the Hall of Fame of the Royal College of Physicians of Thailand (RCPT) at their 2017 annual conference hosted in May in Bangkok, Thailand.

The Royal College of Physicians of Thailand (RCPT) is a national organization of internal medicine physicians endorsed by the Medical Council of Thailand. RCPT is an international society that includes physicians from all specialties such as neurology, cardiology, hematology, nephrology, etc and is the largest medical-specialty organization in Thailand. The award is based on three tracts, academic, teaching and service and is a career achievement award that recognizes the outstanding achievements of its members.

Dr. Apisarnthanarak’s award is on the academic track and based on lifetime academic contributions as well as global recognition.

Somnuek Sungkanuparph, MD, former ID fellow, receives Research Award 2017 of the Royal College of Physicians in Thailand

The Royal College of Physicians of Thailand (RCPT) is a national organization of internal medicine physicians endorsed by the Medical Council of Thailand. RCPT is the largest medical-specialty organization in Thailand. Each year RCPT has selected four internists in Thailand who have most distinguished publication of research and honored with the Research Award. Professor Somnuek Sungkanuparph has received the “Research Award 2017 of the Royal College of Physicians of Thailand” for his research in the field of HIV/AIDS.

Dr. Somuek completed a three year infectious diseases fellowship at Washington University School of Medicine 2002 – 2005. He is now Professor of Medicine, Division of Infectious Diseases at Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.
The faculty of the ID Division at Washington University School of Medicine are working on a variety of research endeavors from basic science to clinical practice. This newsletter will begin a new section showcasing recent publications and the author’s spin on why the publication is relevant and the significance in medicine today.

Below is a list of several publications, followed by the author’s comment.


**Peter U. Fischer, PhD:** A triple drug therapy using ivermectin, diethylcarbamazine (DEC) and albendazole (IDA) shows great promise to improve prospects for elimination of lymphatic filariasis by mass drug administration. In Africa, where onchocerciasis is endemic, this approach cannot be used because DEC can induce serious adverse events in individuals with Onchocerca volvulus microfilariae in the eye. In this viewpoint we discuss strategies how to use IDA in Africa for the elimination of lymphatic filariasis and how to design safe clinical trials of IDA in onchocerciasis patients.


**Peter U. Fischer, PhD:** Neorickettsia (formerly Ehrlichia) are helminth transmitted emerging pathogens of animals and humans. In this paper we describe for the first time the ultrastructure of these intracellular bacteria in adult trematode worms and use a Neorickettsia surface protein antibody for immunolocalization. We show that the endobacteria are localized at the host-parasite interface to enable horizontal transmission as well as in the eggs for vertical transmission.


**Daniel E. Goldberg, MD, PhD:** This paper reports the discovery of a new antimalarial compound that must be activated once it gets into the parasite. The malaria parasite can survive by mutating the gene for the activating enzyme. Then the compound gets in but can't kill the parasite. This is a new mechanism of antimalarial resistance and we show that it applies to other potent compounds as well.


**Jeffrey P. Henderson, MD, PhD:** A subset of patients are highly susceptible to urinary tract infections for reasons that defy standard clinical evaluation. Here we identified a series of human urinary metabolites that activate a human antibacterial protein to diminish bacterial growth. Marked individual differences in these metabolites may correspond to UTI susceptibility.

Dr. Kuhlmann: Leishmaniasis is a globally distributed protozoan infection exacerbated by the presence of a virus termed Leishmania RNA Virus, or LRV. We identified compounds that target LRV, serving as leads to develop adjunctive therapies that can alter disease outcomes as well as further probe the role of LRV in Leishmania pathogenesis.


Jennie H. Kwon, DO, MSCI: This prospective cohort study emphasizes the importance of appropriately selecting patients for Clostridium difficile testing, including a clinical evaluation for signs and symptoms consistent with *C. difficile* infection, as well as potential alternative causes of diarrhea.


Steven J. Lawrence, MD, MSc: The use of half-matched donors (haploidentical) for stem cell transplants is a rapidly emerging strategy that allows greater opportunity for patients with high-risk blood cancers such as leukemia to receive a potentially curative stem cell transplant. This study is the first published comprehensive look at infectious complications that occur with this kind of transplant.


Liang, MD: Central nervous system (CNS) infections, including meningitis, encephalitis, and brain abscess, are rare but time-sensitive emergency department (ED) diagnoses. This review covers pearls and pitfalls of diagnosis and management of CNS infections for emergency physicians.

Jennifer A. Philips, MD, PhD: This study found that a factor secreted by Mycobacterium tuberculosis, called EsxH, inhibits infected antigen presenting cells from being able to efficiently activate CD4+ T cells. These findings provide a molecular explanation for the failure of CD4+ T cells to promote sterilizing immunity to M. tuberculosis.


Makedonka Mitreva, PhD: This study compares genomes among fasciola isolates from North America and South America and surprisingly, the comparison led to the first ever discovery of an endobacteria Neorickettsia in this species. With immunohistochemical analysis we also identified putative routes for fluke-to-fluke and fluke-to-host transmission.


Makedonka Mitreva, PhD: The parasite that causes river blindness infects about 37 million people in parts of Africa and Latin America, causing blindness and other major eye and skin diseases in about 5 million of them. A study now sheds light on the genetic makeup of the parasite, a step toward the goal of eradication.


Margaert Olsen, PhD: We used nationally representative emergency department data to analyze the utilization of urinary catheters. We found that women catheterized in the ED were more likely to lack an appropriate indication for catheterization than men, suggesting over-utilization of urinary catheters in women. Interventions in the ED focused on women may be useful to decrease inappropriate urinary catheterization and thus prevent catheter-associated urinary tract infections.

Margaret Olsen, PhD: Thirty-day readmissions after hospitalization due to heart failure in Medicare patients is a quality measure used by the Centers for Medicare and Medicaid Services, with reduced hospital reimbursement for hospitals in the highest quartile of 30-day readmissions. We analyzed 30-days readmissions in all patients hospitalized for heart failure in three large states from 2007-2011. We found that 70% of the readmissions were not due to heart failure, but were due to other coexisting chronic and acute conditions. In this population over 11% of the readmissions were due to infection, most often bloodstream infection, pneumonia, urinary tract infection, and Clostridium difficile infection. Our results suggest that interventions to reduce readmission need to focus on other common conditions in the elderly, rather than solely on heart failure.


Rachel M. Presti, MD, PhD: This is a review of the major non-infectious pulmonary complications seen in HIV-infected patients on current antiretroviral therapy. The major complications are chronic obstructive pulmonary disease, lung cancer, and pulmonary hypertension. Several of the major mechanisms underlying the high prevalence of these conditions in HIV-infected patients are discussed, including high rates of smoking, the effect of HIV, antiretroviral therapy, opportunistic infections, which all lead to inflammation and oxidative stress resulting in lung damage.


Rupa Patel, MD, MPH, DTM&H: In this article, we describe the outcomes of HIV testing and pre-exposure prophylaxis (PrEP) linkage to care that involved the use of a geosocial networking (GSN) smartphone application as part of a community-based organization’s HIV prevention program for men who have sex with men (MSM) in Missouri. This program led to detection of previously undiagnosed HIV infection in African American MSM and demonstrated an ability to connect GSN application users to PrEP providers with successful PrEP initiation. Outreach through GSN applications can help facilitate PrEP uptake, contributing to a decrease in transmission among at-risk sexual networks.

Andrej Spec, MD: This paper demonstrates that Infectious Disease physicians reduce mortality in patients with cryptococcosis. They do this by appropriately but more aggressively working up patients for disseminated disease, using amphotericin and flucytosine more often and for longer, and by improved management of intracranial pressure.


David K. Warren, MD, MPH: This study examined how often hospitalized patients were tested for the presence of bacteria in their urine, and if other urine tests were done at the same time to look for evidence of infection, specifically white blood cells in the urine. Bacteria in the urine (bacteriuria) is common among older adults and people with urinary catheters in place. Bacteriuria by itself does not mean that a patient has a urinary tract infection. In a previous study done at Barnes-Jewish Hospital, over 8% of patients without any clinical evidence of a urinary tract infection had bacteriuria at the time of admission. The detection of asymptomatic bacteruria can lead to unnecessary antibiotic treatment, increasing the cost of care and increasing the risk of antibiotic resistant bacteria. Our study found that one in five patients who had a urine culture done at Barnes-Jewish Hospital, did not have any additional testing to look for evidence of infection. These patients were more like to be in the ICU, be in the hospital for more than one day, and have a urinary catheter in place at the time of testing. Results from this study are being used to improve clinician practice and prevent unnecessary antibiotic treatment.

continuing medical education

Infectious Diseases Society of St. Louis presents

Current Conundrums in STI Management: Syphilis, LGV, and More

Bradley Stoner, MD, PhD
Medical Director, St. Louis STD/HIV Prevention Training Center
Membership Secretary, International Union Against Sexually Transmitted Infections (IUSTI)
Associate Professor of Anthropology and Medicine, Washington University in St. Louis

Thursday, June 22, 2017
6:00 pm Reception (meet & greet) 7:00 pm Meeting Commences
Engineer’s Club of St. Louis 4359 Lindell Blvd. St. Louis, MO 63108

register at: www.wustl.edu/etransact scroll to Infectious Diseases Society and Event Registration
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.

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. Leon Robison III
Susan Wightman
In Memory of Sharon Maxwell

Your Donations Are Greatly Appreciated!

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

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Infectious Diseases Division
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