Researchers have found that an antiviral compound may protect the brain from invading pathogens.

Studying West Nile virus infection in mice, scientists at Washington University School of Medicine in St. Louis showed that interferon-lambda tightens the blood-brain barrier, making it harder for the virus to invade the brain.

The blood-brain barrier is a natural defense system that is supposed to keep pathogens out of the brain. Sometimes, however, bacteria or viruses circulating in the blood slip past the blood-brain barrier, turning routine illnesses into serious infections.

Interferon-lambda is produced naturally in the body in response to infection, but the new research suggests that larger amounts of the antiviral compound may tighten the blood-brain barrier against pathogens or possibly even faulty immune cells that can attack the brain and cause conditions such as multiple sclerosis.

By blocking interferon-lambda’s receptors in the brain, it may be possible one day to open the barrier to chemotherapies to treat specific diseases in the brain, such as tumors. Such tumors now are not optimally treated with chemotherapy drugs because the drugs can’t cross the blood-brain barrier.

The findings are available online in Science Translational Medicine.

“We have identified a new antiviral function of interferon-lambda that doesn’t involve directly attacking a virus but stems viral invasion into the brain,” said co-senior author Robyn Klein, MD, PhD, professor of medicine. “This suggests the possibility of multiple new applications. We’re testing one of these right now, conducting studies in mice to see if interferon-lambda can help prevent brain inflammation in a mouse model of multiple sclerosis.”

Other forms of interferon have shown potential for influencing the blood-brain barrier, but interferon-lambda may have significantly fewer side effects.
Infections with West Nile virus occur globally. No treatments exist for the virus, which crosses the blood-brain barrier in an estimated 1 percent of infected people, causing a debilitating neurological condition that can be fatal.

Klein and co-senior author Michael Diamond, MD, PhD, professor of medicine, looked closely at West Nile virus infections in mice to learn more about how viruses cross the blood-brain barrier. This barrier typically keeps large molecules, such as immune cells, drugs and pathogens, out of the brain while letting in essential nutrients such as glucose.

In earlier research, Klein showed that West Nile virus can open the blood-brain barrier to enter the central nervous system, but that the barrier usually quickly closes, preventing immune molecules from following to attack the virus.

In the new study, the scientists studied mice that lacked the interferon-lambda receptor. Compared with normal mice, the mice without the receptor had higher levels of West Nile virus in the brain. The researchers found the blood-brain barrier was much more permeable to the virus in these mice, suggesting that loss of the receptor through which interferon-lambda acts had loosened the barrier.

The scientists then gave normal mice West Nile virus along with interferon-lambda. The mice received the antiviral compound at the start of the infection and two and four days later. Typically less than 20 percent of normal mice survive such a high dose of the virus, but survival rates rose to more than 40 percent after treatment with interferon-lambda.

“Viruses are most dangerous when they enter the brain,” said Diamond. “Compared with untreated mice, we found significantly lower concentrations of the virus in the brain among mice treated with interferon-lambda.”

If further studies of interferon-lambda prove fruitful in stemming the spread of viruses to the brain, a major hurdle remains. By the time symptoms of viral infections are serious, the virus is already in the brain. This reality suggests earlier diagnosis is critical. But, the researchers note, interferon-lambda may be a better way to influence what gets into the brain than other forms of interferon, which are associated with significant side effects such as fever, chills and fatigue.

“Interferon-lambda has significantly fewer receptors in the body, which may mean using it as a treatment is likely to have fewer side effects,” Diamond said. “It’s also possible that interferon-lambda may influence other protective barriers in the body, such as those in the skin and the gut, an area of research my laboratory is investigating.”


In 1988 as a brand new medicine intern at Barnes, I learned from the best. Vicky Fraser, Clay Dunagan and Tom Bailey were first year ID fellows. Matt German, Pablo Tebas and Sunil Sultan were my ID fellows in arms starting in 1992. From 1993 to 1997 in the excellent lab of Dan Goldberg, I made some observations about the formation of malaria pigment called ‘hemozoin’ and its inhibition by the quinolines. Lois Bauer Sullivan, MD and I left for Baltimore in late 1997, where I joined the Molecular Microbiology and Immunology department at Johns Hopkins Bloomberg School of Public Health where I have remained. Lois continues to be a sharp, successful pediatrician in private practice. We have raised three boys with the first, Luke, starting at the Naval Academy this year (July 1, 2015), while his brothers Ben and Ronan are both in high school where they run cross country.

I am currently Professor in the School of Public Health, working on malaria diagnostics and drugs as well as malaria epidemiology in Bangladesh and Zambia as part of the Johns Hopkins Malaria Research Institute. I attend on the ID consult service at JHU Bayview Hospital a month each year as well as teach five separate courses on malaria and parasitology. I am glad to pass along the Infectious Diseases pearls learned from such a great Washington University ID Division in the 90’s.

Baltimore and St. Louis are similar in many ways with baseball, football, and ethnic neighborhoods amid great medical centers. While I have moved on to the Orioles and Ravens with our boys, Lois remains a Cardinals fan which as of this writing is the best team.
### RECENT AWARDS

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<td>Jacco Boon, Ph.D.</td>
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### special recognition

The Executive Council of Washington University Medical Center Alumni Association voted to name a Distinguished Alumni Scholarship in honor of Thomas C. Bailey, M.D. The Alumni Scholarships are four-year, full-tuition scholarships named for alumni faculty members who are especially esteemed as colleagues and outstanding citizens of the School of Medicine. These merit-based scholarships are a significant factor in attracting students of exceptional academic and personal achievement.

### congratulations...

On August 27, 2015, the School of Medicine hosted the installation of Dr. Daniel E. Goldberg, M.D., Ph.D. as the David M. and Paula L. Kipnis Distinguished Professor. The installation preceded a talk by Dr. Goldberg, “Stalking the Malaria Parasite, a Fascinating Foe”. A reception followed at the Eric P. Newman Education Center.

Daniel E. Goldberg, M.D., Ph.D.  
David M. and Paula L. Kipnis Distinguished Professor  
Department of Medicine  
Co-director, Infectious Diseases Division
Jennifer A. Philips, M.D., Ph.D., Assistant Professor of Medicine

I grew up in Milwaukee, WI and moved east for college to attend Columbia University. I was enticed to leave NYC for northern California, where I pursued my medical and graduate training at the University of California, San Francisco. My graduate mentor, Ira Herskowitz, imparted a strong appreciation for the power of model systems and genetic approaches to answer basic cell biological questions, providing a foundation that continues to inform my work. I moved back to the east coast for residency training in Internal Medicine at Brigham and Women’s Hospital, followed by an Infectious Diseases fellowship in the Partner’s program (Brigham and Women’s Hospital and Massachusetts General Hospital joint program). As an ID fellow, I met my husband, a neurology resident at the time, when I consulted on patients with cryptococcal meningitis and Lemierre’s disease.

After my clinical training in infectious disease, as a post-doctoral fellow in the laboratories of Norbert Perrimon and Eric Rubin, I turned my focus to tuberculosis. I was motivated by the disease’s medical importance, enormous gaps in the understanding of the interaction between the bacteria and host macrophages, and the fact that novel technologies offered new ways to fill those gaps. My contribution towards understanding TB pathogenesis started with genome-wide RNAi screens in Drosophila using Mycobacterium fortuitum, a distant relative of Mtb. After completing my fellowship, I worked for two years as a Translational Medicine Expert in Infectious Diseases at Novartis Institutes for BioMedical Research in Cambridge, MA on early stage anti-microbials and anti-virals. There I came to appreciate the enormous efforts that are required to truly translate basic discoveries into advances in human health. After Novartis, I started my own laboratory at NYU School of Medicine continuing the work I had started as a post-doctoral fellow and attended on the Infectious Disease consult service at Bellevue Hospital. I also had two lovely children, Ellison, now 5 years old, and Satyana, 3 years old.

I was pleased to join the Infectious Disease Division at Washington University School of Medicine in July, where I am continuing my work on Mtb pathogenesis. Mtb disrupts anti-microbial pathways of macrophages, cells that normally kill bacteria. It establishes persistent infection despite inducing robust antigen specific T cell responses. How Mtb undermines these host immune functions is the focus of our work. We are identifying and characterizing host-pathogen interactions that provide mechanistic insight into how Mtb alters cellular trafficking, antigen presentation, and cytokine responses of macrophages and dendritic cells. In studying the molecular mechanisms by which Mtb sabotages cellular functions, we hope to make fundamental observations that ultimately enable better therapeutics and vaccines for Mtb.

Michael J. Durkin, M.D., Instructor of Medicine

Mike grew up in suburban Chicago. After receiving his MD degree from Medical College of Wisconsin, Mike served his residency in Internal Medicine at Wash U/BJH. While there, Mike participated in clinical research with Bernard Camins, M.D. He was enrolled in the Clinical Scientist Training and Research (CSTAR) program, received research funding through a Mentors in Medicine research grant, and won the Karl-Flance firm teaching award. Following residency Mike was hired by Washington University as faculty in the division of hospital medicine and worked as a hospitalist at Barnes. During this year, Mike’s sweetheart Julie Ruppel was completing her orthodontic residency program at St. Louis University. Forest Park will always have a special significance for both of them, as Mike proposed to Julie while kayaking in the Grand Basin. Luckily the kayak didn’t tip over.

In June 2012 Michael and Julie were married in Chicago. They then moved to Durham, NC. Mike had a fellowship in Infectious Disease at Duke University and Julie worked in private practice in Cary, NC. While there, Mike worked with the Dan Sexton and Deverick Anderson in the Duke Infection Control Outreach Network and enrolled in MPH classes at the University of North Carolina at Chapel Hill.

Mike and Julie plan on buying their first home in University City. In their free time, Mike and Julie like to travel, try new cuisines, and hike with their 1 year-old puppy. Mike also enjoys collecting regional/local liquors when travelling - Julie thinks that most are disgusting. In the last year, they have been to the US and British Virgin Islands, Disney World, New York City, and Ocracoke Island, NC.

Mike’s current research interests include infection control, antimicrobial stewardship, and the microbiome.
welcome to our 2015 fellows

Jason Burnahm, M.D.
I am originally from Houston, Texas. I graduated from the University of Texas Medical Branch (UTMB) School of Medicine in Galveston. I completed a residency program at Washington University School of Medicine. My lovely wife is a dermatologist and we have a cute, but shy dog.

Why did you chose an ID fellowship?
I chose ID fellowship because I have wanted to study infections since the first time I read about smallpox in fourth grade. I chose Wash U for fellowship training because I loved working here so much as a resident.

Batool Eldos, M.D.
I’m from Jordan and graduated from Jordan University of Science and Technology (JUST) in Jordan in 2007 and completed Family Medicine residency in JUST in as well in 2012. I’m married and have an 18 month old daughter named Mariam.

Why did you chose an ID fellowship?
I have chosen ID fellowship because ID is not quite well established in Jordan and would like to apply the knowledge and skills that I will learn during my fellowship to contribute in advancing the medical care in Jordan. I have chosen WashU for it’s reputation as a prominent school, ranking high nationally and internationally with great research opportunities. I know I will get great exposure to many different infections that will help enhance my career.

Mati Hlatshwayo, M.D.
I am originally from Harare in Zimbabwe. I received my medical school training from the Cleveland Clinic Lerner College of Medicine (of Case Western Reserve University), and I completed my residency at University Hospitals Case Medical Center. During my time in Cleveland I was awarded the Richard J. Fasenmayer award for HIV research, with a stipend of $25,000. As a graduating senior resident, I was also awarded the Harold C. Klein M.D. Humane Practice Award. I will be getting married in September! My fiancé is doing his pediatric residency here in St. Louis.

Why did you chose an ID fellowship?
Selecting this fellowship program was a no-brainer for me. It provides strong training in all areas of Infectious Disease, and I was particularly struck by how invested the department is in supporting fellows as they develop their careers. As far as the future goes, I would like to pursue a career in HIV having become drawn to the multifaceted care required for HIV positive patients, and in seeing the potential there lies in translational research and public health endeavors going forward. Having said that, I am really excited for the busy year ahead and seeing what areas in infectious diseases I will naturally gravitate towards!

Brett Jagger, M.D., Ph.D.
I was born and raised in LaPorte, Indiana. I attended the Indiana University School of Medicine in Indianapolis, IN. During medical school I went to Bethesda, MD as a Howard Hughes Medical Institute research scholar to do basic virology research, investigating influenza viral pathogenesis and evolution. Subsequently I earned a PhD from the University of Cambridge through the NIH Oxford-Cambridge Scholars Program, describing a novel influenza viral protein and its impact on influenza disease. I matched into the Physician Scientist Training Program here at Barnes-Jewish Hospital, where I trained in internal medicine. I am married to my wonderful wife Rebecca and we have two daughters, Elizabeth and Margaret.

Why did you chose an ID fellowship?
From my undergraduate days in microbiology class, I have been fascinated by the microbial world, and this interest has only grown with each stage of my training. In comparing with other institutions of comparable academic stature, WashU is more collegial and supportive for those pursuing an academic career path. Just as important, the Division has a track record of training and supporting physician-scientists with strong mentorship and career development. These factors are the perfect complement for the strong clinical training environment and excellent case mix.

Darrell McBride, D.O.
I am originally from Baltimore, Maryland. I graduated from Lake Erie College of Osteopathic Medicine in Erie, PA and completed residency at MetroHealth Medical Center/Case Western in Cleveland, OH.

Why did you chose an ID fellowship?
My primary focus will center around epidemiological and/or clinically based studies regarding domestic HIV populations. I chose Washington University because of its many resources and funding regarding research, its varied patient population/myriad of endemic disease processes, and the structure of its ID program.
fellows’ corner

awards

Abigail Carlson, M.D., and Mike Durkin, M.D. (instructor medicine now) received the Jonathan Freeman Scholarship Award from SHEA Spring 2015 meeting: Science Guiding Prevention in Orlando, FL. The Jonathan Freeman Scholarship was established by SHEA to promote the training of outstanding infectious disease fellows who demonstrate interest in the field of healthcare epidemiology.

Abigail Carlson, M.D., received the Outstanding Citizen Award from Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI). This award is given each year to top Clinical Research Training Center scholars who are identified by the Directors as the most engaged, respectful, and always willing to provide support and constructive feedback to their peers and the program.

SHEA 2015

Abigail Carlson, M.D., presented a poster at SHEA 2015 conference titled: Urine Culturing Practices in a Large Academic Medical Center.

Jennie Kwon, D.O., presented a poster at the SHEA 2015 conference titled: Correlation of Clostridium difficile Enzyme Immunoassay Results with Clinical Signs and Symptoms of Clostridium difficile infection.

ISHAM 2015

Andrej Spec, M.D., presented a poster, End Stage Liver Disease is a Strong Predictor of Mortality in Cryptococcosis, at the 19th International Society of Human and Animal Mycology (ISHAM 2015) Congress in Melbourne, Australia

CINCH 2015

Andrej Spec, M.D., 3rd year fellow in training, was selected to serve as a Substudy Steering Committee Member of Cryptococcus Infection Network Cohort Study for non-HIV patients (CINCH), sponsored by the NIH/NIAID.

ID WEEK 2015

Congratulations to Jennie Kwon, D.O., 3rd year fellow in training and Cynthia Monaco, M.D., Instructor of Medicine, for receiving IDWEEK Trainee Travel Grants to help defray the costs of attending the IDSA 2015 Conference.
IDWeek 2015 presenters & posters

The Vincent T. Andriole ID Board Review Course- October 6, 2015
Philip Budge, MD – Assistant Professor of Medicine
Presentation Title: Parasitic Infectious Disease (40 minutes)

IDWeek Oral Presentations

Ige George, MD, 3rd year fellow
Session Date: Thursday, October 8, 2015
Presentation Time: 3:00 PM-3:15 PM
Presentation Title: Epidemiology of Cryptococcal Disease (CD) and Cryptococcal Meningitis (CM) in a Large Retrospective Cohort of Solid Organ Transplant (SOT) recipients

Kerry Bommarito, PhD, Instructor in Medicine
Session Date: Friday, October 9, 2015
Presentation Time: 11:42 AM-11:54 AM
Presentation Title: The Incidence of Postpartum Infections at Delivery, Post-Discharge Emergency Department (ED) Visit, and Six Week Readmission

IDWeek Poster Presentations

October 8, 2015  12:30 PM - 2:00 PM

Hitoshi Honda, MD and David Warren, MD  Assoc. Prof. of Medicine
Factors associated with treatment mismatch and mortality in geriatric patients with bacteremia: A target for antimicrobial stewardship #186

Stephen Liang, MD Asst. Prof. of Medicine
Presentation Title: Current management of cardiac implantable electronic device infections: results of an Emerging Infections Network survey #302

October 9, 2015  12:30 PM - 2:00 PM

Cynthia Monaco, MD, PhD  former 3rd year fellow (Inst in Medicine)
Expanded Enteric Virome and Altered Bacterial Microbiome in AIDS #754

Carlos Santos, MD – Asst. Prof. in Medicine
Epidemiology of Bloodstream Infections in a Multicenter Retrospective Cohort of Liver Transplant Recipients #1190

Jennie H. Kwon, DO 3rd year fellow
Autologous fecal microbiota transplantation as a strategy to prevent colonization with multi-drug resistant organisms following antimicrobial therapy #762

Andre Spec, MD 3rd year fellow
Predicting Candida Species with Decreased Fluconazole Susceptibility in Candida Blood Stream Infections #829

Jennie H. Kwon, DO 3rd year fellow
The Food of Hospitalized Patients as a Risk Factor for Acquisition of Clostridium difficile: A Modeling Study #938

Jennie Kwon, DO 3rd year fellow
The Changing Epidemiology of Cryptococcal Disease – a Retrospective Population-Based Study #1686

Lemuel Non, MD 2nd year fellow
Nap1 positivity predicts metronidazole failure in a cohort of patients with Non-severe Clostridium difficile-associated diarrhea #960

Kathleen M. McMullen, MPH, David Warren, MD, Associate Professor of Medicine
Impact of a Pulsed Xenon Ultraviolet Light (PX-UV) Light Room Disinfection System on Clostridium difficile Rates #1714

October 10, 2015  12:30 PM - 2:00 PM

Alexandra Dretler, MD, chief resident, Stephen Liang, MD Instructor in Medicine
Treatment patterns for sexually transmitted infections among superusers of an urban emergency department #1554

Sam Reinhardt, MD – resident in medicine, Steven Lawrence, MD – Assistant Professor of Medicine
Chronic Renal Disease is an Independent Risk Factor for Mortality in Older Adults with Pneumococcal Disease #1592

Ige George, MD – 3rd year fellow
The Changing Epidemiology of Cryptococcal Disease – a Retrospective Population-Based Study #1686

Gerome Escota, MD  Instructor in Medicine
Lower CD4 Cell Count is Independently Associated with Unsuccessful Physical Aging Among HIV-infected Persons #1665


Infectious Diseases Division Newsletter  September/2015 • 7
The Infectious Diseases Outpatient Practice left its original home at 4570 Children's Place, known as the Storz Building, after nearly 25 years. The practice, along with the AIDS Clinical Trials Unit/ID Clinical Research Unit (ACTU/ID-CRU), have recently moved to a new facility at 620 S. Taylor Ave, St. Louis MO.

The new building is known as the Taylor Avenue Building Extension, or TABX for short, just south of the Taylor Avenue Building which houses the Institute of Public Health.

Patients are now welcomed to bright, spacious and modern waiting areas, expanded consult rooms and exam rooms with computer technology in each exam room. The practice retained in-office phlebotomy services but with Barnes Jewish Laboratories being the new lab provider. Complimentary parking is convenient in the lot adjacent to the building and the location is less than two blocks from the Metrolink.

The ID clinic occupies the entire first floor with 16 exam rooms and plenty of space for residents, fellows and pharmacy students as well as case management and clinic administration. There are large break rooms provided for the staff and faculty. The second floor is shared between the ACTU/ID-CRU, Neurology, and Weight Management. The ACTU/ID-CRU has five exam rooms, a consult room, a lab processing area with hoods, an outpatient investigational pharmacy, and dedicated study monitor space. There is also a separate nutrition station in the clinical research unit to provide snacks for fasting research participants.

The offices are equipped with the latest technology in ergonomic design. The modern conference room is divided in two by a movable partition with each side equipped with large screen TV monitors and table top receptacles with USB & AC power.

Demolition of the Storz Building is complete. Washington University School of Medicine and BJC HealthCare are busy constructing a 14 story office building on the site. The new building, on Children’s Place, will provide about 40,000 square feet of space per floor and will house offices for the dean and administrative staff and corporate offices for BJC HealthCare. It also will include a WUSM/BJH joint security center, a bookstore and café, and conference rooms.

Before the Storz building opened in 1946, the site was used to store coal needed to fuel the nearby power plant. Coal was delivered by rail to the plant, which now uses natural gas to produce electricity. In addition to the Infectious Diseases clinical and research location, the building also housed Weight Management, Geriatric Medicine, and Endocrine/Metabolism/Lipid Research. The new building is expected to be completed in 2017.

Congratulations...

The Infectious Diseases Division recognizes the following individuals celebrating length of service awards at Washington University School of Medicine.

Susan Wightman, RN, BSN (30 years)
Debra DeMarco, BSN, ACRN (20 years)
Sondra Sieler, BA (20 years)
Tina Robinson (15 years)
**IDSA Reunion 2015**

**Date:** Friday, October 9, 2014  
**Time:** 7:00 p.m. - 10:00 p.m.  
**Location:** Marriott Marquis San Diego Marina  
(adjacent to the convention center)  
**Room:** Catalina Room  
4th Floor, South Tower

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**Washington University School of Medicine**

**IDSA Reunion**

**2015**

RSVP to Alicia Cicerelli at acicerel@dom.wustl.edu

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**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.

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).

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**Thank you to our recent donors**

Dr. Leon R. Robison III and Mrs. Ann R. Robison  
Dr. Mitsuo Kitahara

To donate by mail, simply send your tax-deductible contribution payable to Washington University Infectious Diseases to the address below.

Dan Korte, Division Administrator, Infectious Diseases Division  
Campus Box 8051, 4523 Clayton Ave., St. Louis MO 63110  
phone: 314-454-8354    email: dkorte@dom.wustl.edu

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