BOSTON UNIVERSITY

/NEIDL National Emerging Infectious Diseases Laboratories

# Annual Report
# Fiscal Year 2016

*Photo Credit Paul Duprex*

# Table of contents

**Boston University** National Emerging Infectious Diseases Laboratories

620 Albany Street
Boston, Massachusetts 02118
bu.edu/neidl

September 1, 2016

# Letter from the Director

Events during this past year continue to remind us of the prominent role that emerging infectious diseases plays in the world's public health arena. At the time of this writing, there has been an unprecedented yellow fever outbreak in Angola and the Congo, a Lassa fever outbreak in Nigeria. Ebola virus disease, which had been declared over in the west African countries of Liberia, Sierra Leone and Guinea, continued to surprise us with a new cluster of cases, which as of this writing appear to be sexually transmitted from a person who survived the disease and was declared virus free over 500 days earlier. These viruses continue to amaze, and we learn new properties of viral infection with each outbreak. These events underscore the need for research into the pathogens that cause infectious diseases. We are humbled by how little we really know. This has also been emphasized with the spread of the Zika virus. This virus marched quietly, with little concern, around the globe, because it was thought to cause only mild disease in 20% of infected individuals. However, it has now been linked to birth defects, including microcephaly, is known to cause Guillan-Barre syndrome in adults, and may have other neurologic sequela. This is a call to action for scientists in the NEIDL. As we continued to try to help with the response to the Ebola virus outbreak in Sierra Leone, we also looked at the NEIDL as a resource to develop a Zika program, and engage scientists from around the university, many who have never done experiments with viruses, to rapidly connect with NEIDL investigators and begin to do so. Zika virus reminds us of how interdisciplinary research into emerging viruses needs to be, and why the NEIDL must reach out and link with the broader BU faculty. An expanding Zika program is in place and we look forward to contributing to our understanding the virus, what it does in a human host, and how this results in the diverse manifestations of the disease. The rapid spread of the Zika virus to the western hemisphere and then to the US also reminds us that, in a globalized society, infectious diseases knows no borders.

Reflecting back on this past year, we have much to be proud of, and I am confident the NEIDL will continue to build its faculty and staff to fulfil its missions. This annual report reflects on those successes. Scientifically, our faculty continue to be highly successful and are recognized nationally and internationally because of the quality of their research programs. We have added three new investigators to the NEIDL faculty. These scientists have diverse research interests, and come from 3 schools of the university. These include:

1. Rachel Fearns, Ph.D., Associate Professor of Microbiology in the School of Medicine. Rachel is an expert virologist specializing in respiratory syncytial virus (RSV), a virus that causes respiratory disease in infants and is one of the leading causes of hospitalization of young children. Rachel is also developing a collaborative program with another member of the NEIDL faculty, Elke Mühlberger.
2. John Samuelson, M.D., Ph.D. Professor of Molecular and Cell Biology, Goldman School of Dental Medicine. John is an expert in parasitic diseases and the protozoan pathogens that cause these diseases. One of these, Cryptosporidium, has been identified by the World Health Organization as the second most important cause of severe diarrhea in children in developing countries.
3. Horacio Frydman, Ph.D., Associate Professor of Biology, College of Arts and Sciences. Horacio, like other faculty in the NEIDL, focuses on host-microbial interactions, but the ones he studies are quite unique. Horacio is an expert in the parasitic bacterium *Wolbachia*, an organism that infects many arthropods, including insects such as mosquitoes. He is interested in using *Wolbachia* to understand what is needed for mosquitoes to transmit viruses such as Zika virus.

During this year, we also have begun recruiting for new faculty, and have had a number of candidates visit the NEIDL, give seminars and meet with the faculty and trainees. We anticipate that these activities will continue during the coming year, and look forward to successfully recruiting outstanding new scientists to Boston University

and the NEIDL. NEIDL investigators were supported by over $21 million in funding for their work during FY16, by any measure a demonstration of their success in their respective fields. Nevertheless, colleagues regularly ask me (and other NEIDL faculty) “when will you be open”. This, of course, is in response to ongoing permitting process for operating the NEIDL’s BSL-4 laboratories, necessary for the facility to be considered “fully open”, although we have been conducting research in the BSL-2 and BSL-3 laboratories for some time. We are well into the process for permitting with both the Centers for Disease Control (CDC) and our local regulator, Boston Public Health Commission (BPHC). We look forward to meeting the requirements of both the CDC and BPHC so that we can undertake research into pathogens that require BSL-4 containment.

We have had our challenges this year as well. In March, we had a major incident with our building automation system, resulting in airflow anomalies in our BSL-3 containment laboratories. In keeping with our culture of safety and transparency, we reported the system failure immediately, voluntarily suspended BSL-3 work (even though the system was quickly brought back on line and has continued to function normally and did not affect the integrity of the primary containment system - the biosafety cabinets in which all work with a pathogen is conducted), and did a complete forensic investigation.

We now know what happened, and have put a number of changes in place to prevent these occurrences from happening again. We also put new operational and facilities leadership in place to make sure we are well prepared for the future. We also informed the public of the event, once we had an understanding of what had happened, and also have now been keeping our Community Liaison Committee informed. Even so, we have not yet resumed BSL-3 work, and will not do so until both CDC and BPHC are comfortable with our systems, procedures and supervision. We also shared the engineering report with the NIH and other laboratories that use a similar building automation system as well.

Despite this setback, we continue with plans for an “Inaugural Symposium” which we look forward to hosting in mid-September of this year. The symposium has attracted an international cadre of scientists that are among the world’s experts in the field, and is structured to identify the gaps in our understanding of emerging infectious diseases. Important to our mission to communicate with the public, the symposium opens with a session oriented to the general public session to discuss emerging diseases, the importance of science, and the importance of clear communication of the complexity of the subject and research with the public.

Ronald B. Corley, Ph.D.
Professor of Microbiology
Director, National Emerging Infectious Diseases Laboratories

# Mission Statement and Strategic Plan

The Boston University National Emerging Infectious Diseases Laboratories (NEIDL) mission is: To generate and translate fundamental knowledge on high priority emerging infectious diseases for the benefit of the public health, locally, nationally and globally.

Emerging infectious diseases are defined as those that have newly appeared and been recognized in the population, or have existed but are rapidly increasing in incidence or in geographic range. To meet our missions the NEIDL will:

1. Perform innovative basic, translational and clinical research on emerging infectious diseases, especially those identified as high priority category A, B, and C agents (http://www.niaid.nih.gov/topics/biodefenserelated/biodefense/pages/cata.aspx), in order to develop diagnostic tests, treatments and vaccines to promote the public's health.
2. Provide education and training in these areas of research, in order to develop the next generation of scientists in this field, and to support a national response in the event of a biodefense emergency.
3. Establish a research facility with the highest attention to community and laboratory safety and security.

To successfully implement and achieve these goals, NEIDL has developed and is implementing a strategic plan to:

1. Partner with academic departments across the university to recruit a cadre of investigators, as well as to develop research staff with expertise in the scientific disciplines required to investigate the pathogenesis of emerging infectious diseases caused by category A, B and C agents. We encourage and support the development of national and international research collaborations in order to carry out our mission.
2. Develop physiologically relevant models for the comparative study of these pathogens, mimicking as closely as possible the human disease process. Not only does this require that we recruit faculty with expertise in animal modeling and veterinarian pathology, but also develop the needed services to support these investigations.
3. Move promising basic research as rapidly as possible to translational, preclinical and clinical research in animals and humans in partnership with appropriate collaborators.
4. Create and establish the methodologies needed to advance the development and testing of vaccines, therapeutics and diagnostics for these agents.
5. Train scientists and related support personnel in the requirements to perform maximum containment research in a safe and secure environment.
6. Maintain the flexibility needed to support a national response in the event of a biodefense emergency.
7. Ensure a "safety first" environment for the conduct of all activities in the NEIDL.

# Faculty and Staff

## Scientific Leadership

**Ronald B. Corley, PhD**
Professor and Chair, Department of Microbiology
Director, NEIDL
Director, Immunology Core
*Dr. Corley's Research interests:*

- *Innate and adaptive immunity*
- *Innate-adaptive interface*

**Gerald T. Keusch, MD**
Professor of Medicine, Section Infectious Diseases
Professor of International Health
Associate Director, NEIDL
Director, Collaborative Research Core
*Dr. Keusch's research interests:*

- *Global science and health collaborations*
- *Global impact of infectious diseases*
- *Molecular pathogenesis of infectious diseases*

## Principal Investigators

**Nahid Bhadelia, MD, MA**
Assistant Professor of Medicine
Section of Infectious Diseases, BMC
Director, Infection Control, NEIDL
*Dr. Bhadelia's research interests:*

- *International pandemics strategy and policy*
- *Healthcare worker disaster preparedness*

**John H. Connor, PhD**
Associate Professor, Microbiology
Member, Bioinformatics Graduate Program
*Dr. Connor's research interests:*

- *Virus-host interaction*
- *Viral domination of protein synthesis*
- *Novel approaches to virus detection*

**Paul Duprex, PhD**
Associate Professor, Microbiology
Director, Cell & Tissue Imaging Core
*Dr. Duprex's research Interests:*

- *Paramyxovirus pathogenesis*
- *Virus-cell interactions*
- *Zoonosis; cross-species infection*

**Rachel Fearns, PhD**
Associate Professor, Microbiology
*Dr. Fearns' research Interests:*

- *Negative strand RNA virus nucleocapsid organization*
- *Negative strand RNA virus polymerase activities*
- *Mechanisms of action of polymerase inhibitors*

**James Galagan, PhD**
Associate Professor, Biomedical Engineering
Associate Professor, Microbiology
*Dr. Galagan's research interests:*

- *Systems biology*
- *Infectious Diseases; Tuberculosis*
- *Computational Biology and Genomics*

**Horacio Frydman, PhD**
Associate Professor, Biology
*Dr. Frydman's research interests:*

- *Niche tropism of insect endosymbionts*
- *Mechanisms of Wolbachia-insect interactions*

**Thomas B Kepler, PhD**
Professor, Microbiology
Professor, Mathematics and Statistics
Member, Bioinformatics Graduate Program
*Dr. Kepler's research interests:*

- *Quantitative Systems Immunology*
- *Vaccine Development*

**Igor Kramnik, MD, PhD**
Associate Professor, Medicine and Microbiology
Director, Aerobiology Core
*Dr. Kramnik's research interests:*

- *Genes controlling host resistance and susceptibility to TB*
- *Biology of tuberculosis granulomas*
- *Mechanisms of macrophage activation and differentiation*

**Elke Mühlberger, PhD**
Associate Professor, Microbiology
Director, Biomolecular Production Core
*Dr. Mühlberger's research interests:*

- *Host response to filovirus infection*
- *Molecular mechanisms of filovirus replication and transcription*

**John R. Murphy, PhD**
Adjunct Professor of Medicine, Infectious Diseases, and Microbiology
*Dr. Murphy's research interests:*

- *Recombinant biotherapeutic molecules to alter immune responses to infection, autoimmune diseases, and cancer*
- *Tuberculosis and TB therapeutics*

**John C. Samuelson, MD, PhD**
Professor of Molecular and Cell Biology, BUGSDM
Professor of Microbiology, BUSM
*Dr. Samuelson's research interests:*

- *Mechanisms of pathogenesis of protozoan parasites.*
- *Structures of parasite walls and glycoproteins.*

## Researchers and Laboratory Staff

**Andrew S Acciardo ***
Research Technician
Microbiology, Duprex Lab

**Patricia M Aquino**
Postdoctoral Research Associate
Engineering, Galagan Lab

**Bidisha Bhattacharya**
Postdoctoral Research Associate
Medicine, Kramnik Lab

**Erik P Carter**
Research Technician
Microbiology, Connor Lab

**Alexander Devaux***
Research Study Technician
Microbiology, Connor Lab

**Sujoy Chatterjee**
Postdoctoral Research Associate
Medicine, Kramnik Lab

**Gregory W Ho***
Research Technician
Microbiology, Duprex Lab

**Adam J Hume**
Research Scientist
Microbiology, Mühlberger Lab

**Ronald Killiany, PhD**
Associate Professor, Anatomy & Neurobiology
Director, Whole Animal Imaging Core

**Bang Bon Koo**
Postdoctoral Research Fellow
Whole Animal Imaging Core

**Jacob Koster**
Senior NEIDL Core Technologist, Quality Control

**Maohua Lei***
Research Study Technician
Microbiology, Connor Lab

**Linda J Murphy**
Senior Research Scientist
Microbiology, Duprex Lab

**Shamkumar Nambulli**
Research Scientist and Laboratory Manager
Microbiology, Duprex Lab

**Emily V Nelson**
Postdoctoral Associate
Microbiology, Mühlberger Lab

**Judith Olejnik**
Senior Research Scientist
Microbiology, Mühlberger Lab

**Michelle T Olsen**
Postdoctoral Research Associate
Microbiology, Connor Lab

**Jennifer R Pacheco**
Research Technician
Microbiology, Mühlberger Lab

**Kristen Peters***
Postdoctoral Research Associate
Microbiology, Connor Lab

**John Ruedas ***
Postdoctoral Research Associate
Microbiology, Connor Lab

**Alexandra Soucy***
Research Study Technician
Microbiology, Connor Lab

**Natasha Tilston-Lunel***
Postdoctoral Research Associate
Microbiology, Duprex Lab

**Judy Yung-Ju Yen**
Senior NEIDL Core Technologist

**Xiaoman Zhang***
Research Technician
Biomedical Engineering, Galagan Lab

## Students

**Jake A Awtry ***
Undergraduate Student
Microbiology, Connor Lab

**R Baer**
PhD Student
Microbiology, Galagan Lab

**Mingfu Chen ***
Graduate Student
Biomedical Engineering, Galagan Lab

**Tessa Cressey**
PhD Student
Microbiology, Mühlberger and Fearns Labs

**Uros Kuzmanovic**
Graduate Student
Engineering, Galagan Lab

**Whitney Manhart**
PhD Student, Microbiology
Mühlberger and Mostoslavsky Labs

**Katherine Norwood ***
PhD Student
Bioinformatics, Connor Lab

**Grace Olinger**
PhD Student
Microbiology, Duprex Lab

**Stephanie D'Souza ***
PhD Student
Microbiology, Kepler and Mühlberger Labs

**Xavier DeLuna ****
Graduate Student
Medicine, Connor Lab

**Yuying Guo ***
Visiting Researcher
Microbiology, Connor Lab

**Michaela J Smith ***
Graduate Student
Biology, Frydman Lab

**Emily Speranza ***
PhD Student
Bioinformatics, Connor Lab

## Animal Research Support

**Yulianela Diaz-Perez ***
Veterinary Research Technician

**Christopher Dubois ****
Veterinary Research Technician

**Oscar M Furtado**
Veterinary Research Technician

**Sara Gross ***
Veterinary Research Technician

**Kath Hardcastle, BVet Med DVM**
Core Director, Animal Services

**Marc Jean-Baptiste ***
Veterinary Research Technician

**Andrew G Kocsis, DVM ***
Research Clinical Veterinarian

**James Levin, DVM DACLAM ***
Director, Animal Science Center

**Sergio Roman ***
Veterinary Research Supervisor

**Jonathan W Sturgis**
Operations Manager, ASC/NEIDL

**Larry P Vintinner**
Assistant Director of Operations, ASC

## NEIDL Operations Leadership

**Thomas Daley**
Director
NEIDL Operations

**J Scott Rusk**
Core Director, Facilities & Maintenance Operations

**Ron L Morales**
Core Director, Environmental Health and Safety


**Thomas G Robbins**
Core Director, Biosecurity
Chief, Boston University Police

## NEIDL Administration

**Ronald B. Corley**
Director, NEIDL

**Thomas Daley***
Director, Operations

**Bettina Durkop**
Administrative Coordinator

**Richard P Trevino**
Director, Finance & Research Administration

## Community Relations

**Valeda J Britton**
Executive Director, Community Relations
Boston University Government Affairs

**Chimel Idiokitas**
Assistant Director, Community Relations
Boston University Government Affairs

## Facilities Maintenance & Operations

**David M Ananian**
Maintenance Mechanic

**Juana V Baires**
Custodian

**Joseph T Corbett**
Control Center Technician

**Stephen Coupal**
Intern

**Elijah Ercolino** *
Director, Building Automation Services

**William S Galloway**
General Mechanic

**Jonathan Gendron**
General Mechanic

**John F Holland** *
General Mechanic

**John H Mccall**
Director, Information Technology

**Tracy E Keane** *
Administrative Assistant

**Derek Mosca**
Shipping/Receiving Clerk

**Matthew D Rarick**
Director, Facilities

**Mario Rodriguez**
Custodian

**Scott Rusk** *
Director, Facilities Maintenance & Operations

**Richard Vecchia** *
General Mechanic

## Environmental Health & Safety

**Joshua C Ames**
Program Manager, Research Safety

**Daniel Banh** *
Research Safety Specialist

**Joseph A Barbercheck**
Associate Director, Research Safety

**Tracy S Bastien**
Administrative Coordinator

**Guillermo Madico, MD PhD**
Scientific Safety Officer

**Michael Malmberg** *
Senior Research Safety Specialist

**Ron L Morales**
Core Director, Environmental Health and Safety

**Stephen A Morash**
Director, Emergency Response Planning

**Gene G Olinger, PhD**
Associate Director, Training

**Martin S Rogers**
Manager, Biocontainment Operations

**John Tonkiss, PhD** *
Associate Director, High Containment Safety

**Kevin M Tuohey**
Executive Director, Research Compliance

**Aron J Vinson**
Program Manager, Emergency Response Planning

* Staff who joined during FY16
* Staff who left during FY16

## Public Safety

**Rae T Annese**
Public Safety Officer

**Christopher L Barros**
Public Safety Officer

**Jeffrey P Barros**
Public Safety Officer

**Anthony Carbo**
Electrician/General Mechanic

**Mark J Coffey**
Public Safety Officer

**Joseph M Duffy**
Public Safety Officer

**Robert W Elia**
Systems Integrator

**John Gallivan**
Public Safety Officer

**William Gibbons**
Director, Biosecurity Core

**David J Granados**
Public Safety Officer

**Tracy Harris** *
Systems Integrator

**Joseph H Maldonis**
Public Safety Officer

**Sean R O'Hara** *
Public Safety Officer

**Justin Phelps**
Public Safety Officer

**Jacob Saad** *
Public Safety Officer

**Adil Salhi**
Public Safety Officer

**David F Spellman**
Public Safety Officer

**Stephen A Taranto**
Public Safety Operations Supervisor

**Michael T Tupe**
Public Safety Officer

**Paul M Wynne**
Public Safety Officer

**Sean C Wynne**
Public Safety Officer

**Melody L Zarth**
Personnel Suitability Specialist

*It's impossible to get even half the investigators and staff together at any one time, but our first attempt was a start!*

# Research

The research activities of the NEIDL faculty focus on pathogenesis of emerging viral, bacterial, and protozoan parasitic pathogens and continue to be supported by significant external grant funding (see below). The faculty come from four Schools of Boston University (Medicine, Dental Medicine, Engineering, and Arts and Sciences), as is appropriate for a University Center. Most of these faculty have developed multidisciplinary programs that engage the expertise of faculty, staff and trainees with diverse backgrounds across the university. These collaborations include scientists not only in the faculty's home departments (Microbiology, Medicine, Molecular and Cell Biology, Biomedical Engineering, Biology) but also from the Center for Regenerative Medicine, the Photonics Center, and from Engineering and Chemistry. Many NEIDL investigators collaborate actively with faculty external to Boston University, including from both US and international institutions. Research programs also engage a wide array of undergraduate and graduate students, including those from Graduate Programs in Microbiology (Host Pathogen Interactions), Immunology, Bioinformatics, MCBB (Molecular Biology, Cell Biology and Biochemistry) and Engineering. These types of collaborative programs and training activities exemplify the "research style" that has become a hallmark of the NEIDL.

NEIDL investigators have successfully competed for $21.3M in research and support during the current FY16 year. Funding comes from a variety of competitive sources, including the National Institutes of Health, the Department of Defense, the pharmaceutical industry, and private foundations, as well as subcontracts with faculty at collaborating institutions.

The funding diversity reflects the research mission of the NEIDL, which encompasses everything from basic research to understand the nature of pathogens and their interactions with a host during infection, to more translational and applied research to develop diagnostics, therapeutics and vaccines. These research programs continue to attract outstanding postdoctoral researchers and staff scientists into NEIDL faculty laboratories.

Publications resulting from our research efforts during this past fiscal year are detailed below.


**Bhadelia, N.** (2016). *Prospective cohort study of pregnant Brazilian women elucidates link between Zika virus infection and fetal abnormalities.* Evid Based Med. doi:10.1136/ebmed-2016-110476

**Bhadelia, N.** (2015). *Rapid diagnostics for Ebola in emergency settings*. Lancet, 386(9996), 833-835. doi:10.1016/S0140-6736(15)61119-9

Hochberg, N. S., & **Bhadelia, N.** (2015). *Infections Associated with Exotic Cuisine: The Dangers of Delicacies*. Microbiol Spectr, 3(5). doi:10.1128/microbiolspec.IOL5-0010-2015

**Bhadelia, N.** (2015). *Lessons for pulmonary critical care from treatment of Ebola virus disease in developed countries*. Lancet Respir Med, 3(12), 919-921. doi:10.1016/S2213-2600(15)00432-4

Ortega, R., **Bhadelia, N.,** Obanor, O., Cyr, K., Yu, P., McMahon, M., & Gotzmann, D. (2015). *Videos in clinical medicine. Putting on and removing personal protective equipment*. N Engl J Med, 372(12), e16. doi:10.1056/NEJMvcm1412105

Hochberg, N, **Bhadelia, N**, *"Exotic and Trendy Cuisine" in Schlossberg, Infections of Leisure, Fifth Edition*, 2015. [In Press]

Scherr SM, Daaboul GG, Trueb J, Sevenler D, Fawcett H, Goldberg B, **Connor JH**, Ünlü MS. (2016) Real-Time Capture and *Visualization of Individual Viruses in Complex Media.* ACS Nano. 2016 Jan 22. [Epub ahead of print] PMID: 26760677

Seymour E, Daaboul GG, Zhang X, Scherr SM, Ünlü NL, **Connor JH**, Ünlu MS (2015) *DNA-Directed Antibody Immobilization for Enhanced Detection of Single Viral Pathogens.* Anal Chem. 2015 Oct 20;87(20):10505-12 PMID: 26378807

Sharp CR, Nambulli S, Acciardo AS, Rennick LJ, Drexler JF, Rima BK, Williams T, **Duprex WP**. *Chronic Infection of Domestic Cats with Feline Morbillivirus, United States*. Emerg Infect Dis. 2016 Apr;22(4):760-2. doi: 10.3201/eid2204.151921. No abstract available. PMID: 26982566

Nambulli S, Sharp CR, Acciardo AS, Drexler JF, **Duprex WP***. Mapping the evolutionary trajectories of morbilliviruses: what, where and whither.* Curr Opin Virol. 2016 Feb;16:95-105. doi: 10.1016/j.coviro.2016.01.019. Epub 2016 Feb 26. Review.PMID: 26921570

MacLoughlin RJ, van Amerongen G, Fink JB, Janssens HM, **Duprex WP**, de Swart RL. *Optimization and Dose Estimation of Aerosol Delivery to Non-Human Primates.* J Aerosol Med Pulm Drug Deliv. 2016 Jun;29(3):281-7. doi: 10.1089/jamp.2015.1250. Epub 2015 Dec 8. PMID: 26646908

Millar EL, Rennick LJ, Weissbrich B, Schneider-Schaulies J, **Duprex WP**, Rima BK. *The phosphoprotein genes of measles viruses from subacute sclerosing panencephalitis cases encode functional as well as non-functional proteins and display reduced editing.* Virus Res. 2016 Jan 4;211:29-37. doi: 10.1016/j.virusres.2015.09.016. Epub 2015 Sep 28. PMID: 26428304

Munday DC, Wu W, Smith N, Fix J, Noton SL, Galloux M, Touzelet O, Armstrong SD,Dawson JM, Aljabr W, Easton AJ, Rameix-Welti MA, de Oliveira AP, Simabuco FM,Ventura AM, Hughes DJ, Barr JN, **Fearns R**, Digard P, Eléouët JF, Hiscox JA. *Interactome analysis of the human respiratory syncytial virus RNA polymerase complexidentifies protein chaperones as important cofactors that promote L-protein stability and RNA synthesis*. J. Virol. 2015. 89: 917-930.

Noton SL, **Fearns R***. Initiation and regulation of paramyxovirus transcription andr eplication*. Virology 2015. 479-480C: 545-554. (Diamond Edition, invited review).

Dickey LL, Duncan JK, Hanley TM, **Fearns R**. *Decapping protein 1 phosphorylationmodulates IL-8 expression during respiratory syncytial virus infection.* Virology 2015. 481:199-209.

Noton SL, Nagendra K, Dunn EF, Mawhorter ME, Yu Q, **Fearns R**. *Respiratory syncytialvirus inhibitor AZ-27 differentially inhibits different polymerase activities at the promoter.* J. Virol. 2015. 89: 7786-7798.

Deval J, Hong J, Wang G, Taylor J, Smith LK, Fung A, Stevens SK, Liu H, Jin Z, Dyatkina N, Prhavc M, Stoycheva AD, Serebryany V, Liu J, Smith DB, Tam Y, Zhang Q, Moore ML, **Fearns R**, Chanda SM, Blatt LM, Symons JA, Beigelman L. *Molecular basis for the selective inhibition of respiratory syncytial virus RNA polymerase by 2´-fluoro-4´-chloromethyl-cytidine triphosphate*. PLoS Pathog. 2015 11:e1004995.

McCutcheon KM, Jordan R, Mawhorter ME, Noton SL, Powers JG, **Fearns R**, Cihlar T, Perron M. *The interferon type I/III response to respiratory syncytial virus infection in air way epithelial cells can be attenuated or amplified by antiviral treatment.* J. Virol. 2015.90: 1705-1717.

Aljabr W, Touzelet O, Pollakis G, Wu W, Munday DC, Hughes M, Hertz-Fowler C, Kenny J, **Fearns R**, Barr JN, Matthews DA, Hiscox JA*. Investigating the influence of ribavirin on human respiratory syncytial virus RNA synthesis using a high-resolution RNASeqapproach*. J. Virol. 2015. JVI.02349-15 (Epub ahead of print).

Warren TK, Jordan R, Lo MK, Ray AS, Mackman RL, Soloveva V, Siegel D, Perron M, Bannister R, Hui HC, Larson N, Strickley R, Wells J, Stuthman KS, Van Tongeren SA, Garza NL, Donnelly G, Shurtleff AC, Retterer CJ, Gharaibeh D, Zamani R, Kenny T, Eaton BP, Grimes E, Welch LS, Gomba L, Wilhelmsen CL, Nichols DK, Nuss JE, Nagle ER, Kugelman JR, Palacios G, Doerffler E, Neville S, Carra E, Clarke MO, Zhang L, Lew W, Ross B, Wang Q, Chun K, Wolfe L, Babusis D, Park Y, Stray KM, Trancheva I, Feng JY, Barauskas O, Xu Y, Wong P, Braun MR, Flint M, McMullan LK, Chen SS, **Fearns R**, Swaminathan S, Mayers DL, Spiropoulou CF, Lee WA, Nichol ST, Cihlar T, Bavari S. *Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesusmonkeys.* Nature 2016. 531: 381-385.

Duvall JR, VerPlank L, Ludeke B, McLeod SM, Lee MD 4th, Vishwanathan K, Mulrooney CA, Le Quement S, Yu Q, Palmer MA, Fleming P, **Fearns R**, Foley MA, Scherer CA. *Novel diversity-oriented synthesis-derived respiratory syncytial virus inhibitors identified via a high throughput replicon-based screen*. Antiviral Research. 2016. 131: 19-25

John Barr and **Rachel Fearns** *"Genetic Instability of RNA Viruses*". In Kovakchuk I. and Kovakchuk O. (Eds), Genome Stability. Cambridge: Elsevier Inc. In Press (book chapter)

Sridevi Ranganathan, Guangchun Bai, Anna Lyubetskaya, Gwendowlyn S. Knapp, Matthew W. Peterson, Michaela Gazdik, Antonio L. C. Gomes, **James E. Galagan**, Kathleen A. McDonough. *Characterization of a cAMP responsive transcription factor, Cmr (Rv1675c), in TB complex mycobacteria reveals overlap with the DosR (DevR) dormancy*

*regulon*. Nucleic Acids Res. 2016 Jan 8; 44(1): 134–151. Published online 2015 Sep 10. doi: 10.1093/nar/gkv889 PMCID: PMC4705688

Jared D. Sharp, Atul K. Singh, Sang Tae Park, Anna Lyubetskaya, Matthew W. Peterson, Antonio L. C. Gomes, Lakshmi-Prasad Potluri, Sahadevan Raman, **James E. Galagan**, Robert N. Husson . *Comprehensive Definition of the SigH Regulon of* Mycobacterium tuberculosis *Reveals Transcriptional Control of Diverse Stress Responses.* PLoS One. 2016; 11(3): e0152145. Published online 2016 Mar 22. doi: 10.1371/journal.pone.0152145 PMCID: PMC4803200

Christopher D. Garay, Jonathan M. Dreyfuss, **James E. Galagan** . *Metabolic modeling predicts metabolite changes in Mycobacterium tuberculosis.* BMC Syst Biol. 2015; 9: 57. Published online 2015 Sep 16. doi: 10.1186/s12918-015-0206-7.PMCID: PMC4574064

Aquino P, Honda B, Jaini S, Lyubetskaya A, Hosur K, Chiu JG, Ekladious I, Hu D, Jin L, Sayeg MK, Stettner AI, Wang J, Wong BG, Wong WS, Alexander SL, Ba C, Bensussen SI, Bernstein DB, Braff D, Cha S, Cheng DI, Cho JH, Chou K, Chuang J, Gastler DE, Grasso DJ, Greifenberger JS, Guo C, Hawes AK, Israni DV, Jain SR, Kim J, Lei J, Li H, Li D, Li Q, Mancuso CP, Mao N, Masud SF, Meisel CL, Mi J, Nykyforchyn CS, Park M, Peterson HM, Ramirez AK, Reynolds DS, Rim NG, Saffie JC, Su H, Su WR, Su Y, Sun M, Thommes MM, Tu T, Varongchayakul N, Wagner TE, Weinberg BH, Yang R, Yaroslavsky A, Yoon C, Zhao Y, Zollinger AJ, Stringer AM, Foster JW, Wade J, Raman S, Broude N, Wong WW, **Galagan JE**. *Coordinated Regulation of Acid Resistance in Escherichia coli.* BMC Syst Biol. In Revision.

Knapp, G. S., Lyubetskaya A., Peterson M. W., Gomes A. L., Ma Z., **Galagan J. E.**, McDonough K. A. (2015) *Role of intragenic binding of cAMP responsive protein (CRP) in regulation of the succinate dehydrogenase genes Rv0249c-Rv0247c in TB complex mycobacteria*. Nucleic acids research.43(11):5377-93 PMCID:PMC4477654

Minch, K. J., Rustad T. R., Peterson E. J., Winkler J., Reiss D. J., Ma S., Hickey M., Brabant W., Morrison B., Turkarslan S., Mawhinney C., **Galagan J. E**., Price N. D., Baliga N. S., Sherman D. R. (2015) *The DNA-binding network of Mycobacterium tuberculosis*. Nature communications.6:5829 PMCID:4301838

Zhang, R., Verkoczy, L., Wiehe, K., Munir Alam, S., Nicely, N.I., Santra, S., Bradley, T., Pemble, C.W., Zhang, J., Gao, F., **Kepler, T.B** et al. (2016). *Initiation of immune tolerance–controlled HIV gp41 neutralizing B cell lineages*. Science Translational Medicine 8: 336ra362-336ra362.

Bonsignori, M., Zhou, T., Sheng, Z., Chen, L., Gao, F., Joyce, M.G., Ozorowski, G., Chuang, G.-Y., Schramm, Chaim A., Wiehe, K., **Kepler, T.B** et al. (53 authors) (2016) *Maturation Pathway from Germline to Broad HIV-1 Neutralizer of a CD4-Mimic Antibody*. Cell, 165: 449-63.

Bradley, T., Fera, D., Bhiman, J., Eslamizar, L., Lu, X., Anasti, K., Zhang, R., Sutherland, Laura L., Scearce, Richard M., Bowman, Cindy M., Stolarchuk, C., Lloyd, K. E., Parks, R., Eaton, A., Foulger, A., Nie, X., Karim, S.S.A., Barnett, S., Kelsoe, G., **Kepler, T.B.,** Alam, S.M., Montefiori, D.C., Moody, M.A., Liao, H.-X., Morris, L., Santra, S., Harrison, S.C., Haynes, B.F. (2016). *Structural Constraints of Vaccine-Induced Tier-2 Autologous HIV Neutralizing Antibodies Targeting the Receptor-Binding Site*. Cell Rep. 14: 43-54.

Kuraoka M, AG Schmidt, T Nojima, F Feng, A Watanabe, D Kitamura, SC Harrison, **TB Kepler**, G Kelsoe (2016) *Complex Antigens Drive Permissive Clonal Selection in Germinal Centers*. Immunity 44:542-52.

Schmidt, Aaron G., Do, Khoi T., McCarthy, Kevin R., **Kepler, Thomas B.,** Liao, H.-X., Moody, M.A., Haynes, Barton F., and Harrison, Stephen C. (2015). *Immunogenic Stimulus for Germline Precursors of Antibodies that Engage the Influenza Hemagglutinin Receptor-Binding Site*. Cell Reports 13: 2842-2850.

Feng F, **Kepler TB**. (2015). *Bayesian Estimation of the Active Concentration and Affinity Constants Using Surface Plasmon Resonance Technology*. PLoS One **10**(6):e0130812. PMID: 26098764

Nelson, C.S., Pollara, J., Kunz, E.L., Jeffries, T.L., Duffy, R., Beck, C., Stamper, L., Wang, M., Shen, X., Pickup, D.J., **Kepler TB** et al. (2016). *Combined HIV-1 Envelope Systemic and Mucosal Immunization of Lactating Rhesus Monkeys Induces Robust IgA-Isotype B Cell Response in Breast Milk*. J Virol. 90: 4951-65. PMID 26937027.

Schmidt AG, Therkelsen MD, Stewart S, **Kepler TB**, Liao HX, Moody MA, Haynes BF, Harrison SC. *Viral receptor-binding site antibodies with diverse germline origins.* (2015). Cell **161**(5):1026-34. PMID:25959776

Francica JR, Sheng Z, Zhang Z, Nishimura Y, Shingai M, Ramesh A, Keele BF, Schmidt SD, Flynn BJ, Darko S, Lynch RM, Yamamoto T, Matus-Nicodemos R, Wolinsky D; NISC Comparative Sequencing Program, Nason M, Valiante NM, Malyala P, De Gregorio E, Barnett SW, Singh M, O'Hagan DT, Koup RA, Mascola JR, Martin MA, **Kepler TB**,

Douek DC, Shapiro L, Seder RA. (2015). *Analysis of immunoglobulin transcripts and hypermutation following SHIV(AD8) infection and protein-plus-adjuvant immunization*. Nature Communications **6**:6565. PMID:25858157

Niazi MK, Dhulekar N, Schmidt D, Major S, Cooper R, Abeijon C, Gatti DM, **Kramnik I**, Yener B, Gurcan M, Beamer G. *Lung necrosis and neutrophils reflect common pathways of susceptibility to Mycobacterium tuberculosis in genetically diverse, immune-competent mice.* Dis Model Mech. 2015;8(9):1141-53. doi: 10.1242/dmm.020867. PubMed PMID: 26204894; PMCID: PMC4582107.

Bhattacharya B, Chatterjee S, Devine WG, Kobzik L, Beeler AB, Porco JA, Jr., **Kramnik I.** *Fine-tuning of macrophage activation using synthetic rocaglate derivatives.* Sci Rep. 2016;6:24409. doi: 10.1038/srep24409. PubMed PMID: 27086720; PMCID: PMC4834551.

**Kramnik I**, Beamer G. *Mouse models of human TB pathology: roles in the analysis of necrosis and the development of host-directed therapies.* Semin Immunopathol. 2016;38(2):221-37. doi: 10.1007/s00281-015-0538-9. PubMed PMID: 26542392; PMCID: PMC4779126.

Nelson, E. V., Schmidt, K. M., Deflubé-Owen, L. R., Doganay, S., Banadyga, L., Olejnik, J., Ryabchikova, E., Ebihara, H., Kedersha, N., Ha, T., and **Mühlberger, E**. *Ebola virus does not induce stress granule formation during infection and sequesters stress granule proteins within viral inclusions.* under review.

Schmidt, K. M. and **Mühlberger, *E***. *Marburg virus reverse gentics systems. Viruses*, in press.

Brauburger, K., Boehmann, Y, Krähling, V., and **Mühlberger, E**. 2016. *Transcriptional regulation in Ebola virus: effects of gene border structure and regulatory elements on gene expression and polymerase scanning behavior*. J. Virol. 90: 1898-1909. PMID: 26656691.

Pinto, A., Williams, G., Szretter, K., White, J., Proenca-Modena, J., Liu G., Olejnik, J., Brien, J., Ebihara, H., **Mühlberger, E**., Amarasinghe, A. Diamond, M., and Boon, A. *Human and murine IFIT1 do not restrict infection of negative sense RNA viruses of the Orthomyxoviridae, Bunyaviridae, and Filoviridae families*. J. Virol. 89: 9465-9476. PMID: 26157117.

Chatterjee A, Ratner DM, Ryan CM, Johnson PJ, O'Keefe BR, Secor WE, Anderson DJ, Robbins PW, **Samuelson J.** *Anti-Retroviral Lectins Have Modest Effects on Adherence of Trichomonas vaginalis to Epithelial Cells In Vitro and on Recovery of Tritrichomonas foetus in a Mouse Vaginal Model*. PLoS One. 2015; 10:e0135340.

Chatterjee A, Bandini G, Motari E, **Samuelson J**. *Ethanol and isopropanol in concentrations present in hand-sanitizers sharply reduce excystation of Giardia and Entamoeba and eliminate oral infectivity of gerbils by Giardia cysts*. Antimicrob Agents Chemother. 2015; 59:6749-6754.

# FY16 Funded Research

The work which resulted in the publications outlined above would not have been possible without the ability of our faculty to competitively seek funding to support their research activities. NEIDL faculty members received over $21 Million in funding in FY16 for the following projects:

| PI | SCHOOL-DEPT | TITLE | SPONSOR | PROJECT PERIOD | FUNDS AWARDED IN FY16 |
|---|---|---|---|---|---|
| The following are faculty whose work is carried out within the NEIDL facility: | | | | | |
| CONNOR | MED-MICRO | DEVELOPMENT OF NEAR REAL-TIME, MULTIPLEXED DIAGNOSTICS FOR VIRAL HEMORRHAGIC FEVER | NIH/NIAID | 8/1/2011 - 7/31/2016 | 708,299 |
| CONNOR | MED-MICRO | POINT-OF-CARE NANO-TECHNOLOGY DIAGNOSTIC FOR DIFFERENTIAL FEVER DIAGNOSIS | BECTON, DICKINSON & Co | 10/1/2015 - 9/30/2016 | 777,700 |
| CONNOR | MED-MICRO | COMBINED VIRAL LOAD AND SEROLOGY PANEL FOR RAPID POC EBOLA DIAGNOSTICS | NEXGEN ARRAYS LLC | 3/1/2015 - 2/29/2016 | 65,185 |
| CONNOR | MED-MICRO | ROLE FOR POLYAMINES IN EBOLA VIRUS REPLICATION | NIH/NIAID | 2/1/2016 - 1/31/2018 | 246,251 |
| CONNOR | MED-MICRO | BIOMARKER DISCOVERY | JOHNS HOPKINS U | 3/10/2015 - 3/31/2016 | 362,534 |
| CONNOR | MED-MICRO | ELIMINATION OF PATHOGENIC IGE IN CYSTIC FRIBROSIS | BRIGHAM & WOMEN'S | 2/1/2016 - 7/31/2017 | 92,788 |
| | | | | | |
| CORLEY | MED-MICRO | NATIONAL EMERGING INFECTIOUS DISEASES LABORATORIES OPERATIONS | NIH/NIAID | 6/1/2016 - 5/31/2020 | 11,500,000 |
| | | | | | |
| DUPREX | MED-MICRO | INVESTIGATING FELINE MORBILLIVIRUS MOLECULAR EPIDEMIOLOGY IN CATS IN THE NORTH EASTERN Us | ZOETIS, LLC | 8/26/2014 - 12/31/2015 | 49,377 |
| DUPREX | MED-MICRO | GENERATION OF PREDICTIVE MODELS OF VIRAL PATHOGENESIS | BATTELLE MEMORIAL INST | 11/6/2015 - 9/16/2016 | 300,000 |
| DUPREX | MED-MICRO | DISSECTING THE PATHOGENESIS OF FELINE MORBILLIVIRUS | ZOETIS, LLC | 3/11/2016 - 3/10/2019 | 446,100 |
| DUPREX | MED-MICRO | SHIFTING A PARADIGM IN VACCINE SAFETY: FROM EMPIRICAL TO RATIONAL ATTENUATION | NIH/NIAID | 6/1/2016 - 5/31/2018 | 409,250 |
| | | | | | |

| PI | SCHOOL-DEPT | TITLE | SPONSOR | PROJECT PERIOD | FUNDS AWARDED IN FY16 |
|---|---|---|---|---|---|
| GALAGAN | ENG-BIOMEDICAL | IDENTIFYING MOLECULAR SIGNATURES OF DRUG SUSCEPTIBILITY IN ENTEROCOCCUS FAECIUM | PHILIPS HEALTH CARE | 12/15/2015-6/15/2017 | 423,901 |
| GALAGAN | ENG-BIOMEDICAL | SYSTEMS BIOLOGY OF THE CIRCADIAN CLOCK OUTPUT NETWORK | TEXAS A&M UNIV | 1/15/2015 - 12/31/2018 | 129,229 |
| GALAGAN | ENG-BIOMEDICAL | ORGANIC BIOSENSORS FOR PERSONAL PHYSIOLOGIC MONITORING | DOD / DARPA | 4/11/2016 - 4/10/2017 | 693,133 |
| | | | | | |
| KRAMNIK | MED-PULMONARY | NOVEL TB TREATMENT STRATEGY - OPTIMIZATION OF MACROPHAGE RESPONSIVENESS TO IFNY | NIH/NIAID | 3/11/2015 - 2/28/2018 | 491,100 |
| KRAMNIK | MED-PULMONARY | GENETIC-BASED SUSCEPTIBILITY TO PULMONARY TUBERCULOSIS | TUFTS UNIV | 4/15/2015 - 3/31/2017 | 16,368 |
| KRAMNIK | MED-PULMONARY | NECROSIS IN PULMONARY TB GRANULOMAS: DYNAMICS, MECHANISMS, THERAPIES | NIH/NHLBI | 5/1/2016 - 4/30/2020 | 709,385 |
| | | | | | |
| MUHLBERGER | MED-MICRO | SPR: NOVEL SPR BARRIER TECHNOLOGY (THE USAID AGREEMENT ) | SPR ADVANCED TECH INC. | 3/1/2015 - 2/29/2016 | 28,292 |
| MUHLBERGER | MED-MICRO | DEEP CHARACTERIZATION OF ROUSETTUS AEGYPTIACUS IMMUNE SYSTEM: USE OF BATS/NONHUMAN PRIMATES TO COMPARE IMMUNE RESPONSES DURING ASYMTOMATIC/SYMPTOMATIC FILOVIRUS INFECTIONS | THE GENEVA FOUNDTN | 1/15/2014 - 3/14/2017 | 130,001 |
| MUHLBERGER | MED-MICRO | ANTIVIRAL RESPONSES IN IPSC-DERIVED HUMAN PRIMARY CELLS TO EBOV INFECTION | NIH/NIAID | 6/30/2016 5/31/2018 | 270,000 |
| | | | | | |

| PI | SCHOOL-DEPT | TITLE | SPONSOR | PROJECT PERIOD | FUNDS AWARDED IN FY16 |
|---|---|---|---|---|---|
| The following are affiliated NEIDL investigators whose labs are located outside the NEIDL: | | | | | |
| FEARNS | MED-MICRO | INITIATION AND REGULATION OF RSV MRNA TRANSCRIPTION AND GENOME REPLICATION | NIH/NIAID | 8/7/2014 - 7/31/2018 | 415,000 |
| FEARNS | MED-MICRO | A STRUCTURE ANALYSIS OF THE INTACT VIRON AND REPLICATIVE COMPLEXES OF HUMAN RESPIRATORY SYNCYTIAL VIRUS | UNIV OF GLASGOW | 11/30/2014 - 11/29/2015 | 76,983 |
| FEARNS | MED-MICRO | DEVELOPMENT OF A NON-RADIOACTIVE ASSAY FOR THE RSV POLYMERASE | MERCK, SHARP & DOHME CO | 11/12/2015 - 11/11/2016 | 85,227 |
| FEARNS | MED-MICRO | DEVELOPMENT OF AN IN IVTRO ASSAY FOR PARA-MYXOVIRUS POLYMERASES | ALIOS BIO-PHARMA, INC. | 5/16/2014 - 5/15/2017 | 82,090 |
| FEARNS | MED-MICRO | TREATING RESPIRATORY SYNCYTIAL VIRUS INFECTION BY TARGETINGA VIRUS-ASSOCIATED KINASE | THE HARTWELL FOUNDTN | 4/1/2015 - 3/31/2018 | 100,000 |
| | | | | | |
| KEPLER | MED-MICRO | CHAVI-SRSC J COMPUTATIONAL BIOLOGY | DUKE UNIV | 7/15/2012 - 6/30/2019 | 297,982 |
| KEPLER | MED-MICRO | B CELL LINEAGE ENVELOPE IMMUNOGEN DESIGN FROM RV144 ANTIBODIES, PHASE 2 | DUKE UNIV | 11/1/2014 - 10/31/2016 | 110,000 |
| KEPLER | MED-MICRO | STRUCTURE-FUNCTION ANALYSIS OF INFECTION AND VACCINE-INDUCED B-CELL REPERTOIRES (CORE D) | CHILDREN'S HOSPITAL, BOSTON | 1/1/2012 - 6/30/2016 | 25,105 |
| KEPLER | MED-MICRO | STRUCTURE BASED DESIGN OF ANTIBODIES AND VACCINES | VANDERBILT UNIV | 12/1/2015 - 4/30/2016 | 74,177 |
| KEPLER | MED-MICRO | MODELING AFFINITY MATURATION AT MOLECULAR RESOLUTION | NIH/NIAID | 4/15/2015 - 3/31/2020 | 1,587,693 |
| | | | | | |
| SAMUELSON | SDM-MOL & CELL BIO | STRUCTURE AND DEVELOPMENT OF OOCYST AND SPOROCYST WALLS | NIH/NIAID | 8/1/2015 - 1/31/2020 | 625,333 |
| | | | | | |
| | | **TOTAL** | | | **$21,328,483** |
| | | | | | |

## Seed Funding, 2015 - 2016

The NEIDL is fortunate to be able to provide financial support for pilot programs to investigators to develop new innovative science initiatives to further the NEIDL mission, to support proof of principle studies, or infrastructure support. The expectation is that this funding will be leveraged to improve the research enterprise, promote multidisciplinary studies between NEIDL investigators and investigators across the institution, and/or to develop new programs within the NEIDL. The following programs received seed funding during this fiscal year.

## NEIDL commitment to Zika virus research

With the spread of Zika virus in South America and the now confirmed local transmission of the virus in Florida, the NEIDL provided funding to establish a core Zika virus laboratory to develop expertise in this virus, and use this expertise to enable other scientists around the university to develop collaborative research programs relevant to understanding Zika virus pathogenesis. Through the efforts of NEIDL investigator **John Connor**, a number of strains of the Zika virus from diverse locations including Africa, Asia, South and Central Americas as well as the Caribbean were obtained. His lab began working on identifying antiviral strategies to limit the replication of these viruses using dedicated space in the NEIDL. Their growing experience with the Zika virus facilitated productive collaborations with other investigators around Boston University, Boston Medical Center, the biotechnology community within Boston and visiting students from Brazil. Collaborative activities have included i) working with members of the Neurobiology and Anatomy department to develop a mouse model of Zika virus interruption of brain development, ii) working with faculty in Obstetrics and Gynecology and also the Infectious Disease section of Medicine to identify the primary target cells in the placenta that support Zika virus infection, and working with faculty in biophysics department to visualize the creation of Zika virions within infected cells. Finally, work with the biotech industry has revolved around work with a bio-imaging startup to establish methods that allow the direct visualization of Zika virus particles in biological fluids like serum and urine. We expect these research efforts to continue and to grow in the near future, and lead to new funding as these initial efforts develop into more mature research efforts in the coming year.

Interest in Zika virus also enabled the establishment of insect cell culture and virus growth protocols for the study of how Zika virus infects and persists in mosquito cells with Biology faculty member and NEIDL investigator **Horacio Frydman**. Dr. Frydman is an expert on the parasitic bacterium Wolbachia, which infects arthropod species including mosquitos. Infected mosquitos may be less able to replicate viruses such as Zika, Dengue, or Chikungunya. Dr. Frydman is interested in using Wolbachia as a tool to determine what genes may suppress Zika virus replication in insect cells and in insects. Support for an MCBB graduate student in Dr. Frydman's laboratory, Michaela Smith, has helped catalyze this new line of investigation. She was also supported to train in an arenavirus laboratory at Florida Gulf Coast University to develop the requisite expertise to bring back to BU and the NEIDL.

The NEIDL continues to support an innovative project begun last year between **Elke Mühlberger** and Gustavo Mostoslavsky from the Center for Regenerative Medicine on studies to develop inducible pluripotent stem cells from reservoir species of animals for the study of zoonosis and virus-host interactions. These studies form the foundation for the dissertation research of Microbiology graduate student Whitney Manhart.

Other funds were used for proof of principal projects to help further the NEIDL mission.

- Funds were also provided to **Dr. Mühlberger** to develop molecular clones of the Lloviu cuevavirus, a distant relative of the know filoviruses. While the virus has never been isolated, RNA from it was recovered from a Rosettus bat in Spain. The clones were to be generated to develop probes to investigate this interesting new virus.
- Funds were used to support travel expenses for **Nahid Bhadelia** in her efforts to develop a concept training program between NEIDL and investigators in West and Central Africa.
- Funds were provided to support the two members of the NEIDL scientific staff, **Emily Nelson** and **Judy Yen,** to go to Erasmus University in the Netherlands to train on field techniques required before deploying to work in a mobile Ebola diagnostic laboratory in Sierra Leone during the Ebola virus outbreak in 2015.

The NEIDL also purchased an Odyssey CLx infrared imaging system to permit quantitative western blotting, an instrument that is used by most NEIDL investigators and is too expensive for any given lab to purchase.

## Update on FY2015 seed funding initiatives

**James Galagan** received funding to help perform the first whole genome sequencing and analysis of strains of Mycobacterium tuberculosis (MTB) from India. Through collaborative links between colleagues in India and the NEIDL, he gained access to DNA for over 100 strains of MTB from two different sites in South India. His analysis provided a detailed view of the genetic diversity of MTB in India, which is suffering the world's largest TB epidemic when measured by the number of infected patients. The analysis also revealed the genetic underpinnings of MTB drug resistance in India, and highlights the limitations of current sequence based diagnostics for drug resistance diagnosis. A manuscript describing their analysis is currently in preparation.

**Elke Mühlberger** received funding to support a graduate student (Whitney Manhart) during the summer to initiate a long-term collaborating project between the Mühlberger lab and the Center for Regenerative Medicine investigator Gustavo Mostoslavsky. The ultimate goal of the research is to learn how to establish inducible pluripotent stem cells from *Rosettus aegyptiacus* bats and other reservoir species to provide a source of different cell types for the study of virus-host interactions in reservoir species of Marburg and other filoviruses.

This seed funding, which fostered the collaboration between the Mühlberger and Mostoslavsky labs, led to the successful application of a new R21 grant proposal which was recently awarded (**R21 AI126457**; *Antiviral responses in iPSC-derived human primary cells to Ebola virus infection*). Using the seed funding, Ms. Manhart was trained to generate iPSC-derived human liver cells which will be used for Ebola and Marburg virus infection studies once the NEIDL BSL-4 facility is operational.

**John Connor** received support to purchase an SP-1000 single particle imaging microscope from NexgenArrays, which allows the visualization of viral particles that are not able to be seen using a conventional microscope. The purchase of this specific instrument allowed his lab to conduct collaborative experiments with IRF Frederick and RML Hamilton on the size and shape characteristics of hemorrhagic fever viruses. This initial work has led to follow-on projects on using the SP-1000 and related nanoparticle imagers to visualize Ebola and other high-consequence pathogens, projects that are still ongoing. .

# Research in the News

## Fighting a Deadly Virus - Hartwell Award to help MED prof explore new ways to tackle RSV

### Original article from BU Today, by Barbara Moran, June 22, 2016

Respiratory syncytial virus, or RSV, is a highly contagious virus that attacks people's lungs and airways. For healthy adults, infection often leads to mild symptoms that feel like a cold. But for children and babies, the effects can be severe. RSV is a major cause of pneumonia in infants and young children in the United States, and the leading cause of viral death in infants.

**Rachel Fearns**, a School of Medicine associate professor of microbiology, hopes that a deeper understanding of RSV may lead to better treatments. She has won a 2014 Hartwell Individual Biomedical Research Award from the Hartwell Foundation, which gives her $300,000 over three years to study the molecular mechanisms that allow RSV to replicate and multiply. Fearns hopes that her research might eventually lead to antiviral drugs and vaccines to treat and prevent RSV disease and give insight into how related viruses could also be controlled.

Fearns studies a protein within the virus called a polymerase, a complicated enzyme with two different jobs: first, it copies the RSV genome into messenger RNAs to make viral proteins, a process called transcription; it also makes more copies of the genome, a process called replication. She was the first scientist to isolate and purify RSV polymerase, a "technically challenging" process, she says, that took her six years, from 2004 to 2010. One of the challenges was that RSV polymerase is so large—more than five times larger than the average cellular protein—and therefore is difficult to make efficiently and correctly. "Most normal people would have given up," she says, with a smile.

*Rachel Fearns, a MED associate professor of microbiology and winner of a 2014 Hartwell Individual Biomedical Research Award, studies the molecular mechanisms within RSV, a common virus that is a major cause of pneumonia in infants and young children. Photo by Cydney Scott*

Fearns wanted a pure copy of the protein so she could study its function in detail. "We wanted something we could work with in a test tube," she says. "How does this one protein do both transcription and replication, and how does it choose which one to do? It's a big scientific question."

So far, scientists studying RSV polymerase have learned that it has at least three distinct parts with three different functions, as well as other parts that are not well understood. "We want to understand those unexplained parts," says Fearns, "because any essential protein activity is potentially a good target for antiviral drugs." She also notes that RSV is closely related to measles, mumps, and some emerging viruses such as Marburg and Ebola. "In the long term, anything we learn with RSV would likely be applicable to those other viruses," she says.

Each year, the Hartwell Foundation awards grants to faculty who are involved in innovative, cutting-edge biomedical research that will potentially benefit children. For each researcher funded, the sponsoring participating institution will also receive a Hartwell Fellowship to fund one postdoctoral candidate. For Fearns, it means a chance to pursue science that is high risk, with a potentially large payoff. "It's exciting science," she says, "and I'm glad to have the opportunity to work on it."

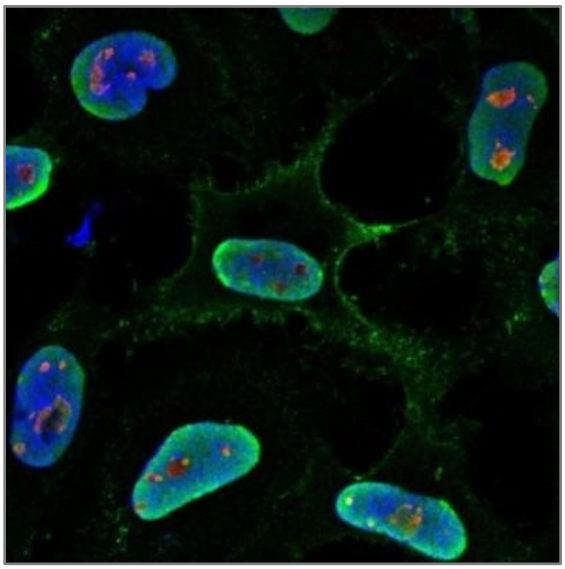
---

## Researchers identify protein role in pathway required for Ebola replication

## May provide insight into novel therapeutic approaches

### Original article from Science News, July 26, 2016

A newly identified requirement of a modified human protein in ebolavirus (EBOV) replication, may unlock the door for new approaches to treating Ebola.



EBOV is one of the most lethal human pathogens known and causes severe hemorrhagic fever in humans. When EBOV makes copies of itself inside cells, it does so by taking over and hijacking parts of that host cell's basic machinery to make its own proteins. The most recent outbreak in 2014 has illustrated the lack of understanding of viral pathogenesis and highlighted the need for increased study of how the Ebola virus replicates.

In the study, fragments of the virus that were not infectious were used to study viral gene expression. Small molecule drugs were used to inhibit the function of a cellular pathway associated with protein synthesis. These drugs and other pathways decreased viral gene expression which suggested that the pathway the drugs blocked is important for the replication of EBOV. To confirm this, the team worked with collaborators at the University of Texas Medical Branch who tested what happened to the ability of EBOV to make copies of itself in the presence of one of the small molecules that they had studied. They found the EBOV made fewer copies of itself when the drug was added. The findings appear in the journal *mBio*.

To explore why this occurred, the study looked at what happened to specific viral proteins when the pathway was on and off. They found that one of the EBOV proteins, VP30, accumulates in cells when the pathway is on, and it does not accumulate when pathway is turned off. These results suggest that VP30 is the only virus protein for which this happens.

"One protein made by the virus requires an unusual component of the host protein synthesis machinery. We found that if you block the function of this component the virus has problems making copies of itself. Thus, by decreasing how well the virus can make one protein we have an effect on the entire replication cycle," explained corresponding author John Connor, PhD, associate professor of microbiology at Boston University School of Medicine.

According to the researchers these findings identify a uniquely modified human protein that is required for Ebola virus to grow in cells. "Targeting this human protein could represent a new target for Ebola therapeutics. These studies can help us to understand and combat active and dormant Ebola virus infections," he added.

### Journal Reference:

Michelle E. Olsen, Claire Marie Filone, Dan Rozelle, Chad E. Mire, Krystle N. Agans, Lisa Hensley, **John H. Connor**. **Polyamines and Hypusination Are Required for Ebolavirus Gene Expression and Replication**. *mBio*, July 2016 DOI: 10.1128/mBio.00882-16

---

## Facing Down the World's Deadliest Pathogens in a BSL4 Lab

## Researchers reach a crucial milestone despite the challenges of working under astronaut-like conditions

### Original article from Scientific American, Bob Roehr on April 5, 2016

*Infection of human cells with Hendra virus (green) is critically dependent on fibrillarin (red), a host protein that resides deep within the cell nucleus (blue). Credit: Deffrasnes C, Marsh GA, Foo CH, Rootes CL, Gould CM, Grusovin J, et al. (2016)*

Ebola, smallpox, plague—the rogue's gallery of highly infectious deadly pathogens is frighteningly long and their potential for havoc is great, which is why they can only be studied within the tightly controlled confines of a

biosafety level 4 (BSL4) facility. The precautions make work in a BSL4 extremely demanding, slow and physically taxing, which is one reason such research lags behind studies of less-lethal organisms.

An Australian research team, however, recently reached a milestone when it became the first to screen and catalogue all of the genes activated by a BSL4 pathogen when it infects human cells. Their focus was the obscure but deadly Hendra virus, which causes respiratory disease in horses and can cross over into humans; they recently published their findings in PLoS Pathogens.

The researchers used siRNA—small bits of synthetic RNA employed to silence an individual gene—in cells placed in the well of a microarray plate, then exposed the cells to the virus and examined where the Hendra thrived and where it died. Little or no virus in a well meant that the siRNA-suppressed gene was important for viral replication, explains molecular biologist Cameron Stewart, who led the effort at the Commonwealth Scientific and Industrial Research Organization (CSIRO), Australia's national science agency.


*A scientist walks through the first air pressure resistant (APR) door at a biosafety level 4 (BSL-4) laboratory Credit: NIAID*

The approach was simple but the scale was enormous, as there were multiple wells for quality control and the process was repeated for each of the approximately 20,000 human genes. It would have been difficult in a regular lab, but took years of work in the physically challenging setting of a BSL4.

"Several hundred proteins are involved to cause infection, but the one with the largest impact was a protein called fibrillarin," Stewart says. "If you reduce the catalytic activity of fibrillarin you can block Hendra virus infection." That was surprising, he explains, because "fibrillarin resides deep within the nucleolus of the host cell…[where it] methylates ribosomal RNA molecules, which then go on to form ribosomes," but its full function may not be completely understood.

Silencing the gene that produces fibrillarin also stopped Nipah virus from replicating. Nipah is another henipavirus, a close cousin to Hendra with a high mortality rate in bats and humans in a zone stretching from Australia to Bangladesh. In fact, fibrillarin's function appears to be similar across the entire paramyxovirus family, which includes measles and mumps, so perhaps understanding fibrillarin as a target for intervention and designing the right treatment for it could work against a broad range of viruses.

## BSL4 Facilities

The continued emergence of deadly infections such as Ebola, MERS and SARS, as well as the terrorist use of anthrax in 2001—when spore-laced letters sent to elected officials in Washington and the news media killed five people and sickened 17 others—made government leaders aware of the need for more and better BSL capacity,

and they have since provided substantial, sustained funding to support such facilities. Still, only a few dozen labs in the world are certified as BSL4 facilities; some are very small and only work on diagnostics, or cell cultures, or a single species of animals.

Most descriptions of a BSL4 facility focus on the physical aspects: elaborate negative-flow air filtration systems, airlocks to enter the "hot" space containing the pathogens, "space suits" with their own air supply systems, and rigorous decontamination procedures when exiting. In some ways it is as arduous as exploring the polar regions or outer space.

As are the demands placed upon the men and women who work every day in the bulky suits and restricted environment.

"Very quickly you learn not to have a coffee or go in feeling hungry," says Glenn Marsh, the molecular biologist who did much of the physical work inside the Australian BSL4. "The negative airflow through the suit dehydrates you fairly quickly, so we try to be no more than about three hours at a time in a suit. It is very tiring."

**"**There is nothing worse than being in the suit and having a runny nose," says Lisa Hensley, deputy director of NIH's Integrated Research Facility at Fort Detrick, Maryland. "You can't blow your nose, so people got very creative with towels around their neck so they could blot their nose. And what do you do if you sneeze? You can't clean your face shield." That's why they urge researchers to use judgment about when to "suit up."

Equipment failure is another challenge. "On more than one occasion Glenn would call me up and say, 'The robotics are broken. We can't fix it.' We just had to turn everything off. The equipment had to be removed from the BSL4 lab, and it had to be decontaminated before it could be fixed," Stewart recalls. And the cells that had taken two weeks to develop had to be discarded. It added even more time to the multi-year Australian project.

Hensley says the Fort Detrick lab was designed to minimize some of these issues. It is one of the largest BSL4 labs in the world, and one of the few built to include imaging capacity for animals using CT scans and MRIs. That equipment requires a lot of maintenance, so the facility was creatively designed with much of the machinery in a "cool" portion of the lab, where normal precautions are sufficient, and a tube running in from the strictly controlled "hot" part of the lab; the research animal is placed on a moving bed in the tube for imaging.

Another way researchers have sought to reduce time in a BSL4 facility is by constructing a pseudotype virus, a chimera that artificially combines elements from two different viruses which can be studied under less-restrictive conditions. Boston University microbiologist **John Connor** has done this with Ebola. He says he combined glycoproteins from the outer shell of the virus, which "unlocks a pathway for the virus to get into the cell," with core functional genes from the vesicular stomatitis *virus,* which poses little risk to humans. This allows him to work in a lower-level BSL2 facility. Connor says the approach can work with some stages of the viral life cycle but not with others, and experiments on a pseudotype will always have to be confirmed using the actual virus; sometimes the two organisms behave differently.

The ultimate goal of BSL4 research is not simply to generate knowledge, but to advance toward prevention and treatment of deadly diseases. Stewart says his team's initial work has not only identified fibrillarin as essential for viable paramyxovirus replication—it also has shown that one can "deplete fibrillarin from cells or block its catalytic activity and the vast majority of cellular proteins still get made within the cell," which suggests it is a safe target for intervention. He hopes they can develop an antiviral drug that will be effective against the entire family of paramyxovirus.

## Ebola Returns: 2nd Case of Relapse Raises Questions

### Original article from: LiveScience posted on October 20, 2015 by Ashley P. Taylor

Scottish nurse Pauline Cafferkey — who became sick with Ebola about a year ago and recovered, but then became very ill again last week with what may be a relapse of the deadly virus — is now improving.

"Pauline Cafferkey's condition has improved to serious but stable," representatives from London's Royal Free Hospital said in a statement Monday (Oct. 19).

Hospital representatives said on Oct. 9 that the nurse had developed an "unusual late complication" of the virus, and reported last week that she was "critically ill." Cafferkey originally became sick with the disease in 2014 while

caring for Ebola patients in Sierra Leone, becoming the United Kingdom's first Ebola patient. The nurse is now being "treated for Ebola in the high-level isolation unit," according to the hospital's statement last week.

Post-Ebola complications have been reported from both the 2014 outbreak and previous ones, **Dr. Nahid Bhadelia**, an infectious-disease specialist at Boston University, told Live Science. Another health care worker who also became infected while treating patients in Africa, U.S. physician Ian Crozier, has reported that he suffered from hearing loss, back pain, seizures and vision problems since he recovered from Ebola last year. These are the kinds of symptoms many Ebola survivors have, Bhadelia said.

But cases of Ebola relapse, or recurrence — severe, sudden illness associated with the detection of the virus in the body — are different from these complications, said Dr. Jesse Goodman, an infectious-disease expert at Georgetown University. Cafferkey's case is the second documented instance of probable viral relapse in a recovered Ebola patient, Goodman said.

The other case was Crozier, Goodman said. Nine weeks after Crozier's blood was found to be Ebola-free, he suffered severe inflammation (uveitis) of his left eye. Tests of the fluid within the eye revealed that the Ebola virus was still there, and replicating.

The distinction between "complications" and "relapse" is somewhat blurry, Goodman said. After the acute infection subsides, Ebola seems to persist in several parts of the body where the immune system is less active, such as the eye, where Crozier's Ebola flared up; the brain; the placenta; and the testes, Bhadelia said.

It's possible that the rare cases of relapse, as well as the more common post-Ebola complications, could be related to the lingering virus, Goodman said.

## Disease relapse

Although little is known about Ebola relapses, other viruses are known to linger in the body and then come back after a person has recovered from an initial infection, Bhadelia said.

For example, varicella-zoster virus (VZV), which causes chicken pox, "hides away in your nerve roots" in a dormant, inactive state, Bhadelia said. When the immune system is weakened, either by disease or aging, the virus can reactivate and return as shingles, she said.

Other viruses in the herpesvirus family, which includes VZV, are also known to have this life cycle of infection, latency and reactivation, Bhadelia said.

However, unlike herpesviruses, Ebola and similar viruses that cause hemorrhagic fever have not been previously known to go through phases in which they lie latent, waiting in the body, Goodman said.

"That's part of the reason why everybody's so surprised" by the cases of Crozier and Cafferkey, in whom the Ebola virus seems to have hidden away and then returned, he said.

## New questions

The big question that remains is how frequently relapses may occur among the tens of thousands of Ebola survivors in West Africa, Bhadelia said.

The two cases of probable relapse "tell us that this can happen," but not how frequently, Goodman said. "It's likely not to be that common because it hasn't been described in previous outbreaks," he said.

Goodman stressed that these cases of relapse should not be a reason to cast stigma on Ebola survivors because there have been no documented cases of disease transmission as a result of casual contact with Ebola survivors.

"We have no evidence that survivors in general, who may have some small amount of virus in their immune-protected sites, are any threat to the public at all," Bhadelia added.

Editor's note: This article was updated on Oct. 21 so that joint cartilage is no longer listed among the sites in the body where the Ebola virus has been found to persist after a person has recovered from their infection.

*Follow Ashley P. Taylor* @crenshawseeds. *Follow Live Science* @livescience, Facebook & Google+. *Original article on* Live Science.

## Moving from A Culture of Outbreak Response to One of Outbreak Prevention

### Original article from Science Views the News, by Elke Mühlberger and Nahid Bhadelia, June 27, 2016

The 2014-2015 Ebola epidemic was the largest filovirus epidemic in recalled human history. It claimed over 11 thousand lives, leading to twice as many total cases, and affecting the health of an exponentially larger population by debilitating already straggling health systems.

Evaluating factors that led to the emergence and spread of Ebola in West Africa at just an alarming rate is just as important as examining how the epidemic enfolded in relative slow motion -into the disaster it was- over a span of two years without swifter action from the international community.
Many commissions and reports in the wake of the epidemic have posited recommendations to address these issues.

As a clinician who cared for Ebola patients in this outbreak in West Africa and a researcher who has worked on this pathogen for more than 25 years, we offer some insight into lessons learned by us in the aftermath of the last two years.

*Freetown in August 2014, a typical roadside checkpoint for temperature (By Nahid Bhadelia)*

## Preventing epidemics

First and foremost, the events in West Africa reiterated the importance of a reliable public health and health delivery system in preventing outbreaks from becoming epidemics. At the terminal end of the international surveillance system for emerging diseases are communities without access to care and health facilities with varying capacity to test and report infections.

This creates a consistent blind spot in our ability to conduct early detection of human cases and we lack the ability to swiftly respond with preventative measures. Ebola virus was not identified as the causative agent of the recent epidemic until 3 months after the index case.

The poor quality of data and sometimes its complete dearth also makes it impossible to ascertain the dimensions of ongoing outbreaks, as is the case with the current Lassa fever outbreak in West Africa.

Additionally, lack of longitudinal engagement between patients who suffer from emerging pathogens such as Ebola virus and good quality medical care also deprives us of information regarding the complete clinical presentation of these diseases.

The post Ebola virus disease syndrome revealed the full scope of what this virus can do in humans. It took the detection of these symptoms in returning American and European clinicians to determine that this disease entity was widely experienced not just by Ebola survivors in this epidemic but also prior ones.

The current Zika epidemic provided the same lesson in quick succession, revealing how microcephaly and neurological diseases such as Guillain-Barré were present among those infected over two years ago in French Polynesian outbreak.

Hence, we as an international community need to stop moving from outbreak to outbreak and put in the hard work required to create good sentinel surveillance and patient care. This lesson is particularly poignant in light of the recent shift of funding from Ebola recovery meant for health systems strengthening to Zika efforts by the US government.

Secondly, when it comes to outbreak response, we believe there is a false dichotomy between research and disaster relief, which is often created due to resource limitations. When there are limited physical and human resources, clearly outbreak response should be paramount.

However, we believe that the care of patients with emerging diseases is in fact research as such care is often based on little evidence and each patient is adding data to our knowledge base and in turn improving care for all subsequent patients. Compared to large number of Ebola cases seen over the last two years, the knowledge gathered about this disease is minuscule.

By the time many diagnostic platforms and medical countermeasure trials were initiated in West Africa, the outbreak was already ending. By reframing the special case of outbreak response with emerging diseases as research, we can draw attention to the unique ethical issues related medical care in these situations and redefine the amount and type of resources needed to address these outbreaks at the outset. Additionally, such reframing also then reveals the need to strengthen research capacity in affected areas as a long-term strategy.

*Infection control training for survivors in Port Loko and Kono district of Sierra Leone. Here Ebola survivors who wanted to be employed to return to ETUs to help are undergoing training in infection control and use of personal protective equipment (by Nahid Bhadelia)*

## Lessons learned

An important lesson of both the Ebola and Zika outbreaks is that we have to take emerging pathogens seriously even if the worst-case scenario has not happened yet and invest in research.

It was only because considerable NIH and DoD funding was put into Ebola virus remedies years before this devastating outbreak happened that we were in a fortunate situation to have promising vaccine candidates which have successfully been used in ring vaccination campaigns to prevent the re-ignition of the Ebola epidemic in West Africa.

Work on Zika virus was deemed to be unfundable before the pictures of the microcephaly babies made their way around the globe. Now we are begging for a vaccine, but it will take time and resources to come up with one that can be used in humans. And Zika virus won't be the last of unwelcome guests raising major public health concerns.

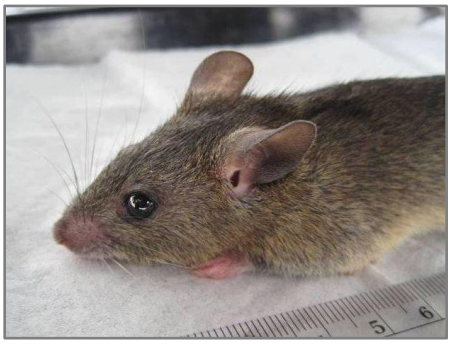
They are out there, in remote areas, and they do not ask for permission to make their way into the human population. The question is not if but when we will be hit by the next HIV, Ebola, Zika, and what we can do to be prepared.

http://www.scienceviewsthenews.com/moving-from-a-culture-of-outbreak-response-to-one-of-outbreak-prevention/

## "Zika Isn't The Only Outbreak; Nigeria Struggles To Rein In Lassa Fever"

**Original article from National Public Radio: Goats And Soda. Online.**
**Nahid Bhadelia and Olukemi Adekanmbi, March 4, 2016.**

*The multimammate mouse can transmit Lassa virus to humans. The virus is likely spread when the rodent urinates or defecates on grain supplies. US National Library of Medicine, National Institutes of Health*



In the world of public health, a lot of the media attention is focusing on the Zika outbreak in Latin America, but that's not the only disease on the rise. Nigeria is experiencing a smoldering Lassa fever outbreak. Since August 2015, almost 20 states have seen 175 confirmed and suspected cases and 101 deaths. The outbreak has poured into neighboring Benin, where 68 cases and 23 deaths have been reported.

Lassa fever, which is caused by an arenavirus, can affect multiple organs and cause bleeding in late stages. It's seen with some regularity every year in Nigeria. Since 2012, there have been 1,723 cases and 112 deaths, according to Nigeria's Center for Disease Control.

But in the current outbreak, Nigeria's ability to control the spread has been limited. There are concerns that patients are not seeking care in time either because they can't afford it, can't get to a health facility or don't recognize the symptoms as a sign of potentially serious illness. And so there is no true sense of the scope of the outbreak.

How is it possible that Nigeria, which not too long ago was widely praised for averting the Ebola outbreak, is having trouble controlling an outbreak that occurs almost seasonally? The Lassa outbreak reveals a few inherent cracks in Nigeria's system and raises good lessons in determining how a country or region can best respond to emerging infections.

Nigeria's response to Ebola was no doubt impressive, particularly given the fact that the spread of the disease in Lagos, the capital city and home to some 20 million people in Africa's most populous nation, would have been disastrous. On July 20, 2014, Patrick Sawyer, a Liberian national, arrived in Nigeria on a commercial flight. He was ill on the flight and was immediately taken to a private hospital. This imported case resulted in 20 confirmed infections and claimed eight lives.

Nigeria quickly made the diagnosis in the initial case of Ebola within its borders. That diagnosis allowed the mobilization of a public health infrastructure, which is much stronger than other countries in West Africa due to the investment made as part of the campaign to eradicate polio over the past 20 years. The polio campaign led to creation of emergency operations centers at the national and state levels. So Nigeria was able to effectively implement contact tracing and monitoring of exposed individuals, curtailing the outbreak in the country.

But Nigeria's ability to rapidly control Ebola was also related to a series of fortunate small coincidences rather than a foolproof system. The first of these breaks was the fact that Ebola was already rampant in neighboring countries before it arrived in Lagos, giving Nigeria the time to organize its response. Second, as opposed to the rampant, unchecked spread of Ebola in rural areas of Sierra Leone, Guinea and Liberia, Ebola first came to Nigeria through Lagos, and specifically, to a fairly well-quipped hospital with experienced doctors. An astute clinician, the late Dr. Stella Adadevoh, took care of Patrick Sawyer. She had the clinical acumen to suspect the diagnosis and ensure that her patient was tested. She herself later succumbed to the infection.

The Lassa virus, which is carried and transmitted by rodents for the most part, poses different challenges. Generally, 80 percent of those infected remain asymptomatic, while others can present with fever, weakness, nausea, vomiting, diarrhea and, in advanced cases, bleeding and coma. Overall mortality is 1 percent, while in severe cases it can be up to 15 percent. Most cases are mild and treatment is available with an antiviral medication, ribavirin, if given early in the disease. Interestingly, the death rate in the current outbreak is much higher than previously seen — almost 70 percent of the 83 laboratory confirmed cases died. The reasons are unclear.

The virus can be transmitted when food contaminated with rat excrement and urine is eaten or person-to-person if there is direct contact with the bodily fluids of an infected patient. As expected, poorer communities that are plagued by a larger rodent population are at higher risk, requiring government investment in rodent control (and causing a run on rat poison in local markets).

Public behavior change is also required to stop the spread of the disease, including hand washing, proper storage of food to keep rodents at bay and encouragement to seek care. Although the Nigerian government has been actively investing in radio jingles, posters and TV ads, the response from the public has been lackluster. That was not the case when Nigeria launched Ebola awareness campaigns. Perhaps Lassa does not seem to invoke the same sense of urgency in the general public.

Additionally, Nigerian hospitals, particularly in the public sector, are poorly equipped when it comes to infection control resources. Many patients actually buy the gloves for their doctors to use and keep them at their bedside. Hospitals and laboratories have been shown to be potential sources for the spread of not only Lassa, but many communicable diseases.

The Lassa outbreak also brings to the forefront the huge gap still to be covered in data collection and information management in the Nigerian public health system — an issue that still plagues most resource-limited countries. Cases may be missed when the patients were either not tested because they lived in a region that simply could not

perform diagnostic exams or because their physician didn't report the case. Nigeria still needs to invest in modernization of its reporting system as well as engage physicians to actually report cases in a timely manner.

The biggest barrier by far is lack of access to medical care. For a case to be diagnosed, patients actually have to visit a health facility. In Nigeria, individuals must pay out-of-pocket for a large chunk of health care expenses, and more than 70 percent of the population lives in poverty. So many people delay seeking medical attention until it might be too late to make a difference — and meanwhile could be spreading disease to others.

On March 1, Nigerian press reported a cluster of three deaths from Lassa fever in Kaduna State in the northwest part of the country. A pregnant woman came in to a hospital for a caesarean section. She turned out to have Lassa fever and later died of the disease. The physician and nurse who cared for the woman became ill and died; they were diagnosed with Lassa after dying. These cases sadly exemplify the impact of delayed diagnosis. Had the pregnant woman been diagnosed, measures could have been put in place to protect the health care workers. These failures in the system outline the work ahead for Nigeria.

*Olukemi Adekanmbi is an infectious diseases physician at University of Ibadan College Hospital in Nigeria.*

*Nahid Bhadelia is an infectious diseases physician at Boston Medical Center and Director of Infection Control and Medical Response at National Emerging Infectious Diseases Laboratories.*

http://www.npr.org/sections/goatsandsoda/2016/03/04/468955167/zika-isnt-the-only-outbreak-nigeria-struggles-to-rein-in-lassa-fever

# NEIDL Faculty Recognition

An indication of the reputation of faculty is best exemplified by their selection as invited speakers in national and international forums, service on review panels and service on editorial boards of journals. Other forms of recognition include being sought after because of their experience and ability to use their expertise to explain a story to the news media about current events. NEIDL faculty continue to be recognized as summarized below.

## Invited Speakers (National and International Forums)

**Nahid Bhadelia**

- *Lessons from Ebola*. North Carolina Central University, Blue Cross Blue Shield of North Carolina Speaker Series. October 27, 2015
- *Insight for Animal Model Research from West African Clinical Experience*. Filovirus Animal Non-Human Research Group, Clinical Subcommittee. October 20, 2015

**John Connor**

- *Virus Detection Through Photonics and Transcriptomics*. Rocky Mountain Laboratories, Hamilton MT. July 2015
- *Hemorrhagic fever viruses: addiction to host factors and host responses to infection.* Mt Sinai School of Medicine, NYC, NY. August 2015
- *I Inhaled What? The Immune Response to Aerosolized Viruses*. Boston University School of Medicine (Pulmonary Section). October 2015
- *Detecting viruses outside the cell, and blocking their replication inside.* University of Arkansas Medical School. March 2016

**Paul Duprex**

- *Illuminating pathogenesis: when viruses "jump"!* Friedrich Loeffler Institute, Insel Riems, Germany. September 29, 2015
- *Illuminating pathogenesis: when viruses "jump"!* Department of Microbiology, Cornell University, Ithaca, PA, USA. October 10, 2015
- *Modeling the evolutionary trajectories of an ever expanding morbillivirus genus: getting in, getting about and getting out and about.* Harvard Medical School, Boston, MA, USA. March 16, 2016

**Rachel Fearns**

- *Initiation of paramyxovirus transcription and genome replication*. Harvard Medical School, Boston, USA (September, 2015)
- *Analysis of the activities of the RSV polymerase*. Novartis Institutes of Biomedical Research, Emeryville, USA (October, 2015)
- *Analysis of the activities of the RSV polymerase*. Merck, West Point, USA (October, 2015)
- *Initiation of paramyxovirus transcription and genome replication*. University of Glasgow, Glasgow, UK (June, 2016)

**Horacio Frydman**

- *Wolbachia manipulation of gut microbiota*. 9th International Wolbachia Conference, Lamington Plateau, Queensland, Australia. (July, 2016).
- *Wolbachia and the mosquito stem cell niches.* Harvard T. H. Chan School of Public Health, Department of Immunology and Infectious Diseases. (December, 2015)

**Thomas Kepler**

- *Statistical Phylogenetic Analysis of Post-Immunization Clonal Dynamics.* Tenth Annual Immunotherapies and Vaccine Summit. Novel Vaccines: Emerging Technologies. Marriott Long Wharf, Boston MA. 25-26 August 2015
- *Evolutionary Dynamics in the Antibody Response.* Innovations in Biological Computation Symposium, UNC Chapel Hill, NC. October 27, 2017

- *B cell lineage dynamics during serial immunizations*. Vaccines Against Antigenically Variable Viruses. Ames, IA. November 6-8, 2015
- *The Ig Repertoire of the Rhesus Macaque.* Antibody Engineering and Therapeutics Annual Meeting, San Diego CA. December 7-10, 2015.
- *Evolutionary Dynamics in the Antibody Response.* Laufer Center for Quantitative Biology Seminar. Stony Brook University, NY. March 11, 2016.
- *B-Cell clonal dynamics in the repeated anthrax vaccine in humans.* 12th Annual Protein and Antibody Engineering Summit, Boston MA. April 27, 2016
- *B-Cell clonal dynamics in the repeated anthrax vaccine in humans*. Influenza Immunology: Data, Systems and Models. Yale University. June 24, 2016.
- *2016 Adaptive Immune-Receptor Repertoire.* (AIRR) Community Meeting II: Progress in Standards, Tools, and a Common Repository, NIAID Campus, Rockville MD. June 27-30, 2016. (Co-organizer with Felix Breden and Jamie Scott, Simon Fraser University)

**Igor Kramnik**

- *Host directed therapy of TB: small molecules that regulate macrophage responses to Interferon-gamma.* RePORT Meeting, Boston, MA. September 22-24, 2015.
- *Strategies for the development and pre-clinical testing of the "necrotic granuloma"-directed therapies US*. Japan TB/Leprosy Panel Meeting, Bethesda, MD. January 11 – 14, 2016.
- *Control of Lung Damage and Carcinogenesis in TB: Genes Meet the Microenvironment*. Keystone Meeting "Tuberculosis Co-Morbidities and Immunopathogenesis" , Keystone, CO. February 2 - March 3, 2016
- *Necrosis in pulmonary TB granulomas: mechanisms and therapeutic approaches*. Lung Tissue Inflammation: Pathogenesis, Regulation and Immune Response. Moscow, May 11 -13, 2016.

**Elke Mühlberger**

- *Loud and quiet – how human macrophages respond to ebolavirus infection*. NIH/NIAID Rocky Mountain laboratories, Hamilton, MT. May 11, 2016.
- *Loud and quiet – how human macrophages respond to ebolavirus infection*. Annual Conference 2016 of the Society for General Microbiology, ACC Liverpool, UK. March 21-24, 2016.
- *Loud and quiet – how human macrophages respond to ebolavirus infection.* Women in Science and Engineering Research (WISER), Mayo Clinic Center for Biomedical Discovery, Rochester, MN. December 18, 2015.
- *Not so silent – How primary human macrophages respond to Ebola virus infection.* Dept. of Microbiology, University of Rochester, Rochester, NY. October 6, 2015.
- *Kill the killers – Inactivation of BSL-4 pathogens*. 2015 New England Biosafety Association Symposium. Broad Institute, Cambridge, MA. September 10, 2015.

## International Meeting Organizers/Chairs

**Gerald Keusch**. Co-Chair of the Committee on Clinical Trials during the 2014-2015 Ebola Outbreak, National Academies of Sciences. (*more information on this committee is presented below*)

## Honors

**Nahid Bhadelia**

- Alumni Active Citizenship and Service Award, Tufts University, Medford, MA. 2016
- Fletcher Women's Leadership Award, Fletcher School of Law and Diplomacy, MA. 2016
- Woman of the Year, India New England News, MA. 2015
- Sara's Wish Foundation Grant for Ebola Survivors Infection Control Training, MA. 2015 – 2016

**John Connor**. American Society of Virology Ebola FAQ team

**Rachel Fearns**. Hartwell Individual Biomedical Research Award, 2015

**James Galagan**. Distinguished Faculty Fellow, College of Engineering, Boston University, 2016

## Editorial Boards

**Paul Duprex**

- mSphere, American Society for Microbiology, Senior Editor
- Journal of General Virology
- FEMS Microbiology Reviews

**Rachel Fearns**

- Virology

**James Galagan**

- BMC Infectious Diseases
- Fungal Genetics and Biology

## Study Sections and Grant Review Panels

**John Connor**

- Reviewer NIAID international grant panel November 2016
- Reviewer NIAID SRG DDR study section 2016
- Reviewer Zika R21 study section 2016

**Rachel Fearns**

- Special Emphasis Panel ZRG1 IDM-W, NIH (July 2015)
- Special Emphasis Panel ZRG1 IDM-B, NIH (December, 2015)
- NIAID Investigator Initiated Program Project ZAI1 EC-M, NIH (January 2016)
- NSF (February 2016)

**James Galagan**

- Philips Genomics for Infectious Disease Advisory Board Member
- NIH, Prokaryotic cell and molecular biology study section
- NIH, Modeling and analysis of biologic systems study section
- Joint Genome Institute, Community Sequencing Program

**Igor Kramnik**

- PAR15-360 Mycobacterial Induced Immunity in HIV-Infected and Uninfected Individuals. April, 2016
- Canadian Institutes for Health Research
- National Research Foundation, South Africa

**John Samuelson**

- Ad-Hoc reviewer for three NIH study sections: Foreign RO1s, New Innovators, and R21/R33 for novel therapeutics.

## Advisory Council and Program Memberships

- Nahid Bhadelia and Elke Mühlberger. Filovirus Animal Non-Clinical Group (FANG), Bethesda, MD. FANG Human Clinical Data Subgroup, US Government Interagency
- Paul Duprex. 2010-2016 European Society for Virology Advisory Council
- Paul Duprex. 2015- 2018 American Society of Virology (Scientific Programs Committee Member)
- Paul Duprex. 2016-2019 American Society for Virology Communications (Committee Member)

## Committee on Clinical Trials during the 2014-2015 Ebola Outbreak

In late 2015, Gerald T. Keusch, MD, Director of the NEIDL Collaborative Research Core, was named Co-Chair of the Committee on Clinical Trials during the 2014-2015 Ebola Outbreak, by the National Academies of Science, Engineering and Medicine (NSF).

The NSF was commissioned to conduct a study by a joint group of government agencies comprised by National Institute of Allergy and Infectious Diseases (NIAID), the Food and Drug Administration (FDA), and the Office of the Assistant Secretary for Preparedness and Response (ASPR) at the Department of Health and Human Services. The goal of the study was to review the clinical research on therapeutics and vaccines conducted in Guinea, Sierra Leone and Liberia during the 2014-2015 Ebola virus disease (EVD) outbreak, in order to "explore and analyze the scientific and ethical issues related to clinical trial design, conduct, and reporting to draw conclusions and make recommendations on how to be better prepared in the future". You can obtain further information about the committee via this link:
http://www.nationalacademies.org/hmd/Activities/Research/ClinicalTrialsDuringEbolaOutbreak.aspx

According to Dr. Keusch, it was, to say the least, an interesting challenge for the committee, and an exercise that might in fact have some future benefits by taking an objective look back to identify lessons learned, including what to do and what not to do, and provide guidelines to improve the process from design to implementation and engage local professionals, the community, and community based organizations in the process. It was also clear this was no simple assignment; that getting clinical research up and running during a humanitarian disaster with products somewhere in the preclinical research phase, and little in the way of resources in place to care for patients and conduct clinical trials was an unparalleled challenge.

It was not until two months later, towards the end of February, that the members of the committee, a group of 16 respected U.S. and international colleagues, were identified and confirmed and the first meeting was held at the National Academies in Washington DC. Since then the committee has met in London, again in Washington DC, and Monrovia Liberia.

Nahid Bhadelia, who is also a member of the NEIDL Collaborative Research Core, provided her perspectives on the integration of clinical research and patient care in maximum containment to the committee at the June meeting, based on her experiences working in Sierra Leone during 2014-2015, an important theme to address and gain insights for improvement so that we are all better prepared the next time such a situation occurs. In the process NEIDL is becoming better known globally and we are learning more about setting our research priorities to increase our knowledge so that it can be applied to the development of solutions.

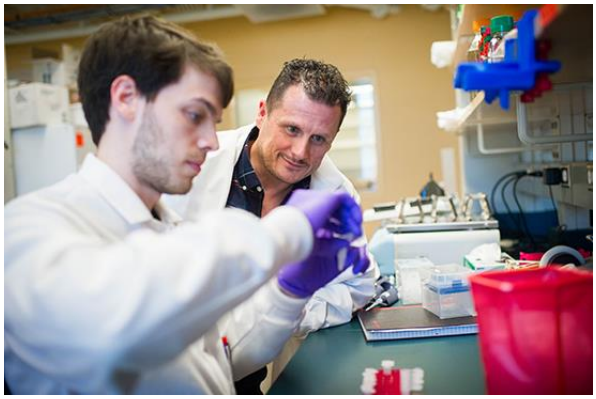
In late September of 2016, the committee will meet again in Boston, here at the NEIDL, to query and analyze the lessons learned from information gathered, and sort this massive amount of information into findings leading to conclusion, and from this derive recommendations for the future that will help advanced preparations, build human skills and infrastructure capacity, and better organize global governance and identify funding sources to be able to make the process of developing and implementing clinical trials in the course of outbreaks more efficient, effective and able to generate interpretable data on drugs and therapeutics without compromising clinical care and public health interventions. After the meeting, the final report will be written, reviewed, edited during the upcoming months and is expected to be release in the spring of 2017.

While NEIDL research priorities are largely at the earlier research stages of R&D for emerging infections, this assignment is relevant to our work and will surely provide insights for us that will help to shape our research agenda. It is central to our mission and role as an important component of a global research network to address EIDs, and to our efforts to reach out to colleagues around the world in different laboratories and hot-spots for disease emergence. It is directly related to the work our colleagues did during the West Africa Ebola outbreak during 2014-2015, and to the role of the Collaborative Research Core at NEIDL.

## Promotions

**From BU Today posted on March 11, 2016.**
**By Joel Brown**

**Paul Duprex**, originally from Northern Ireland, specializes in the genetics of viruses. Haiyan Gong (GRS'91), a native of China, has spent nearly three decades studying a single system in the eye and its relation to glaucoma, a leading cause of blindness worldwide. The two are among eight BU Medical Campus faculty recently promoted to full professor.



**"These promotions signify a major milestone in our faculty's careers," says Karen Antman, dean of the School of Medicine and provost of the Medical Campus. "Achieving the rank of professor recognizes their outstanding contributions plus their national and international reputations."**

Duprex, a MED professor of microbiology and director of the cell and tissue imaging core at BU's National Emerging Infectious Diseases Laboratories (NEIDL), studies the pathogenesis and spread of human and animal viruses, and has worked on the molecular biology of paramyxoviruses for more than 20 years. These include measles, mumps, and canine distemper viruses, which require Biosafety Level 2 containment. As a molecular virologist, he uses genetic techniques to manipulate the genomes of these viruses and make them glow green, red, or blue when they infect a cell. This allows him to illuminate diseases and track the spread of viruses inside and between hosts.

One side of his work is mapping the parts of the genes that build viruses and cause disease. The flip side is trying to identify changes in the genes that can transform viruses from killers into vaccines.

Duprex grew up in Lurgan, a small market town outside Belfast. He takes pride in his roots, but the self-described "child of the Troubles" grew up thinking a lot about the inequities of the world, and is a proponent the idea of global health. He arrived in Massachusetts a decade ago on a Bill and Melinda Gates Foundation Grand Challenges in Global Health grant to work at Johnson & Johnson as principal scientist on a project to make heat-stable vaccines.

"Millions and millions and millions of people are alive today because of vaccines," Duprex says, "and they're not just the preserve of us in the developed world—they really have been sent to all corners of the developing world, and that's brilliant."

Duprex earned a BSc in biochemistry and genetics at the Pirbright Institute and Queen's University Belfast, and a PhD in molecular virology from Queen's University, where he became a senior lecturer before coming to BU in 2010.

A special focus of his team's research is understanding what allows an animal virus to jump to a human population or prevents that from happening. "You need to pick apart these processes slowly and systematically," he says. "Here's the virus and here's a human cell. Can it get in? Can it replicate? Can it get out to spread infection? And can it spread from this host to that host? Understand all of those stages, and you begin to identify the weak points, and it's potentially possible to stop it."

*Paul Duprex (right) works with research technician Andrew Acciardo inside the NEIDL virology lab. Photo by Jackie Ricciardi*

Read Full Article in BU Today

# Education

The NEIDL participates in a number of educational opportunities for the broader community. It sponsors a seminar series for the scientific community, continues to sponsor its Biosafety & Biosecurity Grand Rounds, to promote the culture of safety, and sponsors symposia.

## FY16 Emerging Infectious Diseases Seminars

| Date | Speaker | Title |
|---|---|---|
| 09/16/15 | **Cesar Muñoz-Fontela, Ph.D.**<br>Heinrich Pette Institute | "Ebola Virus Immunology: A Tale of Mice and Humans" |
| 09/30/15 | **Emily Nelson** and **Judy Yen**<br>Boston University School of Medicine | "Ebola Virus Diagnostics in Sierra Leone" |
| 10/07/16 | **Kathleen A. McDonough, Ph.D.**<br>New York Department of Health | "Keeping up with the Neighborhood: Environmental Gene Regulation in *M. tuberculosis*" |
| 11/04/15 | **Benhur Lee, M.D.**<br>Mt. Sinai | "Henipaviruses: Not that Rare, Much more Diverse, Still too Dangerous?" |
| 11/19/15 | **Gary Kobinger, Ph.D.**<br>Public Health Agency of Canada | "A Decade of Ebola Work in the Field and on Vaccine and Therapeutics Culminating with the Biggest Outbreak and Real Solutions" |
| 12/03/15 | **Heinz Feldmann, M.D., Ph.D.**<br>NIH/NIAID | "Vaccines for Highly Pathogenic Viruses" |
| 01/13/16 | **Richard Webby, Ph.D.**<br>St. Jude Children's Research Hospital | "Transmission of Influenza Viruses at the Human-Animal Interface" |
| 01/20/16 | **Ulrich von Andrian, Ph.D.**<br>Harvard Medical School | "Vaccination to Prevent Mucosal Infections" |
| 02/03/16 | **Sean Whelan, Ph.D.**<br>Harvard Medical School | "Structure, Function and Inhibition of Large Proteins of Negative sense RNA Viruses – Single Polypeptide Chains that Catalyze Every Step of mRNA Transcription" |
| 02/22/16 | **Michael Katze, Ph.D.**<br>University of Washington | "Computational Biology, Genomics, (Epi)Genetics, and Systems Approaches: Unlocking the Mysteries of Deadly Virus Diseases in the 21st Century" |
| 03/23/16 | **Raul Andino, Ph.D.**<br>University of California San Francisco | "Virus Evolution during Acute Infection: Population Dynamics and Pathogenesis" |
| 04/20/16 | **Pamela Schwartzburgh, M.D., Ph.D.**<br>Nat Human Genome Research Inst, NIH | "Tuning T cell Responses" |
| 04/27/16 | **Trevor Siggers, Ph.D.**<br>Boston University | "Examining the Specificity of Immune Regulators using Protein-binding Microarrays" |
| 05/04/16 | **Matthias Schnell, Ph.D.**<br>Thomas Jefferson University | "Rabies Virus-based Vaccine Platform Against Emerging Infectious Diseases" |
| 05/11/16 | **Ronald Germain, M.D., Ph.D.**<br>NIAID, NIH | "Imaging Immunity: Developing a Spatiotemporal Understanding of Host Defense" |
| 05/18/16 | **Anita McElroy, M.D., Ph.D.**<br>Emory University School of Medicine | "Immune Responses to Highly Pathogenic Viruses–Do They Help or Harm the Host?" |
| 06/03/16 | **Marshall Bloom, M.D**.<br>NIAID, NIH | "The Enigmatic Biology of Vector-borne Flaviviruses" |
| 06/08/16 | **Darryl Falzarano, Ph.D.**<br>International Vaccine Centre<br>University of Saskatchewan | "Development of Animal Models and Countermeasures for Emerging Viruses" |

| | | |
|---|---|---|
| 06/15/16 | **Pedro F C Vasconcelos, Ph.D.**<br>Instituto Nacional de Ciencia e Technologia para Hemorrhagias Virais, Brasil<br>Belém-Pará, Brasil | "Zika Virus Epidemic in Brazil: Present Situation and Perspectives" |
| 06/22/16 | **Cesar Muñoz-Fontela, Ph.D.**<br>Heinrich Pette Institute | "Correlates of Immunity to Hemorrhagic Fever Viruses in Humans and Animal Models" |
| 06/29/16 | **Alyson A. Kelvin, Ph.D.**<br>Immune Diagnostics and Research | "Viral Pathogenesis and Transmission in the Mother-Infant Dyad: From Influenza to Zika" |

## Biosafety & Biosecurity Grand Rounds

| Date | Speaker(s) | Topic |
|---|---|---|
| 08/19/15 | **Matthew Rarick**<br>Director, NEIDL Facilities | "What is that Smell? – Growing Pains of an Expanding Operation" |
| 09/23/15 | **Bill Gibbons**<br>Director, NEIDL Biosecurity Core & Director of Public Safety, BUMC | "Insider Threat" |
| 01/20/16 | **John Tonkiss, PhD, SM(NRCM), CBSP**<br>Associate Director, Research Safety in High Containment | "Incidents, Near Misses & Safety Investigation Reports: 2015" |
| 02/17/16 | **Josh Ames**<br>Sr. Safety Specialist | "Waste Disposal: Issues, Concerns, and Close Calls" |
| 03/18/16 | **Jim Levin**<br>Director Animal Science Center | "Non-Human Primates from Tulane" |
| 05/25/16 | Research Occupational Health Program | "Random Drug Testing" |

## NEIDL supported educational symposia

### "Ebola, the Disease, and Immune Privilege"

**Symposium hosted by Boston University School of Medicine's**
**Office of the Associate Dean for Research**
**Thursday, October 29, 2015**

The Symposium featured invited guest speaker ***Ian Crozier, MD***, an infectious disease specialist who while helping to fight against the Ebola outbreak in Kenema, Sierra Leone in August 2014, contracted the disease and was evacuated to Emory University Hospital where he recovered. Two months later, after complaints of fading vision, it was discovered that while his blood was Ebola-free, the eye was not. The second invited speaker was ***Steven Yeh, MD***, Louise M. Simpson Professor of Ophthalmology, Emory Eye Center. He led the team that saved his vision.

The symposium included additional talks and discussions on immune privileged tissues, filovirus infections, infection control and testing, and the sequential care needed for patients surviving Ebola.

- **"Welcome & Introduction to Immune Privilege"**

  *Andrew W. Taylor, PhD*
  *Associate Dean for Research* and *Professor of Ophthalmology*

- **"Not so silent – How primary human macrophages respond to Ebola virus infection"**

  *Elke Mühlberger, PhD*
  *Associate Professor, Microbiology*

- **"2014-2015 Ebola epidemic: Clinical presentation and case management".**

  *Nahid Bhadelia, MD, MALD*
  *Assistant Professor, Medicine*

- ***"Ebola Dx and the U.S. clinical laboratory: From practical to practice to promise"***

  *Nancy S. Miller, MD*
  *Assistant Professor, Pathology & Laboratory Medicine*

- **"Eye Disease in Ebola Survivors: Individual and Global Health Implications"**

  *Steven Yeh, MD*
  *Louise M. Simpson Professor of Ophthalmology*
  *The Emory Eye Center -Atlanta, Georgia*

- **"A survivor's story -Dual citizenship at the Ebola bedside"**

  *Ian Crozier, MD*
  *Infection Disease Specialist*

- **Questions & Answers**

## Combatting Disease, Pursuing Cures: Infectious Diseases Research at BU

Research
Fall 2015 Events
FOR FACULTY, STAFF, AND STUDENTS

**Hosted by Ronald B. Corley, PhD**
**Director, National Emerging Infectious Diseases Laboratories**
**November 11, 2015**

This was one of a series of informal gatherings called and hosted by Boston University Office of Research to foster networking and research collaboration opportunities university-wide. This event featured infectious disease experts at BU.

**Participating researchers and presentation titles:**

| Name | Department | School | Title |
|---|---|---|---|
| Andrew J. Henderson, PhD | Medicine, ID<br>Microbiology | MED | Establishment and maintenance of HIV latency |
| Manish Sagar, MD | Medicine, ID<br>Microbiology | MED | Understanding HIV transmission to develop prevention strategies |
| Rachel Fearns, PhD | Microbiology | MED | Polymerase small molecule inhibitors |
| W. Paul Duprex, PhD | Microbiology | MED | When viruses "jump"! |
| Elke Mühlberger, PhD | Microbiology | MED | A rose is not a rose in Ebola virus-infected cells |
| Davidson H. Hamer, MD | Global Health Medicine | SPH<br>MED | GeoSentinel, an emerging infection surveillance network |
| Helen E. Jenkins, PhD | Biostatistics | SPH | Pathogens in space: predicting the next outbreak |
| Lawrence D. Ziegler, PhD | Chemistry | CAS | A nanoparticle enhanced light scattering approach for rapid bacterial diagnostics |
| James E. Galagan, PhD | Biomedical Engineering<br>Microbiology | ENG<br>MED | New approaches to antibiotic resistance |
| Kevin Outterson, LL.M., JD | Health Law | LAW | New business models for antibiotics |
| Muhammad H. Zaman, PhD | Biomedical Engineering | ENG | Good drugs or bad: How would you know? |
| Daniel Segrè, PhD | Biology<br>Biomedical Engineering | CAS<br>ENG | Modeling and engineering microbial communities |
| Lee M. Wetzler, MD | Medicine, ID<br>Microbiology | MED | Use of innate immunity to enhance vaccines |
| Thomas B. Kepler, PhD | Microbiology<br>Mathematics Statistics | MED<br>CAS | Antibody response evolutionary dynamics |
| John C. Samuelson, PhD | Molecular and Cell Biology<br>Microbiology | GDM<br>MED | Good fences make good neighbors: walls of pathogenic parasites |

## BUMC Provost Research Seminar
## Zika Virus: What we know clinically, public health aspects, and basic virology

**Tuesday, March 22, 2016, 3-5 pm**

### Welcome
**Karen H. Antman, MD**
BUSM Dean and BUMC Provost

**Ronald B. Corley, PhD**
Professor and Chair, Department of Microbiology, BUSM
Director, National Emerging Infectious Diseases Laboratories

### What We Know Clinically
**Robin Ingalls, MD**
Associate Professor, Medicine and Microbiology, BUSM
*Clinical Overview of Zika and Related Arboviruses*

**Athanasios I. Zavras, DDS, DMD, DScM**
Professor and Chair, Department of Pediatric Dentistry, GSDM
*Zika Virus Related Concerns in Dentistry (salivary transmission of the virus)*

### Public Health Aspects
**Donald M. Thea, MD, MSc**
Professor, Department of Global Health, BUSPH
Director, Center for Global Health and Development, BUSPH
Director, MD/MPH Program
*Zika: Epidemiology, Transmission and Population Risk*

### Basic Virology
**Rachel Fearns, PhD**
Associate Professor of Microbiology, BUSM
*Zika Virus Biology: Genetic and Phenotypic Differences between Old World and New World Zika Virus Strains*

### Public Health Aspects
**Davidson Hamer, MD**
Professor, Global Health, BUSPH
Professor, Medicine, BUSM
*Travel-associated Zika Virus Infection: Preliminary GeoSentinel Network Results*

### Panel Discussion
Moderated by:

**Christina Yarrington, MD**
Assistant Professor of ObGyn, BUSM
Maternal and Fetal Medicine, BMC
Director, BMC Community Health Center screening, identification and education of pregnant population

**John Connor, PhD**
Associate Professor of Microbiology
Boston University School of Medicine

**Joseph Finkhouse, PhD**
Associate Director, Health, Safety and Security
BU Global Programs
Former Fulbright Scholar to Columbia University

**Horacio Frydman, PhD**
Associate Professor of Biology
College of Arts and Sciences

## Medical Campus Experts Gather to Confer about Zika
## NEIDL acquires sample of virus for further study

**Barbara Moran, BU Today March 25, 2016**

After weeks of BU researchers trying to procure a sample of Zika virus, the pathogen linked to microcephaly and other neurological syndromes, the vial finally arrived at BU's National Emerging Infectious Diseases Laboratories (NEIDL) on March 22. NEIDL director **Ronald B. Corley**, a School of Medicine professor and chair of microbiology, announced the acquisition that day at a BUMC Provost Research Seminar. Zika, like dengue, mumps, and measles, is a Biosafety Level 2 pathogen, defined by the Centers for Disease Control and Prevention (CDC) as an agent that poses "moderate hazards to personnel and the environment."

*Donald Thea, director of the BU Center for Global Health & Development, spoke on the public health aspects of the Zika virus at a BUMC Provost Seminar March 22. "We are at the cusp of a really interesting part of the Zika virus investigation," Thea said. Photo by Cydney Scott.*

After weeks of BU researchers trying to procure a sample of Zika virus, the pathogen linked to microcephaly and other neurological syndromes, the vial finally arrived at BU's National Emerging Infectious Diseases Laboratories (NEIDL) on March 22. NEIDL director Ronald B. Corley, a School of Medicine professor and chair of microbiology, announced the acquisition that day at a BUMC Provost Research Seminar. Zika, like dengue, mumps, and measles, is a Biosafety Level 2 pathogen, defined by the Centers for Disease Control and Prevention (CDC) as an agent that poses "moderate hazards to personnel and the environment."


The sample was of the strain originally isolated in 1947, and it will allow scientists to grow and propagate the virus for study. The 1947 strain is the precursor to the virus causing the current outbreaks in South America and the Caribbean. Because samples of the modern virus are proving difficult to obtain, scientists at NEIDL will begin their work using the 1947 isolate while using published genetic data to make a clone of the modern Zika strain.

"There's a real need for us to be doing research on this virus. It's been seen in Boston and will be again," said John Connor, a MED associate professor of microbiology and a NEIDL researcher, who acquired the Zika sample from the Biodefense and Emerging Infections Research Resources Repository, a supply house for scientists studying infectious diseases. "Having the virus will allow us to ask important questions, like: what is driving the pathogenesis? How is the virus getting across the placental barrier? What is its replication like in mosquitos?" Connor said. "Without understanding the virus, it's hard to know how to block it."

Karen H. Antman, dean of MED and provost of the Medical Campus, began planning the Zika workshop about six weeks ago, when she became aware that people from BU's medical, dental, and public health schools were all talking about the virus, but not necessarily collaborating. "It's a rapidly emerging field—we want everyone doing research on this in the same room," says Antman. "Clinical people have blood specimens, lab people have techniques. We wanted them all talking to each other."

Zika grabbed the world's attention in fall 2015 when scientists in Brazil began to suspect a connection between the virus and microcephaly—babies born with small heads and neurological deficits—and also Zika's possible link to other neurological syndromes like Guillain-Barré. Since January 1, 2007, 59 countries and territories have reported transmission of Zika virus, according to the World Health Organization (WHO), and on February 1, 2016, the WHO declared the cluster of microcephaly cases and other neurological disorders a health emergency. So far, 258 cases have been reported in the United States, all introduced from other countries.

*The Aedes aegypti mosquito, the leading culprit in the spread of Zika virus. By James Gathany, CDC, via Wikimedia Commons.*

The Research Seminar, which included updates from virologists, epidemiologists, and physicians, revealed what scientists have learned about the virus since the 2015 outbreak in Brazil and how many questions remain.

"Zika is difficult to diagnose; the clinical symptoms are really vague," Robin Ingalls, a MED associate professor of medicine and microbiology, said during her clinical overview of Zika. Ingalls noted that an estimated 80 percent of people infected with Zika show no symptoms at all. Most people who get sick have a red, pimply rash that Ingalls called "very subtle," along with other symptoms—like fever, headache, fatigue, and malaise—that overlap with dengue fever and chikungunya, making the disease even more difficult to diagnose.

Lab tests "don't really make it much easier," she said. "While we can detect virus in the blood, it is only there for about a week after infection." After the first week, physicians can order blood tests that measure antibodies specific to Zika. Laboratories are reporting a backlog in these tests, however, with results taking as long as six weeks. Also, the tests can be difficult to interpret because of cross-reactions with similar viruses, like dengue, the patient may have been exposed to.

Many questions about transmission, especially from mother to fetus, remain unanswered, Ingalls said. "How can Zika evade the immune response of placenta? What is the critical time for exposure of the fetus? Is there something unique about Brazil that is increasing the risk of microcephaly?" she asked. "We're just seeing the tip of the iceberg, and we don't know what the long-term consequences of infection will be."

"It appears pretty convincing that Zika is linked to microcephaly," said Donald M. Thea, a School of Public Health professor of global health and director of the BU Center for Global Health & Development, who spoke on the public health aspects of Zika. "From an epidemiological perspective, the question is, how high is the risk?"

Much of Thea's talk focused on what scientists know about the transmission of Zika from mosquitos to humans, and from one human to another. He noted that scientists have isolated the virus from 10 species of *Aedes* mosquito, and from several other mosquito families as well. While *Aedes aegypti* is the best known, he said, *Aedes albopictus*—introduced into the United States in 1985—is the most worrisome because of its hardiness and wider range. "If efficient transmission is limited to *Aedes aegypti,* then the virus shouldn't get beyond Texas and the southeastern United States," areas with warm, moist air where that mosquito can thrive, he said. But if *Aedes albopictus* can spread the disease just as well, larger areas of the world may be exposed.

*BU's NEIDL received a sample of Zika earlier this week, which will allow scientists to grow and propagate the virus for study. Photo by Cydney Scott.*

Thea also explained what scientists currently know about human-to-human transmission. They have found that patients carry low levels of Zika virus in their blood after symptoms begin, but higher levels of the virus in urine, saliva, and semen for a longer time. (Scientists have also found Zika virus in cerebral spinal fluid and in breast milk.) Thea said that the risk of transmission through semen is especially worrisome. "The amount of virus in semen is very high," he said, noting that the viral count in semen can be 100,000 times higher than that in blood, and that scientists have measured Zika virus in semen as late as 62 days after infection. "A patient's semen contains virus before the onset of symptoms, but we're not sure how long the virus remains infectious. We are at the cusp of a really interesting part of the Zika virus investigation."

Also speaking at the seminar were Davidson Hamer, Athanasios I. Zavras, and Rachel Fearns. Hamer, an SPH professor of global health, explained how the GeoSentinel Network—a clinic-based global surveillance system that focuses on travelers, immigrants, and refugees—allows scientists to detect new infections and disease patterns, all with lab-confirmed diagnoses. He expects to publish preliminary GeoSentinel Network findings on Zika in the coming months. Zavras, a School of Dental Medicine professor and chair of pediatric dentistry, discussed the detection—and possible transmission—of Zika virus through saliva. Fearns, a MED associate professor of microbiology, described mutations in the Zika genome that may be helping the virus replicate, and spread among people, more efficiently.

"Up until about four years ago, proposing to study Zika was a dead end for funding. It wasn't very prevalent," Connor said during a discussion panel at the end of the seminar. "It's only the recent rapid spread and new adverse outcomes associated with infection that have made research to understand this virus a high priority."

http://www.bu.edu/federal/2016/03/25/medical-campus-experts-gather-to-confer-about-zika/

## Other NEIDL educational contributions

The NEIDL offers a number of opportunities for education and training outside of the conventional laboratory based training of undergraduate, graduate and postgraduate students. Given the nature of the NEIDL and its specialized infrastructure, we can offer unique training and educational opportunities to the BU and wider community not otherwise available. Two examples are identified below.

First, John McCall, the Core director of NEIDL IT in the BSL-4 laboratory, has been working with Engineering faculty and the Engineering Product Innovation Center (EPIC) to develop projects for students that will benefit the research programs in the NEIDL. McCall challenged the a team of Mechanical Engineering students (Zachary Kink, Grey Nagle, Tommy Sullivan, and Osi Van Dessel) "to supplement the methods available for monitoring the welfare of animals within containment rooms as well as to reduce the need for human entry in certain circumstances". The solution that the team developed is the ARGUS modular robotic system. This system allows for remote operation from outside the containment area. The robot requires no changes to existing laboratory protocols or safeguards. This gives veterinarians, technicians, and scientists an additional tool to observe the health and behavior of the non-human primates being studied. Additionally, the modular nature of the system permits future engineers to develop and implement new capabilities that will assist scientists in additional ways. Working again this year with Dr. William Hauser and David Campbell of EPIC, additional refinements are being planned.

Second, our Facilities core has created opportunities for engineers in training to intern in the NEIDL as part of their undergraduate training. Originally, NEIDL Facilities brought aboard one engineering student from Massachusetts Maritime Academy to build and test the program. That student just completed his third rotation in the NEIDL and has proven to be a valuable engineer and member of the Facilities staff. Our second student is about to begin her second rotation and a third student is coming on board in the September 2016. Both students are at Boston University. The students are given basic tasks to start, such as steam trap surveys, fire door regulations and NEIDL compliance, which familiarizes them with building systems and codes. They gain more knowledge of specialized systems, such as breathing air, humidifiers, HVAC, etc. as they are asked to assist with the mechanics and vendors on preventive and reactive maintenance issues. Our goal is to teach the students, which takes time and effort, but also to recover the investment by giving them meaningful tasks that build in complexity during their tenure. Ultimately, we hope that our program brings in serious and ambitious students that learn from us as much as we gain from them.

Finally, as outlined below (Community Engagement), the NEIDL continued for a second year to work with the School of Education to prove STEM education through an infectious disease/public health educational program called Identifying Infectious Diseases (ID2). More information can be found below.

# Community Engagement

Engaging and sharing information with the community is an important component of the NEIDL's mission. To succeed in this endeavor, the Community Relations Core ensures that the local community is informed in a timely, transparent and ongoing basis about the operations, safety, research and expertise of NEIDL personnel. We must continue and improve our efforts to inform and educate the community about what we do and why, while at the same time building and sustaining community trust about the NEIDL and its mission. Below are the highlights from this past year's activities.

## Web Site

The first place where the community can find out the latest information on the NEIDL is the website, which provides up-to-date information on the facility and the activities of NEIDL staff and researchers (www.bu.edu/NEIDL). Plans designed to support the culture of safety at the NEIDL and throughout the University are posted, as it the Incident Report for the NEIDL, which is posted quarterly. There is also a link to the Institutional Biosafety Committee and its public minutes. These postings are one way we can increase transparency with the community. Press releases and articles from local newspapers with information about the NEIDL and its faculty are also posted on the website. The minutes of our Community Liaison Committee are also found on the NEIDL web site.

## Community Liaison Committee (CLC)

The CLC continues to be an important group for promoting public participation and transparency at the NEIDL. Meetings are open to the public and provide an opportunity for key NEIDL personnel and researchers to provide regular updates on operational, regulatory, and scientific matters impacting the NEIDL. Community Relations has been actively involved in expanding the CLC to increase diversity and depth of expertise. This spring, we solicited applications in several local newspapers and received approximately eighteen (18) applications to join the CLC. The ten (10) community members selected will complement the existing seven CLC members. This expanded committee will allow the CLC to more clearly define its role, responsibilities and level of engagement. It will also permit the NEIDL to take advantage of the CLC's talents and expertise in ensuring effective communication and collaboration on programs involving the NEIDL and the community. They will be a key component in helping to develop strategies for additional community outreach and engagement activities. This expanded group will begin meeting in late September.

To ensure that community representatives continue to be involved in vetting research agendas before research is permitted, two members of the CLC have volunteered to extend their terms on the IBC. Previously, three members of the CLC gave their time and expertise to the Boston Biosafety Committee, the advisory group to the Boston Public Health Commission with respect to the BSL-4 permit and have agreed to continue to be resources as the need arises. As the CLC expands, other oversight groups will be interested in their knowledge and experience as additions to these committees.

Further, it should be noted that CLC members are invited, attend and participate in both tabletop and active simulated emergency response planning drills and exercises for the NEIDL with first responders (emergency, medical and other public safety personnel) to enable them to understand how emergency response procedures for incidents affecting the NEIDL are designed, evaluated and improved and implemented. This year they were involved in simulations involving transport of an injured NEIDL staff member to the Patient Isolation Unit at BMC and viewed the response of NEIDL staff and first responders to a simulated accident involving a truck transporting select agents to the NEIDL. They were very interested in our communications and transportation incident plans.

## Community Meetings

Representatives from the Community Relations Core are active in the community and will continue to attend neighborhood and local business meetings as well as community events on a regular basis. We sponsor and fund community activities either by the contribution of cash or through provision of University resources. We continuously seek and take advantage of opportunities to provide information on the NEIDL as appropriate and to be regularly seen in the community as a resource. In addition, this presence allows us to answer questions and identify and understand issues of neighboring residents.

## Tours

The Community Relations team plans, provides, and coordinates NEIDL tours both to the internal BU community (alumnae, faculty, staff and BU students) as well as external communities (local public health, regulatory officials, elected officials, business organizations, nonprofit community agencies, residents, and middle and high school students). These tours are beneficial in introducing these stakeholders to the NEIDL and giving them a first-hand view on how it functions and why. The addition of tour guides from other areas of the NEIDL, including Facilities, EH&S and Animal Core has proven informative and beneficial for both the guides and the attendees. It should be noted that as part of a summer tour with a group of teenage girls interested in STEM, we hosted a career panel composed of NEIDL researchers. From youth to retirees, all have been impressed with the facility and become ambassadors for the NEIDL.

In the past year, we have given over 34 official tours to a number of local community organizations such as: Retired Men's Association, Young Achievers School, and Boston Skeptics. Among the City and State government representatives who have taken tours this year are: BPHC Executive Director Monica Valdes Lupi, Secretary of Health and Human Services Mary L. Sudders, and City Councilor at Large Annissa Essaibi-George. In addition, students and faculty with varying research and academic interests, from the Medical and Charles River campuses, such as BU Summer Pathways Program, BU's AIM and RISE Programs have toured as have visitors from the Museum of Science, Harvard University, Harvard Institute for Learning in Retirement, MIT, Children's Hospital, South Korean delegates, University of Damman in Saudi Arabia, and Sanofi Pasteur. The largest group of visitors (50) this year was the Knight Science Journalism Program in Science, Technology and Society at MIT. This group of science writers was affiliated with major academic institutions and science publications nationwide.

## NBL/RBL Network Coordination

The NBL/RBL network is an organization of the NIAID funded centers from 13 academic research institutions which promotes sharing of practices for improving the operations and safety of these facilities. The NEIDL community relations staff collaborates regularly with other members of the NBL/RBL network via meetings, conferences and teleconferencing for the purpose of sharing information on community activities of each member and adopting best practices learned during these interactions. This April, the NEIDL and the Medical Campus hosted the 8th Annual NBL-RBL Networking Meeting. Representatives from 13 academic research institutions met for three days with peers from such areas as Biosafety, Lab Animal Care and Operations and Maintenance to discuss and share best practices. Executive Director Welch of the Elizabeth R. Griffin Research Foundation entertained us over a working dinner. In addition, we heard from and were educated about new trends in Biosecurity (Edward You-FBI), received information about Federal Policy Updates in Biosafety and Biosecurity (Dr. Chris Viggiani), Strengthening the Culture of Safety (Dr. Monroe-CDC) and tips on a Duty of Care: A New Lens for Viewing Biological Risk and a Culture of Safety (Dr. Nancy Connell- Rutgers Medical School). We will see our peers at the 9th Annual NBL-RBL Networking Meeting in April 2017 in Galveston, Texas.

*NBL/RBL network representatives at the 8th Annual NBL-RBL Networking Meeting, April 10-12, 2015*

## Educational Programs: Infectious Disease and Career Development

Identifying Infectious Diseases (ID2) is an infectious disease/public health educational program developed in partnership with NEIDL researchers and the School of Education to deliver a hands-on, participatory class to Middle School students. It is focused on infectious diseases and answers a variety of different questions. The ID2 class, taught by NEIDL researchers and post docs has been well received by both faculty and students.
In this fun and informative course, students perform hands-on work with the researchers, putting on personal protective gear (masks, goggles, gloves and coats), using pipettes, building biosafety cabinets, and answering important questions about infectious diseases: What do infectious diseases look like? How are they identified? What are their components? How are they transmitted? How is the research of infectious disease done in safe laboratory environment?

This year, we presented to 6th and 7th grade students in three diverse schools (traditional, pilot and total immersion Spanish); the William Monroe Trotter Innovation School, the Joseph J Hurley School, and the Lilla Fredrick Pilot Middle School.

Below are a few quotes from the students at the Trotter school:

"I wanted to thank you for picking me during CS. I'm happy that I did it and would want to do it again. It was awesome! I liked all three activities and the teachers are very good." -- Lee'el, age 11, Roxbury
"Thank you for taking the time to come out here and do a lesson with us. My favorite part was when we made our own viruses because in that part we learned different types of diseases that affect certain parts of your body." -- Kayleen, age 12, Dorchester


"My favorite part was the viruses and combining the viruses. You can see where and how viruses are made and how they can be stopped. Thank you because it was fun and it taught be more about science. When I'm older, I want to learn more about science. I already liked science before the class, but now I like it even more!" -- Welinson, age 12, Jamaica Plain

"I learned more about what's in your body. Like when we made the stuff with the candy, I learned how stuff looks like in the pictures from your body. I understood everything better when I made it myself. I learned about stuff with blood and about diseases. Before the class, I heard about stuff like Ebola but I didn't know anything more than the name and I didn't know how it affects and what it looks like. From the last station, we had a box and a machine that blows out smoke and we had to use gloves - and I liked how we had to use team work to find a way to work on it without it spreading. Before the class, I didn't think of science too highly, but now I am more interested in diseases and stuff." - Raynard, age 13, Roxbury

The Hurley School grade 7 comments were anonymous and are enclosed herewith: “We liked the quiz and the candy viruses”. “Please give souvenirs like erasers with NEIDL on them”. “We got to investigate stuff and we learned”. “It’s really interesting and you learn new stuff”. “I loved every station”. “Experimenting with viruses, making a B. S. C. and viruses”

In March, Community Relations coordinated Job Shadow Day with the Boston Private Industry Council (Boston PIC) on the BU Med Campus. Over 5 local high schools were represented and students were paired with BU professionals from Public Safety, EH&S, Radiation, Dental, IT, Community Relations and Facilities Operation. We also volunteered with other City agencies to participate in “mock job interviews” during Career Day at Madison Park Technical Vocation High School, the largest vocational high school in Roxbury.

## NEIDL scientists continue serving in West Africa

The West African outbreak of Ebola virus disease (EVD), which began in early 2014, was an unprecedented outbreak of global public health concern unlike any other EVD outbreak in history. Following the mission of the NEIDL to advance public health, the NEIDL supported four volunteers to serve in the front lines of the Ebola epidemic in Sierra Leone.

Last year Nahid Bhadelia donated her time and expertise by providing field training and clinical care at an Ebola Treatment Unit in Kenema, Sierra Leone. Adam Hume, worked in a mobile diagnostic laboratory deployed in the remote district of Kono, Sierra Leone. Again this year, we were fortunate to support two additional scientists to serve in West Africa - Judy Yen and Emily Nelson.

With years of working in EVD research and previous experience at Centre International de Recherches Medicales de Franceville (CIRMF) in Gabon, **Judy Yen** was eager to return to Africa and help out in this outbreak. **Emily Nelson**, motivated by her PhD dissertation research and expertise on Ebola virus and her interest in international public health, was also enthusiastic about this volunteer opportunity.


Supported by NEIDL, Partners in Health (PIH) and Erasmus University Medical Center in the Netherlands, in late June of 2015 Ms. Yen and Dr. Nelson spent one week in Rotterdam training for the specific task of EVD and Malaria diagnostics in the mobile lab setting. They then traveled from Rotterdam to the Koidu City in the Kono district of Sierra Leone for five weeks, where, in addition to four other Dutch team members, tested hundreds of oral swabs and blood samples for the presence of Ebola virus and Malaria.

*Emily Nelson (left) and Judy Yen (right) at work reviewing blood in Kono, Sierra Leone*

They were also responsible for educating and training local hospital staff on EVD and specifically the proper handling of patient samples. Unfortunately, funding issues lead to the closure of the Dutch Mobile lab, and therefore Yen and Dr. Nelson were part of the last team to participate in this diagnostic effort. The two spent their last week in Kono closing and decontaminating the lab and ensuring that all RNA samples were properly accounted for and stored. Both Yen and Dr. Nelson found the experience to be incredibly rewarding and are thankful to NEIDL, PIH, Erasmus University and the people of Sierra Leone for the opportunity.

---

## After Ebola: NEIDL Infectious Diseases Expert Returns to Africa

## Nahid Bhadelia launches effort to help unpaid local health teams

### Original Article from BU Today, by Susan Seligson, August 28, 2015

Last August, Nahid Bhadelia traveled to Sierra Leone during the Ebola epidemic's peak, hermetically clad in the protective spacesuit-like gear of a biosafety level 4 researcher. Funded by the World Health Organization (WHO), Bhadelia went there to share her expertise on infection control and to help care for patients infected with the virus.

A year later, the School of Medicine assistant professor of infectious diseases and director of infection control and medical response at BU's National Emerging Infectious Diseases Laboratories (NEIDL) returned, this time ungloved and unmasked, to interview African health care and burial workers, many still unpaid for their work during the epidemic. Appalled by their financial plight, Bhadelia recently launched a GoFundMe campaign, Support Sierra Leonean Ebola Workers, with the goal of raising at least $50,000 to help compensate them. As of August 26, donations had reached $13,026.

The Centers for Disease Control and Prevention estimates that 13,470 people in Sierra Leone were infected during the 2014 Ebola outbreak and that nearly 4,000 died, along with another 2,500 in neighboring Guinea and 4,800 in Liberia. In May, *Newsweek* reported that burial workers as well as health care workers were sidelined as $3.3 billion in international relief funds poured in last year to fight the epidemic. Rather than paying frontline workers, most of the money went to United Nations agencies and a score of nongovernmental organizations, fueling

protests in Sierra Leone and Liberia. Having witnessed firsthand the tireless efforts of these frontline workers, Bhadelia, who specializes in infection control issues related to emerging pathogens and highly communicable infectious diseases, launched her fundraising campaign on June 19.

She says that one of the nurses has used some of the proceeds "to pay a year of rent for a house farther from water. His last tiny place was by a stream in the dry season, and now it's regularly flooded in the rainy season. This arrangement will keep his family healthier." Another nurse, she says, has used money she received from the campaign to take care of, feed, and clothe her own son and the son of a fellow nurse who died in August 2014.

As well as clinical training in infectious diseases, Bhadelia has a master's degree in international affairs from the Tufts University Fletcher School of Law and Diplomacy and a background in international affairs and human security. She has worked on projects with the UN International Strategy for Disaster Reduction and the Global Fund to Fight AIDS, Tuberculosis and Malaria and was a senior policy and technical advisor to the Partners in Health Ebola response program in Sierra Leone.

*BU Today* asked Bhadelia about her return to the former Ebola zone, her inspiration for the fundraising effort, and the challenges those who helped fight the epidemic continue to face.

*BU Today*: Is your fundraising campaign the only one you're aware of aimed at compensating nurses, ambulance drivers, and other Ebola workers who have received little or no pay?

**Bhadelia:** I know that some of my co-expat Ebola response volunteers are also interested in helping out, and I am hoping that those avenues open up soon for more help for these health care workers. None of us are trying to replace pay for the Ebola workers. That is not sustainable, and it is not our place. We are trying to help our friends in Sierra Leone and their families make ends meet during this hard time.

How have you been able to contact the workers you're hoping to help?

I was able to meet six of the health care workers I knew from last summer and distribute the first set of funds to them at the beginning of July. It was a powerful day to spend time with them and hear about what they have gone through over the last year. I sent the second set of funds for three more health care workers with a friend traveling to Sierra Leone at the end of July. We are hoping to send more funds later this month.

In documenting the workers' stories, what have you found they have in common, and what are some stories that particularly moved you?

They all spoke about staying and continuing to work in the Ebola treatment units despite the fear they felt, because they knew it was the right thing to do. One of the nurses shared this with me: "The hardest thing for me was when we admitted health care workers to our Ebola unit, because I would look at them and I would think, she is a nurse and I am a nurse and tomorrow this will be me."

Tell us about the stigma associated with treating, transporting, or burying Ebola victims. What can be done to fight it?

One of the nurses was kicked out of her mom's house because she was working with Ebola patients. Health care workers in Sierra Leone routinely shared stories about how they had been driven out of villages. Another nurse, who was pregnant, went to the capital to clarify why she had not been paid and was thrown in the back of an ambulance with an Ebola patient without any protection and told that since she worked with Ebola patients, she too must have the disease. It wasn't until she reached the treatment center that she was released.

Many of my expat coworkers would tell stories about having their children disinvited from parties and being told not to return to work by their employers. I was asked not to return to my apartment building by management and was given a month's rent to stay away after I returned the second time from Sierra Leone. It's fear that drives the stigma, and it's lack of information and education that drives fear. We need to see beyond our fear and continue to see the humanity of those around us. This is what allowed the Ebola workers to continue their work, and their doing that is what kept all of us safe.

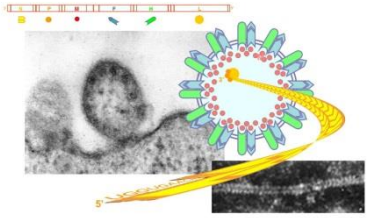
Why was so little of the international donations earmarked for frontline workers? How can people like you raise awareness so that more will go to them in the future?

The issue was not just that such a small amount was earmarked for them in the first place, but also that the amount that was earmarked has been taking a very long time to make it to them. It is hard to work for months without pay, because as human beings we need to continue to pay for food and shelter. I am hoping that by

putting a face to these brave people and bringing their stories to the forefront, we can create pressure to rectify these injustices, but also ensure that they are not overlooked during the next crises.

What is life like now for the health care workers who treated Ebola patients? Has Sierra Leone honored or acknowledged their sacrifices in any way?

Many of them are working as volunteers in their hospitals, as there is no pay. One of my nurse friends who received part of the funds we've raised had not been paid since February. I heard that there may be a fund that is being put together for the families of deceased health care workers, but it is not clear if the funding is getting to where it needs to be. Many health care workers I spoke with said that they felt the world had stopped thinking about them now that the epidemic was over: "We were your first soldiers and we fought naked, and many of us paid with our lives. Now we are forgotten." They felt that the international donors were only interested in Ebola survivors, and in related research, and in making new jobs for people in higher ranking positions. Nothing had changed for them. If anything, they had lost their position in society, they had lost their friends to this disease, and they had spent months risking their lives in their jobs.



The workers you are hoping to help—what is their standard of living?

Nurses in Sierra Leone make the equivalent of about US $150 to $200 a month. It is usual for their pay to be delayed due to the poor administrative structure of the national system. Their living standard is at the subsistence level. As I mentioned earlier, one of the nurses and his family lived in a small house that was constantly flooded during the rainy season. The gratitude that they feel to the amazing people on this side who contributed to the fund is immeasurable. Even the $400 to $600 that each of them has received through this fund drive has changed the lives of their families for months to a year.

You must have made friends in Sierra Leone when you worked there. Can you talk about the commitment of the health care workers and what you admire most about them?

Kenema Government Hospital, where I worked last summer, lost 35 health care workers to Ebola and a total of 50 contracted the disease. We can only imagine continuing to work when we see so much death around us, when we are losing our own friends to the disease, and when we aren't getting paid or getting recognized for the work that we do. If that is not a testament to the heroism of these workers, I am not sure what is.

As someone at the outbreak's epicenter, what are the most important lessons you took away from the epidemic?

As has been said many times over the last few months, we need to invest in the health care delivery and public health systems of countries like Sierra Leone. Our common global health security depends on it. But as we move toward putting money into the efforts to build these systems, we cannot forget the importance of economic justice for health care workers.

# Events

## Boston Skeptics in the Pub - Paul Duprex

**Paul Duprex, April 25, 2016**

Viruses are all around us. Some don't bother us. Others will do us in if given half a chance. Fortunately, there are scientists dedicated to studying these wee beasties, finding out what makes them tick and, more importantly, how to prevent them from making us sick.
This month, Boston Skeptics is very excited to welcome Paul Duprex, Director of Cell and Tissue Imaging at Boston's highly controversial BSL-4 lab, the National Emerging Infectious Diseases Laboratories (NEIDL). He will talk about why we need to work with viruses in labs under high containment, why vaccines are amazingly effective and have saved countless lives, and that you can't trust celebrities (cough*Jenny McCarthy*cough) on topics like this.
https://www.facebook.com/groups/bostonskeptics/

## Preventing further spreading of Zika

**CNBC video aired on Tuesday, 12 Apr 2016 | 2:12 PM ET**


Discussing the effects of the Zika virus on people, what needs to be done in order to prevent further spreading and research funding, with Nahid Bhadelia, Boston University of Infection Control & National Emerging Infectious Diseases Lab - View video

## Fear and Stigma in the Age of Ebola

**TEDx Talk with Nahid Bhadelia, March 29th, 2016**


Outbreaks of deadly infectious diseases can elicit intense fear and confusion in our society, stigmatizing both patients and caregivers. As an infectious diseases expert and a frontline Ebola physician, Dr. Bhadelia understands the challenge of balancing public safety and patient care during an emerging epidemic. She discusses her first-hand experience in Sierra Leone and the unexpected surprises she encountered upon returning to the U.S.

Nahid is the Director of Infection Control and Medical Response at National Emerging Infectious Diseases Laboratory (NEIDL) at Boston University. She served as a frontline physician during the recent Ebola outbreak in Sierra Leone and understands the global challenges of addressing epidemics in a modern world.

Nahid gave this talk at a TEDx event using the TED conference format but independently organized by a local community – Natick, MA. http://tedxtalks.ted.com/video/Fear-and-Stigma-in-the-Age-of-E;search%3ANatick

## Super Science Tuesday with John Connor

**February 29, 2016**


**John Connor** is an associate professor of microbiology at Boston University.

Throughout the 2016 presidential campaign, The Science Coalition is asking people to answer the question: Why should science matter to the presidential candidates? For more videos and information, visit www.ScienceMatters2.me.
View video

## Public Awareness and Transparency

In keeping with its commitment to transparency in its operations, the NEIDL and BU leadership openly reported on a major systems failure that occurred on March 21. The description of this incident reported in the press is below:

## BU lab temporarily halts TB research after safety lapse
## Says public was never in danger

### Original Article from the Boston Globe, by Kathy McCabe, June 2, 2016

Boston University has temporarily halted tuberculosis research at its high-security biolab after a malfunction forced a partial shutdown of the South End facility's ventilation monitoring system in March, university officials said Wednesday.

A faulty network switch impeded air flow from two laboratories, prompting an eight-hour shutdown, BU officials said. The National Emerging Infectious Diseases Laboratories was closed at the time, and the shutdown posed no threat to public safety.

The malfunction was immediately reported to the Boston Public Health Commission and the federal Centers for Disease Control and Prevention, a BU spokesman said.

"We reported the incident, as required, within 24 hours to the regulators," Colin Riley said.

BU has suspended research in the affected laboratories until an outside engineering firm completes a review of the system. Freezer units containing pathogens were not affected by the malfunction, officials said, and redundant safety systems operated as intended.

In a statement, the city's public health commission said there was "no public impact from the ventilation shutdown." The commission will review the engineering report and inspect the lab before it reopens.

"Boston University followed the proper protocol in responding to and reporting the mechanical malfunction," the commission said. The issue was reported Wednesday by BU Today, a university publication.

The university decided not to make the incident public until it had received a preliminary report from Merrick & Co., the Colorado-based engineering firm hired to review the incident and BU's response.

"We chose to wait until they could provide their own analysis," Riley said.

The firm's preliminary recommendations include increased monitoring and improving the mechanism that shuts off air supply units when the exhaust fans are not working, the university said.

The firm is expected to complete its report in the next several weeks, Riley said.

The incident renews safety questions at the seven-story building on Albany Street, where scientists research some of the world's deadliest diseases, such as Ebola. Local residents vigorously opposed the laboratories, which were built with $200 million in federal money on the campus of BU's medical school.

The incident occurred at 8 p.m. on March 21, when a component on a network switch failed, prompting the ventilation monitoring system to temporarily shut down. The malfunction caused exhaust fans to stop working, which increased air pressure in the laboratories, the university said.

The switch was repaired by midnight, and the system was restored at about 4:45 a.m. the next day.

*Kathy McCabe can be reached at* Katherine.McCabe@ globe.com*. Follow her on Twitter* @GlobeKMcCabe*.*


**Boston University** National Emerging Infectious Diseases Laboratories

**620 Albany Street**
**Boston, MA 02118**
**http://www.bu.edu/neidl**


**Boston University** National Emerging Infectious Diseases Laboratories

**620 Albany Street**
**Boston, MA 02118**
**http://www.bu.edu/neidl**