



Annual Report FY2015



National Emerging
Infectious Diseases
Laboratories



Table of Contents

Mission and Strategic Plan	0
Letter from the Director	1
Faculty and Staff	3
Faculty Recognition.....	9
Research	13
Research Programs.....	13
Publications.....	21
FY15 Funded Research.....	26
Education and Training	29
Community Outreach	31
NEIDL Scientists serving in West Africa.....	33
Events and Programs	37

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. To 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. As rapidly as possible move promising basic research 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.

September 1, 2015

Letter from the Director

This is the first annual report since the NEIDL Institute officially became a University Center on October 01, 2014. With this transition, the NEIDL changed its reporting structure from the Dean of the School of Medicine to the Associate Provost and Vice President for Research of Boston University. This change is important for two reasons. First, the change in reporting recognizes the significance of the current and future investments made by the University into the NEIDL, and for the field of emerging infectious diseases, as a focal point of research for the University. Second, it underscores the importance of embracing the breadth of research within in the University into the NEIDL as we recruit faculty. The study of emerging infectious diseases is by its very nature interdisciplinary, and leveraging expertise via joint recruitments with departments across the university will ensure a robust and innovative research portfolio necessary for the future success of the Institute. This diversity of expertise will be an important differentiator for the NEIDL.

Coincident with the change, I had the privilege of being appointed as Director of the NEIDL. I do not take this responsibility lightly. With it comes not only the responsibility for establishing the scientific vision for the foreseeable future, together with many stakeholders across Boston University, but to also continue fostering the culture of safety in all that we do. We also have the responsibility to the public to be completely transparent in what we do. Public trust is essential to the future success of the NEIDL. Emerging infectious diseases research requires rigorous biologic containment facilities and practices, each requiring high levels of attention to the safety of the staff and the public. We aspire to be innovative not only in science, but in safety and safe practices. The NEIDL will also serve as a training center for the next generation of scientists, and this requires that we pass on the safety first culture to them as well.

During this first year, the NEIDL completed the permitting process for undertaking biosafety level 3 (BSL-3) research, obtaining all remaining permits from the Boston Public Health Commission as well as the Centers for Disease Control. These were major hurdles, requiring the outstanding teamwork of the NEIDL staff. The hard work of facilities staff, members of Environmental Health and Safety, Security, and Research Occupational Health all played critical roles in the permitting process. All BSL-3 work will now be undertaken in the NEIDL; other BSL-3 containment research facilities on the medical campus have been or will be decommissioned shortly. We are also working to secure permits for BSL-4, and we look forward to having completed all requirements for BSL-4 work soon, and to begin to undertake work safely in this remarkable facility.

To ensure that everyone in the NEIDL is part of the culture of safety, we instituted a “Biosafety and Biosecurity Grand Rounds” during this year, which engages staff throughout the NEIDL in continuing discussions about safety and security. These serve to provide a forum for frank exchanges of information between the NEIDL’s staff, faculty, and trainees, and keep our emphasis on safe and secure practices at the forefront. We are, of course, here to do cutting edge science. During this year, our scientists have continued to be recognized for the quality of their research, setting a high bar for those we will recruit.

Their quality is reflected not only in their excellence in publications, but their success in competing for external funding to support their science. Some of these successes are highlighted in this report. Our faculty also recruited a strong cadre of graduate students and postdoctoral fellows to their laboratories, a key component in our mission to train the next generation of scientists. We have also developed educational programs for the local public schools (“Identifying Infectious Diseases, aka **ID2**) and participated with news programs to disseminate science to the public, including our participation with Al Jazeera America’s TechKnow program for a piece on emerging infectious diseases research (<http://america.aljazeera.com/watch/shows/techknow/articles/2015/2/23/inside-a-biosafety-level-four-lab.html>). In sum, as we turn our attention to recruiting new faculty and further building the NEIDL research portfolio, we have used this year to set the expectations for science, education, safety and community engagement and outreach.



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

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*



Jerrold J. Ellner, MD

Professor, Department of Medicine

Section Chief, Infectious Diseases

Associate Director, NEIDL

Dr. Ellner's research interests:

- *TB and HIV interactions*
- *TB diagnostics*



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*



John R. Murphy, PhD

Professor of Medicine, Infectious Diseases, and Microbiology

Associate Director, NEIDL

Dr. Murphy's research interests:

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



Principal Investigators

Nahid Bhadelia, MD, MA

Assistant Professor of Medicine
Section of Infectious Diseases
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*
- *Antiviral compounds*
- *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*



James Galagan, PhD

Associate Professor, Biomedical Engineering
Associate Professor, Microbiology

Dr. Galagan's research interests:

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



Thomas B Kepler, PhD

Professor, Microbiology
Member, Bioinformatics Graduate Program

Dr. Kepler's research interests:

- *Quantitative Systems Immunology*
- *Vaccine Development*



Igor Kramnik, MD, PhD

Associate Professor, Medicine
Division of Pulmonary, Allergy, Sleep & Critical Care Medicine
Associate Professor, Microbiology
Director, Aerobiology Core

Dr. Kramnik's research interests:

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



Gene G Olinger, PhD

Adjunct Associate Professor of Medicine
Section of Infectious Diseases
Associate Director, Maximum Containment Training

Dr. Olinger's research interests:

- *Vaccine Development for filoviral outbreaks*
- *Viral Therapeutics*



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*



Scientific Staff

Bidisha Bhattacharya

Postdoctoral Research Associate
Medicine, Kramnik Lab

Erik Paul Carter

Research Technician
Microbiology, Connor Lab

Sujoy Chatterjee

Postdoctoral Research Associate
Medicine, Kramnik Lab

Laure Deflube-Owen*

Postdoctoral Research Associate
Microbiology, Mühlberger Lab

Claire Marie Filone*

Postdoctoral Fellow
Microbiology, Connor 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 Associate
Whole Animal Imaging Core

Shamkumar Nambulli

Laboratory Manager
Microbiology, Duprex Lab

Judith Olejnik

Senior Research Scientist
Microbiology, Mühlberger Lab

Michelle Olsen

Postdoctoral Research Associate
Microbiology, Connor Lab

Jennifer Rose Pacheco

Research Technician
Microbiology, Mühlberger Lab

Linda J Rennick

Senior Research Scientist
Microbiology, Duprex Lab

Dan Rozelle*

Postdoctoral Fellow
Microbiology, Connor Lab

John Ruedas *

Postdoctoral Research Associate
Microbiology, Connor Lab

Judy Yung-Ju Yen

Senior NEIDL Core Technologist

Students

Patricia M Aquino

PhD Student, Biomedical Engineering
Galagan Lab

Jake A Awtry

Undergraduate Student, Biochemistry
Connor Lab

R Baer

PhD Student, Microbiology
Galagan Lab

Declan Bowman*

Undergraduate Student, Biomedical Engineering
Galagan Lab

Molly Braun

PhD Student, Microbiology
Galagan Lab/Ferns Lab

Whitney Manhart*

Graduate Student, Immunology
Muhlberger Lab/Mostoslavsky Lab

Shane McCormack

Undergraduate Student, Biomedical Engineering
Galagan Lab

Garrett Moore * *

Undergraduate Student
Kramnik Lab

Emily V Nelson

PhD Student, Microbiology & Immunology
Mühlberger Lab

Katherine Norwood

PhD Student, Bioinformatics
Connor Lab

Katherine Callaway **

Undergraduate Student, Biomedical Engineering
Galagan Lab

Shreya Deshmukh*

Undergraduate Student, Engineering
Galagan Lab

Tessa Didonato

PhD Student, Microbiology
Mühlberger Lab/Fearns Lab

Grace Olinger

PhD Student, Microbiology
Duprex Lab

Ignacio Sanchez-Caballero

PhD Student, Bioinformatics
Connor Lab

NEIDL Administration

Betina A Durkop *

Executive Coordinator

Tracy E Keane

Administrative Assistant

Richard P Trevino

Director, Finance & Research
Administration

Animal Core Operations

Kath Hardcastle, BVet Med DVM

Core Director, Animal Services

Andrew G Kocsis, DVM

Clinical Veterinarian

James Levin, DVM DACLAM

Director, Animal Science Center

Britney Morea **

Veterinary Research Technician, BSL-4

Sergio Roman

Veterinary Research Supervisor

Cynthia A Pinkus * *

Veterinary Research Technician, BSL4

Jonathan W Sturgis

Operations Manager, ASC/NEIDL

Larry P Vintinner

Assistant Director of Operations, ASC

Community Relations

Valeda Britton

Executive Director, Community Relations
Boston University Government Affairs

Chimel Idiokitas

Assistant Director, Community Relations
Boston University Government Affairs

Environmental Health & Safety

Joshua C Ames

Senior Research Safety Specialist

Tracy S Bastien

Executive Assistant

Keith Leblanc*

Senior Research Safety Specialist

Guillermo Madico, MD PhD

Scientific Safety Officer

Kyle McGovern*

Senior Research Safety Specialist

Stephen A Morash

Director, Emergency Response Planning

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

Ron L Morales
Core Director, Environmental Health and Safety

Facilities Maintenance & Operations

David M Ananian
Maintenance Mechanic

Juana V Baires
Custodian

Sean J Cooper *
Engineering Operations Manager

Joseph T Corbett
Control Center Technician

Jillian Deluca *
Administrative Assistant

William S Galloway
General Mechanic

Jonathan Gendron *
General Mechanic

John F Holland
General Mechanic

John H Mccall
Director, Information Technology

Jeff Morris *
General Mechanic

Derek Mosca
Shipping/Receiving Clerk

Matthew D Rarick
Director, Facilities and Maintenance Operations

Mario Rodriguez
Custodian

Richard Vecchia *
General Mechanic

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

Joseph H Maldonis
Public Safety Officer

Justin Phelps
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

* Staff who joined during FY15

* Staff who left during FY15

NEIDL Faculty Recognition

An indication of the recognition of faculty is their participation as invited speakers in national and international forums, service on review panels and service on editorial boards of journals. These recognitions are summarized below.

Invited Speakers

- Nahid Bhadelia. Keynote Speaker, “Ebola Epidemic: Lessons Learned from One Year of Cases” - NIAID National and Regional Biocontainment Laboratories Network, Annual Meeting, Galveston, TX. April 13, 2015
- Nahid Bhadelia. Panelist: “Epidemic Ebola: Looking Back, Lessons Learned, Looking Ahead” -2015 Conference Plenary VIII Consortium of Universities for Global Health. March 28, 2015, Boston MA
- Nahid Bhadelia. Keynote Speaker, “Building Sensible Health Safety Policies and Procedures/Threats from Emerging Pathogens” - International Association of Health Security and Safety, 47th Annual Conference & Exhibition, St. Louis, MO. May 3, 2015
- John Connor. Science for the Public (science outreach organization), November 2014
- John Connor. Biosensors Conference, Berlin Germany, March 2015
- John Connor. Microbiology & Infectious Diseases Asia Congress (plenary speaker, session chair) Singapore, National University Singapore (Duke-NUS) June, 2015
- John Connor. Rocky Mountain Laboratories, Hamilton MT. July 2015
- John Connor. Mount Sinai School of Medicine NYC, NY. August, 2015
- Paul Duprex. Mapping the steps required for adaptation of animal morbilliviruses to human cells: evolution, structural modeling and prediction. DARPA Prophecy Program Annual Meeting, Washington DC, USA. 2014.
- Paul Duprex. Illuminating paramyxovirus pathogenesis: when is a respiratory virus not a respiratory virus? Society for General Microbiology Annual Meeting, Liverpool, England, UK. 2014.
- Paul Duprex. Morbilliviruses crossing the species barrier: virus eradication, both a reality and a potential risk? 7th European Meeting on Viral Zoonoses, St. Raphaël, France. 2014.
- Paul Duprex. CDV vaccines: past, present and future. Vaccines for Conservation Meeting: convened by The Wildlife Conservation Society (WCS), Cornell University's College of Veterinary Medicine and the University of Glasgow's Institute of Biodiversity, Animal Health and Comparative Medicine Programme. Bronx Zoo, Bronx, NY, USA. 2015
- Paul Duprex. The multitropic meanderings of morbilliviruses: getting in, getting about and getting out. “Second N-RENNT Symposium on Neuroinfectiology” Department of Pathology, University of Veterinary Medicine, Hannover, Germany. 2015
- Paul Duprex. Morbilliviruses crossing the species barrier: virus eradication, both a reality and a potential risk? Mount Sinai School of Medicine, New York, NY, USA. 2015

- Paul Duprex. The multitropic meanderings of morbilliviruses: getting in, getting about and getting out. The Medical Research Council (MRC) Centre for Virus Research, Glasgow, Scotland, UK. 2015
- Paul Duprex. National Science Advisory Board for Biosecurity (NSABB), invited keynote speaker "Gain-of-function studies ... their history, their utility and what they can tell us", October 22, 2014, Washington, DC
- Igor Kramnik. Keystone Symposia on Molecular and Cellular Biology: "Host Response in Tuberculosis", and "Granulomas in Infectious and Non-Infectious Diseases". January 22-27, 2015, Santa Fe, New Mexico
- Elke Mühlberger. Interaction of Ebola virus with the infected cell. University of Virginia, Dept. Microbiology, Immunology and Cancer Biology, Charlottesville, VA . November 4, 2014
- Elke Mühlberger. Interplay of Ebola virus with the host defense machinery. Fluomics Symposium, Salks Institute, La Jolla, CA. January 7, 2017
- Elke Mühlberger. Interaction of Ebola virus with the infected cell. Microbiology and Molecular Genetics Symposium Frontiers in Microbial Biology, Emory University, Atlanta, GA. May 1, 2015
- Elke Mühlberger. Department of Microbiology and Immunology, University of Louisville, Louisville, KY, Title: TBA. June 24, 2015
- Elke Mühlberger. University of Rochester, Title: TBA. October 6, 2015
- Elke Mühlberger. Keystone Symposia on Hemorrhagic Fever Viruses. New Mexico, Title: TBA. December 4, 2016

International Meeting Organizers/Chairs

- Paul Duprex. Symposium Chair, Society for General Microbiology, April 14-17, 2014, Liverpool, UK
- Paul Duprex. Session Chair, 7th European Meeting on Viral Zoonosis. St. May 24-27, 2015, St. Raphaël, France
- Paul Duprex. Organizer, Negative Strand Virology Meeting, June 14-19, 2015 Siena, Italy
- Gerald Keusch. Organizer, Consortium of Universities for Global Health, 6th Annual Meeting, March 26-28, 2015, Boston, MA
- Elke Mühlberger. Session Chair, 7th International Symposium on Filoviruses, March 25-28, 2015, Washington DC

Honors

- Ronald B. Corley. 2015. Elected Fellow of the American Association for the Advancement of Science
- Thomas Kepler. 2014 Norman L. Letvin Scholar, Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery
- Gerald Keusch. 2015 Member, National Academy of Medicine

Editorial Boards

- Igor Kramnik. The American Journal of Physiology – Lung Cellular and Molecular Physiology
- John Connor. Journal of Virology
- Paul Duprex. FEMS Microbiology Reviews
- Paul Duprex. Journal of General Virology

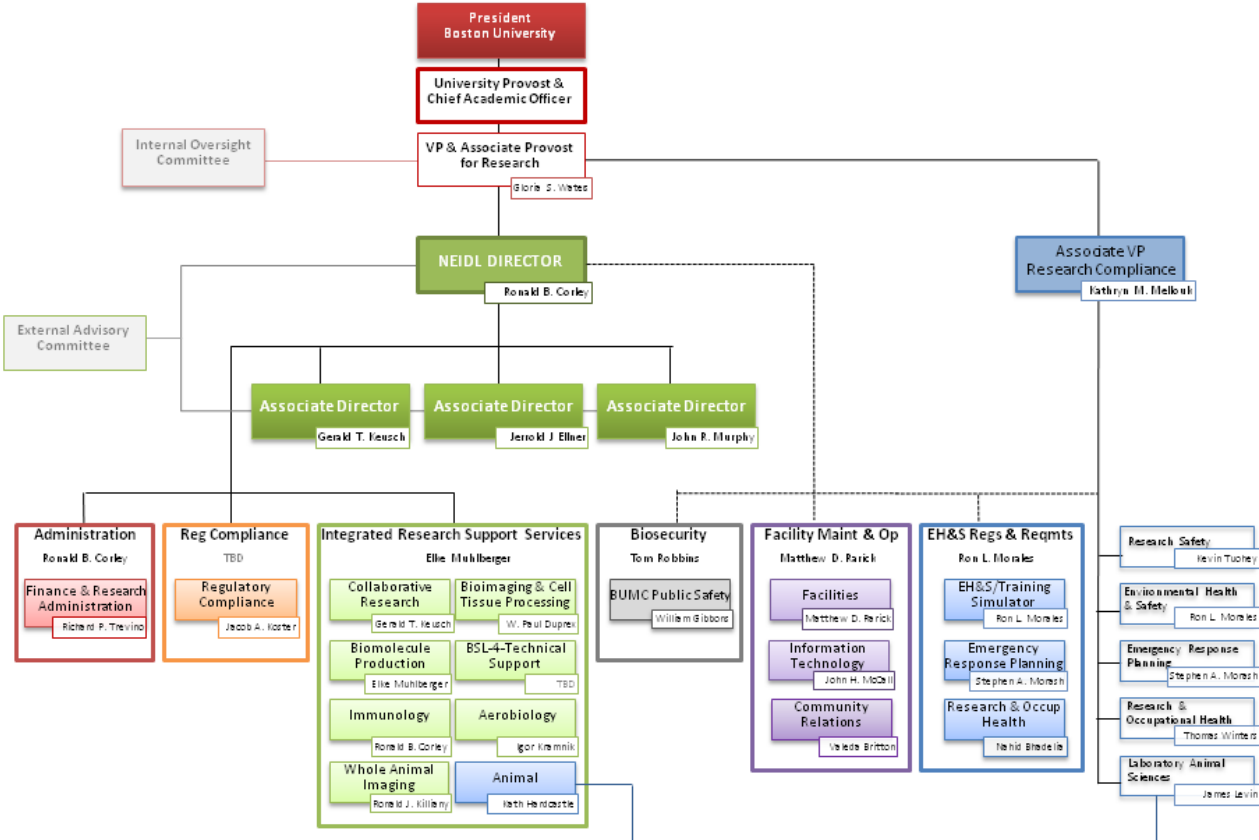
Study Sections and Grant Review Panels

- Paul Duprex. 2014 - VIRGO consortium (a public private partnership of 7 academic institutions, 3 research organizations and 10 private sector companies). Supported by part of an 81 million Euro grant from The Netherlands Genome Initiative
- John Connor. 2014 NIAID review panel and American Society for Microbiology's Ebola virus FAQ response team.
- John Connor. 2015 Reviewer NIAID review panel U24.
- James Galagan. 2015- Hariri Institute Data Science Initiative Leadership Board
- James Galagan. 2014-present - Editorial Board Member, BMC Infectious Diseases
- James Galagan. March 20, 2014, NIGMS, National Centers for Systems biology (P50) Review Panel
- James Galagan. 2014 - Department of Defense, Military Infectious Diseases Research Program; Computational Science Panel
- Igor Kramnik. 2014 – External reviewer for National Research Foundation, South Africa
- Gerald Keusch, Wellcome Trust, Global Clinical Trials Program, 2014-2015
- Elke Muhlberger. 2009-2015 – NIH/NIAID

Memberships

- Nahid Bhadelia and Elke Muhlberger. FANG Human Clinical Data Subgroup, US Government Interagency Filovirus Animal Non-Clinical Group (FANG), Bethesda, MD.
 - Ronald Corley. 2011 – 2014 SmithGroup JJR Science & Technology Advisory Board
 - Paul Duprex. 2010-2016 European Society for Virology Advisory Council
 - Paul Duprex. 2015- American Society of Virology (Scientific Programs Committee Member)
 - Tom Kepler. 2007-present – Science Advisory Board, Immune Response Consortium, MIT
 - Tom Kepler. 2009-present - Scientific Working Group, NIAID Systems Biology of Infectious Disease National Institute of Allergy and Infectious Disease
 - Tom Kepler. 2014–present - Center For AIDS Research External Advisory Committee, Duke University Life Sciences Representative, SIAM News (Society for Industrial and Applied Mathematics)
-

NEIDL Organizational Chart



Research

The research activities of the NEIDL faculty focus on pathogenesis of emerging viral and bacterial pathogens and continue to be supported by significant external grant funding (see below). Most of the faculty have developed multidisciplinary programs that engage the expertise of faculty, staff and trainees with diverse backgrounds across the university. These collaborations include faculty not only on the medical campus in microbiology and infectious diseases, but also the Center for Regenerative Medicine, the Photonics Center, and faculty 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 students, including those from Microbiology, Bioinformatics and Engineering as documented above. These types of collaborative programs and training activities exemplify the “research style” that has become a hallmark of the NEIDL.

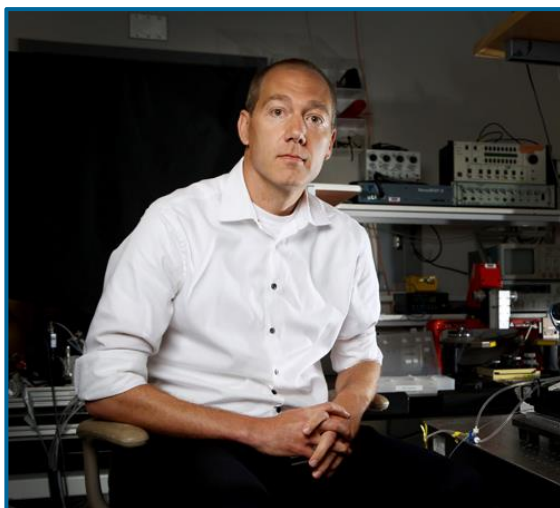
NEIDL investigators have successfully competed for \$17.8M in research and support during the current FY15 year. Funding comes from a variety of competitive sources, including the National Institutes of Health, the Department of Defense, private foundations and subcontracts from collaborating institutions.

During the year, a number of NEIDL research programs were highlighted for the university community because of the unprecedented nature of the Ebola epidemic and the international engagement required to help contain the outbreak and attend to those affected. These highlights included reports in BU Today and BU Research, some of which are reprinted below.

Diagnosing Disease before Symptoms Strike BU School of Medicine team develops technique for early detection of Ebola-like viruses.

BU Research, Barbara Moran, November 20, 2014

<http://www.bu.edu/research/articles/diagnosing-disease-before-symptoms-strike/>



John Connor, senior author on the study. Photos by Michael D. Spencer

In October 2014, nurse Kaci Hickox returned to her home in Maine after treating Ebola patients in Sierra Leone with the group Doctors Without Borders. State officials ordered her to stay in her house for 21 days—the longest possible incubation period for Ebola—even though she showed no symptoms of the disease. Hickox defied the quarantine, setting off a swirl of controversy among state officials, civil rights advocates, legal experts, health care workers, and scientists. Her 21-day monitoring period ended on November 10, without incident.

The Hickox case highlights a thorny problem with the Ebola virus and similar hemorrhagic fevers—a person can be infected long before they show symptoms, and before doctors can diagnose the disease. This can lead to delays in treatment, controversial quarantines, and unnecessary fear.

Now, researchers from Boston University's School of Medicine (MED) have developed a way to detect signs of infection before the virus enters the bloodstream and symptoms emerge. By examining RNA within circulating immune cells, they have been able to detect—and distinguish—infection by two different hemorrhagic fever viruses, Marburg and Lassa, before they could be detected in the blood. Their research was published in the journal *BMC Genomics*. They are now testing whether the technique will work for Ebola as well. Although the research is still preliminary, the ultimate goal is to provide an alternative diagnostic tool for Ebola and other hemorrhagic fevers.

“We want to catch it early, before symptoms emerge and the person becomes contagious,” says John Connor, senior author on the study, a MED associate professor of microbiology, and a researcher at Boston University's National Emerging Infectious Diseases Laboratories (NEIDL). “The earlier one can start treatment, the more likely the patient is to survive.”

Hemorrhagic fevers are a tough nut to crack. When a person first becomes infected, the virus is not detectable in the blood. After an incubation period, virus particles spill out of cells into the patient's bloodstream, where it can finally be detected by conventional methods. At this point, the person becomes contagious and also develops symptoms, like fever.

“Fever is a good indicator of disease, but it's not specific,” says Connor, noting that many diseases, from malaria to influenza, also show fever as an early symptom. “The question we asked was: ‘can you detect infection before the fever, and also get specific information about the disease?’”

The research team decided to look inside white blood cells of infected monkeys to see if the cells themselves showed any changes that might signal infection. They worked with collaborators Jay Goff, Anna Honko, and Lisa Hensley at the US Army Medical Research Institute of Infectious Diseases (USAMRIID), who infected one group of macaques with Lassa virus and another with Marburg virus. The USAMRIID researchers took samples of white blood cells at several different times after infection. Then, they extracted messenger RNA (mRNA)—the molecule responsible for transcribing genes into protein—from the cells and sent it to MED for analysis.

The scientists suspected that the white blood cells might recognize an infection early and activate genes to help fight it. And if certain genes were activated, there should be a corresponding uptick in the amount of mRNA in the cells. This technique has been used successfully in the past for detecting influenza, bacterial infections, and respiratory syncytial virus (RSV), according to Ignacio Caballero, a PhD candidate in the Graduate Program in Bioinformatics and lead author of the study.

“People have found distinct differences in mRNA during bacterial and viral infection, without trying to detect the virus or bacteria itself,” says Caballero. “It makes sense that the immune system would respond before the virus is visible in the blood. This gives us the advantage of seeing patterns in the cells, rather than pathogens in the blood.”

“The immune cells definitely knew that there was something going on. We saw very specific changes to gene expression,” says Connor.

Most of the hundred or so genes turned on in the immune cells were the same for both the Lassa and Marburg monkeys, a general immune response alerting other cells to the presence of a viral invader. But



Ignacio Caballero developed a technique for early detection of Ebola-like viruses.

the scientists also found that a handful of the activated genes were different, allowing the scientists to distinguish between cells infected with Lassa versus those infected with Marburg.

The scientists weren't focused on what the unique genes do, as much as on how soon they could detect the changes. "How fast can we get to an answer?" asks Connor, who notes that treatments differ among hemorrhagic fevers and early intervention can be the key to survival.

The team is now expanding the research in two directions, using the technique to try to detect Ebola in primates, and also testing human blood samples from the field for similar patterns of gene expression.

Caballero notes that much more work is needed before these techniques are practical for widespread use. But he hopes that the work will eventually lead to a better understanding of these diseases. "We want to expand our understanding to make detection earlier," he says, "but we also want to pinpoint specific genes that are activated during infection. We hope that could open some doors and move the field forward."

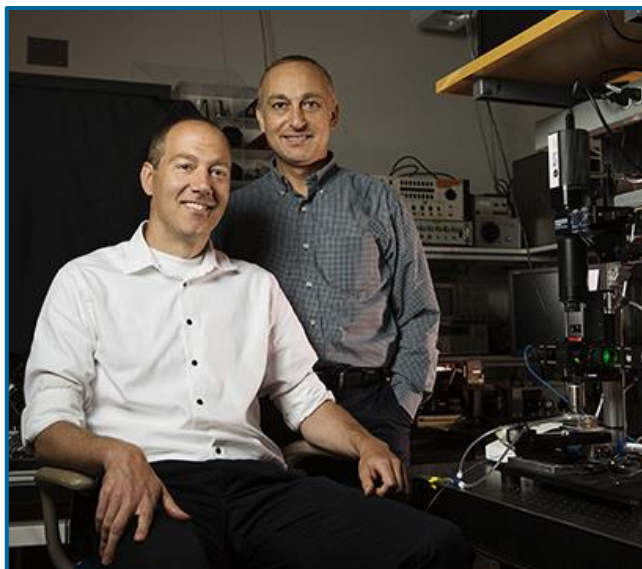
Containing Ebola with Nanotechnology BU team's device detects virus quickly and on site.

BU Today, Mark Dwortzan, September 30, 2014

<http://www.bu.edu/today/2014/containing-ebola-with-nanotechnology/>

By late January, 1.4 million people in Liberia and Sierra Leone could be infected with the Ebola virus. That's the worst-case scenario of the Ebola epidemic in West Africa recently offered by scientists at the US Centers for Disease Control and Prevention. The CDC warns that those countries could now have 21,000 cases of the virus, which kills 70 percent of people infected.

One of the big problems hindering containment of Ebola is the cost and difficulty of diagnosing the disease when a patient is first seen. Conventional fluorescent label-based virus detection methods require expensive lab equipment, significant sample preparation, transport and processing times, and extensive training to use. One potential solution may come from researchers at the College of Engineering and the School of Medicine, who have spent the past five years advancing a rapid, label-free, chip-scale photonic device that can provide affordable, simple, and accurate on-site detection. The device could be used to diagnose Ebola and other hemorrhagic fever diseases in resource-limited countries. The first demonstration of the concept, described in the American Chemical Society journal *Nano Letters* in 2010 and developed by an ENG research group led by Selim Ünlü,



John Connor, a MED associate professor of microbiology (left), and Selim Ünlü, a College of Engineering professor and associate dean for research and graduate programs, have developed a rapid chip-scale photonic device that can detect viruses, including Ebola, on site. Photo by Steve Prue



a professor of biomedical engineering, electrical and computer engineering, and materials science and engineering, in collaboration with Bennett Goldberg, a College of Arts & Sciences professor of physics, showed the ability to pinpoint and size single H1N1 virus particles. Now, after four years of refining the instrumentation with the collaboration of John Connor, a School of Medicine associate professor of microbiology, and other hemorrhagic fever disease researchers at the University of Texas Medical Branch, the team has demonstrated the simultaneous detection of multiple viruses in blood serum samples—including viruses genetically modified to mimic the behavior of Ebola and the Marburg virus.

Mentioned in *Forbes* magazine as a potentially game-changing technology for the containment of Ebola, the device identifies individual viruses based on size variations resulting from distinct genome lengths and other factors. Funded by the National Institutes of Health, the research appears in the May 2014 *ACS Nano*.

“Others have developed different label-free systems, but none have been nearly as successful in detecting nanoscale viral particles in complex media,” says Ünlü, who is also ENG associate dean for research and graduate programs, referring to typical biological samples that may have a mix of viruses, bacteria, and proteins. “Leveraging expertise in optical biosensors and hemorrhagic fever diseases, our collaborative research effort has produced a highly sensitive device with the potential to perform rapid diagnostics in clinical settings.”

NexGen Arrays prototype of SP-IRIS, which detects pathogens by shining light from multicolor LED sources on viral nanoparticles bound to the sensor surface by a coating of virus-specific antibodies. Image courtesy of NexGen Arrays

Whereas conventional methods can require up to an hour for sample preparation and two hours or more for processing, the current BU prototype requires little to no sample preparation time and delivers answers in about an hour.

“By minimizing sample preparation and handling, our system can reduce potential exposure to health care workers,” says Connor, a researcher at the University’s National Emerging Infectious Diseases Laboratories (NEIDL). “And by looking for multiple viruses at the same time, patients can be diagnosed much more effectively.”

The shoebox-sized prototype diagnostic device, known as the single particle interferometric reflectance imaging sensor (SP-IRIS), detects pathogens by shining light from multicolor LED sources on viral nanoparticles bound to the sensor surface by a coating of virus-specific antibodies. Interference of light reflected from the surface is modified by the presence of the particles, producing a distinct signal that reveals the size and shape of each particle. The sensor surface is very large and can capture the telltale responses of up to a million nanoparticles.

In collaboration with BD Technologies and NexGen Arrays, a start-up based at the Photonics Center and run by longtime SP-IRIS developers David Freedman (ENG’10) and postdoctoral fellow George Daaboul (ENG’13), the research team is now working on making SP-IRIS more robust, field-ready, and fast—ideally delivering answers within 30 minutes—through further technology development and preclinical trials.

SP-IRIS devices are now being tested in several labs, including a Biosafety Level-4 (BSL-4) lab at the University of Texas Medical Branch that’s equipped to work with hemorrhagic viruses. Other tests will

be conducted at BU's NEIDL once the facility is approved for BSL-4 research. Based on the team's current rate of progress, a field-ready instrument could be ready to enter the medical marketplace in five years.

Dr. Paul Duprex Presents at The National Science Advisory Board for Biosecurity

Paul Duprex, PhD, Associate Professor of Microbiology and Director of Cell and Tissue Imaging at the National Emerging Infectious Diseases Institute (NEIDL), presented a talk entitled, "*Gain-of-function studies ... their history, their utility and what they can tell us*" at the request of NSABB on Wednesday October 22, 2014 in Washington D.C. In his presentation he argues that cross-species infection studies have already helped to improve surveillance in the field, have shed new light on basic influenza virus biology and could assist in growing vaccine viruses better.

As a founding member of **Scientists for Science** www.scientistsforscience.org a group who "are confident that biomedical research on potentially dangerous pathogens can be performed safely and is essential for a comprehensive understanding of microbial disease pathogenesis, prevention and treatment" and as NEIDL investigator, he emphasized that virologists are responsible scientists who appreciate good communication and transparency is critical.



The National Science Advisory Board for Biosecurity (NSABB) is a federal advisory committee that addresses issues related to biosecurity and dual use research of concern (DURC) at the request of the United States Government. The NSABB has up to 25 voting members with a broad range of expertise including molecular biology, microbiology, infectious diseases, biosafety, public health, veterinary medicine, plant health, national security, biodefense, law enforcement, scientific publishing, and other related fields. The NSABB also includes non-voting ex officio members from 15 federal agencies and departments.

Watch the video at: <http://www.bu.edu/neidl/2014/11/18/dr-paul-duprex-presents-at-the-national-science-advisory-board-for-biosecurity/>
Dr. Duprex's presentation begins at 68:00

Point of View: Battling Ebola. It's our Problem too.

BU Today Special Report, Paul Duprex, August 8, 2014
<http://www.bu.edu/today/2014/pov-battling-ebola-its-our-problem-too/>

I can't hear the three words "point of view" without instantly thinking of my dad! "Here's my point..." is probably one of his favorite phrases, and I guess he's not alone. Doesn't everyone have some point or other they want to get across in conversation, on the Internet, in the press? So let's cut to the chase, here's my first point and it's short and snappy: I do not have a death wish. We will return to my father and his points later on.

Second point, I am fascinated by viruses! As nature's nanomachines, they are incredibly diverse and come in more "flavors" than all the plants, animals, fungi, bacteria, and other unicellular organisms on earth put together. Why? Because as the nursery rhyme says, "Big fleas have little fleas, upon their

backs to bite 'em, and little fleas have lesser fleas, and so, *ad infinitum*." Long before we knew what they were, we saw what they did. Paralysis and, if you survived, lifelong disability due to polio; foaming and snapping animal jaws and the deadly hydrophobia in humans infected by rabies virus; the death of tens of millions in the 1918 influenza pandemic; and so on. As invisible, transmissible harbingers of disease, it's really no wonder they don't have such a great press, why the general public knows so little about them, and why they engender such fear.

Taming, and even eradicating, some of these pathogens from the face of the globe has been a triumph of medical research. Observing the resistance to smallpox of milkmaids previously infected with cowpox led Edward Jenner to develop the principle of vaccination. Proving that he also didn't have a death wish and was also a father capable of making a point, he showed that people, including his own son, who had been exposed to pus from cowpox lesions, were protected from smallpox, albeit in a very eighteenth-century manner. Of course this new idea was not adopted without some controversy, and there is a classic 1802 *Punch* cartoon entitled, "The Cow Pock—or—the wonderful effects of the new inoculation!" showing people sprouting cow-like appendages from various parts of their bodies. I think of this as the nineteenth-century equivalent of a tweet from the anti-vaccination advocate Jenny McCarthy.

Over the years, the "isolate, attenuate, and vaccinate" paradigm was developed. Take poliovirus as an example: the agent was isolated from patients, grown in the laboratory, and then it was weakened (or attenuated). Following immunization, the vaccine replicated in people, did not cause disease, and led to the generation of antibodies which could fight off infection by the wild-type virus.

So here's the challenge! How do we balance our desire to create a vaccine with the need to isolate and attenuate dangerous agents when the first stage of the process demands we bring agents that paralyze, cause apparent madness, blister the skin, lead to hemorrhaging, cause heart and lung failure, or dreadful pneumonia into the laboratory from the wild? How can we dissect the critical steps involved in virus infection, spread, and transmission as viruses continue to emerge from animal reservoirs to infect people when they do just that—make people sick? Can we, should we, continue to work to tame these agents of disease in the laboratories of the world?

Someone once said, "Keep your friends close and your enemies closer," a mantra adopted by scientists worldwide as one pathogen after another has been isolated from nature and grown in laboratories. This "know your enemy" approach has served society well and has been critical in the development of vaccines against many major human and animal diseases. Smallpox has been eradicated from nature; polio is no longer a global problem, having been eliminated in all but a few countries; and a number of other severe, often fatal, diseases are no longer widespread threats.

We quickly forget that prior to the development of the measles vaccine, between seven and eight million children died every year because of this virus infection. Although measles virus is one of the most transmissible pathogens known, in the 1950s scientists assessed the risk of isolating it, decided that this could be done safely and the risk was worth taking, weakened it, and successfully developed a highly effective vaccine to protect against it. Now, due to widespread measles vaccination the number of global cases has fallen by over 99.9 percent. However, nature is full of surprises such as Middle East respiratory syndrome (MERS), Chikungunya, and Ebola virus, which now dominates social and other mass media outlets. Far from being safe, they are just a plane ride away, and viruses are everywhere, not just in research laboratories.

It's been quite a year for virologists. A new term, "gain of function," has been added to our vocabulary as a catchall for studies that aim to understand what it takes for an influenza virus to spread from one mammal to another. Points have been made about whether it is wise to help influenza become more transmissible in an animal model and that such "risky" experiments should not be undertaken. Recently, trust has been damaged by the surprise finding of 60-year-old samples of smallpox in a freezer at the National Institutes of Health and the inadvertent shipment of infectious anthrax and highly pathogenic

avian influenza virus from the Centers for Disease Control and Prevention. Points have been made about errors in sample tracking and failures to adhere to standard laboratory protocols. In the past few days, the US has been gripped by the arrival in Atlanta of an American doctor and technician who were infected with Ebola virus in Liberia. Points have been made that such individuals should have to suffer the consequences if they get infected and they should not be allowed to return back to the US.

Closer to home, the maximum containment National Emerging Infectious Diseases Laboratories (NEIDL) at BU cleared all the legal challenges and this world-class, state-of-the-art facility is ramping up to secure the necessary permissions to begin work. Points have been made—even by some in the medical community—that we should suspend all research at such laboratories until a review of recent laboratory mistakes at CDC is performed because the perceived risks are believed to outweigh the benefits, and that the number of facilities working on dangerous pathogens should be dramatically reduced. I consider such points misguided.

The good ship *Twitter* acts as a wonderful mixing vessel for the amplification of these points. Just like viruses replicating inside a cell, opinions and points transmit indiscriminately and insidiously and, in the absence of meaningful context, at best simply scare people or, worst case, have significant adverse effects on public health. The influence of anti-vaccine activists has already resulted in more measles cases in the US thus far in 2014 than in the last 20 years combined. Dissecting truth from fiction in a sea of comments when everybody in the world seems to have a point is not a trivial pursuit. This is why I am convinced it's critical for researchers to engage with other scientists and the general public proactively, rather than keep their heads down and attempt to fly below the radar.

To help provide a perspective from the individuals who work on these problems and address some of the concerns being raised, we recently took a big step and founded *Scientists for Science* (SfS) and [#scifsci](#) with a view to developing a forum to inform and educate, and “foster open and unbiased discourse on how to address these important contemporary issues in microbiology.” Collectively, SfS are convinced that banning certain types of experiments or closing facilities is not rational and are “confident that biomedical research on potentially dangerous pathogens can be performed safely and is essential for a comprehensive understanding of microbial disease pathogenesis, prevention and treatment.”

Small steps closer to home are also important. My parents, like many BU staff, City of Boston elected officials, journalists, local community residents, and middle and high school kids were fortunate to tour NEIDL to see my laboratory firsthand and appreciate all the safety and security systems in place. Unsurprisingly, after the tour my dad had a point. “Here’s my point...why would anyone want to work in a place which wasn’t safe?” he said. On that occasion I happily ceded to his point! I do not and will not, and in that I’m pretty representative of all the other virus-taming scientists I know.

Paul Duprex is an associate professor of microbiology at the School of Medicine and director of the Cell and Tissue Core at Boston University’s National Emerging Infectious Diseases Laboratories. He can be reached at pduprex@bu.edu. Follow him on Twitter @10queues.

Could an Ebola Treatment Already Exist?

Research led by a NEIDL scientist finds hope in Zoloft, Vascor

BU Today, Rich Barlow, June 9, 2015

<http://www.bu.edu/today/2015/could-an-ebola-treatment-already-exist/>

What if Zoloft and Vascor—safe prescription drugs that you can pick up at your CVS for depression and heart trouble, respectively—could treat Ebola?

A government study led by a researcher at BU's National Emerging Infectious Diseases Laboratories (NEIDL) suggests that this may be the case. If confirmed effective in humans—a finding that immunologist Gene Olinger says will take several years—doctors might sprint to a treatment well ahead of the standard 15-year, \$1 billion-and-up process of developing and marketing a new drug.

When the researchers treated 10 mice infected with Ebola with Vascor (bepridil), customarily used to control blood pressure in heart patients, all the mice survived the often-deadly virus. When they treated 10 mice with the antidepressant Zoloft (sertraline), 7 survived. The next step, Olinger says, will be to test the drugs in guinea pigs and monkeys.

Olinger is associate director for maximum containment training at NEIDL and a School of Medicine adjunct associate professor of infectious diseases. His study's drug analysis was done at his lab in Maryland, where he works as a contractor with the National Institutes of Health. NEIDL, on the Medical Campus in Boston's South End, is awaiting approval for Biosafety Level 4 research, which would include on-site, live-virus Ebola studies.

"This is exactly the type of work that the NEIDL was designed to support," says NEIDL director Ronald Corley, a MED professor. Olinger's research, like NEIDL's, he says, aims at "taking our basic understanding of pathogens and translating that information into potential therapies."

Olinger's work with viral hemorrhagic fevers (VHF) such as Ebola began a dozen years ago, when he was a civilian employee with the Army. Ebola has killed more than 11,000 Africans in an outbreak that began a year and a half ago alone.

"We started to develop a drug screen using a live virus" that might find effective therapies, Olinger says. Given the time and expense—and failure rate—of developing new drugs, "I was tasked to find a way to do something quickly." It made sense to screen existing Food and Drug Administration–approved drugs, not just for the time saved, but because "the repurposing approach has been used in infectious diseases before," he says. He cites two prominent examples: Viagra was originally a heart treatment drug before its effectiveness against erectile dysfunction was discovered, and thalidomide—used for nausea in pregnant women until it was found to cause birth defects—today is "a very good cancer drug."



Immunologist Gene Olinger, in the attire of his profession, thinks existing drugs for depression and heart disease might be effective against Ebola. Photo courtesy Gene Olinger 20

Olinger and his team screened 2,600 drugs, representing 90 percent of the FDA-approved pharmaceutical library, he says. Of those screened, 80, ranging from antihistamines to treatments for breast cancer, heart disease, and depression, appeared to have some effectiveness against Ebola. The drugs were put in dishes along with cells infected with the disease, to see if the drugs might block the virus. Those that looked most effective were tested in mice. Olinger says the effective drugs appear to work by damming up cellular pathways through which Ebola enters. "We do know there are synergistic

combinations that are possible,” he says, meaning that an ultimate therapy might involve a cocktail of several drugs, similar to the way HIV is treated.

The findings of Olinger and his team, published last week in the journal *Science Translational Medicine*, surprised even him. “I was shocked at the breadth of the type of drugs that had an impact,” he says, such as drugs blocking estrogen receptors in the cells. “Why would a virus need an estrogen receptor?” he says. “I could see years of research just on a basic level just off that one finding.”

Olinger is a co-developer of ZMapp, an experimental drug that has shown promise against Ebola during the recent African outbreak. He had hoped to go to Africa to help with the outbreak, he says, but was thwarted when the private firm he works for couldn’t get insurance to cover any evacuation costs. Instead, he filled in for colleagues who did go during meetings in Geneva of the World Health Organization.

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FY15 Funded Research

NEIDL faculty members received almost \$20 MM in funding in FY15 for the following projects:

Principal Investigator	Dept	Grant Title	Sponsor	Total Project Period	Amount Funded in FY15
The following are faculty whose work is done in the NEIDL					
Connor, John	Micro	Development of Near Real Time Multiplexed Diagnostics for Viral Hemorrhagic Fever	NIH/NAID	8/1/2011-7/31/2016	872,644
Connor, John	Micro	Evaluation of the Mechanism of Action of FDA-approved Compounds that Show Activity Against Ebolavirus	USAMRRA	8/18/2014-8/17/2016	287,024
Connor, John	Micro	Biomarker Discovery	IARPA/ Johns Hopkins	3/10/2015-1/31/2016	180,000
Corley, Ronald	Micro	National Emerging Infectious Diseases Laboratories Operations Grant	NIH/NIAID	6/1/2014-5/31/2016	12,477,891
Duprex, Paul	Micro	Shifting a Paradigm in Vaccine Safety: From Empirical to Rational Attenuation	NIH/NIAID	6/1/2013-5/31/2018	409,250
Duprex, Paul	Micro	Investigating Feline Morbillivirus Molecular Epidemiology in Cats in the North Eastern United States	Zoetis	8/26/2014-11/30/2015	105,486
Duprex, Paul	Micro	Mapping the Adaption of Animal Morbilliviruses to Human Cells: Evolution, Structural Modelling and Prediction	DARPA	9/30/2013-9/29/2015	449,280
Galagan, James	ENG-BME	Global mapping and analysis of a bacterial transcriptional regulatory network	NIH/NIGMS	6/1/2015-5/31/2019	570,271

Principal Investigator	Dept	Grant Title	Sponsor	Total Project Period	Amount Funded in FY15
Kramnik, Igor	MED-Pulmonary	Novel TB Treatment Strategy-Optimization of Macrophage Responsiveness to IFNy	NIH/NIAID	3/11/2015-2/28/2018	491,100
Kramnik, Igor	MED-Pulmonary	Genetic-based susceptibility of Pulmonary Tuberculosis	Tufts Univ	4/15/2015-3/31/2016	16,052
Muhlberger, Elke	Micro	Deep Characterization of <i>Rousettus aegyptiacus</i> Immune System Filovirus Replication: Initiation	DTRA /The Geneva Fdn	1/15/2014-1/14/2019	150,000
Muhlberger, Elke	Micro	Filovirus Replication: Initiation Mechanism and Role of RNA Secondary Structures	NIH/NIAID	8/5/2014-7/31/2016	163,700
Muhlberger, Elke	Micro	IMVC Pilot Project: Mechanisms of Ebola Virus-Induced Vascular Dysfunction	NIH/NIAID/Georgia Regents University	5/1/2013-4/30/2015	12,645
The following faculty are NEIDL Investigators but do not have labs in the NEIDL (affiliated)					
Kepler, Thomas	Micro	Modeling Affinity Maturation at Molecular Resolution	NIH/NIAID	4/15/2015-03/30/2020	1,616,696
Total					17,802,039

Seed Funding

Pilot funding to help support new innovative science and to further the NEIDL mission will be leveraged to promote multidisciplinary studies between NEIDL investigators and investigators across the institution. The following three programs received funding during this year.

John Connor used the seed funding to purchase an SP-1000 single particle imaging microscope from NexgenArrays. The SP-1000 is a newly designed microscope that allows the visualization of particles that are below the diffraction limit of visible light. Using the SP-1000 we are able to use green light to image and count virus particles that are normally only seen by electron microscopy. The purchase of this specific instrument allowed us 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.

James Galagan performed 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, we gained access to DNA for over 100 strains of MTB from two different sites in South India. Our analysis provides 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. Our analysis also reveals the genetic underpinnings of MTB drug resistance in India and highlights the limitations of current sequence based diagnostics for drug resistance diagnosis. A paper is currently in preparation and is expected to be submitted this quarter.

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

Education and Training

While the NEIDL does not directly sponsor educational programs or courses at the current time, it's faculty teach in a variety of curricula across the university, including in the School of Engineering, School of Medicine, School of Public Health, and School of Arts and Sciences. As noted earlier, it draws undergraduate and graduate students from across the university as part of its mission to train the next generation of scientists. Mentoring is a major commitment of every faculty member, each of whom is part of one or more established training programs, including: the Training Program in Host-Pathogen Interactions, the Bioinformatics Program, the Immunology Training Program, and Engineering.

The seminar program sponsored by the NEIDL brings in scientists from a variety of external academic institutions, research institutes and federal agencies.

NEIDL/Emerging Infectious Diseases Seminars		
Date	Speaker	Title
9/8/2014	Thomas Hoenen, Ph.D. Rocky Mountain Laboratories	"Reverse Genetics as a Tool For Studying the Biology of Ebolaviruses"
9/24/2014	Igor Kramnik, M.D., Ph.D. BU School of Medicine	"The Process of Dying: Thanatogenesis in Inflammatory Lesions – A Common Pathway and a Therapeutic Target"
10/1/2014	Marc Jenkins, Ph.D. University of Minnesota	"Tracking the Activation of CD4+ T Cells During Infection"
11/5/2014	Ekaterina Heldwein, Ph.D. Tufts U School of Medicine	"Mechanisms of Host Manipulation by Herpesviruses"
12/10/2014	Kevin Francis, Ph.D. Elena Dubikovskaya, Ph.D. École Polytechnique Fédérale de Lausanne, Switzerland	"Recent Advances in Preclinical Imaging of Infectious Diseases and Inflammation"
12/17/2014	Hideki Ebihara, Ph.D. NIAID, NIH	"In vitro and in vivo Approaches to Unraveling the Mechanisms for Replication and the Pathogenesis of Ebola and Marburg Viruses"
1/14/2015	Amanda Jamieson, Ph.D. Brown University	"Tolerance of Polymicrobial Infections of the Lung: Innate Immune Response and the Microbiome"
2/3/2015	Path/NEIDL Fac Candidate James Brien, Ph.D. Washington U in St. Louis	"Immune Recognition and restriction of Re-emerging Flaviviruses"
2/25/2015	Immunology Fac Candidate Anthony Rongvaux, Ph.D. Yale U School of Medicine	"Studying Innate Immunity using Mouse and Humanized Mouse Models"
3/5/2015	Immunology Fac Candidate Amelia Pinto, Ph.D. Washington U in St. Louis	"The Impact of Type I Interferon on Flavivirus Disease"

Date	Speaker	Title
6/11/2015	Student Invited Speaker Michael Katze, Ph.D. University of Washington	"Systems Virology: Can we help stop the Influenza, AIDS, and Ebola Epidemics"
3/18/2015	Matthew Frieman, Ph.D. University of Maryland	"SARS and MERS Coronavirus: Mechanisms of Pathogenesis"
4/15/2015	Mariano Garcia-Blanco, M.D., Ph.D. UTMB	"Flaviviral Host Factors: A Love-Hate Relationship"
6/3/2015	Adam Hume Boston University NEIDL	"Ebola Diagnostics in Sierra Leone; Field Experience"
6/22/2015	Qin Yu, Ph.D. Astra Zeneca	"RSV Inhibitors: Mechanisms of Action and Resistance"

As discussed earlier, safety and security are embedded in the fabric of the NEIDL as an essential component of emerging infectious diseases research. Monthly Biosecurity and Biosafety Grand Rounds serves as a forum to have informative conversations about the importance of conducting research in a safe and secure way.

Biosafety & Biosecurity Grand Rounds		
Date	Speaker(s)	Topic
10/21/2014	John Tonkiss Assoc Director, Biosafety Martin Rogers Mgr, Biocontainment Ops	An analysis of the formaldehyde room decontamination incident and learnings from the event
12/17/2014	Matt Rarick Director, Facilities	Maintenance Activities Risk Assessment (MARA) and an incident that occurred during a recent breathing air maintenance and repair by a contractor
1/22/2015	Steve Morash Director, Emergency Response Planning	Effluent Decontamination System (EDS) Emergency Drill on Simulated Leak; Report and Analysis
2/26/2015	Nahid Bhadelia, MD, MALD Director, Infection Control	Field Experiences in Ebola stricken Sierra Leone
3/18/2015	Jim Levin DVM DACLAM Director, ASC	Animal Care – Report & Analysis of Tulane NHP incident
6/24/2015	Matt Rarick Director, Facilities Dr. Tom Winters Director, ROHP	How to report incidents of exposure and injury to ROHP

Community Outreach

Effective communication with the community is an important component of the NEIDL's mission and purpose. To succeed, the Community Relations Core has been created to ensure that our local community is informed in a timely, transparent and ongoing basis about the operations, research and expertise of NEIDL personnel. We must continue to share and exchange information as well as to build trust through an education program focused on safety, relevance and the benefits of BSL-4 research. Below are the highlights from this past year's community outreach activities.

Community Liaison Committee (CLC)

The CLC serves as an ongoing means by which the NEIDL and the community engage and share information. It has been an effective tool for promoting public participation and transparency at the NEIDL. The group is comprised of a broad array of neighborhood, resident and community interests. Monthly meetings are open to the public and provide an opportunity for key NEIDL personnel and researchers to provide regular updates on operational, regulatory and other matters impacting the NEIDL.

Topics addressed this year included: NEIDL permitting process (CDC and the Boston Public Health Commission); antibodies, vaccines and computational biology; Ebola questions and answers; Ebola epidemic-lessons from one year of cases. In addition, CLC members have participated in emergency response planning drills and exercises 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 developed, evaluated, and implemented.

It should be noted that two of the CLC members sit as community representatives on the Institutional Biosafety Committee (IBC) and three of the CLC members participated as community members on the Boston Public Health Department's advisory committee for the NEIDL's BSL-4 permit.

Community Meetings

Representatives from the Community Relations Core have been active in the community by attending neighborhood and local business meetings as well as community events on a regular basis. The Community Relations team continuously seeks and takes advantage of opportunities to provide information on the NEIDL as appropriate and to be regularly seen in the community as a resource. During the fall, the NEIDL was asked to attend a question and answer session at one of the neighborhood association meetings. We discussed CDC and NIH best practices after the lab incidents involving smallpox, anthrax and bird flu. This opportunity allowed us to discuss NEIDL best practices and emphasize our culture of safety and rigorous oversight procedures.

Website

The NEIDL website (www.bu.edu/NEIDL) is designed to provide extensive, accurate and timely information on the NEIDL. It has proven to be a valuable source of information on the facility and is regularly updated, and designed to be user friendly. CLC minutes are posted here as are the safety plans designed to support the culture of safety at the NEIDL and throughout the University. The Incident Report for the NEIDL, including all of the University laboratories, is posted quarterly. Also, there is a link

to the IBC and its public minutes. Press releases and articles from local newspapers with information about the NEIDL are posted here as well. BU Today published a series of timely articles about Ebola that featured a number of our researchers as subject matter experts. These articles were posted on the website and widely distributed to the community. The response was positive. These articles were really informative and educational. They helped to drive home the need for facilities such as the NEIDL.

Tours of the NEIDL facility

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. Ultimately, these visitors become ambassadors for the NEIDL.

In the past year, a number of local community organizations have taken tours of the NEIDL facilities, such as: Boston Private Industry Council (bostonpic.org), Upward Bound at BU (bu.edu/ub), Youth Enrichment Services Boston (yeskids.org). Among the City and State government representatives who have taken tours this year are: BPHC Interim Commissioner Dr. Huy Nguyen, State Senator Jason Lewis (D - Winchester), State Representatives Kate Hogan (D - Stow), Daniel Hunt (D-Dorchester), Evandro Carvalho (D-Dorchester), and Daniel Cullinane (D-Dorchester), and Massachusetts State Department of Public Health's Director of Epidemiology Dr. Lawrence Madoff.

In addition, students and faculty with varying research and academic interests, from Medical and Charles River campuses, as well as students and staff from Harvard University, MIT, State University of New York, Stonehill College, and Lancaster University, UK have been shown around the NEIDL facility.

For the first time since the opening of the NEIDL facility, the Community Relations team organized a Family Day. On a snowy Saturday in January the NEIDL opened its doors to NEIDL employees' family members, who for a long time have been interested in taking a look inside the building and learning about its mission and the important work done in this unique and highly secured facility. Over 100 family members, including spouses, children, parents, and significant others, all escorted by NEIDL employees, participated in this internal yet important community outreach event.

Engagement with senior scientists. As part of the NEIDL's mission to engage globally, we continue to meet with scientists from academia, government and pharma from international organizations. This is critical to our goals of engaging broadly and globally to further our missions. The NEIDL continued to host visits with a number of accomplished scientists and physicians from national and international organizations. Among them this year include: Rajata Rajanathan, Minister of Health of Thailand; Jeremy Farrar, Director of the Wellcome Trust, UK; Oyewale Tomori, President of the Nigerian Academy of Science; Victor Dzau, President of the National Academy of Medicine; Christian Mandl, Novartis Vaccines' Global Head of Research; Michael Rosenblatt, Chief Medical Officer for Merck.

Consortium of Universities for Global Health (CUGH)

Through the efforts of the Community Relations Core, some 40 students in the 11th and 12th grades from schools in and around Boston and their science teachers attended the last day of a conference on global health issues, including Ebola. NEIDL played a leading role for this conference, as Dr. Gerald Keusch was the principal organizer, and the university and the School of Public Health were among the principal sponsors of this three (3) day conference. Dr. Peter Piot and Muyembe Tamfum, the original discoverers of the Ebola virus, and the NEIDL's Dr. Nahid Bhadelia, were among a group of eminent panelists to

discuss “Ebola Epidemic: Looking Back, Lessons Learned, Looking Ahead”. The students and their science teachers enjoyed the event and asked to be invited to future events that highlight important science and public health issues.

Educational Programs: Infectious Disease

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 and High School Students. It is focused on infectious diseases and answers a variety of different questions. What do they look like? How are they identified? What are their components? How are they transmitted? Why do we need safe containment facilities to research these emerging infectious diseases?

In the spring of 2015 the **ID2** program was delivered to 5th and 6th grade classes at the Trotter Elementary School (Dorchester) and Hurley School (Boston).

The students had fun working with the NEIDL researchers, putting on personal protective gear (masks, goggles, gloves and coats), using pipettes, and building biosafety cabinets. Feedback from students and faculty alike has been strongly positive.



NEIDL Faculty serving in West Africa

The Ebola outbreak in West Africa in 2014 caught the international community off guard, as instead of being self-limited in isolated rural areas in Central and East Africa it reached the urban centers of three West African countries and seemed to be out of control. The speed of progression soon outstripped the usual measures and international responses to such outbreaks. Among the many who responded were members of the NEIDL who volunteered to serve in the front lines of the Ebola epidemic.

We were fortunate to be able to support two members of the NEIDL to donate their expertise to the outbreak giving clinical care (Dr. Nahid Bhadelia) and to work with a Dutch Team in a mobile diagnostic laboratory (Dr. Adam Hume).

U.S. Doctor to Travel to Sierra Leone to Help Ebola Victims

NPR, Kelly McEvers, August 20, 2014

<http://www.npr.org/2014/08/20/341826136/>

Dr. Nahid Bhadelia, an infectious diseases expert at Boston University, is going to Sierra Leone to help care for Ebola patients. She talks to NPR reporter Kelly McEvers about the challenges she expects to face. Transcript:

KELLY MCEVERS, HOST:

One reason the Ebola virus is so hard to treat overseas is it's difficult to find volunteers to help patients. But some Americans are heading right into the heart of the epidemic. Doctor Nahid Bhadelia is one of them. She's an infectious disease expert at Boston Medical Center in Boston University. She and two of

her colleagues are going to Sierra Leone with the World Health Organization. We talked to her just before she got on the plane. I asked her what made her decide to do it.

NAHID BHADDELIA: This outbreak is becoming truly a complex humanitarian emergency in the truest sense of the word. You know you have not just the elements of the disease but then add to that the elements of violence that we've seen and also the need for a military presence in some instances and such. So, all those things I think make this a historical moment and I feel compelled to help if I have the skills to do so.

MCEVERS: And I do have to ask are you afraid?

BHADDELIA: I have to say the thing that weighted most on my mind was actually the international travel between now and getting there. I'm eager to get started. I have had experience working with blood-borne pathogens in the past. So, whatever anxieties I may have I've been able to put those behind me.

MCEVERS: How do you do that? How do you put those fears behind you?

BHADDELIA: I think you click on this mode of being the caretaker. We do it all the time as physicians, you know. And I would say it's something that a lot of us are doing since the news of my own departure was published I received so many phone calls and e-mails from other physician who've said they're either going or they want to go. And I personally know of other doctors who feel the same way, you set the fear aside and say hey this is my job.

MCEVERS: And we've heard a lot of reports about, you know, the lack of the most basic equipment like latex gloves. Are you and your colleagues traveling with lots of protective gear? And I mean not just for yourselves but for others on the ground?

BHADDELIA: Yes, actually most of my luggage is personal protective equipment that I'm taking down. It sounds like that is still an issue. And so certainly we're doing that. What's made it difficult is I had a few boxes of donations as well that I was going to ship out ahead of us but the shipping carriers many of them stopped shipping to that area.

MCEVERS: And what do you hope to learn for this?

BHADDELIA: Personally I think it's one of those things - Henry Ford said man's greatest discovery is the fact that he can actually do something he was afraid he couldn't. I'm paraphrasing but something along those lines. And for me that personally will be the largest achievement. I'm excited to go down there, to be able to do this. And honestly I have to tell you one of the biggest reasons is I hope that it inspires more people to go.

MCEVERS: Doctor Nahid Bhadelia, thank you so, so much for this and good luck on your trip.

BHADDELIA: Thank you. Thank you for having me.

MCEVERS: We'll be checking in with Doctor Bhadelia from time to time here on MORNING EDITION. And she'll be blogging about helping with the Ebola outbreak on our global health blog at npr.org. It's called Goats and Soda.

What a Boston Doctor Learned Treating Ebola Patients in Sierra Leone.

WBUR's Morning Edition, Bob Oakes, October 14, 2014

Bob Oakes interviews Dr. Nahid Bhadelia. View interview highlights here:

<http://www.wbur.org/2014/10/14/bhadelia>



Dr. Nahid Bhadelia, back in Boston (Robin Lubbock/WBUR)

Dr. Nahid Bhadelia traveled to Sierra Leone in August, working as a WHO physician treating Ebola patients. She's an infectious diseases doctor at Boston Medical Center and director of infection control at Boston University's National Emerging Infectious Diseases Laboratories.

She joined WBUR's *Morning Edition* to speak about the outbreak in West Africa.

On the lack of health care workers there

"We had a limited number of doctors and so when you have a large number of patients — the census at the Ebola treatment unit that I was at was about 80 to 100 — there were about four or five physicians and the local nurses and other health care workers. It limited the amount of interaction you could have with the patients. You needed to prioritize who you could save."

What more resources would mean for West Africa

"People survive this disease. For those who made it into our care in time, the mortality rate was less than 40 percent, and that is with the limited number of people and limited physical resources. A majority of people can survive this disease and that is with more resources and more hands."

What's different here in America — and what needs to happen here

"One of the reasons that this epidemic has propagated so much in West Africa, it truly is lack of basic resources or cleaning up potential contamination and such. Here we have all those resources, training becomes a big part of that now here. We have to train our staff."

Mobile Diagnostics in Sierra Leone

During the summer of 2014, while the worst Ebola epidemic recorded in history was raging in the Western African countries of Liberia, Guinea, and Sierra Leone, **Dr. Adam Hume**, had expressed interest in volunteering at a local diagnostic lab to help in the efforts of containing the epidemic. As a postdoctoral research scientist at the NEIDL, Adam knew he was well qualified for this type of work. He had hands-on experience using the diagnostics technique called real time Polymerase Chain Reaction or PCR used for testing Ebola and, more importantly, he had experience working with Ebola virus in a high-containment BSL-4 lab at the Texas Biomedical Research Institute in San Antonio. Adam's research at BU is primarily focused on determining the mechanism(s) that *Rousettus aegyptiacus*, a species of bat which is a natural reservoir of Marburg virus (closely related to Ebola virus), uses to control virus infection and prevent severe morbidity and mortality.

Adam was able to volunteer in the spring, 2015 supported by Partners in Health (PIH), a Boston-based public health organization that had been actively participating in the fight against Ebola in West Africa. PIH oversees a mobile Ebola diagnostic laboratory in the eastern district of Kono in Sierra Leone. This lab was donated and financially supported by the Dutch government through the Netherlands Enterprise Agency, and supplied and staffed by Erasmus University, in Rotterdam.



Dr. Adam Hume on the far right, with lab team members and local PIH volunteers.

Dr. Hume spent five weeks in a mobile lab, where he and his team tested over 400 samples of tissue and blood for the presence of Ebola.

In numerous occasions local residents of Kono expressed their gratitude to the team for the work they were doing. Personally for Adam, like for many laboratory scientists whose work is far removed from clinical/patient care and seldom acknowledged by those who ultimately benefit from his work, these personal interactions with the people of Kono and their recognition were extremely rewarding.

Events and Programs

Expert Panel Discussion:

The Truth about Ebola for New England: Fact vs. Hype

Speaking at a public forum on Ebola at Boston University's National Emerging Infectious Diseases Laboratories (NEIDL) on November 7, 2014, NEIDL director Ronald B. Corley stressed the importance of scientists engaging with the public about the realities of the disease. The NEIDL, he said, has mounted an education outreach campaign to do just that.

"It's not just about Ebola," Corley told the audience of several dozen people from the business and health care community. "It's about infectious diseases in general. It's about research. We have to show we're not just nerds working in a facility. We want to exchange information—not just with our nerd colleagues, but with the public in general. It's not something we've done well over the last 10 to 20 years and it's up to us to change, I think."

The forum was convened by The New England Council, a business organization that has been a strong supporter of research at the NEIDL. Corley was joined by Nahid Bhadelia, a physician who is director of infection control for the NEIDL and who traveled to Sierra Leone in August to help care for Ebola patients; Paul Biddinger, chief of the division of emergency preparedness and medical director for emergency department operations at Massachusetts General Hospital; and Jamie Childs, a Yale School of Public Health senior research scientist and lecturer in epidemiology.

Original article from: BU Today posted on November 20, 2014. By Sara Rimer

Rhett Talks w/ Paul Duprex

Bringing Viruses in from the Cold and Heating them Up!

"I am fascinated by viruses! As nature's nanomachines, they are incredibly diverse and come in more "flavors" than all the plants, animals, fungi, bacteria, and other unicellular organisms on earth put together. Why? Because as the nursery rhyme says, "Big fleas have little fleas, upon their backs to bite 'em, and little fleas have lesser fleas, and so, ad infinitum." I will discuss why and how pathogen taming scientists bring these invisible, transmissible harbingers of disease in from the wild rather than leave them to their own devices."

Filmed on November 20, 2014. View video here (21 minutes):

<http://www.bu.edu/neidl/rehtt-talk-duprex>



Nahid Bhadelia speaks at The Consortium of Universities for Global Health 2015 Conference

“Epidemic Ebola: Looking Back, Lessons Learned, Looking Ahead”

The world faced the largest outbreak of Ebola virus disease ever in three poor West African countries. This panel includes experts on Ebola from multiple disciplines, diverse perspectives on the agent itself, first-hand experience on its epidemiology and transmission, the clinical care of affected individuals, systematic infection control on the ground, the ethics of prevention and treatment with unproved vaccines and therapeutics and how to conduct clinical trials during an outbreak. Wherever the world is in the course of the epidemic the approach of the panel is to be a look back to identify lessons learned, and then how to plan ahead so this does not happen again.

Moderators:

Michele Barry, Senior Associate Dean for global Health, Stanford University
Peter Piot, Director & Professor of Global Health, London School of Hygiene and Tropical Medicine;

Speakers:

Peter Piot, Director & Professor of Global Health, London School of Hygiene and Tropical Medicine;
Jean-Jacques Muyembe Tamfum, Director, Institut National de Recherche Biomedicale (NRB);
Beth P. Bell, Director, National Center for Emerging and Zoonotic Infectious Diseases (CDC);
Larry Madoff, Editor, ProMed Mail;
Oyewale NMI. Tomori, President, Nigerian Academy of Science;
Nahid Bhadelia, Director of Infection Control, Boston Medical Center and National Emerging Infectious Diseases Laboratory, Boston University;
Larry Gostin, Faculty Director, O'Neill Institute for National & Global Health Law.

A full recording of the conference available at: <https://cugh.org/resources/videos/2015-conference-plenary-vii>



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