



## DEAN'S MESSAGE: What's On My Mind



What's on my mind this month is the tenacity, bravery and dedication of the healthcare professionals who volunteer to go to the front lines of deadly infectious disease outbreaks because of their commitment to preserving the well-being of all people.

Since the news of an Ebola outbreak in Guinea was announced in March of this year, every day we hear updates about the toll this virus has taken on the people of West Africa. Ebola hemorrhagic fever has swept through multiple countries, killing an estimated 1 in 2 people who have become infected. The September 23, 2014 *Morbidity and Mortality Weekly Report*, published by the Centers for Disease Control and Prevention (CDC), estimated that, under a worst-case scenario, 1.4 million people could be infected with the virus by January 20, 2015, and a similar report, published in the *New England Journal of Medicine*, predicted that Ebola might become endemic to Africa, along the lines of HIV/AIDS.

These dire forecasts do not take into account the commitment of healthcare workers, physicians, research scientists and physician-scientists around the world who have mobilized against the Ebola outbreak. **I am pleased and proud that School of Medicine faculty members are among those on the front lines of the public health counterstrike against Ebola.**

For example, **Alan Schmaljohn, PhD**, a professor in the Department of Microbiology & Immunology, developed an antibody against Ebola and is the co-inventor of one of the antibodies used in the cocktail that successfully treated two American aid workers who became infected with the virus. He is currently developing Ebola vaccine candidates.

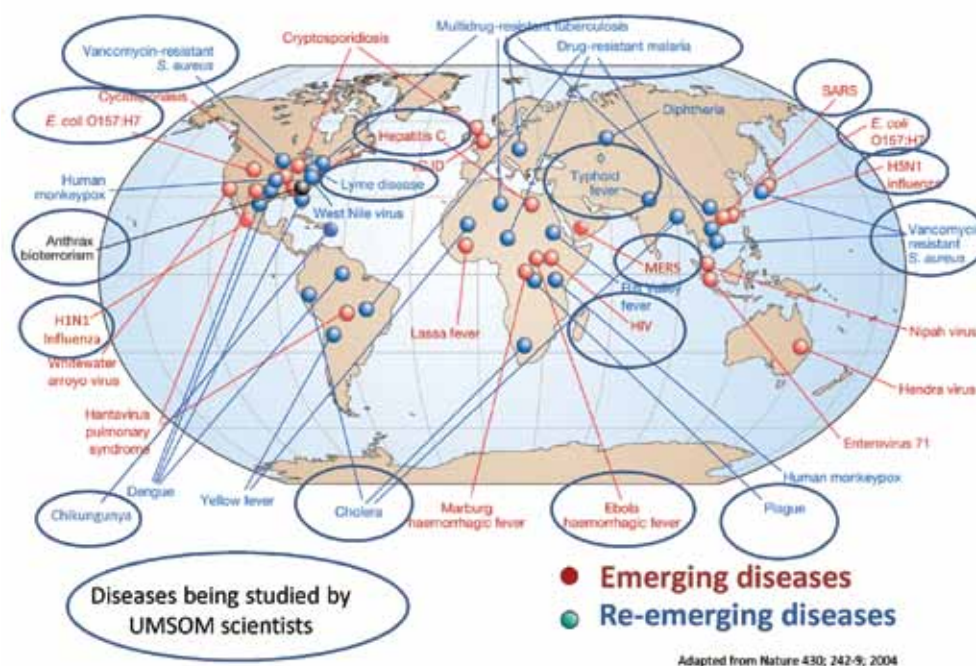
At the end of August, we announced that **Myron "Mike" Levine, MD, DTPH**, founding director of the Center for Vaccine Development (CVD) and a professor in the Department of Medicine, has been asked to lead Ebola vaccine clinical trials in Mali, along with CVD-Mali's director **Samba Sow, MD, MS**, an adjunct professor in the Department of Medicine.

However, combating a major public health threat is not new for our faculty. For decades, the School of Medicine has established and built up robust programs in biomedical research and clinical care, making us poised and ready to respond to any new public health threats that emerge or re-emerge. **As the May and August issues of SOMnews highlighted, respectively, our faculty in the CVD and Institute of Human Virology (IHV), as well those working across all our academic units, have investigated some of the most devastating pathogens of the last two centuries, from malaria to HIV/AIDS, cholera to tick-borne diseases, Severe Acute Respiratory Syndrome**

**Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), to pandemic influenza virus, hepatitis C virus, and enteric diseases.**

Our work has dramatically impacted efforts to combat infectious diseases on nearly every continent. Because of our deliberate decisions to invest and reinvest in strategically focused research programs years ago, today, it is almost **more** difficult to identify where we **are not** working than to pinpoint where we **are** working. This

### Emerging & Re-emerging Infectious Diseases Worldwide



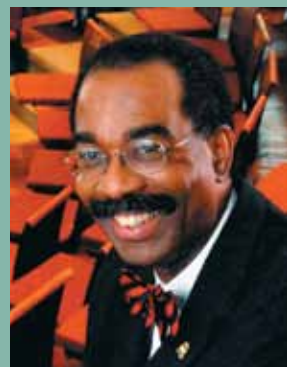
is something that truly sets the School of Medicine apart from our sister institutions. We are privileged to have colleagues who work tenaciously to improve the well-being of people here in the United States and around the world. Much of our impact in the area of infectious diseases has been felt by people in developing nations who are the most vulnerable to illness, because they often live in austere conditions with very little access to health care.

This month, we highlight the efforts of our investigators working to combat Ebola, but I applaud our entire School of Medicine community, because you have dedicated your careers to understanding and enhancing the health of all people through the basic research, translational studies, and clinical work you conduct here each and every day.

In the relentless pursuit of excellence, I am

Sincerely yours,

E. Albert Reece, MD, PhD, MBA  
Vice President for Medical Affairs, University of Maryland  
John Z. and Akiko K. Bowers Distinguished Professor and  
Dean, University of Maryland School of Medicine



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## The School of Medicine Plays a Role in

# the Fight Against Ebola

University of Maryland School of Medicine Begins Human Trials of Experimental Ebola Vaccine



The University of Maryland School of Medicine (UM SOM) Center for Vaccine Development (CVD), in conjunction with its sister institution, The Center for Vaccine Development of Mali (CVD-Mali) and the Ministry of Health of Mali, have begun a clinical trial to evaluate a promising experimental Ebola vaccine.

The trial, which began in early October, will test the vaccine on 37 Malian health care workers.

"This research will give us crucial information about whether the vaccine is safe, well-tolerated and capable of stimulating adequate immune responses in the highest priority target population, health care workers in West Africa," said Myron Levine, MD, DTPH, director of the CVD as well as a professor of medicine, pediatrics, epidemiology, public health, microbiology and immunology at the UM SOM.

"If it works, in the foreseeable future it could help alter the dynamic of this epidemic by interrupting transmission to health care and other exposed front-line workers."

The vaccine, which was developed by investigators at the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, MD, consists of a chimpanzee adenovirus (cold virus) that does not cause illness in humans, and has been modified so that it cannot multiply in humans but produces a single attachment protein of Ebola virus. Immune responses directed against this protein have been shown to be highly protective in animal studies. Researchers hope this response will be robust enough to protect humans too.

The clinical trial in Mali brings to fruition two months of work by a consortium dedicated to move the vaccine into clinical studies in West Africa. The consortium, assembled in mid-August at the behest of the World Health Organization (WHO), also includes the VRC (which developed the vaccine), the Jenner Institute at the University of Oxford (which carried out clinical trials in UK adults paving the way for the African trial), the CVD-UM SOM and CVD-Mali (carrying out the first clinical trial of the vaccine in West Africa), GlaxoSmithKline (GSK) Biologicals (manufacturer of the vaccine) and the Wellcome Trust, UK (funder of the clinical trials in UK and Mali), with additional funding provided by the Medical Research Council (MRC), UK and the UK Department for International Development (DFID). Ordinarily it would take six to 11 months to move a vaccine that had not previously been tested in humans from animal studies to a clinical trial in a developing country where subjects are at risk of the disease itself. But with all consortium members working together, it took just two months to undertake the initial trials in an industrialized country and to obtain the ethical reviews and administrative and political approvals to begin the trial in Mali.

"This is just the critical first step in a series of additional clinical trials that will have to be carried out to fully evaluate the promising vaccine," said

The West African trial will ensure that the research takes into account differences between populations in the developed world and West Africa, which might affect clinical acceptability or immune responses.

Professor Samba Sow, Director General of CVD-Mali. "However, if it is eventually shown to work and if this information can be generated fast enough, it could

become a public health tool to bring the current, and future, Ebola virus disease epidemics under control."

"Malian health care workers are showing keen interest in participating in the clinical trial to help evaluate this vaccine," said Dr. Milagritos Tapia, a key clinical investigator overseeing the trial in Mali.

"Ebola is among the most urgent international public health issues that the world is facing. This clinical research will play a key early role in helping to solve it," said E. Albert Reece, MD, PhD, MBA, Vice President for Medical Affairs, University of

Maryland and the John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine. "Dr. Levine, Dr. Sow and Dr. Tapia have done an extraordinary job, and are working hard to contribute their expertise to the worldwide effort to fight this virus."

Pre-clinical research in primates by the VRC and Okairo, a biotechnology company acquired last year by GSK, indicates that the vaccine provides protection in non-human primates exposed to Ebola without significant side effects. The recent increase in funding for Ebola vaccine research is also enabling GSK to begin manufacturing at least 10,000 additional doses of the vaccine, even as the first clinical trials are occurring.

"An impressive communal effort by multiple groups allowed this trial to get off the ground very quickly," said Dr. Levine. "It is a testament to everyone's commitment to fighting Ebola as aggressively as possible."

This collaborative multi-trial approach will help ensure fast possible progress to determine the best candidate vaccine approach and delivery. The West African trial will ensure that the research takes into account differences between populations in the developed world and West Africa, which might affect clinical acceptability or immune responses.

Researchers hope the first Malian trial will be largely finished by the end of 2014, after which Phase 2 clinical trials involving larger numbers of subjects, particularly health care workers, including in countries heavily affected by Ebola, could commence in 2015. Much depends on GSK's ability to optimize manufacturing methods to increase the yield of vaccine doses for larger clinical trials.

CVD-UM SOM has earned an international reputation for creating and testing vaccines against cholera, typhoid, non-typhoidal *Salmonella*, *Shigella* dysentery, malaria, and multiple other infectious diseases, including influenza. In addition to its research and outpatient facilities in Baltimore, the CVD conducts extensive research in Africa, Asia and Latin America.

## SOM Scientist at the Forefront in Developing a Vaccine for the Ebola Virus

In September, a patient with undiagnosed Ebola entered the United States, and subsequently died of the disease. As his delayed diagnosis showed, the medical community has much to learn about how to diagnose and treat the virus. In fact, some experts point out that the number of medical professionals who can properly diagnose Ebola and recommend the next steps for treatment is alarmingly small.

Some scientists, however, like Alan Schmaljohn, PhD, a professor in the Department of Microbiology & Immunology at the University of Maryland School of Medicine (UM SOM), have spent decades studying Ebola and similar viruses, identifying key characteristics that have aided in the development of vaccines, antivirals and treatment methods.

As a leader of research and chief in the Viral Pathogenesis and Immunology Branch with the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Dr. Schmaljohn helped identify three of the key antibodies that are used currently in combination with each other to treat patients infected with Ebola.

Dr. Schmaljohn is now one of the scientific leaders in the UM SOM partnership with Department of Defense contract recipient Paragon Bioservices in the manufacture of an Ebola virus vaccine for initial safety testing in humans.

"Several vaccine candidates for Ebola virus are proceeding through initial manufacture toward safety testing in human volunteers," Dr. Schmaljohn said. "Different vaccine candidates are based upon different 'platforms' in which selected viral proteins may be made 'in the test tube' and purified for injection, or may be added genetically as passengers of a

different variety of virus that is weakened. Only human trials will provide the final answers as to which vaccines are best on the basis of many criteria, foremost being safety and efficacy."

Dr. Schmaljohn was one of the original leaders in determining what kinds of immune responses are required for protection against viruses like Ebola, and he was part of the team that first identified antibodies capable of protecting certain animals from Ebola. "Subsequently," he said, "three of these antibodies have been developed as a candidate mixture for human therapy against Ebola

virus, which seems to be true with an American who was infected with Ebola virus during the current outbreak." However, he cautions that many scientific questions remain unanswered.

E. Albert Reece, MD, PhD, MBA, Vice President for Medical Affairs, University of Maryland and the John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine, said, "We are grateful to have scientists at the UM SOM like Dr. Schmaljohn who have studied viruses like Ebola for decades. We can now build on that knowledge and understanding to focus on bridging the science to the development of new vaccines. The University of Maryland School of Medicine is well-positioned to play an integral role in addressing this serious public health issue."

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## SOM Faculty Working on Ebola



► **Myron M. Levine, MD, DTPH**, Director of the Center for Vaccine Development (CVD). In October 2014 the CVD, in conjunction with the Center for Vaccine Development of Mali (CVD-Mali) and the Ministry of Health of Mali, began the first-ever human trial in West Africa of an experimental Ebola vaccine. Dr. Levine has been working on vaccines for more than four decades but on Ebola vaccines only since August 2014 when requested to do so by the World Health Organization.



► **Samba Sow, MD, MSc**, Director General of CVD-Mali, is playing a key role in the Ebola vaccine trial in Mali, as the local principal investigator of the trial.



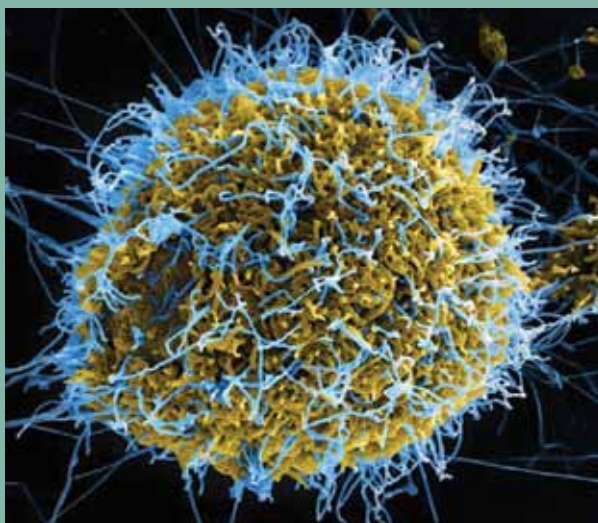
► **Milagritos Tapia, MD**, Assistant Professor of Pediatrics and faculty member of the CVD, travels back and forth between Baltimore and Bamako, Mali. She is the Maryland Principal Investigator of the first Ebola vaccine clinical trial in Mali.



► **Kirsten Lyke, MD**, Associate Professor of Medicine and faculty member of the Malaria Group in the CVD, is also involved in Ebola vaccine clinical trials.

► **Alan Schmaljohn, PhD**, Professor

of Microbiology and Immunology, has spent decades studying Ebola and similar viruses, identifying key characteristics that could lead to the development of vaccines and treatments.



## A Perfect Ten: Grant Success is Within Our Reach

On June 27th, 2014 Dr. Robert Bloch of the physiology department, was notified that his R21 grant application had not only been well received by the NIH, but had scored a perfect 10 impact rating upon review.

Ecstatic, he rattled off congratulatory notes to all personnel involved and left for the weekend with an excitement rarely witnessed within the halls of HSF I. Why such enthusiasm?

It's no secret that the economic climate in recent years has adversely affected funding for scientific research and that competition for those limited funds is at its peak. As young scientists we are regularly reminded of how tenuous our funding may be and we are often encouraged to seek alternative opportunities outside of academic research. Dr. Bloch's story provides a shining example that, while it does not come easy, grant success is still within our reach.

The R21 grant is an NIH award for exploratory and developmental research. Its goal is to fund projects that are in the early and conceptual stages of development. Applications are reviewed for scientific and technical merit and the impact score is based on 5 major areas: significance, investigator, innovation, approach, and environment.

Dr. Bloch's proposal involves using a novel xenografting approach to study a complex form of muscular dystrophy, facioscapulohumeral muscular dystrophy, or FSHD. To date, the molecular pathophysiology of FSHD has been poorly understood owing to the fact that the causal genetic dysregulation is not reproducible in animal models. Instead, Dr. Bloch is now funded to develop and optimize a technique in which he engrafts immortalized human myogenic precursor cells, previously isolated from FSHD patients and unaffected relatives, into the tibialis anterior compartment of a mouse hindlimb. Using firefly luciferase luminometry he is able to track the success of the xenografted muscle over the course of several weeks. He proposes to vary many of the experimental conditions to ultimately produce a fully mature and functional human tibialis anterior muscle within the mouse hindlimb. He then plans to use his optimized approach to assay the pathophysiology of the FSHD muscle and perform therapeutic testing in ways that are not possible using current models.

A maximal impact score does not mean that the proposal was initially accepted wholly without question. Dr. Bloch received no less than 20 comments from the four reviewers, each of which he was able to address upon resubmission. So then, what is the recipe for this grant's success? The compelling nature of the problem combined with the novelty of Dr. Bloch's approach, his encouraging preliminary data, his positive responses to the reviewers' concerns, and the potential for groundbreaking therapeutic outcomes all contributed to his grant receiving an impact rating of 10. With his hard work and dedication Dr. Bloch has given us a rare and inspiring tale of R21 funding.

Dr. Bloch would like to thank the members of his laboratory and everyone who collaborated to make this grant a success.



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## Another Successful Mini-Med School Comes to an End

Mini-Med School is an exciting initiative by the University of Maryland School of Medicine. It offers a series of tuition-free classes on important health conditions that affect many in our local community. These classes are open to everyone, young and old. One of the major aims of Mini-Med School is to provide participants with easy-to-digest information on critical healthcare issues.

The 2014 Mini-Med School session commenced on September 10 with a welcome speech from E. Albert Reece, MD, PhD, MBA, Vice President for Medical Affairs, University of Maryland, and the John Z. and Akiko K. Bowers Distinguished Professor and Dean, University of Maryland School of Medicine. The five-week program consisted of a series of diverse lectures focusing on obesity; the Affordable Care Act; dermatologic diseases; diabetic retinopathy; joint replacement surgeries; HIV testing and living with HIV; proton therapy; children's mental health, and the science behind addiction. There were two classes each night, with the exception of the last, each of which concluded with a question and answer session. The graduation ceremony was held on the last night, October 8, with Dean Reece handing out graduation certificates to those who had attended at least four sessions.

This Mini-Med School program stressed the interdependence of basic research and medical technology and informed the participants about the groundbreaking research conducted at the School of Medicine. Well-received by our neighbors in downtown Baltimore, Mini-Med continues to grow every year. If you would like to participate as an instructor for next fall's session, please contact Caelie Haines at [chaines@som.umaryland.edu](mailto:chaines@som.umaryland.edu).



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 ▲ E. Albert Reece, MD, PhD, MBA, Vice President for Medical Affairs, University of Maryland, and Dean, University of Maryland School of Medicine ▲ Chris Hardwick, Executive Editor ▲ Caelie Haines, Managing Editor  
 ▲ Tom Jemski and Mark Teske, Head Shot Photos ▲ Brushwood Graphics Design Group, Design  
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UNIVERSITY of MARYLAND  
 SCHOOL OF MEDICINE  
 655 West Baltimore Street  
 Baltimore, Maryland 21201-1559



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