

Ebola Research Begins at BU

After years of review, lab receives first BSL-4 pathogen

EIGHT MONTHS AFTER receiving final approval from the Boston Public Health Commission to conduct research at Biosafety Level 4 (BSL-4), Boston University's National Emerging Infectious Diseases Laboratories (NEIDL) has begun work with its first Level-4 pathogen, the Ebola virus.

"This is clearly an important step for the NEIDL," says Ronald B. Corley, NEIDL director and a School of Medicine professor of microbiology. "This will permit us to fulfill our mission of studying emerging pathogens and developing diagnostics, therapeutics, and vaccines for these pathogens, even those that require BSL-4 containment. It has taken a very long time to get to this point, but the time that has passed has not dampened our enthusiasm—and excitement—to be able to start BSL-4 work."

NEIDL microbiologist Elke Mühlberger says the lab's first Level-4 projects will examine how the Ebola virus damages cells in the liver, and why it triggers such a powerful inflammatory response. Answers to those questions, she says, could speed the development of a therapy for Ebola virus disease, which sickened tens of thousands of people and led to more than 11,000 deaths in West Africa in a 2014–2016 outbreak, and sickened 59 people and killed 97 in an outbreak in the Democratic Republic of Congo this year.

Ebola virus causes a rare but life-threatening disease that has become a global public health threat, traveling to the United States and Europe during the 2014 outbreak. There is no available FDA-approved vaccine or therapy for the virus, which along with the related Marburg virus arrived at NEIDL in August.



Microbiologist Elke Mühlberger (left) and research scientist Adam Hume hope to learn how the Ebola virus damages human liver cells.

Mühlberger, a MED associate professor of microbiology, says the researchers' plans include at least three projects involving the Ebola and Marburg viruses, all funded by the National Institute of Allergy and Infectious Diseases, which also provides more than \$10 million a year to help underwrite the cost of operating the BSL-4 in the NEIDL.

The first project will use human liver cells generated from induced pluripotent stem cells at BU's Center for Regenerative Medicine by stem cell biologist and tissue engineer Gustavo Mostoslavsky, a MED associate professor of medicine and microbiology.

"We are excited to use these cells," says Mühlberger, "because the liver is one of the main target organs of Ebola virus infection. We will use Gustavo's cells to find out why Ebola virus is so devastating for the liver."

A second project, which follows up on research conducted by NEIDL researcher John Connor, a MED associate professor of microbiology, will examine why the

Ebola virus triggers an inflammatory response in specific immune cells. Mühlberger says researchers will also work with the Marburg virus, hoping to learn why it kills humans but not Egyptian fruit bats, a mystery that has been studied by Thomas Kepler, a MED professor of microbiology.

"The need for this facility is even more acute today than when it was first built," says Corley. "And we remain committed to being completely transparent in our operations, and maintain the NEIDL with the greatest attention to safety and security."

In December 2017, after more than three years of review, BSL-4 research at the NEIDL was approved by the Centers for Disease Control and Prevention, and last December the lab received final approval from the Boston Public Health Commission. All BSL-4 research conducted at the NEIDL must also be approved on a case-by-case basis by BU's Institutional Biosafety Committee, which was created under National Institutes of Health guidelines to review research involving biohazardous materials. **ART JAHNKE**