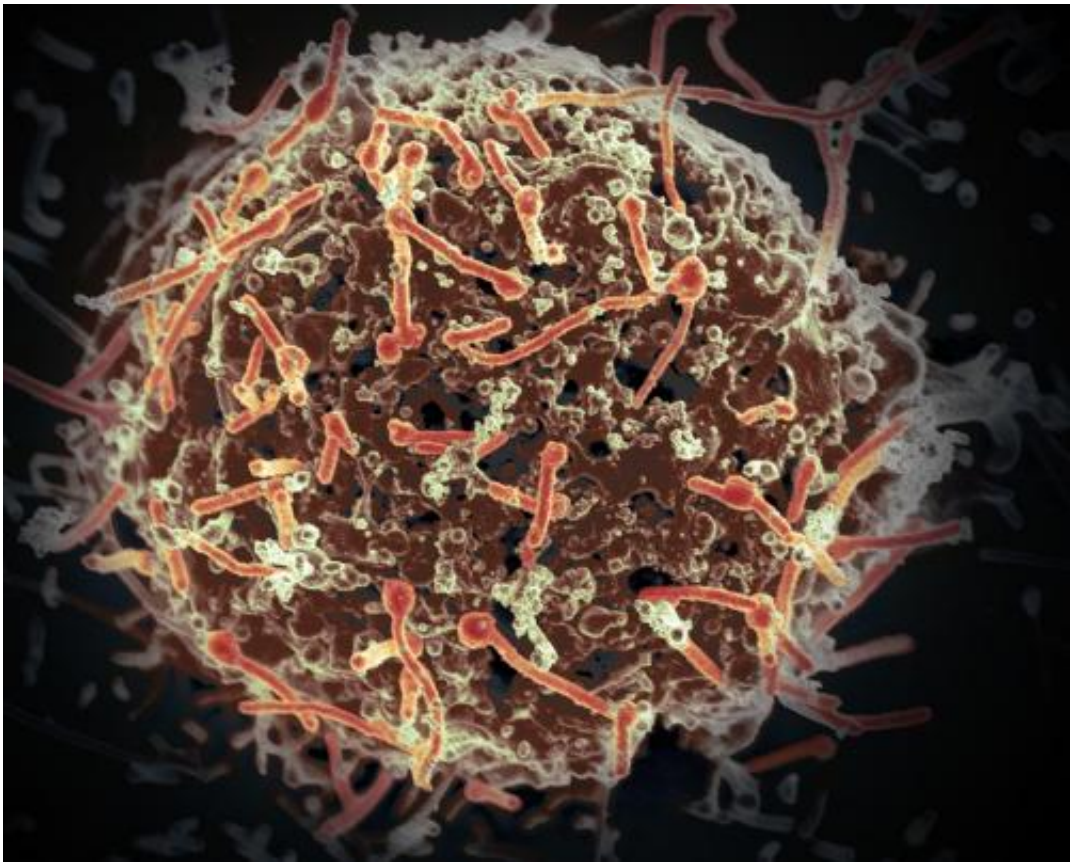
MedicalXpress

Experimental immunotherapy zaps two most lethal Ebola virus strains

January 13 2016



The Ebola virus, isolated in November 2014 from patient blood samples obtained in Mali. The virus was isolated on Vero cells in a BSL-4 suite at Rocky Mountain Laboratories. Credit: NIAID

Researchers at Albert Einstein College of Medicine and the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) have

engineered the first antibodies that can potently neutralize the two deadliest strains of the virus that causes Ebola hemorrhagic fever. The findings, made in mice, are a significant step toward immunotherapies that are effective against all strains of Ebola virus that cause human disease. The study was published online today in *Scientific Reports*.

"A broadly effective immunotherapy for Ebola virus would be a tremendous advance, since it's impossible to predict which strain of the virus will cause the next outbreak," said study co-leader Jonathan Lai, Ph.D., associate professor of biochemistry at Einstein. The other study co-leader is John M. Dye, Ph.D., branch chief of viral immunology at USAMRIID.

Zaire Ebola virus (EBOV) was responsible for the 2014 Ebola outbreak in West Africa, the largest in history. The next-most pathogenic strain of Ebola virus is Sudan Ebola virus (SUDV). "This strain is also a concern because outbreaks are occurring more frequently, and it has been responsible for large outbreaks in the past," said Dr. Dye.

Although a Zaire-specific vaccine is in clinical trials, no vaccine has yet been approved for preventing infection from any strain of Ebola virus. And therapies for people who become infected are very limited. ZMapp, a cocktail of three monoclonal antibodies, is the most promising of several experimental immunotherapies for Ebola virus now in development. But ZMapp's antibodies are specific for EBOV and would not work against the other two Ebola strains that have caused major outbreaks. (In addition to Zaire and Sudan, the third major strain is Bundibugyo.)

In previous work, Dr. Lai and his colleagues used a technique called synthetic antibody engineering to create the first humanized antibodies against SUDV. Those antibodies were designed to bind to SUDV's surface glycoprotein, which the virus uses to gain entry into host cells.

Since SUDV's glycoprotein shares just 55 percent of amino acid sequences found in EBOV's glycoprotein, antibodies against SUDV do not neutralize EBOV.

In the current study, Dr. Lai's team engineered "bispecific" antibodies that contain key glycoprotein-binding sequences from both the EBOV and SUDV antibodies. The bispecific antibodies effectively neutralized both EBOV and SUDV in tissue culture studies. In addition, the antibodies provided high levels of protection for mice that had been exposed to lethal doses of either of the viruses.

The bispecific antibodies must still be tested in larger animals and in humans to know whether they'll be effective. If the new immunotherapy proves safe and effective for people, said Dr. Lai, it might best be suited for preventing local outbreaks from getting out of hand, as happened in the recent West Africa Ebola virus epidemic. "It's also possible," he noted, "that a therapy like this could be used prophylactically, to protect health workers or family members who come into contact with Ebola virus patients."

There are currently no plans to further test the new immunotherapy. But if a pharmaceutical company were interested, said Dr. Lai, "it could probably move the antibody fairly rapidly along the evaluation process." Meanwhile, Dr. Lai has broadened his approach to Ebola virus therapy. He is developing antibodies and antibody cocktails aimed at neutralizing the three most dangerous Ebola virus species (Zaire, Sudan and Bundibugyo) as well as Marburg virus, a deadly pathogen closely related to Ebola virus.

The study is titled "Bispecific Antibody Affords Complete Post-Exposure Protection of Mice from Both Ebola (Zaire) and Sudan Viruses."