The hunt for an Ebola drug

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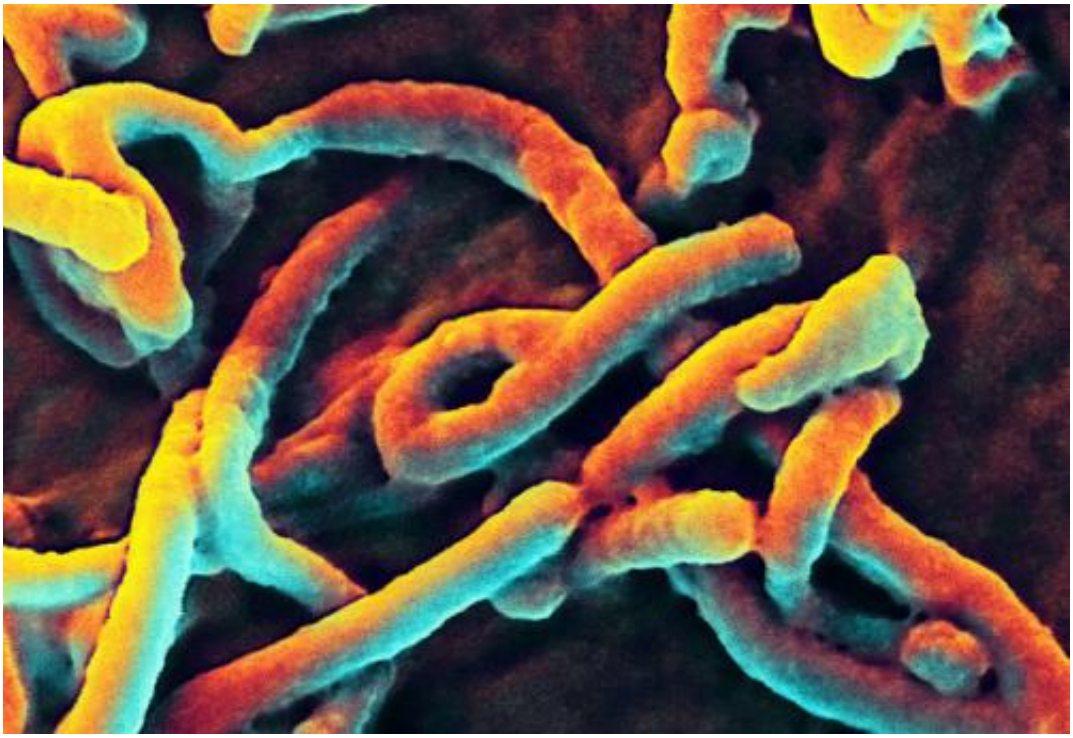

A scanning electron micrograph of Ebola virus budding from a cell (African green monkey kidney epithelial cell line). Credit: NIAID

In December 2013, a 2-year-old boy in a small village in Guinea fell ill and died. Days later his 3-year-old sister and their pregnant mother also died. That was the beginning of the largest Ebola outbreak in recorded history, during which the virus spread rapidly across West Africa, killing more than 11,000 people in two years.

Since then, scientists have been diligently working to create what would

be the first Food and Drug Administration-approved vaccine or treatment for the deadly virus. At Georgia State, professor and world-renowned virologist Christopher F. Basler and his colleagues are trying to uncover how filoviruses, including Ebola, manage to replicate while evading the body's immune system.

"By the time the immune response finally kicks in, the virus has replicated so fast that you can't fight it off," says Priya Luthra, assistant professor in the Institute of Biomedical Sciences and a researcher in Basler's lab. "And that's when the disease takes hold."

One potential target for an Ebola drug would be the machinery and activities required for RNA synthesis, a part of viral replication.

Luthra and others in the Basler lab screened a library of 200,000 small molecule compounds to identify potential inhibitors of Ebola RNA synthesis, and identified 56 that impeded virus activity while showing limited toxicity to human cells. Of those, three were particularly potent against the Ebola virus, and one—benzoquinoline—also showed antiviral activity against other viruses, including the highly fatal Marburg virus and the Zika virus. Their findings were published in the journal Antiviral Research in March 2018.

Identifying the compounds is part of a broader effort to better understand how the Ebola virus grows and then to develop new treatment strategies, Basler says. Benzoquinoline could eventually become an active ingredient in a drug aimed at Ebola, although Luthra cautions there's still a lot of work to be done.

"We need to learn more about how the compound is actually working," Luthra says, "and we have to evaluate how a person's genes may affect their response to the drug."

Researchers are also still searching for other molecules that may work against the virus.

"The search never stops," Luthra says. "The goal is to find a drug that could be given prophylactically during the virus's incubation period and a drug that could be given therapeutically after symptoms begin and also a vaccine. You want all these things so clinicians have a full toolkit to use."

Fighting Ebola in animals

There are five known species of the Ebola virus, four of which can cause the disease in people. The fifth, known as Reston virus, affects primates and pigs but not humans. It was discovered nearly 30 years ago during an outbreak in monkeys that were brought to an animal facility in Reston, Va., from the Philippines. Now, Basler has received more than $400,000 from the National Institutes of Health to study the Reston virus and how it differs from other strains of Ebola.

"We're trying to better understand how the virus grows, how it replicates and how the disease that it causes in animals differs from what you see with Ebola," he says. "If we can understand what's different, that may suggest ways to reduce the severity of the disease."

Basler and his co-investigator, Thomas Geisbert of the University of Texas Medical Branch at Galveston, are also interested in a protein found in the Ebola virus known as VP35, which suppresses the body's immune response. The pair have identified mutations that can be inserted into VP35 to disable this function, preventing the virus from spreading. They plan to apply the same approach to engineer a Reston virus that doesn't cause disease in animals.