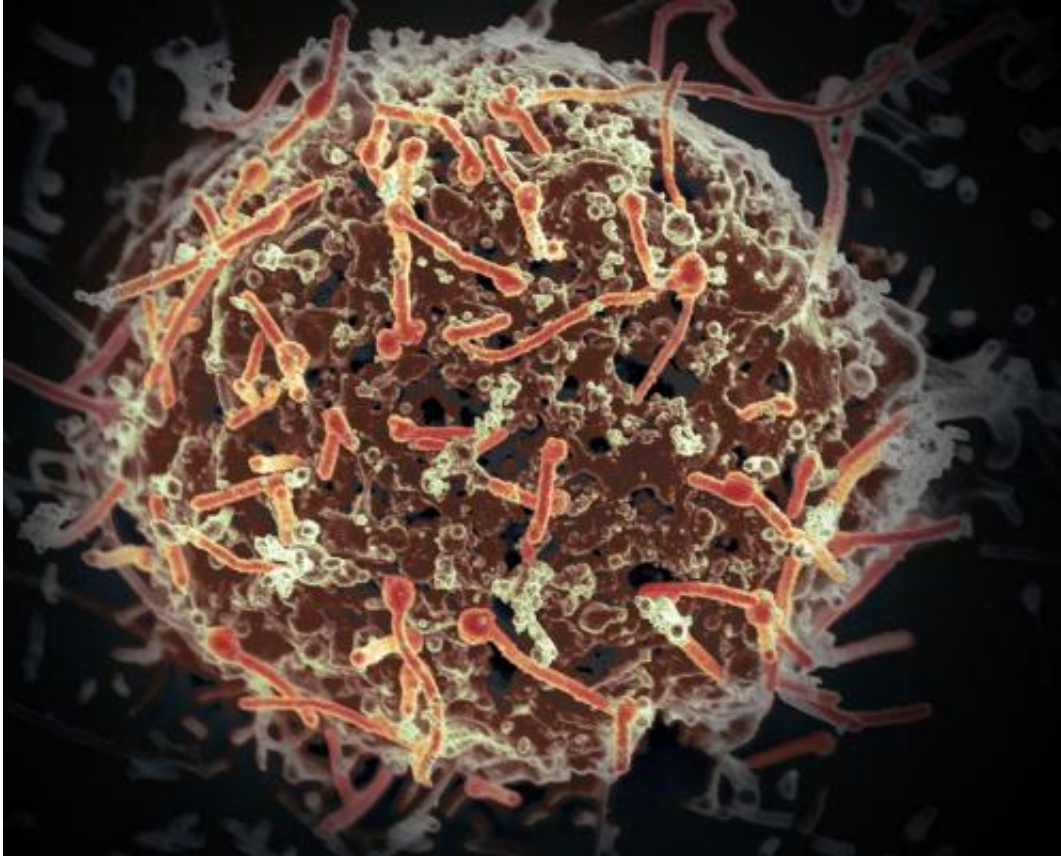


Sequencing Ebola's secrets

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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

Last June, in the early days of the Ebola outbreak in Western Africa, a team of researchers sequenced the genome of the deadly virus at unprecedented scale and speed. Their findings revealed a number of

critical facts as the outbreak was unfolding, including that the virus was being transmitted only by person-to-person contact and that it was picking up new mutations through its many transmissions.

While [public health officials](#) now believe the worst of the epidemic is behind us, it is not yet over, and questions raised by the previous work still await answers.

To provide them, a global team from Harvard University, the Broad Institute, the U.S. Centers for Disease Control and Prevention (CDC), and the National Institute of Allergy and Infectious Diseases (NIAID, part of the National Institutes of Health), along with many other institutions, sequenced more than 200 additional genomes from Ebola virus samples, to capture the fullest picture yet of how the virus is transmitted and how it has changed over the long-term [outbreak](#).

In an effort to enhance the global response, this team made their data publicly available as it was produced throughout last year. "One of the most rewarding aspects of working in this outbreak response is the connections we have made with so many extraordinary individuals through open data sharing", said senior author Pardis Sabeti. The global team that assembled as a result has now described their analysis in a June 18 paper published in *Cell*.

"Our early work tracked the virus's movements over just three weeks as the outbreak emerged in Sierra Leone," said Sabeti. "Now with a view of the virus over seven months, we can understand how it has been moving and changing over the long term."

"One insight we gained from this high resolution sequence data is that later in the outbreak, there was very little cross-border exchange of the virus," said lead author Danny Park. "That's important, because the three main affected countries—Sierra Leone, Liberia, and Guinea—are often

described as having 'porous borders' which allowed people to travel back and forth."

While cross-border contact may have helped fuel the early days of the outbreak, Park said it's now clear that, once underway, the virus didn't migrate in the ways many had predicted. "This is very reassuring to know that measures to contain the outbreak at borders can work," he said, "and allows attention to be focused on within-country movement."

The new sequencing also provides insight into viral evolution over the sustained outbreak. Early in the outbreak, as the virus spread rapidly, it accumulated many mutations, a disproportionate share of which could affect protein function. Last August, the researchers noted that most of these were likely to be damaging to the virus, but that the outbreak hadn't gone on long enough for natural selection to weed them out yet.

Over the longer term, the team observed that many of these mutations did not persist very long, and that the rate of change in the [viral genome](#) has become more in line what is expected over the longer term. "Ebola has never been exposed to humans for so long, and through so many transmissions, it has begun to weed out mutations that do not benefit it," Park said.

The team also identified other changes of the [virus](#) that are expected over the longer-term. For example, in some patients, they saw evidence of human enzymes editing the viral genome. This has never before been seen for Ebola, and is only seen previously with viruses that have long-standing interactions with humans.

"The many [mutations](#) we saw early in the outbreak and the evolution we saw over the long-term have been observed for other viruses before, and the genomic data only helps illuminate known evolutionary phenomena." Sabeti says. "The data just remind us what we have always known, that

we must get this viral lineage to zero."

Provided by Harvard University

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