INFECTIOUS DISEASES

# Delays hinder Ebola genomics

## For months, no sequences from the virus have been released

*By* **Gretchen Vogel**

As the Ebola epidemic sweeps through West Africa, scientists lack key genetic data to answer a question that has provoked much worried speculation: Is the virus becoming more transmissible or more deadly, or acquiring changes that would let it evade diagnostic tests or vaccines? Thousands of blood samples from Ebola patients have been sitting in refrigerators in Africa and Europe, untouched. And, as *Science* went to press, the few groups that have new sequence data have not made them public.

Researchers are eager for a close-up look at how the virus may be evolving. Besides answering questions about its virulence, genomic data could reveal details about the epidemic, including hotspots of transmission and how often the virus has escaped from its animal reservoir to humans, says Andrew Rambaut, an evolutionary biologist who studies infectious diseases at the University of Edinburgh in the United Kingdom. "If it can be done on a timely basis, you can really get insight into what is going on." But faced with the all-consuming public health response to the epidemic, bureaucratic obstacles, and chaotic record keeping, scientists have had to wait.

In August, the world got its closest molecular look at the virus so far, when researchers published 99 genomes of viruses from 78 patients who were infected in or around Kenema, Sierra Leone, from late May to mid-June. That analysis, published online on 28 August in *Science*, included more than half of the known cases in Sierra Leone at the time.

The sequence data, which the researchers deposited in public databases as soon as they were generated, showed how the virus changed as it passed from person to person at the start of the Sierra Leone outbreak, with one variant disappearing as another gained prominence among later cases. Since then, the outbreak has exploded into an epidemic—it has now sickened more than 13,000 and killed 5000—but the team, led by Pardis Sabeti and Stephen Gire at the Broad Institute in Cambridge, Massachusetts, has been unable to import any new samples from Sierra Leone. Other groups have been similarly stymied.

Several researchers say that getting export approval from beleaguered health ministries has been tough. "I can only assume that the system is so overwhelmed that processing samples beyond simple diagnostic tests is not high priority," says Rambaut, who was a co-author on the August sequence paper.

Stephan Günther, a virologist at the Bernhard Nocht Institute for Tropical Medicine (BNI) in Hamburg, Germany, and coordinator of the European Mobile Laboratory (EMLab) consortium, says they have been unable to export samples from Nigeria or Liberia. But BNI has been receiving samples from the EMLab mission in Guinea since March and now has close to 3000, he says. (BNI is storing them in its high-security lab on behalf of the Guinean government, which still owns them.)

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>
> **Stephan Günther**, Bernhard Nocht Institute for Tropical Medicine

Günther and his colleagues have not yet sequenced any of the samples, because consortium staff members have been busy supporting diagnostic centers in affected countries. "We are all busy with fieldwork," Günther says. "Personnel is a bit of a problem." That should ease, he says, with a new €1.7 million ($2.1 million) award from the European Union to EMLab for Ebola research.

In France, the Institut Pasteur, where early samples from Guinea were first identified as Ebola, also experienced delays exporting samples from West Africa but plans to start sequencing new viral genomes soon. The institute's lab in Dakar recently received samples from Guinea, says Felix Rey, who is coordinating the institute's Ebola task force in Paris. The Dakar lab will extract RNA and send it to Paris for high-throughput sequencing. "We hope to have sequenced viruses from a couple of hundred samples in the next month or so," Rey says.

Sabeti and her colleagues should soon get their Sierra Leone samples, which finally were cleared for export and arrived in the United States last week, says Robert Garry of Tulane University in New Orleans, Louisiana, who collaborates with Sabeti. But to speed the research, she and her colleagues are trying to secure funding to send sequencing machines to West Africa. "If we can't get the samples here, we will get the sequencers there," she says. The effort will build on the researchers' ongoing work with the African Centre of Excellence for Genomics of Infectious Diseases, a consor-

### A changeable foe

The proteins that enable the Ebola virus to spread and cause disease are encoded by seven protein-sheathed genes. Mutations in the gene for the glycoprotein could affect the efficacy of antibody-based treatments. Other genes, such as those for polymerase and transcription factor VP30, can affect how quickly the virus replicates.

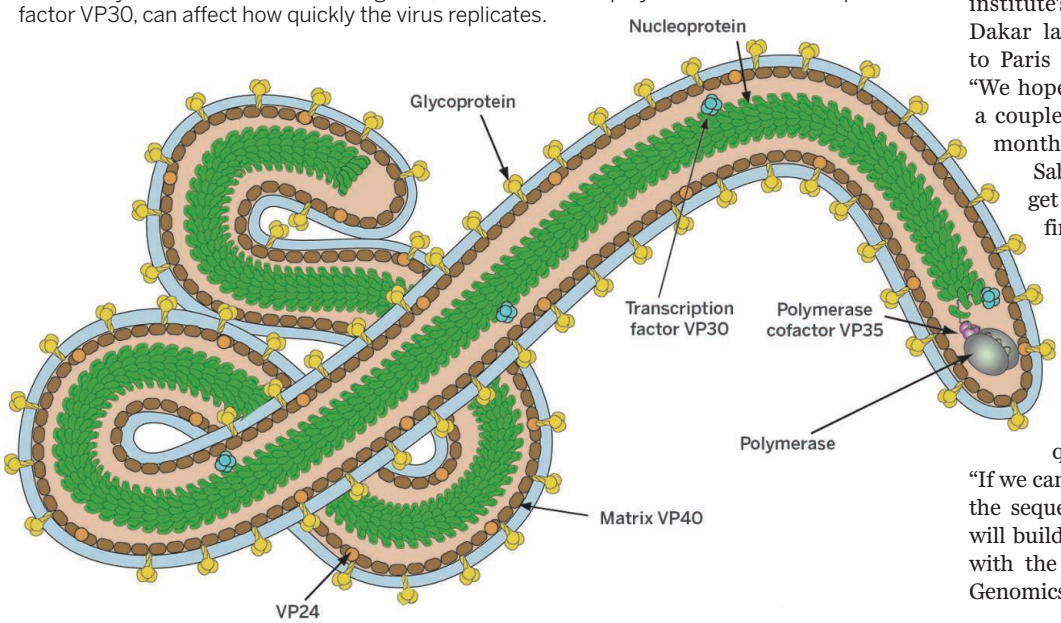


ILLUSTRATION: VIRALZONE/SIB SWISS INSTITUTE OF BIOINFORMATICS

tium of universities and research institutes in the United States, Nigeria, Sierra Leone, and Senegal, which for several years has been training African researchers in the use of genomics tools.

Blood samples alone aren't enough for genomic studies. Investigators need to know at least where each patient was from; ideally they will also have clinical information such as whether he or she survived. "Only when you have those pieces of information can you come up with useful information from the sequences," Günther says—and because of spotty record keeping, that information is often missing. He and his colleagues are working with Doctors Without Borders and the World Health Organization to match samples with relevant information, but setting up a database is time- and labor-intensive, he says.

Meanwhile, the few Ebola virus sequences that have been generated since that initial batch from Sierra Leone have not been made public. The U.S. Centers for Disease Control and Prevention (CDC) announced in August that it had sequenced Ebola virus samples from patients treated in the United States. But the data have not been placed in any public sequence repositories. That's unfortunate, Rambaut says. "As the U.S. cases are from Liberia and we have zero sequences from there so far, even one genome would be interesting and potentially useful," he says. Duncan MacCannell, a bioinformatics specialist at CDC in Atlanta, told *Science* that the sequences had been "actively shared and discussed with the public health community." He says CDC is working to submit the sequences to a public database.

New sequences probably won't show that the virus is finding new ways to attack or spread, Rambaut says. Instead, the prize is a clearer picture of the outbreak. A cluster of closely related viruses might point to a hotspot of transmission, he says, while unexpectedly diverse sequences would suggest that many cases were going undetected. Sequence data could also help researchers tell whether there has been more than one animal-to-human introduction.

Earlier sequence data did suggest that the virus was undergoing rapid changes, but that is not necessarily a sign that it is becoming more dangerous, Rambaut says. "Most RNA viruses mutate quickly, but adaptation and functional change is a much slower process." Measles mutates nearly as quickly as Ebola virus, but it has never evolved to escape the lifelong immunity of previously infected or vaccinated individuals. Even in an outbreak this big, Rambaut says, "I see no reason to suspect the virus will radically change its life cycle or its mode of transmission." ■

Sami herder Per Anders Eira wrangles a reindeer calf in northern Norway.

PHOTO: KNUT LANGELAND

ECOLOGY

# What's killing the reindeer?

## Conservationists and herders in Norway differ about whether to blame predators or overpopulation

*By* **Eli Kintisch**, *in Nordkapp, Norway*

An ecologist's study of reindeer has touched off a firestorm in this land of ice, tundra, and Sami herders, who tend vast numbers of the semi-domesticated animals. Each year, the herders file compensation claims for tens of thousands of reindeer deaths that they blame on carnivores, primarily lynx and wolverines. Ecologist Torkild Tveraa, however, pins the blame on overpopulation: The land simply cannot support the herds, which number roughly 180,000 here in Finnmark, Norway's most northern region.

Tveraa, who is with the Norwegian Institute for Nature Research in Tromsø, first presented his case in a government-funded report last year, and he added new analysis in a study published in the October issue of the *Journal of Applied Ecology*. The government has pointed to the findings as exonerating the threatened lynx and wolverines, which are already protected by strict hunting limits. To the Sami, however, the study threatens an economic lifeline.

To receive compensation, a herder must prove that a dead reindeer was killed by a lynx or wolverine. That's hard when herders find remains of only 5% to 10% of the reindeer that they lose. The government approved just a quarter of more than 60,000 such applications in 2011. The claims nonetheless are lucrative: That year, Sami herders in Norway received $11 million in predator payments, or two-thirds of what they received from meat sales.

To find out how much damage the predators really do, Tveraa's team combined their own data on reindeer health since 2000 with herd sizes reported by herders, observations of lynx and wolverines, and satellite data on grazing areas. They found that as a factor in reindeer mortality, food scarcity was two to three times more significant than lynx, and more than 20 times more significant than wolverines.

"Tveraa has a very solid basis for these findings—a very large data set collected over a very long time series," says Terje Bø, head of wildlife management in the Norwegian government's environment division in Trondheim. In the global canon of human-carnivore conflict research, Tveraa's "robust" study, says Matt Hayward, an ecologist at Bangor University in the United Kingdom, "goes against the grain of papers saying, 'It's the predators' fault.' " Other experts agree that the findings are plausible. "It's sort of official: We have too many reindeer," says Emil Halvorsrud, a wildlife official in Lakselv. Large herds are becoming less sustainable, he says, as a warming subarctic climate results in more slush and rain in winter, leaving pastures covered in ice.

Ellinor Jåma, with the Sami Reindeer Herders' Association of Norway in Karasjok, agrees that overpopulation is a factor in some deaths. "We may have too many reindeer in some areas of Finnmark," she concedes. "But in the middle of the country, reindeer health is good—and we still have heavy losses," which she blames on predation.

Bø hopes Tveraa's findings will show how ecological data could underpin a new compensation system the government has proposed to launch in 2017. Tveraa underscores that he doesn't take sides in the debate. "We hear: 'Oh, since your research is paid for by the government, you are only there to protect the carnivores,' " he says. That's not so, he insists: "The data speak for themselves." ■

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