Team discovers the ancient origins of deadly Lassa virus

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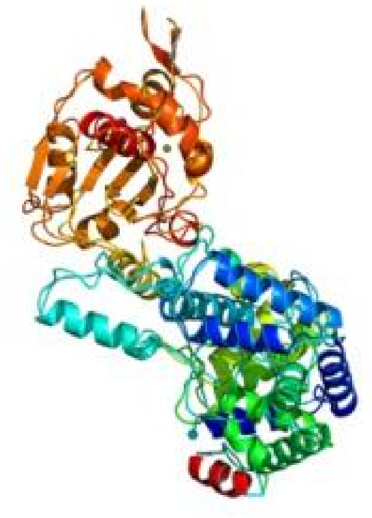

A subunit of the Lassa nucleoprotein. The C terminal domain at top and the N-terminal domain at bottom.

Working as part of an international team in the United States and West Africa, a researcher at The Scripps Research Institute (TSRI) has published new findings showing the ancient roots of the deadly Lassa virus, a relative of Ebola virus, and how Lassa virus has changed over time.

"This gives us a clear view of how the virus is evolving, which is important to know as we develop vaccines and therapies," said TSRI biologist Kristian G. Andersen, a lead author of the new study.

At least 5,000 people die each year from Lassa fever. The virus is spread through contact with urine and droppings from infected *Mastomys natalensis* rodents (which are a natural "reservoir" of the virus)—and the disease can spread from human to human.

In the new study, published August 13 in the journal *Cell*, the team—whose senior members included Pardis Sabeti and Joshua Levin of Harvard University and the Broad Institute, Robert F. Garry of Tulane University and Christian Happi of Nigeria's Irrua Specialist Teaching Hospital and Sierra Leone's Kenema Government Hospital—used a technique called next-generation sequencing to analyze genomes of Lassa virus samples taken from wild *Mastomys natalensis* and human patients in Nigeria and Sierra Leone.

The genomic data showed that far-flung strains of Lassa virus share a common ancestor that can be traced back more than 1,000 years to an area today known as Nigeria. This surprised the researchers, as Lassa fever was first described in Nigeria in 1969. "The virus has very ancient roots," said Andersen.

The researchers found that the virus spread out of Nigeria about 400 years ago and over the past couple of hundred years moved into Guinea, Liberia and Sierra Leone—the same part of the world where the largest outbreak of Ebola virus has been raging since 2013. As Lassa virus spread, the virus mutated and seemed to better adapt to mammalian hosts.

The new data also show that most Lassa fever cases are caused by frequent "spillover" infections from the wild rodent reservoir to humans, rather than spreading from human to human. "The reason Lassa hasn't yet grown into this huge epidemic is because there is limited transmission between humans," said Andersen. "That's a major difference between Lassa virus and Ebola virus."

Andersen noted that local scientists in West Africa were key for this new study and will be crucial for future studies in the region. He views the next step in this research as understanding how the virus mutates within individual hosts as it confronts the immune system.

More information: "Clinical sequencing uncovers origins and evolution of Lassa virus," *Cell*, 2015.

Provided by The Scripps Research Institute

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