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Genomic Analysis Sheds Light on Ebola Virus Disease Outbreak in Liberia

Majority of Cases Linked to Single Introduction, Subsequent Spread

Scientists have performed the first comprehensive genomic analysis of Ebola virus sequences from Liberia, one of three countries widely affected by the devastating outbreak that began in 2013 in Western Africa. Their work, published today in *Cell Host & Microbe*, traces the introduction and spread of the virus in Liberia and also sheds light on how the virus moved between the neighboring countries of Guinea and Sierra Leone.

"The scope of this study has allowed us to piece together a complete picture of the Liberian portion of the outbreak," commented senior author Gustavo Palacios, Ph.D., of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID). "It also allowed us to investigate potential patterns of adaptation to the human host."

Ebola virus (EBOV) causes severe hemorrhagic fever in humans and nonhuman primates with high mortality rates and continues to emerge in new geographic locations, including Western Africa, the site of the largest recorded outbreak to date. Over 28,000 confirmed, probable and suspected cases have been reported in Guinea, Liberia and Sierra Leone, with over 11,000 reported deaths, according to the World Health Organization.

According to first author Jason Ladner, Ph.D., of USAMRIID, viral genome sequencing played a key role in identifying chains of EBOV transmission as the outbreak was unfolding. Now, that information can also help scientists to better understand general patterns of spread and inform efforts to control future outbreaks of Ebola virus disease (EVD).

The study is the first of its kind to cover the entirety of one of the three countries most affected by the outbreak, the first to cover the entire temporal span of the outbreak within a country, and the first to combine genomic datasets from Liberia, Guinea and Sierra Leone, Ladner said.

In the paper, Palacios and his team describe their analysis of 140 new EBOV genome sequences from Liberia, combined with 782 previously published sequences from throughout Western Africa. Their findings suggest that the majority of cases in Liberia are consistent with a single virus introduction, followed by spread and diversification within the country. In addition,

reintroductions from Liberia also served as a source for the continuation of the outbreak in Guinea.

"The scope of this outbreak has provided an unprecedented opportunity for Ebola virus to evolve within the human host," Palacios said. "We also wanted to explore the genetic changes occurring in the virus during the outbreak to see whether we could detect signatures of adaptation. This would allow a better understanding of the dynamics of the interaction between EBOV and humans."

Interestingly, the study's authors saw little evidence for ongoing adaptation of EBOV to the human host. Although they were unable to reconstruct the changes that occurred during the first few months of the outbreak, due to the lack of available samples, the large number of sequences they were able to utilize covered four countries and about one year of the outbreak. These samples included representatives from a large number of distinct transmission chains, thus providing a powerful dataset for detecting genomic changes in the virus.

According to Ladner, one of the team's next steps is to expand beyond Liberia to include Guinea and Sierra Leone. While the current study included many sequences from those countries, they were primarily utilized to provide a broader context for the Liberian portion of the outbreak.

"Over the next few months we will be combining forces with other research groups to look carefully at the commonalities and differences of Ebola virus spread and diversification within and between these three countries," he said. "This analysis should help to shed light on the most successful approaches for controlling the spread of the virus."

Another future direction, according to Palacios, is to begin to functionally examine the different genetic mutations that have occurred during the outbreak.

"Computational analysis can help to highlight changes that are likely to have resulted in a functional change to the virus, but in the end, these changes need to be evaluated experimentally to assess the impact on viral fitness and pathogenicity," Palacios said. "In particular, it will be very interesting to examine several of the changes that occurred early during the Western African outbreak."

The study was made possible by the in-country laboratory capability established by USAMRIID in collaboration with the Liberian Institute for Biomedical Research (LIBR) and the Liberian Ministry of Health and Human Welfare. This state-of-the-art, high-throughput sequencing facility allows the team to conduct near real-time genomic sequencing.

In addition to five USAMRIID personnel who have rotated through the laboratory in the past year, the Institute has trained several local scientists to run the sequencer, including study co-author Lawrence Fakoli. Another co-author, Suzanne Mate of USAMRIID, just returned from LIBR, where she was working to process samples related to the latest cases of Ebola virus disease in Liberia.

USAMRIID's mission is to provide leading-edge medical capabilities to deter and defend against current and emerging biological threat agents. The Institute plays a key role as the lead military medical research laboratory for the Defense Threat Reduction Agency's Joint Science

and Technology Office for Chemical and Biological Defense. USAMRIID is a subordinate element of the U.S. Army Medical Research and Materiel Command. For more information, visit www.usamriid.army.mil

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Cell Host & Microbe, Ladner, Wiley, Mate et al.: “Evolution and Spread of Ebola Virus in Liberia, 2014–2015” http://dx.doi.org/10.1016/j.chom.2015.11.008

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