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Fort Detrick, MD

CONTACT: Caree Vander Linden

(301) 619-2285

teresa.l.vanderlinden.civ@mail.mil

**Gene Sequencing Tools Pinpoint Origins of Bundibugyo Virus Disease Outbreak**

New research sheds light on the origins of a 2012 Bundibugyo virus disease outbreak in the Democratic Republic of the Congo, according to a report published online this week in the journal *Cell Reports Medicine*. The work also demonstrates the importance of using high throughput sequencing to understand virus “spillover” events in order to more effectively manage disease outbreaks.

In the study, an international team led by the U.S. Army Medical Research Institute of Infectious Diseases demonstrates how high throughput sequencing—one of USAMRIID’s core competencies—can be used retrospectively to pinpoint the origins of a disease outbreak and provide key information about emerging pathogens of military and public health importance.

Bundibugyo virus is one of four ebolaviruses known to cause human disease, and multiple outbreaks have occurred on the African continent. It is characterized by flu-like symptoms that are sometimes followed by diarrhea, vomiting, chest pain, and hemorrhage. Survivors may suffer from joint pain, blurred vision and hearing loss.

As is the case with other ebolaviruses, the “reservoir” of Bundibugyo—meaning the primary host that harbors the virus—remains unknown, according to the authors. Thus, the ecology of the virus and its transmission mechanism into the human population are poorly understood.

The 2012 outbreak resulted in 38 laboratory-confirmed cases of human infection, 13 of whom died. However, only 4 patient specimens from that outbreak had been sequenced until now, according to MAJ Jeffrey R. Kugelman, Ph.D., one of the study’s lead authors.

USAMRIID’s analysis of sequences from 7 additional patients shows that multiple virus “spillover” events contributed to the outbreak—not a single event, as previously described—and that one of the spillover events likely occurred weeks earlier than previously thought.

“Analysis of the molecular epidemiology and evolutionary dynamics of the 2012 outbreak with these additional isolates challenges the current hypothesis that the outbreak was the result of a single spillover event,” said MAJ Christine Hulseberg, Ph.D., the paper’s first author. “In addition,

phylogenetic analysis suggests that the initial emergence of the virus occurred 50 days earlier than previously accepted.”

In addition to playing a key role in identifying chains of transmission as an outbreak unfolds, viral genome sequencing helps scientists to better understand general patterns of spread, and informs public health efforts to control future outbreaks. It also allows for examination of genetic mutations that may affect the ability of the virus to survive and cause disease.

This study was conducted at USAMRIID as part of an ongoing Ebola virus response and surveillance effort under the project, “Assessment of Human Clinical Samples from Viral Hemorrhagic Fevers of Known and Unknown Etiology.” It is also among the first of several planned collaborations with the Icahn School of Medicine at Mount Sinai, New York, laying a foundation for future joint research initiatives to protect national and global public health. USAMRIID’s partnership with ISMMS is designed to maximize the impact of DoD’s research, development, and testing and evaluation investment by ensuring integration and cooperation with biomedical infectious disease research centers with similar goals.

Other collaborators include the National Biodefense Analysis and Countermeasures Center, Frederick, MD; Metabiota, Inc., Kinshasa, Democratic Republic of the Congo; Institut National de Recherche Biomédicale, Kinshasa, Democratic Republic of the Congo; and the Integrated Research Facility at Fort Detrick, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Frederick, MD.

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#### **About the U.S. Army Medical Research Institute of Infectious Diseases:**

For over 50 years, USAMRIID has provided leading edge medical capabilities to deter and defend against current and emerging biological threat agents. The Institute is the only laboratory in the Department of Defense equipped to safely study highly hazardous viruses requiring maximum containment at Biosafety Level 4. Research conducted at USAMRIID leads to medical solutions – vaccines, drugs, diagnostics, information, and training programs – that benefit both military personnel and civilians. Established in 1969, 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 laboratory of the U.S. Army Medical Research and Development Command. For more information, visit [www.usamriid.army.mil](http://www.usamriid.army.mil).

#### **Reference:**

Palacios, Gustavo et al.: "Molecular analysis of the 2012 Bundibugyo virus disease outbreak." Cell Reports Medicine, published online 27 July 2021. DOI: 10.1016/j.xcrm.2021.100351 Article link: [https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(21\)00200-7](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00200-7)