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## **The 454 Genome Sequencing System Detects a Novel Virus Responsible for South African Hemorrhagic Fever Outbreak**

*The newly discovered arenavirus caused the deaths of four of five infected individuals in South Africa in October, 2008.*

A study published online today in PLoS Pathogens reports that researchers at Columbia University, the South African National Health Laboratory Services, the US Centers for Disease Control, and 454 Life Sciences have discovered a new virus that is responsible for a highly fatal hemorrhagic fever outbreak in Zambia and South Africa late 2008(1). The previously unknown arenavirus, which is distantly related to the Lassa virus and Lymphocytic choriomeningitis virus, was characterized using the rapid and sensitive sequencing technology of 454 Life Sciences. The new species, named “Lujo virus” for the geographic origin of the outbreak (Lusaka, Zambia and Johannesburg, South Africa), is the first hemorrhagic fever-associated arenavirus from Africa identified in the past three decades. Characterization of the novel virus confirms the utility of unbiased high-throughput sequencing for pathogen discovery and provides an opportunity for public health efforts to quickly curb emerging viral pandemics in the future.

In September and October, 2008 five cases of undiagnosed hemorrhagic fever were recognized in South Africa after air transfer of a critically ill individual from Zambia. The disease was fatal in four of the five cases, including the originally infected individual, the paramedic who attended the patient during air transfer, the nurse who attended the patient in the intensive care unit in South Africa, and a member of the hospital staff who cleaned the room after the death of the patient. Unbiased, high-throughput sequencing with the 454 Sequencing system revealed the presence of a previously undiscovered Old World arenavirus. While the distantly related Lymphocytic choriomeningitis virus is generally harmless in healthy humans, the Lujo virus demonstrates an unprecedented high case fatality rate of 80% and unusual degree of pathogenicity.

“Within 72 hours of the sample arriving at JFK Airport, we identified the novel virus using high throughput sequencing,” said Thomas Briese, Associate Director of the Center for Infection and Immunity at the Mailman School of Public Health of Columbia University.

“It is reassuring that we now have the tools needed to rapidly detect and respond to the challenges of previously unknown killer viruses. A key challenge that remains is deployment of these technologies to the ‘hot spots’ where new viruses frequently emerge,” explained Ian Lipkin, MD, John Snow Professor of Epidemiology and Professor of Neurology and Pathology at Columbia University and the director of the Center. “We remain committed to this important public health effort as it represents a unique opportunity to prevent the next pandemic, be it a threat like HIV or SARS.”

The unbiased, high-throughput 454 Sequencing System has been shown to be a powerful pathogen discovery tool in a series of recent studies. In early 2008, a study published in the New England Journal of Medicine reported the identification of a new virus responsible for the death of three transplant recipients using the technology of 454 Sequencing (2). Another study published last year employed the sequencing system to uncover a novel ebola virus responsible for a 2007 hemorrhagic fever outbreak in Uganda (3).

“454 Sequencing enables researchers to quickly identify the organisms present in a complex sample,” explained Michael Egholm, study co-author and Chief Technology Officer and Vice President of Research and Development at 454 Life Sciences. “Our work with Lipkin and colleagues, in developing a comprehensive approach to pathogen detection, has borne fruit in resolving a number of recent disease outbreaks and confirms that it has the potential to be a critical tool for public health. We were honored in this most recent example to work with outstanding investigators at the Centers for Disease Control, World Health Organization, and the National Institute for Communicable Diseases in South Africa. ”

454 Life Sciences, a center of excellence of Roche Applied Science, develops and commercializes the innovative 454 Sequencing System for ultra-high-throughput DNA sequencing. Specific applications include de novo sequencing and re-sequencing of genomes, metagenomics, RNA analysis, and targeted sequencing of DNA regions of interest. The hallmarks of the 454 Sequencing System are its simple, unbiased sample preparation and long, highly accurate sequence reads, including paired-end reads. The technology of the 454 Sequencing System has enabled hundreds of peer-reviewed studies

in diverse research fields, such as cancer and infectious disease research, drug discovery, marine biology, anthropology, paleontology and many more.

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- (1) Briese et al. Genetic detection and characterization of Lujo virus, a new hemorrhagic fever-associated arenavirus from southern Africa. (2009) PLoS Pathogens. ePub April xx.
- (2) Palacios et al. A new arenavirus in a cluster of fatal transplant-associated diseases. (2008) New England Journal of Medicine 358: 991-998.
- (3) Towner et al. Newly discovered ebola virus associated with hemorrhagic fever outbreak in Uganda. (2008) PLoS Pathogens 4(11): e1000212.

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