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Ebola, Marburg viruses edit genetic material during infection

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Filoviruses like Ebola "edit" genetic material as they invade their hosts, according to a study published this week in *mBio®*, the online open-access journal of the American Society for Microbiology. The work, by researchers at the Icahn School of Medicine at Mount Sinai, the Galveston National Laboratory, and the J. Craig Venter Institute, could lead to a better understanding of these viruses, paving the way for new treatments down the road.

Using a laboratory technique called deep sequencing, investigators set out to investigate filovirus replication and transcription, processes involved in the virus life cycle. They studied the same Ebola virus species currently responsible for an outbreak in West Africa, and also analyzed a related filovirus, Marburg virus, that caused a large outbreak in Angola in 2005 and recently emerged in Uganda. The scientists infected both a monkey and human cell line with both viruses, and analyzed the genetic material produced by each virus, called RNA.

Their results highlight regions in Ebola and Marburg virus RNAs where the polymerase of the virus (a protein that synthesizes the viral RNA) stutters at specific locations, adding extra nucleotides (molecules that form the building blocks of genetic material like DNA and RNA), thereby "editing" the new RNAs. The study found new features at a described RNA editing site in the Ebola glycoprotein RNA, which makes the protein that coats the surface of the virus. Their work also identified less frequent but similar types of editing events in other Ebola and Marburg virus genes – the first time this has been demonstrated.

Because of these messenger RNA modifications, Ebola and Marburg are potentially making proteins "that we previously didn't realize," said Christopher F. Basler, PhD, senior study author and professor of microbiology at Mount Sinai.

"The bottom line is we know these changes occur but we don't yet know what it really means in the biology of the virus," Basler said. There are many aspects of how the viruses replicate that aren't yet understood, he said, "so we need a complete description of how they grow to develop new strategies used to treat the infections."

The study also illustrated how the filoviruses express their genes, and deep sequencing identified all seven messenger RNAs within six hours of infection.

"Our study suggests that the Ebola virus is making forms of proteins previously undescribed," said lead author Reed Shabman, PhD, an assistant professor at the J. Craig Venter Institute in Rockville, Md. Shabman was at Mount Sinai when the study was initiated. "Understanding the products of these viruses is critical to understanding how to target them."

In addition, he said, proteins produced by the glycoprotein editing site are associated with virulence in animals, "so it's of great interest to understand how that protein is made, and in as much detail as possible."

"We infer that this probably contributes to how the virus grows in a person or an animal," Basler said.

Further study is needed to determine the biological significance of these findings and how these processes are regulated, Basler said.

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