

Ebola's secret weapon revealed

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Researchers have discovered the mechanism behind one of the Ebola virus' most dangerous attributes: its ability to disarm the adaptive immune system.

University of Texas Medical Branch at Galveston scientists determined that [Ebola](#) short-circuits the immune system using proteins that work together to shut down cellular signaling related to interferon. Disruption of this activity, the researchers found, allows Ebola to prevent the full development of dendritic cells that would otherwise trigger an immune response to the virus.

"Dendritic cells typically undergo a process called 'maturation' when they're infected by a virus—they change shape and present antigens on their surface that tell T-cells to attack that particular virus, thus generating an adaptive immune response," said UTMB professor Alexander Bukreyev, senior author of a paper on the discovery now online in the *Journal of Virology*. "But Ebola prevents dendritic-cell maturation and produces a severe infection without an effective [adaptive immune response](#). We found that its ability to do this depends on several specific regions of two different proteins."

Bukreyev's research group made the discovery after a series of procedures that started with a clone of the Ebola Zaire [virus strain](#). Working under maximum-containment conditions in a biosafety level 4 facility in UTMB's Galveston National Laboratory, the team introduced mutations into the virus' [genetic code](#) at four locations thought to generate proteins that affected immune response.

They then infected human dendritic cells with each of the resulting new strains and compared the results with those produced by unmutated Ebola Zaire. Each of the four new viruses, they found, was unable to suppress dendritic-cell maturation.

"We saw two very interesting things," Bukreyev said. "First, that these mutations restore maturation of dendritic cells very effectively, and second, that a mutation in even one of these genetic domains makes the virus unable to suppress maturation. That means that the virus needs multiple combined effects in order to undermine the immune system in this way."

Ebola's ability to evade the human immune response is one of the factors that accounts for its high mortality rate—up to 90 percent in humans—and the notoriety that it gained after its first appearance in Zaire in 1976, in an outbreak that killed 280 people. Zaire—now the Democratic Republic of the Congo—is the home country of Ndongala Lubaki, lead author on the paper and a postdoctoral fellow at UTMB.

Provided by University of Texas Medical Branch at Galveston

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