

How Ebola Virus Avoids The Immune System

ScienceDaily (Jan. 30, 2009) — Researchers at the University of Pennsylvania School of Medicine have likely found one reason why the Ebola virus is such a powerful, deadly, and effective virus. Using a cell culture model for **Ebola virus** infection, they have discovered that the virus **disables a cellular protein called tetherin that normally can block the spread of virus from cell to cell.**

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Tetherin represents a new class of cellular factors that possess a very different means of inhibiting viral replication," says study author Paul Bates, PhD, Associate Professor of Microbiology at the University of Pennsylvania School of Medicine. **Tetherin** is the first example of a protein that affects the virus replication cycle after the virus is fully made and prevents the virus from being able to go off and infect the next cell." These findings appear online this week in the Proceedings of the National Academy of Sciences.

When a cell is infected with a virus like Ebola, which is deadly to 90 percent of people infected, the cell is pirated by the virus and turned into a production factory that makes massive quantities on new virions. These virions are then released from that cell to infect other cells and promote the spreading infection.

Tetherin is one of the immune system's responses to a viral infection. If working properly, tetherin stops the infected cell from releasing the newly made virus, thus shutting down spread to other

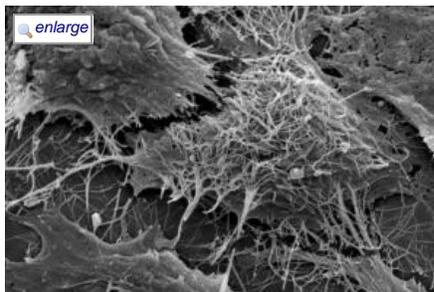
cells. However, this study shows that the Ebola virus has developed a way to disable tetherin, thus blocking the body's response and allowing the virus to spread.

"This information gives us a new way to study how tetherin works," says Bates. "Binding of a protein produced by Ebola to tetherin apparently inactivates this cellular factor. Understanding how the **Ebola protein** blocks the activity of **tetherin** may facilitate the design of therapeutics to inhibit this interaction, allowing the **cell's natural defense systems** to slow down viral replication and give the animal or person a chance to mount an effective antiviral response and recover."

Previous research had found that **tetherin** plays a role in the immune system's response to HIV-1, a retrovirus, and that **tetherin is also disabled by HIV.** These new studies reveal that human cells also use this defense against other types of viruses, such as Ebola, that are not closely related to HIV-1.

"Because we see such broad classes of viruses that are affected by tetherin, it's possible that all enveloped viruses are targets of this antiviral system," says Bates. "If so, then understanding how tetherin works and how viruses escape from the effect of tetherin will be very important."

Rachel L. Kaletsky, Joseph R. Francica and Caroline Agrawal-Gamse of the University of Pennsylvania School of Medicine are co-authors of this study. This work was funded by the Public Health Service Grants and the Philip Morris External



Scanning electron microscope image of Ebola virions (spaghetti-like filaments) on the surface of a tetherin-expressing cell (center). (Credit: Paul Bates, PhD, University of Pennsylvania School of Medicine)

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