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## Small Molecules May Prevent Ebola Infection

***Ebola, a virus that causes deadly hemorrhagic fever in humans, has no known cure or vaccine. But a new study by University of Illinois at Chicago scientists has uncovered a family of small molecules which appear to bind to the virus's outer protein coat and may inhibit its entry into human cells.***

The results are to be published in the Journal of Medicinal Chemistry and are now online.

Previous studies have shown that small molecules can interfere with the Ebola infection process, says Duncan Wardrop, associate professor of chemistry at UIC and corresponding author of the new study. But almost all of these compounds "appear to exert their effects by altering the cells' response to the virus once it's entered the cell -- by which time it's too late," he said.

The new findings demonstrate that it is possible for a small molecule to bind to the virus before it has a chance to enter the cell and thereby prevent infection, he said.

Wardrop collaborated with UIC virologist Lijun Rong, who created a screening system that uses a chimeric HIV-Ebola virus bearing the protein coat of the Ebola virus. The chimera looks like Ebola but isn't life-threatening for scientists to work with.

After screening more than 230 candidate compounds, Wardrop and Rong found two molecules that inhibited cell entry, but only one that demonstrated specificity for the Ebola virus -- plus a bonus.

"We found that our lead compound also inhibits Marburg," Wardrop said, referring to a related virus that, along with Ebola, is one of the deadliest pathogens known. "That was a nice surprise. There's growing evidence the two viruses have the same cell-entry mechanism, and our observations appear to point to this conclusion."

In an effort to find even more potent anti-Ebola agents, Wardrop and graduate student Maria Yermolina synthesized a series of derivatives of the lead molecule -- a member of a family of compounds called isoxazoles -- and found several that displayed increased activity against Ebola infection. Exactly how and where these small molecules bind to the virus's protein coat is now being determined through nuclear magnetic resonance spectroscopy, done by Michael Caffrey, associate professor of biochemistry and molecular genetics.

While it's too early to predict whether the findings will lead to a new treatment for Ebola or Marburg infections, Wardrop said the positive results so far raise hope. The next step would be to see if small-molecule treatments prove effective in animal models.

The UIC scientists also hope their findings will provide further insight into mechanisms the Ebola and Marburg viruses use to enter human cells.

"This knowledge may spur development of new anti-viral agents," Wardrop said.

"From a wider perspective, we're searching for compounds to use as probes to study biological processes. Small molecules which bind to specific proteins and alter their function are invaluable to understanding what these proteins do in living cells," he said.

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