Research finds HIV-killing compound

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(Medical Xpress) -- A powerful topical preventative for HIV, the virus that causes AIDS, could soon be in the works thanks to a newly discovered molecular compound that research at Texas A&M University and the Scripps Research Institute shows dissolves the virus on contact.

The ability of the synthetic compound known as “PD 404,182” to break apart the AIDS-causing virus before it can infect cells was discovered by Zhilei Chen, assistant professor in the university’s Artie McFerrin Department of Chemical Engineering, and her team of researchers. Their findings appear in the November online edition of *Antimicrobial Agents and Chemotherapy,* a journal of the American Society for Microbiology.

“This is a virucidal small-molecule compound, meaning that it has the ability to kill a virus; in this case that virus is HIV,” Chen says. “Basically, it acts by breaking the virus open. We found that when HIV comes in contact with this compound, it breaks open and loses its genetic

material. In a sense, the virus 'dissolves,' and its RNA becomes exposed. Since RNA is pretty unstable, once it is exposed it's gone very quickly and the virus is rendered non-infectious."

In other words, the compound works by quickly ripping open the virus before it can inject its genetic material into a human cell. What's more – and perhaps even more important -– the compound, Chen explains, achieves this by acting on something within the virus other than its viral envelope protein, meaning that the virus can't alter its proteins to bolster its resistance -– something that's made HIV notoriously difficult to treat.

"We believe this compound is not working on the viral protein of the viruses but on something else common in all the viruses on which we tested it -- some cellular material common in these viruses," Chen notes. "Because this compound is acting on a component that is not encoded by the virus, it will be difficult for the virus to evolve resistance against this compound."

While not a cure for HIV, the compound demonstrates significant potential for use as a preventative, specifically in the form of a topical gel that could be applied in the vaginal canal, Chen explains.

"We conducted a number of tests to demonstrate that this compound remains active in vaginal fluid and is not rendered ineffective," Chen says. "In the form of a vaginal gel, the compound would serve as a barrier, acting almost instantaneously to destroy the virus before it could infect a cell, thereby preventing HIV transmission from one person to another."

Surprisingly, Chen and her team did not set out to discover an HIV preventative. Instead, they were conducting screenings of molecules for use in potential drug therapies targeting hepatitis C virus, which causes the dangerous and often fatal disease of the liver. Employing a screening

system developed by Chen, the team screened thousands of molecular compounds, in search of those that could block aspects of the HCV life cycle.

During the course of the screenings, the team made an interesting discovery: Not only was PD 404,182 an HCV inhibitor, it also worked on lentiviruses (the group's negative control in its experimental procedures). Intrigued by that finding, Chen then tested PD 404,182 on HIV, which itself is a lentivirus and found the compound to be even more effective on HIV than on HCV.

"We believe PD 404,182 acts through a unique and important mechanism," Chen notes. "Most of the known virucidal compounds interact with the virus membrane, but our compound does not appear to interact with the virus membrane. Instead, it bypasses interaction with the membrane and still compromises the structural integrity of the virus."

The ability of the compound to avoid interaction with the virus membrane is important because human cells have similar membranes, Chen notes. If the compound were to disrupt the structure of the virus membrane, it could also disrupt and ultimately kill human cells. PD 404,182 doesn't interact with these membranes and is therefore a more attractive option for clinical treatment, Chen says.

As is the case with any potential pharmaceutical, several key steps are still needed before it winds up on drug store shelves. In addition to several rounds of animal studies to ensure the compound is safe for humans, further collaborations with chemists are needed to continue to improve the efficiency of the compound. Chen says. What's more, Chen also plans to further explore the mechanism by which PD 404,182 breaks apart HIV.