MedicalXpress

How photosensitization can stop viruses from infecting cells

February 28 2014, by Enrique Rivero

A UCLA-led team of researchers has found evidence that photosensitizing a virus's membrane covering can inhibit its ability to enter cells and potentially lead to the development of stronger, cheaper medications to fight a host of tough viruses.

The UCLA AIDS Institute study, published in the February issue of the *Journal of Virology*, is part of ongoing research on a compound called LJ001, a "broad-spectrum" antiviral that can attack a wide range of microbes.

The current paper advances the science by showing that the process of photosensitization—heightening a biological organism's sensitivity to certain damaging processes induced by light—applies to more than just LJ001. This could pave the way for a cost-effective way to make blood products safer, which is particularly important in resource-poor countries where deadly viruses run rampant.

There are two categories of viruses: lipid-enveloped and non-enveloped. Enveloped viruses, including many that are of great public health concern, have a membrane that serves as a mechanism through which the microbe inserts its genome into a host cell, infecting it.

Photosensitizers, which have the ability to damage a virus's genetic material, can in many cases prevent infection, according to first author Frederic Vigant, who conducted the study as a postdoctoral researcher in microbiology, immunology and molecular genetics at the David Geffen

School of Medicine at UCLA.

"The ability of photosensitizers to inactivate many different viruses has been known for decades," Vigant said, pointing out their well-known ability to cross-link the DNA and RNA of lipid-enveloped viruses, causing irreversible damage. "It must have seemed so obvious this was how photosensitizers work that no one ever looked in detail at the oxidation of the lipids. Oxidation of lipids by light—termed photo-oxidation—is also very well known."

For the current study, an international research team led by Dr. Benhur Lee, adjunct professor of microbiology, immunology and molecular genetics at the Geffen School, nailed down how photo-oxidation of the viral lipid envelope can be a general method for compromising the ability of such viruses to enter cells.

In an earlier proof-of-principle study published in 2010, the researchers described an antiviral small molecule—a rhodanine derivative they dubbed LJ001—that is effective against numerous viruses, including HIV-1, influenza A, filoviruses, poxviruses, arenaviruses, bunyaviruses, paramyxoviruses and flaviviruses. These viruses cause some of the world's deadliest diseases, such as AIDS, Nipah virus encephalitis, Ebola hemorrhagic fever and Rift Valley fever. This LJ001 compound could also be effective against new, yet-to-be discovered enveloped viruses, the researchers said.

In a subsequent paper published in April 2013 in *PLOS Pathogens*, the team found that the LJ001 broad-spectrum antiviral, and its more potent second-generation derivatives, could affect not just some but any lipid-enveloped virus via photosensitization of the envelope. It was the first time this process was identified and used as an antiviral strategy, Lee said.

The new *Journal of Virology* paper, Lee said, shows that this new paradigm for antivirals applies to more than just LJ001. The team examined another broad-spectrum antiviral compound called dUY11, which had been thought to act as a "wedge" by inserting itself into viral membranes and compacting the lipids, impairing fusion and entry into cells. The new research demonstrates that the process is unlikely to happen on its own because it is inactive in the dark. It turned out to behave as a photosensitizer in all the experiments they performed.

As with LJ001 and its derivatives, dUY11 enters the viral membranes, is activated by light and then changes the lipid composition of the viral coating, resulting in the inability of the virus to fuse with and enter cells.

"In other words, instead of the compound itself acting as a physical constraint on the membrane, we show that it actually works through photochemical reactions that end up changing the biophysical properties of the virus membrane that make it unable to mediate fusion," Vigant said.

More information: "The Rigid Amphipathic Fusion Inhibitor dUY11 Acts through Photosensitization of Viruses." Frederic Vigant, Axel Hollmann, Jihye Lee, Nuno C. Santos, Michael E. Jung, and Benhur Lee. *J. Virol*. February 2014 88:3 1849-1853; published ahead of print 27 November 2013, DOI: 10.1128/JVI.02907-13

Vigant F, Lee J, Hollmann A, Tanner LB, Akyol Ataman Z, et al. (2013) "A Mechanistic Paradigm for Broad-Spectrum Antivirals that Target Virus-Cell Fusion." *PLoS Pathog* 9(4): e1003297. DOI: 10.1371/journal.ppat.1003297

Provided by University of California, Los Angeles