Compound found that targets wide range of viruses

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(PhysOrg.com) -- The compound was found to be effective against viruses that cause some of the world's deadliest diseases, such as AIDS, Ebola and Rift Valley fever.

Viruses are insidious creatures. They differ from each other in many ways, and they can mutate — at times seemingly at will, as with HIV — to resist a host of weapons fired at them. Complicating matters further is that new viruses are constantly emerging.

One potential weapon is a small-molecule "broad spectrum" antiviral that will fight a host of viruses by attacking them through some feature common to an entire class of viruses. For example, there are two categories of viruses: lipid-enveloped and non-enveloped. Enveloped viruses are surrounded by a membrane that in effect serves as a mechanism through which a virus inserts its genome into a host cell, infecting it. Is there something out there that might disrupt that action in as many viruses as possible — and not produce unwanted side effects?

A group of researchers led by a team from UCLA and including others from the University of Texas at Galveston, Harvard University, Cornell University and the United States Army Medical Research Institute of Infectious Diseases may have found just such a compound.

In a proof-of-principle study published online in Proceedings of the National Academy of Sciences, the researchers have identified an antiviral small molecule 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.

Even better, the compound — a rhodanine derivative that the researchers have dubbed LJ001 — could be effective against new, yet-to-be discovered enveloped viruses.

"Since the government has changed its priorities to support development of broad spectrum therapeutics, more and more groups have been screening compound libraries for antivirals that are active against multiple viruses in a specific class," said Dr. Benhur Lee, associate professor of microbiology, immunology and molecular genetics at the David Geffen School of Medicine at UCLA and the primary investigator of the four-year study.

U.S. Food and Drug Administration-approved broad spectrum antivirals do exist but are rare, for various reasons. Ribavirin, for instance, affects both the virus proteins and the host cell and is effective on only a limited number of viruses, such as respiratory syncytial virus and Lassa fever virus. And α-interferon, which is used against the hepatitis C virus, produces unwanted side effects and is too expensive for widespread use.

But the putative mechanism for LJ001 is surprising, according to Lee, who is also a member of the UCLA AIDS Institute.

"We provide evidence that the small molecule binds to both cellular and viral membranes, but its preferential ability to inactivate viral membranes comes from its ability to exploit the biogenic reparative ability of metabolically active cells versus static viral membranes," he said. "That is, at antiviral concentrations, any damage it does to the cell's membrane can be repaired, while damage done to static viral

membranes, which have no inherent regenerative capacity, is permanent and irreversible."

Lee and his collaborators developed their concept of LJ001 as interfering only with enveloped viruses after testing 23 pathogens in cell culture. Studies of nine of those agents — including Ebola virus, Nipah virus and Rift Valley fever virus — required high- or maximum-containment facilities and were carried out in the biosafety level 3 and 4 laboratories of the University of Texas Medical Branch at Galveston (UTMB) and USAMRIID.

"Once we started testing more and more, we figured out that it was only targeting the enveloped viruses," said Alexander N. Freiberg, director of UTMB's Robert E. Shope, M.D., Laboratory.

The Shope BSL4 lab was also used for mouse experiments with Ebola and Rift Valley fever virus that further confirmed the protective value of LJ001.

While the exact mechanism of viral membrane inactivation is unknown, the researchers are pursuing some promising leads that could answer that question.

Additionally, the drug does not appear to be toxic in vitro or in animals when used at effective antiviral concentrations.

UCLA has filed for a patent on the use of the compound.

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