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Researchers find smallpox drug may also target adenovirus

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Scientists at Saint Louis University have made two key discoveries that could lead to the first-ever human testing of a drug to target the adenovirus, which causes a number of severe upper-respiratory infections and is one of many viruses that causes the common cold.

There are currently no drugs approved specifically to treat adenovirus infections in large part because there has been no animal model in which to test drug candidates, a key prerequisite before testing in humans.

SLU researchers and their collaborators, however, have made two breakthrough findings: an animal model suitable for adenovirus testing – in this case using Syrian hamsters – and a drug that successfully attacks the adenovirus in those animals. The drug, hexadecyloxypropyl-cidofovir or CMX001, is currently under development by Chimerix, Inc. as a biodefense agent to meet the threat of smallpox or monkeypox viruses and as an antiviral agent in transplant patients.

The SLU research is published the week of May 19 in an early online edition of the *Proceedings of the National Academy of Sciences*.

“This is exciting news and a major step forward in finding a drug to treat adenovirus infections in humans,” said William Wold, Ph.D., professor and chair of the department of molecular microbiology and immunology at the Saint Louis University School of Medicine and the study’s lead author.

One of the key obstacles to finding an animal model for adenovirus testing involves the fact that the virus is generally species-specific; meaning the human version of the virus doesn't replicate well in animals commonly used in laboratory research.

The SLU researchers, however, found that the adenovirus replicates in Syrian hamsters (also called golden hamsters) with suppressed immune systems in much the same manner as it replicates in humans whose immune systems are weakened – making Syrian hamsters ideal for animal model testing.

"We are pleased to see that CMX001, a drug candidate showing broad antiviral activity that is being developed under a federal grant for smallpox, also has potential benefit against adenovirus," said George R. Painter, Ph.D., president and CEO of Chimerix.

Said Samuel Stanley Jr., director of the Midwest Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research (MRCE): "It is exciting to see work funded by the National Institute of Allergy and Infectious Diseases' MRCE program lead to potential new therapies for this important virus."

There are 52 known serotypes, or strains, of adenovirus in humans. They generally cause acute upper respiratory infections including colds, tonsillitis and ear infections, but they can also cause conjunctivitis, gastroenteritis and bladder infections.

Most people are able to recover from an adenovirus infection, but in some young children and people with weakened immune systems, adenovirus infections can turn virulent and even deadly. Adenovirus can also cause disease and even death in organ transplant recipients. Severe adenovirus outbreaks have occurred among groups of military recruits likely due to crowded living conditions.

CMX001 is an oral pro-drug, or derivative, of cidofovir, a drug developed by Gilead Sciences, Inc. to treat a type of retinitis in AIDS patients. Chimerix licensed from Gilead the rights to develop CMX001.

Cidofovir has long been a possible candidate to treat a number of virus infections, including the herpes virus, poxvirus and adenovirus infections in humans. The drug, however, is quite toxic to the liver and kidneys and is not available in oral form, which limits widespread use.

Using the new animal model, the SLU researchers found that CMX001 provided protection from the adenovirus when it was administered prophylactically (before infection with the virus) or therapeutically (after infection). The scientists found that the drug worked by greatly reducing the ability of the virus to replicate in key organs, mostly notably the liver.

The SLU team also found that CMX001 was much less toxic and far more powerful than cidofovir. In addition, scientists discovered, two weeks after infection with the virus CMX001 had reduced the viral load in the liver and blood to undetectable levels.

Source: Saint Louis University