AIDS Protection for Vaginal Sex?

For the first time, a vaccine appears to protect monkeys from vaginal transmission of a virus that closely resembles HIV, the virus that causes AIDS, a team of investigators reported this week. They hope that such studies will lead to the development of human vaccines that will prevent HIV from being transmitted through heterosexual intercourse.

Heterosexual activity is the dominant form of HIV transmission worldwide, notes virologist Preston A. Marx, the study's lead researcher. Indeed, the World Health Organization estimates that most of the 13 million people infected with HIV since 1981 were exposed through heterosexual intercourse. The team details its findings in the May 28 SCIENCE.

The monkey vaccine represents a promising development in the effort to stop the spread of this lethal disease, AIDS researcher Anthony S. Fauci told SCIENCE NEWS. However, it may take years before researchers can begin human trials of a similar vaccine, warns Fauci, director of the National Institute of Allergy and Infectious Diseases.

In 1989, Marx showed that monkeys could be vaginally infected with the simian immunodeficiency virus (SIV), a virus that is genetically similar to HIV. Indeed, those same monkeys went on to develop an AIDS-like illness, says Marx, now at New Mexico State University's primate laboratory at Holloman Air Force Base.

Investigators have developed vaccines that protect monkeys from intravenous injections of SIV (SN: 8/19/89, p.116). But those vaccines failed to shield female monkeys who were vaginally exposed to SIV, notes co-researcher John H. Eldridge of the University of Alabama at Birmingham.

The researchers began their experiment by dousing SIV with a lethal dose of a chemical called formalin. Next, they enclosed the inactivated SIV in microscopic beads of a biodegradable polyester material. They gave six female monkeys intramuscular injections of this vaccine, a step designed to rev up their immune systems, Eldridge says.

The monkeys then received a series of booster treatments aimed at triggering the part of the immune system that protects the mucous membranes lining the vagina. Researchers gave three of the monkeys an oral booster and sprayed vaccine directly into the windpipes of the remaining three.

All six monkeys had antibodies to SIV in their vaginal fluid after such booster treatment. But would these antibodies confer protection against the lethal virus? To find out, the team rinsed the vaginas of the monkeys with fluid containing high concentrations of SIV.

The researchers repeatedly tested the blood of the monkeys for evidence of SIV infection. Eight weeks after exposure, only one of the monkeys had become infected. Another monkey seemed to show signs of infection, but later tests were negative. The other four monkeys remained SIV-negative throughout this part of the study.

To determine whether the protection would last, the team gave those four monkeys another series of boosters and then exposed them to SIV. This time, three of the four remained infection-free.

It is very difficult to predict whether an approach that works with monkeys will benefit humans, comments virologist Shiu-Lok Hu of the University of Washington in Seattle. However, this study does raise the hope that scientists may one day develop a vaccine that would protect women, and eventually men, from contracting HIV through heterosexual activity. It's easier for women to become infected with the AIDS virus during intercourse with an HIV-positive man than vice versa. In men, scientists theorize, HIV invades the body through the mucous lining of the urethra.

The scientists caution that additional animal studies will be needed before the vaccine can be tested in humans. "I'm not predicting that [a human vaccine] will be available next year," says Marx. "It took me five years to get to this point."

– K.A. Fackelmann

Flu virus shows spring-loaded mechanism

Viruses have evolved complex and cunning methods of infecting their preferred hosts. Now, researchers believe they have discovered a twist in viral cleverness – a spring-loaded mechanism within the protective outer membrane of the influenza virus. This mechanism apparently helps the virus spill its DNA into cells, causing the misery known to millions as "the flu."

Spring-loading offers an explanation for how the virus brings out of hiding short bits of protein, called peptides. These peptides start a critical stage of infection known as membrane fusion, report structural biologists Chavela M. Carr and Peter S. Kim in the May 21 CELL. "We've provided a possible solution to a long-standing puzzle," says Kim, a Howard Hughes Medical Institute investigator at the Massachusetts Institute of Technology. Kim and Carr base their model on flu-membrane research they conducted at the Whitehead Institute for Biomedical Research in Cambridge, Mass.

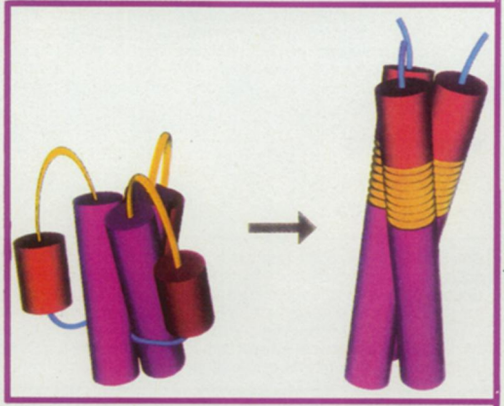
During infection, Kim explains, a flu virus latches on to a cell, causing part of the cell's outer membrane to bulge inward, seal off, and break free. This encloses the virus in a free-floating bubble called an endosome. But to move to the next stage of infection, the virus must fuse with the endosome and spill its DNA into the cell.

To do this, certain peptides normally hidden within the viral membrane must be lifted above the surface. Special spring-loaded regions of the membrane, triggered by increased acidity within the endosome, accomplish this feat. Strands of amino acids in the viral membrane – usually held under tension – spring up, causing the peptides to make contact with the inside surface of the endosome. This connection kicks off membrane fusion.

Successful infection depends on membrane fusion, making it a prime target for antiviral drugs. "If you could prevent membrane fusion, I think there's no question you could prevent infection," says Kim.

The researchers have also found that the outer shell of HIV, the virus that causes AIDS, contains an amino-acid pattern strongly resembling that of the spring-loaded region of the influenza virus. The spring structure may thus prove critical in the life cycle of other kinds of viruses.

– D. Pendick



Carr & Kim/© 1993 Cell Press

Proposed spring-loaded mechanism in the influenza virus before (left) and after it deploys its peptides.