New Drug Sweeps Clean in HIV Model

A team of researchers has tested a drug that apparently stops the animal equivalent of HIV, the AIDS-causing virus, in its tracks. Researchers gave the drug, PMPA, to 25 macaque monkeys as late as a day after inoculating the animals with simian immunodeficiency virus (SIV). The virus failed to infect any of the 25 animals.

"I've tested a variety of antivirals over the last several years, and such a response is extremely unusual," says Che-Chung Tsai of the University of Washington's Regional Primate Research Center near Seattle, who leads the team.

In its effect on the simian virus, PMPA seems to act as a more effective, less toxic version of the widely used AIDS drug AZT (zidovudine). The new drug may be most useful soon after exposure to the virus, the scientists suggest in the Nov. 17 SCIENCE. Tsai says the macaque research "forms a basis for future studies of the drug on HIV infections."

The simian virus provides the best model scientists have for HIV. Monkeys infected with SIV usually go on to develop an incurable, AIDS-like illness. They can also be infected with HIV but remain free of disease.

As retroviruses, both SIV and HIV carry their genetic material in the form of ribonucleic acid (RNA). They use their RNA as a template to form DNA, which then attaches itself to a host's genetic material. Retroviral drugs such as AZT disrupt this process by interfering with the enzyme that forges DNA subunits into a whole molecule. AZT acts as a bogus subunit, or analog, that ties up the enzyme.

But AZT has many drawbacks. Viruses frequently mutate and form a new enzyme that is unaffected by AZT, Tsai says. Moreover, many cells fail to treat AZT as a potential subunit. Even if they do, the drug doesn't last long inside cells. "[It] has a short half-life," says Tsai.

The new drug may overcome those problems. PMPA's structure ensures that cells will treat it as a subunit, and it stays within a cell far longer than AZT. "This long intracellular half-life may be the reason for the powerful antiviral effects of PMPA," Tsai says. So far, in test-tube studies of the drug's effectiveness against SIV, the researchers have seen no signs that the virus can mutate out of PMPA's hold.

In the animal experiments, the team gave 25 macaques daily doses of PMPA for a month, starting 48 hours before, 4 hours after, or 24 hours after giving the monkeys SIV injections. The investigators looked for laboratory and clinical evidence of SIV infection for more than a year but found none, even in lymph nodes.

Ten other macaques given SIV but not PMPA all became infected.

"We found no evidence that PMPA harms the animals," Tsai says, adding that they found no significant changes in blood chemistry or cells. AZT, on the other hand, causes many side effects at far lower doses.

"Such protection with no toxicity is unprecedented in the monkey model of AIDS," says Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases in Bethesda, MD. "It suggests a possible role for PMPA in preventing HIV in health care workers or others accidentally exposed."

The researchers have set their sights on using the new drug to eliminate HIV in babies born to infected mothers. "Some 70 percent of transmission occurs during labor," Tsai says. "We would love, one day, to be able to give this [drug] to newborns at risk," he adds. Tsai and other researchers are now considering how to study PMPA's effectiveness in blocking maternal SIV transmission in macaques.

Tsai's group plans to investigate how long after the introduction of SIV the drug can block the spread of the virus and will continue to monitor possible toxicity. They also expect that PMPA may eventually have an important role in combination therapies against established HIV infections. — *M. Centofanti*

Explaining the moon's two-faced appearance

The far side of the moon looks unfinished, as though its geological development stalled early on. Although vast volcanic eruptions resurfaced much of the moon's near side more than 2.5 billion years ago, the far face shows little repaving.

Using data collected last year by the Clementine spacecraft, two planetary geologists now proffer an explanation for the moon's unequal volcanic history. The thicker lunar crust on the far side inhibited large eruptions there, suggest R. Aileen Yingst and James W. Head of Brown University in Providence, R.I. They discussed their work at the annual meeting of the Geological Society of America in New Orleans last week.

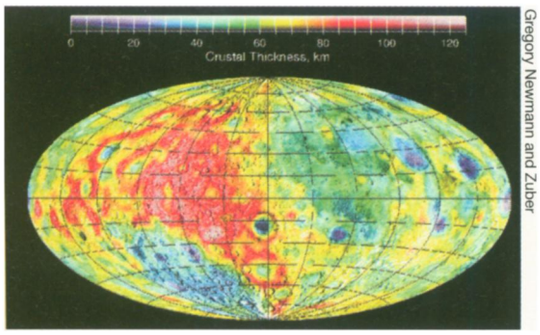
Yingst and Head focused their study on two giant basins carved by impacts on the far side. The basins contain "ponds" of erupted basalt much smaller than the vast seas of rock, or maria, on the near side.

Most of the ponds appear in regions where the crust was relatively thin, less than 50 kilometers deep. In the 2,500-km-wide South Pole–Aitken Basin, for example, Yingst and Head found that 94 percent of the erupted rock occurs in areas of thin crust.

This trend supports a theory, proposed previously by Head, that explains how eruptions occurred during the moon's volcanic phase. Because the lunar crust has a low density, molten basalt would not have been buoyant enough to rise passively through the crust. Instead, the basalt got trapped beneath the crust in reservoirs until enough pressure accumulated to force the molten rock upward. According to this theory, basalt reached the surface most easily through areas of thinner crust on the near side.

Maria T. Zuber of the Massachusetts Institute of Technology questions the theory, however. "That doesn't explain the whole story, because some of the thinnest crust on the moon is on the far side," says Zuber, who used Clementine data to map lunar crustal thickness. Zuber notes that the South Pole–Aitken Basin on the far side has regions of extremely thin crust. Even so, this area lacks the vast basaltic maria that sit atop areas of thicker crust on the near side.

To explain the volcanic deficit on the far side, some scientists have suggested a deeper reason. The lunar interior beneath the far side may have had limited quantities of radioactive elements, making it colder than rock under the near side. — *R. Monastersky*



Gregory Newmann and Zuber

In this map of the lunar crust, red indicates thick areas, and blue shows thin spots. The right half of the map represents the near side, the left half the far side.