# Enzyme study suggests anti-AIDS strategy

Biochemists working to understand HIV infection may have found a way to slow or stop replication of the AIDS virus before it really starts.

A research team from the National Cancer Institute (NCI) in Bethesda, Md., and Temple University in Philadelphia has pinpointed the site where a key HIV enzyme latches onto RNA belonging to the infected cell. In the Nov. 12 BIOCHEMISTRY, the group also reports creating small molecules that can settle into this site. These molecules may represent a first step toward developing therapeutic compounds that can prevent the virus from co-opting a cell, says Samuel H. Wilson, who codirected the NCI work with Dolph L. Hatfield.

"[The new results] will provide us with the information necessary to design compounds that can block or interfere with the actions of the enzyme," says Wilson, who is now at the University of Texas Medical Branch at Galveston.

"It might represent a new mechanism of inhibiting the [enzyme known as] reverse transcriptase, and any novel mechanism is important," comments David K. Stammers, a biochemist with Wellcom Research in Beckenham, England. Zidovudine (AZT) also affects reverse transcriptase, but in a different way.

Indeed, according to Robert J. Suhadolnik, who led the Temple University contingent, the group has made specific binding inhibitors for reverse transcriptase. Suhadolnik and colleagues from Germany and France reported promising results from such a compound in the Feb. 26 BIOCHEMISTRY. "[Such inhibitors] could either complement AZT or lower the concentration of AZT needed, [so that one could] get away from the toxic effects," he says. "Our goal right now is to find a method by which this could be delivered into the human cell without damaging the cell."

Reverse transcriptase enables the virus to run the infected cell's genetic machinery in reverse. Usually, the coding of a cell's DNA provides instructions to RNA, which then arranges amino acids into specific proteins. HIV uses reverse transcriptase to get RNA to instead create new DNA coding that includes the virus' genetic information.

The enzyme binds to one part of a specific piece of host transfer RNA, so called because it transports amino acids for protein synthesis. To locate this binding site, the NCI-Temple group first made probes – molecules resembling transfer RNA but also containing radioactive phosphorus – and mixed them with reverse transcriptase, Wilson says. The researchers then chopped the enzyme into small pieces and scanned the pieces. They discovered that a 100-amino-acid-long section near the center of the 560-amino-acid-long enzyme had latched onto the probe.

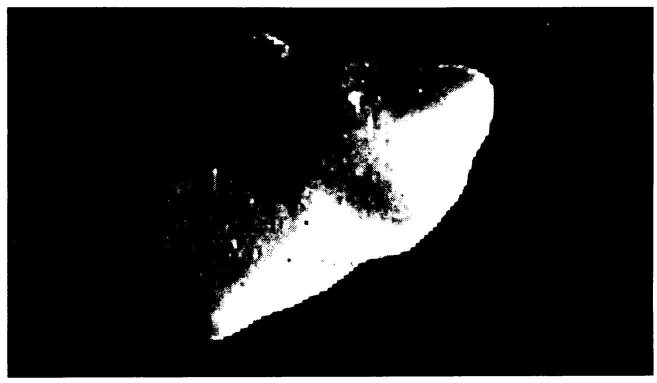
"Now we'll be able to focus on this small domain," Wilson says.

The investigators also studied the formation and stability of the RNA-enzyme complex in solutions with increasing concentrations of salt. From those studies, they concluded that the enzyme's docking site for transfer RNA consists of a groove with hydrophobic (water-repelling) protuberances as well as charged sections along the indentation. "That tells us to think in terms of developing hydrophobic compounds [to block the binding of RNA]," Wilson says.

In separate, unpublished work, molecular biologist Stuart F.J. Le Grice of Case Western Reserve University in Cleveland has identified the binding region as a smaller stretch of amino acids in the same part of the enzyme. Le Grice contends, however, that the form of the enzyme used by the NCI-Temple researchers was not the "biologically relevant" form that is active in the cell, and he expresses concern that some of the materials they used may not have been as pure as they thought.

"I doubt that the work is wrong," Le Grice says. But he thinks the story is more complicated than the new report suggests. *– E. Pennisi*

# Galileo snaps first close-up of an asteroid


JPL

*Galileo's view of the asteroid 951 Gaspra.*

Asteroids have intrigued skywatchers since astronomers first detected these rocky bodies nearly 200 years ago. From Earth, they appear only as faint streaks of light, leaving many unanswered questions about their origin, shape and chemistry. Last week, that state of knowledge changed dramatically as the Jupiter-bound Galileo craft radioed back the first close-up images ever taken of an asteroid.

On Oct. 29, Galileo's camera snapped 150 pictures as it passed within 1,600 kilometers of a tiny asteroid called 951 Gaspra. The images – only a few of which actually show the asteroid – were stored in an on-board tape recorder because researchers have been unable to open the craft's main antenna (SN: 8/3/91, p.79).

As recently as mid-October, researchers doubted they could retrieve any Gaspra images before December 1992, when the craft swings around Earth again to gain speed on its way to Jupiter. The problem: Relying on a small antenna that transmits at the painfully slow rate of 80 hours per picture, Galileo would be unable to radio more than a few images during the two weeks following the Gaspra flyby. Scientists decided the transmission effort wouldn't be worth the bother, since they wouldn't even be able to determine which stored images contained the asteroid.

As Galileo closed in on Gaspra, however, an unusually successful navigation enabled engineers to identify four likely asteroid images among a mosaic of 36 photographs. In fact, the two visible-light and two near-infrared pictures relayed to an Australian radio receiver show Gaspra at dead center, scientists reported at a briefing last week at the Jet Propulsion Laboratory in Pasadena, Calif.

These images offer graphic testimony to Gaspra's violent history, says Cornell University astronomer Joseph Veverka. The irregularly shaped asteroid, which he likens to a dented football pitted with craters, measures about 12 by 20 by 11 kilometers, he says. The craters that pepper its surface range in diameter from 2 kilometers to 160 meters – the smallest features visible in the images.

Researchers believe Gaspra is a fragment chipped from a larger object. "We suspect [Gaspra] is a survivor of a series of catastrophic collisions . . . , in which a succession of parent bodies got broken down into smaller and smaller pieces," Veverka says. On the basis of the degree of cratering discerned in the photographs and the estimated frequency of collisions that Gaspra would suffer at its current location – about 411 million kilometers from Earth, near the inner edge of the asteroid belt – astronomers calculate that the asteroid may have taken its present shape a relatively scant 300 million years ago. Before the flyby, Richard P. Binzel and Noriyuki Namiki of the Massachusetts Institute of Technology reported a similar estimate in the June GEOPHYSICAL RESEARCH LETTERS.

Gaspra's brush with violence didn't end there, Veverka notes. A series of apparent ridges or grooves on its surface suggests