Monkey virus may lead to anti-HIV insights

Developing new drugs to combat HIV, the virus that causes AIDS, can cost hundreds of millions of dollars and require a decade or more of research and development.

To leapfrog some of this expenditure and investment of time, many researchers are using powerful computer programs and structural information about HIV's key proteins to design highly specific anti-HIV compounds.

Now, researchers have taken another important step toward bringing this approach to bear against HIV. At a meeting of researchers this week in Washington, D.C., two teams of investigators announced that they have elucidated the structure of a key protein manufactured by the simian immunodeficiency virus (SIV), which causes an AIDS-like illness in monkeys. The protein, SIV protease, enables the virus to make copies of itself, which then infect other cells.

At the meeting, sponsored by the National Institute of General Medical Science, Robert M. Stroud of the University of California, San Francisco (UCSF), and Sherin Abdel-Meguid of SmithKline Beecham Pharmaceuticals in King of Prussia, Pa., exhibited three-dimensional, computer-generated portraits of SIV protease showing the exact locations of its constituent atoms.

Each scientist represented a large group of collaborators that independently solved the structure.

In HIV infection in humans, a nearly identical enzyme — HIV protease — enables infected cells to assemble new virus particles. Scientists unlocked the structure of HIV protease in 1987 and have since discovered scores of molecules that inhibit the enzyme's function in laboratory-grown cells.

But no one yet has demonstrated that disarming HIV protease can halt the proliferation of virus that leads inexorably to AIDS. Structural information on SIV might help resolve whether disabling the HIV replication protein is a viable therapeutic approach.

"Knowing the structure of SIV gives us a way to develop drugs faster that can then be tested in monkeys," says Charles S. Craik, a UCSF biochemist who has worked extensively with HIV protease. And because SIV and HIV are so similar, identifying a nontoxic drug that stops SIV from reproducing in monkeys could establish the feasibility of using protease-blocking drugs to combat HIV infection in humans, he adds.

By incorporating this structural information about SIV protease into computer programs, explains UCSF's Stroud, researchers can match various kinds of molecules against the shape of the active site on the SIV protease. The computer can tell which molecules are likely to bind strongly to the enzyme, gumming up viral replication. Animal studies could then prove which of the compounds prevent HIV from proliferating.

Evidence suggests that HIV-II, the virus strain that causes most cases of AIDS in Africa, evolved in primates and then made the jump to human hosts, Stroud points out.

"The disease used animals to develop this virus and give it to humans," Stroud says. "Now, we're turning it around. Using that misfortune of nature, we're going to use those same animals to help get a cure."

— D. Pendick

Mystery flu hits Southwest

A virus carried by field mice and other rodents may prove responsible for the deadly flu-like illness that has erupted mostly in Arizona and New Mexico, according to public health officials.

The ailment, which is known as acute respiratory distress syndrome, has killed 11 people and made nine others severely ill. The symptoms appear remarkably like those of the flu. Victims spike a fever, start coughing, and develop muscle aches and inflamed, reddened eyes. Most, although not all, of the victims lived on or near the Navajo reservation located in the Four Corners area of Arizona, New Mexico, Utah, and Colorado.

The illness primarily has hit apparently healthy people in their 20s and 30s, says epidemiologist Stuart Castle of the New Mexico State Health Department in Santa Fe. Patients have trouble breathing, and some have died of suffocation within hours of getting ill, he adds.

U.S. Department of Health and Human Services Secretary Donna E. Shalala has sent federal investigators to help state and local epidemiologists nab the culprit in this deadly cluster of cases. Preliminary evidence suggests that the illness is caused by airborne spread of dried urine or fecal matter from rodents infected with some type of virus, possibly a *Hantavirus*. Health officials have urged people living on or near the reservation to avoid rodent nests.

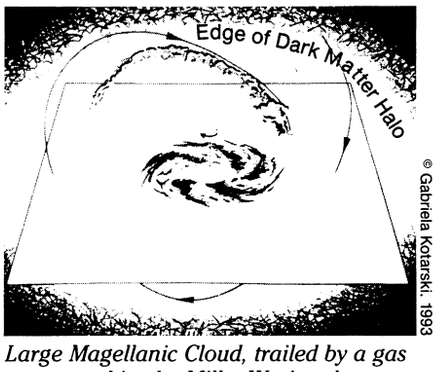
The disease does not appear to be transmitted by contact with infected people, Castle adds. No health workers have become infected. Furthermore, the investigators turned up only one instance in which several members of the same family got sick. □

Nearby galaxy sheds light on dark matter

Astronomers have measured for the first time the movement across the sky of a galaxy other than our own. Using the new data, which characterize the orbit of the Milky Way's nearest galactic neighbor, California researchers have made what they consider the most accurate estimate to date of the amount and shape of dark matter in our galaxy. Dark matter — hypothetical material thought to make up 90 to 95 percent of the mass in the universe — doesn't emit light, yet it exerts a gravitational tug.

According to the new calculations, the mass of the Milky Way contains five to 10 times as much dark matter as visible stars. Moreover, the team infers that this unseen material lies in a giant halo at least six times larger than the visible disk of the galaxy. A halo this big would not only dwarf the visible Milky Way, it would extend far beyond the Milky Way's nearest neighbor and satellite galaxy, the Large Magellanic Cloud (LMC).

While astronomers had already derived similar estimates for the size and mass of dark matter in the Milky Way, "this measurement is much more reliable than all previous measurements," says Douglas N.C. Lin of the University of California, Santa Cruz. He and his Santa Cruz colleagues, Burton F. Jones and Arnold R. Klemola, reported the work this week at a meeting of the American Astronomical Society in Berkeley, Calif.



Large Magellanic Cloud, trailed by a gas stream, orbits the Milky Way's poles.

Since dark matter can't be seen, astronomers use its gravitational influence on visible objects as an indirect means of detecting it. To search for dark matter in the Milky Way, therefore, Lin and his coworkers decided to study the motion of the LMC, bound to our galaxy in an orbit that takes it above and below the Milky Way's disk. Many astronomers had previously measured the LMC's radial velocity, or motion along the line of sight to the Milky Way. But Lin's team sought its transverse velocity — its motion across the sky — which no one had ever measured for any galaxy but our own.

Such motion is extremely difficult to