Second protein opens cells to HIV's entry

Scientists have long puzzled over how HIV, the AIDS virus, gains entry into the human immune cells it infects. They know the virus attaches itself to a human cell surface molecule called CD4. Yet they also know that HIV does not fuse to most animal cells, even after the gene for CD4 has been added to them.

"The binding [with CD4] was not enough. Something else was required for the fusion process to happen," says Edward A. Berger of the National Institute of Allergy and Infectious Diseases in Bethesda, Md.

That something else, at least for certain strains of HIV, is another human cell surface protein, Berger and his coworkers contend in the May 10 SCIENCE.

Other researchers hail the long-awaited identification of this protein, which Berger's group calls fusin, as a major advance in scientists' knowledge of HIV's life cycle. "It really affords new opportunities to study, at the molecular level, how HIV infects cells," says Robert W. Doms of the University of Pennsylvania Medical Center in Philadelphia.

While researchers can conceivably develop therapeutic agents that block HIV's interaction with fusin, says Berger, a more immediate impact of fusin's discovery may be to help researchers understand why some people resist HIV infection and why some HIV-infected people do not develop AIDS. By adding the genes for CD4 and fusin to animals such as rabbits, investigators also hope to create laboratory models in which they can study HIV infection.

Fusin arrives center stage almost 3 years after a French research group announced that a molecule called CD26 was the elusive HIV fusion cofactor. Many labs were unable to reproduce the finding, however. In contrast, the discovery of fusin by Berger's group has so far garnered rave reviews.

"There's no controversy about this. It's already been reproduced in several labs. There's no question it's correct and it's a highly significant piece of work," says John Moore of the Aaron Diamond AIDS Research Center in New York City.

To identify the HIV fusion cofactor, Berger's group developed a novel means of testing the importance of many human proteins in the fusion process. The researchers added to one mouse cell line the gene for CD4 and to another, the gene for Env, a protein on the surface of HIV that the virus uses to bind to CD4.

They also added to the mouse cells containing the CD4 gene a large library of genes taken from human immune cells that HIV can infect. One or more of the proteins encoded by these human genes endowed the CD4-bearing mouse cells with the ability to fuse to the mouse cells displaying Env, Berger's team found. By winnowing the genetic library down to fewer and fewer genes, the investigators finally found a single gene whose protein was required for cell-cell fusion.

A further battery of experiments solidified the case for fusin. In one test, Berger's group added the genes for CD4 and fusin to mink cells, which normally resist HIV infection: HIV then penetrated the altered cells.

Not all HIV strains depend upon fusin, notes Berger. Strains that preferentially infect immune cells called macrophages appear to use a different cofactor, though Berger suspects it closely resembles fusin.

"In some ways, this could be the tip of the iceberg. Different HIV strains might utilize different members of [a fusin] family," says Doms.

The gene for fusin was actually identified several years ago in research unrelated to HIV, notes Berger. As yet, researchers haven't discovered the normal role of fusin or the proteins with which it naturally interacts. Curiously, says Berger, fusin resembles a molecule that binds to a chemokine called interleukin-8. Chemokines are a small family of proteins, some of which have recently been found to suppress HIV infection (SN: 12/9/95, p. 388).

Fusin's similarity to a chemokine receptor raises the possibility that chemokines interfere with HIV's ability to use fusin or fusinlike proteins to infect cells, says Doms. "We're not saying fusin is a chemokine receptor, but the chemokines may be a good place to start looking," adds Berger.

Berger's group plans to examine exactly how fusin's presence allows HIV to enter a human cell. They also hope to study whether HIV's interaction with fusin might explain how the virus kills immune cells, a fundamental question that remains a mystery. — *J. Travis*

A new instrument could spot faintest stars

To learn about the births and deaths of distant galaxies, astronomers must catch the handful of photons that make it to Earth from the farthest reaches of the universe. A new electronic device that can detect high-energy photons promises to make that task easier.

Astronomers use charge-coupled devices (CCDs)—light-sensitive semiconductors that register almost every photon that hits them—to catch the scant rays from distant objects. Yet even CCDs fail to perform well at short wavelengths of light. Moreover, they do not record the energy of the photons that hit them, so astronomers must combine them with other optical devices in order to measure spectra.

Now, Anthony Peacock, an astrophysicist at the European Space Agency in Noordwijk, the Netherlands, and his colleagues have built an optical measuring device that they maintain "can overcome the limitations" of conventional CCDs for optical astronomy.

Describing their new "superconducting tunnel junction" (STJ) in the May 9 NATURE, the researchers explain that it can detect the position, arrival time, and energy of individual photons whose wavelengths measure as little as 200 to 500 nanometers—from near ultraviolet to visible light. In theory, they say, the current device can detect photons with wavelengths near 20 nm—and with improved superconductors, the wavelength limit could fall as low as 8 nm.

"This is an extremely exciting development," says Charles C. Steidel, an astronomer at the California Institute of Technology in Pasadena. "This new instrument should enable astronomers to obtain images and do spectroscopy simultaneously on every object in their field of view. In the next few years, such devices could make an amazing difference in observational astronomy."

To analyze a celestial object, astronomers first compose images by measuring photon locations and then form spectra from photon energies. These observations demand separate procedures, both of them time-consuming for faint objects.

The new device may enable astronomers "to gather thousands of spectra simultaneously just by taking an image," says Steidel. "For someone studying very faint galaxies, this technology could bring significant gains."

Indeed, the new instrument could "enormously increase the amount of useful information at our disposal," says Francesco Paresce, an astronomer at the European Southern Observatory in Garching, Germany.

"Right now, no instrument can make 3-D panoramic views of the sky and at the same time record the position and time of a photon's arrival, as well as its energy level," says Paresce. The new technology will enable astronomers to analyze large portions of the sky that today must be studied piecemeal, he adds.

"There are distant galaxies whose redshifts we can't measure accurately because bigger telescopes are needed to funnel a small number of photons into the spectrometers," Paresce says. "That precludes us from studying many very faint objects.

"This new instrument," he adds, "could replace many tons of steel in telescopes on land and in space." — *R. Lipkin*