intensities," says Klaus Heinz, head of the Erlangen-Nürnberg team. "If those calculated intensities coincide with those you measure, you're pretty sure you have the correct structure. But normally, you have to modify your model through trial and error. And in cases of complex structures, it may not ever be possible to find the correct structure."

In 1990, however, Saldin and Pedro de Andres of the Universidad Autonoma de Madrid suggested that the diffuse diffraction pattern generated when electrons scatter from a disordered surface might be interpreted as a hologram—a three-dimensional image captured in an interference pattern. Holograms are created when a beam scattered off an object interferes with a reference beam that has bypassed that object. Saldin and de Andres realized that they might be able to generate such a pattern if the surface has a single atom sticking out prominently, which can split the incoming electron beam. Half the beam bounces off the prominent atom and back to the detector, creating the reference beam, explains Heinz. The other half goes on to the other surface atoms and then scatters back to the detector, producing an object beam. The two interfere to produce the holographic image, which can be extracted from the LEED data.

Heinz's group collaborated with Saldin and his colleagues to produce atomic-resolution holograms of disordered oxygen and potassium atoms on a nickel surface. But measuring the intensity of a diffuse diffraction pattern accurately enough to extract a hologram was extremely difficult; only a few labs in the world could do it. Surface scientists also tend to be much more interested in ordered surfaces than in disordered ones because, says Starke, "those are the ones you can reproducibly prepare."

Heinz and his colleagues then realized that, with some modification, the same holographic reconstruction algorithms could work on the much brighter diffraction patterns that result from crystalline surfaces. The result is the pioneering image in the *PRL* paper: an electron hologram of a well-ordered atomic surface—in this case, silicon carbide.

Not every surface will give up its secrets to electron diffraction holography. It only works on materials with the occasional prominent atom, although such atoms can be chemically attached to a surface of interest before it is imaged. What's more, the technique can achieve a resolution of only 0.5 angstrom, compared to 0.1 angstrom for conventional LEED. For now, says Saldin, the technique is best suited to providing a quick first guess to plug into the LEED algorithm, which can then generate the correct, well-resolved structure. "It is a direct method of very quickly getting an approximate view of the structure," he says—a quick, surface impression of a material.

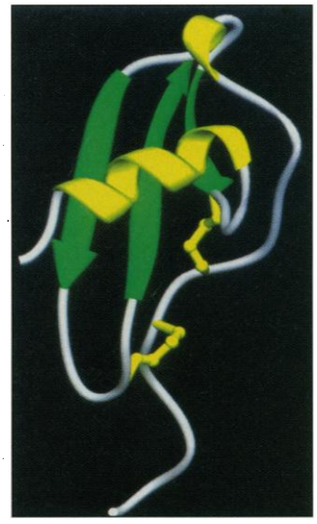
–Gary Taubes

AIDS RESEARCH

Chemokine Mutation Slows Progression

One of the most insidious features of the AIDS virus, HIV, is its habit of lurking in the body for years before causing overt disease. Why HIV takes so long to destroy the immune system of most infected patients is a central question in AIDS research. Now, findings presented in this issue may provide fresh clues to the mystery—as well as suggest new therapies that could slow or stop progression of the disease.

On page 389, geneticists Stephen O'Brien, Cheryl Winkler, and their colleagues at the National Cancer Institute in Frederick, Maryland, together with collaborators from other institutions in the United States and Japan, report that HIV-infected patients who have a mutant gene for a molecule called SDF-1 progress much more slowly to full-blown AIDS or death than do people with a normal version of the gene.



M. CRUMP/PENCE

Protector? SDF-1 chemokine may tie up T cell receptors.

SDF-1 is a member of a class of molecules called chemokines, which help recruit immune cells to sites of inflammation. It normally binds to a receptor molecule on T lymphocytes—the cells targeted by HIV—called CXCR4, which the virus also uses to enter T cells during later stages of the disease. The results suggest that the mutant gene, called *SDF1-3'A*, helps protect infected people from the ravages of these late-stage viruses. These findings mark the first time that a mutation in a gene coding for a chemokine, rather than a chemokine receptor, has been shown to affect the course of HIV infection.

O'Brien's team found the mutation during a genetic screen of blood samples taken from 2419 HIV-infected patients in study cohorts across the United States, as well as 435 people who had been exposed to HIV but remained uninfected. In earlier work on these patients (*Science*, 27 September 1996, p. 1856), the team found that people with two mutant copies of the gene coding for CCR5—a chemokine receptor targeted by HIV in the earlier stages of infection—are highly resistant to infection. The new study indicates that subjects who are homozygous for the SDF1-3'A mutation—meaning they carry two copies of it—are also protected, but primarily against progression of the disease after infection. Disease progression in homozygous Caucasians, for example, takes three times longer than in similar individuals who possess only one mutant copy or none at all.

The SDF1-3'A variation, which occurred in homozygous form in less than 5% of the patients studied, is located in a part of the gene that is not "translated" into the building blocks of SDF-1. Instead, it is in an adjacent, untranslated portion whose sequence is conserved among mammalian species, indicating that it may have an important regulatory function. O'Brien and his colleagues suggest that this segment may control the production or transport of the chemokine. If so, the mutation may protect infected individuals by increasing the production or availability of SDF-1, which would bind to CXCR4 and block the virus from entering the T cells.

The study provides no direct evidence for this idea, but other researchers told *Science* that it is a reasonable—and attractive—interpretation of the results. Viral immunologist Jean-Louis Virelizier of the Pasteur Institute in Paris says that an increased level of the chemokine is the "simplest explanation" for the findings. Although SDF-1 has previously been shown to block CXCR4-using viruses in the test tube, Virelizier says the new results "provide the first evidence" that the chemokine "may participate in vivo in the host's defense against HIV infection." And Dan Littman, an AIDS researcher at the New York University Medical Center, says that if the mutation does affect SDF-1 levels, "it would be very exciting indeed, because it would suggest that progression to disease is in large part dependent on HIV interacting with CXCR4." That is a popular, but not yet proven, hypothesis for how HIV becomes increasingly lethal to its target cells.

The next step, researchers say, will be to prove that the mutation really does increase SDF-1 levels. If O'Brien's hypothesis is right, the findings could point the way to development of new anti-HIV drugs: SDF-1 or a laboratory-modified version of the molecule "may have antiviral effects even at late stages of HIV infection," says Virelizier. Indeed, O'Brien argues that the protective effects of the SDF1-3'A mutation could be considered a first clinical test of that appealing possibility. "This was not done in the test tube, but with patients infected with HIV," he says. "It has parallels with a clinical trial. The results are very provocative."

–Michael Balter