of its work. So when Matsuda learned about Herkenham's marijuana receptor map, she walked down the hall to see him. They compared maps—and got a flash. The marijuana receptor concentrations were high in just those brain sections where the Brownstein group's gene was active.

She and her colleagues immediately went to work to test the hypothesis that their gene encodes the receptor. They introduced the cloned gene, for example, into Chinese hamster ovary cells and tested the ability of cannabinoids with varying potencies to inhibit adenylate cyclase in the cells. Only cells carrying the transferred receptor gene responded, and then, Brownstein says, "The rank order of the the compounds [in inhibiting the enzyme] was the same as the rank order of those compounds in producing highs." That and other results convinced the researchers that their long search for a function for their gene had paid off.

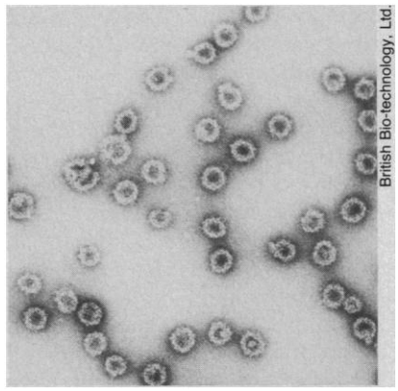
The next big step is to try to find out what the receptor binds naturally. And that could require another protracted search. "We don't even know the chemical nature of the ligand [binding substance]," Brownstein says. "It could be a prostaglandin, a peptide, whatever." Neurobiologists, it turns out, can't expect the instant gratification of marijuana smokers. They have to work long and hard for their highs.

■ JEAN MARX

U.K. Vaccine Trial: Stalking Horse for the Future

The trials of a new AIDS vaccine are set to begin in London next month. And the world will be watching—not just to see how well the vaccine does, but because the protocol will, in several respects, presage future AIDS vaccine trials.

The phase I trials, first under the U.K. Medical Research Council's AIDS Directed Programme, are innovative in three ways. Clinically, the vaccine could prove more effective as a form of immune therapy than as a preventative. Ethically, issues that will arise in later vaccine trials are being given careful consideration. And scientifically, the vaccine's delivery system may be the forerunner of a whole generation of new antiviral immunizations.



Special delivery. *These "virus-like particles" deliver an experimental AIDS vaccine.*

That delivery system consists of virus-like particles, or VLPs. VLPs are made up of proteins and are of the same size and structure as viruses, but contain no DNA or RNA and are therefore not infective. The particles can be engineered to include foreign proteins, serving as the vehicle for presenting antigens—including HIV antigens—to the human immune system.

The first step toward using VLPs as a delivery system was taken in 1984 by Alan Kingsman, a biochemist at Oxford University, who discovered that yeast cells have a gene—named Ty—whose protein has remarkable properties. Ty is a transposon: a piece of DNA that can insert itself in many different spots in the genome. Transposons were already known, but Kingsman and his wife Susan, also an Oxford biochemist, showed that Ty is no ordinary member of that group. Ty is a retrotransposon: like a retrovirus, it reproduces itself via an RNA intermediary and the enzyme reverse transcriptase.

Kingsman went on to show that if he fused another gene to Ty, the yeast cell would make a hybrid protein that assembles itself into VLPs, carrying on their surface antigens corresponding to the foreign gene. And that makes VLPs excellent immunization vehicles. As Kingsman told *Science*, "producing antigens as particles makes them significantly more immunogenic than [they are as] globular proteins."

The Kingsmans' work on VLPs was patented by British Bio-technology, Ltd. Working part time at the firm, where he is associate director of research, Kingsman and his colleagues created hybrid VLPs carrying the p24 protein that forms part of the HIV core. The HIV hybrid has already shown promise—one reason it is proceeding to human trials.

The trials will be conducted by Jonathan Weber, infectious disease specialist at the Royal Postgraduate Medical School in Hammersmith, London. Weber is assembling a panel of 20 healthy young men, not infected with HIV and not in any risk group. The initial phase of the trial is to determine what kind of immune response the VLPs elicit, not to test it against actual infection.

The trial group has taken precautions to ensure that none of the volunteers might be thought to have HIV infection—which could subject them to discrimination. The volunteers will have a positive response to p24—one thing measured by AIDS diagnostic tests. But they will also have a positive response to the Ty protein, distinguishing them from HIV carriers. And, since no HIV envelope protein is included in the vaccine, the volunteers "will absolutely not have an anti-envelope response," Kingsman says. Therefore volunteers in the trial should have no difficulty obtaining life insurance. But such questions will be more sharply posed in the future—particularly if a vaccine containing HIV DNA should ever be tested.

Most workers on AIDS vaccines are cautious about the value of VLP-p24 as a preventative. "The approach is scientifically very interesting," said Reinhard Kurth, director of the Paul Ehrlich Institute near Frankfurt in Germany, "but from the immunological point of view I have my doubts that such a small [antigen] can confer protection." Weber agrees. But, he adds, an effective vaccine may require structural proteins like p24 as well as HIV envelope proteins. Hence the current round of tests might lead to one component of an eventual vaccine.

More promising is use of VLP-p24 as a form of immune therapy. As Kingsman says, "there is a long-standing observation that patients with high anti-p24 levels early in infection tend to have longer onset times." That implies that boosting the level of anti-p24 antigen through the VLPs might delay full-blown AIDS. Kingsman admits that the link between high anti-p24 and delay of AIDS is "controversial." But, he says, it's "worth a try. Anything in the AIDS field is worth a try."

Trying VLPs is worthwhile for another reason—because they can deliver practially any antigen. Hence they might, according to Keith McCullagh, chief executive of British Bio-technology, have "the potential of leading to the creation of a new generation of antiviral vaccines." As one example, Kingsman sees a "much cheaper hepatitis vaccine." And the promise, he thinks, is unlimited: "We can put anything in [VLPs]." ■ JEREMY CHERFAS