Mouse model tests AIDS drug efficacy

Researchers report success in using mice transplanted with human immune cells to test the efficacy of an AIDS drug. The work bolsters hopes that this animal model can help scientists assess the potential of various drugs against the AIDS-causing virus, or HIV.

Investigators currently screen experimental AIDS drugs in cultured human immune cells infected with HIV. Compounds showing promise in the laboratory become candidates for pilot trials to evaluate safety and efficacy in humans.

But because that method can expose volunteers to high levels of potentially dangerous drugs, scientists have sought a small-animal model that could bridge the gap between laboratory culture and human trials, giving them some idea of a drug's potential toxicity. The search remained frustrating until 1988, when several research teams transplanted components of the human immune system into mice—whose own tissues naturally resist HIV infection—and then injected HIV into the mice (SN: 12/24/88, p.404).

In the Feb. 2 SCIENCE, one of those teams reports using zidovudine (AZT), the only federally approved anti-HIV drug, to suppress HIV infection in immunodeficient mice. Led by Joseph M. McCune of SyStemix of Palo Alto, Calif., the group started by transplanting thymus and lymph node tissue from human fetuses into mice born without immune systems.

The researchers injected 40 of these mice with HIV. At the end of a two-week period, a genetic technique called polymerase chain reaction (PCR) showed all 40 mice positive for the virus. The team then took 17 other mice and treated them with zidovudine for 24 hours before injecting them with HIV and for two weeks immediately after. At the end of those two weeks, the researchers removed and tested some of the transplanted human tissue, finding no hint of HIV when they used the PCR. But when they tested the tissue with an even more sensitive technique called *in situ* hybridization, they found a few cells infected with HIV. After the mice went four more weeks without zidovudine, the PCR showed HIV replication in tissue from each of the 17.

"It is a demonstration that these kinds of models are going to be useful for drug testing," says Donald E. Mosier of the Medical Biology Institute in La Jolla, Calif., who created a similar AIDS model by implanting white blood cells from human adults into immunodeficient mice. Mosier says such models may also help scientists study other viral diseases. His team, for example, has infected mice with Epstein-Barr virus, which in humans can cause a cancer called Burkitt's lymphoma. — *K.A. Fackelmann*

Suicide thoughts drop in HIV positives

Thoughts of suicide actually decrease in the two months after a person tests positive for infection with the AIDS-associated virus (HIV) and participates in two short counseling sessions, according to a research report in the Feb. 2 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

The finding is "somewhat reassuring" for people in the early stages of HIV infection, say Samuel Perry of Cornell University Medical College in New York City and his colleagues. In contrast, two previous studies of men whose HIV infections had progressed to AIDS charted a suicide rate up to 36 times greater than that of men without AIDS.

Nearly 16 percent of the individuals in Perry's study group who requested an HIV test experienced substantial emotional distress both before and after the procedure, regardless of the results, the researchers found. About one in 50 study participants not only thought about killing themselves but also reported the desire or intent to commit suicide both before and after notification of test results. These same individuals also reported symptoms of severe depression and may require psychiatric treatment, the scientists assert.

Perry and his co-workers administered free HIV tests to 244 male and 57 female volunteers recruited in New York City. All volunteers received counseling the day blood samples were drawn and two weeks later when notified of their test results. A psychiatric nurse conducted the one-hour counseling sessions, which included a standard depression inventory and education about HIV infection.

Among all volunteers, the rate of suicidal thoughts dropped from 30.2 percent at the start of the study to 18.8 percent one week after notification; it fell to about 16 percent at the two-month follow-up. When contacted two months after notification, subjects testing positive for HIV reported about the same rate of suicidal thoughts as those testing negative.

But 10 participants reported suicidal wishes or intent before testing, and five of them continued to consider suicide two months after notification. All five tested negative for HIV.

Routine counseling before and after HIV testing may identify similar individuals who are at high risk for severe depression and suicide, the researchers maintain. — *B. Bower*

Fetal-cell recipient showing improvements

A tiny sample of human fetal cells transplanted into the brain of a man with Parkinson's disease appears to have survived and grown there for at least eight months, significantly reducing his symptoms, European researchers report.

The 49-year-old Swedish man's improvement contrasts with two disappointing attempts by the same researchers, who attribute their latest results to changes in surgical technique. The accomplishment "supports the idea that neural grafting can be developed into an effective therapy in Parkinson's disease," they conclude.

Several U.S. neuroscientists told SCIENCE NEWS that the report — the most complete analysis of a successful fetal graft to appear in a scientific journal — still falls short of proving the procedure's ultimate value. But they add that further technical improvements may well lead to more definite successes, which would almost certainly complicate the already heated debate about the ethics of the controversial procedure.

In the Feb. 2 SCIENCE, Olle Lindvall of the University Hospital in Lund, Sweden, Anders Björklund and nine others describe the surgery, performed last March. They used 60 microliters of fetal tissue retrieved from four fetuses aborted in the first-trimester. In this latest attempt, the team used a smaller tool to implant the fetal tissue and shortened the interval between tissue retrieval and transplant.

Two months later, the patient showed reduced rigidity, improved motor function and less need for medication, the researchers report. In the months since, he has maintained these improvements. Brain-imaging PET scans performed five months after surgery indicated the fetal cells were alive and producing the neurotransmitter dopamine, which is in short supply in Parkinson's patients.

However, notes neuroscientist Curt Freed of the University of Colorado Health Sciences Center in Denver, "PET scans are very difficult to interpret, especially with the small changes seen in these transplants." He and others say researchers need even more refined tests to measure survival of grafted cells and to show that any clinical improvement results from those cells. Some experiments in animals have hinted that the trauma of brain surgery itself can spur new growth of dopamine-secreting neurons.

Despite such caveats, the work is "quite exciting," says Irwin Kopin, a neuroscientist whose unprecedented request in 1988 to perform a similar operation at the National Institutes of Health led to a ban on U.S. federal funding for human fetal cell transplants. — *R. Weiss*