Experimental cell grafts for Huntington's

Physicians last week reported what appears to be the first surgical grafting of adrenal tissue into the brain of a patient with Huntington's disease. The experimental procedure, using the patient's own adrenal tissue, was performed in early March at the Vanderbilt University Medical Center in Nashville, Tenn. It is similar to an experimental therapy used on patients with Parkinson's disease, another neurological disorder. The Parkinson's surgeries, which have now been reported at several medical centers in the United States and elsewhere, have so far met with uncertain results.

"It will be several months before we know if [the Huntington's therapy] works," says George S. Allen, director of Vanderbilt's neurotransplant program. The rationale behind the therapy comes from evidence that the neurological problems associated with Huntington's may be due in part to brain damage caused by a brain chemical, quinolinic acid. Experiments with rats suggest that transplants of tissue from the adrenal medulla to the caudate nucleus in the brain may be able to block such damage.

Between 500 and 1,000 new cases of Huntington's are diagnosed in the United States each year. This hereditary disease, which typically doesn't become apparent until middle age, results in severe neurological degeneration and death. Vanderbilt says it plans to perform experimental adrenal transplants on a total of 24 Huntington's patients.

Retinoblastoma cells lack receptors

Researchers seeking to uncover the biochemical defect behind retinoblastoma, a hereditary cancer of the eye, have found that retinoblastoma tumor cells lack a class of chemical receptors involved in inhibiting growth. The exact function of the so-called transforming growth factor-beta 1 (TGF-beta 1) receptors, first characterized in 1985, is still not well understood. Scientists suspect, however, that the receptors—located on the surface of some cells—are important in regulating cell proliferation. In some cases they appear to protect against the effects of cancer-causing genes, or oncogenes.

As reported in the April 8 SCIENCE, researchers at the Weizmann Institute of Science in Rehovot, Israel, The Whitehead Institute for Biomedical Research in Cambridge, Mass., and the University of Massachusetts Medical School in Worcester tested the responses of retinoblastoma tumor cells and normal retinal cells to various growth-inhibiting factors. When the tumor cells proved insensitive to the growth inhibitor TGF-beta 1, they tested the cells for TGF-beta 1 receptors. None was found.

"Loss of TGF-beta 1 receptors, which is a rare event even among tumor cells, may represent one mechanism through which these cells escape from negative control and form retinoblastoma," the researchers report.

Scientists discovered years ago that retinoblastoma involves the failure of a particular gene, the RB gene, to function properly. Little is known about the protein normally coded for by the RB gene, although it is believed to act directly on DNA. It is possible, the new report concludes, that the RB protein might directly affect the expression of TGF-beta 1 receptors. Alternatively, it might interact with the receptors in a way that affects receptor structure and function, allowing cell proliferation and tumor formation.

"Right now we can't really draw a link," says Sela Cheifetz, a Whitehead Institute researcher and coauthor of the report. "The apparent lack of TGF-beta receptors may not be the direct cause of these cells being tumorogenic, but rather might be a consequence." More research needs to be done, she says, to find out exactly what the RB gene product is and its role in cell growth.

AIDS: Envelope research update

Two published reports dealing with the structure and function of the AIDS virus, a retrovirus known as HIV, are providing some hope — and some cautions — about the possibility of stemming the virus' infectivity.

Researchers at Stanford University Medical Center report in the April 8 CELL that they have inhibited HIV infection in cultured cells by making a minor rearrangement of the HIV envelope protein. The envelope protein, called gp160, is normally cleaved into two pieces during viral replication inside white blood cells. Only after the protein is cleaved into gp120 and gp41 components is the AIDS virus able to bind to and infect other white blood cells. Under the direction of Joseph M. McCune, the Stanford researchers made a specific mutation in the gp160 protein. In doing so, they prevented enzymatic splitting of the protein into its component pieces, rendering the virus biologically inactive.

The research supports the notion that a drug capable of blocking enzymatic splitting of gp160 inside a cell might inhibit HIV's infectivity. Along similar lines, the researchers note, custom-designed antibodies directed against gp41 or gp120 *after* enzymatic splitting might also prove effective, since those pieces appear critical to infectivity. Previous research on other retroviruses had suggested such approaches to blocking infectivity might work, but the work had not been done on HIV.

Other research, however, appearing in the April 9 LANCET, strikes a cautionary note for scientists who are developing such antibodies or are developing vaccines that would stimulate the production of such antibodies. Researchers at Vanderbilt University School of Medicine report they have partially characterized two components in HIV-positive blood serum — one of them apparently an HIV-induced antibody — that together enhance rather than deter infection by the HIV virus. The researchers reported preliminary evidence of one such factor last year.

In the latest research, the scientists describe the presence of a suspected immunoglobulin that they believe is an antibody to some part of the HIV virus, and a second factor they say is likely to be complement—a biological compound that often interacts with antibodies to destroy cells. Together, they hypothesize, these two factors might work to enhance HIV infection.

It is still not clear which part of the AIDS virus might stimulate the production of such an infection-enhancing antibody, they say, adding that vaccine developers will have to be careful to choose parts of the AIDS virus that will stimulate production of protective antibodies exclusively.

They conclude that if part of the AIDS virus "can be correlated with the induction of antibodies that together with complement enhance HIV-1 infection, then candidate vaccines should obviously be devoid of such antigenic stimuli. Those vaccines already being tested should be evaluated for their ability to stimulate infection-enhancing antibody formation."

Botulism: More than a passing fancy

A recent report suggests there may be more long-term problems associated with botulism than scientists have assumed. Researchers led by Felissa L. Cohen of the University of Illinois at Chicago looked at the long-term effects of botulism in 28 persons who became ill after eating sauteed onions in congealed margarine. She found that although "the patient may appear to be fully recovered after a period of time . . . 50 percent of the patients became easily fatigued three years after contracting botulism." Other long-term effects included muscle weakness, headache and blurred vision.

Botulism is an acute bacterial poisoning often associated with home-canned foods, but increasingly traced to restaurants.

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