Biology

Elizabeth Pennisi reports from Miami at the annual meeting of the Society for Neuroscience

Gene therapy for brain diseases

A simple surgical procedure involving genetically altered cells may someday halt disintegration of the brain caused by any number of diseases. Such a procedure remains at least a decade away. But tests in animals that show symptoms of human disorders indicate that innovative uses of gene therapy can reverse or prevent the development of these symptoms, several research teams report.

Sometimes, gene therapy involves altering cells from the individual needing treatment. Other times, it makes use of genetically modified cells from other organisms. Either way, it promises to deliver protective or restorative substances to specific parts of the brain, says Allan J. Tobin of the University of California, Los Angeles.

"What you have in situ is a little drug factory," he explains.

For example, the dementia that characterizes people with Alzheimer's disease seems to occur because nerve cells in a part of the brain essential to memory die off. Researchers have injected Alzheimer's patients with human nerve growth factor, a substance that can prevent cell death, but it caused unwanted nerve development and did not seem to help much.

Supplying nerve growth factor locally seems more promising, says Mark H. Tuszynski of the University of California, San Diego. His team removed skin cells from seven monkeys whose brains had been damaged in such a way that they would lose nerve cells similar to those lost in Alzheimer's disease. The researchers grew the skin cells in the laboratory and modified them to produce large amounts of nerve growth factor. When placed in the decaying part of the monkeys' brains, these skin grafts generally reduced cell loss by 75 percent and sometimes by more than 90 percent, depending on the placement of the graft, Tuszynski reports.

Dwaine F. Emerich of CytoTherapeutics, a biotechnology firm in Providence, R.I., also aims to deliver nerve growth factor locally. He and his coworkers package genetically altered skin cells from baby hamsters in thin polymer capsules. Once in the brain, the walls of the capsules allow nerve growth factor to ooze out and nutrients to seep in, but they keep the immune system from attacking these cells, Emerich explains. Tests of the capsules in seven young and six old monkeys yielded results similar to those seen with skin grafts, he reports.

A third team is developing the skin-graft approach to fight Parkinson's disease, a neuromuscular disorder involving deficits in the brain messenger dopamine. In this case, the skin cells produce extra amounts of the enzyme that helps make dopamine, says Krzysztof S. Bankiewicz of Somatix Therapy Corp., a biotech company based in Alameda, Calif. His group has tested these grafts in monkeys with chemically induced symptoms of Parkinson's on one side of their bodies. "The clinical improvement is very rapid," he says.

At Yale University School of Medicine, Matthew J. During is developing a more direct gene therapy for Parkinson's. His team has modified the harmless adeno-associated virus to carry the genes for two enzymes critical to dopamine production. In green monkeys, the modified virus can infect brain tissue and within 10 days cause an increase in the brain's output of at least one of these enzymes, he says.

No one knows whether these therapies will pan out, but their implications are far-reaching, the researchers suggest. Before tests in people can begin, scientists need to make drug delivery more consistent. Nevertheless, "the potential of this technology [gene therapy] extends not only to these two diseases, but also beyond that to reprogramming individual types of cells in the brain," Tobin says. "That's something the whole neuroscience community is excited about."

Environment

Food bags: Which plastic protects best?

Each year, pesticide applicators fumigate some 200,000 U.S. buildings — many of them residences — to kill termites, wood-boring beetles, and other particularly tenacious household pests. Whenever they use one of two especially effective agents — the respiratory irritant sulfuryl fluoride or the neurotoxic methyl bromide — fumigators instruct their customers to either remove all foods or wrap them in two layers of plastic. A new study now argues compellingly for using nylon rather than polyethylene, until recently the plastic of choice, for any bagging.

Researchers at the University of Florida in Gainesville double-bagged a number of common household foods — from milk, ground beef, and dry dog food to cooking oil, lettuce, and dry cereal — in either nylon or polyethylene. They refrigerated perishables and stored the other items on shelves during the subsequent 20-hour fumigation with various concentrations of sulfuryl fluoride or one concentration of methyl bromide.

In the October JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, Rudolf H. Scheffrahn and his coworkers report that bags made from thin nylon-polymer film effectively shut out the sulfuryl fluoride except occasionally, at the highest test concentration — one considerably above any that should occur with a properly administered fumigation. Polyethylene proved less protective, often permitting 2 to 10 times more of the gas to taint foods.

In contrast, neither plastic offered a foolproof barrier to methyl bromide, though nylon was more effective. Indeed, polyethylene allowed up to 900 times more of this fumigant to reach the bagged contents. However, Scheffrahn points out, "these findings are almost moot," as methyl bromide will be phased out over the next 6 years as a fumigant.

If your larder was one of the millions exposed to pesticides in the past without the protection of nylon bags, don't assume your family ingested high quantities of even the methyl bromide, Scheffrahn says. Both fumigants typically volatilize out of foods within a day or so. And where does one get nylon bags? Responsible fumigators should provide them or suggest where to buy them, says Scheffrahn.

Bioengineering regulations go public

Insert a virus fragment into a squash and, like humans given a vaccine, the squash will develop an immunity to the viral disease that would normally destroy it. Some people call this a dream come true, with the promise of high yields and reduced use of chemical pesticides. Others say it's a nightmare — that such genetic engineering may wreak ecological havoc and unleash unknown forces in nature.

Now, the Environmental Protection Agency has weighed in with proposed new regulations for plants genetically modified to resist pests and disease. EPA calls the resulting pesticides, along with the genetic material used to produce them, plant-pesticides. The agency published its recommended regulations in the Nov. 21 FEDERAL REGISTER.

Several plant-pesticides have reached the testing phase already. One of the most common takes genetic material from the bacterium *Bacillus thuringiensis,* or B.t. This material produces a compound known as a delta endotoxin, which kills certain types of insects but doesn't harm humans. By inserting B.t. genes into plants such as corn, researchers have enabled these crops to make their own delta endotoxin.

Despite the proposed regulations, a number of concerns remain. "We think it's appropriate that the EPA develop policies to oversee these transgenic plants," says plant pathologist Jane F. Rissler of the Union of Concerned Scientists in Washington, D.C. However, she adds, the proposed regulations exempt certain types of genetically engineered plants for which there are "unresolved risk issues."