Presentable oral vaccines

By introducing a bacterial protein transport system into an orally delivered vaccine, a team of researchers has managed to coax the immune system into producing a different type of response. Attenuated strains of *Salmonella* are considered attractive vaccine delivery vehicles, but their inability to elicit a major histocompatiblility complex (MHC) class I-restricted immune response—the most effective response against many intracellular pathogens—has been a serious drawback. In a paper in *Science* (**281**:565–568, 1998), scientists at the State University of New York at Stony Brook and the University of Nebraska-Lincoln have fused genes for antigens to a bacterial gene that encodes a secreted protein. The fusion protein is secreted from the bacteria inside cells, processed by the MHC, and efficiently presented on the cell surface. Using an oral vaccine based on this approach, the scientists were able to elicit a class I response that completely protected mice from infection with murine lymphocytic choriomeningitis virus. "We have ways of manipulating the system so that the epitopes of the particular protein that *Salmonella* is delivering can be [channeled] into a class II or a class I system, so we can use this very same approach to stimulate both types of responses," explains Jorge Galan, an author on the study.

Synthetic secretory granules

A technology modeled from nature could one day be exploited as a drug delivery system. Researchers at Duke University (Durham, NC), Access Pharmaceuticals (Dallas, TX) and The Glynn Wilson Group (Issaquah, WA) have coated a microgel with a stable lipid layer to form microbeads that mimic the secretory granules found in granulocytes (*Nature* **394**:459–462, 1998). Using existing technology, they synthesized beads of polymethacrylic acid that had a swollen diameter of 6.5 μm at neutral pH. They then loaded the beads with the anticancer drug doxorubicin, condensed them by lowering the pH, and added a lipid bilayer coating. In vitro experiments demonstrated that the lipid coating remained intact, preventing diffusion of the drug, when the beads were suspended in saline for several days at neutral pH. In addition, rapid and controlled release of the drug could be accomplished by applying an electric pulse that ruptured the lipid coating. According to the authors, beads could also be engineered to respond to other types of external stimuli (e.g., ultrasound, illumination at a particular wavelength, or temperature). The approach promises a 10–100-fold higher drug capacity than liposomes or protein microspheres.

Fetal cell transplants for Parkinson's

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

Courtesy L. Studer et al.

Recent research at the National Institutes of Health (NIH; Bethesda, MD) and the University of Massachusetts (Worcester, MA) may eventually make a promising, but controversial, treatment for Parkinson's disease—transplantation of neuronal tissue from aborted fetuses into patients—more widely available. In the new work, reported in *Nature Neuroscience* (**1**:290–295, 1998), researchers obtained stem cells from the brains of fetal rats and cultured them in a medium containing basic fibroblast growth factor (bFGF), causing the cells to multiply and form clusters. When the bFGF was removed, the cells differentiated into different types of neurons, including some clusters of the dopaminergic neurons (left panel) that are lost in Parkinson's disease. When these cells were injected into the brains of a rat model of the disease (right panel), the animals showed substantial recovery. In addition to reducing the need for fetal tissue, growing explanted cells in culture may be useful for treating conditions other than Parkinson's. "The problem with brain grafting is not really putting something precisely into someone's head, it's knowing what to put there. This [result] suggests that you can get all kinds of neurons in rather large numbers," explains Ron D.G. McKay, a senior author on the study. McKay adds that the approach could be further refined by introducing new genes into the cells before implanting them.

Promiscuous pollination

Fears that cross-pollination between transgenic cultivated plants and their wild relatives could result in "superweeds" have been reignited by research reported at a recent meeting. Such hybrids were thought to have lower reproductive fitness than wild-type weeds, minimizing the danger of horizontal gene transfer. But at the annual meeting of the Ecological Society of America (Baltimore, MD, August 6), researchers at Ohio State University (OSU; Columbus) have presented data showing that at least some hybrid weeds can reproduce normally. When the OSU scientists crossed herbicide-resistant rapeseed, which is used to make canola oil, with a related wild plant, the progeny not only were herbicide resistant, but also produced the same number of seeds as their weedy parents, suggesting comparable fitness. Similar experiments are underway with squash and sunflower plants and their wild relatives. While acknowledging that relatively few weeds can breed with cultivated plants in the field, Lawrence Spencer, who co-presented the work, recommends caution: "I would err on the side of not releasing new transgenic plants until you test the possibilities," he warns. New techniques, such as inserting transgenes into chloroplasts to limit their transfer in pollen, may also help to keep resistance genes down on the farm.

Caspase knockout

New results published in *Cell* (**94**:1–20, 1998) provide insights into a neuronal cell death pathway that might lead to drugs that specifically target neurological disease. Scientists at Yale University Medical School (New Haven, CT), Tokyo Metropolitan Institute of Medical Science (Tokyo), and Vertex Pharmaceuticals (Cambridge, MA) have generated a knockout mouse that lacks caspase 9, an aspartate-specific protease that mediates apoptosis (the process by which cells are programmed to degenerate and die). Many of the knockout animals were found to die perinatally, with severe malformation of the brain due to a reduction of apoptosis in the proliferative neuroepithelium. "This finding not only constitutes the first demonstration for an essential role of caspase 9 in vivo, but it also takes us a long way to establishing links between particular caspases and specific tissue damage," says Vicki Sato, Vertex CSO and senior vice president of research and development. Caspase 9 is a key activator of cell death pathways induced by cytochrome c from damaged mitochondria and the knockouts should aid in delineation of the caspase cascades activated by different stimuli. "The research has opened a wide opportunity for therapeutic intervention," claims Soto. "The results suggest that it would be possible to design a therapeutic approach targeting neuronal death linked to neurological diseases without general adverse effects."

Research News Briefs written by Alan Dove, Andrew Marshall, and Regina Raz.