Biomedicine

Pitting viruses against each other

Set a thief to catch a thief. Scientists trying to combat HIV have taken that message to heart and created novel viruses that infect only cells the AIDS virus has already broken into.

The new work stems largely from the recent understanding of how HIV enters immune cells. In the key event, two proteins on HIV's surface, gp120 and gp41, bind to two specific proteins on the surface of immune cells. Once inside the cells, HIV starts reproducing, in the process placing many copies of gp120 and gp41 on the surface of the infected cell.

Armed with this knowledge, investigators wondered how a virus displaying the immune cell proteins that bind to gp120 and gp41 would behave. A group led by Karl-Klaus Conzelmann of the Federal Research Center for Virus Diseases of Animals in Tübingen, Germany, created a virus covered with such proteins and found that it would infect only cells in which HIV had taken up residence and was producing gp120 and gp41. The virus, which cannot reproduce, could deliver therapeutic genes or proteins to HIV-infected cells, the investigators suggest in the Sept. 5 CELL.

A second group, led by John K. Rose of Yale University School of Medicine, added the genes for the two normal immune cell surface proteins to a different virus. This enabled the virus to enter the HIV-infected cells and reproduce inside them, killing them. In test-tube experiments on cells infected with HIV, also described in the Sept. 5 CELL, the investigators found that the new virus dramatically reduced HIV production.

"The research boldly demonstrates that it is now possible to reverse the aim of the biochemical grappling hooks HIV uses to enter cells and to employ them against the virus," Garry P. Nolan of Stanford University School of Medicine writes in a commentary for CELL.

Nolan cautions against any immediate plans for using such altered viruses to treat people infected with HIV, citing concern that the viruses might spread to and harm uninfected people. "Any use of a self-replicating 'drug' . . . should go to the highest levels of ethical and medical reviews," writes Nolan. As a safer alternative, researchers might endow nonviral systems, such as the fatty spheres called liposomes, with the same ability to target HIV-infected cells, he suggests. —*J.T.*

Parkinson's protein in brain clumps

The mystery of Parkinson's disease, in which brain cells that produce the neurotransmitter dopamine gradually die, may be nearing a resolution. In June, scientists reported that some inherited cases of the disease result from mutations in the gene that encodes a protein called alpha-synuclein (SN: 6/28/97, p. 396).

The investigators speculated that alpha-synuclein aggregates to form the so-called Lewy bodies, mysterious clumps that invariably show up in the brain cells of people with Parkinson's. Studies using antibodies that highlight the protein show that this is indeed the case, Maria Grazia Spillantini of the University of Cambridge in England and her colleagues report in the Aug. 28 NATURE.

Instead of examining people who had inherited the brain disorder, the researchers scrutinized Lewy bodies from Parkinson's patients who did not have a mutation in the alpha-synuclein gene. Such people make up the majority of Parkinson's patients. The discovery of normal alpha-synuclein in their Lewy bodies suggests that other genes, or some unknown environmental factors, induce the protein to aggregate. The scientists also report that alpha-synuclein exists in the Lewy bodies characteristic of another brain disorder, a type of dementia. While they have not yet proven that Lewy bodies kill brain cells, scientists are already exploring ways to prevent alpha-synuclein aggregation. —*J.T.*

Environment

Lacing food with an estrogen mimic

Bisphenol A, a building block of polycarbonate plastics, can mimic the effects of the body's natural estrogens (SN: 7/3/93, p. 12). In tests meant to simulate the use and cleaning of plastic food ware, a Food and Drug Administration study now shows that bisphenol A (BPA) can leach into liquids.

This raises public health concerns because a variety of estrogen mimics can alter the development of animals (SN: 1/8/94, p. 24)—and perhaps people (SN: 1/22/94, p. 56).

Polycarbonates are made by joining BPA molecules into long chains. Not every molecule gets linked, however, leaving some BPA free to migrate from the finished product. John E. Biles and his coworkers at FDA in Washington, D.C., found that polycarbonate baby bottles and juice cups contained from 7.4 to 46.7 micrograms of unbound BPA per gram of plastic.

Heating tests that simulated stove-top sterilization triggered the bottles to release 5 percent of the unbound BPA into a mixture of alcohol and water designed to mimic the baby formula and fatty foods that might be stored in polycarbonate containers. Repeated treatments released smaller amounts. In exaggerated conditions—where the plastic was bathed at a lower temperature, about 150°F, for 10 days in a solution of 50 percent alcohol in water—"migration as high as 368 percent of the original residue level of BPA [31.5 micrograms per gram of plastic] . . . was observed," FDA chemists report in the September JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY. The latter, very high numbers "strongly suggest there is hydrolysis," a breakdown of some of the plastic, freeing up more BPA, says Biles.

In a less extreme experiment, distilled water was held in large polycarbonate containers for 39 weeks at room temperature. Some BPA migrated, eventually contaminating the water at concentrations of almost 5 parts per billion.

Though others have observed qualitatively that BPA can leach from plastic, "these numbers are more quantitative than what had been reported," says Ana Soto of Tufts University School of Medicine in Boston. "This demonstrates that we can measure BPA and should, to determine how much people—especially children—can be exposed to [in foods]." —*J.R.*

A pollutant that can alter growth

Fetuses are particularly vulnerable to the effects of hormones. To tease out the potential consequences of prenatal exposure to bisphenol A (BPA), Frederick S. vom Saal and his colleagues at the University of Missouri in Columbia fed pregnant mice on days 11 to 17 of gestation with food containing BPA at concentrations equivalent to 2 parts per billion of the rodents' body weight. The dose was meant to represent an amount that people could be exposed to from all sources, including dental sealants (SN: 4/6/96, p. 214) and foods in plastic-lined cans (SN: 6/3/95, p. 341). At birth, all of the offspring were transferred for nursing to foster moms—females that had not been treated with the estrogen-mimicking pollutant.

The brief, early exposure had lasting effects. Compared to mice from untreated mothers, offspring exposed to BPA were 10.6 percent bigger at weaning and entered puberty 2 days earlier. Vom Saal's group presented portions of the study in July at a federally sponsored Estrogens in the Environment conference in Arlington, Va.

In a related study, vom Saal's team now finds that comparable exposure to BPA during the same period of gestation alters slightly the development of testes and accessory male reproductive organs in mice.

"The jury's still out on what this means for humans," vom Saal says. However, he notes, there have been reports that high concentrations of other estrogen-mimicking pollutants alter children's stature, behavior, and intellectual development (SN: 11/11/95, p. 310). —*J.R.*