Biomedicine

Poison-packed LDLs: Cancer weapons?

All cells need cholesterol to make new membrane, and cancer cells, which are rapidly dividing, need more of the compound than others. In their search for ways to kill cancer cells without harming healthy tissue, several research teams have begun to explore the ways cells respond to LDLs (low-density lipoproteins), the body's cholesterol delivery vehicles.

Most laymen know LDLs for the troublemaking role they can play in fostering disease of the heart and blood vessels (SN: 7/21/84, p 38). But Raymond A. Firestone and co-workers at Merck Sharp and Dohme Research Laboratories in Rahway, N.J., are more interested in the ways LDLs might serve as poison-packed Trojan horses that could selectively invade cancer cells and kill them. Their most recent work, with colleagues at the Massachusetts Institute of Technology and the University of Texas Health Science Center in Dallas, is published in the August Journal of Medicinal Chemistry and suggests that, despite a few roadblocks, such an approach may prove useful.

The normal LDL molecule consists of a core of modified cholesterol chains in a phospholipid coat. MIT's Monty Krieger has been working on the best ways to unzip the coat, replace the core with a new material, then rezip the coat, making sure that the "seams" are sealed so that none of the new toxic core leaks out before the LDL gets inside the cell.

Firestone has focused on the core itself, as he tries to develop potent poisons that can easily be anchored inside the LDL. The most promising compound so far, he says, is a modified nitrogen mustard, which has the added benefit of being most toxic to rapidly dividing cells. Presumably, he says, doses of the compound could be devised that would spare the healthy cells of organs like the adrenal gland, which divide more slowly. (The adrenal gland is a special concern in such an approach because it uses a great deal of cholesterol in its manufacture of hormones, and relies heavily on LDLs.)

All of their work thus far has been performed in cultured cells, rather than in whole animals, Firestone stresses, so it is much too soon to predict how safe or effective such an anti-cancer treatment might be in humans, or which types of cancer would be best suited to the approach. While some types of cells are known to rely heavily on LDLs for a supply of fully assembled cholesterol, other cells can make their own. Most types of cancer have yet to be surveyed in this regard, he says.

First chimps infected with AIDS virus

Giving an animal AIDS, the immune system scourge that has struck more than 5,500 human victims to date, has proven almost as difficult as slipping a camel through the eye of a needle. Marmosets, rhesus monkeys and chimpanzees have all been inoculated with blood cells or serum containing viruses thought to cause the disease, but none—until now—has shown signs of ill health, although a similar disease has spontaneously infected two colonies of rhesus monkeys (SN: 3/15/83, p. 151). However, two recent studies hint that at least four chimps may be developing the first stages of the human disease—the most promising news yet for those seeking an animal model.

In one Centers for Disease Control study conducted at Yerkes Regional Primate Center in Atlanta, researchers have, for the first time, detected the virus LAV in samples of white blood cells from infected chimps. Though the animals still have no clinical symptoms, they have begun to show the dip in immune cells that is associated with AIDS in humans.

In a separate study, National Institutes of Health researchers have found evidence of infection with the virus HTLV-III in two chimps. One has developed the severely enlarged lymph nodes that are an AIDS trademark. HTLV-III and LAV have been strongly linked to AIDS, and are thought by most researchers to be different names for the same virus.

Technology

EMP: Guaging strategic vulnerability

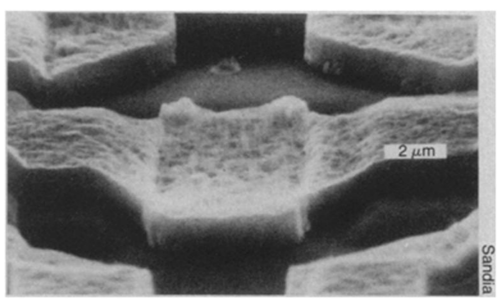
In response to a Defense Department request, the National Academy of Sciences' research council reviewed current techniques for estimating the vulnerability of strategic systems — such as communications- and electric-power networks, aircraft electronics and missile-guidance circuitry — to crippling by electromagnetic pulses (EMPs). This devastating electronic fallout is showered by high-altitude nuclear detonations (SN: 5/9/81, p. 300). The Academy's 111-page report, issued last week, concludes that shielding entire subsystems vulnerable to EMP-induced burnout — essentially boxing them in metal screens known as Faraday cages — is preferable to "hardening" (or strengthening) the subsystems' most vulnerable individual components. In particular, the report says, statistical techniques necessary for tackling the latter approach—known as "tailored hardening" — are not only deceptively difficult, but also very poorly understood by the defense-electronics community.

Amorphous switch for EMP surges

One way to protect electronic systems that contain components vulnerable to EMP is to precede them in the circuit path with the equivalent of a fast-acting, automatically resetting circuit breaker. Such a device would have to respond in less than 1 nanosecond (ns) — a billionth of a second — and recover, or reset, within 100 ns. And according to Mike Sheldrick of Energy Conversion Devices (ECD) in Troy, Mich., the company's "Ovonic threshold device" should do the trick.

ECD is best known for its pioneering work on high-efficiency, low-cost photovoltaic cells (SN: 12/9/78, p. 406). Among the amorphous (randomly structured) materials it explored early on was a class known as chalcogenide glasses. The firm's new threshold switch is also a chalcogenide device. Sheldrick says it's able to switch a circuit (to ground) in response to a threshold that can be tailored to as low as 2 volts. And for a current density of 20,000 amperes per square centimeter, he says a device with a radius of less than 2 millimeters could sustain 2,000 amps. Scaling to larger sizes would permit survival of correspondingly larger currents. In addition to offering protection against EMP, the device might be used to protect the extensive electronic circuitry within today's automobiles and computers from burnout initiated by lightning-induced voltage surges.

A hard row to etch



By refining and carefully controlling the process of plasma etching, researchers at the Sandia National Laboratories in Albuquerque, N.M., can now produce extremely narrow, sharp-edged aluminum lines on the surface of a silicon wafer. The resulting electronic devices prove to be very reliable and resistant to large radiation doses, say the researchers. In plasma etching, a mixture of the gases boron trichloride and chlorine is pumped into a reaction chamber. Radio waves ionize the gas, turning it into a plasma. These ions bombard the unprotected parts of a thin aluminum film coating a silicon wafer and react with the aluminum to form aluminum trichloride, which subsequently evaporates from the wafer. Although plasma etching itself involves ionizing radiation, Sandia researchers report little radiation damage during the fabrication of "radiation-hardened" integrated circuits using this technique.