Biomedicine

Fusion factor in AIDS cells identified

Researchers report identifying a molecule on the surface of white blood cells that helps AIDS-infected cells fuse with — and pass their infection to — uninfected cells. The work helps explain how the AIDS-causing virus, HIV, spreads from cell to cell in infected individuals. Clinical applications remain speculative, but researchers say the new information may prove helpful as physicians experiment with novel means of controlling AIDS progression in HIV-infected individuals.

Scientists know that HIV-infected cells can bind to and then fuse with other cells, thus allowing an exchange of viral contents. They refer to the process of cell fusion as syncytium formation. In AIDS patients, cell-cell binding is mediated in part by a viral protein, gp120, which HIV-infected cells feature on their outer membranes. This binds to a receptor called CD4 on uninfected cells, providing cell attachment — the first step in syncytium formation.

James E. K. Hildreth and Rimas J. Orentas of Johns Hopkins University School of Medicine in Baltimore knew from other work that cells often use a molecule called LFA-1 to stabilize interactions mediated by cell-surface receptors. They report in the June 2 SCIENCE that LFA-1 plays a similar, critical role in the fusion of cellular membranes that follows cell attachment between HIV-infected and uninfected cells. When the scientists blocked the action of LFA-1 with antibodies, they prevented fusion of HIV-infected, cultured human cells.

Clinicians probably can't provide AIDS patients with large quantities of LFA-1 antibodies, because antibodies would block both useful and harmful actions of the multipurpose LFA-1 molecules. "You'd screw up too many things," says Richard O. Hynes of the Massachusetts Institute of Technology in Cambridge. However, he and Hildreth say, a limited course of LFA-1 antibodies may prove useful in AIDS patients undergoing an experimental therapy involving bone marrow transplants. While it's too early to tell, they say the antibodies may someday become part of a broader effort to keep new blood cells from becoming infected by residual, infected cells in the body.

Scientists see new hope for old drug

A "sleeper" drug, long available in the United States but rarely called upon, has emerged as a promising anti-cancer drug. Scientists developed suramin in the 1920s as a treatment for African sleeping sickness. But researchers at the National Cancer Institute (NCI) in Bethesda, Md., report it shrank tumors by more than 50 percent in four of eight patients with advanced prostate cancer unresponsive to normal therapy.

While the numbers are small, researchers express optimism — in part because of the drug's mechanism of action. Suramin blocks a hormone called fibroblast growth factor, which prostate tumors make in large quantities and which stimulates further tumor growth. The drug "breaks the loop that tumors use to promote their own growth," explained NCI's Charles E. Myers at the annual meeting of the American Society of Clinical Oncology in San Francisco last month. "We believe the drug is the first of a class of growth-factor-inhibiting drugs."

Myers says pharmaceutical companies have begun testing chemical relatives of suramin that may prove as effective against cancer but less toxic to healthy cells. The drug kills nerve cells at high doses, and clinicians must closely monitor blood levels of the compound in patients receiving it.

Veterinarians first used suramin in 1916 to treat sleeping sickness in African cattle. Scientists tested it in humans in 1926. Today it is available through the Centers for Disease Control as an "orphan drug," one rarely used in the United States.

Prostate cancer is the most common cancer among U.S. men and the second leading cause of U.S. cancer deaths after lung cancer.

Chemistry

Giving neurotransmitters a second wind

While some medical scientists strive to find a cure for mentally debilitating diseases, others hope to find chemical compounds for fighting the symptoms. Called "nootropic agents," these compounds counter the neurochemical abnormalities that underlie learning and memory losses linked to ailments such as Alzheimer's disease. One promising compound — huperzine A — comes from a club moss species indigenous to China and known for centuries to Chinese herbalists, says chemist and neuroscientist Alan P. Kozikowski of the University of Pittsburgh.

In the May 24 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, he and co-worker Yan Xia (now at the National Institute on Aging) describe a short and practical laboratory procedure for synthesizing huperzine A. Animal studies in China, Switzerland and the United States have shown the club moss chemical improves animals' performance in tasks that involve memory. Kozikowski notes Chinese researchers have reported evidence the compound improves the memory of elderly people suffering memory problems. Presently, it takes a ton of the club moss to yield small fractions of a gram of huperzine A. Kozikowski says his 12-step laboratory synthesis (and perhaps another similar procedure just published by Chinese researchers) can produce gram amounts of the chemical, enough to begin clinical testing.

Huperzine A works by blocking acetylcholinesterase, an enzyme that breaks down the neurotransmitter acetylcholine after it has passed neural information from one neuron to another or to muscle fibers. Alzheimer's disease slowly wrecks the machinery for making acetylcholine in some areas of the brain. By blocking the natural destruction of the neurotransmitter, huperzine A and other less active, but similarly acting, nootropic agents empower the lower amounts of acetylcholine in diseased brains to work overtime, Kozikowski told SCIENCE NEWS. With funding from a Pennsylvania program, he has started a company to scale up synthesis of huperzine A and other nootropic agents.

Soaking up the rays to make fuel

Using natural photosynthesis as a model, scientists have constructed a device that harnesses solar energy for liberating the hydrogen bound in sea water.

In the chloroplasts of green plant cells, thin pigment-studded membranes harvest sunlight, which incites some negatively charged electrons to travel to one side of the membrane, leaving regions of positive charge near the other. The separated charges then participate in different chemical reactions — the building of carbon dioxide into energy-rich compounds such as glucose or the breaking apart of water into molecular oxygen and hydrogen. The hydrogen then participates in other reactions in independent watery compartments flanking the membrane.

In the May PHOTOCHEMISTRY AND PHOTOBIOLOGY, biophysicist H. Ti Tien of Michigan State University in East Lansing describes a device using features of photosynthetic membranes. In place of the biological membrane, Tien uses a light-absorbing septum made of a thin film of the semiconductor cadmium selenide painted on nickel foil. When excited enough by light, electrons in the semiconductor travel into the nickel where they break sea water into hydroxyl ions and hydrogen, which many chemists envision as a widely used fuel in the future. On the semiconductor side of the septum, electrons from iron-containing compounds dissolved in the sea water flow into the semiconductor to complete the circuit.

Given the limited supplies of fossil fuels and the environmental problems of nuclear power, Tien says, "Sooner or later, we will have to rely on solar energy."