Biomedicine

Abortion pill may battle brain tumors

The controversy surrounding RU486 (mifepristone) centers on its use as an abortion-inducing drug. Early safety testing suggests that this so-called abortion pill may have another use, this time as a treatment for a type of brain tumor.

Researchers led by Steven M. Grunberg, an oncologist at the University of Southern California School of Medicine in Los Angeles, recruited 19 women and nine men suffering from meningioma, a slow-growing, noncancerous tumor. Treatment typically consists of surgery to remove the tumor, which affects the tissue lining the brain and spinal cord. But in some cases, surgery is too risky. In such cases, the tumor continues to grow and can cause blindness, paralysis, and seizures. All 28 people in the study had inoperable tumors.

Cancer specialists have observed that meningiomas occur more frequently in women than in men. Symptoms of these tumors often worsen during pregnancy, when a woman's body produces increased amounts of the sex hormone progesterone. Indeed, meningioma cells often contain progesterone receptors, Grunberg says. Men also produce progesterone.

These observations have led researchers to hypothesize that progesterone fuels the growth of such tumors. Grunberg's team wondered whether mifepristone, which blocks progesterone receptors, would slow the tumor's progress. To test that theory, they gave each of the 28 patients low-dose mifepristone daily for approximately a year.

It's too early to tell whether mifepristone will prove an effective tumor fighter, but initial results are encouraging. At the American Cancer Society's (ACS) 35th Science Writers Seminar, held in San Diego last month, Grunberg reported that eight of the 28 people benefited from the treatment. In six of these patients, the tumors shrank slightly during the trial. A seventh patient, who was nearly blind in one eye, reported dramatic vision improvement in that eye after treatment with mifepristone, Grunberg says, and another had less dramatic vision improvement.

So far, side effects associated with the drug include fatigue, hot flushes, some thinning of the hair, and a rash.

The team has already launched a larger study, comparing mifepristone to a placebo pill in a double-blind, randomized trial of 200 people with meningioma.

Anticancer drug targets calcium

A novel drug treatment seems to reduce tumor growth and may also dampen cancer's ability to spread to distant parts of the body, according to researchers at the National Cancer Institute (NCI) in Bethesda, Md.

Conventional anticancer drugs work by killing dividing cells. But chemotherapy doesn't always prevent a few malignant cells from breaking away from the primary tumor and getting into the bloodstream. These cells can travel to distant parts of the body, where they take root and create another cancer, a process called metastasis.

The steps in that deadly process involve calcium. Thus, Elise C. Kohn and her colleagues at NCI hypothesized that a drug that prevents cells from taking in calcium might help to prevent the growth and spread of tumors.

The NCI team developed an experimental drug called carboxyamido-triazole, or CAI. Preliminary results from a pilot trial of CAI appear promising, says Kohn, who described those findings last month at the ACS Science Writers Seminar.

She and her co-workers gave CAI to 13 people with a variety of advanced cancers. Eleven of the 13 patients showed no increase in tumor size during treatment, Kohn says. The researchers hope that CAI and other drugs like it may usher in a new era in cancer treatment—one in which physicians approach cancer as a chronic disease.

Chemistry

Karen F. Schmidt reports from Denver at the American Chemical Society meeting

New way to embed proteins in polymers

The age of plastics arrived decades ago, when chemists learned to string together chemical units, called monomers, to make polymers. Today, scientists endow these materials with biological talents — for use primarily in chemical separation and sensing devices — by attaching proteins to them.

A new technique for building proteins directly into polymers now promises to expand the variety of biologically active materials that can be synthesized. Researchers might one day use the method to make an artificial heart from materials containing an enzyme that prevents blood clotting, for example, or to develop a hormone-containing polymeric glue that encourages bone deposition while keeping artificial hips fixed in place.

"This strategy opens up whole new vistas for incorporating proteins into different materials," says Alan Russell, one of the chemical engineers who developed the method at the University of Pittsburgh.

Many of the most commonly used polymers — such as the acrylates used to make Plexiglas, contact lenses, and materials that can control the release of drugs — must be synthesized in organic solvents. Because proteins don't dissolve in these solvents, chemists who combine proteins with polymers have had to use polymers that can be made in water. The Pittsburgh team has now removed this limitation by finding a way to incorporate proteins into polymers that can be made in organic solvents.

Russell and co-worker Darrell Williams converted the enzyme subtilisin into a "biomonomer" that can link up with other monomers. As a first step, they attached a chemical group called polyethylene glycol to the enzyme. This made it soluble in organic solvents. Then they hooked this unit to a methyl methacrylate monomer. Working with several common organic solvents, they polymerized these biomonomers into a material that looks and feels just like polymethylmethacrylate but has subtilisin's catalytic ability. Because the enzyme is chemically bound to the material, it remains stable and can't be leached out. The team is now eager to try the technique with other enzymes and polymers.

Heat shapes handedness of enzyme products

Many organic molecules come in right- and left-handed mirror-image versions. Because one form may smell like mint and the other like caraway, or one act as a sedative and the other as a poison, chemists try to control which of these chemical isomers they make. Often, they accomplish this with the help of enzymes, which in the body prefer to catalyze chemical conversions of just one isomer.

Outside of cells, however, enzymes can pull some unexpected tricks. Robert S. Phillips of the University of Georgia in Athens has found that enzymes can flip their preferences from one isomer to the other. Furthermore, heat can sometimes boost an enzyme's selectivity.

"It was surprising to us that by increasing heat, which increases disorder, or entropy, you can actually get greater selectivity," Phillips says. As temperature increases, ordinary chemical reactions tend to generate equal proportions of the two isomers, producing so-called racemic mixtures.

Phillips studied secondary alcohol dehydrogenase, an enzyme taken from a bacterium. When the enzyme converted the substrate 2-butanone into 2-butanol at 15°C, it favored the left-handed form, which made up 55 percent of the product. At room temperature, the product became a racemic mixture. At 50°C, the balance shifted to 90 percent right-handed 2-butanol.

Phillips' message to drug and chemical manufacturers: "By changing the temperature, you might make an impractical reaction nearly practical."

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