Biomedicine

Carol Ezzell reports from Houston at the annual meeting of the American Association for Cancer Research

Stopping cancer cells in their tracks

Most cancer drugs work by killing tumor cells as they grow and divide. But cancer's lethality stems from the ability of malignant cells to break off from the initial tumor and spread to distant tissues, seeding new tumors. Scientists are now investigating a drug that works by halting the spreading cancer cells in their tracks.

The compound, called CAI, "constitutes a new approach to cancer therapy," asserts Lance A. Liotta, head of the pathology laboratory at the National Cancer Institute (NCI) in Bethesda, Md. He says his group expects to begin testing it in humans within the next six months.

Although CAI (carboxamide-amino-imidazole) was originally developed as an antifungal drug by the Merck Institute for Therapeutic Research, Liotta's team discovered that it also trips up traveling tumor cells.

Now, Liotta and Elise C. Kohn of NCI have uncovered the mechanism behind CAI's anticancer effect. Normally, the spread of cancer cells through the bloodstream is triggered by signals received from other cancer cells. Liotta reports that CAI shuts down this line of communication by blocking a chemical pathway involving arachidonic acid, a cell-membrane protein known to enable cells to receive signals from each other.

Last year, Kohn and Liotta found that CAI prevented malignant melanoma cells from moving around in a culture dish. They also showed that mice injected with human ovarian cancer cells and treated with CAI lived more than two times as long as mice receiving the cancer-cell injections but no CAI.

Liotta says cell-culture experiments by his group have shown that CAI acts against 20 different types of cancer. He adds that the compound offers several advantages over conventional cancer drugs: Patients can take it orally, a single dose stays in the bloodstream for as long as three days, and the treatment causes few side effects.

Homing in on a key lung cancer gene

After years of sleuthing, scientists have identified a gene they believe is responsible for up to half of all cases of lung cancer.

Collaborators from eight U.S. institutions have turned up evidence that the gene's absence leads to large-cell lung carcinoma, one of the most common forms of cancer in both sexes. The gene directs the production of PTP-gamma, a member of a family of enzymes called protein-tyrosine phosphatases. These PTP enzymes act as receptors on the outer membranes of cells, receiving and translating incoming messages that tell the cell when to stop dividing.

The gene "is a candidate for being involved in lung cancer, but we don't have proof at this point that it is definitely the gene which is involved," cautions study director Carlo M. Croce of the Fels Institute for Cancer Research and Molecular Biology at Temple University School of Medicine in Philadelphia.

The team found that one copy of the PTP-gamma gene was missing in half of the lung tissue samples taken from 10 patients with various types of lung cancer. In contrast, patients with unrelated diseases had two copies of the gene in their lung tissue.

The PTP-gamma gene resides on the short arm of chromosome 3, the researchers discovered. Previous studies have shown that pieces of chromosome 3 are missing in many lung cancer patients.

Croce and his colleagues are now working to isolate a complete copy of the gene – a challenging task because of the gene's large size. To confirm its role in lung cancer, they plan to splice the gene into cultured lung cancer cells. If it reverses the cells' cancerous traits, says Croce, this will prove that it is a so-called tumor-suppressor gene – a gene that keeps cells from multiplying uncontrollably and causing cancer.

Carol Ezzell reports from Houston at the annual meeting of the American Society of Clinical Oncology

Chemical tip-off to ovarian cancer

Ovarian cancer's high fatality rate stems in part from the difficulty of detecting the disease and monitoring its spread. Most physicians rely on time-consuming and expensive imaging techniques, such as CT scans, to find and track ovarian tumors. But a new blood test already in use in the Netherlands may soon improve their ability to follow the course of the disease.

M.E.L. van der Burg, an oncologist at the Daniel den Hoed Clinic in Rotterdam, reports that a blood serum protein called CA 125 is an effective indicator of the recurrence of ovarian cancer. In some cases, she says, the presence of CA 125 is a better tip-off of ovarian cancer's spread than are standard imaging techniques.

Most human tissues contain low levels of CA 125. The protein, whose normal function remains unknown, is also secreted by tumors of the ovaries, colon, cervix and breast, and shows up in elevated levels in blood samples from patients with these malignancies.

Van der Burg's team used CA 125 blood tests to detect the recurrence of ovarian tumors in 113 women over an average of seven years. The test proved accurate in 61 percent of the patients who suffered relapses during the study. Moreover, it detected these relapses an average of 4.5 months before imaging techniques revealed the new tumors, she reports. CT scans usually do not detect tumors until they have grown larger than 1 centimeter, she notes.

"I believe in it," says van der Burg, who now uses the CA 125 test to monitor relapses among all of her ovarian cancer patients. "I think it is an advance."

She adds, however, that the test has a false-positive rate of 4 percent, which means that 4 percent of patients who test positive do not in fact have the cancer. False-positive results, she says, can arise from noncancerous conditions such as endometriosis – a condition characterized by uterine cysts that spread throughout the abdominal cavity.

Genetic cause for some cervical cancers

Although studies have linked 80 percent of cervical cancer cases to infection with some types of human papilloma virus (HPV), physicians continue to see fast-growing cervical cancers in women who test negative for HPV infection. French scientists now suggest that a cancer-causing gene, or oncogene, may be to blame for some of these extremely aggressive cervical cancers.

Guy Riou of the Gustave Roussy Institute in Villejuif, working with researchers at the Institut Pasteur in Paris, studied 94 women treated for early-stage cervical cancer, some of whom progressed to advanced cervical cancer. The team found that women who were not infected with HPV – but who carried the c-*myc* oncogene – had a 33-fold higher risk of later developing advanced cancer than did women who were infected with HPV and did not carry the gene.

Riou says this suggests that very aggressive cervical cancers and slower-growing tumors may spring from different causes.

However, he says his group did not find the c-*myc* oncogene in all HPV-negative patients who developed fast-growing cancers. HPV-negative women who lacked the oncogene were still nine times more likely to develop advanced cervical cancer than were the HPV-positive women.

Riou says he hopes his group's results will help doctors identify women who are likely to develop aggressive cervical cancers so that these patients can get intensive therapy in the early stages of their disease. But before physicians can routinely use the presence of c-*myc* to spot individuals at high risk for advanced cervical cancer, he says, "we need to evaluate these findings in a larger number of patients."