

Cancer's genes and chemotherapy

Some cancer cells protect themselves from the chemotherapy drug methotrexate with high levels of a protein that detoxifies the drug; the cell makes these high protein levels with extra copies of the responsible gene (SN: 1/3/87, p.12). Researchers studying another type of resistance, in which a different protein disarms several other drugs, have now found that such "multidrug-resistant" cells also make extra protein, but not by producing extra genes.

Instead, the protein's gene becomes more productive, report Ira Pastan and Michael M. Gottesman of the National Cancer Institute (NCI) and their colleagues at NCI and at the University of California at Los Angeles. They have also discovered that the gene is active in certain normal cells. The findings, they say, may enable predetermination of tumor resistance.

Multidrug resistance is dependent on p-glycoprotein, a cell surface molecule that pumps a variety of chemotherapeutic drugs out of the cells. The researchers, who previously reported that such resistance can occur in the absence of gene amplification (production of extra copies), thought the extra p-glycoprotein could be coming from an overactive gene.

In a series of experiments described in the January PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (Vol. 84, No. 1), the researchers measured the levels of p-glycoprotein messenger RNA (mRNA). Messenger RNA is the "working copy" of DNA and its levels indicate actual protein production.

They found high mRNA levels in cells from human tumors of types that are often resistant to chemotherapy. They also observed a six-fold increase in before-and-after samples from a tumor that was initially sensitive to drugs but then became resistant.

In addition, some normal digestive system cells also had high levels of p-glycoprotein gene expression, presumably to help the cells deal with toxic chemicals in food. "Tumors derived from these tissues are intrinsically drug resistant," says Gottesman. "I'd hypothesize that might be because the tissue is already able to handle [toxins]."

In the future, physicians might be able to use increases in p-glycoprotein mRNA to predict inherent resistance or as an early signal of the development of resistance.

Estrogens exonerated in breast cancer

In the tangled epidemiology of postmenopausal estrogen use, the hormone has been linked with an increased incidence in breast cancer and endometrial cancer and both an increase and a decrease in heart disease (SN: 5/3/80, p.278; 11/2/85, p.279). Now a study from the Centers for Disease Control (CDC) in Atlanta indicates that the estimated 2 million to 3 million women in the United States who take estrogens after natural menopause or removal of their ovaries are *not* putting themselves at a significantly higher risk of breast cancer.

The CDC researchers studied 1,369 women 25 to 54 years old with breast cancer and 1,645 cancer-free women of the same age. The study, reported in the Jan. 9 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, is the largest such case-control comparison to date. The 1980 study that had found a link between estrogen use and breast cancer involved 131 breast cancer patients and 262 matched controls.

After adjusting for confounding factors, the researchers found that the rate of breast cancer was the same overall in women who had used estrogens as in those who had not. Women who went through natural menopause and subsequently used estrogen were at 80 percent of the risk of women who had not used estrogen, and women with surgically induced menopause and a history of estrogen use had a 30 percent higher chance of breast cancer than a similar group who had never used estrogen.

JANUARY 24, 1987

A science tax on information?

When it came to funding "targeted programs" like AIDS and the Strategic Defense Initiative for fiscal year 1987, "Congress was very good," says Philip Speser, executive director of the Washington, D.C.-based National Coalition for Science and Technology (NCST). However, he points out, "across the board, there was a 4.2 percent cut from the administration's request for general science." And no windfall materialized to boost the research community's ailing infrastructure, including facilities.

So NCST, the only registered lobby of scientists for science, announced last week that it has crafted a plan to generate additional revenues for future science budgets: a tax of 0.1 percent on the sale of printed or electronic information. Speser says, "The idea has generated considerable interest on Capitol Hill, and formal legislation is being prepared."

Commerce Department statistics suggest, he says, that the "information industry" has gross revenues of \$94.15 billion annually. Based on those figures, the tax NCST is proposing would generate \$94 million a year: \$28.9 million from the sale of newspapers, \$15.7 million from periodicals, \$11.2 million from books, \$22 million from computer software, \$4.5 million from videocassettes and \$9.5 million from cable television.

Speser says one-quarter would go to the National Endowments for the Arts and Humanities, since some of the tax would be derived from literature and art, and the rest would go to a new Science Trust Fund. The science portion, administered by the National Science Foundation along guidelines established by a government interagency committee, would be spent on education, on buildings, equipment and maintenance and on "blue sky" basic research.

Research opportunities for undergrads

Hoping to lure more young people into careers in science, math and engineering, the National Science Foundation is initiating a new program to fund the participation of roughly 2,000 undergraduates in active university research. Interested research institutions must apply for the money—about \$4,000 per student involved—by March 1, 1987. Special priority will be given for programs that would involve the participation of women, minorities or physically disabled students.

Coming: Student Nobelists

A new program to award \$50,000 American Nobel Fellowships to graduate students in physics, chemistry, medicine and economics was announced last month by the Westport, Conn.-based American Nobel Anniversary Committee (ANAC). The nonprofit organization was set up in 1941 by Albert Einstein and French emigré Jacques Ferrand to honor Alfred Nobel and U.S. winners of the award named for him.

The new fellowships, to be awarded every other year, will go to students "who show tremendous aptitude, skill and innovative ability in some of the subdisciplines that complement the Nobel awards," according to Henry Singer, ANAC's executive officer. Winners, who will be able to use the fellowships to complete their graduate studies or to finance research, will be chosen by Nobel laureates, Singer says. The first awards are scheduled to be made on Dec. 9, 1988.

Though ANAC is not affiliated with the Stockholm-based Nobel Foundation, which offers the Nobel Prize (SN: 10/25/86, p.262), Singer says the Nobel Foundation has offered the ANAC fellowships program its enthusiastic support. Money for the program is to come from corporate sponsors. And these can name the fellowship they endow after anyone they choose, Singer says, "so long as [the fellowship's] ultimate objective is to enhance and nurture the growth and development of future Nobel laureates." An anonymous donor has already contributed the \$250,000 needed to set up the chemistry fellowship.

57