

## Biomedicine

John Travis reports from Washington, D.C., at the annual meeting of the American Association for Cancer Research

### Genetic flaw causes double trouble

Researchers now believe that a gene they've studied for years may function as a tumor suppressor in liver, breast, and other tissues. This gene, which encodes a cell surface protein that binds to growth-inhibiting molecules, is missing in certain cancer cells, report investigators at Duke University Medical Center in Durham, N.C.

Tumor suppressor genes help prevent a cell from growing and dividing uncontrollably. Like most genes, tumor suppressors come in pairs, and a cell can usually keep the brakes on its growth as long as one copy functions. Delete or mutate both copies, however, and the cell is in trouble.

The cell surface receptor encoded by the apparent tumor suppressor gene binds to two different molecules and can suppress cell growth in at least two ways, says Duke's Randy L. Jirtle. First, by attaching to a molecule called transforming growth factor-beta, the receptor sends a strong growth-inhibiting signal to its cell. Second, the receptor deactivates insulin-like growth factor-II, which normally stimulates cell growth.

Last year, Jirtle and his colleagues found that in many liver cancer cells, both copies of the gene for this receptor are either deleted or mutated. "It's like going down the highway with your brakes cut and your foot on the accelerator," says Jirtle.

The Duke group, whose results are scheduled for the May ONCOGENE, now reports that an absence of the receptor also appears to contribute to breast cancer. In 12 out of 40 breast cancer patients who were missing a copy of the receptor gene, the investigators found mutations in the other copy. Jirtle notes that at least one copy of the receptor gene is often deleted in other cancers, including ovarian cancer.

Jirtle hopes that knowing whether this receptor is missing in a cancer patient will help physicians tailor treatments. For example, promising cancer drugs called monoterpenes bind to the receptor. Patients who lack the receptor may not respond as well to these drugs, says Michael N. Gould of the University of Wisconsin-Madison.

Gould has recently finished a preliminary clinical trial with one monoterpene, a compound found naturally in lavender oil. In a follow-up study, says Gould, investigators will document the receptor's presence or absence in each cancer patient to determine whether it influences the outcome of the treatment.

### Bombs away against cancer cells

The war on cancer may one day have a new weapon: the gene bomb. Luis T. Da Costa and his colleagues at the Johns Hopkins University Medical Institutions in Baltimore are mastering the novel cancer-fighting strategy. To construct the bomb inside a tumor, he explains, investigators would insert at least two foreign genes into the cancer cells.

The first gene, which Da Costa calls the trigger, encodes a protein that binds to another protein made only by cancer cells. That pairing then turns on the second transplanted gene, which codes for a bacterial toxin that can destroy the cancer cell and the cells around it. "If the cell is normal, the bomb just stays there and the cell isn't harmed. A cancer protein will pull the trigger and the bomb will go off," says Da Costa.

The gene bomb will probably end up killing some normal cells, Da Costa acknowledges. Most cancer proteins are actually mutated forms of normal proteins, so it's difficult to guarantee that the bomb's trigger will not be pulled by a normal protein. Da Costa notes, however, that surgeons usually remove healthy tissue surrounding a tumor to ensure that no cancer cells escape.

In test-tube experiments, Da Costa's group has shown that this new approach can kill groups of cancer cells, including some that didn't contain the gene bomb but were near cells that did. Da Costa cautions that researchers must find more efficient ways of delivering the gene bomb into tumors.

## Science & Society

### Finally, the fiscal year's budget . . .

In late April, 5 months before the end of fiscal year 1996, Congress and the President agreed on the year's allotment for those federal agencies that had yet to receive their final budgets, including six that fund research and development. The President signed some agencies' FY 1996 R&D appropriations into law earlier in the year (SN: 2/10/96, p. 86).

You may want to hold your applause, however. The funding for R&D at all but one of the agencies came in below FY 1995 levels, after factoring in an estimated 2.7 percent rate of inflation. (Percentages in this article are adjusted for inflation.)

The final total FY 1996 R&D budget stands at \$71.2 billion, \$285 million more than in FY 1995—but after inflation it is 2.3 percent less. Defense-related R&D took home \$38.5 billion of that pie, 1 percent less than in FY 1995. Nondefense R&D received \$32.7 billion, a 3.8 percent reduction, according to the American Association for the Advancement of Science.

Of the six agencies that had been operating without a firm R&D budget, only Health and Human Services secured an increase for R&D. It received \$12.1 billion, a 2.2 percent increase over FY 1995.

In contrast, the R&D budget at the Department of Commerce plummeted from \$1.1 billion to \$948 million, a 17.9 percent crash, AAAS reports. Republicans in Congress had targeted for demolition Commerce's Advanced Technology Program, and they succeeded in cutting its budget in half. The program, which supports innovative, but risky, technologies, received \$207.7 million.

The National Institute of Standards and Technology, also part of Commerce, received \$400.7 million in FY 1996, 30 percent less than the previous year.

Second in line for outstanding cuts is the Department of the Interior, which received \$622 million for R&D, 9.6 percent less than in FY 1995, AAAS reports.

Although it fared better than some analysts had expected, the Environmental Protection Agency faces a 7.4 percent drop in its R&D budget, down from \$554 million to \$528 million. Funding for enforcement, however, got a boost.

The R&D budget of \$9.4 billion for NASA is 3.2 percent less than the FY 1995 allotment. The National Science Foundation received \$2.4 billion for R&D, a 2.9 percent drop, AAAS reports.

Although the FY 1996 numbers look bleak, the House had originally proposed cuts of over 10 percent, notes Kei Koizumi, a AAAS budget analyst in Washington, D.C.

### . . . A Conservation Reserve Program

The Department of Agriculture's Conservation Reserve Program pays farmers to take millions of acres of highly erodible land out of production (SN: 1/20/96, p. 44). Last year, Congress threatened to weaken the program by preventing the agency from enrolling new acres when farmers' contracts expire.

In early April, however, Congress and the President approved legislation that allows USDA to continue enrolling new acres and thereby maintain its current acreage of about 34.6 million.

However, most landowners are now permitted to end their contracts without USDA approval. With grain prices high, some farmers will no doubt do so.

### . . . And an endangered species list

As part of the budget negotiation, Congress has agreed to lift a ban that prevented the Fish and Wildlife Service from listing additional species as endangered or threatened (SN: 3/23/96, p. 188). How soon FWS will sign up the 250 species that meet the criteria for listing remains unclear, an agency spokesman says.

The agency received a 4.7 percent cut in its budget for fiscal year 1996. About \$60.3 million of FWS' \$501 million allotment is going to the endangered species program.