SCIENCE NEWS OF THE WEEK

Cancer View: Roughing Up the Chromosomes

Massive rearrangements of genetic material, rather than local subunit changes, are the underlying cause of most cancer, says John Cairns of the Imperial Cancer Research Fund in London. This view reflects the new era in understanding of genetic information, he told the International Symposium on Aging and Cancer held recently in Washington. Previous work focused primarily on tiny changes in the genetic information, the equivalent of typographic errors in an encyclopedia, which gradually set the finely tuned cell mechanisms awry. Now Cairns suggests that the cell's own proofreading system can identify and correct such small mistakes. But it is the "chopping and switching" of larger pieces of the chromosomes, whole pages of the encyclopedia deleted or inserted in the wrong volume, that initiates malignancies. "Agents that drive such changes are causing cancers," Cairns says.

Movement of large segments of DNA is now in vogue in several areas of biology. Recent techniques for analyzing extensive areas of genetic material have revealed that genes rearrange during development (SN: 12/11/76, p. 372) and during evolution (SN: 7/7/79, p. 13).

Cairns was persuaded that massive rearrangements and not small changes are the basis of cancers by the study of persons with a genetic disorder called Xeroderma pigmentosa. The cells of those persons are defective in the ability to repair small changes in DNA, such as those caused by ultraviolet radiation from the sun. Such persons are unusually susceptible to skin cancer. But when Cairns examined the records of 114 patients with the genetic defect he found no excess of other types of cancer. If small changes in DNA are responsible for cancer, those patients should have far more such local lesions than the average person. Since they do not develop more than the average number of internal cancers, Cairns concludes that the instigation of cancer is not, on the whole, due to local changes in the DNA.

In contrast to the Xeroderma pigmentosa patients, Cairns considered, as a "pseudocontrol," people with another inherited disease. Patients with Bloom's syndrome develop cancer 100 times more frequently than does the general population. The syndrome is characterized by unrepaired chromosome breakage, and a high incidence of chromosome rearrangements and deletions. "The main causes of human cancer must be the things Bloom's syndrome patients make a mess of," Cairns reasons. Another clinical association of high cancer incidence and chromosome rearrangements turns up in Werner's syndrome, a rare disease of accelerated aging, discussed by George M. Martin of the University of Washington (see p. 216).

Another speaker at the meeting raised the possibility of chromosome changes underlying particular cancers. Janet D. Rowley of the University of Chicago reports that certain chromosome changes are seen repeatedly in leukemic cells of patients with various types of acute leukemia. Particular chromosome rearrangements are associated with specific subtypes of leukemia, she says. In addition, both the incidence of acute leukemia and the frequency of certain chromosome changes increase with age.

A genetic element, such as one found in yeast, could be responsible for the large genetic changes required to commit a cell to the cancerous state, says Gerald R. Fink of Cornell University. In yeast, pieces of DNA called transposons insert into a chromosome in many places. Fink reports that a transposon can subvert normal control by causing a high frequency of gene mutation and by rearranging genes to cause dramatic changes in chromosome structure.

When the arrangement of genes on a chromosome is changed, the cell's characteristics are likely to be altered. James A. Shapiro of the University of Chicago reviewed several examples of rearrangements that provide control of gene expression. In the world of microorganisms, inversion of specific sequences determines which of two types of flagella appear on a Salmonella bacterium (SN: 3/12/77, p. 164) and which group of bacteria a virus known as Mu can infect. The mating type of yeast is determined by insertion at a specific location of an extra copy of one of two stretches of DNA (SN: 3/12/77, p. 164). Similarly, the protozoan parasite trypanosome adds an extra copy of a gene to alter its surface molecules to avoid its host's immune system. Shapiro suggests that moving genes to different positions on a chromosome can change their expression. More obviously adding or subtracting copies of a gene, thereby changing the gene dose, can alter a cell's characteristics.

Massive changes of genetic material also occur in development in higher animals. Robert T. Schimke of Stanford University reports that cells achieve drug resistance by attaching to their chromosomes multiple copies of an appropriate gene (see p. 216). Susumu Tonegawa described his most recent work in plotting rearrangements of the DNA sequence during normal differentiation of the cells responsible for producing antibodies. Earlier work showed that genetic material coding for one region of the light chain of an antibody molecule comes together with the genetic material for the other region during maturation from embryonic to adult cells (SN: 12/11/76, p. 372). Now Tonegawa has shown the same phenomenon for the antibody heavy chain and has mapped out more details of the rearrangement.

In the search for the agents responsible for human cancer, Cairns predicts scientists will need to change their strategy. Instead of looking primarily for substances that make small changes in DNA, such as those detected with the Ames bacterial test, they need to detect chemicals and viruses that promote extensive chromosomal changes. □

Politics: Making something of space

"We are taking the space constituency as a real part of the political constituency," says Michael Fulda, a professor of political science at Fairmont State College in West Virginia. And apparently as a significant part. Working with the campaign of independent presidential candidate John Anderson, Fulda wrote the policy statement (and helped with the resultant platform plank) in which Anderson calls for an expanded space program, at a time when such proposals are less than universally supported.

Except as it is sometimes related to national defense, space development is not one of the more visible issues in the campaign. Fulda, however, is now the Anderson campaign's "Coordinator for the Space Constituency," and by the end of this week

NASA

The space shuttle, being transported between its launch pad and assembly facility.

was expecting to have established state-level coordinators in as many as 15 states, emphasizing those with appreciable portions of the country's space business.

William Van Cleave, senior defense policy advisor for Republican candidate Ronald Reagan, is setting up a "space science committee," but, he says, "I think there are no plans at all to go campaigning on space." Instead, according to Van Cleave, the committee is one of several being established "with an eye toward January 20," planning ahead on policy matters on the assumption of Reagan's election.

Anderson's space policy calls for "an expanded space program based generally on [the National Aeronautics and Space Administration's] current five-year plan." That plan, however, the policy statement avers, "does not include funding for several vital programs needed for the development of space science, technology and industrialization. Most of these programs, included in earlier plans and cut from the current proposal by the Carter Administration, should be reinstated." The areas identified by the Anderson policy include:

- "An intensified effort to achieve routine operational use of the Space Shuttle, with improvements in lift and on-board capabilities."
- "A more adequate fleet" of shuttle orbiters—five, says Fulda, instead of the Carter administration's four.
- "Establishment" of an operational Landsat-type earth-resources satellite survey system, "in lieu of the hesitant, half-hearted motions" of the administration.
- "Proper support of a long-term program" of solar system exploration, with specific mention of the Galileo orbiter and probe of Jupiter (already under development), the Venus Orbiting Imaging Radar (now being sought in NASA's FY 1982 budget after two unsuccessful attempts) and a flyby of comet Halley. (Some U.S. scientists fear that plans for a U.S. Halley mission, already well behind the Venus flight on NASA's "new start" priority list, may finally succumb to the alternative of U.S. cooperation with the European Space Agency's planned Halley effort.)
- "Establishment of a permanent U.S. presence in space through planning and design of a general-purpose orbiting space station."
- "Vigorous" continued studies of the feasibility of solar power satellite systems "until a rational basis has been established for deciding whether to develop it or not."

The Anderson statement does not cite specific cost estimates, but Fulda says that the non-shuttle portions of such a program could cost about 17 to 25 percent more in the course of NASA's 1981-1985 planning interval than they might in the sort of program inferred from Carter administration activities. Even so, the statement asserts, the space program "is one of the few taxpayer-supported programs which can show a greater return (by several fold) than our initial investment."

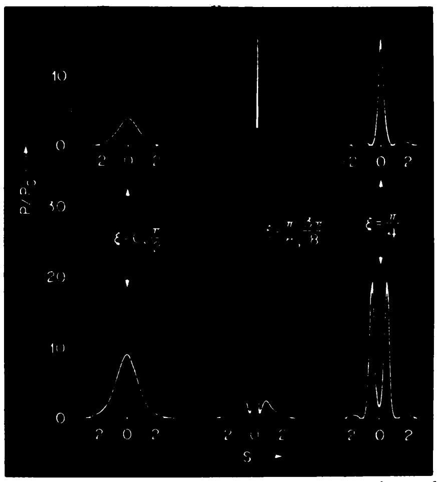
Echoing a General Accounting Office report from earlier this year (SN: 2/16/80, p. 102), the statement advocates encouraging greater participation by private industry. "Private industries should be allowed accelerated depreciation in all areas, not merely those related to space, for their capital stock and the existing investment tax credit should be extended to qualified research and development expenditures." Satellite-borne earth-resources systems and space manufacturing technology both should receive increased federal support, the document says, citing aviation and communications satellites as examples of government-initiated fields that have been successfully adopted by private enterprise. "There is no reason to suspect," according to the policy statement, "that the remote-sensing and space-manufacturing industries will not follow." It also calls for eased government regulations "to allow easier entry of private enterprise into space programs."

Besides teaching about space policy and energy policy at Fairmont State, Fulda is a member of several pro-space organizations including the industry-oriented National Space Institute and the Planetary Society (started by Carl Sagan and by Jet Propulsion Laboratory director Bruce Murray). NASA and the "responsible space constituency" generally agree on the overall distribution of the civilian space budget, says the policy statement. "One expects some disagreements among program offices as to the proper division of the space budget pie, but there is almost unanimity of opinion that there is a pressing need for a larger pie."

Predictably, the statement advocates increased international cooperation in space projects and, on the military side, the U.S. development of anti-satellite technology (unless the Soviet Union will agree to a ban).

A civil space policy issued by the Carter administration in 1978 was declared by NASA administrator Robert Frosch to consist of "straightforward directives and provide the basis for an exciting and productive space program in the years ahead." Critics claimed that the policy was not specific enough, in part because it seemed to defer key decisions until after the space shuttle demonstrated its ability. "As the resources and manpower requirements for shuttle development phase down" the Carter policy stated, "we will have the flexibility to give greater attention to new space applications and exploration, continue programs at present levels or contract them." At the time the policy was presented, however, the shuttle's maiden flight was targeted for last month. Now it is aimed at March of 1981—with an election taking place in the meantime to determine who will set the policies that follow. □

Soliton solutions in an optical fiber



Mollenauer, Stolen and Gordon

Development of first- (upper row) and second-order solitons. Second-order solitons split into two peaks and recombine.

Solitons, or solitary waves, appear in the theories of many branches of physics. Solitons represent solutions to an important and ubiquitous mathematical equation, the nonlinear Schrödinger equation. Now solitons are no longer entirely theory. A report of an experimental demonstration by L. F. Mollenauer, R. H. Stolen and J. P. Gordon of Bell Telephone Laboratories in Holmdel, N.J., was to appear in the Sept. 29 PHYSICAL REVIEW LETTERS.

A soliton is a single wave shape that is not part of a continuous train of waves, but that stands alone. Unlike ordinary pulses of waves, solitons maintain their shape as they propagate their way through the medium that supports them. Dispersion does not make them dribble away and dissipate like ordinary pulses. The experimental work of Mollenauer, Stolen and Gordon demonstrates, they say, the existence and propagation of soliton light pulses in an optical fiber.

For the production of solitons, the material of the fiber (its quartz core, that is) must satisfy two conditions: negative dispersion and nonlinearity. Dispersion is what a prism does to a light beam when it makes a rainbow. In a material medium, like quartz, the speed of light varies according to frequency. In most media this "dispersion" is usually "positive." That is, low frequencies go faster than high frequencies. But in some media over certain frequency ranges dispersion becomes "negative" so that high frequencies go faster.

For low intensity light, the speed of any given frequency in a given medium is a constant number. At the light intensities characteristically given out by lasers, that can change. In these nonlinear media the speed of light for a single frequency varies according to the intensity of the light. This causes a change of phase in one part of the