Gene Relocates During Differentiation

The polypeptide chains that make up antibody molecules seem to disobey a basic rule of modern biology. Rather than a single gene coding one polypeptide, different genes code for the two regions of each chain (SN: 10/19/74, p. 253). Now there is evidence that, during differentiation, one gene is moved adjacent to another antibody chain gene.

A central problem in immunology is how the immune system produces thousands of different antibody molecules to respond to the multitude of possible foreign toxins and pathogens. It would be impractical to have a separate gene for each molecule.

A partial explanation has been found in the combination of a constant portion of an antibody chain with one of a number of variable portions. Further, in ways yet unexplained, changes in the variable region give antibodies their characteristic property of combining specifically with whatever substance elicited their formation.

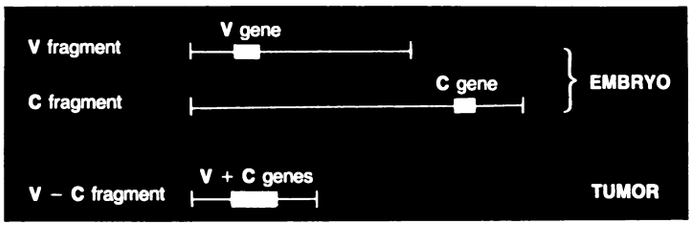
Three mechanisms have been suggested by which two genes could produce a single protein. The genes could move to adjacent positions in the chromosome before they are transcribed to a single messenger RNA, the messenger RNA produced from two separate genes could be joined before the protein is made or the final polypeptide chains could be enzymatically linked.

Twelve years ago W. J. Dreyer and J. Claude Bennett of the California Institute of Technology proposed that genetic material for the variable portion (V) of the chain combines with the constant region (C) gene during differentiation of antibody-producing cells. New evidence from the Basel Institute for Immunology in Switzerland supports this mechanism.

Nobumichi Hozumi and Susumu Tonegawa report in the October PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES that the location of the genes coding for one antibody molecule chain differs between embryonic and differentiated cells. The embryonic genes are some distance apart, while the genes from differentiated cells are contiguous.

Hozumi and Tonegawa analyzed DNA from embryonic mouse cells and from tumor cells derived from mouse bone marrow. Tumor cells, rather than normal adult cells, were used because all cells in a clone produce the same antibody. Antibody production of tumor cells is similar to that of normal cells.

The method of analysis was based on the specific binding of messenger RNA to the DNA sequence from which it was made. The researchers isolated messenger RNA for one of the polypeptide chains of an antibody and also a messenger RNA fragment, half as long, containing only the sequence for the constant region of the polypeptide chain. An enzyme was used to cut the mouse chromosomes into DNA fragments, which could be identified by their different lengths. They then mixed the DNA fragments with each of the messenger RNA molecules.



Genes for a single polypeptide are separate in embryo, but adjacent in tumor, DNA.

Two DNA fragments from the embryonic cells bound to the intact messenger RNA, and one of those fragments bound to the shorter RNA molecule. Therefore the gene for the constant region was in that DNA fragment.

Only one DNA fragment from the tumor cell, however, attached to either of the messenger RNA molecules. That DNA fragment was shorter than the embryonic DNA fragments that bound, but contained both genes (see diagram).

The researchers conclude that a region of DNA moves during differentiation. The details of how the mouse DNA changes position remain to be resolved.

Hozumi and Tonegawa propose that terminology, rather than a basic biological dogma, may need to be changed. There is an alternative to the concept of two genes producing one polypeptide chain. "Rather, there are two segments of DNA, one specifying the V region and the other specifying the C region," they write. "The gene is *created* by joining." □

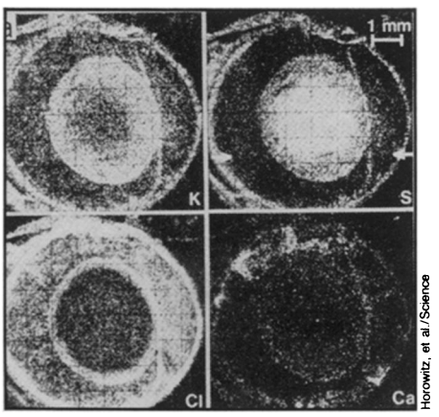
Element mapping in biological samples

Cutting, grinding, dehydrating or embedding a biological sample destroys valuable information about the spatial distribution of its components, so biological analysis demands techniques that can be applied to relatively undisturbed specimens.

A new biological tool has now been used to map out the elements present in a variety of specimens. In the Dec. 10 SCIENCE researchers report the use of the proton microprobe technique to analyze single strands of hair from poisoning victims, and eye and kidney specimens from rats. The technique was developed and applied by Paul Horowitz and Michael Aronson of Harvard University, Lee Grodzins and William Ladd of the Massachusetts Institute of Technology, Jean Ryan of the Lincoln Laboratory in Lexington, Mass., and George Merriam and Claude Lechene of Harvard Medical School.

In the new method a 2-million-electron-volt proton beam, brought out into the air, scans the sample. When elements in the sample are excited by the proton beam, they emit characteristic X-rays. An X-ray detector collects those rays, and the information can be stored in a computer memory. To produce a two-dimensional analysis, linear scans are made repeatedly across the sample and then displayed together on an oscilloscope screen.

The first biological samples examined



Horowitz, et al./Science

Microprobe map of four elements in eye.

were one-dimensional—individual strands of hair from victims of accidental mercury and arsenic poisonings. Along its length, each hair showed a peak of the toxic substance. The location of the peak, combined with the rate of hair growth, provided information about the time of the poisoning. Such analysis of hair might also be used to detect biochemical changes in a person.

The proton microprobe technique is especially applicable to understanding how mobile ions are distributed and concentrated in living tissue. The compartmentalization of ions is a central problem in physiology. Only living or frozen hydrated samples of tissue maintain their

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normal ion distribution.

The photographs show proton microprobe maps of four different elements in a frozen rat eye. (The eye is facing to the right, so that the retina is on the left, the lens in the center and the cornea on the right.) The variations in shading reflect differences in local concentration of the elements potassium, sulfur, chlorine and calcium.

The researchers also examined kidney specimens with this technique. They showed visually, for the first time, gradients of potassium and chlorine in the concentrating kidney.

Because the technique requires the use of one of about 100 proton accelerators available in this country, the proton microprobe cannot be used in most laboratories. Nevertheless the developers of the technique believe its sensitivity and convenience will allow study of many important biological problems that cannot be approached by other methods. □

Door into space unhinged

On Feb. 20, 1962, John Glenn became the first American to orbit the earth, riding a Mercury spacecraft known as Friendship 7. The most visible landmark of the historic flight has been the 145-foot steel service tower at Launch Complex 14 on Cape Canaveral, from beside which an Atlas rocket carried Glenn's capsule into space. On Dec. 1, 1976, five demolition specialists from the U.S. Army's 27th Engineering Battalion wrapped plastic explosives around the base of the landmark, connected their detonators and blew it down.

The reason was money. The deteriorating tower was deemed "hazardous" for the complex's blockhouse (750 feet away), as well as for some rooms beneath its approach ramps, both of which have been in use as storage facilities. The Air Force, from whom the National Aeronautics and Space Administration borrowed the complex in Mercury days, estimates that to have restored the tower, together with an adjacent one at Launch Complex 12, would have cost $500,000, plus another $100,000 a year for maintenance. Complex 12 was "explosively dismantled" on Dec. 3, and the same fate is in store (at a date yet unspecified) for the Project Gemini launch site at complex 19.

All of the orbital Mercury flights—those of Glenn, Scott Carpenter, Walter Schirra and Gordon Cooper—took off from No. 14, whose last launch was that of Applications Technology Satellite C on Nov. 5, 1967. The preceding suborbital flights of Alan Shepard and Virgil Grissom lifted off from a separate pad, number 5, which was dismantled more than a decade ago. A plaque marks the spot. R.I.P. □

A pioneering look 'down' on the sun

While the Pioneer 11 spacecraft was studying Jupiter from close up late in 1974, it was also using the giant planet's gravity to swing around onto a course toward a 1979 rendezvous with Saturn. A fortuitous side-benefit of the Saturn-bound trajectory was that during the trip it would take Pioneer 11 where no other manmade probe had ever been: out of the plane of the ecliptic, far "above" the disk in which the planets orbit the sun, so that it could take an unprecedented look "down" at the solar system.

By February of this year, the spacecraft was about 16° above the ecliptic plane; that is, a line from the center of the sun to Pioneer 11 would have passed through the sun's surface at about 16°N latitude. Measurements from this lofty viewpoint, about 160 million kilometers above the plane, have now given scientists their first direct look at solar outpourings in a region where there used to be nothing but theories. Even with the help of the sun's tilted axis of rotation, spacecraft travelling in or near the ecliptic plane have been limited, by comparison, to heliographic latitudes of 7.25° or less.

Pioneer's results, reported by Edward J. Smith of the Jet Propulsion Laboratory in Pasadena, have now shown that the sun's magnetic field is much more spherical than disklike, extending for billions of miles above and below the solar poles. Within the plane of the ecliptic, Pioneer 11's predecessor, Pioneer 10, has confirmed that the field extends out as far as the orbit of Saturn, and field-strength measurements there combined with Pioneer 11's out-of-plane data suggest that it probably reaches all the way to Pluto, more than 4.5 billion kilometers from the sun.

The northern and southern parts of the sun's field are apparently separated, as are those of Jupiter and the earth, by a warped electrical "current sheet," with the magnetic field lines on one side of the sheet flowing outward and those on the other side bringing the circuit back around to the sun. Because the sheet is not flat, and because the sun's axis is tilted relative to the plane, spacecraft flying within the ecliptic plane have encountered field lines oriented sometimes in one direction, sometimes in the other. Pioneer 11 has added strong support to the likelihood of this warped sheet, mitigating against the competing idea that the sun's magnetic field was just cantankerously erratic.

The sun was a major topic this week at the annual autumn meeting of the American Geophysical Union in San Francisco, where Smith presented his Pioneer 11 findings, and the slowly evolving picture of the sun's nonequatorial latitudes was discussed in nearly a dozen presentations. Both the magnetic field and the solar wind have revealed latitude correlations in data from the two German Helios probes, for example, which are so close to the sun—inside even the orbit of Mercury—that a small change in distance from the ecliptic plane represents a relatively large change in heliographic latitude. In March of 1975, Helios 1 provided a particularly rich data harvest when it travelled from 6°S to 6°N in only two weeks. □

Tracking quake data and predictions

Two government agencies have embarked on widely different programs for gathering information on earthquakes, their origin and their prediction. The National Science Foundation has just announced new cooperation with the Soviet Union in an international network of seismic instruments, and the U.S. Geological Survey is starting a file of earthquake predictions to see whose are most reliable.

In the NSF program, an American seismometer, which produces digital data on tape cassettes for analysis in the United States, has been installed in Garm, a remote village in the Soviet Republic of Tadjikistan. The installation is the seventh in a worldwide network that may eventually include 15 to 20 units. A geophysicist who has helped set up the network, Jonathan Berger of the University of California at San Diego, told SCIENCE NEWS that this marks the first permanent installation of an American seismic instrument in the Soviet Union.

The new network has unusual funding—each country involved pays for operation of instruments on its land, NSF is paying for setting up the network, and the instruments themselves were donated privately by Cecil Green (a founder of Texas Instruments, Inc.) and his wife Ida. In honor of their gift, the project is called IDA, which can also stand for International Deployment of Accelerometers.

The object of the network is to gather data on the extremely long wavelength vibrations set up in the earth by earthquakes deep below the surface. The data are analyzed by a computer in San Diego. Berger says this analysis should help to develop a model of earth's elastic structure, which in turn can be used to analyze the "source mechanism" of particular quakes. Although the immediate aim is one of fundamental research, the study of such source mechanisms may eventually help scientists predict when more damaging quakes—those nearer the surface—will occur.

The USGS National Earthquake Information Service in Denver has started a computerized file of earthquake predic-