Human gene partially synthesized

In the murky underworld of the mammalian cell, several hundred thousand genes may be carrying out cellular activities at an astounding speed. Further, the transcription of DNA into RNA into protein occurs in such minuscule quantities that human vision cannot detect it without the help of the electron microscope. Nonetheless molecular biologists are finding ways of indirectly mapping genes on mammalian strands of DNA as they have done with DNA from lower species. They are also learning how to manipulate mammalian DNA in similar fashion.

One of the latest and most intriguing manipulations has been accomplished, almost simultaneously, by three independent research groups. They have succeeded in partially synthesizing the gene from the rabbit, and from man, that codes for red blood cell protein—or hemoglobin. Evidence for such a coup is fairly concrete: Hybridization experiments show that the product synthesized binds to hemoglobin messenger RNA, but not to other kinds of RNA.

The researchers are Jeffrey Ross, Haim Aviv, Edward Scolnick and Philip Leder at the National Institutes of Health; Inder Varma, Gary Temple, Hung Fan and David Baltimore at the Masachusetts Institute of Technology; D. L. Kacian, Sol Spiegelman, A. Bank, M. Terada, S. Metafora, L. Dow and P. A. Marks of Columbia University. The NIH group's work appears in the January PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. Research by the MIT and Columbia investigators is in press with NATURE.

Only a few genes have been synthesized to date. They are from the yeast cell, which is far less complex than a mammalian cell. Also, the complete DNA sequence of the yeast genes had to be known before they could be made. The NIH, MIT and Columbia scientists have taken another tack to gene synthesis. Without knowing the entire DNA sequence of the mammalian gene they were trying to make, they called upon the enzyme "reverse transcriptase." This enzyme identified in the summer of 1970 (SN: 7/25/70, p. 54) by Baltimore and Howard Temin of McArdle Laboratory, Madison, Wis., makes RNA into DNA. This is in contrast to the dogma due to Francis Crick that genetic information in cells is usually passed from DNA to RNA.

Actually, as far as artificial synthesis of genetic material is concerned, this partial synthesis of a rabbit hemoglobin gene and a human hemoglobin gene is probably the biggest job the reverse transcriptase enzyme has been given to date. Previously it has been used to make viral RNA's into DNA's. It has also been used to make synthetic polynucleotides. Nucleotides are the building blocks which go into the DNA molecule.

The challenge now facing the NIH, Columbia and MIT researchers is to provide still more evidence that the DNA material made with the reverse transcriptase is indeed what they claim—part of the hemoglobin gene. To do so they will first have to change the single DNA strand into a double strand. (Two strands comprise a gene.) They will then have to take this double strand and have it make some messenger RNA. If this m-RNA appears to be the hemoglobin messenger, they will try to make a hemoglobin protein with it. Such an accomplishment, NIH's Leder asserts, "would constitute virtually conclusive proof that the DNA made so far is, in fact, part or most of the hemoglobin gene."

Brain prosthesis for a paralyzed limb

Some medical researchers have entertained the possibility of bringing a stroke victim's paralyzed limb back to life by placing electrodes into the limb and stimulating it into action. Such an idea does not appear to hold much clinical promise, though. Some 30 muscles are needed for a movement as simple as arm flexion. Such a technique would require an electrode to be placed in each of these muscles to flex an arm. An error in electrode stimulation could make the arm perform an undesired movement.

Then a team of neurophysiologists, psychologists and engineers at the Stanford Research Institute and the Stanford University School of Medicine, headed by L. R. Pinneo, came up with the idea of a brain prosthesis for a paralyzed limb. Such a procedure would consist of stimulating those parts of the brain stem that can involuntarily control limb movement even though voluntary control, usually provided by the cerebral cortex, has been negated by stroke.

The California scientists spent several years mapping those parts of the brain stem that can control limb movements. When they found analogous functions among homologous brain stem parts from several species of laboratory animals, they assumed man's brain stem must work in a similar manner. They charted various patterns and intensities of electrode stimulation that would be needed if the desired limb movements were to be induced by electrically stimulating the brain stem. After the patterns were set, they were programmed into a computer.

The team members then felt that they were ready actually to test their method on an animal. Cerebral cortex tissue normally controlling voluntary limb movement was surgically removed from a monkey. As anticipated, the tissue removal put one limb out of operation, just as if the monkey had had a stroke. Electrodes were then attached to the monkey's brain stem and linked to the computer. The computer program indeed caused the monkey's paralyzed limb, via brain stem stimulation, to perform simple tasks, such as reaching for food or scratching.

The technique has been successfully applied to a handful of monkeys. One animal was trained in several weeks to switch on computer programs by itself.

However "a lot more work will be needed on the technique before it becomes available to stroke victims," Pinneo cautions. "We need to see whether we can indeed keep electrodes in the brain stem for long periods. We also need to develop a small computer that would do what our large now does." □

Nursing home fire: Commission snubbed

On Jan. 26 another nursing home experienced a tragic fire (SN: 1/15/72, p. 39). Nine women died in the blaze at the Green's Nursing Home in Lincoln Heights, Ohio.

Three members of the President's Commission on Fire Prevention and Control, including chairman Richard Bland, flew immediately from Washington to Cincinnati to investigate. But Ohio's fire marshal, Robert Lynch, left instructions that commission members were not to be allowed on the premises of the burned nursing home, under any circumstances. The marshal was not available for comment to the commission. Nor was Eugene Jewel, chief arson investigator for Ohio. The commission members consider these circumstances peculiar indeed. One of them told SCIENCE NEWS, "We are going to damn well find out what they mean."

Such matters will undoubtedly be brought up at Senate hearings on the nation's fire problems, to be held Feb. 15-17. The commission also touched briefly on the peculiarities surrounding the Ohio nursing home fire when it met with the National Academy of Sciences' Committee on Fire Research on Jan. 28. □

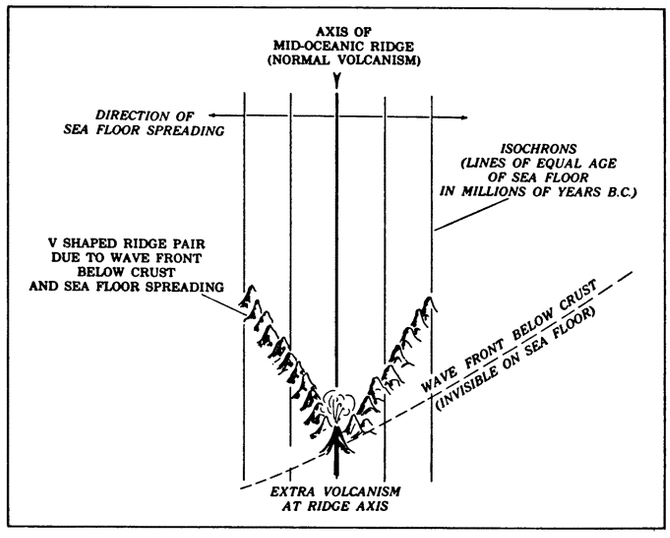
A V-shaped clue to the mantle's flow

Most of the major theories on the motivating force for continental drift involve thermal convection in the earth's mantle (SN: 7/25/70, p. 74). Last March, W. J. Morgan of Princeton University proposed that the mantle hot spots that have been detected in various locations around the world are convection plumes where hot magma from deep in the mantle wells up into the asthenosphere, the fluid part of the mantle. The magma then spreads out, dragging continents along with it. Morgan proposed about 20 such plumes throughout the world (SN: 3/13/71, p. 180).

Now Peter Vogt and Leonard Johnson of the U.S. Naval Oceanographic Office have found a peculiar topographic feature on the ocean floor in the North Atlantic that lends partial support to Morgan's theory. They found a V-shaped ridge flanking the Reykjanes ridge which they believe is a manifestation of convective flow from a hot spot below Iceland.

The scientists theorize that a convection plume under Iceland brings five to ten cubic miles of semimolten basalt upward, to spread out in the asthenosphere. The upwelling does not appear to be a steady process, says Johnson; instead, waves of magma seem to spread out periodically from Iceland. They believe that whenever one of these waves crosses below the Reykjanes ridge, a midoceanic spreading center, it causes a volcanic burst on the sea floor in which an extra dose of magma wells up to form a topographic peak. As normal sea-floor spreading at the Reykjanes ridge continues, this peak, originally located at the ridge crest, would split, and the two halves be pushed aside, to be added to the arms of the V. Meanwhile, the wave that created the first peak moves southward to form another.

As the flow spreads southward, the theory continues, it loses momentum and slows down, so that each successive topographic peak is closer to the one before it, and the V's become progressively narrower. The angle between the limbs of a V-shaped structure and the axis of the Reykjanes ridge, Vogt says, are thus a measure of the rate of flow from the Iceland plume. This rate, at the point where Vogt and Johnson made their observations (about latitude 61 degrees north), is about six centimeters per year. Johnson says the mantle wave that formed the V they found probably left its source under Iceland 5 million to 7 million years ago.



In the Vogt and Johnson model, mantle waves passing under midocean ridges form V-shaped patterns like the wake of a ship.

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The rate of spreading at the Reykjanes ridge is about a centimeter per year. If mantle convection from the plume moves the crustal plates, Vogt says it is encouraging that the calculated outward flow from Iceland is greater than the rate of ridge spreading. "It had to be greater; otherwise it couldn't exert enough viscous traction to crack or separate the crust and then drive the two plates apart." Vogt and Johnson believe mantle plumes may not be the only force driving the plates, but that they are important in certain locations.

Though the two researchers found only one such V-ridge, Johnson points out that bathymetric charts of the ocean south of Iceland reveal V-shaped shallow contours that may, he believes, be ridges such as the one they found. The researchers predict that similar V-ridges may be found near other hot spots, such as one in the Azores. □