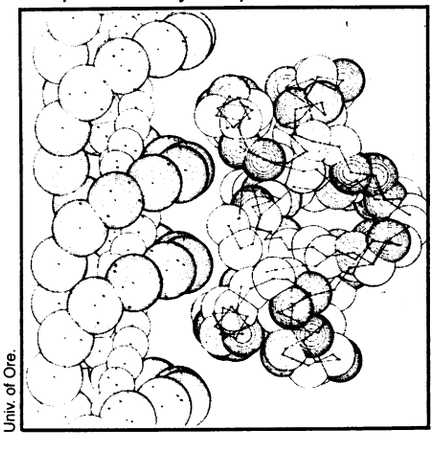
How the DNA switch is thrown

The deoxyribonucleic acid (DNA) in the human liver cell is the same as the DNA in the human skin cell. In fact, all of the cells in the human body contain the same DNA. But the liver cell, for example, uses only the genetic information on the DNA necessary for it to function as a liver cell. Similarly, the skin cell uses only a part of its genetic information. What enables a cell to ignore part of the message encoded on the DNA molecule, and thus to differentiate, is a complex gene regulation system that includes molecular "switches" that bind to and turn on or off various portions of DNA. Now, in an effort to shine more light on this system that long has intrigued researchers, two groups of biochemists have determined the three-dimensional structures of two different molecules that function as switches in lower organisms. Coincidentally, both groups published their work in the April 30 NATURE.

One group, Brian Matthews of the University of Oregon at Eugene and colleagues, determined the structure of "cro" — a protein that turns *off* portions of DNA in the very simple, virus-like organism, bacteriophage lambda. The other group, David B. McKay and Thomas A. Steitz of Yale University in New Haven, Conn., ascertained the structure of "CAP" — a protein that turns *on* portions of DNA in the common bacterium *Escherichia coli*. For structure elucidation, both groups used X-ray crystallography — a technique that involves irradiating crystals of a compound with an X-ray beam and collecting the resulting scattered X-rays on a photographic plate.

Once the structures were determined, both the Oregon and Yale researchers asked the same question: How does the molecular switch recognize the specific portion of DNA that it must turn on or off? The answer in both cases seems to be that specific helices on the switch molecules recognize specific grooves on the DNA molecule. Every twist of the double-stranded DNA molecule creates one major and one minor groove. Basing their theories on their respective models, the Oregon and Yale researchers both guess that two helical, or spiral-like, regions on their switch molecule fit into two successive major grooves of the DNA molecule.

The model of cro, right, and DNA, left, was drawn with a plotter that was fed data obtained through X-ray crystallography and processed by computer.



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But that is where the Yale and Oregon researchers part company. While Matthews and colleagues found that two helices of cro seem to fit two successive grooves of the more usual right-handed form of DNA (see diagram), Steitz and McKay found that the CAP helices are complementary to the left-handed version of DNA (SN: 12/29/79, p. 420). Steitz says this may indicate that CAP converts DNA from the right-handed to the left-handed form in regions where it binds.

The CAP and cro research contributes two pieces to the giant gene regulation puzzle. Since certain diseases can be traced back to malfunctions in regulation, completing that puzzle may be important for designing drugs that will interact with and regulate DNA. □

Spine manipulation for low back pain

Can spinal manipulation, as provided by physicians, osteopaths or chiropractors, help people with low back pain? The few controlled scientific studies that have explored this question have produced conflicting answers, perhaps because the placebos used in the studies (painkilling drugs or slight elevation of temperature of back tissues) were inadequate control procedures for an evaluation of a manual technique. So Fred K. Hoehler and his physical medicine colleagues at the University of California Irvine Medical Center in Orange, Calif., decided to see whether spinal manipulation can help patients with low back pain by comparing it to a placebo that they considered much more appropriate than those used in previous trials because patients wouldn't be able to distinguish it from spinal manipulation. It was massage of the soft tissues of the back. And as they report in the May 8 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, the results of their trial suggest that spinal manipulation is effective in relieving low back pain, at least over the short term.

Of the 95 subjects selected for the study, 56 received spinal manipulation. In this maneuver a patient lay on his or her side facing the manipulator with the inside leg extended and the outside leg flexed, thus tilting the outer side of the pelvis toward the manipulator, yet with the outer shoulder rotated away from the manipulator. The manipulator then gave the patient's pelvis a short, high-speed thrust, which opened the joints of the lower back and stretched its muscles. The other 39 control patients received only soft-tissue massage of the lower back, with the thrust omitted. The number of treatments that each patient in both groups got varied at the discretion of the treating physician. Throughout the treatment period patients in both groups subjectively rated the pain relief they obtained and were also examined objectively for pain relief.

The patients who received spinal manipulation reported significantly more pain relief after their first treatment than did the patients who had gotten soft-tissue massage. Objective measurements confirmed their subjective observations. But by the time of discharge the patients in the spinal manipulation group reported no more pain relief than did patients in the soft-tissue massage group; yet *both* groups reported substantial improvement in pain relief. Objective measurements once again jibed with their subjective observations.

So spinal "manipulation may facilitate recovery" of low back pain, Hoehler and his team conclude. They point out, however, that the long-term effectiveness of this technique would be more difficult to evaluate, primarily because given enough time, many patients with low back pain recover without treatment. □

First 'test-tube' baby

After a year and a half of trying to get a lab-fertilized human egg to develop into a fetus in a woman's womb, the first "test-tube" baby clinic in the United States, located at the Eastern Virginia Medical School in Norfolk, has succeeded.

The head of the clinic, Howard Jones, refused to identify the prospective parents or to say how far the pregnancy had progressed for fear of publicity disturbing the course of events. However, the patient, like others who seek the help of the clinic, had elected to undergo the procedure because she either had no Fallopian tubes or defective Fallopian tubes. Thus the eggs she manufactured in her ovaries could not pass through the tubes to be fertilized by her husband's sperm and then move into her womb to develop into a fetus. Doctors at the Norfolk clinic used techniques similar to those that have led to the birth of several "test-tube" babies in England, Australia and India (SN: 10/11/80, p. 231). First they inserted a glass-fiber instrument called a laparoscope into her abdomen around the time of ovulation and visualized a ripe egg cell in one of her ovaries. They suctioned the egg cell out of the ovary with a suction needle, removed the egg from the cell and placed it, along with sperm from her husband and certain chemicals, in a culture dish. One of the sperm fertilized the egg. The egg was then inserted through the woman's cervix into her womb and is now developing there as a fetus. □