Genetic engineering: Myth or reality?

Prospective engineers put the timetable for human genetic engineering at 20 to 100 years but other possibilities of the New Biology may be closer

by Joan Lynn Arehart

"The code of life has been cracked and genetic engineering is on its way. . . ."

"Within a year a scientist will fertilize a human egg in a test tube, Dr. James Watson told a House of Representatives science subcommittee hearing Tuesday. . . ."

"Under the magic wand of biology man is now gradually becoming quite different from what he was. . . ."

In the past year or two much fuss has been made in the popular press about human "genetic engineering" and the "New Biology." Some of the articles have been patently tongue-in-cheek, others sober but chock full of chilling predictions for the future. The total impact of such material has left both the public and scientists outside the immediate realm of the publicized biological feats confused, if not alarmed. How much is doomsday and science fiction, and how much is reality? What is genetic engineering anyhow?

The best way to gain an understanding of genetic engineering and whether it will soon be upon us is to talk with some of the specialists engaged in its development. One such man is Dr. James Danielli, a biologist who works at the State University of New York at Buffalo. Dr. Danielli received worldwide publicity, both praise and concern, last December when he announced, with Drs. Joan Lorch, Kwang Jeon and Charles Ault, the first synthesis of a living cell (SN: 12/12/70, p. 443).

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Danielli: Maybe 20 years away.

Dr. Danielli is one of some 20 scientists in the world actively working toward life synthesis. Yet contrary to opinion in many quarters, he is taking cell parts out and reassembling them not to control humankind but to understand how a cell works. "Only when we arrive at some theories of the genome [set of genes in a germ cell] can we hope to safely repair defective parts."

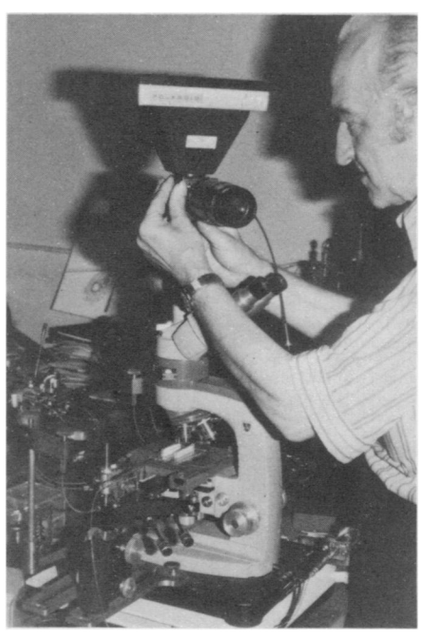
Actually the underlying revolutionary temper in biology isn't altogether science fiction and press fabrication, Dr. Danielli said in an interview, because biology, during the past century or so, has been turning from observation to analysis to synthesis. Scientists are now entering the age of biological synthesis, he says, but they must first arrive at some general theories on the basis of observational and analytical data amassed so far. Presently Dr. Danielli is trying to develop such theories, and to encourage molecular biologists to come up with techniques which will provide the basis for genetic engineering.

As now practiced by biologists on lower animals and plants, genetic engineering means minor alteration of a cell's nucleus or more basic genetic material. This is usually done with surgical techniques, although viruses have been tried.

The most immediate practical spinoff of such efforts, Dr. Danielli predicts, will be to create a plant rich in those amino acids that humans need. Yet Dr. Danielli believes that genetic engineering will eventually mean artificial assembly of human genes and chromosomes to replace defective ones. At least this is his anticipated hope. Cloning, or duplication of identical organisms, as has been achieved with frogs, is not genetic engineering in the real sense, he asserts, nor are efforts to create test-tube babies, although cloning and creating life in a test tube are often canopied under the heading of genetic engineering.

Still, Dr. Danielli admits it will probably be 20 to 50 years before human chromosomes with defective genes might be replaced. Yet he is confident human genetic engineering is coming. "If you started thinking about gas molecules, you would never attempt chemistry," he says. "Similarly if you get caught up pondering that there may be as many as a million genes in a human cell, you would never tackle genetic engineering."

Standing in sharp contrast to Dr. Danielli, who believes in striking out to meet a challenge, however problematical, is New York University's M. J. Kopac. A jazz pianist before becoming a scientist, Dr. Kopac subsequently studied under Dr. Robert Chambers, a New York University biologist and a pioneer in cell surgery. Like Dr. Chambers, Dr. Kopac staunchly follows the philosophy that a scientist



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Kopac: Gene surgery not imminent.

must know as much about a cell and microsurgery as possible before seriously considering manipulating human genetic material. Dr. Kopac has been less optimistic than Dr. Danielli about the prospects of human genetic engineering. Yet he has designed or improved on some of the most intricate microsurgical instruments in the world and has passed ideas on microsurgery on to other scientists to pursue in their own labs.

Although Dr. Kopac admits that correction of genetic diseases, by operating on human genetic material, is the ultimate goal of microsurgeons of his genre, he stresses that such advances are far from imminent. In operating on the nucleus or more minute genetic material of either animal or plant cell, various critical factors must be considered, he explains. Will the cell surface withstand puncture? What kind of nuclear surgery will be tolerated? Should the microneedles or pipettes penetrate the cell and nucleus rapidly or slowly? How many needles or pipettes should be used? From what angle will they best probe and excise? Has the operation been properly recorded with still or motion picture photography? Will the cell recover? Can the operation be repeated successfully?

Dr. Kopac was at first skeptical when he heard Dr. Danielli had "synthesized a cell." After all, biochemists for several decades have been experts at taking living systems apart and reassembling some subsystems. Dr. Kopac no longer doubts Dr. Danielli's achievement but asks, can he repeat it? Dr. Lorch replies: "We can repeat the assembly of an amoeba from nucleus, cytoplasm and cell membrane, although it is still technically difficult, and we have not gone beyond this feat to break down the cytoplasm into its constituents."

All these factors must be considered, and more, Dr. Kopac stresses, if cell microsurgeons wish to engineer human material. Dr. Kopac's team has been trying to manipulate mice-egg chromosomes to change the sex of the fetuses. "Our success so far," he admits, "has by no means been howling."

Dr. Kopac believes much more will have to be known about human genes—where they are located on various chromosomes, what they control—before microsurgeons start tampering with human genetic material. Actually such manipulation is already possible on human somatic (nongerm) cells, should some scientist really get the urge. Dr. Kopac says that while no one actually knows how many genes are found on each of the 46 human chromosomes, he puts the number at 100,000.

Some 100 human genes have been identified for what they do, a handful of them have been located on the X sex chromosome, and a select few of these genes have actually had their precise geographical location on the X chromosome mapped. Yet even when the day comes when a number of human genes have been identified, located and mapped, Dr. Kopac believes, surgery on these genes would be exceedingly risky. The naked eye can see one mouse egg in diameter. The light microscope magnifies this egg 500 times, revealing its chromosomes. The electron microscope reveals the helical DNA chains on these chromosomes, but where individual genes start and stop on these DNA chains is not known. The band of DNA that can be seen under the electron microscope is roughly 25 angstrom units in diameter. A gene might stretch 10,500 angstrom units along a DNA chain—or 420 times longer than the cross section of the gene (DNA) which can be refracted at one time. But even if the electron microscope were refined to magnify a whole gene, Dr. Kopac states, existing microneedles and pipettes would be grossly inadequate for operating on a single gene.

Still, assuming scientists will soon, or someday, get to where they can improve on human genes with surgery, they will be faced with performing this surgery on the human egg cell shortly after it is fertilized, before the cell divides many times. Although it is not yet possible to tell when fertilization occurs in women, it is possible in female mice.

Like Dr. Kopac, Dr. Bentley Glass, a geneticist at the State University of New York at Stony Brook, says in regard to what he interprets as genetic engineering—alteration of the gene in the genotype by some kind of substitution of DNA—"I do not think we are anywhere near that." However, he believes scientists are much closer to fertilizing a human egg in the lab and implanting the embryo into a foster mother.

Similarly Dr. Theodore Dobzhansky, a geneticist at Rockefeller University, says that genetic engineering in its narrow sense—"artificial change of the gene"—won't be possible on human material for a hundred years at least.

Whether genetic engineering is around the corner or not, a more basic question presents itself: Should scientists be moving in this direction? Not a few people feel that the more profound areas of life should be off-limits to scientific experimentation. But genetic engineering could ultimately mean correction of genetic diseases, and Dr. Joshua Lederberg of Stanford University asserts that such an attitude is as prejudicial as thinking of surgery as "anatomical manipulation," education as "psychological control" and scientific nutrition as "molding a superbaby." In any event most scientists believe that man was made to discover all he can, and it is up to society to decide how the knowledge is to be applied.

Nonetheless, Dr. Danielli admits that genetic engineering achievements could be abused like any knowledge. Having worked on the therapeutic side of chemical warfare in World War II, he particularly fears abuse by the military. Still he, Dr. Kopac and other prospective engineers of human genetic material concur that public opinion will determine the future of genetic engineering.

To assist the public in making informed decisions, centers for probing ethical problems raised by the New Biology have been formed—the Life Sciences and Social Policy Committee of the National Academy of Sciences and the Institute of Society, Ethics and the Life Sciences at Hastings-on-Hudson, N.Y. Some of the foremost participants in these groups are precisely those scientists contributing to New Biology. Dr. Dobzhansky, for example, is on the board of directors of the Hastings-on-Hudson center. The New Biologists, contrary to their science fiction image, are deeply concerned about the power they hold to shape human destiny and are anxious to see that their achievements are not abused. □

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Lorch: "Life synthesis" confuses the public. "Cell reassembly" is better.