SPECIAL FEATURES

1981: Molecular Genetics Comes of Age

Joshua Lederberg
President, Rockefeller University, New York, New York

The biology of *DNA*, the science of molecular genetics, has for the general public been a quiet sideroad on the map of "pure" scientific research for the last four decades. In 1981, it exploded into public prominence. A host of practical applications of this arcane science were announced in medicine, agriculture, energy, and the chemical industry.

Only 37 years ago, O. T. Avery, Colin MacLeod, and Maclyn McCarty at the Rockefeller University discovered that DNA was the substance that carries genetic information in bacterial cells. This finding changed the direction of all fundamental biological research. With renewed confidence scientists have striven for *chemical* explanations of structure and function in cells, tissues, and organisms.

DNA was discovered by the German pathologist Miescher in 1865. It was found to be a gummy nitrogenous substance of very high molecular weight which formed stringy threads in solution and was somehow associated with the nuclei of living cells.

But it took almost another 75 years for proof that DNA, rather than the protein and other substances in cell nuclei and chromosomes, was responsible for determining the genetic characteristics of the cell and, indeed, of all organisms. This discovery in 1944 promptly stimulated much more incisive research into the structure of DNA, culminating nine years later in the famous *double helix*, a structure proposed by Watson and Crick on the basis of the images produced when X-rays are scattered by specimens of DNA.

During the last thirty years, research into many new methods of chemical analysis and for the manipulation of segments of DNA has been carried on in laboratories throughout the world. Today we have a fairly comprehensive picture of the way this master substance is accurately reproduced at the moment of cell division in order that the information of the parent is precisely and accurately distributed to both daughter cells.

Scientists also sought to relate their findings on the DNA of simple viruses and bacteria to more complex organisms, including human cells. A further consequence of DNA research has, therefore, been the enrichment of what we know about the general biology of simpler organisms, as well as the molecular structures common to all forms of life.

At the present time, scientists believe that only about 1% of the DNA in our body is informationally active. The function of the remaining 99% is obscure; it may simply be "filler." The one percent, which contains about 30,000,000 nucleotides in our 23 pairs of chromosomes, is sufficient to provide the informational code for about 100,000 distinct proteins. The complexity of the research task before us can be measured by the fact that we now have detailed knowledge of less than 1,000 of these proteins.

The scientific task before us can be compared to rearranging a haystack, every straw of which is important but only one of which may correspond to the particular protein in which we are interested. One of the important recent advances in genetic engineering has been the ability to cut up or segment the huge DNA filament into a large number of manageable "straws," each of them containing a limited number of genes or units encoding a single protein. A familiar task in many laboratories today is to search for one particular straw in the huge haystack—a search that has been successful already in synthesizing such important substances as insulin and interferon. The most exciting applications of this technology are in the preparation, on a large scale, of human proteins which would otherwise be extremely costly, if not impossible, to procure.

Insulin. Insulin may be the first of these proteins on the pharmaceutical market. There is already a well-authenticated demand for it and there are a large number of diabetic patients who can benefit. Today, insulin is procured almost entirely from the pancreases of pigs, goats, or cattle and these substances, although closely related, are not identical to human insulin. While most scientists believe there will be definite advantages in using a substance identical with human insulin in place of its animal equivalents (and it is most unlikely that there will be any disadvantages!), this will not be known for sure until large-scale production and trial of biosynthetic insulin is achieved during the next few years.

Interferon. A far more precious substance than insulin, since it can be produced only in microgram quantities even from large quantities of tissue cells, is interferon. It is certainly effective in mitigating some virus infections and has had some promising results in the treatment of some forms of cancer. However, we will not know its full applicability in medicine until it also is available on a large scale for clinical trial and application. One of the more important findings about interferon is that it represents a rather large class of substances rather than one, and this encourages optimism that several variant forms of interferon will be found, each of them perhaps having an important role in medicine.

Other Applications. Besides these human proteins, genetic technology will produce an ever-increasing number of vaccines that would otherwise be most difficult to obtain. A vaccine for hoof-and-mouth disease (a serious affliction of cattle) is already in test. Improved vaccines for hepatitis and influenza will certainly be in clinical trials in the very near future. Vaccines for difficult diseases like gonorrhea and malaria are more speculative, but leads toward their development are promising and particularly important because they would be very difficult to produce by other approaches.

The engineering of microbial strains will also have important applications in the energy and chemical industries. For example, we are seeing even more efficient ways to produce fuel alcohol, not only from corn starch but also from cellulose waste. Improved processes for the production of crystalline fructose—a cheaper and slightly less caloric alternative to cane sugar—have also been announced. These are surely only the first innovations in this sphere.

DNA technology for plant cells is less advanced, but together with other innovations, it also promises a revolution in plant breeding. This will result in new crops, enhance the efficiency of fertilizer, and develop croplands that are now marginal. With the looming pressures of population on food supply in many parts of the world, and the precariousness of reserves which could be imperiled by one or a few bad crop years, these promising developments may come none too soon to protect mankind against recurrent catastrophe.

Genetics and the Law. These developments have proceeded so quickly that we are still catching our breath with respect to the legal and institutional framework which will mold this progress. Questions like the proper place of patent rights in specifically "engineered" microorganisms; the relative roles of government, the universities, and of industry; the conflicts that will arise as between the different legal systems of different countries in a large international market—these are some of the issues that will be at the center of attention during the next decade.

Although public attention naturally focuses on technological advances that have prompt practical applications, these may not be the most important result of the new genetics. The same research that has such value for industry is equally indispensible for the rapid unraveling of many scientific puzzles. Already, very important new information about the genetic basis of antibody formation, and its aberrations constituting a whole family of immunological diseases, has been found. The evolution of the aberrant genes that are connected with sickle cell and other hemoglobin diseases has been traced. Very important advances in our understanding of cancer as a lesion within the DNA of afflicted cells permitting them to escape normal bodily regulation have been made. There is no aspect of embryonic development and of aging that is not profitably being studied with these more powerful tools; and we can soon expect revolutions of insight that will be even more important than the revolutions of production in the field of biology.

The DNA technologies have already shown that it is possible to find molecular labels for individual chromosomes. This can be done to such an extent that we will soon be able to trace in a given pedigree exactly which offspring have received segments of which chromosomes. It will then be possible to trace correlations of genetic factors like heart disease or intelligence through particular chromosomal labels. Once this is done, we will be able to help people to avoid specific risks and to design individual educational strategies. Probably far more important, we all gain a better understanding of the development of these traits.

Paradoxically, the most important application of this insight is not to *do* genetics but to *transcend* genetics. At the point that we understand the operation of a specific genetic factor in the development of the individual, we can design the environmental interventions that can compensate for and enhance the working efficacy of the particular genetic code with which that individual begins his existence.

1982

INFORMATION
PLEASE
ALMANAC
ATLAS & YEARBOOK

NOV 16 1981