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DEVELOPMENTS IN CONTEMPORARY BIOLOGY

The term "biology" was introduced in 1802 by a German, Treviranus, and by a Frenchman whose name would remain well known to posterity, Jean-Baptiste Lamarck.

Just as in any other scientific discipline, it is obviously impossible to locate precisely what marked the beginnings of biology in terms of actual realizations and concepts. At the beginning the life sciences, when not of a strictly theological inspiration, were derived from practical considerations. These arose quite naturally from an awareness of the human body and its diseases, its nutrition, its survival. On the one hand there was man and his anthropocentric, animist or mystical vision of living things, and, on the other, animals and plants. We cannot yet speak of sciences as such. The term "art" would be more appropriate, for this was much more a matter of a "corpus" of recipes that, in the

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case of medicine, depended on the services of the barber and, for the vegetable world, on the work of the farmer. However, Antiquity had seen some remarkable precursors, often subjects of ingenious premonitions. Democritus, for example, six centuries before Christ, had the intuition that psychic activity emanates from the brain and not from the heart. Hippocrates described epilepsy. Herophilus and Erasistratus, in the 7th century, were dissecting cadavers and learning with astonishment that nerves originate in the brain and spinal column, and not in the heart. A Greek doctor, Galen, around the year 50 A.D., discovered the grey substance that he called "ventricles of the brain". He was, in fact, one of the first persons to propose a natural cause for diseases, thereby contradicting religious explanations attributed to them since Antiquity. In the 15th century, an Italian doctor, Fracastor, born in Verona, devoted his initial experiments to syphilis. Vesalius, in the 16th century, developed anatomy, publishing his fascinating work on the construction of the human body; and Harvey, in 1628, discovered the circulation of the blood.

Comparatists and Evolution

But everyone seems to be in agreement with the fact that the life sciences were truly developed by naturalists in the 18th century. First of all it was necessary to determine the similarities between the enormous variety of species and, in order to do this, to establish classifications that brought out clearly the first principles of phylogenetic units. The distinction between botany and zoology probably came about as a result of the work of Carl Von Linné, the botanist doctor of the King of Sweden, a great naturalist who invented binary classification. Buffon published his *Histoire naturelle* between 1749 and 1778; he is no doubt the first person to deserve the name biologist. In fact, not content simply to classify, he attempted to explain his observations by proposing that a gradual evolution, based on widening filiation from the beginning, links all known living species.

We know how Lamarck viewed evolution. Opposing the partisans of "fixism" or of "catastrophism," such as Linné and

Cuvier, for whom species appeared abruptly, with no interdependence and without the environment intervening as cause of this evolution, Lamarck became the champion of transformism, based on the heredity of acquired characteristics. His hypothesis was to be proven wrong, but it at least had the merit of bringing about a profound analysis of the mechanisms at play in phylogeny.

Cellular Theory—Spontaneous Generation—the Birth of Genetics

Around 1859 Charles Darwin published *The Origin of the Species*, in which he stated that natural selection is responsible for characteristics that serve to differentiate the various species today making up the living world. We can thus say that theories of evolution were the first to state our knowledge of living beings. Naturally we should not overlook cellular theory, expressed in 1839 by Schwann and which stated, "All life emanates from a pre-existing cell". This theory assumed great importance in the work of Louis Pasteur. In Pasteur's day several biologists were still fervent believers in spontaneous generation. Van Helmont, a Belgian, was remembered in his times for having proposed the spontaneous generation of leeches, snails and frogs from swamp muck, and that of mice through "the transmutation of a sack of grain wrapped in a dirty cloth"! L. Pasteur, a follower of Schwann, provided a brilliant confirmation of cellular theory by applying it to explain the most common diseases of that time, namely infectious diseases.

But at the beginning of the 19th century an astonishing development occurred with the discovery of the laws of heredity by Gregor Mendel. It was in 1866, when Pasteur was in his prime. By showing through his experiments in cross-breeding peas that hereditary characteristics are borne by invisible elements, sorts of particles present in parental cells, Mendel introduced the first reductionist explanation of heredity. Johannsen in 1860 gave these particles the name "genes"; and Morgan and Müller, Americans, demonstrated that they are present in our chromosomes. Genetics was born.

We can say, then, that biology acquired its full status at the end of the 19th century. Heredity, evolution, reproduction and the diversification of species began to be explained.

But life is not only reproduction. By 1920 another intellectual concern was apparent. How does a cell function? Until then biology had developed rather much in a "closed circuit," so to speak. By that I mean that it had already achieved a certain degree of formalism (for example by drawing on statistics to explain the distribution of hereditary characteristics in early generations, by establishing the existence of phyla, genuses and species, and by recognizing cellular unity in all organized living beings). But, apart from the ideas of Mendel (that were forgotten and ignored for forty years), biology was overall more descriptive and holistic than reductionist and explicative.

Chemical Reductionism and Biochemistry

Several attempts were made, however, to reduce biological complexity to simplified referential models. After the theories of Descartes on the animal-machine, after the trend of robots and then of cybernetics, and finally cellular energy under the instigation of Lavoisier, hope was born that properties of living things could be explained from the chemical components that can be extracted from them. In 1828 Whöler successfully completed the first synthesis of a substance from the inanimate kingdom and yet characteristic of living beings: urea. Pharmacological "powers" of plants were attributed to the chemical properties of defined molecules; these included narcotine extracted by Derosne in 1817, morphine extracted by Pelletier, then emetine and quinine. The first enzymatic juices were described by Büchner, who extracted the first enzyme, zymase of yeast, in 1897, earning him the Nobel Prize in 1907. Summer was the first to succeed in crystallizing an enzyme, urease, and then was it realized that cellular life is catalyzed by definite molecules, proteins. Biochemistry was born. A new era of life sciences, biological kinetics and thermodynamics, began with the work of Michaelis and Henry. The problem was to learn if life conforms to the principles of thermodynamics. Life is

the catalyst, the enzymes are catalyzers. To supply all the energy for this there is ATP.* The chemical unity of all living things was gradually discovered before World War II. For example it was noted that the energy processes of two phenomena as dissimilar as the fermentation of sugar by yeast and muscular contraction obey the same mechanisms and employ the same chemical intermediaries.

In the early forties, biologists thus had the illusion of having explained everything and of having revised the basic "logic" of living things (an error committed regularly in the history of the sciences!) Everything did seem simple. Genes control enzymes, which control cellular functions. Researchers did not suspect that the real conceptual revolution was yet to come and that there was still a long road to be followed before distinguishing the most important characteristics, or even laws, relating to biological systems. Until then biology had been primarily a science of inventory and classification with 19th-century comparatists, a statistical science with the geneticists and an analytical science with pre-war biochemists; now it was to become the science of "codes," strangely related to micro-electronics and data processing.

Birth of Molecular Biology

The principal question was, "what are genes made of"? What is their physical-chemical structure? What is the code to their diversity? After statisticians, chemists and thermodynamicists, solid physicists and crystallographers had the most to say. Biology became molecular. "What is life?," asked the great physicist Schröedinger. In 1952 Watson and Crick supplied an initial element of a response. Life can be explained by genes, and genes are present in a very long molecule shaped like a double spiral and inserted into every cell: DNA. Its structure was quickly confirmed

* ATP: adenosine triphosphate, primary chemical intermediary in metabolic energy reactions.

by X-rays. It was then noticed that this same structure can be used remarkably well to explain the transmissibility of characteristics at each cellular division since the molecule has double symmetry and is formed of complementary chains capable, after being separated from one another, of forming two double spirals when brought together, identical to the original structure.

From that point on discoveries multiplied at an implacable rate. In barely more than a decade, the genetic code was broken along with the regulatory circuits, mechanisms for transfer of genetic information and the formation of protein; messenger RNA was discovered, and the complexity of the reproductive systems of genetic matter at the molecular level was unraveled.

Biology had certainly become more precise. Biologists and physicists could now speak the same language. But by doing so, biology and biologists, to a certain extent, cut themselves off from the world, meaning by that from certain concrete realities proper to the socio-economic realm. Biology had become esoteric and, with very few exceptions, around 1955 society was little interested. Biology had become a matter for an elite. There was a feeling that by reducing life to molecular interactions, life sciences had passed over the major questions involving man, his health, his well-being or his environment.

Biology of Growth and Pathology

A whole series of causes, however, (the relative importance of which is difficult to appreciate) was quick to restore molecular biology to the heart of social preoccupations. We can note here:

– the development of the post-war pharmaceutical industry, in large part due to the discovery of antibiotics;

– the reform of medical studies that tended to bring fundamental biology and medicine closer together. In this way disciplines that had seemed to be within the realm of doctors only (virology, immunology, cancerology, neurobiology) began to learn lessons from molecular biology. The term "biomedical" appeared. As Dr. L. Thomas, former director of the Sloan Kettering Institute in New York, noted ironically, "Doctors were flattered to see their

clinical activities take on the prestige of biology, thanks to the prefix 'bio-', while biologists hoped to find in medicine a new source for their research". In a certain manner the life sciences once again became "organismic". Their most significant objectives on this score were the study of infectious aggression or auto-immune diseases, the study of socio-professional diseases, of hereditary anomalies, of cancer, of behavioral problems, and, more generally speaking, of human reproduction and aging. Moreover, under pressure from consumer movements, there was a nascent interest in ecosystems.

But all of this does not suffice to explain the popularity of the life sciences today, nor their appearance at the center of the social stage.

Birth of Genetic Engineering

It was certainly in 1973 that the decisive turn was taken. That year saw the beginning of a new and revolutionary technique, formed directly from the molecular biology of the gene: "genetic engineering". For the first time the public as a whole would discover the life sciences and even realize that they are "disturbing," in the same way as nuclear physics. The world of decision-makers—politicians and industrialists—would become aware of the fact that a modern technology had been born, with important and even totally revolutionary practical consequences for the fields of health, agriculture, the environment, and that it represented a considerable potential for the macro-economic balance of the planet. Biology, until then a contemplative science, became an interventional science, sometimes even a "business" science.

Having thus traced very schematically the picture of the life sciences from their origins to our own times, I would now like to illustrate my point with a few examples of major realizations from among the most significant aspects of contemporary biology.

To do this I will refer to four sets of data that have to do with various realms of the biology of development and neuroscience. By doing so I am aware of neglecting entire sectors of knowledge,

particularly everything involving the conceptual revolution in the realm of vegetable cells.

Theoretical Consequences of Genetic Engineering

One of the most important consequences that resulted from the use of the technology of genetic engineering, in addition to being able to direct as desired the biosynthetic capacities of single-cell organisms, was the appearance of means for marking, called "genetic probes," which, when used, make it possible to draw a precise cartography of the human genome. Using the techniques of recombinant DNA, it is possible to clone larger or smaller fragments of chromosomes taken from animal or human cells into the cells of micro-organisms. The latter propagate and amplify the chromosome fragments so they can be sorted and purified. Once a sufficient amount is available for analytic research, two operations are possible. The first consists in characterizing these fragments by studying the manner in which they are split by a series of restriction enzymes; this is what is called the "physical cartography". The other consists in determining the chemical sequence, that is the sequential order of millions of constitutive elements; this is the "sequencing" operation.

Before the discovery of genetic engineering the existence of genes could only be deduced from the consequences of mutations taking place within them. A change in the pigment of an eye, in the morphology of a member, in behavior, or through being susceptible to a disease pointed to the existence of an hereditary trait. With its location on the chromosome discovered, it could also be inferred from studies of cross-breeding, based on the frequency of combination or segregation of characteristics during the recombination of parental chromosomes. This was only "indirect" genetics. At best coarse alterations in chromosomes could be observed thanks to optical or electronic microscopes: breaks, transposition, amplification. On the other hand, after 1973, genetic engineering made it possible to "materialize" a gene. Although it represents no more than one millionth of a human person's hereditary patrimony, it can now be purified like a molecule; it

becomes accessible chemically and physically speaking. It is not only possible to analyze it, but, as everyone knows, to manipulate it, to subject it to microsurgery thanks to restriction enzymes. In short it can be treated like an ordinary molecule, even though, it should be stressed, its structure remains complex.

The consequences of this are multiple for the basic knowledge of living things. I can cite the discovery of genetic mechanisms that are at the origin of the diversity of antibodies, the fine study of the genetic polymorphism of individuals, the discovery of cancer genes, or oncogenes, to which I will be returning. But for the moment, let us look at the medical consequences; I wish to speak here of the study of hereditary diseases.

Medical Applications of Genetic Engineering—Hereditary Diseases—Prenatal Diagnosis

In France each year thousands of children are born suffering from serious, often fatal, hereditary diseases. Such afflictions are responsible for about half of infantile mortality: myopathy, mental problems, metabolic intolerance, muscular dystrophy, blood diseases, fragility of the X chromosome, serious auto-immune deficiencies of "bubble" children. And this is but the tip of the iceberg. In fact, as our knowledge grows, doctors and biologists note that already at birth our genes contain numerous risk factors, or a susceptibility, even though they may not contain the severe mutation responsible for monogenic diseases. The discovery of genes with properties for controlling compatibilities of organ or of tissue transplants between individuals (Dausset) has shown that certain mutations within these genes considerably increase—in certain cases by a factor greater than one thousand—the probability for the individual to develop serious diseases (spondylarthritis, rheumatic fever, auto-immunity, etc.).

However, the possibility of establishing the chemical sequences of genes or their physical organization provides enormous perspectives for prenatal or preclinical diagnosis. Such "detection," as clinicians call it, was already possible through study of the karyotype or the enzymes, but these tests are not very reliable and,

especially, can only be performed very late in the development of a fetus. On the other hand, diagnoses using genetic probes can be performed by the eleventh week. More than ten serious diseases can thus be detected and the type of mutation specified.

This "new genetics" may also lead to an enormously vast project, whose nature and premises are presently exciting American opinion almost as much as the problem of AIDS. This is a project that consists in establishing the sequence of the three and a half billion chemical elements that make up the complete genetic code buried in the forty-six human chromosomes. It is hoped to be able to localize a very large number of mutations responsible for hereditary diseases whose causes are yet unknown. Out of nearly three thousand described hereditary diseases, barely more than a few dozen can be "localized" precisely with regard to corresponding genetic alterations. Out of the one hundred to one hundred and fifty thousand genes in man, barely one thousand five hundred have been localized, but we know the sequence of only five hundred of them. Is such a project justified, when it would cost three billion dollars and mobilize hundreds of researchers for ten to fifteen years? We will not get into that discussion. However, this example makes it clear to what extent the techniques of recombinant DNA have revolutionized genetics. And we still have not spoken of the prospects of "genetic therapy". It is perhaps known that for five years now biologists have demonstrated that a foreign gene transferred into a somatic cell, such as the lymphocyte cell of human bone marrow, can function normally. This led to the idea of compensating for defective genes by transplanting "normal" genes, implanting in the patient marrow cells that include the "normal" gene. Specialists estimate that this genetic prosthesis can be envisaged shortly, particularly in order to save immunodeficient children. The transfer of a non-altered gene into a fertilized ovocyte, followed by reimplantation into a surrogate mother to obtain descendants in whom a serious hereditary risk would be overcome definitively, naturally raises an unsettling series of ethical problems. These are in addition to the already difficult issues surrounding the practices of *in vitro* fertilization and surrogate motherhood.

Oncogenes and Recent Theories on Cancer

Molecular biology and genetic engineering have opened another area of human biology and medicine: that of cancer.

With the discovery of a particular category of genes called "oncogenes," a discovery that dates back barely a dozen years, it is now possible to explain for the first time the genetic origin of cancer and its unexpected appearance as a result of mutations or viral attacks. We cannot linger here to examine this very important problem, but first we should note what Philippe Meyer has stated. "The discoveries that have just been made are not simply an enhanced description of the damages of cancer. These are discoveries that can be termed 'key', that can lead to the development of totally new therapeutic strategies. An objective analysis of the state of anti-cancer research makes it possible to affirm that an early victory over cancer is not impossible."

It should be recalled that the principal families of carcinogenic viruses were isolated during the first half of this century. The first of this kind was described in 1914 at the Rockefeller Institute of New York by the American biologist Peyton Rous who identified a virus capable of causing a sarcoma in a chicken in a few weeks. Since that time more than thirty carcinogenic viruses have been isolated. In the last ten years there has been a growing conviction that many human cancers are linked to oncogene viruses. The best known are the Hepatitis B virus, frequently associated with early cancer of the liver in tropical zones; the Epstein-Barr virus, responsible for cancers of the jaw in Africa and Asia (while in Europe it only causes a benign disease, infectious mononucleosis); papilloma viruses responsible for neck cancers. But we should also mention the RNA viruses or retroviruses. Among these have been discovered the agents of leukemia (HTLV1 and 2) and the viruses responsible for AIDS, called LAV, HTLV3 or HIV, which are also responsible for certain cancers like Kaposi sarcoma.

It was noted that the carcinogenic power of these viruses was linked to the presence of a particular gene in their genetic matter. However, in 1976 there was great surprise at the discovery that all animal cells (including human cells) normally include in their chromosomes genes that are very close to cancer genes previously

detected in viruses alone. Among the several hundred thousand human genes, barely more than thirty oncogen genes have been discovered. This discovery already provides explanations for phenomena that are extremely important for understanding the mechanisms leading to a tumoral condition.

1. If carcinogenic viruses include cancer genes, this means they "stole" them from the cells they had previously invaded. These viruses are, so to speak, cellular sub-products that have acquired a certain degree of autonomy.

2. Most agents responsible for the appearance of cancer (viruses, chemical agents, mutations, etc.) owe their properties to the fact that they activate and deregulate the normal function of certain cellular oncogenes.

3. Since deregulating cellular oncogenes can lead to the appearance of extremely diverse cancers, that is manifestations of deregulation in cellular growth, we are led by symmetrical reasoning to believe that under normal circumstances oncogenes have a central and permanent role in the control of the cellular processes of division and recognition.

It has in fact been demonstrated that oncogenes are nothing other than genes for communication between cells. Some encode growth factors for the exogenous chemical signals involved in the process. Others determine the production of receivers for these signals, receptors located in the cellular membrane. Still others produce substances that, once the signal arrives at the receiver, "carry" it to the chromosomes so that cellular division is begun. These substances are phosphorylation enzymes or proteins with a great affinity for DNA and capable of exercising a regulatory effect.

And so it seems that the development of a cancerous condition has been generally explained. Precise knowledge of the phenomena set off by the activation of oncogen genes should make it possible to conceive new inhibiting products that set themselves against cancerous transformation, perhaps opening the way to a new therapy, particularly since we have begun to discover that the activity of certain genes (TNF) seems directed at blocking effects brought on by oncogen genes.

But all has not been said in this matter. Some human cancer specialists are not convinced that the theory of cellular oncogenes

is sufficient to explain the appearance of the neoplastic condition in man, and especially the nature of tissue specificity found in primary cancers. Enthusiasm should be moderated somewhat. Nevertheless, it does look as if a major step has been taken toward explaining the cancerous condition.

Homeotic Genes and Embryonic Development

We could refer to many other important consequences that have resulted from the spectacular progress made in molecular biology of the gene. It would be necessary, for example, to discuss the extraordinary breakthroughs that have just been made, barely three or four years ago, in the realm of genetics of reproduction. Here it was discovered, or rather rediscovered, but with a more precise approach thanks to molecular biology, that the development of the embryo, from insects to humans, was "modular". In the first stages of such development, for example, we find that the fly embryo is composed of stacked "discs"; that the human embryo has, in certain regions such as the mesoderm, segments known as "somites" with a very precise embryological role.

But each of these modules possesses an autonomous genetic determinism and can, under certain conditions, for example as a result of certain mutations, evolve "on its own," which leads to morphologically abnormal individuals. Genes that control the identity and future of segments are called "homeotic". Several homeotic genes correspond to each module. In general embryogenesis is normal because these homeotic genes communicate among themselves thanks to a complex series of chemical sequences of interaction. But if this does not happen, a malfunction occurs that opens the door to teratogenesis. For the first time a sturdy bridge has been constructed between embryogenesis, a hitherto descriptive science, and genetics. This is a major breakthrough in the study of development.

It would be necessary also to describe the remarkable progress made in the study of the *differentiation of tissues* and particularly the results of biologists analyzing genetic regulation of higher organisms. The discovery of regulatory sequences present on the

chromosome and acting at a very great distance from the genes themselves (enhancers or silencers) and the discovery of proteins that attach themselves thereto, help explain the intimate mechanisms that ensure proper temporal functioning of our genes in the course of development of our tissues.

Neuroscience and Diseases of the Nervous System

I would, however, like to conclude by borrowing from a no less fascinating area, neurobiology. No one will contest the fact that, organized beings that we are, there are two "master objects" that account for most of our characteristics. These are our genes and our neurons. And naturally the nature of the "gene-neuron" dialogue is a central problem for biology.

"The term 'neuroscience' is relatively new", remarked Paul Laget, professor of psychophysiology at the Pierre and Marie Curie University. "Only shortly before other terms were preferred, such as neurochistology, neurophysiology, neuroanatomy. This globalizing neologism brings to light the necessity for a pluridisciplinary approach resulting from growth in our knowledge from study of the functioning of the nervous system." But this progress, in the second half of our century, and most especially in recent years, has been remarkable!

It would be completely misleading to try to be exhaustive. But before furnishing a few significant illustrations, we can ask what were the reasons for a trend in favor of the neurosciences. With Paul Laget we can find at least three:

– The necessity to produce new methods of treatment for diseases of the nervous system since these included no less than several hundred affections resulting from hereditary changes.

– The nature of the social problems confronting our civilization, particularly the return to phenomena of violence, which has led neurophysiologists like P. Karli to study the physiological bases for aggression, for example.

– The greater accessibility of life sciences and neurobiology (in relation to the physical sciences), which makes it easier to "popularize" them and contributes to making them part of what is necessary to be an educated man in our day.

I will not dwell on the formidable arsenal of physical techniques that have made it possible to remove material obstacles to the study of the human brain: gaseous encephalography, arteriography and especially tomodensitometry, imagery by magnetic resonance, the use of position cameras. We should likewise mention the enormous progress made in microscopic observation of neurons.

But even if we limit ourselves only to technological aspects, it is undeniable that here again there are two principal disciplines of modern molecular biology—immunology, with the use of monoclonal antibodies, and especially genetic engineering—that have accelerated the study of the neurons. By now most important proteins and neuropeptids have been cloned. Genetic probes achieved have made possible extraordinarily fine analyses of the biosynthetic activities of isolated neurons and specifying the molecular structure of mediators and even more so that of receivers and ionic channels.

Thanks to the combined efforts of biochemistry, genetic engineering and pharmacology, the idea has gradually taken root, over the last decade at least, that nerve cells can not only transmit information of a physical nature, such as potentials for action, but also of a chemical nature. Certainly the speed of this chemical transmission is slow (a few mm/hour) relative to the speed of nerve impulses (several meters/second). But it is considerably important because it is much more diversified. Today, in addition to classic neuromediators (ach, noradrenalin, etc.), we know of some twenty neuropeptids. Since each neuron can secrete combinations of neurotransmitters, we believe this represents one of the explanations for the diversity of transconnectional information, in addition to well-recognized neuroanatomical diversity.

Without going so far as to say that the brain secretes thoughts like the liver secretes bile, we must admit that discoveries relative to the fine biochemistry of neurons had important extensions into pharmacotherapy (e.g. use of largactil, l-dopa, valium, etc.).

Nevertheless, it is too early to say if reductionist enthusiasm in this realm is exaggerated or not. Psychophysiologists think that conceptions in the realm of the molecular biology of the neuron will be like the past vogue for micro-electrophysiology. In any event, a new field—that of molecular neurobiology—is now open,

and it has already yielded a great harvest of fruits.

But we must never forget the pluridisciplinary nature of neuroscience. Without recourse to neuroanatomy, neurophysiology, neurohistology and the study of neuropathological behavior or affections, it would be useless to hope to understand major cognitive functions and memory.

But it is also true that behavioral genetics is in full development as well. Naturally it can only explain simple behavioral stereotypes, such as the song of a cricket, reproduction of aplysia, short term learning in the drosophila and its memorization, etc. Obviously the study of neurogenetic diseases (for example thanks to recent breakthroughs concerning the localization of mutations responsible for Huntington's chorea or Alzheimer's disease) is only in its early stages, but we sense new prospects taking shape for modern neurogenetics, as disturbing for their ethical implications as they are filled with hope for the medicine of tomorrow.

The Ethical Dimensions of the Problem

My presentation has left in the shadows many aspects of an emerging biology as well as already existent biology. I have not spoken of the immense area of biotechnological applications. It would have been necessary to cover the new pharmaco-medical paradigm that genetic engineering techniques allow us to surmise, by forging a number of molecules endowed with new therapeutic activities. I have not mentioned the vast sector of microbial genetics, nor the molecular revolution now being experienced by vegetal biology, long left on the sidelines of the major modern breakthroughs. For example, we are beginning to know how to perform transgenosis in plants, to understand the chemical communications set up between them and symbiotic bacteria. The physical plan of vegetal genes is now accessible thanks to genetic engineering. It could well be (and the probability here is great) that the next millennium will see prodigious developments in vegetal genetics, with results that are good or bad, but definitely important for agriculture: we need only think of new micropropagation techniques.

Any respectable science—and here biology is only one example among many others—evolves with a sort of autocatalytic acceleration for reasons that can be easily imagined. But biology in a certain manner touches us even more profoundly. Emmanuel Kant wrote the following: "I see in biology a disposition of sensitivity that is quite favorable to morality and at least prepares us for it". Can we continue to maintain this opinion, to retain such a view of the life sciences, when we observe certain evident deviations in the past, present or to come, concepts and techniques developed from this science, such as scientific eugenics, degradation of living things, standardization of the living world through biotechnological procedures?

Genetic "Typing" of Man

Before dealing with the problem of eugenics, we must first discuss for a moment new procedures that make it possible to perform an extremely fine analysis of human genes, thereby leading to increasingly accurate predictions about the intimate characteristics of each individual.

Astonishing progress made in genetics has made it possible today, as we have seen, to have "copies" of genes called "genetic probes". These may be significant fragments of genes obtained by chemical synthesis methods. These synthetic probes are then produced by machines whose operations can today be reproduced and standardized. These may also be probes obtained from genetic engineering processes. In any case, thanks to these chemical copies of genes as determined by biologists, it is possible, using a special molecular "molding" process called hybridization, to test the degree of functionality of the gene for which we have a copy. For example, hybridization with a probe of the hemoglobin gene of an individual's chromosomes provides exact information about the presence or absence of mutations in this gene. Any alteration, even minimal, will be expressed by easily measured changes in the nature of the hybrids. The techniques employed do not require complicated equipment; they only depend on the availability of the probes. Before too long it will be possible to perform them in

pharmacies or in a physician's laboratory as hybridization procedures become more standardized.

In 1974 two American doctors, Kan and Dozy, were no doubt the first to apply hybridization techniques to human pathology by looking at genetic alterations affecting the properties of hemoglobins.

Since then use of genetic probes to study the human genome has expanded, and we have already described the applications that have begun to result for detecting hereditary defects or alterations. From the early Seventies to the present time, the number of prenatal diagnoses performed in France has increased from around twenty to several thousand today. It is possible to detect nearly a dozen serious diseases either in the early stages of pregnancy or in women who risk being "carriers" because of a mutation in an important gene of their X chromosomes.

The trend toward systematic testing is growing. This is based not only on a desire to advise couples about the advisability of procreating when one member of the couple comes from a "risk" family, but also, and certainly even more so, in order to be able to develop predictive medicine! Its purpose will be to have available a sufficient amount of genetic data about the fetus to plan when necessary for certain forms of treatments, from the moment of birth, or at least to anticipate more frequent medical observation.

Sequencing the Human Genome—Eugenics

It is all the more evident that there is an increasing trend toward *avant-garde* genetic diagnostic practices given that we are moving toward almost total knowledge of the human genome (see p. 10). The question being asked, however, is this: to what extent does this trend, inspired by preventive public health considerations, exceed its objective? When relatively precise lists of the "genetic" formulae of individuals become possible, will there not be a temptation to put them to a more general use? As long as the rules of confidentiality are respected, the benefits (informing a family, planning early therapeutic measures) will outweigh the risks. But

if these rules should be transgressed, if access to these genetic files should be commonly opened up to insurance companies, employers, or even family members, we can easily imagine what would be the consequences!

An even more serious danger would seem to be that of so called "scientific" eugenics. Certainly it must be admitted that a certain form of eugenics occurs as soon as a serious threat appears to the life of an unborn child and genetic advice is sought. Nevertheless, everyone will react to the information provided by pre-natal diagnosis in accordance with one's personal feelings, personal ethics or beliefs. But given the systematization of the study of human genes and their comparative analysis at the individual level, we must be careful that there is not a gradual shift from control of hereditary characteristics of a pathological or fatal nature to control of hereditary characteristics that do not conform to a given norm, the norm of the ethnic majority, for example. However, although it is true that genetic polymorphism is the rule, in man as in every species, and that we cannot speak of a standard gene or a reference gene, we must recognize that the line is thin between a "mutated" and abnormally functioning gene and a mutated gene with normal or nearly normal functioning. If this shift should occur, there would be considerable expansion of prenatal diagnosis with the intention of standardizing the genetic patrimony of individuals. Prudence, and even in certain cases intransigence, is necessary if we wish to avoid practicing systematic molecular eugenics. While convinced that firmness and respect for the rules of medical ethics are perfectly compatible with unlimited acquisition of knowledge, I do not think, however, that conformity with these rules is automatic, no matter how pure the initial scientific effort. More generally, as we learn more about certain rules of molecular evolution in the human genome, or certain laws concerning the prevalence of hereditary anomalies in one or another group, there will be a growing risk of "categorizations". Once again it will require much wisdom in order to remain faithful to scientific truth while avoiding the dangers of ideological take-overs.

Industrial Use of Living Creatures—Biology and Merchant States

But the danger of seeing living beings "cheapened" by an attempt to reduce vital characteristics and behavior to genetic formulae can also arise from operations in another area of concern, that of the industrial production and use of animal and vegetable cells or their genes.

Jurists are particularly concerned with the patenting of micro-organisms and plants; in 1983 the United States court agreed that the isolation by Chakhrabarty of bacteria capable of breaking down certain chemical pollutants could be patented. Until then, because of the principle of inalienability of living beings, only inanimate objects could benefit from a patent.

Today jurists note that gradually, since the end of the last world war, there has been a progressive lifting of prohibitions against patent protection for living things, particularly microbial strains, plant seeds, etc. In general there has been, according to some, a sort of abdication of law to the pressure of bio-industrial imperatives. It is true that the argument advanced by leaders in the fermentation or seed-producing industry is that these are strains or seeds that have been transformed by man using new methods. Although authorities such as the EPA (Environmental Protection Agency) continue to hinder the use for commercial purposes of plants modified by genetic engineering or animals obtained through transgenosis, it is no doubt more because of pressure from unconditional opponents of this type of genetic engineering or for reasons of ecological harmony than for reasons stemming from the commercial nature of these modified biological objects. In fact, as this is being written, the United States has just granted two American researchers the right to patent a particular race of mice they produced in which mammary gland tumors appear spontaneously.

Thus the tendency to consider the biological world as merchandise rather than patrimony is growing. On the one hand we cannot avoid the observation that the new genetics, even more than the old (the one based on the techniques of cross-breeding and selection), is on the brink of producing transformations that should

prove to be of great economic and even bio-ecological importance (for example by leading to the elimination of pesticides or phytosanitary chemical treatments and perhaps even—in the very long term—to the reduction of the use of nitrogen fertilizers, etc.). On the other there is a risk of increased standardization of agricultural and horticultural consumer products due in particular to the extraordinary "identical reproduction" represented by cloning techniques. This could lead to an impoverishment of the natural genetic patrimony and also threaten the balance of trade with developing countries whose economy is based on exploiting local natural resources while maintaining their own specific characteristics.

Pushing the argument a little bit further, we can compare these observations to those surrounding the commerce of human organs. (Some would even point to the prospect of buying and selling fertilized ovocytes or viable embryos).

Biology and Respect for "The Other"

Between those who dream of science that can do anything, including redesigning species—even the human species—in order to attain a sort of biological paradise, and the Cassandras who see in science but a powerful menace that must be exorcised at any cost, there is fortunately room for an attitude more in keeping with the trends of contemporary society. This attitude rests fundamentally on the postulate of scientific progress. It favors unbridled but responsible research whose primary end is naturally knowledge (especially of man), but also knowledge that is inseparable from respect for "the other" (as well as respect for self).

Often it is said that science progresses faster than man. This impression is even very common and nourishes an ethic with increasing numbers of adherents and with growing support among political leaders who are beginning to take stock of the immediate impact of biology. That morality is unable to keep up with knowledge is not a new phenomenon; this is one of the cornerstones of philosophy. But, without analyzing the extent and consequences any further, I would come back quite simply to biology.

We will always have need of this science and of the methods on which it is based, no doubt even increasingly so if we hope to one day be able to answer the questions that challenge man and that have often haunted him since his origins. Where do we come from? Of what stuff are we made? What are our limits and how far can our hopes go? Obviously these questions exceed and transcend the biological dimension, but biology should be able to throw greater light on these matters.

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