The main scientific and technological advances that have increased our ability to act so as to influence biology and call into question our idea of what constitutes a human being, have been made in the fields of genetics, and of embryology and cell therapy. These two fields of knowledge have often been confused, but for the specialist involved in these kinds of research, they are entirely distinct, although some of the ethical problems that arise from them occur at the interface between these types of knowledge and these technologies. So, let us start by discussing the changes in medical prospects, and the questions that stem from our improved understanding of the genetic program of human beings as a result of the human genome project.

The genetic program

First of all, a brief reminder of some facts and concepts: on February 15, 2001 two competing consortia, one multinational and private, and the other a public university, published the almost-complete sequence of the human genome. According to the theory of evolution, the first living cell appeared on earth four billion years ago, and all living organisms are descended from this original life form. As a result, some biological properties are shared by all forms of life. From 1972/73 it became possible to develop methods based on the following principle: if all life forms are indeed derived from a single original cell, then the mechanisms by which the program is executed, which account for the biological properties of organisms, can also be expected to be conserved. As a result, a gene transferred from one living organism, to another, including one belonging to a different species, - or even another "kingdom" - can be expected to find the conditions it requires to function in its new environment. The methods used to transfer genes from one organism to another are known as genetic engineering. Genetic engineering became possible once tools had been created that could cut DNA, separate the genes, amplify them, determine their sequence and transfer them at will from one organism to another. What the concept of evolution made it possible to envisage, i.e. that this method would permit the genetic use of any living being to express part of the genetic program of another being, has indeed been confirmed. This method has also been used to achieve the sequencing of the human genome. The basic method consists of the following series of steps:

- To begin with, the DNA is cut into fragments, using special enzymes
- Each of these fragments is then inserted into bacteria.
- Each bacterium containing a fragment proliferates and after a few days yields colonies of several million cells. Each of these colonies also contains millions of replicas of the DNA fragment inserted into the bacterium used to produce the colony.
- This fragment of DNA can then be isolated and sequenced.

The genetic program is a message written using four letters: A, C, G and T. In what sense is it a program? It is a program because, like a text written using, for example, the latin alphabet, it can carry instructions. In our every-day language, the shortest series of the twenty-six letters that make up our alphabet that has an individual meaning is a word. In the genetic program, the shortest series of the four letters A, C, G and T with an individual meaning is a "gene". This parallel between language and the genetic program can be taken further. It is obvious that the meaning of a sentence, and to an even greater extent, the meaning of a work of literature consisting of sentences, can in no way be reduced to the meaning of a word: the word contributes to this greater meaning through an interplay of
juxtapositions. The meaning of a word is very often determined by its context. In the same way, a single gene never determines all the biological properties of a cell, let alone those of an entire organism. The body of an adult human being contains ten thousand billion cells. Its intrinsic biological properties are determined by the combination of several tens of thousands of genes. However, the meaning of a combination of genes is not that of an immutable program of destiny. It is essential to highlight the difference between a genetic program, which is that of the intrinsic biological properties, and an inevitable destiny. Their confusion has given rise to many ideological aberrations in the past and present - it is to be feared - will continue to do so in the future. Destiny results from the encounter between biologically programmed beings and their environment, in the widest sense of the word, which is not genetically determined. This environment is defined by the air we breathe, the food we eat, the climate we encounter and - for us humans - by the symbolic world within which we construct ourselves, the culture with which we are surrounded, the education we receive, the many events that shape our life. And of course, none of this is genetically programmed. This means that even if I were to know someone's genome and know how to interpret this information, I would still be totally incapable of predicting his or her religious, political, sexual, cultural or artistic choices. I would be even less capable of saying much about what is going to happen to this person, even though I could perhaps have some idea about some of the illnesses he or she is likely to contract. Consequently, this "human genome program", as it was more-or-less fully elucidated in the publications of 15 February 2001, must be viewed as being like a dictionary that we are just beginning to compile. A dictionary contains a series of words to which a definition can be assigned. In our "dictionary", we have a series of "annotated" genes, that is genes for which an initial definition can be proposed. While a dictionary is being compiled, and even after it is fairly complete and of excellent quality, it still cannot be used to produce literary works, such as Proust's "À la recherche du temps perdu", for instance, although it can help to analyse such works. Similarly, the sequence of the genome in no way removes the need to study the biological properties of organisms, but it can make it easier to do this.

Progress attributable to the genome program

Some people claim: "The genome program is going to lead to extraordinary medical breakthroughs". Others say: "That's not true, the gene is not important. It's all about selling the dream and the shares of the genome companies". What are we to make of these claims, which are as sweeping as they are contradictory? As is often the case, we are oscillating here between scientific information and ideological interpretations. The affirmation that everything is genetic is just as ideological as the claim that genes have no influence. The genome undeniably does have a coding function because a gene codes for a protein - that is a molecule essential for the structure and function of cells- and the mutation of a gene, associated with a change in a protein, can indeed induce disease. It is incontestable that the genetic "dictionary" will lead to medical progress. Cells and organisms contain essential molecules that determine their structure and their properties; these are the proteins, and they are directly encoded by the genes. This means that knowing about genes allows us to find out about proteins. In fact, in a rather reductionist way, many diseases can be related to a functional change in one or more of these proteins. The gene(s) coding for one or more protein(s) can therefore provide a way of understanding the mechanism underlying the disease and new approaches to discovering new drugs. This is not limited to genetic diseases or to gene therapy. Diseases as a whole can be classified in terms of a dividing line, to the left of which are the truly genetic diseases (such as Duchenne's myopathy or hemophilia), and to the right of which are non-genetic disorders (such as a fracture of the neck of femur, on a rainy day as a result of slipping on a wet surface.), and, in the middle the diseases that are neither entirely genetic, nor completely independent of the influence of the diasthesis. This latter group includes diseases such as diabetes, hypertension, arteriosclerosis, Alzheimer's disease, etc. The genome program should make it possible to improve the treatment of all these disorders. Let us take the example of a fracture of the neck of femur, an accident that is clearly not genetically determined. For the neck of femur to mend, there must first be a sort of biological glue that will knit together the broken ends of the bone. Then this tissue has to calcify. All this happens under the influence of hormones and growth factors, which are usually proteins and are therefore encoded by genes. Characterizing these genes therefore provides access to the hormones that promote and improve the quality of bone repair. Hormones of this type are already being used in medicine.

The therapy that it is hoped to obtain from advances in genetics will doubtless not be limited to gene therapy, which is in fact only a minor aspect, and often somewhat illusory. In fact, the treatment of common illnesses can also be expected to benefit from this knowledge of the genome. I have already mentioned the example of Alzheimer's disease, which is a form of senile, and sometimes presenile, dementia, and which, given the increased longevity of the population, may well affect one person out of four or five in the near future. There are some unusual genetic forms of this
There is another reason why the genome program, even though it can contribute to progress in medicine, cannot bring us into a world of universal good health. Medical progress actually makes only a relatively minor contribution to the general improvement of health. When we try to identify the contribution made by various factors to the difference in life expectancy that exists between individuals and populations, we can divide it into three thirds: one third is clearly linked to poverty, to deprivation in itself and to the conditions of life that it leads to. It is the lack of hygiene, the contamination of water supplies, malnutrition and lack of access to medicine that are responsible for the dramatic difference between the life expectancy in Africa and that in Europe or the USA. The second third probably results from the inequalities themselves - independently of absolute poverty - in that they lead to high-risk behavior, smoking, alcoholism, drug abuse, stress and psychological stress. Finally, the differences in access to modern treatments seem to account for only one third of the discrepancies in life expectancy. However, unfortunately any improvement of possibilities, in this case medical, does not necessarily mean that there is any increased political will for these new possibilities to benefit those who need them, but are unable to pay for them. Something more than science is needed; political will is called for, based on the uncomfortable observation that one of the consequences of the incontestable advances in medical techniques in the world is a staggering increase in inequalities. At the beginning of the 20th century life expectancy was not very different for someone born in Bobo-Dioulasso (which was then a French colony in Upper-Volta) or in Paris: about 40 years in Bobo-Dioulasso, versus 48 years in Paris. Nowadays, the life expectancy at birth of a French child, whether boy or girl, is 79/80 years, whereas it has remained about 45 years in Burkina Faso. This means that a century of fabulous scientific progress, but without the political will to make it also one of progress for Mankind, has led to an increase in the worst possible inequalities, those experienced when confronting disease and death. Progress that leads to increased inequalities is not acceptable.

The medicine of prediction

It is sometimes said that decoding the human genome will make it possible to predict the biological susceptibility of individuals to developing specific diseases, and thus to implement truly preventative medicine. This is what is known as predictive medicine or, more accurately, "the medicine of prediction". Disease susceptibility can sometimes be detected before birth, or even before the single-cell embryo, the zygote, has been implanted in the mother's womb: this is what is known as prenatal or pre-implantation diagnosis. However, a genetic diagnosis can also be done in anyone who, despite showing no sign of
disease, comes to find out whether he or she runs a particularly high risk of developing a disease. Being able to answer this question can be a considerable progress. For instance, there is a very common disorder, hemochromatosis, which is characterized by the presence of excessive iron in the liver and other organs. The gene conferring susceptibility for this disorder is found in about one person in ten, and the disease itself strikes about one person in four hundred. If the genetic abnormality responsible for the condition can be detected even before the individual is affected, it is possible to prevent this overload of iron developing and therefore prevent the onset of symptoms: as the blood contains a high level of iron, all the person has to do to avoid the onset of hemochromatosis is to donate blood regularly. There are already quite a lot of examples of this type. However, the situation is often much more complicated.

Let us start with the example of breast cancer: this strikes one woman in nine, and 5% of these cancers are genetic. In these individuals, corresponding to about one woman in two hundred - constitutional susceptibility to breast cancer is one of the most widespread genetic diseases - the risk of developing breast cancer is of the order of 55%. It is therefore a considerable threat. Let us imagine the case of a woman in whose family a mother or an aunt has been affected by this disease and that the mutation of a susceptibility gene has been identified, and who comes to her doctor asking for a test. If the test turns out to be negative, the woman will be rather relieved. In other cases, sadly, the test may confirm that this woman herself faces a high risk. What can the doctor propose? Certainly he or she can offer to help the woman, who has just found out that she faces a real danger, to manage her anxiety, which may not actually be any worse that she had experienced before the test was done. The doctor can also offer to follow-up the patient more regularly, and this may make it possible to save about 30% of the lives lost to breast cancer. However, the method that is by far the most effective involves the preventative removal of both breasts and both ovaries; in this case, 95% of the lives under threat can be saved. Obviously, this type of prevention, may be acceptable for the breast, but would be much less so in the case of a genetic susceptibility for brain cancer!

In such a situation, which is always dramatic, the only freedom that this woman has is that to chose between a risk that the doctor cannot carry for her, and accepting a mutilation with potentially enormous physical and psychological consequences. She is like a condemned prisoner who is allowed to chose the method of execution. Despite this, in a context of established familial risk and at the request of a worried woman, one will not refuse to do this test.

In contrast, there is no reason to offer this test routinely to the general population. The hereditary forms of breast cancer are in fact the rarest ones, and so a woman testing negative still has a risk of one in twelve of going on to develop breast cancer. Routine screening for genetic susceptibility to breast cancer therefore has little to recommend it in terms of medical or ethical logic. However, there is another view: the genome program involves considerable financial interests. The drugs market is of the order of two hundred and fifty billion dollars, at present. If we add to this all the other biotechnology markets, the figure rises to four hundred billion dollars. Genetic tests can also generate considerable income. Tests for the susceptibility to breast cancer have been patented by an American Company, which is trying to gain exclusive rights to carry out these tests for the modest sum of two thousand six hundred dollars a time. Let us imagine that as a result of advertising by this company, 10% of the women in the rich countries have the test. We can just hear the line "You really cannot behave like ostriches and ignore the fact that it is now possible to detect this susceptibility in your daughters and in yourself". There are four to five hundred thousand million women in these rich countries, that comes to fifty million tests at two thousand six hundred dollars each: that's a market of nearly one hundred billion dollars for just one genetic test! And there will be dozens of such tests …!

**Gene law**

I was the person responsible for promoting a campaign to increase public understanding in France about the subjects I am talking about here today. This campaign was known as "the gene train". A survey was done after this travelling exhibition, to find out whether it had achieved its aims. More than five thousand people who had attended the exhibition were asked to complete a questionnaire. One of the replies we got seemed to be particularly interesting: in response to the question "Are you in favor of undergoing genetic tests, even if they cannot help to improve your health?", 90% of the people answered that they were. So, even if the genetic test has no preventative or curative effect, nine people out of ten say that they still want to know. This suggests that it is highly probable that in the future people will become more and more aware of the factors that determine their biological future and their susceptibility to disease. Yet just knowing this, even if there are no medical consequences, can have huge implications from an economic standpoint, affecting bank loans, private insurance policies and job prospects. Tomorrow we will be living in societies in which powerful economic interests will be able to profit from knowing the genetic predispositions of individuals, and the vast majority of people still say that they want to know their genetic future. There is probably nothing more difficult to protect than ones genetic privacy. There are information circuits and files, in which I think it is impossible to prevent overlaps. This means that there is a high risk that the
economic agents involved will have access to the relevant genetic information about people. This is a real danger, and, if we are not careful, unstoppable mechanisms will mean that the freedom of people living in the human community, one that is theoretically based on their common humanity, will be severely restricted on the basis of biological determinants. The article of the Declaration of Human Rights which states that "all people are born and remain equal in dignity and before the law" will give way to rights that depend on their genes. In other words, we will see the principle of human rights being replaced by the rights of genes. A sinister shift. One has to understand this to be able to prevent it. It can still be done, but one must be aware of the problem.

The gene, a raw material

In addition to their purely scientific aspect, the genome programs involve considerable economic interests. As I have said, the potential market for biotechnologies using genetic engineering amounts to several hundred billion dollars. The raw material of this industry is a gene. We have therefore seen a whole series of stratagems being constructed around the gene, which are exactly the same as the industrial and political stratagems used to ensure special access to other raw materials, such as oil, uranium, diamonds etc. Private biotech. companies have made deals with democratic states in order to obtain exclusive rights to prospect, not the earth beneath the countries concerned, but the genetic diversity and medical records of an entire population. Such agreements have been signed by Iceland and the Tonga islands. Is there not something sinister, something incompatible with human dignity and specificity about reducing the genetic diversity of a people to a "mineral resource" for which one can be win prospecting rights? In addition, if the gene has market value of this sort, it would be better to prevent ones competitors also getting access to it, even if there have been no negotiations to obtain exclusive prospecting rights. This is why we are witnessing a process by which the gene is assimilated to a patentable commodity. Yet the gene is in fact simply something we know about the natural world, a molecule that has the power to encode some of the biological properties of individuals. It cannot in any way be viewed as an invention. The gene can be used to produce an invention, that is a different question, but the gene itself is not an invention. But because there is an economic advantage in viewing the gene as an invented product, patents for genes have been registered not only in the United Sates, but also elsewhere throughout the world. For the first time ever, a European Directive actually obliges the fifteen member states to include the patentability of genes as part of their national law.

Cell therapy and embryo research

Two of the great advantages in tomorrow's medicine that are mentioned are, firstly, the fallout from genetics, from the decoding of the genome; and, secondly, regenerative medicine. This is the concept underlying a form of medicine in which many diseases, notably those linked to the fact that aging cells are functionally impaired or have degenerated, can be treated using young, fully functional cells, that are tolerated by the person treated. In principle, these cells could be obtained from two sources: from the embryo or from differentiated tissues.

Let us begin with the differentiated tissues. In all differentiated tissues, whether those of a new-born infant, of a fetus, or of an adult, and even a fairly elderly adult, there are still in the heart of the tissues, cells that are able to regenerate themselves. For the last three or four years, it has been known that in reality these regenerative cells do more than just repair the tissues in which they occur. Thus, a regenerative cell from the skin can give rise not only to skin, but also to neurones, which may make it possible in the future to treat neurodegenerative diseases, such as Parkinson's disease of Alzheimer's disease. The bone marrow contains not only cells able to repair the blood by making red blood cells and white blood cells, but also cells that could regenerate the heart, bone, tendons, liver, nerve tissue and perhaps, tissues of every type. There is still a lot of work to be done to transform this theoretical possibility into a therapeutic reality, but it does hold out a real hope, particularly because this approach does not raise any ethical problem.

The second possible source of cells is the embryo. The embryos of mammals, of whatever type, develop up to the stage of forming a hollow cavity surrounding a ball of cells, known as the internal cell mass, from which the embryo properly so-called later develops. The rest of the egg will contribute to the placenta and the membranes. If the embryonic stem cells of the internal cell mass are removed, thus sacrificing the embryo, they can be multiplied and cultured for a very long time. Under some culture conditions, however, these cells have the ability to produce all the tissues in the body. They can be used to produce insulin-secreting cells, which could be used to treat diabetes; into dopamine-secreting cells, which could be transplanted into people suffering from Parkinson's disease; into heart cells with the potential of boosting a heart weakened by a myocardian infarction, etc. As a result, research is now being conducted to try to transform these theoretical possibilities into realities. There is still a lot of work to be done, before either of these strategies can be adopted. There are probably only a few of the stem cells known as "adult" stem cells, it is not easy to recognize them, they are sometimes difficult to culture, they may decrease in number with age; like embryonic stem cells, if they are
not differentiate they have a propensity, to produce a type of cancer, a teratoma. Transplanting such undifferentiated embryonic cells into a patient, not only would not cure him or her, but could trigger the onset of an embryonic tumor. In addition, we are still far from being able to control the mass differentiation of the embryonic cells into a given type of cells to fit the disease we are trying to treat, cells secreting insulin for diabetes, for example, of cardiomyocytes for myocardial infarction, dopaminergic neurons for Parkinson's disease, etc.

**Therapeutic cloning**

The production of human embryos by cloning could have two indications, or purposes, one is therapeutic and the other reproductive. In the first case, the embryonic cells that are obtained are genetically, and therefore probably immunologically, identical to those of a patient waiting for cell transplant for a wide range of diseases: neurodegenerative diseases such as Parkinson's or Alzheimer's disease, cancer, diabetes, hepatocellular failure, burns... etc.

For such a program to be effective, the biologists must be able to control the differentiation of cells isolated from a cloned embryo, and this, as we have seen, is not yet the case, although it is not impossible. In the future, someone suffering from Parkinson's disease or diabetes could ask his wife or daughter to give him some oocytes, or could obtain them from donors, whether paid or unpaid. The doctor would then replace the nucleus of these ova by that of specific cells from the person to be treated and then culture the cloned embryo thus created for 6 to 7 days under laboratory conditions until it has been converted into blastocyes. At this stage, as we have already seen, the cells in the internal cell mass constitute the precursors of the fetus. This is the origin of the embryonic stem cells about which I have already spoken at length. If it is possible to order them to differentiate, by changing the culture conditions, to form brain cells or pancreas cells, they could then be transplanted into the patient to treat his/her Parkinson's disease or diabetes. The transplant should theoretically take perfectly, because the cells transplanted will be essentially similar to those of the person receiving them.

It should be noted that the description that we have just given of a cloning protocol intended for human therapeutic purposes is still very theoretical. In fact, several teams have attempted to reproduce cloning by nuclear transfer in non-human primates (macaca and rhesus monkeys), but without success. According to the results reported by scientific journalists, the cloned embryos obtained degenerate very quickly, after only a few divisions; and accumulate chromosome anomalies for a reason that is not understood. These negative findings make it highly unlikely that any attempt to carry out human cloning will be successful, if it were to be performed today. This view was strengthened at the end of November 2001 by the highly publicized announcement that the American Company Advanced Cell Technology had made a breakthrough in developing cloning methods for therapeutic purposes. A closer look (The Journal of Regenerative Medicine of November 25, an on-line Internet publication), reveals that the transfer of fibroblast nuclei into human oocytes was always unsuccessful, and 71 attempts to inject cumulus ovarian cells yielded two 4-cell stage embryos and 6-cell stage embryo. In every case, the development of these embryos was spontaneously aborted within 24 hours or even less. When we recall that embryonic stem cells are isolated from a blastocyte, that is from a stage of development corresponding to the 6-7th day after fertilization, i.e. to more than one hundred cells, we realize just how far we still are from obtaining a human embryo usable for human cloning, whether for therapeutic or reproductive purposes.

Despite this, the rumor in the specialist media is that Chinese teams have managed to obtain cloned human embryos reproducibly capable of developing to the blastocye stage, and therefore of providing embryonic stem cells. If this news is confirmed, the method will doubtless be reported in a scientific publication ... and could therefore be used throughout the world by specialist teams. The ability to obtain cloned human embryos is essential for anyone trying to produce cloned babies, as well as for cell therapists who dream of having a supply of immuno-compatible ES cells. This aspect of the question obviously looks crucial now that declarations of intent to carry out human reproductive cloning are increasing in number. The Raelian cult has set up a Biotechnology Company dedicated to this project, that is known as Clonaid. A group of eminent reproductive biologists led by the Italian Severino Antinori has also announced that they have been commissioned by two hundred sterile couples to produce cloned babies from the cells of sterile fathers. Dr Zavos, Antinori's American co-worker dangled before our eyes the prospect of a new kind of birth scheduled for 25 December, the birth of cloned human embryos. These two companies have the facilities they need to succeed. The mechanisms of cult subjection do indeed provide the Raelians with hundreds of young female "volunteers" to donate ova and lend their uterus for the transfer of cloned embryos. As for Antinori and his co-workers, they have considerable clinical experience in reproductive biology. The only obstacle facing these would-be cloners is that in fact, as we have seen, they are apparently still incapable of producing normal cloned human embryos. Once the method has been developed for the needs of therapeutic cloning, this obstacle will have been overcome, and we will not have long to wait before it is announced that pregnant women are carrying cloned fetuses.
Another cause of concern is the risk of further "commodification" of the female body to which widespread use of cloning could not fail to lead. The public or private teams doing these experiments would have to have access to a large supply of human ova. At present, one to two hundred ova would be required for each attempt. As demand inevitably creates a market, at least in many countries, we can well imagine that large numbers of women in need would be enrolled to constitute cohorts of paid ovum donors. Under contract they will agree to undergo repeated ovarian stimulation, plus the health checks necessary to confirm the quality of the ovum-producers and their ova.

Furthermore, for some people, the question arises of the respect due to the unique nature of the human embryo as a possible future person. For many believers, for instance, the creation of human embryos with the aim of destroying them in order to isolate research tools or cell populations for therapeutic purposes, would be at loggerheads with the respect to their unique nature. Without wishing to enter into this debate here, I must point out that as a matter of common sense, it should not have led to the trench warfare we now see raging throughout the world between those in favor and those opposed to therapeutic cloning, both of whom are ferocious. In fact, the reality of the therapeutic prospects offered is far from sure. A technique that requires several hundred women's ova for each patient treated, in order to clone human embryos and try to culture potentially carcinogenic cells of which the efficacy remains to be demonstrated, hardly justifies the promises that have been made so confidently. Even apart from the ethical concerns and the remaining technical and scientific obstacles, this is a typical example of a rather selfish approach, that would be very costly in terms of time and personnel and it is hard to see, even in the best of cases, how it could possibly constitute the basis for the treatments now hoped for by tens of millions of people.

We do not think that the seriousness of the moral objections to the production of human embryos by cloning is outweighed at present either by the reality of the therapeutic hopes based on their use, nor by the urgency of the research needs. It would seem that the movement which is growing today in favour of authorizing therapeutic cloning at least comes from two sources. The first is the impatience of researchers to see themselves allowed access to new study materials, especially when they are so promising in terms of celebrity, if not of real medical efficacy. The second is the perceived supreme value of Progress, conceived as offering the hope or even guarantee of an improvement in the human condition. And yet, the 20th century that has just finished, has been flamboyant in every sense of the word, lighting the fires of the spirit as well as those of concentration camp ovens, and clearly illustrates the ambiguity of the power conferred on human beings by the scientific and technical progress. Human freedom implies the possibility of Good and Evil, and consequently, Progress can be used to the advantage of either. It is definitely not just because something is possible that it is necessarily good. It is still necessary to be able to show how a proposed innovation, to which a human being is subjected, could improve his or her condition whilst still complying with the moral principles on which human dignity and autonomy are based. This is not yet true, at least for therapeutic cloning.

I wanted to paint a wide picture of the medical prospects held out by gene and cell therapies. The purpose of science is to confirm the truth of phenomena and this leads onto the development of techniques and the valuation of their effects. However, science in itself cannot claim to decide what should be done, and in any case, is not capable of doing so. The question of how to use the power conferred by knowledge faces a being who claims to be free. This freedom to choose implies that all human power can be used to benefit or harm others. This is exactly what we are discussing: how can we collectively face up to the new responsibilities that result from developments in science and technology, and the consequent increase in our power?