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Commentary

Basic Biological Research at the Dawn of a New Century

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I am delighted to be here and have this opportunity to speak with you, particularly because this ceremony marks the successful completion of the studies you have undertaken. So first, I want to congratulate you for an achievement you can be very proud of and second, since you are now professional, I mean, card-carrying chemists and biochemists, I want to tell you a few things about the fields you have selected and discuss a couple of very serious and controversial problems that will confront us in the years to come, and that will not be solved without the contribution and help of people with your background and formation.

I believe it is the right time to bring up these issues because the advances that have occurred in those areas in the last 10 or 20 years are absolutely without precedent. If the first half of the century that just ended was that of nuclear physics, with Einstein's relativity and Max Planks' quantum theory, atomic energy etc., there is no doubt that the second half belonged to biology. It gave us incredibly sophisticated new instrumentation and technologies, such as genetic engineering with gene cloning, manipulation, and expression without which we would know essentially nothing about our genetic make-up, hereditary diseases such as muscular dystrophy or diabetes, viral diseases such as AIDS, or cancer. And with the pervasive presence of the computer that allows us to analyze and display data, store them and retrieve them at the touch of a button, the scientists of today have at their disposal an incredible array of techniques undreamed of just a few years ago.

The first problem I want to mention is world hunger. Indeed nowadays, more than 3/4 of a billion people remain chronically undernourished and over 180 million children are on the verge of starvation. But the agricultural environment has already been taxed to its limit and there are few realistic opportunities for opening up new land. Soils are eroding and losing their fertility, precious water supplies are being squandered, fish stocks are declining worldwide and have already been depleted in many parts of the world oceans, and forests have been devastated by the push of urbanization, by wars, fires, acid rain, toxic wastes, etc. Therefore, this new century will have to rely on biologists to feed a population that will exceed 8 and a half billion in 20 years. The task will be enormous because today, world population is increasing faster than agricultural productivity. So, unless one can curb overpopulation world-wide (and I don't mean in developed countries only, but globally: after all, the

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world is a closed system and if there is an explosion of population in one of its quadrants, inevitably, it will spill over everywhere; thermodynamics tell you that) frankly, I don't see how our civilization can survive without following new avenues such as making use of genetically modified plants.

Okay, it is absolutely true and we all agree that modern agriculture has remarkably increased food production without having recourse to genetic engineering, but it has been able to do so only by the use of massive amounts of fertilizers and pesticides that are not only extremely costly (prohibitive for developing countries) but are already causing a major pollution of our waterways and the atmosphere—and I don't even mention the health-hazard they present. So any further increase in food productivity can only be considered under conditions that would both conserve our natural resources and protect the environment. This will be extremely difficult and, frankly, I don't see that it can be done without taking advantage of molecular genetics, i.e., by introducing new traits in transgenic plants. This technology has already allowed us to reduce heavy losses of crops due to predatory insects, pests and diseases, but it has the further capability of allowing us to grow plants in very harsh environments, such as in soils of high salinity or under drought conditions where no present plant would survive.

For sure, absolutely rigorous, stringent, airtight regulatory measures will have to be put in place to identify and monitor any potential health or environmental hazard, just as should be done for the introduction of any new technology. But as I said, unless one can put an end to the increase in world population, for me, there is no alternative, unpalatable as this prospect might be.

Now, we all know that there is a worldwide opposition to the use of genetically modified plants and, for that matter, toward any kind of genetic engineering, particularly outside of the United States. Some of these concerns are understandable and probably justified, but there is another factor to consider, i.e., the fact that there has been a distinct change in the way the general public perceives science today. While no previous century has contributed so extensively to our health and well-being, by the same token, no previous century has generated such a high level of apprehension and distrust toward science. Today, when a new discovery is announced, the first question that seems to come to mind is "in what way might this discovery endanger the environment, menace our health if not destroy our civilization altogether?" To such an extent that many wonder whether humankind will be able to survive this third millennium. For me, it is not science that is dangerous, it is ignorance. And of course, the way some people might want to utilize science.

Of course, no one can predict what the next millennium has in store for us, because one cannot simply extrapolate the present. All that is absolutely certain is that the world that will surround us will be completely, totally different from the one we live in today. And it is no more possible for us to imagine that world than it would have been possible for Christopher Columbus a few centuries ago, to imagine that people would cross the Atlantic in a few hours, or that man would walk on the moon. One cannot imagine what one cannot conceive and it would be totally senseless, if not silly or even arrogant to try to do so.

Let me give you a few examples. Just a hundred years ago, at the turn of the last century, William Thompson—perhaps the most reputed physicist of his days who became the first Lord Kelvin because of his studies on absolute temperature that gave us the degrees that bear his name, etc.—made three astounding predictions: 1) That radio waves would be of little utility and therefore had no future; 2) That no machine heavier than air would ever fly; and 3) That x-rays that had just been announced by Roentgen most certainly did not exist, and were probably a scientific fraud. Clearly, Lord Kelvin was more at ease with thermometers than with a crystal ball.

Incidentally, he became a bitter opponent of Darwin, claiming that the Earth was far too young to allow for all the mutations required for Darwinian evolution. Of course, poor Darwin had neither the expertise in physics nor the prestige Kelvin enjoyed to fend off those brutal attacks. We know today that in his calculations, Kelvin had underestimated the age of the Earth by nearly 4 billion years.

Another example: After the telephone was adopted in this country (and, by the way, Western Union was so unimpressed by Alexander Graham Bell's invention that it declined to buy the patent), a group of British experts who studied the question concluded that "the telephone may be appropriate for our American cousins, but not here because we have an adequate supply of messenger boys." Finally, quite recently, after the computer had been invented in the mid 1940s, few people could see much need for such clunky and cumbersome machines. To such an extent that in 1947, Thomas Watson who was then the Chairman of IBM, declared "I think there is a world market for maybe five computers." That was only 50 years ago.

On the other hand, there are certain predictions that can safely be made because they are for the near future: we know the problems to be solved and know the approaches needed to solve them. So let me now turn to human biology, which is really my field. To begin with, medicine as you know it will never be the same in the years to come. Most households will be directly linked to core medical facilities through the Internet, not only for diagnostic purposes, as already done today, but even for health management. We will have cures for most forms of cancer because we begin to understand its complexity. Thirty, forty years ago, everybody's dream was to discover the agents responsible for the initiation and progression cancer: we were really in the dark. Today, most of these have been identified. We know that cancer arises from a series of genetic changes that occur over a period of years, and that these trigger multiple oncogenic events that collectively contribute to the advanced stages of the disease. But we know many of these steps and have characterized most of the major pathways involved. To such an extent that, I'm convinced, sooner rather than later (and probably sooner than later), we will be able to put all this information together and bring many forms of cancers under control.

Gene therapy (already used to target various hematopoietic diseases) will become a reality and we will learn how to regenerate many tissues through the use of pluripotent stem cells. And this brings me to the second very serious and just as controversial problem I want to mention, namely, the possibility of using pluripotent stem cells for therapeutic purposes. You all have heard about stem cells and know the tremendous potential they have to cure various diseases because of their ability to develop and to differentiate into any types of tissues or organs. Indeed, they can be coaxed to become a heart cell that beats, a pancreatic cell that produces insulin, a brain cell that might be used one day to cure Alzheimer's or Parkinson's disease, or a nerve cell that might help us repair a spinal cord injury. But we don't know the commands that will tell those cells to go where they are supposed to go, to become what they are meant to become. We know that these involve the addition or removal of a maze of hormones, neuromediators, growth factors, cytokines, etc., but we don't know what these signals are. It is an enormously complicated problem that must be investigated, but for that, we need all the help we can get. And foremost among these is the possibility of utilizing pluripotent embryonic stem cells.

Now, of course, I am well aware of the bitter controversies that have surrounded this issue, deeply rooted in highly personal, emotional, and religious considerations and further complicated by very volatile, if not irrational, politics. Indeed, some people in the Senate are trying to introduce a bill that would not only ban the use of somatic cell nuclear transfer to produce human stem cells for therapeutic purposes, but to make it a crime punishable by imprisonment for anyone that would use imported therapies developed outside of the United States involving these technologies, which makes no sense to me. Frankly, personally, I cannot see any immorality whatsoever in utilizing embryonic stem cells for therapeutic purposes when those same cells are piling up in the freezers of fertility clinics and are destined to be discarded anyway. On the contrary, for me, the immorality is to destroy uselessly those cells that are so enormously precious; to prevent health scientists from studying this very complex problem, from applying all the knowledge they have acquired, all the wisdom, experience and expertise they have accumulated, when this knowledge could help us cure diseases and be placed at the service of humanity. It is as if I had in hand a drug that would cure a sick person asking for my help, and I would refuse to give it to him.

For me, this is what is tragic but, I guess, this is what biology has to face today: some see it as the universal panacea, as the remedy to all our ills while others suspect it of harboring dark imperialistic, if not monstrous, designs. Biology deserves neither this excess of praise nor this indignity.

To conclude, let me say a few words about Science itself and the nature of scientific research, for those of you who would want to go in that direction. At the onset, when a research scientist selects his research project, he must rely heavily on his imagination and on his intuition. In a way, he must create his field of investigation just like an artist creates a new work of art. Like a visionary, he must see things that don't yet exist, but might. His success will depend on the depth and originality of his vision. To paraphrase Ed Wilson, the Harvard entomologist "To the inept hunter, the woods are always empty."

But this is where the analogy between the sciences and the arts ends because in science, every result obtained must be checked and rechecked before it can be finally accepted; nothing is acquired for good, nothing is absolutely definitive. As Einstein once said "No number of experiments can ever prove that I am right, but a single experiment, at any time, can prove that I am wrong".

Some see this element of doubt as one of the weaknesses of science; I see it as one of its finest qualities, its real grandeur: the fact that there is no absolute truth and that one might be wrong. If everybody could accept the idea that they might be wrong, it would put an end to all forms of fanaticism: political, moral, racial and, particularly, religious fanaticism.

Anyway, this is where the sciences and the arts go their separate ways. Because from this point on, science builds on science where each answer obtained suggests the next logical question, and each question asked suggests the next experiment, so that what will not be done today by one scientist will almost inevitably be done tomorrow by another. For instance, if Newton, Darwin, or Einstein had never existed, how long would it have taken for others to come up with the same discoveries? Probably not that many years. For instance, Einstein's ideas about relativity were already kicking around, and all the things he did would have eventually been done. Not by one single person, of course not: this was Einstein's extraordinary genius, but by many, working independently and arriving ultimately at the same result. What this means is that in science (and I consider this a rather humbling thought), very few people are really indispensable.

This is in sharp contrast with what occurs in the Letters or the Arts. Because if Mozart had never existed, nobody but nobody, would have ever written his *G-minor symphony,* or *Don Giovanni,* or *Cosi fan Tutte.* Or Schubert, his *Schöne Müllerin.* Not in a million years. This is why works of arts, paintings, sculptures, the treasures of architecture are so enormously precious and are to be protected at all cost. Because once they are destroyed, they are gone forever.

As Nadine Gordimer, the South African Nobel Leaureate writer and poet once said "Writers are not orchestrated; poets sing unaccompanied." Scientists do not sing unaccompanied. Science nowadays evolves at such an incredible pace that it is inconceivable that anyone would work alone, in isolation or in a vacuum. Scientific exchanges, scientific collaborations among colleagues, among schools, countries or continents are indispensable if one wants Science to move forward.

And this is where you, the graduates of today, come into the picture. Because you are those on whom we count to work and collaborate with us, to help us with your innovative ideas and your fresh imagination. And, much more importantly, to carry the ball and take over after us. To each and every one of you, I wish all the success in the world in whichever direction you propose to go. Good luck and thank you for listening.