Treb. Soc. Cat. Biol., Vol. 41 (1990) 89-91

WHERE IS BIOTECHNOLOGY GOING?

Extracte de la conferència impartida pel Professor Julian E. DAVIES de l'*Institut Pasteur* a París, França, durant la celebració del 2n. Congrés Espanyol de Biotecnologia (BIOTEC-88) a Barcelona, el dia 22 de juny de 1988.

It has been my privilege to spend fifteen exciting years working in modern biotechnology. Biotechnology has, in fact, contributed to man's health and well-being for more than ten thousand years. However, biotechnology can be clearly divided into two distinct phases: before 1973, and after 1973, which is to say before and after COHEN and BOYER. Before 1973 biotechnology was essentially an art: you took an organism and you took what that organism could do for you. All manipulations of industrial processes in biotechnology were largely determined by the properties of the organism being used. After 1973 biotechnology became a real science. The discovery of recombinant DNA, and the development of genetic engineering technology brought about a revolution; organisms could be tailored at will. If someone had said in 1970 that *Escherichia coli* K12 would be an industrial microorganism, people would have laughed at this idea. If the same person had said that, in addition, mammalian cells, and insect cells would be used extensively in industry, this person would have been locked up in an insane asylum!

However, these are the *new* industrial microorganisms. Another very important change in biotechnology which occurred after 1973 was the development of entrepreneurship. This incredible race to develop commercial products from recombinant DNA played a crucial role in the rapid growth of the new science. Small biotechnology companies with their academic-industry combination accelerated discovery, and have been making highly significant contributions. Companies like *Genentech* (whose scientists published more than two hundred papers in 1987) may have been formed to make money, but their scientific contributions have been awesome.

Something else has happened since 1973. Not only has the application of recombinant DNA produced many new and important medical products such as human insulin, human interferon, and human growth hormone, but biotechnology has developed into a subject; it has evolved into a new science in its own right. Biotechnology is not routine. It is something more than the cloning of proteins in *E. coli*. Everything that could be cloned (from knowledge of its existence and properties) has been cloned. This has led scientists into developing the field into the true realm of science: the discovery and analysis of new biological phenomena.

Murray GELL-MANN, Nobel Prize win-

ner in physics, talked about modern science in the following way.

"New subjects, highly interdisciplinary in traditional terms, are emerging, and represent in many cases the frontiers of research. These interdisciplinary areas do not link together the whole of one traditional discipline with another: particular sub-fields are joined together to make a new subject."

We saw this first in the development of molecular biology, but in my opinion this is no case more true than with biotechnology. It is in this context that I see the real future of the science of biotechnology: a new fusion of traditional sub-fields providing new ways of both analysing biological phenomena and developing these fundamental discoveries to improve the human condition.

Let me give you a few examples of this type of fusion. If we consider the now commonplace procedure of cloning and secretion of a heterologous protein, we can see how this implicates knowledge and application of a variety of sub-fields such as cell physiology and genetics, membrane structure, secretion mechanisms, gene expression, enzymology, protein structure, computing and chemical engineering.

A more recent example concerns the development of the polymerase chain reaction PCR, which is surely going to be one of the most significant advances in the field. The technology will revolutionise several fields: clinical diagnosis, crime detection (identifying a person by the analysis of a single hair!), basic cloning methodology, to name just a few of them. The PCR system would not have been developed without a successful marriage of specific aspects of fields such as enzymology, nucleic acid chemistry, synthetic organic chemistry, physical chemistry, engineering and computing.

When considering the future of biotechnology it is worthwhile remembering that our major concern will be with *interactions* between biological systems: many of these interactions are already under intensive study and new information is rapidly forthcoming.

It is easy to see how sub-field specialities are being used to analyse these interactions and to provide tools and products; for example, the growth of receptor biology. In this particular case, the role of traditional gene cloning is simply one of isolation and availability; the pharmaceutical products of the future will come from the study of receptor/ligand interactions, the receptors having been identified and isolated by techniques which are already well established. In this example, we are not simply considering receptors for proteins such as hormones, but studying receptors for smell, taste, touch by the interactive approaches provided by biotechnology. As the methodology develops (e.g. PCR) we will be able to analyse these relationships with increasing sensitivity and accuracy.

It is all too easy to say that biotechnology has not succeeded in all its attempted applications. This is nowhere more true than in the development of vaccines. During the birth of modern biotechnology, everyone proposed that new, safe, stable vaccines to most diseases would be the easiest and fastest product. And were are we? The major product is a vaccine against hepatitis B, made in *Saccharomyces cerevisiae*. It should be pointed out that this major new vaccine product took only eight years from cloning to market. This can be considered to be a success. Even in the so-called failures, we can look at what we have learned. For example, even though not many vaccines have succeeded, what seemed to be *"failures"* have led to rapid, new diagnostic techniques. Biotechnology has brought indeed a deeper understanding.

I have concentrated on human health aspects of biotechnology, but we must not forget that many other applications will

reach fruition in the future: biomass conversion, energy production, fine chemical production, and a whole host of applications in agriculture, such as herbicide and disease resistant plants, transgenics.

Finally, even though it must be evident that I am very enthusiastic and optimistic about the future of biotechnology, before concluding I would like to express two concerns I have.

The first is with respect to regulation. In the late 70's and early 80's there was much quasi-political activity relative to genetic engineering. Fortunately good sense and reason prevailed, but we are now facing new problems with *«luddism»*. These will undoubtedly be satisfied by an intelligent approach involving free information flow and education. However, the danger is that it may be necessary to dissipate too much energy and funds on things that *might* go wrong. Of course all aspects of the controlled release of genetically-engineered organisms must be considered and studied in detail, but it must be realised that we can only, at the end, use these new products with the reasonable prediction that based on research, there is no finite harm factor. Unfortunately the press can always devise science fiction scenarios!

Another and more serious concern is the future progress of biotechnology. Because of the entrepreneurship and excitement in the development of the field, it is apparent that potential new products and applications are arriving at a faster rate than they can be developed commercially. I would like to see the entrepreneurship of the science being matched by entrepreneurship in government and industry. The future of biotechnology is not limited by our imagination, but only by support –moral, financial and commercial. Only in countries where industry and government provide this kind of support will the real benefits of biotechnology be made available to the population. The others will, by definition, become dependent. I am pleased that the European Community is trying to approach this problem, but even here bureaucracy, slow decisions and lack of funds will limit our benefits unless steps are taken to put entrepreneurship in government as well.