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BIOTECHNOLOGY AND HEALTH IN LATIN AMERICA AND THE CARIBBEAN

The recent explosive expansion of knowledge in microbiology, molecular biology, biochemistry, genetics, and other disciplines has set off unprecedented advances in biotechnology and has given the field of biotechnology an increasingly important part to play in nations' socioeconomic progress. Judicious application of techniques for gene-splicing, production of monoclonal antibodies, protein engineering, and so forth to solve problems in the fields of health, food production, energy, and the environment has given birth to noteworthy technologies in the industrialized countries. The effort to control diseases and improve health through these technologies has already scored triumphs whose implications are publicized almost daily in the mass media.

Biotechnology is a general term for any technique that uses living organisms (parts of organisms or products obtained from such organisms) to produce or alter products, improve animals or plants, or develop microorganisms for specific purposes.

Traditional biotechnological processes arose out of empirical practices such as the production of fermented liquids and bread. Today, the advances made in cell biology, molecular genetics, and biochemistry have spurred the development of a new biotechnology that uses organisms modified by the recombinant DNA technique and also by cell fusion (principally fusion of plant protoplasts and production of hybridomas that secrete monoclonal antibodies).

Among other things, these new techniques permit the cell (or viral) genome to be dissected, yielding organisms without the genes that make them pathogenic. This opens up a new strategy for vaccine production and new ways of controlling animal and plant diseases by substituting modified microorganisms for harmful ones in certain ecologic niches.

Medical Applications

Many gains in infectious disease prevention have been made without any great understanding of the mechanism of immunity or the nature of the responsible pathogens. It is clear, however, that empirical knowledge is not enough to control the infections and parasitic diseases that now plague much of the world's population. Rather, we need to understand the molecular mechanisms that regulate cell differentiation, genetic expression, and the immune response in order to undertake alternative measures against such key diseases as the acute infectious diarrheas, acute respiratory infections, malaria, trypanosomiasis, filariasis, schistosomiasis, leishmaniasis, leprosy, and the enteroparasitic diseases. Designing new drugs for their treatment and obtaining antigens that are useful for preventive interventions and diagnosis will require expanded knowledge of the causative pathogens' molecular biology. Such knowledge can only be gained through research policies conducive to answering the basic questions that must be answered before the practical problems at hand can be solved.

Diarrheal diseases. These are the leading cause of infant mortality in the Americas. Oral rehydration therapy has reduced this mortality considerably but has left morbidity unaffected. (It is estimated that many infants suffer four to six episodes of diarrhea a year.)

Probably a third of all infant diarrhea cases are caused by rotavirus. The rotavirus genome has recently been synthesized in vitro and inserted into *Escherichia coli,* some forms of which are also etiologic agents of diarrhea. In addition, bacterial clones containing copies of rotavirus genes have been identified, and in some cases the amino acid sequence of these genes has been or is being established. Even now, DNA probes can be used for the diagnosis and identification of the virus in feces, and a vaccine is being tested. DNA probes for identification and typing of *E. coli* are also being tested.

Malaria. Over 900,000 malaria cases were reported in Latin America and the Caribbean in 1984, but the real number is estimated as being five times greater.[1] The control techniques used in recent decades—insecticide spraying and chemoprophylaxis—have encountered serious problems arising from development of vector resistance to insecticides and parasite resistance to drugs. Partly for this reason, efforts are now in progress to obtain specific antigen proteins of sporozoites and merozoites for the development of immunizing agents.[2] A simple molecule located on the sporozoite membrane has been identified and seems to be a good candidate for that purpose. While it appears essential for development of the parasite and its entry into liver cells, it

[1] Pan American Health Organization, Status of malaria programs in the Americas, *Epidemiological Bulletin* 7(1), 1986.

[2] Pan American Health Organization, Malaria vaccines: State of the art, *Epidemiological Bulletin* 7(3):6–10, 1986.

also stimulates production of host antibodies that can neutralize sporozoite infectivity. The gene that controls the production of this protein in *Plasmodium falciparum* has already been isolated and cloned, and it has been established that the antigenic portion of the protein has only four amino acids.

P. falciparum antigens can be synthesized chemically or produced in bacteria by recombinant DNA techniques. Monoclonal antibodies, which have played a central role in the isolation of these protective antigens, are also expected to help with detection of antigens circulating in infected humans; detection of infection in vectors; and determination of the plasmodium species infecting the mosquito. This is important for epidemiologic surveys of affected areas and for evaluation of prevention and control measures.

In addition, testing of DNA probes for the diagnosis of malaria infections has recently begun, as has testing of vector control techniques using larvicidal biologicals.

Chagas' disease. The number of Latin Americans infected by *Trypanosoma cruzi,* the etiologic agent of Chagas' disease, is estimated at over 12 million. Study of trypanosome antigens can yield a battery of alternative proteins for use as sensitive and specific antigens in diagnostic tests. Another possibility is that monoclonal antibodies and probes may prove more effective than the methods currently in use for the detection of parasitemia, thus permitting a more objective evaluation of the effects of antiparasitic drugs.

Leishmaniasis. Probes are needed for differential diagnosis of the etiologic agents of leishmaniasis in skin lesions. Such probes would provide a faster method for certifying the diagnosis, inferring the response to current drugs, and evaluating new therapeutic agents.

Thalassemias, other hemoglobinopathies, and other genetic diseases. Until a few years ago, thalassemias and other hemoglobinopathies were the only diseases against which molecular biology could be said to have made some meaningful contribution to practical medicine. Since then, methods based on polymorphisms detected by cleaving DNA with restriction enzymes have yielded important data about other genetic diseases including Duchenne's muscular dystrophy, mental retardation syndrome with a fragile X chromosome, Lesch-Nyhan syndrome, phenylketonuria, and retinoblastoma.

Poliomyelitis. Molecular dissection of the poliovirus has made it possible to identify the immunogenic proteins that elicit neutralizing antibodies. These polypeptide fragments have been chemically synthesized, and their

inoculation into animals has shown that they confer effective protection. Moreover, this protection is as efficient as that afforded by inoculation with the entire protein or the virus itself. As a result, it appears that the procedures involved may constitute the best approach for obtaining vaccines against currently hard-to-culture pathogenic viruses.

With recombinant DNA techniques, viral chimeras can be made that consist of the genome of an attenuated virus of proven immunogenicity plus a gene coding for the immunogenic protein of another virus. The first successful tests have been made of viral chimeras consisting of vaccinia viruses carrying genes of the surface antigen of the hepatitis B virus and vaccinia viruses carrying the gene coding for hemagglutinin from the influenza virus.

Genetic manipulation of the chromosomes of bacteria and viruses will also permit removal of the genes that make them pathogenic and the elimination of adverse reactions to vaccination, while preserving the antigenicity of the microorganisms involved. More generally applied molecular biology can be expected to have a considerable impact in other fields of medicine, particularly in the early diagnosis and treatment of neoplasms, congenital anomalies, and hereditary metabolic diseases.

Impact in Latin America and the Caribbean

The new biotechnology will have an important impact in Latin America and the Caribbean. In many cases this impact will be beneficial—such as when it is expressed through development of vaccines and faster methods of medical and veterinary diagnosis, or through application of the new plant tissue and cell culture methods and recombinant DNA technology to obtain plant species resistant to the high concentrations of aluminum present in tropical soils. In other cases it could have adverse economic and social consequences—such as when raw materials produced by exporting countries are supplanted by other products manufactured or improved by biotechnology in industrialized nations.

Also, however attractive the development of the new biotechnology may prove for the countries in the region, many problems will still require solution through traditional biotechnology, without use of either recombinant DNA technology or monoclonal antibodies. For instance, several countries still do not make their own vaccines, even though the requisite technology was described years ago. Many fermentation industries in Latin America and the Caribbean are still primitive in their operation, and the profits earned from their captive markets are large enough to allow them to disregard so elementary a resource as improvement of microbial strains by conventional methods in order to enhance production. In some cases there is very little use of reactors, despite a need to introduce reactor fermentation technology for the improvement of outmoded production methods.

Actually, the design of biological reactors is a patent necessity for Latin America and the Caribbean. Among other

things, drug production in rural areas requires a classical technology entirely independent of recombinant DNA and monoclonal antibodies, but one that is of great economic and social importance to the rural communities of several countries in the region. Although classical, this technology still involves many problems that are not described in the biotechnology textbooks of the industrialized countries, because they are problems those countries have no need to solve.

Conclusions

In all but a few countries of Latin America and the Caribbean, research and development and the status of industry are closely correlated with economic and social status. The trend is for even the poorest countries to try to develop technologies of their own that will allow them a standard of living commensurate with their expectations. Many countries in the region have some of the human resources needed for successful biotechnology programs, and their policies give technological development priority because it is seen as a vehicle for attaining autonomy and reducing dependence on more advanced countries. However, it will not be easy to convert this theoretical potential into practical results—partly because most new scientific knowledge can be applied to the solution of problems in the region only with the active participation of institutions and individuals from several countries.

The outlook will be favorable only if a serious effort is made to surmount the limitations of the existing basic scientific structure, the lack of communication between academic institutions and the production system, the limited technological infrastructure, the scarcity of financing, and the lack of promotion provided for biotechnology. All technological development and adaptation is based on policies and economic motives. Therefore, any attempt to impose technological innovation in a policy vacuum, without social acceptance and without obvious economic benefits, is doomed to fail. Acceptable development in this area is possible only if virtually all the production-related sectors of a country perceive biotechnology as necessary to national and regional development, for it is only then that personnel devoted to the discipline will find effective employment in the production system and appreciation for their accomplishments.

Source: Pan American Health Organization, Estado actual, tendencias y perspectivas de investigación en biotecnología en América Latina, PAHO Document PNSP/85-25, Washington, D.C., 1985, as reported in Pan American Health Organization, Biotechnology: Its potential for health in Latin America and the Caribbean, *Epidemiological Bulletin* 7(3)10–12, 1986.