BIOTECHNOLOGY DEVELOPMENTS

THE physico-chemical basis of biological systems and the control of their development and interactions are being unravelled in spectacular advances in molecular biology, which had its birth 35 years ago. New techniques are providing much valuable information on molecular-level mechanisms in genetics, reproduction, growth, development and immunology, as well as on interactions between living organisms. Methods are now available for transferring genes from one organism to another, even across species. Genetic engineering incorporates new genetic expression capabilities not previously available in the recipient organism in a gene transfer. Components of whole living systems, such as cells, tissues and organs, can be grown in controlled culture conditions. In plants such tissues can be developed into fully identical whole plants. Microbial systems can be endowed with specific genes of plants, animals or man and be made to produce appreciable amounts of hormones, enzymes, vaccines and 'bioactives' previously not available in more than trace quantities. Enzymes and cells can be immobilized to function as catalysts in chemical-type reactors for prolonged periods to effect specific chemical transformations on an industrial scale. Automated instruments and techniques are available for the determination of detailed chemical structure of genes containing many hundreds of nucleotides and of sequences of amino acids in complex proteins. Automated methods are also available for the synthesis of polynucleotides and proteins for research.

The knowledge from these advances is being sought to be applied on a large scale for the benefit of man in a variety of novel ways. The entire gamut of such techniques and controlled processes is called biotechnology. Propagation of selected plants by asexual methods, large-scale propagation of animals from high-breed parents by *in vitro* fertilization and transfer of embryo for maturing and birth into non-high-quality females, extension of such embryo transfer to humans in the case of infertile couples, control of male and female fertility by birth control vaccines in man and animals, and detection of disease by specific diagnostic methods based on principles of immunology are also included in the broad definition of biotechnology.

The potential of biotechnology for major economic gains in food and non-food agriculture, animal husbandry, industrial chemicals and pharmaceuticals, and for humanitarian applications in detection and control of disease, fertility, health and nutrition is considered immense. Hundreds of large and small companies in developed countries are investing in furthering applications. Governments and research agencies in many countries are promoting basic and applied research. Yet there are apprehensions that genetic engineering, particularly genetically engineered organisms, may lead to unforeseen ill effects, especially under open-field, uncontrolled propagation conditions. Major concerns are also voiced on possible restrictions in technology transfer to and utilization by developing countries arising from inadequate scientific and technological capacity for absorption and commercial consideration.

These developments were discussed recently in two important seminars in India, one, 'Biotechnology and allied sciences', organized by the Commonwealth Science Council at the National Chemical Laboratory, Pune, during 21–27 January 1989, and the second, 'Public policy implications of biotechnology for Asian agriculture', promoted by the Asia–Pacific Development Centre at the National Institute of Immunology, New Delhi, during 6–8 March 1989. The first seminar was inaugurated by Sir John Kendrew, Nobel Laureate, and the second by Dr K. R. Narayanan, Minister of State for Science and Technology, Government of India*. In both excellent summary presentations were made by many leading scientists from India and other countries and there were lively and highly educative discussions. The following is the author's purely personal appreciation of these developments.

Substantial progress has been made in genetic engineering of microbial systems to produce vaccines of high purity and specificity for immunization against bacterial, fungal and viral diseases of man and animals. These could replace vaccines hitherto available by more laborious techniques using animals or animal organs. Production by controlled industrial conditions is elegant. Some of these vaccines will be produced in India soon. There are clear prospects of additions to the list of such products. However, there are as yet no proven vaccines available for numerous parasitic diseases that affect millions in India and in other developing countries. Much more basic work on parasites seems necessary before control can be achieved. There are

*The address by K. R. Narayanan is reproduced in this issue on pages 534–536. (Ed.)

also new techniques for early detection of some diseases, which can then be controlled by chemotherapy. Such research has to be given priority and may be best carried out in developing countries. Bioactives such as human growth hormone, human insulin, interferon, tissue plasminogen activator, and streptokinase and other enzymes are produced in fermenters by genetic engineering, but the products are still very expensive, although valuable in correcting dwarfism or providing relief in heart disease and cancer. Bovine growth hormone so produced could improve milk yields, although there is opposition to such increased production by dairy farmers in USA and Europe. There are also high costs in testing and evaluation and clearance from food and drug control authorities. A one-time injection for permanent male infertility that does not affect libido, developed by the National Institute of Immunology, New Delhi, is undergoing animal trials. There are also promising developments in vaccines for leprosy.

Biological control of agricultural pests and of mosquitoes, which are a vector for the malaria parasite, is sought through selected *Bacillus* microbes, but their success, in comparison with chemical control agents and in terms of efficacy and costs, has to be established. Attempts at incorporation of resistance genes into plants are awaiting safety clearance for open-field use.

There are indications of substantial improvements in conventional fermentation to produce alcohol, butanol, amino acids and bulk chemicals as well as modified penicillins and other antibiotics. Immobilized enzymes and cells would also be increasingly used. There may be value in improving digestibility of straw and other animal feed constituents.

Tissue culture propagation of selected varieties is clearly of much value in plantation crops such as sugarcane, oil palm, coconut, rubber and spices, and in flowers, biomass trees, bamboo, potato and other vegetables, and fruits. There do not seem to be great advantages in biotechnology for cereals, pulses and oil-seeds over conventional plant breeding and propagation except in the case of hybrid varieties. There may be potential for propagation of certain naturally occurring pest-resistant or drought-resistant varieties, or of those cereals with high essential amino acid or vitamin content. There is much potential in paddy because of the availability of 150 varieties, with details of chromosomal make-up and properties. Genetic engineering techniques in plants are becoming simple but the question of open release of transgenic plants remains. Long-term effects in quick-growing tree species are as yet unknown.

Micro-organisms with the property of biological nitrogen fixation could be produced on a large scale and applied usefully on legumes and oil-seeds but not yet to the same extent on cereal crops. Some algae can also perform this function. Genetic engineering to incorporate nitrogen fixation ability in photosynthetic green plants is still a far cry as it is determined by a complex system involving about 26 genes. Chemical fertilizers and pesticides are likely to be continued to be used for the next ten years.

Major international chemical, oil and food companies are entering the area of large-scale seed production and marketing with breeders' rights on high-yielding varieties. It is likely that they would pioneer biotechnology applications suited to large farms and plantations and these developments may not be made available to small-farm agriculture in countries such as India. High-yielding seeds of reliable quality are not available in adequate quantities in this country. New systems of regulation are necessary, which can also promote biotechnology applications. Integrated inputs of services and materials such as soil testing, soil amelioration, fertilizers, pesticides, seeds, planting materials, water management devices, implements and machinery, and buy-back arrangements, credits and insurance are available to farmers 'single-source' from commercial companies in developed countries. These may be a necessary base for biotechnology in agriculture, forestry, animal husbandry, poultry and fish farming.

There are possibilities of producing proteins, fats, cocoa, butter substitutes, perfumery chemicals, spice components, gums, resins, and other high-value items by fermentation or tissue culture in developed countries, replacing imports from developing countries. Tea, coffee and cocoa would be produced in greenhouses by hydroponics. These methods of production pose a threat to exports from developing countries.

In conventional fermentation for antibiotics, vitamins, enzymes and industrial chemicals, cultures are held by secrecy and security and the processes are patented. On the other hand, genetically engineered organisms themselves have been granted patent protection as new products in the USA. Similar practices for transfer of technology may prevail for all biotechnology-based products and high charges will be expected by commercial companies. In the case of open-field propagation in small farms, security against further propagation without payment cannot be ensured and this may limit availability of high-yield seeds and plant varieties. The benefits could be made available to developing countries only through purchase by governments or international organizations from the companies. Research and development in commercial companies may have to be supported by contract research. The earlier conventions of openness and free exchange of information, materials and scientists in agriculture and communicable-disease control are being replaced by intellectual property and technology rights. Innovations to promote research with adequate rewards and returns coupled with systems to make results available to developing countries and to small farmers at low cost are necessary.

The regulation of recombinant DNA research and ensuring safety in large-scale testing and use depend on voluntary adherence to guidelines and cooperation. Good ethics and vigilance are essential, with informed debate on the issues, especially open-field trials and large clinical tests.

In summary, it is highly necessary to nurture and develop facilities and capabilities for basic and applied research in biosciences and biotechnology in developing countries and for quick application of results. Risk investment on a substantial scale should be made possible in fiscal systems. Where necessary, liberal public fund support should be provided for long periods for sustained effort if biotechnology developments are to provide large, social, national benefits in health, agriculture, energy and industry. Biotechnology has special relevance to developing countries as it can bring about a variety of major improvements in key sectors, with relatively low capital investments. It is therefore vital to attach importance to research and development and create favourable conditions and systems for wide application of results.

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