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The Scope of Biotechnology: the Indian Advantage

10 February 2003 | News

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Biotechnology may be as old as human civilization but modern biotechnology is less than three decades old. Traditional Biotechnology that led to the development of processes for producing products like yogurt, Vinegar, alcohol and cheese was entirely empirical and bereft of any understanding of the mechanisms that led to the product. There was no possibility of a deliberate design to produce a desired new product.

In modern biotechnology, we use the in- depth understanding we have gained in the last five decades. The mechanisms that underlie the variety of functions performed by living organisms, to produce a desired new or old product. In the case of an established product, the new biotechnological process is cheaper and better in many respects than the earlier processes.
Modern biotechnology has been, infact, an historical imperative. Its emergence on the world scene was predicted at leastfour decades ago. The term, genetic engineering, was coined independently in 1973 by the author of an article in The Guardian in the UK, and in a syndicated article by the present author in India.

Today's biotechnology consists of at least twenty-five areas each area being characterized by the use of a different set of technologies.

Scope of Biotechnology

Genetic engineering: Genetic Engineering of microbes, plants and animals (including marine animals). Genetic engineering implies conferring new capabilities on an organism by Transferring into an organism the appropriate DNA (De oxyribo Nucleic Acid, the genetic material) of another having these capabilities does this. Then ensures that these capabilities are converted into abilities. Thus the common yeast, Sacchromyces cerevisciae cannot make the protein, human insulin, but we can make it to do so by introducing in it the gene for human insulin (that is, the appropriate DNA fragment coding for this protein). After integrating the insulin gene in yeast DNA, creates condition for the insulin to express itself to produce insulin through the normal process of transfer of information from DNA to protein.

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Pushpa M. Bhargava, one of India's most brilliant scientists, has founded and directed the Centre for Cellular and Molecular Biology (CCMB), Hyderabad.His scientific contributions include the preparation and characterization of primary lever cell suspensions, identification of proteins from the seminal plasma and extensive characterization of one of these proteins and seminal plasmin. He has been awarded with Padma Bhushan, the Legion d'Honneur, the Wattumull Memorial Prize and Goyal Prize.

Genetically engineered microbes are today widely used for producing drugs and vaccines in large scale at low costs that are of great importance (human insulin, erythropoietin, and hepatitis-B vaccine). For example genetically engineered plants that make their own pesticides or are resistant to weedicides- are already in the market. Thus, over 60 percent of the acreage under soyabean in the United States have now genetically engineered soyabean that is resistant to the weedicides, Roundup. The total acreage under genetically engineered crops (for good or for bad) around the world exceeds 100 million acres today.
Genetically engineering plants are also poised to produce vaccines. A few hundred acres of genetically engineered banana plantation can provide enough vaccine to immunize 120 million children every year that need to be protected against four common diseases. One of the future sources of cheap protein-drugs in the coming years, would be genetically engineered animals who would secrete these drugs in abundance (1-15 mg/ml) in their milk. They will be available at a cost of three or more times lower than the current cost.

Gene Therapy: This is in a way, genetic engineering of humans, which would allow a person suffering from a disabling genetic disorder to lead a normal life.

Immunotechnologies: Such as monoclonal antibodies (MABs) for diagnosis and therapy. Antibodies, special sets of proteins present in humans that enable them to fight incursion of their bodies by harmful chemicals or micro organisms. Monoclonal antibodies are single chemical species of antibodies produced in the laboratory by a special technique. Nobel Prize was awarded for this in the 1980's to Cesar Milstein and Georges Kashler. Mouse MAB's can be used for the diagnosis of human diseases. As human MABs are difficult to produce in the laboratory, genetically engineered plants are likely to find wide application in the production of human MABs.

Tissue culture: Tissue culture of both plant and animal cells. These are used for Micro propagation of elite or exotic materials (Such as orchids), production of useful compounds such as taxol (the widely used anti-cancer drug) and vanillin, and preparation in the laboratory of â€œnaturalâ€? tissues such as arteries for arterial graft or skin for burn victims. (Modern tissue culture technologies allow the multiplication in the laboratory of cells isolated from plants and animals. In the case of plants, one can grow in the lab a whole plant from a single cell.)

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Stem cell techniques: Which would involve purification and isolation of stem cells from various tissues and develop into the desired tissue which could then be used, for example, for transplantation. Stem cells can be either totipotent (have the capability to produce any desired cell type or organ of the body under specific conditions) or they could be pluripotent (able to develop into several though not all cell types or organs). As embryonic stem cells are more likely totipotency than stem cells from adult tissues, the immediate emphasis in the area of stem cells is going to be first in the direction of establishing cell lines derived from early human embryos, from which stem cells could be isolated.

Enzyme engineering and technology: Involves immobilized or stabilized enzymes, new classes of enzymes (ribozymes) or new enzymatic routes that produce important organic compounds. Enzymes are biological catalysts (Generally proteins) poised to replace inorganic catalysts, which are used in chemical industry. (Proteins are abundant biological entities made up of twenty amino acids strung together like pearls in a necklace, by a special type of thread- a chemical bond called the peptide bond. One protein differs from another in the total number of amino acids and their sequence in the chain.)

Photosynthetic efficiency: Increasing photosynthetic efficiency for biomass production in the plant with the same amount of light and other inputs.

New DNA technologies: These include DNA fingerprinting, sequencing of genomes, development and use of new molecular markers for plant identification and characterization. Also the development of DNA- based probes for diagnosis of inherited disorders, antisense technologies that are aimed at blockage of the function of a particular stretch of DNA and computing using DNA.

Plant-based drugs: Use of modern biological techniques for validation, standardization and manufacture of indigenous plant-based drug formulations.

Peptide synthesis: Synthasis to make new drugs or other materials of industrial and commercial importance, such as salmon GnRH analogue (Ovaprim) to induce ovulation in fish. (Peptides are small proteins, generally containing less than 50 amino acid moieties.)

Rational drug design: Until a decade or so ago, the only way to discover a new drug was to synthesize a large number of compounds hoping that one of them will be effective against a particular disease. And it cost something between half a billion to a billion dollars for bringing a new drug to the market. As a result we have not added more than ten new drugs per year to the repertoire of medicines already available. In rational drug design, we first identify the molecular target we wish to attack. To do so, it becomes necessary to understand the mechanism of causation of the disease. Once we understand this mechanism and identify the molecular target lead effective computerized programs to design a molecule, which would hit the target. This approach of designing a drug on a rational basis cuts the cost of discovery of a new and reduces the time required (Now 12-15 years) by half.

The coming together of biotechnology and informatics is paying rich dividends. Genome projects, drug design and molecular taxonomy are all becoming increasingly dependent on informatics.

Nutraceuticals: That helps recovery after surgery or an episode of a major disease, or helps protect one against certain medical and health problems. For example, a Swedish company, Probi, has isolated a strain of Lactobacillus planetarum, which is apparently present in the digestive tract of Europeans and Amercians. (Indians have not yet been tested for its presence). The presence of this organism has been correlated with the ability of the person to recover after major surgery or after chemotherapy of cancer; this organism also seems to protect people against a vast range of stomach disorders including stomach ulcerts, irritable bowel syndrome and constipation. Probi is, therefore, marketing this organism in various forms, including a delicious soft drink!

Assisted reproductive technologies: Such as artificial insemination (Using husband's or donor semen), invitro fertilization, intra cytoplasmic sperm injection and techniques involving egg donation, surrogate motherhood or embryo transfer.
New cloning technologies: - Cloning of genetically engineered animals that would produce useful products.

Organ transplantation: Xenotransplantation that is transplantation into humans of organs from other animals. It appears that pig may be the most suitable for this biochemically, anatomically and immunologically. The major problem in xenotransplantation is the hyper-acute immunological rejection of the â€œ foreign organâ€? which occurs in a matter of minutes in enotrans plantation. This problem has been recently overcome by identifying the molecular basis of the hyper-acute rejection and then genetically engineering a pig to avoid it. But in the case of a kidney transplant from one human donor to another human recipient (homotransplantation) this does not occur.

New drug-delivery systems: Such as lipsomes and electrical patches, and the use of circadian rhythms to optimize the effectiveness of the drug. Thus the drug may depending on the circadian rhythm of the individual will be effective when taken at noon and midnight, than if taken at 6 AM and 6 PM.

Production of useful materials: Existing (for example, polyunsaturated fatty acids or beta-carotene, both of which are essential for normal vision) or new, from so far unutilized or under utilized but widely available resources such as marine organisms.

Production of new materials using new ideas: Observations or research findings, such as bacterial ropes or biodegradable polymers. For example, bacterial ropes that essentially consist of certain mutant bacteria that have the ability to grow into spagetti-like structures, when impregnated with certain metal ions can be stronger than steel but much lighter and biodegradable.

DNA vaccines: Which would be much cheaper than protein antigen-based vaccines that are generally used today.
New medical diagnostic technologies: - such as combination of MRI and Pet-SCAN for correlation of structure and function in

normal and diseased individuals.

Biosensor: For example, optical sensors using special thin films for detection of bacteria.

Use of microbes: Microbes selected or genetically engineered for effecting chemically difficult transformations, for example in the field of steroids that are widely used as drugs.

Bioremediadtion: For example of effluents or waste, using biological systems. A septic tank and an oxidation pond are simple examples of such bioremediation. Production of biogas is value-added bioremediation!

Processing of low-grade ores using microorganisms: Commercially viable bio processes are available today for processing such ores of over a dozen metals.

Bioinformatics, including genomics and proteomics: This newly emerging area makes use of the enormous amount of data on biological systems that are becoming available. There are several million species known. The sequence of the building blocks of DNA of just one human being alone will fill nearly 700 books (typed single space) of 500 pages each.

Nanobiotechnology: In which the operating or useful unit is of the scale of, say, a nanometre (millionth of a millimeter).

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Biological warfare: This is defined as the 'employment of biological agents to produce casualties in man or animals or damage to plants. While a biological attack could result in a made-made epidemic of unprecedented scale, the classical principles of clinical medicine and epidemiology would apply. Prompt diagnosis and early interventions could reduce morbidity and mortality, and mitigate the effects of a biological attack.

Advantages of biotechnologies

Biotechnologies are always non-polluting and, often, labour intensive. They make use of replenishable natural resources and help their conservation. They help, directly or indirectly, in saving energy. The cost of products produced through a biotechnological process is almost always less than that of the same product product produced, say, through a chemical synthetic route.

Biotechnologies are less accident-prone. In spite of their high level of intellectual sophistication, it is easier to train people to handle biotechnologies than other technologies. Above all, they are interesting and exciting for all those involved with them.

The Indian advantage

No other country in the world today has the unique set of advantages that India offers for large-scale practice of biotechnology. We have one of the largest bio in the world. We also have one of the largest coastlines anywhere. We have at least seven distinct climatic zones and one of the largest and most varied sets of marine organisms anywhere. The ambient temperature in most parts of the country is just what living organisms need for their activities that result in a biotechnological product. This curtails immensely the cost of cooling or heating which becomes obligatory for the practice of biotechnology in most parts of the Western world. There are places on the Indian coast where there is uninterrupted sunshine for some 340 days in the year so that one can grow marine organisms in open raceways.

We have an enviable infrastructure and a large pool of trained manpower, with experience in most of the areas of biotechnology. Our labor and infrastructure costs are, perhaps, lower than anywhere else where biotechnology can be done and is being done, with the possible exception of China. We have large tracts of land available for growing the desired plants required for agriculture-based biotechnology. We have experience of building world-class institutions in virtually every sector of human endeavor â€“ from outstanding basic research to efficient industrial production. We have, of course, many problems but we also know how to overcome them. In a nutshell the advantages far outweigh the disadvantages. It is a pity that we started much later in biotechnology than we could have but, even now, the prospects for the future are bright.

Dr. P.M. Bhargava