Contents lists available at www.innovativejournal.in

INNOVATIVE JOURNAL OF MEDICAL AND HEALTH SCIENCE

Journal homepage: http://www.innovativejournal.in/index.php/ijmhs

ISSN No. 2277-4939

THE BLEND BETWEEN BIOLOGY AND GENETIC ENGINEERING - OVERVIEW OF HUMAN STRIDES IN MOLECULAR GENETICS.

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ARTICLE INFO

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Keywords: Biology, Genetic engineering, Pharmacogenomics, Gene therapy.

ABSTRACT

Biotechnology is a field of applied biology that involves the use of living organisms and bioprocess in engineering, technology, medicine, public health and other fields requiring bioproducts. Biotechnology also utilizes these products for manufacturing purposes. Modern use of similar terms includes genetic engineering as well as cell and tissue culture technologies. The concept encompasses a wide range of procedures for modifying living organisms according to human purpose-going back to domestication of animals and cultivation of plants through the use of transgenic plants and animals to enhance the desired products. This includes gene testing, gene therapy, pharmacogenomics, discovery of DNA repair in cancer cells, genetically modified food, production of novel substances in crops plants, introduction of genetically engineered products into animals to improve their economic values and revelation of DNA sequencing in soft shell turtle, *Pelodiscus*. The significance of genetic engineering will not be fully ascertained without the knowledge on the importance of genetics on environmental factors, forensic science and genetic microbial biodegradation in the clean-up of oil contaminated environment.

INTRODUCTION

Genetic engineering "is the technological application that uses biological systems, living organisms or derivatives therefore, to make or modify products or processes for specific use". In the modern world, genetic plays a part in more dramatic breakthroughs than any other field of biological study. These breakthroughs have an impact in a wide variety of areas, from curing diseases to growing better vegetables to catching criminals. The field of genetics is in the midst of revolution, and at the centre of this exciting (and , to some minds, terrifying) phenomenon is the realm of genetic engineering: the alteration of genetic material by direct intervention in genetic processes. In agriculture, for instance, genes are transplanted from one organism to another to produce what are known as transgenic animals or plants. This approach has been used to reduce vulnerability of crops to environmental stresses, increase nutritional qualities, pesticides, herbicides and viral – resistant plants, and other agrochemicals, etc. Fruits and vegetables also have been genetically engineered so that they do not bruise easily and have a longer shelf life. Genetically engineered products into animals have improved their economic values as in gene pharming for milk and meat production as well as mass production of identical animals. Biotechnology also draws on the pure biological sciences (genetics, microbiology, animal cell culture, molecular biology, biochemistry and cell biology) and in many instances is also dependent on knowledge and methods from outside the sphere of biology (chemical engineering, bioprocess engineering, information technology). Conversely, modern biological sciences (including even concepts such as molecular ecology) are intimately entwined and dependent on the methods developed through biotechnology and what is commonly thought of as the life sciences industry.

Human strides in modern biotechnology find promising applications in such areas as:

Medicine and Human Health-Related Products

In medicine, modern biotechnology has made achievements in these areas;

- drug production
- pharmacogenomics
- gene therapy
- genetic testing (or genetic screening): techniques in molecular biology is used to detect genetic diseases(Thieman and Palladino, 2008).

PHARMACOGENOMICS

Biotechnology is researching a broad range of human-health-related products. Pharmacogenomics is the study of how the genetic inheritance of an individual affects his/her body's response to drugs. It is a portmanteau derived from the words "pharmacology" and "genomics". It is hence the study of the relationship between pharmaceuticals and genetics. The vision of pharmacogenomics is to be able to design and produce drugs that are adapted to each person's genetic makeup. Pharmacogenomics results in the following benefits:

1. Development of tailor-made medicines. Using pharmacogenomics, pharmaceutical companies can

create drugs based on the proteins, enzymes and RNA molecules that are associated with specific genes and diseases. These tailor-made drugs promise not only to maximize therapeutic effects but also to decrease damage to nearby healthy cells.

2. More accurate methods of determining appropriate drug dosages. Knowing a patient's genetics will enable doctors to determine how well his/ her body can process and metabolize a medicine. This will maximize the value of the medicine and decrease the likelihood of overdose.
3. Improvements in the drug discovery and approval process. The discovery of potential therapies will be made easier using genome targets. Genes have been associated with numerous diseases and disorders. With modern biotechnology, these genes can be used as targets for the development of effective new therapies, which could significantly shorten the drug discovery process.
4. Better vaccines. Safer vaccines can be designed and produced by organisms transformed by means of genetic engineering. These vaccines will elicit the immune response without the attendant risks of infection. They will be inexpensive, stable, easy to store.

Modern biotechnology is often associated with the use of genetically altered microorganisms such as *E. coli* or yeast for the production of substances like synthetic insulin or antibiotics. It can also refer to transgenic animals or transgenic plants, such as Bt corn. Genetically altered mammalian cells, such as Chinese Hamster Ovary cells (CHO), are also used to manufacture certain pharmaceuticals. Another promising new biotechnology application is the development of plant-made pharmaceuticals. Biotechnology is also commonly associated with landmark breakthroughs in new medical therapies to treat hepatitis B, hepatitis C, cancers, arthritis, hemophilia, bone fractures, multiple sclerosis, and cardiovascular disorders. The biotechnology industry has also been instrumental in developing molecular diagnostic devices that can be used to define the target patient population for a given biopharmaceutical. Herceptin, for example, was the first drug approved for use with a matching diagnostic test and is used to treat breast cancer in women whose cancer cells express the protein HER2.

Modern biotechnology can be used to manufacture existing medicines relatively easily and cheaply. The first genetically engineered products were medicines designed to treat human diseases. To cite one example, in 1978 Genentech developed synthetic humanized insulin by joining its gene with a plasmid vector inserted into the bacterium *Escherichia coli*. Insulin, widely used for the treatment of diabetes, was previously extracted from the pancreas of abattoir animals (cattle and/or pigs). The resulting genetically engineered bacterium enabled the production of vast quantities of synthetic human insulin at relatively low cost (Bains, 1987). According to a 2003 study undertaken by the International Diabetes Federation (IDF) on the access to and availability of insulin in its member countries, synthetic 'human' insulin is considerably more expensive in most countries where both synthetic 'human' and animal insulin are commercially available: e.g. within European countries the average price of synthetic 'human' insulin was twice as high as the price of pork insulin (IDF 2003).

Modern biotechnology has evolved, making it possible to produce more easily and relatively cheaply human growth hormone, clotting factors for hemophiliacs, fertility drugs, erythropoietin and other drugs(Feldbaum, 2002). Most drugs today are based on about 500 molecular targets. Genomic knowledge of the genes involved in diseases, disease pathways, and drug-response sites are expected to lead to the discovery of thousands more new targets (Feldbaum, 2002).

Gene Therapy.

"Gene therapy," according to a *Scientific American* review of the field, may "constitute a fourth health care revolution," following those of teaching public health practices, surgery with anesthesia, and antibiotics. "[Introduction] of selected genes into a patient's cells can potentially cure or ease the vast majority of disorders. More than 4,000 conditions [such as cystic fibrosis, cancer, heart disease, AIDS, arthritis and senility] result to an extent from impairment of one or more gene" (Anderson, 1995).

Altering Genes in Sperm.

A method has been discovered for altering genes in sperm(Detjen, 1994). The process will be patented. So far the method has only been applied to animals.

Insertion of Genes from other Species into Human Sex Cells.

This transgenic (cross-species) procedure could improve the quality of life and health of future humans, particularly if it means that they will not experience a genetically transmitted disease or defect.

Somatic Gene Therapy.

Somatic Gene Therapy involves insertion of genes from another species or a human into a sick person. For example, in 1988 a team of scientists wanted to place a bacterial gene into the bodies of terminally ill melanoma patients using a rodent retroviral vector. The purpose was to develop a better understanding of how the immune system fights cancer and whether genes from other organisms could be used for this purpose. National Institutes of Health guidelines required that the research team receive approval from the Recombinant DNA Advisory Committee. The Advisory Committee voted to approve the project and it was carried out (Carmel, 1992). A recent review of National Institutes of Health investments in gene therapy research found that progress is being made but that more attention needs to be paid to basic research (Marshall, 1995).

Insertion of a healthy gene from one person to another to treat a health problem is also possible. In 1989, the first human gene transplant was authorized by a United States District Court in Washington, D.C. (Hartman, 1993). Since then, scientists have demonstrated that it is possible to insert a healthy human gene into the cells in a cystic fibrosis patient's lungs. The implanted gene produces an essential protein to replace one that is defective in cystic fibrosis patients. A second approach is to use genetically-altered common cold virus to act as a carrier of the healthy gene into the body. This approach has been successfully tested in the laboratory (Detjen, 1994). In October of 1995 the first clear gene therapy success was claimed by scientists. Two children suffering from an inherited gene that left them without an immune system received normal genes. One patient's response showed clear improvement (Kolata, 1995).

DIAGNOSTIC PRODUCTS

Biotechnology products have made it easier to detect and diagnose illnesses. Many of these new techniques are easier to use and some, such as pregnancy testing, can even be used at home. More than 400 clinical diagnostic devices using biotechnology products are in use today. The most important are screening techniques to protect the blood supply against contamination by AIDS and the hepatitis B and C viruses. (Reports on National Biotechnology Policy,1991).

ARTIFICIAL ORGANS

Biotechnology is moving beyond transplantation to direct fabrication of body parts and organs. This technology depends on the manipulation, using computer-aided design, of ultrapure, biodegradable plastics and polymers. It has already been demonstrated in animals with an engineered artificial heart valve for lambs. Innovative electronics may be used. For example, "An ultrathin chip, placed surgically at the back of the eye, could work in conjunction with a miniature camera to stimulate the nerves that transmit images"(Robert and Vacanti, 1995).

VACCINES

The cost and availability of potential future vaccines may depend on biotechnology research. For example, efforts are underway to sequence the genome of human pathogens and parasites. The goal is to identify genes in these organisms that influence metabolism and could be drug targets or that encode antigens that could be built into vaccines (Aldehous, 1994) Examples include the agents that cause leprosy and African sleeping sickness.

GENETIC TESTING

Genetic testing involves the direct examination of the DNA molecule itself. There are two major types of gene tests. In the first type, a researcher may design short pieces of DNA ("probes") whose sequences are complementary to the mutated sequences. These probes will seek their complement among the base pairs of an individual's genome. If the mutated sequence is present in the patient's genome, the probe will bind to it and flag the mutation. In the second type, a researcher may conduct the gene test by comparing the sequence of DNA bases in a patient's gene to disease in healthy individuals or their progeny.

Genetic testing is now used for:

- Carrier screening, or the identification of unaffected individuals who carry one copy of a gene for a disease that requires two copies for the disease to manifest;
- Confirmational diagnosis of symptomatic individuals;
- Determining sex;
- Forensic/identity testing;
- Newborn screening;
- Prenatal diagnostic screening;
- Presymptomatic testing for estimating the risk of developing adult-onset cancers;
- Presymptomatic testing for predicting adult-onset disorders.

Some genetic tests are already available, although most of them are used in developed countries. The tests currently available can detect mutations associated with rare genetic disorders like cystic fibrosis, sickle cell anemia, and Huntington's disease. Recently, tests have been developed to detect mutation for a handful of more complex conditions such as breast, ovarian, and colon cancers. However, gene tests may not detect every mutation associated with a particular condition because many are as yet undiscovered, and the ones they do detect may present different risks to different people and population (Feldbaum, 2002).

GENETICS IN FORENSIC SCIENCE.

Forensic science, is the application of science to matters of law. It is based on the idea that a criminal always leaves behind some kind of material evidence that, through careful analysis, can be used to determine the identity of the perpetrator- and to exonerate someone falsely accused. Among those forms of material evidence of interest to forensic scientists working in the field of genetics are blood, semen, hair, saliva and skin, all of which contain DNA that can be analyzed.

ANIMAL AND PLANT PRODUCTS

The projected benefits from genetically engineered animal and plant research products are considerable. The Office of Technology Assessment estimates that agricultural biotechnology will continue to help agricultural productivity to increase at about the same rapid historical rate of the last two decade (U.S. Congress Office, 1992). Table 1 shows what the estimated impact of biotechnology might be on animal and plant-related products. For example, the bushel per acre yield of corn is predicted to increase by as much as 21 percent if more new biotechnology is developed, compared to projected loss of 2 percent if less new technology is used. The application of more new biotechnology could increase the number of calves born per 100 cows by 12 per year. These are significant increases which could have a substantial impact on commodities and the cost of food. Requirements for field testing and regulatory approval, the acceptance of the new methods by farmers, and public acceptance of the new products could significantly influence these projections.

Table 1
The Estimated Impact of Biotechnology on Crop Yield and Animal Production Efficiency by 2000

	Actual 1990	Slow-Down development of New Technology 2000	Most Likely Technology 2000	Rapid Creation of New Technology 2000
Crops				
Corn bu/acre	116.2	113.8	128.5	141.6
Cotton lb/acre	600.0	NA	708.0	NA
Soybeans bu/acre	32.4	37.7	42.6	53.8
Wheat bu/acre	34.8	37.7	42.6	53.8
Beef				
Lbs meat/lbs feed	0.143	0.146	0.154	0.169
Calves /100 cows	90.0	93.7	96.2	102.5
Dairy				
Lbs milk/lbs feed	0.370	0.373	0.389	0.428
Lbs milk/cow/year	14,200.0	17,247.2	19,191.6	20,498.8
Poultry				
Lbs meat/lbs feed	0.370	0.373	0.389	0.428
Eggs/layer/year	250.0	250.5	258.0	273.1
Swine				
Lbs meat/lb feed	0.154	0.174	0.181	0.196
Pigs/sow/year	13.9	14.4	15.8	17.8

Source: Adapted from U.S. Congress, Office of Technology Assessment, 1992

Animal Products

Genetic engineering may improve an animal's economic value. Genetically engineered hormones, transfer of genes from other species, and introduction of human genes to produce specified substances are all being used today for this purpose.

INTRODUCTION OF GENETICALLY ENGINEERED PRODUCTS INTO ANIMALS TO IMPROVE THEIR ECONOMIC VALUE.

Genetically engineered hormones and other biologically active substances may improve animal qualities. For example, pigs that were administered a new bioengineered growth hormone (porcine somatotropin) "show increased average daily weight gains of about 10 to 20 percent, improved feed efficiency of 15 to 35 percent, decreased adipose (fat) tissue mass of 50 to 80 percent, and concurrently increased protein deposition of as much as 50 percent without adversely affecting the quality of the meat. This hormone is currently being reviewed by the federal Food and Drug Administration (FDA) for commercial use."

In 1993, the U.S. Food and Drug Administration approved the use of Posilac, a Monsanto company product containing recombinant bovine somatotropin (rBST) to improve the milk production of dairy cows (California Department of Food and Agriculture, 1992). On average, depending on the management skill of the producer, rBST can increase milk production by about 12 percent (U.S. Congress Office, 1992). Concern has been expressed about possible antibiotic residue levels in milk; however, the California Department of Food and Agriculture's position is that public health is safeguarded.

ANIMALS TRANSGENIC

A transgenic animal contains genes which have been inserted from another species into the egg to generate a particular scientifically useful or marketable characteristic. Offspring include the desired trait. The vast majority of transgenic animals being produced today are laboratory mice with genes inserted from many different species (including humans). Typical is the Oncomouse, which is genetically modified to develop malignant tumors useful for human cancer research. Recently developed transgenic farm animals include cattle, chickens, pigs, rabbits, sheep, fish, and goats (Comstock, 1992).Transgenic cattle and swine have recently been developed to produce human growth hormone. Transgenic animal blood would produce products that are free of HIV and other transmittable human disease organisms (Lacy and Bush,1987).

GENE PHARMING

The term "gene pharming," playing on the words *farming* plus *pharmaceutical*, refers to the production of biologically active drugs using genetically altered animals. For example, Genzyme Transgenic has purchased a farm in western Massachusetts to breed genetically altered goats which produce human therapeutic and diagnostic proteins in their milk. Gene pharming is expected to be a less costly production Mass method than traditional cell culture methods. In August of 1995, the FDA issued guidelines for medicines derived from the milk of genetically altered animals (Detjen, 1994).

Producing Identical Animals

Recent laboratory success in producing identical sheep by cloning "could open the door to gene-altered animals with desirable traits, such as sheep with better wool or pigs with `humanized' organs suitable for transplantation into people" (Weiss, 1996). Each of the biotechnology animal related developments discussed above might be able to use this new technique to maximize benefits by reducing variation between animals.

Plant Biotechnology

The current work in plant biotechnology emphasizes modification of plant-specific characteristics such as resistance to weeds, pests, herbicides, and pesticides, tolerance to stress, and improved nutritional content. Other work focuses on improving traits important to agriculture such as frost resistance and nitrogen fixation (Lacy and Bush, 1987). According to the Biotechnology Industry Organization, all of these activities are directed at improving the yield and reliability of plants in the face of pests, reducing the cost of farming by reducing the need for costly herbicides, improving crop quality, and increasing crop diversity by developing entirely new crops.

Herbicide-Resistant Plants

A little less than half of bioindustry's resources are spent on genetic engineering aimed at producing herbicide resistant crops, rather than disease-resistant crops. Herbicide-resistance research seeks to develop plants that can resist intensive applications of herbicides. In contrast, disease-resistance research seeks to engineer plants that are resistant to diseases and insects. At least 27 herbicide-producing corporations, including the world's eighth largest pesticide producers, are working in this area. Market value of these products is expected to exceed $6 billion by the turn of the century (Gasser and Fraley, 1989). In 1995 the Environmental Protection Agency, for the first time, granted "limited premarket approval for pesticidal transgenic plants. The approval allows these companies to plant experimental crops of pesticide-resistant potatoes, corn, and cotton with the goal of gathering data that could lead to commercialization as early as 1996" (Emst and Young, 1994).

Virus-Resistant Plants

Plant viruses can devastate entire food crops, including corn, wheat, rice, soybeans, and potatoes. Virus-resistant plants have been developed by introducing the genes that encode a key part of the virus into the plant. The new plant retards viral infection and viral replication. Enhanced viral resistance should improve crop quality and yield; it also should decrease the need for insecticides directed against insects that spread the virus. The level of viral material in any plant is "not expected to present a health risk for humans and livestock," according to the American Medical Association's Council on Scientific Affairs (American Medical Association's Council, 1991).

Food Processing

Food-processing research currently focuses on growth and fermentation by yeast and bacteria. These methods are well known technologies used in cheese and bread making. Biotechnology applications include producing fermentation starter cultures with specific taste, texture or other characteristics; creating plant tissue for the production of plant-derived ingredients (starches for example); and improving waste management (such as oil or other waste digesting bacteria). "In principle," one report asserts, "any commodity that is consumed in an undifferentiated or highly processed form could be produced in this manner, and product substitution could be easily introduced. In short, agricultural production in the field could be supplanted by cell and tissue culture factories." (Goodman, et al., 1991).

Research on Environmental Cleanup and New Energy Sources

Renewable sources of energy have been a national priority since the mid 1970s. Environmental cleanup of large toxic spills and of military bases remains a challenge. Biotechnologists are researching ways of addressing these needs.

BIOREMEDIATION

"Bioremediation" involves the use of microorganisms to degrade various types of environmental pollution, such as waste oil and heavy metals, to produce environmentally safe byproducts (Ramos, 1994). This method was used to clean oil spills in the Gulf of Mexico and Prince William Sound, and might be used to decontaminate military bases or to remove heavy metals from soil. It might also be used to clean up nuclear waste. Approval was recently given to release genetically engineered bacteria to "feast on pollutants in Oak Ridge National Laboratory soil"(Zorpette, 1995). Government environmental regulatory efforts to clean up polluting industries and hazardous materials disposal sites are encouraging research and development of bioremediation (Edgington, 1994). Germany recently passed a law requiring manufacturing companies to assume responsibility for their products from cradle to grave. As a consequence, German companies have become quite interested in biotechnological solutions in order to avoid the high costs of traditional cleanup methods.

DNA Sequences Reveal the True Identity of the Soft Shell Turtle *Pelodiscus*

A research team from the Senckenberg Research Institute Dresden has identified many different genetic lineages in the soft shell turtle genus *Pelodiscus*, representing different species.

Traditionally it has been assumed that only the species *Pelodiscus sinnensis* belonged to the genus examined. As a foodstuff, Chinese soft shell turtle are the most economically important turtles in the world, with an animal trade volume of many hundreds of millions of species.

Tiny pieces of tissues were removed from the shells by the Dresden researchers and part of the genetic make up of the turtle were defined with the help of the most up – to – date technique. What is promising here is above all the analysis of the mitochondrial DNA, as these are present to a much greater degree compared to the DNA of the cell nucleus, thus minimizing conservation problem. Unfortunately, the attempt to gain DNA from the first turtle shell failed completely. The remnants of the animal were simply too old and too dried out . However, the second shell proved to be a great success for the research! The analysis of the DNA sequences led to the conclusion that the genus *Pelodiscus* contains at least four and not as previously believed one species. For the first time, and with the help of the sequences from the Berlin sample, which is more or less the "original standard" for the species *Pelodiscus sinnensis*, it could be clarified which of the four specie is actually the "real" Chinese soft shell turtle(Senckenberg, 2011).

Complexities of DNA Repair Discovered

An international team of scientists led by UC Davis researchers has discovered that DNA repair in cancer cells is not a one-way street as previously believed. Their findings show instead that recombination, an important DNA repair process, has a self-correcting mechanism that allows DNA to make a virtual u-turn and start over. "That makes it a very robust process, allowing cancer cells to deal with DNA damage in many different ways. This repair mechanism may have something to do with why some cancer cells become resistant to radiation and chemotherapy treatments that work by inducing DNA damage."

In the current study, Heyer and his colleagues used yeast as a model system to elucidate the mechanisms of DNA repair. They expect their findings, like most that come out of work on yeast, will be confirmed in humans. The research team used electron microscopy to observe repair proteins in action on strands of DNA. They saw a presynaptic filament called Rad51 regulating the balance between one enzyme (Rad55-Rad57) that favors recombination repair and another (Srs2) that inhibits recombination repair. By controlling the balance between the two enzymes, Rad51 can initiate genetic repair or the u-turn as needed."It is a tug-of-war that has important implications for the cell because, if recombination occurs at the wrong time in the wrong place, the cell may die as a consequence." The ability of the repair system to abort ill-fated repair attempts, gives the cell a second shot, improving cellular survival after its DNA is damaged. This is exactly what is dreaded in cancer treatment.

"There are a lot of hints in the scientific literature suggesting that DNA repair contributes to resistance to treatments that are based on inducing DNA damage such as radiation or certain types of chemotherapy." "The ability of cancer cells to withstand DNA damage directly affects treatment outcome, and understanding the fundamental mechanisms of the DNA repair systems will enable new approaches to overcome treatment resistance."Heyer said the team's next step is to look at the enzyme system in humans and see whether they find the same principles at work. One application of this work will be to target the self-correcting mechanism in cancer cells as a way of sensitizing them to radiation and/or chemotherapy treatments."If we can confirm that these types of mechanisms exist in human cells, then we will have an approach for making cancer cells more sensitive to DNA damage-inducing treatments."(Liu, et al., 2011).

CONCLUSION

Today, genetics permeates both the biological sciences and American Culture, surfacing in Research Laboratories, congressional hearings, and courtrooms as well as popular movies and books. Genetics has unified the biological sciences and led to the modern synthesis of evolution theory and biology by demonstrating that organisms share the same basic genetic materials and processes. DNA analysis (such as in semen, skin, blood, hair etc) plays a vital role in primary investigations and the establishment of paternity, while genetic screening, pharmacogenotics, gene therapy gene test and discovery of DNA repair provide hope for those suffering from inherited diseases like sickle-cell anemia, cystic fibrosis blood clotting hemophiliacs or Huntington's disease. Entering the twenty first century, transgenic plants and animals have provided the best window into future impact of genetics. Biotechnology has also gained momentum in the use of genetically engineered microorganism in an effort to find a sustainable ways of cleaning up contaminated environment.

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