CHAPTER 1

UNDERSTANDING BIOTECHNOLOGY - THE CONCEPTS AND TERMINOLOGIES

1.1 INTRODUCTION

The term 'Biotechnology' may sound futuristic, but it is nearly as old as civilization itself. We have begun growing crops and raising animals 10,000 years ago to provide a stable supply of food and clothing.[1] We have been using the biological processes of microorganisms for 6,000 years to make useful food products such as bread, cheese and to preserve dairy products.[2] The term 'biotechnology' has been used to signify activities relating to biological process and technologies. Traditional biotechnology and its development processes were entirely experiential. It was aimed at understanding the mechanisms for improving every activity from farming to food processing. Early farmers selected particular plants to grow crops and saved their seeds for the following season. Over the years, they bred the varieties of seeds they found best and learned how to grow them more efficiently through techniques of irrigation and weed control. The process of choosing certain seeds for their expressed characteristics and learning how to irrigate and rotate the crops was the genesis of earlier days of biotechnology.[3]

The expression 'modern biotechnology' can be differentiated form traditional use of biological process which was commonly termed as classical biotechnology. Even though biotechnology has been in practice for thousands of years, the technological explosion occurred only in the twentieth century. Various branches of science like physics, chemistry, engineering, computer application and information technology helped revolutionise the development of life sciences and it ultimately resulted in the evolution of modern biotechnology.[4] Unlike classical biotechnology,

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[1] Debbie Strickland ed., *The Guide to Biotechnology*, (Biotechnology Industry Organization), p.1. available at; http://www.pacontrol.com/download/BiotechGuide.pdf accessed on 12-11-2009.
[2] Ibid.
[3] Kathy Wilson Peacock, *Biotechnology and genetic engineering*, (New York, Infobase Publishing, 2010), p.11.
[4] A.J. Nair. *Introduction to Biotechnology and Genetic Engineering,* (New Delhi, Infinity Science Press Llc. 2007), p.34.

modern biotechnology operates at the molecular level of life. It is modern in the sense that the techniques are applied mainly to cells and Molecules.[5] Life at the molecular level is the same among every species from humans to bacterium. Every living thing on earth is built with molecules which are similar and there exists hardly any difference among humans, fishes, trees, worms and bacterium at molecular level. Only the deoxyribonucleic acid (DNA) coding is different among various species and it ultimately makes every living thing what it is.[6]

The term biotechnology for the purpose of understanding can be divided in to two 'bio' and 'technology'. 'Bio' means the use of biological processes and 'technology' means to solve problems or make useful products.[7] Biotechnology is a collection of many different technologies. It is a highly multidisciplinary subject. It involves the contribution of scientists from various fields like biology, chemistry, engineers, statisticians, mathematicians, and information technology. It also involves contributions from financial, legal, and managerial experts.[8] It is a rapidly growing technological terrain, recognised by its significant contribution to life science research like the agricultural, medical and pharmaceutical sectors. In order to have a better understanding of the major issues raised by biotechnology, we must have some grasp of what biotechnology and bioscience are. The concepts and jargons frequently used in biotechnology are not familiar to legal researchers. This chapter makes an attempt to familiarise the common concepts and terminologies used in biotechnology for the better understanding of legal issues relating to biotechnology and research data protection.

1.2 DEFINITIONS OF BIOTECHNOLOGY

The simple definition of 'biotechnology' is the commercialization of cell biology". Biotechnology is an umbrella term that covers various techniques for using

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[5] A.J. Nair. *Introduction to Biotechnology and Genetic Engineering,* p. 4.
[6] Ibid.
[7] Debbie Strickland ed., *The Guide to Biotechnology* , p.1.
[8] European Federation of Biotechnology, *What's What In Biotechnology?*, Task Group On Public Perceptions of Biotechnology, p. 1 (2007) available at http://efbpublic.org/Members/admin/library/Library_Card.2004-03-30.4055353969 last accessed on 22-09-2011.

the properties of living organisms to make products or provide services.[9] The Convention on Biological Diversity (CBD) defines biotechnology as: "any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products for specific use."[10] This definition includes medical and industrial applications as well as many of the tools and techniques that are common in agriculture and food production.

According to the definition of the Codex Alimentarius Commission (CAC) adapted from the Cartagena Protocol on Biosafety Section, modern biotechnology is defined as the application of:

1. In vitro nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and the direct injection of nucleic acid into cells or organelles or

2. Fusion of cells beyond the taxonomic family, that overcomes natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection.[11]

The definitions appears to be rather complicated, however a much simpler definition was laid down by the Organisation for Economic Co-operation and Development (OECD). The OECD developed a single definition for the term biotechnology in 2002.[12]

The OECD defines biotechnology as:

> "the application of science and technology to living organisms as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services. [13]"

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[9] Eric S Grace, *Biotechnology Unzipped-Promises and Realities,* (Hyderabad, Universities press, 2004.) p.3

[10] A zaid et al., *Glossary of biotechnology and genetic engineering*, FAO Research and Technology Paper 7. Food and Agriculture Organization of the United Nations, p. iii available at ftp://ftp.fao.org/docrep/fao/003/X3910E/X3910E00.pdf last accessed on 30-11-2010

[11] Food Safety Department, *Modern food biotechnology, human health and development: an evidence-based study*, World Health Organization, p. 1-2 (2005) available at, http://www.who.int/foodsafety/publications/biotech/biotech_en.pdf., last accede on 10-11-2011

[12] Brigitte van Beuzekom and Anthony Arundel, *OECD Biotechnology Statistics 2009*, p. 9 available at. http://www.oecd.org/dataoecd/4/23/42833898.pdf last accessed on 10-4-2011

[13] Ibid.

This definition covers the entire modern biotechnology including the traditional activities. The OECD statistics have given a list of indicative biotechnology techniques. The following are the activities classified under modern biotechnology according to the OECD:[14]

- **DNA/RNA:** Genomics, pharmacogenomics, gene probes, genetic engineering, DNA/RNA sequencing/synthesis/amplification, gene expression profiling, and use of antisense technology.
- **Proteins and other molecules:** Sequencing/synthesis/engineering of proteins and peptides (including large molecule hormones); improved delivery methods for large molecule drugs; proteomics, protein isolation and purification, signaling, identification of cell receptors.
- **Cell and tissue culture and engineering:** Cell/tissue culture, tissue engineering (including tissue scaffolds and biomedical engineering), cellular fusion, vaccine/immune stimulants, embryo manipulation.
- **Process biotechnology techniques:** Fermentation using bioreactors, bioprocessing, bioleaching, biopulping, biobleaching, biodesulphurisation, bioremediation, biofiltration and phytoremediation.
- **Gene and RNA vectors:** Gene therapy, viral vectors.
- **Bioinformatics:** Construction of databases on genomes, protein sequences; modeling complex biological processes, including systems biology.
- **Nanobiotechnology:** Applies to the tools and processes of nano/microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics etc.

Detailed explanations of the terminologies are given in the later portion of this chapter. Another definition given by the Food and Agricultural Organisation (FAO) is as follows.[15]

1. The use of biological processes or organisms for the production of materials and services of benefit to humankind. Biotechnology includes the use of techniques for the improvement of the characteristics of economically

[14] Brigitte van Beuzekom and Anthony Arundel, *OECD Biotechnology Statistics 2009*, p. 9
[15] A zaid et al., *Glossary of biotechnology and genetic engineering*, p. 31.

important plants and animals and for the development of micro-organisms to act on the environment.

2. The scientific manipulation of living organisms, especially at the molecular genetic level, to produce new products, such as hormones, vaccines or monoclonal antibodies."

1.3 CLASSIFICATION OF BIOTECHNOLOGY

Biotechnology is a huge topic. It is hard to define its exact boundaries. Some scientists divide the field into red biotechnology and green biotechnology.[16] Red biotechnology signifies medicine and green biotechnology is related to food. There are other subdivisions of biotechnology as white and blue. White biotechnology which is also called industrial biotechnology uses enzymes and adopts natural processes such as fermentation to create industrial products, which was formerly made of chemicals. Bioplastics made with vegetable oil and starches instead of petroleum are examples of white biotechnology. Blue biotechnology is an area that deals with marine biology. [17]

Academically, biotechnology falls under many umbrellas. It is generally considered a natural science and more specifically a life science. The life sciences include biology, the study of living organisms and their environments. Biology encompasses both botany and zoology. Beyond these classifications are numerous overlapping categories including cell biology, microbiology, molecular biology, physiology, ecology, embryology, genetics, population genetics, epigenetics, proteomics and bioinformatics.[18] These subdivisions are narrowed down on the basis of the area of research.

1.4 HISTORICAL PERSPECTIVE OF BIOTECHNOLOGY

History of biotechnology is as old as human race itself. Agriculture practices are believed to have originated around 10,000 B.C. and so is the history of biotechnology. Humans always had the desire for research; even the selection and preservation of seeds for subsequent crops was the earlier genesis of biotechnology

[16] Kathy Wilson Peacock, *Biotechnology and genetic engineering*, p. 4.
[17] Ibid.
[18] Ibid.

research. Planting techniques, animal husbandry and food processing involved some amount of research. As the food processing techniques improved, the process of fermentation was discovered. The Egyptians were probably the first to brew beer on a wide scale, almost 9,000 years ago even though they did not understand the scientific properties of enzymes and yeast.[19]

The history of biotechnology is interesting. A detailed study shows how the quest for research led to many useful discoveries in biotechnology. One such study which was done in early 500 BC by the Greeks is on inheritance of characteristic features of human beings. According to the Greek mathematician, Pythagoras, heredity was the dominion of males. Females were responsible for nourishment and safety of the unborn; but the father provided all the traits, physical and otherwise, that a child possessed. A few years later, the philosopher Empedocles added to Pythagoras's idea by theorizing that the man's semen mixed with the fluids inside the woman's body, resulting in a child with characteristics of both the parents.[20] Another prominent concept was articulated by Aristotle who formulated his own theory around 350 B.C. He believed that both the mother and father contributed to the physical makeup of their children.

1.4.1 EARLY DEVELOPMENTS - MICROBIOLOGY

The study of microbiology was one of the landmark developments in the field of biotechnology. The science of microbiology started with the invention of the microscope. The English scientist Robert Hooke was the first person to use a microscope for academic studies. He discovered the cellular structure of plants in 1665.[21] He also viewed the fungi which he grew in his laboratory. However Antoni van Leeuwenhoek is considered to be the father of microbiology. He made many improvements on the microscope which helped him to be the first to view bacteria and muscle fibers. He developed a microscope powerful enough to view sperm for the first time and witnessed the fertilization of an egg. This area of research was further developed into a different branch called genetics. These developments in microbiology during the 17th century helped English physician William Harvey to

[19] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.33.
[20] Ibid, at, p.34
[21] Ibid, at, p.35.

explain the process of fertilization inside the woman's body. Harvey's ideas were verified by the Antoni van Leeuwenhoek in 1677.[22]

1.4.2 GENETICS

By 1890's, the invention of better microscopes helped biologists research on basic facts of cell division and sexual reproduction. A number of hypotheses were suggested to explain heredity, but Gregor Mendel an Austrian monk was the only one who got the concept more or less right. Hence Gregor Johann Mendel was considered to be the father of genetics.[23] He discovered the laws of heredity through his breeding experiments with peas. He studied the inherited characteristics of pea plants resulting in the understanding of dominant and recessive phenotypes. Mendel cross-bred pea plants with various characteristics and meticulously observed what physical traits were passed on to the offspring. His in-depth experiments led him to understand which phenotypes predominated when various combinations of plants were bred. Mendel published his landmark paper, "Experiments on Plant Hybridization," in 1866.[24] Though it was ignored by the scientific community earlier, recognition came posthumously in the early 1900s when scientists rediscovered his work and they were able to replicate his findings.

1.4.2.1 DARWIN'S THEORY NATURAL SELECTION

The basic concepts of heredity and evolution were explained in the publication of Charles R. Darwin and Alfred R. Wallace. Their theory of evolution by natural selection was formulated in 1858. The natural selection theory explains that all species of plants and animals have evolved from common ancestors and useful traits are preserved in them, while detrimental ones are extinguished. Charles Darwin's famous book *On the Origin of Species by Natural Selection* was published in 1859. This was one of the major milestones in the history of science.[25] According to him, evolution takes place as members of a species survive and pass their traits on to their offsprings. A genome of a species carries a set of instructions for assembling and

[22] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.35.
[23] A.J. Nair. *Introduction to Biotechnology and Genetic Engineering*, p. 352
[24] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p. 35
[25] Ibid, at, p.37.

operating an organism and it records the organism's evolutionary history.[26] Darwin's theory has proven useful to the study of heredity and environment.

1.4.2.2 EUGENICS

Another development subsequent to genetics was 'Eugenics'. The process of selection and breeding has taken a new dimension when Francis Galton applied these principles to human race to improve the quality of traits. The term 'Eugenes' in Greek means good in stock; hereditarily endowed with noble qualities.[27] 'Eugenics' is the study of the agencies under social control that may improve or impair the racial qualities of future generations either physically or mentally. Francis Galton is considered to be the father of 'Eugenics'. He was the cousin of Charles Darwin and was a renowned intellectual. He was inspired by Darwin and started his own exploration of human variation. He coined the word 'Eugenics' in 1883 in his book "Inquiries into the Human Faculty and Its Development."[28] He defined 'Eugenics' as the improvement of humankind through selective breeding, sterilization, and other forms of intervention. According to Galton, his abilities were inherited from his own eminent, privileged family.

The development of eugenics as a separate branch of science was aimed at improving the overall health or qualities of a race of people by controlling their ability to reproduce. Eugenics is classified as positive eugenics and negative eugenics. Positive eugenics is the practice of encouraging people possessing esteemed genetic traits to reproduce. Whereas, negative eugenics is the practice of discouraging or forbidding (sometimes by force) those who possess undesirable traits from reproducing.[29] The practice of eugenics was widely criticized as unethical.

1.4.3 THE DEVELOPMENTS OF MODERN BIOTECHNOLOGY

The term biotechnology was coined by a Hungarian inventor named Karl Ereky in his book entitled *"Biotechnologie der Fleisch-, Fett- und Milcherzeugung im*

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[26] Jim Chen, *Biodiversity and Biotechnology: A Misunderstood Relation*, p. 57
[27] Francis Galton, *Inquiries Into Human Faculty And Its Development*, Edited by Gavan Tredoux, This edition forms part of the online Galton archives, available at http://galton.org/books/human-faculty/text/galton-1883-human-faculty-v4.pdf accessed on 02-01-2011.
[28] Ibid.
[29] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.325.

landwirtschaftlichen Grossbetriebe" (Biotechnology of Meat, Fat and Milk Production in an Agricultural Large-Scale Farm) in 1917.[30] He described how technology could be used to transform plants and animals into products more useful than in their natural state. The modern biotechnology as a subject is very broad. It applies modern techniques on living organisms or substances to make or modify a product. Biotechnology can be applied to all classes of organisms - from viruses and bacteria to plants and animals - and it has revolutionised the area of modern medicine, agriculture and industry.

The era of modern biotechnology is believed to have started with the discovery of the microscope. The path of genetic manipulation can be said to have started in 1665 when the English scientist Robert Hook published a review of some observations he had made while peering through a microscope. He saw tiny spaces surrounded by walls while he was observing samples of cork. He is the one who coined the word "cell."[31] Ten years later Anton van Leeuwenhoek designed the microscope with magnifying power as great as 270 times. He was the first person to observe and describe micro-organisms which he called "very little animalcules". He was also the first person to observe the "bacteria" which according to him were twenty five times smaller than the blood cells. He also discovered the presence of sperms in semen in human and other animals.[32]

Even though cells were found everywhere from plants to animals, nobody came up with the idea that the cells were fundamental to life. More than 70 years later, two Germen biologists Matthias Schleiden and Theodore Schwann introduced the cell theory which says that all living organism are made of cells. According to them cells are the basic structural and functional units of a living organisms. [33] The research on cells further led to the discovery of deoxyribonucleic acid (DNA) which is believed to be the heart of life. The area of biotechnology developed as a result of man's increasing desire to know the mechanisms that maintain living organisms.

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[30] Fari, M.G. and Kralovanszky, *The founding father of biotechnology: Károly (Karl) Ereky*, International Journal of Horticultural Science, 12 (1): pp 9-12 (2006).
[31] Eric S Grace, *Biotechnology Unzipped-Promises and Realities,* p.3
[32] Ibid.
[33] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.325.

In 1869, the Swiss physician Friedrich Miescher isolated various phosphate-rich chemicals which he called *nuclein* (now nucleic acids) from the nuclei of white blood cells. It paved the way for the identification of DNA as the carrier of inheritance[34]. In 1919 a Russian-born biochemist Phoebus Levene, working at the Rockefeller Institute of Medical Research in New York City, discovered that *nuclein* was a string of nucleotide molecules containing sugar and a base held together with phosphates.[35] He also correctly identified the nucleotides as adenine, guanine, thymine, and cytosine. However, Phoebus Levene believed that each molecule contained only four nucleotides and that nucleotides were much too simple to contain the genetic code. According to him the genetic code was believed to have resided in the protein of a cell. Subsequently Oswald Avery who was also working at the Rockefeller Institute claimed in the year 1944, that DNA is the key component of genes and chromosomes.[36] His work was verified in 1952 by geneticists Alfred Hershey and Martha Chase in the famous Hershey- Chase experiment which earned Hershey a Nobel Prize.

The landmark moment in the history of science occurred on April 25, 1953 when James D. Watson and Francis Crick published "A Structure for Deoxyribose Nucleic Acid" in the journal, Nature.[37] Watson and Crick, along with their colleague Maurice Wilkins, received the 1962 Nobel Prize in physiology and medicine for "their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material.[38]"

The discovery of double helix DNA structure was a huge controversy during that period. In fact the crystallographer Rosalind Franklin, who generated the legendary "photograph 51" using the X-ray diffraction photo, was the first one to reveal DNA's double-helix structure. The controversy was that the Rosalind Franklin's X-ray crystallography image, "photo 51", was shown to Watson and Crick without her knowledge and consent. The image which actually indicated the double-helix structure of DNA, was not the discovery of Watson and Crick which earned

[34] Ralf Dahm, *Friedrich Miescher and the discovery of DNA*, Developmental Biology 278, p.278 (2005).
[35] Ibid.
[36] Ibid.
[37] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.40.
[38] Ibid.

them the Nobel Prize.[39] They could not have proposed their celebrated structure of the DNA without access to the experimental results obtained by Rosalind Franklin, particularly her crucial X-ray diffraction photograph. She was known as the dark lady of DNA[40].

The major development in medical biotechnology was the discovery and development of antibiotics. The first antibiotic was 'moldy soybean curd' used by the Chinese almost 2,500 years ago to treat skin infections. The Sudanese-Nubian civilization of Africa used a form of the same micro organism which created tetracycline as an antibiotic as early as 350 B.C.[41] The traces of tetracycline have been found in human skeletal remains of ancient Sudanese Nubia. The distribution of tetracycline in bones was only understandable after exposure to tetracycline-containing materials in the diet of these ancient people.[42] In the middle ages in Europe, tinctures made from plant extracts or cheese curds were used to ward off infection. The tetracycline as a large family of generic antibiotics was discovered as natural products by Benjamin Minge Duggar in 1948.[43]

The most significant development in the history of mankind was the discovery of vaccines to prevent diseases. History shows that the Chinese used to practise variolation, a primitive type of vaccination in which people were purposely and mildly infected with smallpox to create immunity against future infections. Indian physician Madhav described a similar process in his medical textbook, *Nidana* in eighth century.[44]

The landmark era in biotechnology was that of Louis Pasteur, a French microbiologist and chemist who studied how diseases were transmitted. Louis Pasteur became popular for the discovery of vaccines for the treatment of rabies, cholera, and anthrax. He discovered the anthrax vaccine and bacteriologic agents for diseases such

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[39] Rosalind Franklin and the Secret of ' Photo 51'- the Structure of DNA, available at www.stealthskater.com/Documents/**DNA**_07.pdf , last accesses on 12-09-2010
[40] Ibid.
[41] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.34.
[42] Ibid.
[43] Ibid.
[44] Ibid.

as tuberculosis, diphtheria, typhoid and yellow fever.[45] The cornerstone of Pasteur's contribution to science was the germ theory. Pasteur discovered that fermentation of decaying matter allowed microorganisms to reproduce. According to him Germs were microorganisms and if allowed to reproduce, they would cause diseases. Pasteur's ideas led to the development of basic hygiene. People began to realize that epidemics could be caused by polluted water or food. Louis Pasteur received the U.S. Patent in 1873 for yeast as an article of manufacture.[46]

The Scottish biologist and pharmacologist Alexander Fleming discovered penicillin, the first widely manufactured antibiotic which was developed from the *mold* of the *Penicillium notatum*.[47] Fleming was investigating the properties of staphylococci and discovered the curative properties of penicillin. He received the Nobel Prize for this discovery in1945.[48] It was the miracle drug of the late 1940s and 1950s against many diseases, including strep throat, scarlet fever, diphtheria, syphilis, gonorrhea, meningitis, tonsillitis and rheumatic fever.[49] Although Fleming isolated penicillium and recorded its antiseptic properties, he was unable to transform it into a medically viable treatment. Ernst Chain and Howard Florey at the Dunn School of Pathology at Oxford University in Britain developed the techniques to produce stable penicillin to treat diseases on a large scale.[50]

Polio viral attack was one of the worst problems faced during the 20th century. The problem was caused by Poliomyelitis virus popularly known as polio. In 1952 Jonas Salk, an epidemiologist at the University of Michigan, School of Public Health, discovered the polio vaccine. In 1952, Salk combined three types of polio virus grown in cultures made from monkey kidneys. Using formaldehyde, he was able to "kill" or

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[45] Julie D. Cromer, *It's Hard to Find a Good Pair of Genes: So Why Make Them Free for the Taking?,* 76 UMKC L. Rev.505, p.513 (2007).

[46] Leslie G. Restaino, Steven E. Halpern and Dr. Eric L. Tang, *Patenting DNA-Related Inventions in the European Union, United States and Japan: A Trilateral Approach or a Study in Contrast?,* UCLA J. L. Tech. 2, p.2 (2003).

[47] Penicillium chrysogenum is common in temperate and subtropical regions and can be found on salted food products. But it is mostly found in indoor environments, especially in damp or water damaged buildings.

[48] Stacie L. Derderian, *Alexander Fleming's Miraculous Discovery of Penicillin*, Rivier Academic Journal, Volume 3, Number 2, p.2 (2007).

[49] Ibid.

[50] Neil Z. Miller, *The polio vaccine: a critical assessment of its arcane history, efficacy, and long-term health-related consequences*, Medical Veritas, p.240 (2004). available at, www.thinktwice.com/Polio.pdf

make the viral matter inactivate so that it would trigger an anti-body response without causing the disease.[51] The process adopted by Salk for the polio vaccination was by injecting dead or inactive polio cells into the body. The experiment was termed as double-blind test. His first experimental studies were successfully conducted on schoolchildren. This was the largest medical experiment in history known as the Francis Field Trial.[52] It was the most elaborate program of its kind in history, involving 20,000 physicians and public health officers, 64,000 school personnel and 220,000 volunteers. Over 1,800,000 school children from forty four states took part in the field trial.[53] Within two years of the vaccine's introduction, reported cases of polio had dropped by 90 percent. Salk's research using the double-blind test changed preventative health care forever.

Small Pox vaccine was another most important breakthrough in the history of medical biotechnology. Approximately two million people around the world are believed to have died of the small pox disease. Edward Jenner is known to have invented the immunization which ultimately eradicated the smallpox.[54] A massive vaccination program sponsored by the WHO began in 1967 and by 1979 the disease was declared to have been eradicated. The elimination of smallpox stands as one of the greatest medical triumphs of all time.

Another major havoc which took place during the late 80's and 90's was the 'mad cow disease.' 'Mad Cow Disease' is actually bovine spongiform encephalopathy (BSE), a degenerative neurological condition caused by infectious protein particles known as "prions", which slowly destroy the brain cells.[55] The disease can appear in human beings as "variant Creutzfeldt-Jakob Disease" (vCJD), a fatal condition in which a person's brain is infected by a virus like protein that destroys the tissues.[56] There is increasing evidence that it can pass to humans through diet and cause a related neurological syndrome. Creutzfeldt-Jakob has a long

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[51] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p. 41.
[52] Ibid.
[53] Ibid.
[54] Stefan Riedel, *Edward Jenner And The History Of Smallpox And Vaccination*, BUMC Proceedings 18(1), p.21 (2005).
[55] European Federation of Biotechnology, *What's What In Biotechnology?*, p.3.
[56] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.42.

incubation period of many years. Patients die roughly a year after the first symptoms appear and there is no cure for this infection.

Nearly179,000 cattle had died of BSE and another 4.4 million were destroyed as a precautionary measure.[57] Extensive research was made to discover the cause of the disease. It was found that the culprit was the practice of using animal remains as feed for existing livestock a sort of cannibalism which had been a common practice in Britain's cattle industry since at least 1926. The first sick cow possibly might have contracted BSE from a naturally occurring mutant gene. Once the mutant gene entered the food chain, there was no way to eliminate it other than to kill everything in that chain.

1.4.4 BIRTH OF OPEN COLLABORATIVE CONCEPT IN BIOTECHNOLOGY RESEARCH

1996 witnessed the official beginning of the world's largest collaborative research to sequence human genome called the Human Genome project (HGP).[58] It was coordinated by the U.S. Department of Energy and the National Institutes of Health.[59] It was one of the largest international scientific research projects with the primary goal of determining the sequence of chemical base pairs which make up DNA and to identify and map the approximately 20,000–25,000 genes of the human genome from both a physical and functional standpoint. The project was successfully completed ahead of schedule in 2003.[60]

Another major event in the history of biotechnology was the International HapMap Project (HapMap). The project was another major milestone in collaborative research. The goal of the International HapMap Project was to determine the common patterns of DNA sequence variation in the human genome and to make this information freely available in the public domain. The HapMap was aimed to

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[57] "*The 'Recipe for Disaster' that Killed 80 and Left a £5bn Bill*." Telegraph News (6/19/01). Available online. At; http://www.telegraph.co.uk/news/uknews/1371964/The-recipe-for-disaster-that-killed-80-and-left-a-5bn-bill.html. accessed on 2nd january, 2011.

[58] http://www.genome.gov/10001763 last accessed on 18-06-2011.

[59] Monika Gisler, Didier Sornette, and Ryan Woodard, *Exuberant innovation: The Human Genome*, Swiss Finance Institute Research Paper Series No10 – 12, p. 2 available at http://ssrn.com/abstract=1573682 last accessed on 12-10-2010.

[60] Monika Gisler, Didier Sornette, and Ryan Woodard, *Exuberant innovation: The Human Genome Project*,. p.2

discover the sequence of variants that affect common diseases in order to facilitate development of diagnostic tools.[61] The International HapMap Consortium announced the completion of Phase I of its project in November 2005.[62] From November 2003 to January 2006, the HapMap Consortium made at least twenty separate data releases to the Internet. The growth of biotechnology has taken a new dimension with the HapMap project.

One major mile stone in biotechnology during the 20th century was the initiatives to eradicate epidemics and it was called Influenza Genome Sequencing Project (IGSP). In 1918 'Spanish' flu, one of the most deadly outbreaks in recorded history, killed 30 to 50 million people worldwide; this was estimated to be 2.5 to 5 percent of the planet's population.[63] Epidemiologists therefore worked hard to keep tab on various influenza viruses. This resulted in establishing Influenza Genome Sequencing Project (IGSP) initiated by the National Institute for Allergy and Infectious Diseases (NIAID) which was funded by the U.S. National Institute of Health (NIH) in 2004.[64] The project completed its first genome sequencing in March 2005 and rapidly accelerated since then. The IGSP sequenced more than 1,800 influenza genomes in its first few years of existence. As of mid 2008, over 3000 isolates had been completely sequenced from influenza viruses that were endemic in human flu avian (bird flu) and swine flu populations including many strains of , H1N1 , and H5N1 (avian)[65]. The project is making all sequence data publicly available through GenBank, an international, NIH-funded, searchable online database. This is intended to provide international researchers with the information needed to develop new vaccines, therapies and diagnostics as well as to improve understanding of the overall molecular evolution of Influenza and other genetic factors that determine their virulence.

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[61] The International HapMap Consortium, *The International HapMap Project*, 426 Nature, p.789 (2003).
[62] The International HapMap Consortium, *A Haplotype Map of the Human Genome*, 437 Nature, p.1299 (2005).
[63] Elodie Ghedin, et al., *Large-scale sequencing of human influenza reveals the dynamic nature of viral genome evolution*, 437 Nature, p.1162 (2005).
[64] Lori B Andrews Laura A Shackelton, *Influenza genetic sequence patents: where intellectual property clashes with public health need,* Future Virology, Vol. 3, No. 3, p. 235 (2008).
[65] Elodie Ghedin et al., *Large-scale sequencing of human influenza,* p.1162.

1.5 BIOTECHNOLOGY TERMINOLOGIES

Biotechnology's basic terminologies can be explained easily. However in order understand the more complicated details like Genomes and Epigenomes it requires an extra effort. It is a basic knowledge that every living organism is made of cells and the cell contains a nucleus. The genetic material of an organism is located within the chromosomes which are found in the nucleus of cells. The Chromosomes are structures containing long sequences of dense, supercoiled DNA.[66] There are many genes on a single length of double-stranded, helical DNA and they are super-coiled and form the chromosomes.[67] These basic understandings may not require a special knowledge about biotechnology. However the area of biotechnology that poses a challenge to intellectual property laws is much more complicated and requires a little more sequential understanding of the terminologies and concepts.

1.5.1 GENE

A gene is a molecular unit of heredity material of a living organism. The gene is a sequential organization of the four nucleotides in a unique order resulting in one unit. They are located in a particular position within a chromosome that encodes a specific function. This gene unit is an encoding for a distinct protein product.[68] Genes are the functional information units of the genome and consist of DNA sequences that encode for proteins. It is estimated that there are around 80,000 to 100,000 genes in human DNA.[69] A gene is similar to the binary code of computer language and drives the functions of the organism. The DNA sequence of a gene is translated into the amino acid sequence which, after processing, results in a protein[70]. The genetic composition of an organism depends on its genotype in conjunction with

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[66] Molly A. Holman and Stephen R. Munzer*, Intellectual Property Rights in Genes and Gene Fragments: A Registration Solution for Expressed Sequence Tags*, 85 Iowa L. Rev. 735, p.742 (2000).
[67] Ibid.
[68] Edward J. Baba, *From Conflict to Confluence: Protection of Databases Containing Genetic Information*, 30 Syracuse J. Int'l L. & Com. 121, p.126 (2003).
[69] Molly A. Holman and Stephen R. Munzer*, Intellectual Property Rights in Genes and Gene Fragments:* p.739
[70] Edward Baba, *From Conflict to Confluence*. p.126.

environmental influences. These genetic compositions determine its appearance and physical characteristics of that organism.[71]

1.5.2 DNA (DEOXYRIBONUCLEIC ACID)

Deoxyribonucleic acid (DNA) is the hereditary material of a living organism. The basic difference between a gene and DNA is that, the gene is a functional unit of nucleotide within the DNA sequence. The human chromosomes carry many units of chemical coding in DNA and they are known as base units. The base units in DNA are known as nucleotides. Nucleotides are nitrogen containing molecules that store all the genetic information about an organism. There are four types of nucleotides; adenine, thymine, cytosine and guanine. They are represented by their abbreviation A, T, C, and G.[72] It is the sequence of these bases in the DNA molecules which determines the biochemistry of cells and physiology of organisms."[73] DNA is a good carrier of information and it is relatively motionless.

Each cell in an organism contains a copy of the organism's DNA. The genetic instructions for a living being are set in their genomes which are encoded on DNA.[74] DNA is around 1.6 metres long but only one fifth of a millionth of a centimetre wide.[75] Every cell of the human body contains a copy of this DNA and is divided into 46 parts of discrete length called the chromosomes. These chromosomes exist in the cell as 23 pairs.[76] These are so highly condensed that they can fit into the cell's nucleus which measures 3 to 4 millionths of a metre in diameter.

1.5.3 RNA (RIBONUCLEIC ACID)

The relationship between DNA and protein, according to biochemists is: "DNA-makes-RNA- makes-protein". RNA is similar to DNA, but it has a slightly different chemical structure, and it carries nucleotides adenine (A), guanine (G), cytosine (C) and they are paired with uracil instead of thymine.[77] RNA is usually

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[71] European Federation, *What's What In Biotechnology,* p.1.
[72] Molly A. Holman and Stephen R. Munzer, *Intellectual Property Rights in Genes and Gene Fragments,* p.744.
[73] Ibid.
[74] Ibid.
[75] Edward J. Baba. *From Conflict To Confluence,* p.125.
[76] Ibid.
[77] European Federation, *What's What In Biotechnology,* p.1.

single-stranded and plays an important role in the synthesis of proteins. There are different types of RNA that fulfill different roles within an organism. For example, messenger RNA (mRNA) carries the instructions for a protein construction site in the ribosome[78]. Messenger RNA molecules are copies of genes, which carry instructions and act as templates for protein synthesis.[79] Transfer RNA (tRNA) conveys an amino acid to the construction site as part of the translation process. A protein is then synthesized from the mRNA template in a process called translation. The amino acid sequence of the protein corresponds to the nucleotide sequence of the mRNA.[80]

1.5.4 PROTEIN

Proteins are biologically important macromolecules that act as enzymes, hormones, signal receptors and play many other roles. Most of the cell's activities are carried out by proteins, very large molecules that consist of chains of units called amino acids. Most pharmaceutical products are either proteins themselves or they interact with protein receptors within the body.[81] Virtually all cellular functions of the organism depend on proteins and these functions include complex relationships among various proteins and thus between multiple genes. The intricate relationship among genes, their expression patterns and their protein products, have been the focus of careful research in an attempt to understand the basis of diseases and to create innovative and effective therapies.[82]

1.6 BIOTECHNOLOGY – THE TECHNOLOGY APPLICATIONS.

Biotechnology has a vide range of application in all walks of life. It is playing a significant role in genomic research which is the corner stone of all major research works in medical biotechnology. The main areas are pharmaceuticals, therapeutic research and diagnostics research. Apart from these applications biotechnology has many other industrial uses including crop production and manufacture of biodegradable plastics, vegetable oil, biofuels and environmental uses.[83]

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[78] European Federation, *What's What In Biotechnology,* p.1.
[79] Ibid.
[80] Ibid.
[81] Ibid.
[82] European Federation, *What's What In Biotechnology,* at p.4.
[83] Debbie Strickland, *The Guide to Biotechnology,* p.18.

1.6.1 BIOPROCESSING TECHNOLOGY

The bio processing is the oldest biotechnology use, which employs living cells or the molecular components to produce the desired products. One of the earliest forms of bio-processing is the microbial fermentation. It has been used for thousands of years in process like brewing beer, making wine and for preparing bread and pickle foods. Micro-organisms were discovered in mid 1800's and it was realized that their biochemical machinery was responsible for these useful products. Once it was realised that the micro organisms are responsible for the fermentation, it was greatly extended to industrial use. [84]

Bioprocessing technologist develops design and optimise the biotechnological production processes. These processes use micro-organisms and bio-molecular components to reach a more effective and cleaner production than possible with traditional production methods. The living cells most commonly used are one-celled micro organisms such as yeast and bacteria. The bio molecular components which we use most often are enzymes. They are proteins that catalyze biochemical reactions.[85]

Bioprocessing technology is employed to produce smaller molecules and speciality bioproducts. The bioprocessing technology is used to obtain value-added products and to engineer large-scale, integrated processes in many areas. Recombinant DNA technology coupled with microbial fermentation is used in the manufacture a wide range of products such as human insulin, the hepatitis B vaccine, the calf enzyme and so on. Bio processing technology also includes tissue engineering and manufacturing as well as biopharmaceutical formulation and delivery.[86]

A landmark event began in the early 1970s when scientists used recombinant DNA technology to insert a DNA fragment into the bacterium, *e.coli.* This experiment was aimed at industrial production of insulin. It is achieved by inserting pieces of DNA containing a gene for insulin in to the bacterium. By adopting this method of

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[84] Hylke van der Schaaf, *Design of Digital Learning Material for Bioprocess Engineering Education*, PhD. Thesis, Wageningen University, The Netherlands, p.3 (2006) available at http://library.wur.nl/wda/dissertations/dis4125.pdf last accessed on 23-10-2010.
[85] Ibid.
[86] Debbie Strickland, *The Guide to Biotechnology,* p.18.

bioprocessing technology it was able to produce proteins and enzymes in large quantities.[87]

1.6.2 MONOCLONAL ANTIBODIES

The monoclonal antibodies are one of the major achievements of therapeutic medical biotechnology. The main tools of the immune system are antibodies. Antibodies are proteins that specifically attack the molecules that are foreign to the organism, such as infecting pathogens. Our immune system is capable of creating more than 1000 different types of antibodies. The natural immune response towards a single antigen triggers the production of a mixture of antibodies.[88] A monoclonal antibody is a single species of antibody. An antibody is a protein which is produced by an organism as a result of the presence of a foreign substance in the body and which acts to neutralise or remove that substance.[89]

By combining these natural antibodies with modern methods of their production, it is now possible to obtain antibodies capable of combating virtually any molecule. By using a specially constructed hybrid cell called 'hybridoma[90]' researchers can produce a clone of identical antibodies called "monoclonal antibodies". Monoclonal antibodies are created specifically for a particular antigen or against a disease.

Two revolutionary advances of the 1970s were the introduction of genetic engineering and monoclonal antibody technology. The monoclonal antibody technology was launched in the biotechnology industry during 1980[91]. Nowadays this technology uses immune system cells to make proteins called monoclonal antibodies. Treatment of various diseases including cancer is possible with the help of this technology.

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[87] A.J. Nair. *Introduction to Biotechnology and Genetic Engineering,* p.10.
[88] David S. Goodsell, *Bionanotechnology; Lessons from Nature,* (Hoboken,Wiley-Liss, Inc., 2004) p.55
[89] Ibid.
[90] Hybridoma technology is a technology of forming hybrid cell lines called 'hybridomas' by fusing a specific antibody related to a particular disease.
[91] Directorate for Science, Technology and Industry Committee for Scientific and Technological Policy, *Economic Aspects Of Biotechnologies Related To Human Health*, *Part II: Biotechnology, Medical Innovation and The Economy: The Key Relationships,* OECD, DSTI/STP/BIO(98)8/FINAL, p. 44 (1998) available at http://www.oecd.org/dataoecd/40/25/2351234.pdf last accessed on 12-10-2010.

1.6.3 CELL / TISSUE CULTURE

Cell culture or tissue culture is another significant development in medical and agricultural biotechnology sectors. Cell culture technology is the process of growing cells outside living organisms. Plant Cell Culture is a significant step in creating transgenic crops. It provides an environmentally sound and economically feasible option for obtaining naturally occurring products with therapeutic values. This can be used for production of medicinal and commercial plants.[92] Plant cell culture is also an important source of compounds used as flavors, colors and aromas by the food-processing industry.

1.6.3.1 INSECT CELL CULTURE

Insect Cell Culture is another advantage of modern biotechnology. It is a technology used in producing biological control against insects and pests without harming the beneficial insects or with out using harmful pesticides which endanger the environment. However manufacturing these biological control products in the traditional way to a marketable quantity has been impossible. The new technology of insect cell culture removes these manufacturing constraints. Interestingly, insect cell culture, similar to plant cell culture, is being experimented as a production method of therapeutic proteins. Insect cell culture is also being researched for the production of biopharmaceuticals such as virus- like particle vaccines (VLP) against infectious diseases such as SARS, influenza, and cancer. A patient specific cancer vaccine that utilizes insect cell culture has reached Phase III clinical trials.[93]

1.6.3.2 MAMMALIAN CELL CULTURE

Livestock breeding has used mammalian cell culture as an essential tool for decades. Eggs and sperms taken from genetically superior bulls and cows are united in the lab and the resulting embryos are grown in culture before being implanted in surrogate cows. A similar form of mammalian cell culture has also been an essential component of the human in vitro fertilization process.

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[92] Sachin Chaturvedi, *Status and Development of Biotechnology in India: An Analytical Overview*, Research and Information System (RIS) discussion paper (RIS-DP #28/2002), p. 2.
[93] Gary Walsh, *Biopharmaceutical benchmarks 2010*, Nature Biotechnology 28: 9. p. 917 (2010).

Apart from these, there are other uses like biopharmaceutical use of the mammalian cell culture. The first product of mammalian cell culture to hit the market was Tissue Plasminogen Activator (t-PA). This is an anti-clot drug developed to dissolve blood clots selectively.[94] t-PA is a natural protease secreted by mammalian cells and is used against heart attacks and other problems caused by the formation of blocks in the blood flow. Mammalian cell are selected and cultured in a suitable bioreactor for commercial production of t-PA as a pharmaceutical compound.[95]

1.6.3.3 STEM CELLS CULTURE

Stem cell research is a new scope of today and is also the greatest achievement of biotechnology. This technology enables us to create special cells that teach the body's immune system how to destroy cancer cells or regenerate damaged and diseased organs.[96] The primary line of research on stem cells was on embryonic stem cells. This was widely criticised as unethical.

Researchers are now working at other options of research based on cultured adult stem cells which are found in certain tissues like the bone marrow and brain. The stem cells have wide uses. Researchers have found that adult stem cells can be used by the body to replenish tissues. Adult hematopoietic stem cells[97] could be transplanted into bone marrow to stimulate the generation of the various types of blood cells necessary to rejuvenate an immune system. These stem cells can be harvested in large quantities from umbilical cord blood, but they are difficult to isolate and purify. Stem cells derived from amniotic fluid could have just the right properties for use in future therapies.[98] Unlike stem cells derived from human embryos, the amniotic-fluid does not form cancerous masses when allowed to grow on their own. Researchers also are working on ways to harvest stem cells from placentas and fat. Some are looking at cellular reprogramming as a way to get specialized body cells like skin cells to revert to a primordial state so that they can be coaxed into various types of tissues.

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[94] A.J. Nair. *Introduction to Biotechnology and Genetic Engineering*p. 744.
[95] Ibid. at, p.745.
[96] Ibid.
[97] The stem cells that form blood and immune cells are known as hematopoietic stem cells. They are ultimately responsible for the constant renewal of blood - the production of billions of new blood cells each day.
[98] Nature, Research highlights, Nature biotechnology, Vol 445, p. 128 (2007).

1.6.3.4 EMBRYONIC STEM CELLS CULTURE

Stem cells from embryos have immense scope of research in therapeutic sector. An embryonic stem cell can be turned into any type of cells like brain cells, skin cells or liver cells, and it can reproduce itself. As the name suggests, embryonic stem cells are derived from embryos, specifically those that developed from eggs that are fertilized in vitro (in an in vitro fertilization clinic) and then donated by consent for research purposes. The embryos are typically used in stem cell research is four or five days old and are hollow microscopic ball of cells called the blastocyst[99].

Human embryonic stem cells are isolated by transferring the inner cell mass into a nutrient rich culture medium. There the human stem cells proliferate. Over the course of several days the cells of the inner cell mass, divide and spread all over the dish. Researchers then remove the growing cells and divide them into fresh culture dishes. This process of replanting the cells, called sub culturing, is repeated many times over many months. Each cycle of sub culturing is called a passage[100]. To start a line of stem cell research, an embryo must be cloned or destroyed. This has raised many ethical issues. In one of the most recent cases, the United States District Court for the District of Columbia granted a preliminary injunction blocking the implementation of the federally funded human embryonic stem cell research (hESC) by the National Institutes of Health (NIH).[101] This decision paralysed the area of stem cell research.

1.6.4 RECOMBINANT DNA TECHNOLOGY

Recombinant biotechnology is one of the major milestones in biotechnology. Recombinant DNA is produced when scientists add DNA to an organism's genome to code it for a new trait or to alter an existing trait. The cloning experiments of Herbert Boyer, Stanley Cohen, Paul Berg, and their colleagues in the early 1970s lead in the erena of recombinant DNA technology.[102] The term recombinant DNA means the joining or recombining of two pieces of DNA from two different species. The first

[99] http://stemcells.nih.gov/info/basics/basics3.asp
[100] Ibid.
[101] Ryan P. O'quinn, *Sherley V. Sebelius: Stem Cells And The Uneasy Interplay Between The Federal Bench And The Lab Bench,* Duke L. & Tech. Rev. 002, (2011).
[102] Lizabeth A. Allison, *Fundamental Molecular Biology*, (Blackwell Publishing Ltd, Oxford, 2007) p. 184.

recombinant DNA substance was the synthetic human insulin which was created to treat diabetes.[103]

Recombinant DNA technology allows scientists to alter or rearrange a cell's hereditary structure. The hereditary material in cells consists of molecules of DNA. The gene carries the DNA genetic code and the cell process enables the production of RNA. The information in an RNA molecule determines the order in which amino acids are strung together by the cell's protein manufacturing process.[104] Thus a modification of the genetic code can determine whether a cell will produce large or small amounts of such proteins.

Recombinant technology can be used to produce new medicines and safer vaccines, treat some genetic diseases, enhance biocontrol agents in agriculture, increase agricultural yields, decrease production costs, decrease allergy-producing characteristics of some foods, improve food's nutritional value, develop biodegradable plastics, decrease water and air pollution, slowdown food spoilage, control viral diseases and inhibit inflammation. India's first domestically produced and marketed recombinant DNA product, is Shanvac-B, a Hepatitis B vaccine developed by the Indian biotechnology company Shantha Biotechnics in 1997.[105]

1.6.5 CLONING

As a general terminology, the cloning is the production of genetically identical animals by nuclear transfer from adult somatic (body) cells to unfertilized eggs.[106] Another method is by following the process of selecting a piece of DNA, inserting it into a vector[107] and reproducing many copies of this DNA segment. Using restriction enzymes, a scientist can isolate a DNA fragment and insert it into a vector. By transferring this modified vector into a host and reproducing the vector, the scientist

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[103] United Nations Conference on Trade and Development, *Key Issues In Biotechnology*, UNCTAD/ITE/TEB/10 p. 8 (2002) available at http://www.unctad.org/en/docs/poitetebd10.en.pdf last accessed on 10-10-2010.

[104] Adrienne B. Naumann, *Biotechnology: Recent Developments In Patent Law*. AHA, Journal of Health Law Vol. 20, No. 2, p.17 (1987).

[105] Janice M. Mueller, *Biotechnology Patenting In India: Will Bio- Generics Lead A "Sunrise Industry" To Bio-Innovation?*, 76 UMKC L. Rev. 437, p. 439 (2007).

[106] Lizabeth A. Allison, *Fundamental Molecular Biology*, p. 546.

[107] Vector is an agent that acts as a carrier or transporter or a virus or plasmid that conveys a genetically engineered DNA segment into a host cell.

clones the piece of DNA.[108] Cloning technology allows us to generate identical molecules, cells, plants or animals.

1.6.5.1 MOLECULAR OR GENE CLONING

Molecular or gene cloning is the process of creating genetically identical DNA molecules. It provides a foundation for the molecular biology revolution and is a fundamental and essential tool of biotechnology research and development. Virtually all applications in biotechnology, from drug discovery and development to the production of transgenic crops, depend on gene cloning.

1.6.5.2 ANIMAL CLONING

Animal cloning has helped us to rapidly incorporate improvements in livestock herds for more than two decades. Animal cloning has the potential to overcome the limitations of the normal breeding cycle. The first animal cloning experiments were conducted in the 1950s when developmental biologists Robert Briggs and Thomas King developed a method for nuclear transplantation in the leopard frog, *Rana pipiens*[109]. In 1997 Dolly, the cloned sheep brought animal cloning in the public consciousness. Though the production of an animal clone was not a new development, cloning of mammals using adult somatic cells and the nuclear transfer was not thought to be possible until the cloning of Dolly.[110] Dolly was considered a scientific breakthrough not because she was a clone, but because the source of the genetic material used to produce Dolly was an adult somatic cell.[111] Recombinant DNA technologies, in conjunction with animal cloning, provide us with excellent animal models for studying genetic diseases, aging and cancer. In the future it will help us to discover drugs and other forms of therapy such as gene therapy and cell therapy.

1.6.6 MICROARRAYS AND GENE CHIPS

Growth of computer technology has revolutionised the biotechnology research. The innovations like gene chip and microarray technology have a vital role

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[108] Adrienne B. Naumann, Biotechnology*: Recent Developments In Patent Law*, p. 17
[109] Lizabeth A. Allison, *Fundamental Molecular Biology*, p. 561.
[110] Ibid. at p. 578.
[111] Meredith Wadman, *Dolly: A Decade On.* Special Report, 445NATURE 22, p. 800 (2007).

to play in the analysis of genetic sequences. Microarrays which are also called gene chips are vast libraries of short DNA sequences attached to tiny glass or silicon supports which are used to screen nucleic acid population.[112] Microarrays help the detection and analysis of thousands of genes in a single small sample. Microarrays consist of small DNA fragments, called probes, physically attached to a solid surface such as glass, plastic or silicon chip to form an array. The precise location of each distinct probe is called a feature and thousands or even millions of different features can be contained in a single microarray.[113] This has revolutionised Biotech industry as a result of miniaturization and high output screening of genetic sequences. Consequently, more data can be obtained more quickly than ever before.[114]

Biotechnology Researchers currently use microarray technology to study gene structure and function. There are different types of microarrays such as DNA microarrays, Protien microarrays, Tissue microarrays, Whole cell microarrays, Small molecules microarrays and so on.[115] DNA microarrays have many different purposes. They are generally used to detect mutations in disease-related genes, monitor genes activity, diagnose infectious diseases identify the best anti- biotic treatment, identify genes important to crop productivity, improve screening for microbes used in bioremediation and so on. DNA microarrays have proved to be extremely useful in gene discovery, basic biomedical research, disease diagnosis, drug discovery (pharmacogenomics) and toxicological research (toxicogenomics).[116] DNA microarrays can contain a huge number of different genetic sequences in a single product, each of the sequences representing a different gene or genetic polymorphism. Since genetic sequences and polymorphisms are often patented, a single DNA microarray might infringe many individual patents.[117]

1.6.7 BIOSENSORS

Many applications in medicine and the chemical industry require sensitive methods for sensing small organic molecules. The sense of smell and taste are

[112] Christopher M. Holman, *Biotechnology's Prescription for Patent Reform*, 5 J. Marshall Rev. Intell. Prop. L. p. 340 (2006).
[113] Ibid.
[114] Ibid.
[115] Biotechnology Industry Organization *The Guide to Biotechnology*, p.12.
[116] Christopher M. Holman, *Biotechnology's Prescription for Patent Reform*, p.339.
[117] Ibid at p.340.

designed to perform exactly this sensing task. The immune system of human body also recognizes millions of different molecules and reacts based on the sensing. So in order to make a biosensor two components are needed: the recognition element and some mechanism for reading out the recognised element.[118] Antibodies are primarily biosensors, so they form the basis of development of diagnostic tests and are proved to be a major success of biotechnology.

Biosensor technology uses both common knowledge and biology with the help of advances in microelectronics. A biosensor is composed of a biological component, such as a cell, enzyme or antibody, linked to a tiny transducer. Transducer is a device powered by one system that then supplies power (usually in another form) to a second system. Biosensors are detecting devices that rely on the specificity of cells and molecules to identify and measure substances at extremely low concentrations.[119]

1.6.8 SYNTHETIC BIOLOGY

The synthetic biology is the new hope of today aiming to engineer living organisms. The 'modern biotechnology' has grown ahead of traditional recombinant DNA technology. Instead of simply transferring a pre existing gene from one species to another, synthetic biology aims to make biology a true engineering discipline[120]. Just as electrical engineers rely on standard circuit components and computer programmers rely on programme codes, synthetic biologists create an array of standard, modular gene switches and parts that can be readily synthesized and mixed together in different combinations.[121]

Growth of synthetic biology has a tremendous effect on research. The example of this new initiative is the Massachusetts Institute of Technology (MIT) which is maintaining a Registry of Standard Biological Parts known as Biobrick project.[122] The goal of this project is to record and index biological parts. It also offers services like synthesis assembly and construction of new biological parts, devices, and systems.[123]

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[118] David Goodsell, *Bionanotechnology Lessons From Nature*, p.291.
[119] Debbie Strickland, *The Guide to Biotechnology*, p.22.
[120] Drew Endy, *Foundations for Engineering Biology,* 438 Nature, p.449 (2005).
[121] Richard N. Langlois, *Modularity in Technology and Organization*, 49 J. Econ. Behav. & Org., p.19 (2002).
[122] Dianne Nicol, *Cooperative Intellectual Property in Biotechnology,* Script-ed, Vol. 4:1, p.149 (2007)
[123] Ibid.

The idea behind the Registry of Standard Biological Parts is that these parts could be used in different ways to produce many different types of devices and systems. The Registry currently maintains physical DNA. The role of the Registry is to codify large information and specifications which can be readily fabricated in DNA synthesizers. These fabricated DNA-based functions can be executed in a cell.[124]

Synthetic biology has wide range of possibilities such as constructing an entirely artificial programmable genome from standard parts. Scientists working in field of synthetic chemistry are experimenting on linking artificial RNA and proteins to the genetic code.[125] Synthetic biology can resolve many problems including the possibility of unlimited supplies of previously expensive drugs.[126] Scientists working in the area of synthetic biology hope to use synthetic organisms for economical production of medically relevant chemicals and large variety of industrial materials. The recent development in the area of synthetic biology which drawn the attention of the world recently is the research on low-cost production of green fuels such as cellulosic ethanol.[127]

1.7 CLASSIFICATION OF BIOTECHNOLOGY APPLICATIONS

For the purpose of analysis, biotechnology research can be classified into different categories depending on the field of application. The most relevant application of biotechnology is in the area of medicine and agriculture. Medical application of biotechnology includes health care, medical diagnostics, therapeutic applications, enzyme research, pharmaceutical, food and so on. However agriculture biotechnology covers vetinary, plant biotechnology, aquaculture, vaccines, bio-fertilisers' pesticides, antibiotics and so on.

1.7.1 MEDICAL BIOTECHNOLOGY

Medicine is the science of healing. Medical biotechnology is the use of living cells and cell materials in research to produce pharmaceutical and diagnostic products that help treat and prevent human diseases. Biotechnology has changed medical

[124] Dianne Nicol, *Cooperative Intellectual Property in Biotechnology,* p.149.
[125] Steven A. Benner, *Act Natural*, 421 Nature 118, p.118 (2003).
[126] Vincent J.J. Martin et al., *Engineering a Mevalonate Pathway in Escherichia Coli for Production of Terpenoids,* 21 Nature Biotechnology, p.800 (2003).
[127] Vincent J.J. Martin et al., *Engineering a Mevalonate Pathway in Escherichia Coli,*p.800

science from mere medicine to the era of genetic manipulation. Diseases that were once incurable can now be cured by interfering with a person's DNA. Scientists working on medical biotechnology are now exploring the secrets of the human genome and learning how to manipulate sequences of DNA. DNA manipulations have much potential and can make changes from eye color to memory skills.[128]

Biotechnology tools and techniques play a major role in medical research. Biomedical research opens new research avenues for discovering how healthy bodies work and what goes wrong when problems arise. Knowledge of the genetic base of health and disease, helps improve the methods for treating and preventing diseases. Biotechnology products help quicker and more accurate diagnostic tests, therapies with fewer side effects and new and safer vaccines. The first bioengineered medicine is the synthetic human insulin discovered in 1982.[129] Apart from new treatments for existing disease, recombinant DNA technology has great potential for developing vaccines that could prevent diseases.

Traditionally, doctors used to examine a patient, diagnose the conditions and then prescribe the medicine or antidote. Common problems like High blood pressure, high cholesterol, depression and chronic pulmonary heart disease are all treatable with a large number of common pharmaceuticals. A long interaction between patient and physician is required to find the right medication and the right dosage for the maximum intended effect. The developments of biotechnology have helped scientists to understand how a person's genotype could guide treatment for his or her ailments. We can now identify the genotype, the disease which the person is carrying and the remedial measures in terms of personalized medicine.[130] As more and more research is going on, there emerge more specialized areas in biotechnology. Some of the current relevant areas of research are discussed hereunder.

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[128] UNCTAD, *Key Issues In Biotechnology*, p. 8.
[129] Matthew Rimmer, *Genentech And The Stolen Gene: Patent Law, And Pioneer Inventions,* Bio-Science Law Review, Vol. 5, No. 6, p.200 (2006).
[130] Richard Li-Dar Wang, *Biomedical Upstream Patenting and Scientific Research: The Case For Compulsory Licenses Bearing Reach-Through Royalties*, 10 Yale J. L. & Tech., p. 291 (2007).

1.7.1.1 PHARMACOGENETICS AND PHARMACOGENOMICS

The field of pharmacogenetics has a history dating back to the 1950s. The term pharmacogenomics emerged in the late 1990s and is often associated with the application of genomics in drug discovery. Pharmacogenetics is a specialised area of study about how a person's inherited genetic tendencies interact with specific medicines. [131] Pharmacogenetics has been suggested as the area of genetics with the high potential to provide public health benefits. Scientists working in this field create safer, more effective drugs and vaccines that are modified to meet the requirement of a person's proteins, RNA, and DNA structure. [132]

The pharmacogenomics attempts to tailor drugs to an individual's genetic profile.[133] It helps the development of personalized medicine in which genetic differences among patients are acknowledged and used to design more effective treatments. A medicine's effectiveness and safety often vary from one person to person. Using data acquired in gene analysis, it is possible to identify genetic differences that cause patients to adverse reactions to certain drugs or help them identify other drugs that are best suited for personalised treatment. This tailoring of therapeutics to the genetic makeup of the patient is known as pharmacogenomics where researchers and pharmaceutical corporations attempt to develop pharmacogenomically tailored medicines.[134]

1.7.1.2 PROTEOMICS

Every cell produces thousands of proteins, each with a specific function. This collection of proteins in a cell is known as its proteome, and proteomics is the study of the structure, function, location and interaction of proteins within and among cells. human genome contains 23 chromosomes pairs (22 autosomepairs and a pair of sex chromosomes XX or XY) and every cell may have only 33,000 functional genes.

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[131] Michael M Hopkins, *Putting pharmacogenetics into practice,* Nature Biotechnology, Volume 24, Number 4, p.403 (2006).
[132] Ibid.
[133] Jonathan Kahn, *Race-ing Patents/Patenting Race: An Emerging Political Geography of Intellectual Property in Biotechnology*, 92 Iowa L. Rev, p. 362 (2007).
[134] Jonathan Kahn, *Race-ing Patents/Patenting Race,*p.362

Every human gene is able to code for potentially thousands of proteins. Genes contain gene expression for protein production. [135]

Proteomics is the study of proteins, enzymes, and protein modification for medicinal purposes. Proteins of a person change from cell to cell, whereas a person's genome remains constant. Proteomics means the characterization of the entire array of proteins encoded by our genes.[136] Different types of cells in the human body have different sets of proteins. A single gene can encode for multiple proteins. The protein structures and functions can be modified in many ways. Proteomics is the study of these possibilities of modifications to proteins and enzymes.

1.7.1.3 EPIGENETICS AND EPIGENOME

Epigenetic is the study of chemical modifications of genes that are transmitted from one cell generation to the next. However these modifications do not affect gene expression or alter the DNA sequence. Epigenetics explains the change in the pattern of gene expression that is mediated by mechanisms other than DNA. Certain characteristics of individual, carrying the same pair of genes may be different. This is due to the changes in chemical markers attached to the DNA. Epigenetic changes are regulated by these gene expressions.[137] An epigenome is the description of these modifications across the whole genome. But unlike the genome DNA sequence, each organism has multiple epigenome in different cell types. And these may change during its lifetime in response to environmental changes.[138]

Epigenetics is the study of how the chemical markers attached to the DNA can be altered. It is a set of controls that silence or activate genes by chemically modifying the DNA or by binding them to certain proteins.[139] The study of these modifications, what they are, how they are laid down, and the processes that they control require extensive research. The study of epigenetics is to decode these epigenetic glitches that control, silence or activate genes by chemically modifying the DNA. The latest

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[135] A.J. Nair. *Introduction to Biotechnology and Genetic Engineering*, p.558.
[136] Monika Gisler, Didier Sornette, and Ryan Woodard, *Exuberant innovation: The Human Genome Project*, p.18
[137] Rama S. Dwivedi et al, *Beyond genetics: epigenetic code in chronic kidney disease*, 79 Kidney International 23, p.23 (2011).
[138] Jane Bradbury, *Human Epigenome Project - Up and Running*, PLoS Biology, Vol.1:3, p.316 (2003)
[139] Ibid.

development in this area of research is about the identification of epigenetic mechanisms for human disease. Epigenetic therapies are being developed to find a cure for disease caused by epigenetic factors. Some drugs are used specifically because of their known effects on the epigenome. A class of epigenome-modifying agent for cancer is currently under clinical trials.[140]

1.7.1.4 NUCLEAR MEDICINE

The uses of nuclear substances for diagnostic and therapeutic applications are very common today. One of the significant areas in medial biotechnology using nuclear energy, is the medical imaging. The science of medical imaging to reveal biological processes at the sub cellular level involves the nuclear methods. Nuclear magnetic resonance (NMR) is the best way to study motion in proteins.[141] This often relies on radiopharmaceuticals[142] and medical isotopes.[143] NMR spectroscopy provides advantages over other technologies like X-ray crystallography.[144] X-ray crystallography is a powerful technique used to study the three-dimensional structure of crystals including macromolecules such as proteins and nucleic acids.[145]

NMR spectroscopy can yield useful information about proteins having no well-defined structure, including those that are extremely difficult to crystallize because they assume a shape only when they bind to another protein. NMR spectroscopy could be used to analyse chemical reactions and chemical catalysts.[146] Using NMR spectroscopy protein structures can easily be deciphered and it can check the purity and structure of compounds during organic synthesis.[147]

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[140] Andrew P. Feinberg, *Phenotypic plasticity and the epigenetics of human disease*, 447 Nature, p.438 (2007).
[141] Ad Bax and Dennis A. Torchia, *Molecular machinery in action*, 445 Nature, p. 609 (2007).
[142] Radiopharmaceuticals are medicines that are radioactive when used in patients. They are used in specialised hospital wards, primarily for diagnostic purposes.
[143] A medical isotope is a very small quantity of radioactive substance used in safe, cost-effective imaging and treatment of disease. Medical isotopes can be delivered directly to the site of diseased cells. This is different from external beam radiation treatment where radiation is directed from outside of the body.
[144] Ananyo Bhattachary, *Breaking the billion-hertz barrier*, Nature,Vol 443, p. 605 (2007).
[145] A.J. Nair. *Introduction to Biotechnology*, p. 238.
[146] Ibid.
[147] Ibid.

1.7.1.5 NANOMEDICINE

Nanomedicine is a natural application for bio nanotechnology. Nanomedicine allow researchers to make customized changes to the mechanisms of the human body, correcting defects and curing diseases. Nanomedicine first chooses an area in a human body that causes or contributes to the disease state. A specific nanoscale device is then created to find that target area and correct its function. This works almost like aspirin acting on clots.[148]

Nanomedicine is a very new technology in line with nano-biotechnology. Nanomedicine focuses on diagnosing, treating or preventing diseases and improving human health by making use of the molecular knowledge of the human body[149]. The area is dominated by nano-pharmaceuticals and DNA nanotechnology. Scientists are engineering functional devices at the molecular level to repair human cells with small atomic machinery injected into the body and guide them through the body to create DNA nanotubes[150]. Nanomedicine uses nanosc of mo ale techniques lecular self-assembly[151] for the production of materials such as tissue cell engineering devices, molecular motors and molecules for bio sensory and drug delivery devices.

The emerging field of molecular electronics has made considerable progress in the development of nano-scale electronic components and sensors. One such development is the use of DNA-based nanotechnology which seeks to engineer synthetic DNA polymers to encode information necessary for realization of the desired structures or processes on the molecular level. These structures similar to DNA nanotube[152] has a major role to play in future nanomedicine.[153]

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[148] David Goodsell, *Bionanotechnology Lessons from Nature,* p.237.
[149] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.62.
[150] DNA nanotubes represent a potential breakthrough in the self assembly of nanometer-scale circuits for electronics layout because they can be targeted to connect at specific locations on larger-scale structures and can subsequently be metallized to form nanometerscale wires.
[151] Molecular self-assembly is the process by which molecules adopts a defined arrangement without guidance or management from external source.
[152] A nanotube is a nanometer-scale tube-like cylindrical nanostructure, DNA nanotubes are hollow tubes formed of strands of DNA that are a few nanometres wide. Researches are gong to see how nanotubes can be used to deliver drugs locally to specific diseased cells.
[153] Dage Liu, et al., *DNA nanotubes self-assembled from triple-crossover tiles as templates for conductive nanowires,* PNAS, vol. 101, no. 3 p.717 (2004).

1.7.1.6 THERAPEUTICS AND DIAGNOSTICS

Biotechnology has a very important role to play in medial research. The biotechnology research can be used as a tool to diagnose diseases. It can also be used in treatments of diseases. The techniques of genetic manipulation like recombinant DNA technologies, genetic screening, genetic engineering, gene therapy and so on. play a major role in therapeutic and diagnostic use in medical biotechnology.

1.7.1.7 GENETIC ENGINEERING

Biotechnology is widely accepted as the most appropriate diagnostic and therapeutic techniques for modern treatments. Genetic engineering plays a very prominent role in medical biotechnology. Genetic engineering is a process by which an organism's genome is intentionally altered. It is the manipulation of an organism's genes through cloning or transformation via the addition of foreign DNA.[154] By the process of genetic engineering, we can transfer the property of a single gene from one organism to another.

This process has five steps: [155]

1. Isolation of the genes
2. Insertion of those genes into a transfer vector (a virus or a plasmid used as a conduit)
3. Transfer of the vector to the organism to be modified
4. Transformation of that organism's cells
5. Separation of the genetically modified organism (GMO) from organisms that have not been successfully modified.

1.7.1.8 GENETIC SCREENING

Genetic screening is the process of screening a person's DNA to see if he or she carries a gene that may lead to a certain disease or not. The first successful, wide-scale genetic screening took place in 1971, when Michael Kaback, a pediatric neurologist at Johns Hopkins University, gave 1,800 people of Ashkenazi Jewish

[154] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p.12.
[155] Ibid.

ancestry an enzyme test to determine if they carried the gene for Tay-Sachs[156] disease.[157] The gene screening plays a significant role in health care sector as a diagnostic tool of advanced biotechnology.

2.7.1.9 GENE THERAPY

Gene therapy is the process of treating a genetic disease by replacing a person's defective gene with a new, normally functioning one to cure a disease caused by a malfunctioning gene. Gene therapy is a major achievement in the genetic engineering sector. One of the miraculous achievements in the history of medical biotechnology was in 1990, when doctors performed a groundbreaking procedure on the four-year-old Ashanthi DeSilva Who suffered from severe combined immunodeficiency (SCID). she lacked immunity to such an extent that she could not even stand mild infections. People born with SCID typically die in childhood. Researchers took some of DeSilva's white blood cells, grew them in a laboratory, inserted a missing gene into them, and then put the modified cells back into her bloodstream.[158] Even though the treatment was not a cure, it improved her immune system enough for her to lead a normal life. She had to appear for treatment every few months as the modified cells began to die off and needed to be replaced.

1.7.1.10 GERM LINE GENE THERAPY AND SOMATIC CELL GENE THERAPY

Gene therapy comes in two forms: germ line gene therapy and somatic cell gene therapy. Germ line therapy is normally made on reproductive cells, sperm or eggs that are altered by inserting engineered genes. Changes made this way will alter a genome forever and which will be passed on to future generations. The most famous example of germ line research was Tracy, a sheep whose germ line contained a genetic construction comprising a human gene plus "promoter", which caused Tracy's

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[156] Tay-Sachs disease is a deadly disease of the nervous system passed down through generations. The disease occurs when large quantities of cell membrane components known as gangliosides accumulate in the nerve cells of the brain, resuting in premature death of those cells. As of now, there is no cure or treatment for this disease.

[157] Kathy Wilson Peacock, *Biotechnology and genetic engineering,*p.13.

[158] Ramez Naam. "More Tan Human." New York Times (7/3/05). Available at. http://www.nytimes.com/2005/07/03/books/chapters/0703-1st-naam.html. last accessed on 9-9-2009.

milk glands to produce proteins identical to human ones.[159] Somatic cell gene therapy involves altering the body's somatic cells, or organs and tissue cells that are not involved in reproduction. This type of gene therapy would cure or treat a person's condition, but the changes would not be passed on to future generations.

1.7.1.11 ANTIRETROVIRAL DRUGS

Antiretroviral drugs are medications for the treatment of infection by retroviruses. A virus is an infectious agent that grows or reproduces by attaching itself to a host cell. Viruses do not have cells but has their own genetic material either DNA or RNA. Retrovirus is a type of virus that contains RNA instead of DNA. It replicates by using the enzyme reverse transcriptase that gives them the unique property of transcribing RNA (virus RNA) into DNA. The DNA then integrates itself into the chromosomal DNA of the host cell to be expressed there. The virus then continues to replicate via the host's DNA.[160]

Human immunodeficiency virus (HIV) is a retrovirus. Antiretroviral drugs (ARV) are used to combat retroviruses, but because retroviruses mutate quickly and often, ARV therapy usually involves taking several medications at once in high doses; the course of the treatment may vary. The treatment is now mainly used for HIV virus infections.

1.7.1.12 IN VITRO FERTILIZATION

In-vitro-fertilization is a new reproductive technology, which includes a process in which an egg is removed from a woman's body and fertilized with a man's sperm in a laboratory, with the resulting zygote then implanted in the woman's womb. In-vitro means, outside the body. Fertilization means the sperm has attached itself to and entered the egg.[161] Robert Edwards a British obstetrician and gynecologist, an expert in genetics and reproduction along with Patrick Steptoe originated the process of in-vitro fertilization. Louise Brown, the world's first test tube baby was conceived

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[159] Donna M. Gitter, *Led Astray by the Moral Compass: Incorporating Morality into European Union Biotechnology Patent Law*, 19 Berkeley J. Int'l L., p. 16 (2001).

[160] Definition given by medterms dictionary available at http://www.medterms.com/script/main/art.asp?articlekey=5344 last accessed on 20-6-2011.

[161] Medline Plus, medical encyclopaedia, avilble at; http://www.nlm.nih.gov/medlineplus/encyclopedia.html , last accessed on 20-6-2011.

and born through the in-vitro fertilization process in England in 1978.[162] Robert Edwards was awarded The Nobel Prize in Physiology and Medicine for the development of human in-vitro fertilization (IVF) therapy in 2010.[163]

1.7.1.13 PHARMING: GROWING MEDICINE

Pharming is a new area in biotechnology. The term 'pharming' comes from a combination of the words farming and pharmaceuticals - a melding of the basic methods of agriculture with the most advanced biotechnology. It is also called biopharming or molecular farming which follows a procedure of inserting genes with pharmaceutical benefits into crops that do not normally contain those genes[164]. The crop is then harvested and either consumed for its pharmaceutical properties or refined into a marketable pharmaceutical product. Much of the new genetic material introduced into these organisms are proteins. Most bio-pharming applications target production and storage of the pharmaceutical protein in seeds which naturally accumulate high concentrations of proteins and oils.[165]

Plant-made pharmaceuticals (PMP) could also help malnourished people in developing countries. Golden Rice 2 is a pharming product that contains the provitamin beta carotene which can be converted by the body into vitamin A. This is a genetically modified variety of rice rich in Vitamin A and it was developed for the 100 million people who live in developing countries and suffer from Vitamin A deficiency.[166] In parts of the world where diet staples are low in beta carotene, this rice may alleviate this deficiency.

1.7.1.14 THERAPEUTIC ANTIBODIES

Antibodies are the core components of the immune system. They recognize foreign bodies inside the body and take necessary action to remove the antibodies such as molecules on the surface of body cells, bacteria or viruses, and mark them out for elimination by the immune system. They belong to a class of proteins known as

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[162] A.J. Nair. *Introduction to Biotechnology,* p.8.
[163] http://nobelprize.org/nobel_prizes/medicine/laureates/2010/press.pdf. last accessed on 12-10-2010.
[164] http://learn.genetics.utah.edu/archive/pharming/index.html last accessed on 12-10-2010.
[165] P. Byrne, *Bio-pharming,* Colorado State University, available at http://www.ext.colostate.edu/pubs/crops/00307.pdf accessed on 10-4-2011.
[166] Richard Li-Dar Wang, *Biomedical Upstream Patenting and Scientific Research*, p. 294.

immunoglobulins.[167] In 1972 Cesar Milstein and Georges Kohler, a Nobel Prize winner found a way to produce copies of identical antibody molecules in unlimited amounts. Within a few years these monoclonal antibodies had revolutionised biological research, allowing any desired molecule to be reliably identified and marked. The therapeutic antibodies play a significant role in improving the immunity system.[168]

1.7.1.15 THERAPEUTIC PROTEINS

Modern medical biotechnology uses a wide range of methods to diagnose and treat diseases from the biotechnological production of simple natural products to gene therapy. The most important group of biotechnological drugs are the therapeutic proteins. The use of proteins as therapeutic agents is not a new concept. The protein insulin was first introduced as a treatment for diabetes in the 1920s.[169] The first approved therapeutic antibody was rituximab (Rituxan) manufactured by Genentech, Inc. and Biogen Idec Inc. and is used in the treatment of B-cell non-Hodgkins lymphoma[170] in 1997.[171] Antibodies have since become the fastest-growing class of human therapeutics. Protein-based therapy has become an important strategy that has greatly benefited people suffering from various disorders including cancer, Crohn'sdisease,[172] diabetes and multiple sclerosis.

Most therapeutic proteins are chemical messengers, enzymes or monoclonal antibodies. Therapeutic proteins, the largest group of biopharmaceuticals are made up of dozens, sometimes hundreds of amino acids. They are used as active agents in pharmaceuticals. These molecules act as vital chemical messengers in the body. The target cells that receive and translate the signals bear special receptors on their surface

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[167] F. Hoffmann-La Roche Ltd, *Biotechnology – new directions in medicine*, (F. Hoffmann-La Roche Ltd, Corporate Communications CH-4070 Basel, Switzerland. 2006), p. 45 available at www.roche.com/biotechnology_new_ways_in_medicine.pdf last accessed on 21-06-2011.

[168] Ibid.

[169] Form the editors, *web focus- therapeutic proteins*, Nature Reviews Immunology 6, p.S.4 (October 2006) available at http://www.nature.com/reviews/focus/therapeuticproteins/editors/nri1946.html last accessed on 21-6-2011.

[170] Hodgkin's lymphoma, previously known as Hodgkin's disease, is a type of lymphoma, which is a cancer originating from white blood cells called lymphocytes. It was named after Thomas Hodgkin, who first described abnormalities in the lymph system in 1832.

[171] Form the editors, *web focus- therapeutic proteins*, Nature Reviews Immunology 6,p. S.4.

[172] Crohn's disease, also known as regional enteritis, is an inflammatory disease of the intestines that may affect any part of the gastrointestinal tract from mouth to anus.

into which the corresponding chemical messenger precisely fits. Gene sequences enable the production of therapeutic proteins. Human DNA sequences are primarily used in the context of recombinant production of human therapeutic proteins.[173]

1.7.1.16 NATURAL PRODUCTS AS THERAPEUTICS

Plants have been used as a source of medicine throughout history and they continue to serve as the basis for many pharmaceuticals used today. Arthur Eichengrün and Felix Hoffmann, working at Friedrich Bayer, created the first synthetic drug, aspirin. Aspirin (acetylsalicylic acid) was synthesized from salicylic acid, an active ingredient of analgesic herbal remedies. Penicillin was discovered in 1928 by Alexander Fleming, adding microbes as important sources of novel drugs.[174] Effective use of plant cell culture, recombinant DNA technology and cellular cloning can provide us with new ways to identify naturally produced therapeutic drugs.

Many plants and animals such as certain ticks and bat saliva are sources of new medicines and are proved to be effective anticoagulants. Exenatide is a medication for the treatment of diabetes. Exenatide is a synthetic version of exendin-4, a hormone found in the saliva of the Gila monster and it was first isolated by Dr. John Eng in 1992.[175] The compound was chemically copied from the venom of the Gila monster and was approved in early 2005 for the treatment of diabetes.

The marine organisms provide a rich habitat for potential new medicines. Marine biotechnologists have discovered organisms containing compounds that could be used as therapeutic agents. One of the recent discoveries is that a new genus of actinomycetes[176] called *Salinospora* which produces salinosporamide a potent anticancer agent.[177] These pathogens are found only in the marine environment.

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[173] Geertrui Van Overwalle, *Policy Levers Tailoring Patent Law to Biotechnology. Comparing US and European Approaches,* University of California Irvine Law Review, Forthcoming. p. 8 (2010). Available at SSRN: http://ssrn.com/abstract=1720875 last accessed ON 26-06-2011.

[174] Barbara Schmidt, *A natural history of botanical therapeutics*, Metabolism Clinical and Experimental 57 (Suppl 1) p. s3 (2008)

[175] http://en.wikipedia.org/wiki/Exenatide

[176] Many species of actinomycetes occur in soil and are harmless to animals and higher plants, while some are important pathogens, and many others are beneficial sources of antibiotics. http://www.britannica.com/EBchecked/topic/4401/actinomycete.

[177] Lixin Zhang, Arnold L. Demain, ed.,*Natural Products, Drug Discovery and Therapeutic Medicine* (Totowa, New jersey, Humana Press Inc. 2005) p.36

Marine organisms like shells shrimp and crabs from marine crustaceans are effective agents for drug-delivery.[178]

1.7.1.17 PROTEIN REPLACEMENT THERAPIES

Some times certain diseases are the result of certain missing proteins or defective genes. The diseases are caused when defective genes do not produce sufficient proteins required for the body. In certain disease states, the defective gene product (protein) can be supplemented or replaced. Examples are glucocerebrosidase, a protein supplementation for the treatment of Gaucher's disease and insulin for the treatment of diabetes mellitus.[179]

Today, with the help of recombinant DNA technology and cell culture, we can replace the missing proteins. Replacement protein therapies include treatment for haemophilia. Hemophilia A is an inherited X-linked disorder caused by the deficiency of coagulation "factor VIII (F.VIII)" a protein involved in the blood clotting process.[180] It can be treated by replacement of "factor VIII". We are using replacement protein therapies for the treatment of diabetes which is the result of an inadequate supply of insulin. Insulin is a protein hormone that regulates blood glucose levels and now it can be replaced.

1.7.1.18 CELL TRANSPLANTS

Cell transplantation is one of the new research areas in medical biotechnology. Scientists are investigating ways to use cell culture to increase the number of patients who might benefit from one organ donor. Cell transplantation is one of the therapeutic remedies for certain acute diseases related to liver, diabetes, multiple myeloma[181] and blood cancer. The treatment is basically cell transplantation. Depending upon the

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[178] Lixin Zhang, Arnold L. Demain, ed.,*Natural Products, Drug Discovery and Therapeutic Medicine,* p.36

[179] Directorate For Science, Technology And Industry Committee For Scientific And Technological Policy, *Economic Aspects Of Biotechnologies Related To Human Health, Part II: Biotechnology, Medical Innovation and The Economy: The Key Relationships*, (OECD Working Party on Biotechnology,1998), p. 216.

[180] Timothy C. Nichols et al., *Protein Replacement Therapy and Gene Transfer in Canine Models of Hemophilia A, Hemophilia B, von Willebrand Disease, and Factor VII Deficiency*, ILAR Journal, Volume 50, Number 2, p. 147 (2009).

[181] myeloma is a cancer of the immunoglobulin-producing plasma cells found in the bone marrow. It is a cancer that involves the immune system. The cancerous plasma cells, or myeloma cells, rarely enter the blood stream.

types of transplants they are classifies as stem cell transplant, islet[182]transplation, Hematopoietic[183] cell transplantationand so on.

In the case of stem cell transplant, stem cells are harvested from a myeloma patient following initial therapy and re-infused after high-dose melphalan therapy has been administered. The process can be done using donor stem cells from twin brothers or other family members.[184]

1.7.2 AGRICULTURAL BIOTECHNOLOGY

Humans have always relied on plants and animals for food, shelter, clothing and fuel and for thousands of years farmers have been changing them to meet our evolving needs. Agriculture is the backbone of every economy. Adopting technological applications to agriculture practice is all about agricultural biotechnology. The agricultural practice is as old as the civilisation itself. One of the main objectives of the agricultural biotechnology is to meet the food requirement of the people around the world. Biotechnology can help in achieving the ever raising need to increase yields, decreasing crop inputs such as water and fertilizers and providing pest control methods that are more environment friendly.

Agricultural biotechnology is a collection of scientific techniques used to improve plants, animals and microorganisms. Biotechnology enables improvements that are not possible with traditional cross breeding of related species alone. It has its presence in every sector of agricultural practice from livestock and poultry management, production of high yield verities of rice and wheat to improving agribusiness. Biotechnology helps in increasing productivity and thereby profit. [185]

Transgenic crops are one of the major developments in the biotechnology sector which increases yield resulting in greater harvests. They are more pest resistant

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[182] Islets are clusters of cells in the pancreas that make insulin, a hormone that helps the body use blood sugar or glucose) for energy. When you have type 1 diabetes, your immune system destroys the islet cells that make insulin.

[183] hemopoietic cells is collective term for all bone marrow-derived cell types in the blood

[184] International Myeloma Foundation, *Understanding Stem Cell Transplant,* p. 4 available at http://www.ebmt.org/10.1Patients&Families/Patient&DonorMaterials/9.%20IMF_u-stemcell_d2_web.pdf last accessed on 12-10-2010.

[185] Jonathan H. Adler, *The Cartagena Protocol and Biological Diversity: Biosafe or Bio-Sorry?,* Georgetown International Environmental Law Review, v. 12, p. 16 (2000).

than those grown from farm saved seeds. Transgenic Bt cotton is a typical example of pest resistant cotton plant. Inserting a Bt gene enables crops to produce a defensive protein, protecting them from insect pests and reducing crop damage.[186] Biotechnology has its own role in livestock management. Livestocks are injected with growth hormones to produce more meat at a faster rate, and antibiotics keep animals free of disease in crowded confines. The result is higher productivity so as to meet the food requirement of the people all over the world.

Depending upon the area of activities, biotechnology can be classified in to many areas like crop biotechnology forest biotechnology animal biotechnology aqua culture etc. Apart from these specialised areas, biotechnology has its own role in the food processing sector, industrial sector and in environmental protection application.

1.7.2.1 CROP BIOTECHNOLOGY

Ancient farmers selected plants with the best characteristics and saved their seeds for the next year's crops. Early farmers used to preserve seeds from plants with preferred characteristics for subsequent cultivations and convert wild plants into domesticated crops. All these were long before the science of genetics was understood. Farmers and plant breeders have always relied on crossbreeding, hybridization and other genetic modification techniques to improve the yield and quality of food and fiber crops and to provide crops with built-in protection against insect pests, disease-causing organisms and harsh environmental conditions.

Modern biotechnologies have advanced much forward from traditional cross breeding and hybridization techniques to genetic manipulations. The tools of biotechnology allow plant breeders to select single genes that produce desired traits and move them from one plant to another.[187] The process is far more precise and result oriented than traditional breeding. Biotechnology also helps to move genetic traits among plants and other organisms. This opens up a world of genetic manipulation to benefit food production. We can, for example, take a bacterium gene that yields a protein, toxic to a disease-causing fungus and transfer it to a plant. The

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[186] Jonathan H. Adler, *The Cartagena Protocol and Biological Diversity: Biosafe or Bio-Sorry?,* p. 16

[187] United Nations Conference on Trade and Development, *Key Issues In Biotechnology*, UNCTAD/ITE/TEB/10 p. 8 (2002) available at http://www.unctad.org/en/docs/poitetebd10.en.pdf last accessed on 10-10-2010.

plant then produces the protein and is protected from the disease without the help of externally applied fungicides.[188]

Biotechnology plays a significant role in genetic modification techniques to increase yield, and to increase resistance to diseases caused by bacteria, fungi and viruses. Biotechnology helps enhance the ability of the plants to withstand harsh environmental conditions such as freezes and droughts and to increase the ability to resist pests, weeds and nematodes. Biotechnology advancements enable DNA manipulation to get the desired qualities to various traits. A biotech crop is a crop-plant that has been genetically engineered using recombinant DNA technology either to promote or to prevent the production of a particular protein with the objective of introducing or enhancing a desirable characteristic in the plant or seed.[189]

1.7.2.1.1 BIOPESTICIDES

Another major achievement of biotechnology is the innovations related to biopesticides such as microorganisms and fatty acid compounds that are toxic to targeted crop pests but do not harm humans, animals, fish, birds or beneficial insects. Biopesticides are certain types of pesticides derived from animals and natural materials such as, plants, bacteria, and certain minerals. There are different types of biopesticides.[190]

Microbial pesticides consist of a microorganism as the active ingredient. Microbial pesticides can control many different kinds of pests such as fungi that control certain weeds and fungi that kill specific insects.[191] Another major development in bio- pesticides is Plant Incorporated Protectants (PIPs). They are pesticidal substances that plants produce from genetic material that has been added to the plant. Gene from '*Bacillus thuringiensis'* (Bt) bacterium when inserted to a plant using the recombinant DNA technology can increase pest resistant quality to plants[192].

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[188] Anne Dauwers, *Uganda hosts banana trial*, news, Nature,Vol 447, p. 1042 (2007).
[189] Allen Van Deynze, Kent J. Bradford, And Alison Van Eenenna, *Crop Biotechnology: Feeds for Livestock*, (Publication 8145 The Regents of the University of California, 2004) p. 1 available at http://www.plantsciences.ucdavis.edu/bradford/8145.pdf last accessed on 26-06-2011.
[190] http://www.epa.gov/oppbppd1/biopesticides/whatarebiopesticides.htm last accessed on 18-06-2011.
[191] Ibid.
[192] Jonathan Adler, *The Cartagena Protocol*, p. 16.

1.7.2.1.2 HERBICIDE TOLERANCE

Another major accomplishment of biotechnology is to make crop plants tolerant to specific herbicides. When the herbicide is sprayed, it will kill the weeds but has no effect on the crop plants. This lets farmers reduce the number of application of herbicides and the cost of producing crops with out damage to the environment.

Herbicide-tolerant plant can be produced either by insertion of a foreign gene to the crop or by regenerating herbicide-tolerant mutants form the existing crop germplasm. The herbicide- tolerant plants have a broad spectrum of weed control and they reduce crop injury and most of them are environment friendly.[193]

1.7.2.1.3 HYDROPONIC BIOTECHNOLOGY

Hydroponics is the practice of growing plants without soil. Hydroponic biotechnology is the growing of crops in water-based nutrient solutions. The word hydroponics was coined in the early 1930s by Professor Gericke at U.C.L.A., to describe the growth of plants with their roots suspended in water containing mineral nutrients. The name comes from two Greek words: 'hydro' (water) and 'ponos' (to work, labor), and literally means 'water works.'[194] The definition of hydroponics has gradually been broadened. Today it is used to describe all the ways of growing plants without soil. It is synonymous with the term soil less culture and both terms are restricted to the growing of plants without soil.

Removing soil helps avoiding many of the problems associated with traditional agriculture. It has many advantages over traditional soil farming. For example, farmers can grow plants indoors through out the year using organic techniques; this will also help conserve water and eliminate the need for pesticides and herbicides.

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[193] Stevan Z Knezevic, *Use of herbicide tolerant crops as part of an integrated weed management programme*, (The Board of Regents of the University of Nebraska 2010), p. 2 available at http://elkhorn.unl.edu/epublic/live/g1484/build/g1484.pdf last accesses on 26-10-2011.

[194] Mohsen Daha, *Easy Gardening with hydroponics for teachers students and home hobbyists*, (Foothill Hydroponics,1999) p. 3., available at http://www.foothillhydroponics.com/booklet/booklet.pdf last accessed on 12-6-2011.

1.7.2.1.3.1 FLAVR SAVR TOMATO

Flavr Savr tomato is the first transgenically modified vegetable approved for human consumption by the United States Food and Drug Administration (FDA). The tomato was created by Calgene, Inc., by introducing a gene to the tomato that produces a messenger ribonucleic acid (mRNA) which functions as an antisense copy of the polygalacturonase gene.[195] Polygalacturonase is a gene that causes the decomposition of pectin- a constituent of the tomato fruit cell wall. The newly introduced ribonucleic acid (mRNA) suppresses the production of an enzyme associated with the breaking down of pectin.[196] This, in turn, will give tomatoes lower levels of polygalacturonase to have longer shelf life because their cell walls remain intact for a longer period of time. This was a revolutionary invention in biotechnology. Apart from these, biotechnology helped the production of insect-protected cotton and herbicide-tolerant soyabeans.[197]

1.7.2.2 FOREST BIOTECHNOLOGY

Wood is an important source of energy. It provides us with fuel materials for construction and making paper. But its supplies are declining rapidly. Demand for wood products is increasing as a material for construction. Trees play the primary role in maintaining ecological balance. As trees absorb carbon dioxide, any advancement that allows us to increase tree yields without cutting down forest, could have significant positive effects on global warming. Forest tree biotechnology emerged during the 1980s and it encompasses a developing collection of tools for modifying tree physiology and genetics to aid breeding, propagation and research.[198]

Biotechnology helps the creation of disease-resistant and insect-resistant trees with increased growth rates. Scientists are also learning how to use biotechnology to improve the efficiency with which trees convert solar energy into plant material and to move more of that energy into wood production and less into pollen, flowers or seeds. All these methods of increasing productivity should decrease the pressure on

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[195] Jim Chen, *Biodiversity And Biotechnology: A Misunderstood Relation,* p.71.
[196] Ibid.
[197] Ibid.
[198] David E. Harry and Steven H. Strauss, *Biotechnology and Genetic Engineering in Forest Trees*, available at http://agribiotech.info/details/Strauss and Harry Draft Final 02 print.pdf

natural forests and invariably act as forest conservation techniques. Extensive research is going to increase cellulose contents of the trees an essential raw material for papermaking and to decrease the amount of lignin, a tough molecule that must be removed during papermaking. Changing the cellulose-lignin ratio genetically, has important environmental implications.

1.7.2.3 ANIMAL BIOTECHNOLOGY

Animal biotechnology is the application of modern biotechnology to all animals including livestock, poultry, fish, insects, companion animals and laboratory animals. Animal Biotechnology basically comprises of three primary technologies such as genomics, cloning and transgenics. The objectives of animal biotechnology are to improve animal health, enhancements of productivity in animals, environmental conservation benefits and advances in human health.

1.7.2.3.1 LIVESTOCK

Demand for diary products and meat has increased all over the world. This has lead to the intensification of live-stock breeding process. Historically meat has been expensive and it takes more land, time and resources to raise cattle. Due to the increase in the demand and price of meat, people started thinking of its large scale production. Traditional farms were replaced by factory farms; traditional mode of feeding was replaced by new techniques known as concentrated animal feeding operations (CAFOs).

Biotechnology helps in bringing many modifications to milk production and has helped in adding new proteins to milk or manipulate endogenous proteins. Recently, researchers from New Zealand developed GM cows that produce milk with increased levels of casein protein.[199] Use of such protein-rich milk would increase the efficiency of cheese production.[200]

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[199] Casein proteins are proteins that are commonly found in mammalian milk, and are a major component of cheese.

[200] World Health Organization, *Modern food biotechnology, human health and development: an evidence-based study*, p. 9 available at; www.who.int/foodsafety/publications/biotech/biotech_en.pdf, last accessed on 22-10-2010

1.7.2.3.2 PRODUCTIVITY ENHANCEMENT HORMONE TREATMENT

Another major growth in modern biotechnology is productivity enhancement by hormone treatment. Bovine Growth Hormone (BGH) or Bovine Somatotropin (BST) is a protein generated in the pituitary glands of cows.[201] It can also be produced artificially using DNA containing genetically engineered *E. coli* bacteria, in which case it is known as rBGH or rBST. The drug is administered to cows to increase milk production, despite the chronic oversupply of milk in the United States. It was a highly controversial product when it was introduced for the first time. BGH is currently used by about 10 percent of U.S. dairy groups. Cows injected with as rBGH or rBST may produce ten percent more milk. The injections, however, tend to cause mastitis (a painful infection of the udder), reduce fertility, and increase lameness.[202]

1.7.2.3.3 ANIMAL GENOMICS

Animal Genomic research helps us in identifying individual genes and proteins of livestocks that control commercially and economically crucial functions such as muscle growth and tenderness to disease resistance and reproduction. The identification of the genetic makeup of an individual animal can greatly affect its value for breeding, feed lot or branding purposes.[203]

1.7.2.3.4 ANIMAL CLONING

Animal Cloning is another form of sophisticated assisted reproduction. Cloning allows livestock breeders to create a new animal with exact genetic properties of an existing animal, essentially an identical twin. Cloning animals is a reliable way of maintaining high quality livestock to meet our nutritional needs. Identifying and reproducing superior livestock genetics ensures that the groups are maintained at the highest quality possible.[204]

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[201] A.J Nair. *Introduction to Biotechnology and Genetic Engineering,* p.772.
[202] R. Dohoo et al. *A Meta-analysis Review of the Effects of Recombinant Bovine Somatotropin*. Can J Vet Res. 67(4): p.252 (2003).
[203] Strickland, *The Guide to Biotechnology,* p.18.
[204] Ibid. at p.70.

1.7.2.3.5 TRANSGENIC ANIMALS

Transgenic animals are created by modifying a genetic material of the species from another species added to its DNA. This breakthrough in technology allows scientists to precisely transfer beneficial genes from one species to another. Transgenic technology can improve the nutritional value of animal products through enhanced genes. The technology helps in improveing animal welfare and productivity in order to meet the food demands of a global population.[205]

There are many positive implications of animal biotechnology. It can play a great role in conservation of endangered species. It also has a role to play in environmental balancing. Livestock produce large quantities of manure annually. Animal manure especially that of swine and poultry, is high in nitrogen and phosphorus, but can contribute to surface and groundwater pollution. Animal feeds improved with biotechnology may help us in decreasing phosphorus and nitrogen excretion, total manure excretion and offensive odors.[206] Biotechnology helps us in resolving these issues by genetic manipulations techniques.

Another side of the story is that the transgenic animals created by genetic manipulation are prone to diseases. the Harvard Onco-mouse which stired intense controversy was a transgenic animal and was susceptible to cancer. Another example is the "Beltsville pig," which was inserted with a gene originating from human genetic material and it produced a growth hormone to enable faster growth. Although these pigs did indeed grow faster, carried less fat and passed these traits on to their offsprings, as intended, they suffered from arthritis and were more susceptible to infections.[207]

1.7.2.3.6 XENOTRANSPLANTATION

When there is a scarcity of healthy human organs or tissues for transplantation, the modern biotechnology permits the use of suitable compatible animals such as pigs. This method of transplantation of organs or tissue- grafting from

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[205] Strickland, *The Guide to Biotechnology,* p.70.
[206] Ibid. at p.72.
[207] Donna M. Gitter, *Led Astray by the Moral Compass: Incorporating Morality into European Union Biotechnology Patent Law*, 19 Berkeley J. Int'l L. 1., p.6 (2001).

animals, is called xenotransplantation.[208] This is another major breakthrough in biotechnology. Extensive research has been done on the potential for using biotech animals as blood or organ donors for humans. The primary barriers to successful xenotransplantation include the immune reactions of the recipient to the graft. The possibility that animal tissues or organs might be rejected in a human recipient and also there is a possibility that the xenotransplant might carrying infection. Biotechnology has been used to address the problem of immunorejection. Biotech pigs have been developed with organs that resist rapid rejection by the human immune system. The first successful xenotransplantation trial was conducted, by transplanting a heart from a genetically-engineered pig into a baboon.[209]

1.7.2.3.7 TRANSGENIC ANIMAL-MADE ANTIBODIES

Another achievement is that the Transgenic animal-made antibodies can be produced from animals that have had human antibody genes transferred to them. These animals can then be vaccinated against human diseases and antibodies can be collected from their blood and used for treating diseases in humans.[210]

1.7.2.4 AQUACULTURE

The term aquaculture refers to the growing of aquatic organisms in a controlled environment. The objective of this method is to increase the production of marine food products. By using biotechnology techniques including molecular and recombinant technology, aquaculture scientists study the growth and development of fish and other aquatic organisms to understand the biological basis of traits such as growth rate, disease resistance and resistance to destructive environmental conditions. Researchers use marine biotechnology to identify and combine valuable traits in parental fish and shellfish to increase productivity and improve product quality. The scientists are investigating the possibility of incorporating growth factors and the natural defense compounds in marine organisms to fight microbial infections.

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[208] A.J Nair. *Introduction to Biotechnology and Genetic Engineering,*p.759.
[209] A.J Nair. *Introduction to Biotechnology and Genetic Engineering,* p.9.
[210] Strickland, *The Guide to Biotechnology,* p. 75.

Biotechnology is also attempting to improve productivity through the development of feed additives, vaccines and other pharmaceutical agents.[211]

One of the major achievements of marine biotechnology is the biotech salmon which reach maturity very quickly but do not breed. Breeding will normally cause salmons to loose weight. The genetic modification of the salmon enabled the year-round availability of it. The projected increase in demand for fish suggests that GM fish may become important in both developed and developing countries. Enhanced-growth in Atlantic salmon containing a growth hormone gene from Chinook salmon is likely to be the first GM animal on the food market.[212] Researchers are trying to develop fish that are more resistant to disease, tolerant of low oxygen levels in the water and tolerant to freezing temperatures. Some species of fish naturally produce a protein that allows them to survive in the Arctic. This "anti-freeze" gene has been transplanted to other species of fish so they can survive in very cold water.

1.7.3 NANOBIOTECHNOLOGY

The term nanotechnology was first used by physicist Richard Feynman in a lecture entitled "Room at the Bottom."[213] The word nanotechnology derives from nanometer, which is one-thousandth of a micrometer (micron) or the approximate size of a single molecule. A nanometre is 10^{-9} of a metre. That is the size of about three or four atoms. To illustrate, a human hair is about 25.000 nanometres (= 10^{-4} metres) whereas a DNA molecules about 2nm wide.[214]

Nanotechnology the study, manipulation and manufacture of ultra small structures and machines made of as few as one molecule was made possible by the development of microscopic tools for imaging and manipulating single molecules and measuring the electromagnetic forces between them. Nanobiotechnology is the study

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[211] Ibid. at, p.76.
[212] World Health Organization, *Modern food biotechnology,* p. 8.
[213] David S. Goodsell, *Bionanotechnology Lessons From Nature*, p. 1.
[214] The Royal Society & The Royal Academy of Engineering, *Nanoscience and Nanotechnologies: Opportunities and Uncertainties*, Report on nanotechnologies, p 5, (2004) available at http://www.nanotec.org.uk/report/Nano 20report 202004 20fin.pdf last accessed on 22-7-2010.

of chemical elements for the purpose of creating technical or medical devices. It is also called bionanotechnology.[215]

Nanobiotechnology uses nanometre scale for measuring the shape and size regarding design, characterisation, production as well as the application of structures, devices and systems used in nanobiotechnology. Nanobiotechnology uses nanofabrication tools and processes to build devices to research biosystems. By using nanofabrication techniques and processes of molecular self-assembly, bio-nanotechnology enables the production of materials and devices such as tissue and cellular engineering scaffolds, molecular motors, and biomolecules for sensor, drug delivery and mechanical applications. [216] Nanotechnology is used in developing screening devices as well as approaches to drug discovery to improve diagnostic and therapeutic techniques. It can image cells and sub-cells at a much higher resolution as magnetic resonance imaging,

1.7.4 GENETICALLY MODIFIED ORGANISMS (GMO'S)

Modern agriculture speaks the language of Genetically Modified Organisms. The basic argument put forward in favour of genetically modified (GM) crops is that they can help in providing a stable food supply for the entire world. Genetic engineering has revolutionised the area of agriculture by increasing crop yields, reducing crop losses by insects, diseases and post-harvest storage problems, and enhancing the nutritional value of some crops. GM crops are now being developed to resist stressful conditions such as drought and soil salinity.[217] Another advantage of GM foods is that they have longer shelf life. The longer shell life of the GM food enable it to reach more people at different locations, ensuring variety in people's diets.

However, there are many controversies related to GM crops. GM food differs significantly from its unmodified counterpart. This is because of the belief that GM foods are not equal in nutrition and safety to those that are not modified. Another controversial issue related to GM food is the use of 'Genetic Use Restriction

[215] Kathy Wilson Peacock, *Biotechnology and genetic engineering,* p. 61.
[216] The Royal Society & The Royal Academy of Engineering, *Nanoscience and Nanotechnologies,* p.20.
[217] United Nations Conference on Trade and Development *Key Issues In Biotechnology*, p. 4.

Technologies' (GURTs), or terminator technology.[218] GURT Embedded GM seeds fail to germinate for subsequent seasons because they cause crops to kill their own seed before germination. Farmers are, therefore, forced to purchase new seeds from their suppliers every year. The United States, Canada, and Argentina are strong supporters of terminator technologies despite serious concerns by the CBD and a majority of the international community. The concern was regarding the potential impact of terminator technology on agricultural livelihoods of indigenous and local communities.[219]

One of the major concerns about introducing GM crops is the impact on the environment. One of the potential problems is that the gene might be unintentionally transferred by pollination to other plants including weeds and also wild relatives of the crop species causing Genetic contamination resulting in adverse consequences on the ecosystem[220]. Many others believe that GM crops could cause a loss of biodiversity. They believe that GM crops affect the normal plant and animal life within a given ecosystem, endangering biodiversity corresponding to a healthy ecosystem.

Another major concern is the risks to human health due to food products derived from genetically modified crops. This is where novel genes have been transferred to crops from organisms that are not normally used as food or animal feed products. Many of the researchers fear that this might lead to the introduction of previously unknown allergens into the food chain.[221] The controversy was sparked when a gene from a Brazil-nut was successfully transferred into a variety of soya which was being developed for animal feed. It was confirmed that the allergenic properties of the Brazil-nut were expressed in the soya.[222] However, the counter-argument was that this case demonstrated the effectiveness of scientific testing for safety.

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[218] Ibid. at, p.7
[219] Chidi Oguamanam, *Biotechnology And Traditional Agricultural Practices At The Periphery Of International Intellectual Property Regime Complex,* Mich. St. L. Rev. 215., p. 238 (2007).
[220] United Nations Conference on Trade and Development *Key Issues in Biotechnology*, p. 4.
[221] Ibid at p.5.
[222] Ibid.

1.7.5 BIOINFORMATICS

Modern biotechnology, by nature is an interdisciplinary science which integrates biological sciences with mathematics, statistics, chemical science and engineering. The most recent development is Bioinformatics as a result of the interaction with Information Technology.[223] Computers have the ability to handle large quantities of data and explore the complex dynamics observed in nature. Bioinformatics is the new technology expression used to describe a rapidly developing discipline working in close coordination between computer technology and the life sciences. Bioinformatics helps computational data management of biotechnology research such as genomics and proteomics. Powerful data management tools and computational techniques are required to store, share, study and compare the rapidly increasing library of biological information. Bioinformatics combines the tools of mathematics, computer science and biology for research data analysis.[224]

There is no widely agreed definition for the term 'bioinformatics.' It may be defined as the application of computing power to biological data to reveal new patterns and information below the surface of those data.[225] The definition for bioinformatics, according to oxford dictionary is, "the science of collecting and analysing complex biological data such as genetic codes."[226]

The fundamental role of bioinformatics technologies is the creation and maintenance of research databases for the storage of biological information. From a wider perspective, bioinformatics is a technology using a computer program to analyze gene sequence data in order to determine how a gene related to a particular disease is turned on or off in the cell.[227] This type of information or research data would be very useful in the realm of biotechnology research for drug discovery and development. The ability to use bioinformatics to organize, analyze or make predictions from data collected in the lab has a major role in biological research.

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[223] A.J.Nair. *Introduction to Biotechnology and Genetic Engineering,*p. 15.
[224] A.J.Nair. *Introduction to Biotechnology and Genetic Engineering*, p.171.
[225] Tom Meyers, *Patenting and Financing Bioinformatics Inventions,* 8:1 B.U. J. Sci. & Tech. L. 157, p.6 (2002).
[226] http://oxforddictionaries.com/definition/bioinformatics
[227] Suneeta D'Souza, *Gene Meets Machine: Intellectual Property Issues in Bioinformatics*, 34 Health Law Review, Vol.12:2, p.34 (2004)

Bioinformatics helps the researchers reduce the time required to find solutions to certain biological questions.

In short, bioinformatics is a management information system for molecular biology and it has many practical applications.[228] Bioinformatics is currently being applied to a number of scientific areas including chemistry, genomics, brain mapping, pharmacology, proteomics and structural biology. It brings together the diverse disciplines of mathematics, statistics, engineering, and computer science to map and model genes and proteins. Bioinformatics plays a critical role in mapping the human genome in both the large public and commercial projects. [229]

The purpose of bioinformatics is three fold. First bioinformatics organises data in a way that allows researchers to access existing information and to submit new entries as they are produced. One of the important tasks is the data curation, the information stored in the databases is essentially useless until analysed and arranged properly. The second aim is to develop tools and resources that help the data analysis. There are different types of data analysis programes available for bioinformatics data analysis[230]. For example, after having sequenced a particular protein, it can be compared with previously characterised sequences. This requires more than just a simple text-based search and there are programs. For example software like FASTA and PSI-BLAST enable us to search and compare a biologically significant matches. The third aim is to use these tools to analyse the data and interpret the results in a biologically meaningful manner[231]. Traditionally, biological studies examined individual systems in detail and frequently compared them with a few that were related. In bioinformatics, we can now conduct global analyses of all the available data with the aim of uncovering common principles that apply across many systems and highlight novel features[232].

The area of bioinformatics, similar to biotechnology, has triggered many controversies. It has given rise to many intellectual property issues; some observers

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[228] Luscombe N M, Greenbaum. D.Gerstein. M, *What is bioinformatics? An introduction and overview,* - Review Paper - Yearbook of Medical Informatics 2001.p83-100 available at; http://www.ebi.ac.uk/luscombe/docs/imia_review.pdf last accessed on 19-08-2011

[229] Suneeta D'Souza, *Gene Meets Machine: Intellectual Property Issues in Bioinformatics*, p.34.

[230] N.M. Luscombe, , *What is bioinformatics*, p.84.

[231] Ibid.

[232] Ibid.

argue that bioinformatics is a discovery, not an invention and hence should not be eligible for patents[233]. This objection is largely mooted because many patents are already being granted in the field of bioinformatics. Critics also assert that innovations in bioinformatics are typically sequential; so early patents can hinder later innovation or form barriers to new products[234]. Bioinformatics being the rapidly growing scientific discipline of computational biology, poses some difficult questions for intellectual property policy. Bioinformatics has made some significant contributions to modern biology by the application of computer science and mathematics to biotechnology research databases such as protein sequence information[235]. This new discipline seems to be playing a critical role in the future development of bio-medical science. The intellectual property issues relating to patenting of bioinformatics software are dealt in details in chapter five.

1.7.6 EXPRESSED SEQUENCE TAGS (ESTs)

Expressed Sequence Tags (ESTs) are one of the most significant areas in biotechnology research as it involves many intellectual property issues. It has been an area of controversy as a patentable subject matter since Craig Venter first used the word EST for the gene sequence.[236] In order to understand what is an EST, a basic understanding the gene its structure and composition is required. We have seen the chemical structure of a DNA and RNA and also the gene structure in the beginning of this chapter. Although genes are sequences of DNA that encode proteins, proteins are not synthesized directly from DNA. The DNA serves as a template for the transcription of RNA. First information from a gene is copied from DNA into new strands of messenger RNA (mRNA) by a process called transcription. Then mRNA directs the assembly of amino acids that fold into a completed protein molecule.[237]

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[233] Robert W. Hahn, ed., *Intellectual Property Rights in Frontier Industries Software and Biotechnology,* (Washington, D.C. AEI-Brookings Joint Center for Regulatory Studies, 2005) p.7.
[234] Robert W. Hahn, ed., *Intellectual Property Rights in Frontier Industries,*p.7.
[235] Robert W. Hahn, ed., *Intellectual Property Rights in Frontier Industries*, p.109.
[236] Matthew Rimmer, *The New Conquistadors: Patent Law and Expressed Sequence Tags*, (16)JLIS, p.13 (2007).
[237] Melanie J. Howlett And Andrew F. Christie, *An Analysis of the Approach of the European, Japanese and United States Patent Offices to Patenting Partial DNA Sequences (ESTs)* , International Review of Industrial Property and Copyright, Vol. 34, p.584(2003)

It is interesting to note that only a small fraction of DNA called exons,[238] constitutes genes that code for protein synthesis. Genes are basically coded with exons and within and between these coding regions of genes are non-coding regions called introns[239] majority of which serve no currently identifiable function. Active genes will first express their products as mRNA and then translate them to protein products. Scientists can get a 'snapshot' of these genes being expressed at a given time by extracting the mRNA from cells.[240] The mRNA can be converted into cDNA and the nucleotides can be sequenced, either fully or partially. An expressed sequence tag is a length of cDNA that is generally partial sequence of a gene that is expressed at the time when a specific tissue is sampled. In other words, an EST is not a short stretch of cDNA that was individually selected for sequencing.[241] It was randomly isolated with many other stretches of cDNA from a cDNA library or from the tissue itself. An EST is generally about 400 to 500 nucleotides in length, and encodes about 130 amino acids, whereas full-length genes are generally between 2000 and 25,000 nucleotides.

1.7.7 SINGLE NUCLEOTIDE POLYMORPHISMS (SNPs)

Like ESTs, Single Nucleotide Polymorphisms (SNPs) are also a prime focus area in biotechnology patent**.** An SNP is a DNA sequence variation that occurs when a single nucleotide (A, T, C, or G) in the genome sequence is altered. SNP variation occurs when a single nucleotide, such as an A, replaces one of the other three nucleotide letters—C, G, or T. An example of a SNP is the alteration of the DNA segment AAGGTTA to ATGGTTA, where the second "A" in the first set is replaced with a "T".[242]

SNPs are genetic variations in the form of different alleles (tiny variations) of the same gene. Genes are combination of nucleotides that code for the production of

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[238] Exons and introns refer to specific nucleotide base sequences in the genetic code that are involved in producing proteins. Exons are the DNA bases that are transcribed into mRNA and eventually code for amino acids in the proteins.

[239] An intron is a segment of a gene situated between exons that is removed before translation of messenger RNA and does not function in coding for protein synthesis.

[240] Molly A. Holman and Stephen R. Munzer, *Intellectual Property Rights in Genes and Gene Fragments:* p.748

[241] Ibid.

[242] The explanation given to SNPs by the National Center for Biotechnology Information (NCBI) available at http://www.ncbi.nlm.nih.gov/About/primer/snps.html accessed on 12-10-2010

proteins. An allele is an alternative form of any particular gene. Humans genes are 99.9% same, however that point one percent (.1%) variation amounts to about three million variations.[243] These variations reflect in different frequencies among different groups of individuals. It is estimated that there are approximately 300,000 SNPs in the human genome. SNPs are particularly useful in the identification of the multiple genes underlying such complex disorders as diabetes, hypertension, asthma, common cancers and the major neuropsychiatric diseases. The genes will be identified through the association of particular SNP markers with individuals who have a particular disease.[244]

1.8 CONCLUSION

The subject of biotechnology, the concepts and the terminologies may not be familiar to the experts in the field of law. However in order to understand the legal issues relating to intellectual property rights in biotechnology sector, we must have a basic understanding of the concepts and terminologies. This chapter attempts to give a brief overview of various biotechnology concepts.

The term biotechnology today implies modern biotechnology. It involves many fields like cell biology, microbiology, molecular biology, embryology, genetics, epigenetics, proteomics, bioinformatics and so on. Biotechnology today has a wide variety of uses in the medical field as a diagnostic and therapeutic tool. The growth of biotechnology research leading to the development of genetic engineering and recombinant DNA technologies has a tremendous impact on human life. It makes disease diagnosis and treatments much easier. Researchers are working towards finding a solution to the most complex diseases with the help of genetic manipulations.

As technology grows to a different plane, the issues relating to intellectual property protections are also getting far more complex. The biotechnology has posed many challenges to the traditional intellectual property regime. The biotechnology research relating to genes and gene sequences like ESTs and SNPs are highly

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[243] Jonathan Kahn, *Race-ing Patents/Patenting Race: An Emerging Political Geography* p. 360.
[244] Arti K Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 Nw. U.L. Rev. 77, p.105 (1999).

controversial. The protection of research data and the intellectual property issues relating to them are still unresolved issues which are dealt in detail in subsequent chapters. The research databases and analysis tools such as bioinformatics are also raising many intellectual property issues.

This chapter attempts to familiarize the biotechnology concepts and terminologies in order to have a better understanding of the intellectual property issues and controversies relating to it. Intellectual property management requires conceptual and philosophical backing which can be realized only by familiarizing the nature of activities taking place in the area biotechnology research. Biotechnology research relating to gene and gene fragments are rather exploratory in nature, to uncover the basic structure composition and chemical linkage with in the gene. Hence it shows that biotechnology research on genes and gene fragments are having the nature of discoveries rather than innovations relating to an already existing product of the nature. Since it forms only discovery of the product of the nature, application of patents becomes doubtful. Nevertheless the DNA sequence data is a highly valuable product of an intellectual input. Adequate protection must be ensured to safeguard the data. However the raw genomic data falls under the category of non creative databases which is not protected under the present copyright regime. This raises a complex situation since the application of patents and database protection under copyright fails to extent to genomic databases. Application of intellectual property concepts are justifiable only if the nature and concept of protection required are in line with the Intellectual property philosophy. These issues are analysed in detail in the following chapters. A detailed account of the various patent philosophies and problems confronted by the biotechnology research in ensuring patent protection is explained in the following chapter.