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Narrative Review

Advancement in Medical Biotechnology: A Review

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Abstract

Technology is anything that makes our life convenient or easier, thus any technology that uses bioresources e.g., microorganisms, enzymes, and other bioresources to make human life easier is defined as Biotechnology. The human genome project results are the baseline for various applications of modern medical biotechnology e.g., drug discovery and DNA delivery, medical diagnostic techniques, vaccine development, pre-clinical trials in an animal model, and clinical trials in humans. Medical biotechnology is the use of living cells and cell materials to research and produce pharmaceutical and diagnostic products that help treat and prevent human diseases. This study highlights a brief review of various applications of medical biotechnology including gene therapy, monoclonal antibodies (Hybridoma technology), vaccine technology, recombinant DNA technology, Human Genome Project (HGP), in silico drug designing, RNA-mediated interference (RNAi), Nano-biotechnology, stem cell therapy, and metamaterial application.

Keywords: Biotechnology, Drug Development, Gene Therapy, RNAi, Stem Cell, Metamaterials

Introduction

The term biotechnology was introduced by a Hungarian engineer, Karl Ereky (1917), defining biotechnology as "all lines of work by which products are produced from raw materials with the aid of living things".[1] The term biotechnology is composed of two words biology and technology. Technology makes human life comfortable and easier, thus technology that uses biological agents/ bioresources to make human life easier is termed biotechnology. The Organization for Economic Cooperation and Development (OECD) defined modern biotechnology in 1982 as the "application of scientific and engineering principles to the processing of materials by using biological agents to provide goods and services for improving the quality of life".

The most promising application of biotechnology is observed in the medical field. Biotechnology is the application of biological agents (microorganisms, plant and animal cells, and enzymes) to be used in agriculture, animal husbandry, food production, and medicine industries.[2] The Convention on Biological Diversity (1992) defined biotechnology as ''technological application that uses biological systems, living organisms or derivatives thereof, to make or modify products and processes for specific use''.[2] This definition was accepted by the Food and Agriculture Organization, United Nations (FAO) and the World Health Organization (WHO).

The basics of modern biotechnology in the field of biomedicine were developed using cloning in host organism *E. coli* and discovery of restriction enzymes by molecular biologists W. Arber, H. Smith, and D. Nathans for which they were awarded the Nobel Prize (1978). The recombinant insulin and recombinant human growth hormone were produced in 1980.[3] Vaccines (e.g., hepatitis B vaccine), recombinant human insulin, drugs, and diagnostic tools are being developed by medical biotechnologist for disease diagnosis and treatment such as tuberculosis, malaria, AIDS and pandemic e.g., COVID-19.[4]

Medical biotechnology is described as 'technology of hope' for biomedical applications. It is actually defined as the "use of living resources for the production of pharmaceutical and diagnosing products for the diagnosis, treatment and for preventing diseases" because the healthcare sector is the most important priority worldwide.

Medical Biotechnology

Medical biotechnology is the application of scientific

and engineering principles by using living cells and cell materials to produce pharmaceutical and diagnostic products that prevent and treat human diseases. Most of the medical biotechnologists' work is research-oriented that has applications in industrial settings. The research laboratories experiment according to the existing problem (e.g., development of vaccine for COVID-19) and conduct various experiments in a laboratory setup. it would be scale-up in industrial setup for developing vaccines or drugs and many other products for human use e.g., antibiotics, plantibodies, microbial pesticides, insect-resistant crops, vitamin A-rich rice, and techniques for environmental clean-up.

According to the OECD, biotechnology is defined as "the application of science and technology principles to process materials by using biological agents to provide goods and services". For decades, human beings practiced biotechnological techniques to produce various goods, including curd, cheese, bread, beer and wine, breeding of animals and increasing crop yield by selecting seeds from, especially desirable plants. Modern biotechnology is an interdisciplinary area of study based on the knowledge of biosciences and engineering technologies. Biotechnology applications are classified in four major areas, including health care (medical), crop improvement and agriculture, non-food uses of crops (e.g., biodegradable plastics, biofuels, vegetable oil), and environmental clean-up process.

The discovery of antibiotics was the landmark discovery that changes the world of medicine immensely. Alexander Fleming was recognized for discovering penicillin from the mold penicillium. Using sophisticated biotechnology techniques and a range of microorganisms have been used to produce a variety of antibiotics.

Recombinant DNA (rDNA) Technology

Recombinant DNA (rDNA) technology refers to the process of combining DNA molecules from two different sources and inserting them into a host organism, to generate products for human use (Figure 1). The discovery of DNA double-helix structure was the base of advancement in the field of rDNA technology.[5] The first rDNA molecule was generated by Paul Berg, Herbert Boyer, Annie Chang, and Stanley Cohen in 1973, as they developed a technique to introduce DNA into host organisms e.g., *E. coli* to create a transgenic bacterium.[6] The foundation of rDNA technology was laid by the discovery of restriction enzymes by Werner Aber, Hamilton Smith, Daniel Nathans and received a Nobel Prize for Medicine and Physiology in 1978. In several bacteria, these enzymes naturally occur and serve as part of the restriction-modification system which is a bacterial defense mechanism. The restriction enzymes selectively recognize a specific DNA sequence to cut and remove DNA segments from one organism and recombine it with the DNA of another organism. Today more than a thousand restriction enzymes are available for modern genetic engineering.[7]

Since the year 2019 due to the exposure of COVID-19 pandemic worldwide, biotechnology has had a tremendous scope for the discovery of medicine and vaccine to save human life. The rDNA technology used host organisms to produce therapeutic products for the treatment of human diseases[7] e.g., *E. coli* used for the production of insulin hormone, growth hormones, monoclonal antibody, yeast cells used to produce Hepatitis B vaccine. The basic steps involved in rDNA technology are illustrated schematically below (Figure 1):

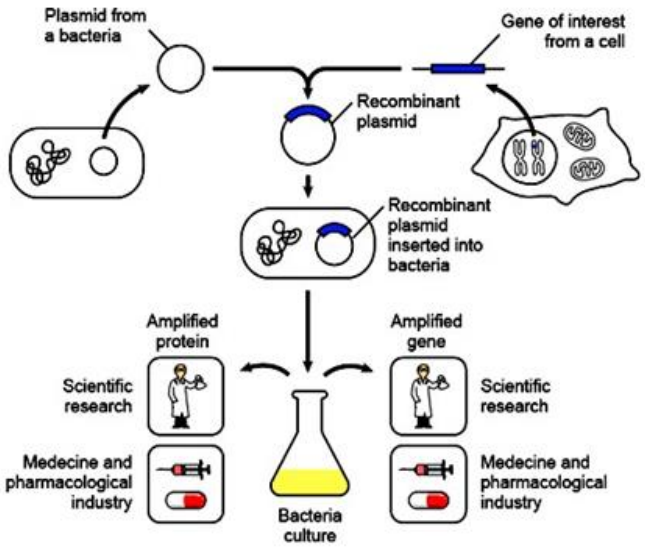

Figure 1. Recombinant DNA Technology Steps and Applications: Treat foreign DNA and plasmid with restriction enzymes and join using ligase. Introduce the recombinant plasmid into host bacteria. Applications of amplified genes and proteins are explained in the diagram.

- Isolation of gene of interest by treating with restriction enzyme that needs to be cloned.
- Formation of a recombinant DNA (rDNA) molecule by insertion of the DNA fragment into a carrier DNA molecule called vector (e.g. plasmid, cosmid)

that can self-replicate within a host cell.

- Transfer of the rDNA into an *E. coli* host cell (transformation)
- Selection of only those host cells carrying the rDNA and allowing them to multiply thereby multiplying the rDNA molecules. The whole process thus can generate either a large amount of rDNA (gene cloning) or a large amount of protein expressed by the insert.

The modern biotechnologists have been classified into the following branches: (a) *In Silico* Biology/ Bioinformatics is an interdisciplinary branch of study, that deals with the application of mathematical, statistics, biology, and informational technique principles to process the biological data to find out the structure and functions of macromolecules (e.g., DNA, Proteins, etc.) and plays an important role in various areas, including genomics, transcriptomics, proteomics that have application as in silico drug designing. (b) Blue biotechnology is based on the use of marine resources to develop new products. (c) Green biotechnology is the application of agricultural technology to improve crops or industrial purposes to generate industrially useful products e.g., paper, detergents, biofuels, pharmaceutical, textiles, substances, designing of transgenic plants, etc. (d) White or industrial biotechnology is the application of industrial processes, enzyme or microorganism to produce chemicals, pharmaceuticals, food ingredients, etc. (e) Red biotechnology is the application of medical technology for producing vaccines, antibiotics, drugs, and curing diseases through genetic manipulation. Therefore, advancement in the field of biotechnology is facilitating scientists for designing safe and effective drugs, vaccines, and other various products.[8-11]

Medical biotechnology has outstanding features of as the contribution of developing a variety of drugs, vaccines for the treatment of microbial infections, chronic renal and respiratory disease, cancer, autoimmune disease, cerebrovascular diseases (e.g., myocardial infarction), diabetes, and dementia/brain-related diseases (i.e., Alzheimer's disease, Parkinson's disease, etc.). Pharmacogenomics-based medications help to understand why individuals respond differently to medicines and it becomes a part of the chronic diseases treatment process. It has developed the base of a safe medication approach according to an individual's genetic makeup.[12]

Genome Editing and Gene Therapy

J. Doudna and E. Charpentier were awarded by the Nobel Prize (2020) in Chemistry for the development of the CRISPR/Cas9 genome editing technique. The CRISPR/Cas9 genetic scissors could change the DNA of humans, plants, and microorganisms with high accuracy. Since the discovery of DNA structure and the recognition of genes, the ability to site-specific local modifications in the human genome has become the goal of medical research.

Therefore, the advancement of gene therapy techniques has the capacity for creating gene improvements by site-directed mutation or modifications that have targeted treatment (Figure 2). Advances in gene therapy, antibiotics discovery, rDNA technology and chemotherapy, and other techniques allow the manipulation of vectors used to deliver genetic material to target cells.[13]

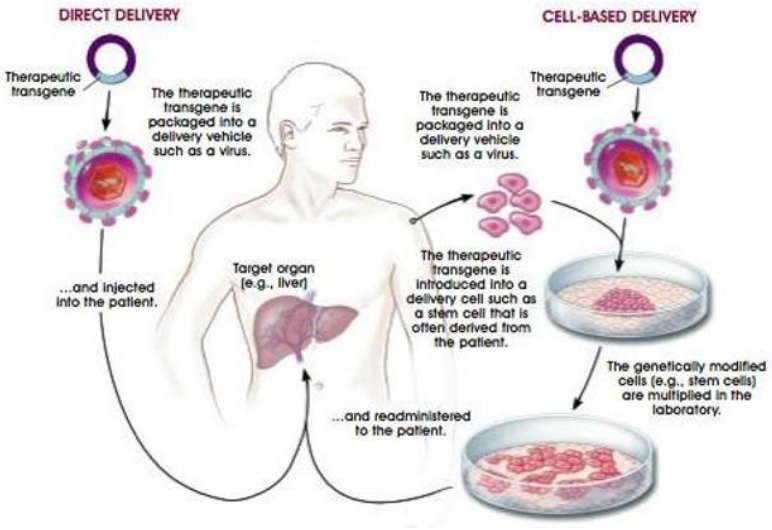

Figure 2. Strategies for Delivering Therapeutic Transgenes.

Tools and methods for gene therapy are used to correct a gene mutation in an inherited embryo disorder. Genetic disease is the outcome of a structural or functional alteration in the DNA that is considered a gene mutation in which the DNA sequence is altered. Three methods can be adopted by gene therapy: (a) replacing a faulty gene with a normal gene; (b) inactivating or 'knocking out' the defective gene; or (c) inserting a completely new gene into the body to treat the disease so that the human body can generate the right protein and thereby eradicating the root causing the disease.[14]

Gene mutation may cause many human diseases such as diabetes, cancer, cardiovascular, autoimmune disorders, and mental illnesses. It is assumed that family history is a strong indicator of the likelihood of genetic inheritance of an individual's disease[15]. Single gene mutation/nucleotide polymorphisms (SNPs) is associated with various diseases including sickle cell anemia, Severe Combined Immunodeficiency (SCID), β-thalassemia, hemophilia, cystic fibrosis, phenylketonuria, etc. Gene therapy focuses on diseases caused by single -gene defects.[16]

The gene therapy may be classified into two types, based on the treated cell types (a) germline gene therapy and (b) somatic gene therapy. Germline gene therapy involves introducing ‘normal’ genes into the eggs or sperm or the fertilized egg or early embryo of the offspring. These genetic changes would be inherited. Germline gene therapy may be performed to eliminate genetic disorders or to enhance genetic variation. Somatic gene therapy involves the introduction of novel genetic material into somatic cells to express therapeutic gene products and its promise to treat both inherited and acquired diseases. In progenies, somatic gene therapy is not inherited. The somatic cells are exposed to a recombinant virus carrying the desired gene and after infection, the desired gene becomes a part of the DNA of the cells. Gene therapy approaches and concepts are still under progress and are being investigated during pre-clinical trials on laboratory animals. The safety aspect of initial clinical trials will lead to the widespread investigation of applications in both medicine and surgery.[17]

Monoclonal Antibodies and Plantibodies

Antibodies present in serum are a heterologous population released by B- lymphocytes and therefore are known as polyclonal antibodies. Monoclonal Antibodies (mAbs) are monovalent antibodies which bind specifically to the epitope on an antigen and are produced from a single B-lymphocyte clone. The mAbshave been increasingly used over the last decades and the concept of using antibodies to selectively target tumors was proposed by Paul Ehrlich through Hybridoma Technology (Figure 3).[18] Ceasar Milstein and George Kohler were honored with the Nobel Prize (1984) for the development of hybridoma technology by fusing antibody-producing B-lymphocytes with myeloma cells using polyethylene glycol. The mAbs were first generated in mice using a hybridoma technique (1975).[19]

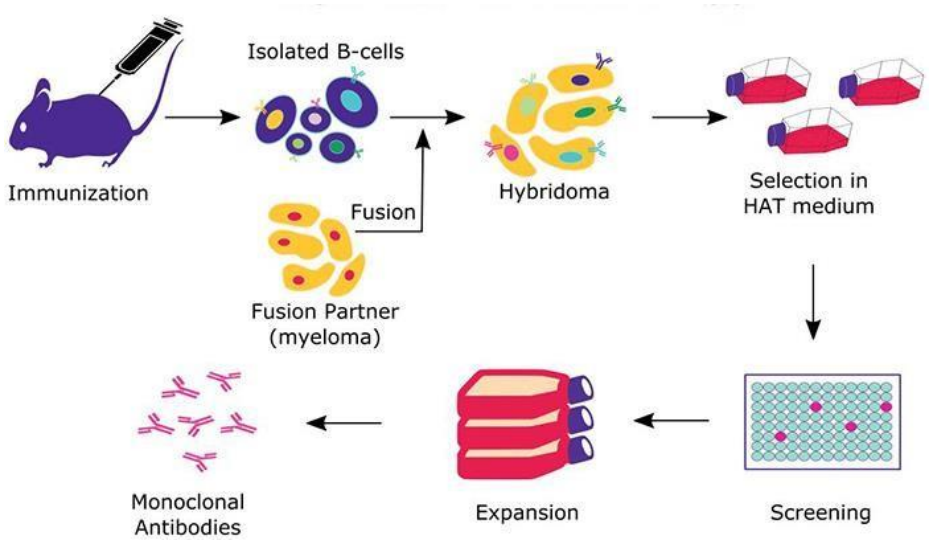

Figure 3. Hybridomatechnology.

Hybridomas are hybrid cells produced by the fusion of antibody-producing lymphocytes with myeloma cells.[20] Monoclonal antibodies are being used in clinical applications, e.g. OKT3 which is the first monoclonal antibody to be used for the prevention of acute rejection of organs. OKT3 binds and blocks the function of cell surface CD3 (Muromonab-CD3) in T cells. The mAbsare important diagnostic substances used in biomedical and microbiological research for the diagnosis of hepatitis, AIDS, influenza, herpes simplex, and for the treatment of infectious diseases and cancer.[21] Pregnancy tests based on selectively detect elevated levels of human chorionic gonadotropin (hCG) in urine or serum by using a combination of mouse monoclonal anti-hCG antibodies and goat polyclonal anti-hCG antibodies. The mAbs can detect unusual serum levels of a prostate-specific antigen, which provides an early warning of developed prostate cancer. The recombinant antibodies have been approved for therapeutic use and have been introduced into human medicine *e.g.*, Muromomab, Abciximab, Rituximab, Infliximab, Trastuzumab, Omalizumab, Efalizumab, Cetuximab, etc.[22] Antibodies can also be produced in transgenic plants by inserting foreign genes and the resulting mAbs are termed as plantibodies. Phage display and plantibody techniques arefor large-scale production of customized mAbs.

Vaccines Technology

Edward Jenner is well known for hisinnovative contribution to immunization and the ultimate eradication of smallpox. Eventually, the eradication of smallpox was one of the major successes of vaccine science. Scientists around the world have been working to develop the SARS-CoV-2 vaccine, the virus that caused the COVID-19 pandemic. The fast-tracked vaccine will likely be launched between the end of 2020 and the middle of 2021. Vaccination is a safe and efficient way to administrate a harmless form of a pathogen to induce a specific adaptive immune response that protects the individual against later exposure to the pathogen and it is the most effective method for disease prevention and control.[23]

Vaccines define as a preparation of immunogenic material used to induce immunity against pathogenic organisms. A vaccine contains the harmless or less harmful form of pathogen's antigens, e.g., the smallpox vaccine contains the antigens specific to smallpox. When a person is vaccinated against smallpox, the immune system responds by stimulating B-lymphocytes cells to produce smallpox antibodies. After vaccination against a pathogen, the body's immune system will be ready with active B-lymphocytes and antibodies to fight against the infection.[24] The advance of novel technologies such as genomics, proteomics, bioinformatics, and recombinant DNA technology are useful for the discovery of new vaccine antigens. The approaches used for vaccine development are based on an improved understanding of the microbial structure, physiology, epidemiology, virulence, host-pathogen interactions, and the scale of microbial intra- and interspecies diversity (Figure 4).[25]

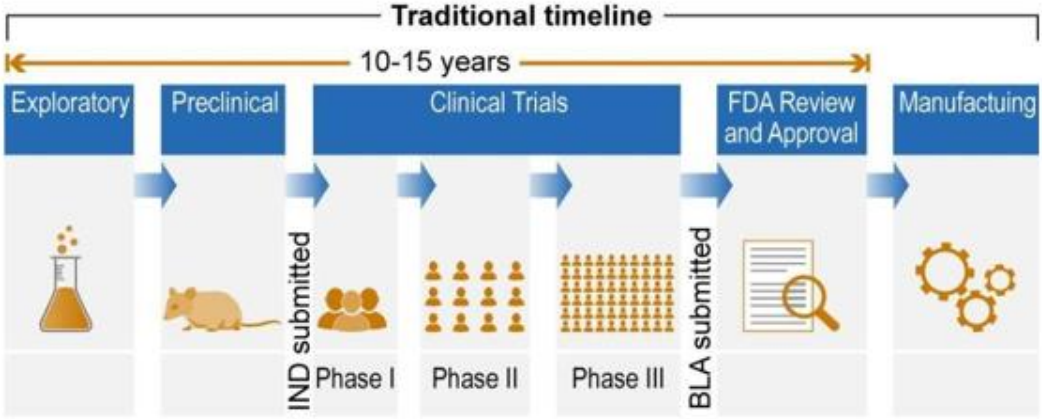

Figure 4. Phases of Vaccine Development.

Most current vaccines can target pathogens that have low antigenic variability and for which protection depends on antibody-mediated immunity. This is the case for tetanus, polio, measles, diphtheria, and hepatitis B.[26]

In Table 1, the vaccination schedule for Indian children according to the Universal Immunization Program (UIP) is explained.

Table 1. Vaccination Schedule for Indian Children's According to UIP

AGE	VACCINE
By birth	Bacillus Calmette – Guerin vaccine (BCG) Oral polio vaccine (OPV) Hepatitis B vaccine (Hep B)
6 Weeks	Diphtheria, Pertussis Tetanus vaccine (DPT) Hemophilus influenzae type B (HIB)vaccine Oral polio vaccine(OPV), Hepatitis B vaccine (Hep B)
10 Weeks	Diphtheria, Pertussis Tetanus vaccine (DPT) Hemophilus influenzae type B (HIB)vaccine Oral polio vaccine(OPV)/ Inactivated polio vaccine (IPV)
14 Weeks	Diphtheria, Pertussis Tetanus vaccine (DPT) Hemophilus influenzae type B (HIB) vaccine, Oral polio vaccine (OPV)
18 Weeks	Inactivated polio vaccine (IPV)
6 Months	Hepatitis B vaccine (Hep B)
9 Months	Measles

Conjugate vaccine is the combination of weak antigen with strong antigen for stronger immune response to the weak antigen e.g., the vaccine against Hemophilus influenzae type B (Hib) is a conjugate vaccine. DNA vaccines could be produced by using antigenic genes that code for the antigens of microbe in the host organism. Vaccines capable of generating neutralizing or opsonizing antibodies against these pathogens are successful.[27]

In Silico Drug Designing

The objective of the drug discovery process is to search for new drug molecules which can bind to a specific target known to be involved in causinga disease and change the target's function.[28] The drug discovery process involves the lead structure identification and is followed by the synthesis of its analogs, and their screening to get candidate molecules for drug development. Even though most traditional drug discovery processes depend on experimental tasks, *in silico* approaches are playing important roles in every stage of this drug discovery pipeline (Figure 5).[30]

Figure 5. *In Silico* Drug Discovery Process.[30]

In silico techniques significantly contribute to the early drug development process and are an important in target and lead discovery.[29] *In silico* drug, designing methods are limiting the use of animal models in pharmacological research, for rational designing of novel and safe drug candidates.[30]

Human Genome Project

The Human Genome Project (HGP) was a multinational collaborative project to determine the sequence of all the genes and map the genome of humans.[31] The estimated budget of $3 billion for the HGP was funded by the United States-National Institutes of Health (NIH) and the Department of Energy (DOE). The project started in 1990 and the International Human Genome Sequencing Consortium published the first draft of the human genome in Nature journal (February 2001).[32]

The main object of the HGP was to provide acomplete and accurate sequence of the 3 billion DNA base pairs that make up the human genome and to find all the estimated 20,000 to 25,000 human genes. The project also aimed to sequence the genomes of several other organisms that are important to medical research, such as the mouse and the fruit fly. The primary method used by the HGP to produce the finished version of the human genetic code is map-based, or "Bacterial Artificial Chromosome" (BAC) based sequencing.

Just about 2% of genes of the human genome encode proteins, and at least 50% of the genomes do not code for proteins termed as "junk DNA" [33]. The initial draft of the rat genome sequence was published in November 2002. The 3 million human genetic variations have been identified as Single Nucleotide Polymorphisms (SNPs); and the generation of complementary DNAs (cDNAs) for more than 70% of known human and mouse genes. Improved knowledge on the genetic basis of diseases provides availability of DNA-based diagnostic methods for neurodegenerative diseases

e.g., Alzheimer's disease, Parkinson's disease, multiple sclerosis, cancers, and hypertension.[34]

RNA Interference

The dsRNA-mediated interference (RNAi) is a natural post-transcriptional mechanism of gene silencing expression in a range of organisms. Gene silencing is a function of RNA degradation into short RNAs that activate ribonucleases to attack homologous mRNA.[35] RNAi works on cells of organisms ranging from flies, nematodes, plants, and mammals, showing its fundamental significance in the selective suppression of protein translation by targeted mRNA encoding degradation. RNAi is considered an essential tool not only for functional genomics but also for gene-specific therapeutic activities that target the mRNAs of disease-related genes, due to its exquisite specificity and efficacy.

In various fields of genetics and genetic engineering, RNAi technology has been used, especially in the engineering of food plants that produce lower levels of natural toxins.[36] The RNAi modification targets the genes involved in pathogenicity, the genes necessary for the survival and metabolism of the pathogen, or the genes associated with the immune and toxicity response of the pathogen, aimed at silencing the particular gene that produces resistance to diseases and pathogens. The therapeutic ability of RNAiis to treat viral infections, cancer tumors, neurodegenerative diseases, renal disorders, etc.[37]

Viral infections can be treated by using RNAi-based therapies by reducing the activity of key viral genes. Cancer is caused by over-excited genes in the cells and retarding their activities could stop the disease progression. RNAi-based therapies stopped the growth of HIV, hepatitis C, polio, and other viruses in human cell culture during clinical trial stages.[38] RNAi-based delivery methods include Liposomal Nanoparticles (LNPs), conjugates, and viral vectors. Synthetic dsRNA is delivered by nanoparticles, while viral vectors deliver a transcriptional template to the nucleus.

Nonspecifically cellular uptake occurs by receptor-mediated endocytosis. Nanoparticles deliver the RNAi trigger to the cytoplasm of the cell. The trigger enters the RNAi pathway at the dicer processing or RNA-induced silencing complex stage. Transcriptional templates generate hairpin RNAs that enter the pathway at an earlier nuclear stage (Figure 6). Finally, an active RISC complex is formed that cleaves the mRNA target. The increased acceptance of gene editing, rapidly expands clinical acceptance of RNAi-based drug delivery for targeting cells and tissues.[39]

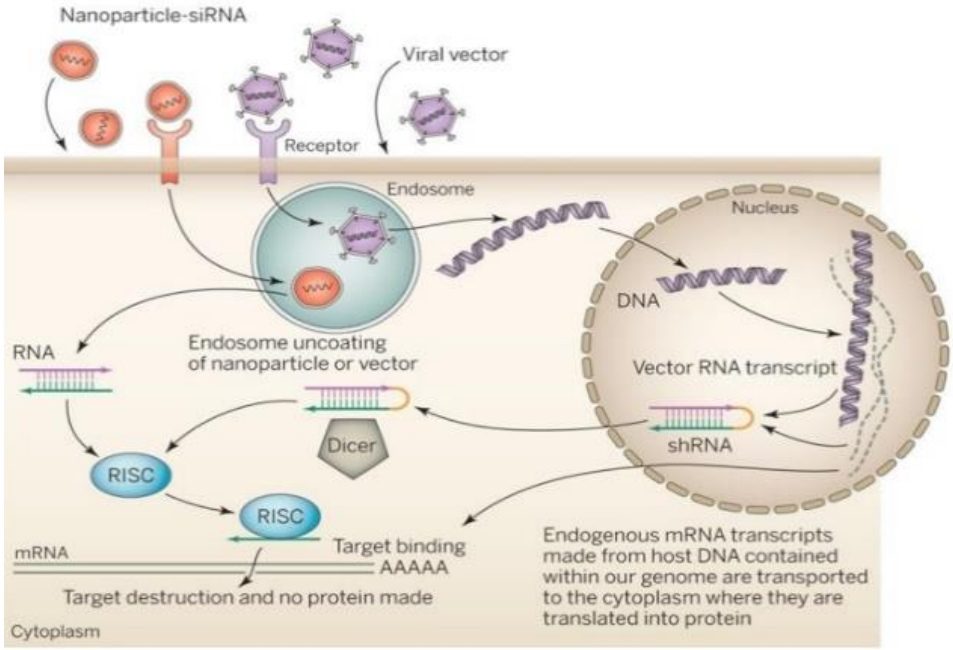

Figure 6. RNAi is the Drug: RNAi delivery approaches include conjugates, liposomal nanoparticles (LNPs), and viral vectors.[39]

Nano-Biotechnology and Nano-Medicine

Nanomaterial refers to a natural, or manufactured material including particles, either in an unbound state or as aggregate wherein external dimensions are in the size range of 1-100 nm for ≥50% of the particles.[40] Nano-biotechnology uses the principles and techniques

of nanomaterials in a biological system to manipulate physical and chemical properties at molecular, genetic, and cellular process levels to develop products and services that are used in various fields from medicine to agriculture.[41] Applications of nanotechnology in medicine involve employing nanoparticles to deliver drugs and engineering particles to be used for diagnosis and treatment of diseases or injuries.[42]

According to the NIH, the applications of nanotechnology for diagnosis, prognosis, monitoring, control, prevention, and treatment of diseases is termed nanomedicine.[43] These involve the identification of precise targets as cells and receptors, related to specific medical conditions and choice of the appropriate nanocarriers for delivery of pharmaceutical, therapeutic, and diagnostic agents to achieve the required responses with minimum side effects. Nanomedicine's main targets are mononuclear phagocytes, dendritic cells, endothelial cells, and cancer cells.[44]

Nanomedicine makes use of nanostructures for applications in different areas of medicine, including biosensors, drug delivery, neuro-electronic interfaces, *in vivo* imaging, and cell-specific molecular interactions. The nanoparticulate drug delivery systems can alter the biodistribution and pharmacokinetics of drugs.[45]

Stem Cell Therapy

Stem cells are undifferentiated cells that can differentiate into specific cell types. The two main characteristics of stem cells are perpetual self-renewal and the ability to differentiate into a specialized adult cell type [46]. The field of stem cell research was established by Ernest McCulloch and James Till (1960). There are two major classes of mammalian stem cells: embryonic stem cells that are isolated from the inner cell mass of blastocysts, and adult stem cells that are found in adult tissues. The embryonic stem cells are pluripotent and can differentiate into any cell in the adult body. The adult stem cells are multipotent and differentiate into the limited population of cells that act as a repair system for the body by maintaining the normal turnover of regenerative organs.[47]

Stem cell therapy is a potentially emerging field to treat disease and injury, and it recently progressed from preclinical to the early clinical trial of a variety of diseases.[48] Stem cell therapy is used for the repair of damaged and diseased tissue with healthy cells provided by stem cell transplant.[49] Under the specific conditions of animal tissue culture, stem cells have the potential to differentiate into heart cells, skin cells, nerve cells, muscles, etc.[50,51]

The embryonic stem cells can be used for disease treatment including leukemia, paralysis, Alzheimer's, Parkinson's, Huntington's, cardiac tissue damage, etc.[52] The adult stem cells are used for the treatment of cancer[53] and are able to repair muscle damaged after heart attacks. The advancement in embryonic stem cells could be used to overcome many of the technical barriers for successful therapeutic gene transfer and clinical success of cell-based gene therapy.[54]

Metamaterials

Metamaterials are complex materials with an artificial structure which have special modified electric features. These features attract many scientists to use metamaterial structure in many medical research areas.[55] The metamaterials can enhance the properties of microwave and optical passive and active components and exceed some performance of devices used in technical equipment. Examples of technical fields which can improve electrical engineeringare micro-and nano-technology, microwave engineering, optics, optoelectronics, semiconductor technologies, and biomedical engineering.[56]

In plasmonic, the interplay between propagating electromagnetic waves and free-electron oscillations in materials are exploited to generate new features and applications. Biomedical scientists use these novel materials in much-advanced equipment and their electromagnetic application in medicine. Some of the applications of metamaterials in medicine are described as cancer detection, medical imaging wireless strain sensing, lens radar absorbing materials, etc.[57] Metamaterials refer to important artificial composite materials in which small artificial elements, through their collective interaction and applications, create a desired and unexpected macroscopic property and response that is not present in conventional materials.[58]

The terahertz electromagnetic frequency region of the electromagnetic spectrum plays an important role in biomedical imaging because biomolecules are very sensitive to vibrational modes for this frequency range. Advantages in broadband terahertz pictures have been rising in biomedical spectroscopy science. Biomedical imaging technology is used to discriminate in the infected e.g., cancer, and the non-infected tissue,[59] which requires broad frequency band and highly

efficient Radar Absorbing Material (RAM) system designs to obtain high-resolution image and study of the tissue.[60]

Conclusion

Biotechnology is defined as the application of scientific and engineering principles to process material to provide goods and services. Its interdisciplinary area of study is to serve mankind. Medical biotechnology is the use of living cells and cell materials to research and produce pharmaceutical and diagnostic products that help treat and prevent human diseases (e.g., cancer, autoimmune disease, and infectious diseases such as tuberculosis, malaria, and AIDS, etc.). In this study various applications of medical biotechnology have been discussed e.g., gene therapy, monoclonal antibodies (hybridoma technology), vaccine technology, recombinant DNA technology, HGP, *in silico* drug designing, RNA-mediated interference (RNAi), nanomedicine, stem cell therapy, and medical metamaterials.

References

1. Gupta V, Sengupta M, Prakash J, Tripathy, BC. An Introduction to Biotechnology. Basic and App Aspects of Biotech. 2017; Singapore. doi:0.1007/978-981-10-0875-71
2. Young FE. Biotechnology: the view from the FDA. Health Matrix. 1986;4(3):10-15.
3. Rezaei M, Zarkesh-Esfahani SH. Optimization of production of recombinant human growth hormone in *Escherichia coli*. J Res Med Sci. 2012;17(7):681-5.
4. HsinIS, Chi-Jung W, Yi-FangT, Chia-Yu C. Fighting COVID-19: A quick review of diagnoses, therapies, and vaccines. Biomedical J. 2020;43(4):341-54.
5. Portin P. The birth and development of the DNA theory of inheritance: sixty years since the discovery of the structure of DNA. J Genet. 2014;93:293-302. doi:10.1007/s12041-014-0337-4
6. Johnson IS. Human insulin from recombinant DNA technology. Science. 1983;219(4585):632-7. doi:10.1126/science.6337396
7. Khan S, Ullah MW, Siddique R, Nabi G, Manan S, Yousaf M, et al. Role of recombinant DNA technology to improve life. Int J of Genomics. 2016;2016:2405954. doi:10.1155/2016/2405954
8. Drews J. Strategic trends in the drug industry. Drug Discov Today. 2003;8(9):411-20. doi:10.1016/S1359-6446(03)02690-4
9. Knowles J, Gromo G. Target selection in drug discovery. Nat Rev Drug Discov. 2003;2(1):63-9. doi:10.1038/nrd986
10. Castle AL, Carver MP, Mendrick DL. Toxicogenomics: a new revolution in drug safety. Drug Discov Today. 2002;7(13):728-36. doi:10.1016/S1359-6446(02)02327-9
11. Vajo Z, Fawcett J, Duckworth WC. Recombinant DNA technology in the treatment of diabetes: insulin analogs. Endocr Rev. 2001;22(5):706-17. doi:10.1210/edrv.22.5.0442
12. Shastry BS. Pharmacogenetics and the concept of individualized medicine. Pharmacogenomics J. 2006;6(1):16-21. doi:10.1038/sj.tpj.6500338
13. Gonsalves GA, Paiva RD. Gene therapy: advances, challenges and perspectives. Einstein (Sao Paulo). 2017;15:369-75. doi:10.1590/S1679-45082017RB4024
14. Misra S. Human gene therapy: a brief overview of the genetic revolution. J Assoc Physicians India. 2013;61(2):127-33.
15. Kardia SL, Modell SM, Peyser PA. Family-centered approaches to understanding and preventing coronary heart disease. Am J Prev Med. 2003;24(2):143-51. doi:10.1016/S0749-3797(02)00587-1
16. Gardlik R, Palffy R, Hodosy J, Lukacs J, Turna J, Celec P. Vectors and delivery systems in gene therapy. Med Sci Monit. 2005;11(4):RA110-21.
17. O'Malley BW, Ledley FD. Somatic gene therapy: methods for the present and future. Arch Otolaryngol Head Neck Surg. 1993;119(10):1100-7. doi:10.1001/archotol.1993.01880220044007
18. Li J, Zhu Z. Research and development of next generation of antibody-based therapeutics. Acta Pharmacol Sin. 2010;31(9):1198-207. doi:10.1038/aps.2010.120
19. Little M, Kipriyanov SM, Le Gall F, Moldenhauer G. Of mice and men: hybridoma and recombinant antibodies. Immunol Today. 2000;21(8):364-70. doi:10.1016/S0167-5699(00)01668-6
20. Kuhler G, Milstein C. Continuous cultures of fused cells secreting antibody of predefined specificity. Nature. 1975;256(5517):495-7. doi:10.1038/256495a0
21. Teicher BA, Chari RV. Antibody conjugate therapeutics: challenges and potential. Clin C Res. 2011;17(20):6389-97. doi:10.1158/1078-0432.CCR-11-1417
22. Chames P, Van Regenmortel M, Weiss E, Baty D. Therapeutic antibodies: successes, limitations and hopes for the future. Br J Pharmacol. 2009;157(2):220-33. doi:10.1111/j.1476-5381.2009.00190.x
23. Riedel S. Edward Jenner and the history of smallpox and vaccination. Baylor University Medical Center Proceedings. 2005;18(1):21-25.
24. Paoletti LC, Rench MA, Kasper DL, Molrine D, Ambrosino D, Baker CJ. Effects of alum adjuvant or a booster dose on immunogenicity during clinical trials of group B streptococcal type III conjugate vaccines. Infect Immun. 2001;69(11):6696-701. doi:10.1128/IAI.69.11.6696-6701.2001
25. Rinaudo CD, Telford JL, Rappuoli R, Seib KL. Vaccinology in the genome era. J Clin Invest. 2009;119(9):2515-25. doi:10.1172/JCI38330
26. Dhouib W, Kacem M, Bennasrallah C, Fredj MB, Abroug H, Zemni I, et al. Hepatitis B birth vaccination, cohort study, Tunisia 2000–2017. Libyan J Med. 2020;15(1):1809223. doi:10.1080/19932820.2020.1809223
27. Nascimento IP, Leite L. Recombinant vaccines and the development of new vaccine strategies. Braz J Med Biol Res. 2012;45:1102-11. doi:10.1590/S0100-879X2012007500142
28. Khan MS, Baig MH, Ahmad S, Siddiqui SA, Srivastava AK, Srinivasan KV, et al. Design, synthesis, evaluation and thermodynamics of 1-substituted pyridylimidazo [1, 5-a] pyridine derivatives as cysteine protease inhibitors. PloS One. 2013;8(8):e69982. doi:10.1371/journal.pone.0069982
29. Baig MH, Ahmad K, Adil M, Khan ZA, Khan MI, Lohani M. Drug Discovery and *In Silico* Techniques: A Mini-Review. Enz Eng. 2014;4:123. doi:10.4172/2329-6674.1000123
30. Brogi S, Ramalho TC, Kuca K, Medina-Franco JL, Valko M. In silico methods for drug design and discovery. Front Chem. 2020;8:612. doi:10.3389/fchem.2020.00612
31. Hood L, Rowen L. The human genome project: big science transforms biology and medicine. Genome Med. 2013;5(9):79. doi:10.1186/gm483
32. Lander ES, Linton LM, Birren B, Nusbaum C, Zody MC, Baldwin J, et al. Initial sequencing and analysis of the human genome. Nature. 2001;409:860-921. doi:10.1038/35057062
33. Qin S, Zhou Y, Lok AS, Tsodikov A, Yan X, Gray L, et al. SRM targeted proteomics in search for biomarkers of HCV-induced progression of fibrosis to cirrhosis in HALT-C patients. Proteomics. 2012;12(8):1244-52. doi:10.1002/pmic.201100601
34. Dulbecco R. A turning point in cancer research: sequencing the human genome. Science. 1986;231(4742):1055-6. doi:10.1126/science.3945817
35. Agrawal N, Dasaradhi PV, Mohmmed A, Malhotra P, Bhatnagar RK, Mukherjee SK. RNA interference: biology, mechanism, and applications. Microbiol Mol Biol Rev. 2003;67(4):657-85. doi:10.1128/MMBR.67.4.657-685.2003
36. Bernstein E, Caudy AA, Hammond SM, Hannon GJ. Role for a bidentate ribonuclease in the initiation step of RNA interference. Nature. 2001;409(6818):363-6. doi:10.1038/35053110
37. Xu W, Jiang X, Huang L. RNA interference technology.

Comprehensive Biotechnology. 2019:560-75. doi:10.1016/B978-0-444-64046-8.00282-2
38. McManus MT, Sharp PA. Gene silencing in mammals by small interfering RNAs. Nature Rev Genet. 2002;3(10):737-47. doi:10.1038/nrg908
39. Haussecker D, Kay MA. Drugging RNAi. Science. 2015;347(6226):1069-70. doi:10.1126/science.1252967
40. Soares S, Sousa J, Pais A, Vitorino C. Nanomedicine: principles, properties, and regulatory issues. Front Chem. 2018;6:360. doi:10.3389/fchem.2018.00360
41. Fakruddin M, Hossain Z, Afroz H. Prospects and applications of nanobiotechnology: a medical perspective. J Nanobiotechnol. 2012;10(1):31. doi:10.1186/1477-3155-10-31
42. Vasir JK, Labhasetwar V. Targeted drug delivery in cancer therapy. Technol Cancer Res Treat. 2005;4(4):363-74. doi:10.1177/153303460500400405
43. Tinkle S, McNeil SE, Muhlebach S, Bawa R, Borchard G, Barenholz Y, et al. Nanomedicines: addressing the scientific and regulatory gap. Ann N Y Acad Sci. 2014;1313(1):35-56. doi:10.1111/nyas.12403
44. Moghimi SM, Hunter AC, Murray JC. Nanomedicine: current status and future prospects. FASEB J. 2005;19(3):311-30. doi:10.1096/fj.04-2747rev
45. Saidi T, Fortuin J, Douglas TS. Nanomedicine for drug delivery in South Africa: a protocol for systematic review. Syst Rev. 2018;7:154. doi:10.1186/s13643-018-0823-5
46. Biehl JK, Russell B. Introduction to stem cell therapy. J Cardiovasc Nurs. 2009;24(2):98-105. doi:10.1097/JCN.0b013e318197a6a5
47. Molofsky AV, Pardal R, Morrison SJ. Diverse mechanisms regulate stem cell self-renewal. Curr Opin Cell Biol. 2004;16(6):700-7. doi:10.1016/j.ceb.2004.09.004
48. Nadig RR. Stem cell therapy–Hype or hope? A review. J Conserv Dent. 2009;12(4):131-8. doi:10.4103/0972-0707.58329
49. Evans MJ, Kaufman MH. Establishment in culture of pluripotential cells from mouse embryos. Nature. 1981;292(5819):154-6. doi:10.1038/292154a0
50. Keller GM. In vitro differentiation of embryonic stem cells. Curr Opin Cell Biol. 1995;7(6):862-9. doi:10.1016/0955-0674(95)80071-9
51. Fortier LA. Stem cells: classifications, controversies, and clinical applications. Vet Surg. 2005;34(5):415-23. doi:10.1111/j.1532-950X.2005.00063.x
52. Barker RA, Jain M, Armstrong RJ, Caldwell MA. Stem cells and neurological disease. J Neurol Neurosurg Psychiatry. 2003;74(5):553-7. doi:10.1136/jnnp.74.5.553
53. Keller GM. *In vitro* differentiation of embryonic stem cells. Curr Opin Cell Biol. 1995;7(6):862-9. doi:10.1016/0955-0674(95)80071-9
54. Iohara K, Nakashima M, Ito M, Ishikawa M, Nakasima A, Akamine A. Dentin regeneration by dental pulp stem cell therapy with recombinant human bone morphogenetic protein 2. J Dent Res. 2004;83(8):590-5. doi:10.1177/154405910408300802
55. Gerrits T. Social and cultural aspects of infertility in Mozambique. Patient Educ Couns. 1997;31(1):39-48. doi:10.1016/S0738-3991(97)01018-5
56. Sundby J. Infertility in the Gambia: traditional and modern health care. Patient Educ Couns. 1997;31(1):29-37. doi:10.1016/S0738-3991(97)01006-9
57. Van Balen F, Gerrits T. Quality of infertility care in poor-resource areas and the introduction of new reproductive technologies. Hum Reprod. 2001;16(2):215-9. doi:10.1093/humrep/16.2.215
58. Ombelet W, Cooke I, Dyer S, Serour G, Devroey P. Infertility and the provision of infertility medical services in developing countries. Hum Reprod Update. 2008;14(6):605-21. doi:10.1093/humupd/dmn042
59. Choudhury B, Reddy PV, Bisoyi S, Jha RM. Soft computing for terahertz metamaterial absorber design for biomedical application. Computers, Materials and Continua. 2013;37(3):135-46. doi:10.3970/cmc.2013.037.135
60. Toner JP. Progress we can be proud of: US trends in assisted reproduction over the first 20 years. Fertil Steril. 2002;78(5):943-50. doi:10.1016/S0015-0282(02)04197-3