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Biotechnological Innovations and their Impact on Modern Medicine

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Annotation: As evidenced by the enormous and rapid growth of industrial and governmental investment in the area of biotechnology over the past decade, it is of little surprise that the application of biotechnologies to modern medicine by the pharmaceutical industry has been immense. The fostering of pharmaceutical biotechnology over the past two decades has gained worldwide acceptance as a means to produce novel, safe, and effective diagnostic tools and drugs. A successful drug development project can take up to 15 years and incur a financial cost on the order of $1.7 billion. Pharmaceuticals continue to be the third highest health-care cost in the United States of America. The development of entirely new drug delivery systems, vaccines, medical imaging agents, and techniques of genetic treatment are the subject of attempts at researching biotechnological solutions. However, the biopharmaceutical revolution of the 20th century, with the approval of more than 300 recombinant dan and peptide products, is likely to make a lasting impact on medical treatment for generations to come. It is also expected that treatments through gene and therapeutic stem cells will have a significant impact on modern medicine. While treating patients on an individual basis with genetically tailored medical care is still well beyond current technology, personalized medicine has started to move away from a “one size fits all” approach to a treatment course that is very much

individualized. The achievement of a pharmacogenomic goal will represent a potential enabling tool for advances towards personalized medicine. In addition, other biologically related techniques, such as nanotech, medical robotics, tissue engineering, and regenerative medicine, bioprinting, synthetic biology, and computer-assisted biotechnology design, to name just a few, are the sources of relentless development into modern medicine. Growingly sophisticated modern technology devices have led to the development of a range of medical techniques, such as MRI, used in the prediction, diagnosis, and monitoring of a wide variety of diseases. Due to transplants of organs, mechanical devices, and regenerative medicine approaches, the dramatic increase in life expectancy and the fight against diseases that were previously incurable are examples of improvement in patient health. Advanced biotechnology research methodology has contributed to the knowledge of human disease processes and led to the development of innovative biotechnologies that have previously been utilized for the study of disease. This innovative technical field encompasses recursive acronomic investigations, proteomics, bioinformatics, microarrays, gene therapy, recombinant immunotherapies, and RNAi technologies for use in genetic, protein and metabolite studies within cells, tissue, and assorted body fluids.

Keywords: biotechnology, modern medicine, gene editing, regenerative medicine, personalized healthcare, nanotechnology, biopharmaceuticals.

1. Introduction to Biotechnological Innovations

Biotechnology is a diverse field, involving the use of living cells or molecules, which have been recumbent for applications oriented toward the human welfare, as the demand on individuals to enlighten life further and cure the complex diseases remains constant and grows. The products of biotechnologies have a major impact on many facets of our lives, and it has wide range of uses and has been termed the “technology of hope” that there should have a major impact in the future on human health as well as the well-being of the other life forms and further on the environment. While it is understood how profound it has revolutionized diagnostics and therapeutics and given rise to the burgeoning biopharmaceutical industry, the major challenges to human beings over the last three decades have been posed by the deadly virus infections, mainly of the human immunodeficiency virus (HIV) and hepatitis C virus (HCV) and the discovery of new viral pathogens of global concern continues. The world has now recognized the Ebola virus that has escaped from the remote foci in Africa and caused the large-scale outbreaks recently. Furthermore, in recent years the concept of personalized medicine has been increasingly

recognized in the healthcare system, particularly in making the choice of the most effective pharmacotherapy for the individual patient. For example, the US department of Food and Drugs Administration (FDA) has amended minute regulations, providing for the accelerated drug approval if they are necessary for targeted therapy on the basis of genomic data [1]. While biotechnology has impacted greatly the economy, it has further opened the new avenues for the environmental improvement, the public being highly concerned about the toxic compounds of natural, agricultural and especially industrial origin that have accumulated in biosphere in the past several decades. Industrialization and urbanization have given rise to environmental pollution prevailing in the quality of air, water and soil. Yet another hazard is the recent discovery of the extremely alarming rate of the large-scale disappearance of bees aggressive pollination [2]. Substantial progress has been made in the comprehension of phagocytosis, regarding the entry of the pathogen into macrophages, and many other fundamental processes implicated in the infection carried out by the deadly microorganisms mentioned above. Major novel targets for the broad-speculative anti-infection agents have been identified, regarding host components, which block, in principle, the infection process. Meanwhile, research of the lethal factors secreted by the pathogen representing the potential molecular target of the highly effective anti-infection agents, including chemical compounds and biopharmaceutical preparations is carrying out. However, the dazzling achievements in the pharmaceutical biotechnology sectors, which have concrete, applied aspects, disclose only the tip of the iceberg, as space limitations do not permit reviewing other findings and ideas.

1.1. Definition and Scope of Biotechnology

Biotechnology is one of the relatively new classical branches of life sciences. It typically deals with the study of protozoa, fungi, bacteria, virus, and biotechnological innovations as well as genetically engineered plants and animals. With the discovery of the DNA recombinant in 1973, it became possible for the first time molecular techniques to manipulate genes with precision predetermination. The DNA recombination technology is marked by the walking of the human genome that culminated in the sequencing of the entire human genome at the beginning of the Twenty-First century. It changed the way of studying and analyzing genetic material. It was just a beginning and laid the foundation of the developing bioinformatics, nanomedicine, and individualized therapy in medicine, biotechnology, pharmaceutics, and veterinary science. With the advent of recombinant DNA technology, unicellular organism was genetically engineered to produce substances having medical importance in human therapy . A paradigm change occurred in medicine with the entry of genetically engineered biopharmaceuticals in 1982. Genetic engineering in biotechnology has revolutionized the concept of drugs/therapeutics. Before 1982, most medical drugs must be obtained from bulk tissues. It was not only very costly but also chances of impurities, side effect and infections were associated with it. Then in 1982, they started producing medical biochemical by genetic engineering. These drugs are less costly, effective with rare side effect; purity is almost cent percent. Strictly speaking, more than 90% of these biopharmaceuticals have exactly the same amino acid sequence as their native compound. Analogous to this, Interferon and Insulin were the first genetically engineered biochemical to reach the market. Since then, more than 1,000 different biopharmaceuticals have been produced and many more are under various stages of clinical trial. Hormone menopausal therapy is used to decrease the hot flush and nausea feeling in female pigs and cats. In the near future, genetically engineered pigs may release a high quantity of estrogen hormone (estradiol 17β- E2) present in the urine having desired medical orientation directly to the human population. For the treatment of syphilitic diseases "Salvarsan" and "Dithiarsan" were used, but these arsenic compounds are highly toxic and caused several deaths. Penicillin discovered during 1928 had greatly reduced the infection of wounded soldiers in World War II. After penicillin was used, the death rate of wounded soldiers decreased drastically. Broadly speaking, every field is linked with the biotechnology to some extent, directly or indirectly. But the modern biotechnological approaches have no existence or roles before 1965. The ongoing biotechnological revolutions are as back to

Nils Bohlin (1920-1981), a Swedish scientist who invented the three-point safety belt in 1958 for which he did not require the patent. Before this invention, the open system does not have any seat belt. Its no doubt save the millions of the human population from road accidents, and then onward, up to 1965 several safety belts were installed in cars (altogether now humanity is expecting biotechnology will answer all needs of the human society). [3][4][5]

2. Historical Development of Biotechnological Innovations

After millennia of contributing to our daily lives with essentials such as bread, beer, and wine, microorganisms took on an extraordinary technological significance in the middle of the 20th century. Since then, the technological application of microorganisms (and/or their derived naturally cultivated metabolic activities), known as microbial biotechnology, has been a critical factor in producing a myriad of vital natural bioactive compounds of universal interest, including the well-known antibiotics, antifungals, anti-tumour agents etc., as well as industrially relevant vitamins, amino acids, solvents, enzymes, and food products, using an exponentially expanding biotechnological armamentarium [6].

Since then, it has had diverse degrees of legal and moral reflection on its implications, such as those resulting from the fact that in the United States of America, in 1980, for the first time in History, the US Supreme Court allowed life to be patented, following the invention of a genetically engineered bacterium capable of breaking down oil slicks. But it was a decade of intense work in several world laboratories that were significantly impronted to the exteriorization of the central message, of the new teaching, especially in the field of molecular biology, also stimulated by conjunctural excitation, within of American official biomedicine itself and even more of Soft-Images - coded by a cinema of distraction and flourishing female liberation, diffusive signs of and concomitant transformations of strong historical contours, with "retro-food" effects, of a kind of psychopathic sclerosis in present day Portuguese spiritual life. The part of the central message corresponding to the interpretation of the genetic code and that invoked the future ability to spell out every nucleotide of any DNA molecule were the most requested, emerging from the instrumentation then ready, which also had to be explained. The couple of geneticists and molecular biologists Jim Watson and Francis Crick entered history as one of the scientifically-based legends of the 20th century with the announcement of the elucidation of the genetic code, thus deciphering the secret of life and faceting an unparalleled and seminal innovative impetus, contributing to the unblocking of the application of recombinant DNA technology.

2.1. Key Milestones in Biotechnology

After the concept of DNA structure was discovered, molecular biology transformed completely by the development of recombinant DNA technology, which enables the transfer of genetic material between distantly related organisms leading to a new field of biotechnology. The key processes that genetically modified organisms carry out are identification of suitable genetic vector and DNA fragments, the cloning of donor DNA from an organism, and the insertion of the cloned DNA into a host organism. Once recombinant organism expresses gene product, it can be harvested for protein products [2]. DNA analysis and sequencing were introduced by the Human Genome Project, which became possible only after the development of recombinant technology, thus allowing more rapid identification and cloning of the disease-related gene. The technologies have become the foundation for the development of other technologies, e.g., bioinformatics, nanomedicine, and individualized therapy by genetic profiling. Many multicellular organisms have been genetically engineered to become mini-factories for substances medically useful to humans. Since the inception of recombinant DNA technology, many revolutionary advancements have taken place. As a consequence, it is now possible to genetically engineer bacteria, yeast, plants, animals, or their cells in culture to produce a wide variety of substances that are either naturally produced or now a gene has been cloned and introduced into a different organism. All these processes can be performed under rigorous

conditions in which the identity of all the genes is clearly established as is the fact that they are free of known hazardous properties. [7][8][9]

3. Biotechnological Tools and Techniques

Microbial biotechnology and genetic engineering have come to play a central role. Pharmaceutical biotechnology techniques are largely based on microbial growth of recombinant genetic structures, as well as the use of adequate conditions which allow the production and extraction of the bioactive necessary compound. Besides, the products and processes developed thereby are implemented on a large scale and are integral to economically viable and sustainable activities. Biotechnological tools and techniques are important in genetic engineering and industrial microbiology, such as mutant selection, protein engineering, recombinant DNA technology, and metabolic engineering. While genetic and metabolic engineers create and/or optimize biological machines using living organisms, microorganisms are the main agents acting in industrial biorefineries, as far as these permit controlled growth on renewable resources in an aerobic environment. On the other hand, complex biotechnological ecosystems have been developed, such as those involving plants in photosynthesis and organic matter degradation in soil, or those comprising both bacteria and fungi in the production of enriched compost. These activities are also of great interest in analyzing and improving bioremediation processes. In order to drive these biotechnological ventures, an important array of tools and techniques have been developed, which range from basic activities such as mutant selection and improved gene transfer methods, to the employment of advanced analytical technologies enabling large-scale genome reduction and reconstruction capabilities. While adaptable to different organisms and settings, the availability of these tools has brought about the development of a number of "-omics" approaches that are discipline-specific and are implemented in order to capitalize on these biotechnological initiatives. Despite the increased understanding these high-throughput methods have brought about microbial cell factories, combined with more recent systems and synthetic biology endeavours, microbial biotechnology-related platforms are still greatly underexploited. An attempt to review the state of the art is presented with this study, expecting to offer a general overview of the developments according to this context. [10][11][12]

3.1. Gene Editing Technologies

A profound revolution and innovation have been driven by gene-editing technologies in agriculture, medicine, biotechnology, and the manufacturing industry. In the past decade, with the discovery and improvement of diverse gene-editing platforms, there has been one innovation after another. Thanks to them, gene editing has currently reached various facets of the human genome. The profound mechanisms involved in the treatment of numerous diseases have been decoded, paving the way for the development of new generation treatments. This review touches on the confluence of the field and medical discovery enhancements, research of gene-editing technologies, and a clear area of change.

Recently, gene editing has become headline news due to the birth of the first genetically edited human babies. This achievement may open the door to a world free of genetic disorders and abundant with individuals possessing desirable traits. The CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)-Cas (CRISPR-associated) system was adapted from the prokaryotes to function as an adaptive immune defence mechanism against pathogens. CRISPR-Cas systems are found in archaea and bacteria and protect the host from foreign mobile genetic elements, such as plasmids and phages, and from specific re-encounters; digestion occurs upon recognition of foreign heterologous nucleotides with a PAM (Protospacer Adjacent Motif) sequence. Variations in the CRISPR-Cas system have led to their classification into two classes with six types and 33 subtypes. However, most class 2 type II CRISPR-Cas systems, in which the single enzyme Cas9 is guided by a mature CRISPR RNA (crRNA) and a trans-activating crRNA (tracrRNA) to cause sequence-specific DNA cleavage at a complementary site, are focused on and used for therapeutic purpose. This process can serve as a protection device for

eukaryotic transgenic material so that patented genes remain proprietary. The recently discovered Cas12a (Cpf1) and Cas12b orthologues have been re-engineered to act like previously known Cas9 nucleases and were described also as new diagnostic tools, SHERLOCK and DETECTR, because they were repurposed after first-to-second ssDNA detection also to detect stable and unstable RNAs, respectively. Although gRNA highlander (crRNA fused with tracrRNA, necessary for Cas9 cleavage) is relatively long, the small size of the complementary sequence allows the designing of their new versions within other CRISPR effectors. These Cas9 variants, e.g. CasXS and CasY proteins, have been engineered to target DNA with a programmable PAM and protospacer recognition. Cas13 family proteins naturally targeting RNA have also been adapted for therapeutics and beyond. DPAS can allow for programmable thermostable CRISPR response inhibition for antimicrobial treatment.

Broad development in the medical applications of gene-editing technologies has been driven by accomplishments in a better acquaintance of their mechanism and improvement and adjusting the systems for precise human applications. This new comprehensive advancement means that the gene editing technology is universally more accessible and, hence, greater exertion is necessary to assess the details of in-vivo applications. Narrow insight is required to manage and connection the information between clinical judgments and the laboratory application of gene-editing therapies [13]. The common developments in genome-editing technologies and the first human trials using the modified cells are now in clinical testing in the collaborative growth of gene-editing technology examination and limitations. The goals for future development research in the implementation of gene-edited cells or in-vivo editing in human trials including facility description details or IND for investigational new biotherapeutic products offer a basic scientific analysis data stepping promoting cell-based and in-vivo based gene-editing technologies and the variables involved in making predictions about the human response to genome-edited organisms proficient in self and in-vivo approaches. [14][15][16]

4. Biotechnological Applications in Medicine

The application of biotechnological tools in medicine is called medical or health biotechnology. Medical biotechnology has alleviated the sufferings of mankind through the development of various treatments and cures. Some biotechnology products in medicine contain live materials and necessitate the reconstitution of the medication immediately before it is used.

The randomized-controlled double-blind trial, a cornerstone of the current modern medical-industrial complex, has its roots in ancient biotechnology. recognized bias and that people should not be responsible for both the collection of the data and its interpretation. The controlled trial, as hailed by , can be considered ancient as it is found in the book of .

Biotechnology tools are being employed today in the production of purified biological therapeutic agents on an industrial scale. Medical biotechnology is employed in the development of such biotechnology products as recombinant pharmaceuticals and vaccines, tissue engineering products, and regenerative medicines including stem cell and gene therapy products. In this other treatment, the biologically active substance is produced by a non-biological process. This process involves the recombination of DNA [2].

4.1. Personalized Medicine

Modern molecular medicine may be said to have begun in 1869 when Friedrich Miescher discovered what he termed nuclein (the present day term is nucleic acid), and recognized it as a distinct molecule. His writings on the subject began to appear in the chemical literature in 1871. Much of what Miescher achieved at his home laboratory in Tübingen, included the subsequent discovery of the acidic nature of the molecule he extracted, went unacknowledged during his lifetime, only later to be recognized incrementally as determining many aspects of what is viewed today as modern biology [17]. Beginning in 1896, Sir William Osler, Sir Arthur Schuster, and Sir William Bragg collaborated in establishing the usage of x-ray photography in

medicine as a method for diagnosing kidney stones. The work of Frederick Sanger elucidating the sequence of biochemical reactions involved in disease is indicative of the type of work that has led to the golden age of molecular biology. The name of the disease officially changes in publications to kinase activation disease, being previously known as acute lymphocytic leukemia. Given the relatively common occurrence of disease, the widespread interest in it was predictable. Current subscription statistics indicate a marked and steady rise in the number of academic and commercially sponsored journals on the subject of treatment. The subject of molecular biology is specifically mentioned in the articles' methodology section, and the continued use of the Sanger machine is indicated.

In 1865, Karl Landsteiner identified distinct variations in human blood, making the connection between blood type and the immune response of recipients to donor blood. The practical application of Landsteiner's insights into blood transfusion occurred 16 years later in 1907, as pioneered by Reuben Ottenberg and Ludvig Hektoen at the Cook County Hospital in Chicago. They attempted blood transfusions on 80 hospitalized patients while trial and error matching the more recently discovered blood types for observable hemolysis. By this point, the clinical approach of blood transfusions itself was practically half a century old. Instead of attempting fresh blood, a connection between donor and recipient blood compatibility was made.

5. Ethical and Regulatory Considerations in Biotechnology

Commercial application of biotechnology innovations have developed faster than associated ethical, legal, and social implications can be sufficiently considered. To garner better understanding of these implications, a literature review was conducted. The broader public attends to values-based considerations when deliberating new technologies. Problems arise during their development when a diversity of attention or concern limits a technology's acceptance or potential for deployment. A taxonomy is proposed to guide biotechnology innovators toward assessing how and why a range of publics may oppose a technology's application. Such a taxonomy highlights mitigation strategies to address the adverse dimensions of attention to new biotechnologies. Attention is recommended to focus on hot-button issues throughout a technology's development. Diverse risks stemming from biotechnology innovations could engender variation in public attention according to risks' variability and the properties of organisms modified. Broadening the diversity of genetically engineered organisms beyond domesticated species may splinter biotechnology backlash, rendering silent or unknown problems more conspicuous and actionable [18].

At the cusp of the 21st century, society faces a cornucopia of unasked-for gifts, or perhaps pernicious piranhas, emanating from the "scientific, technological and industrial revolution" sketched in the 6th Kondratieff wave of economic development. To continue in this metaphor, the slippery fish wriggling in the net include biotechnology innovations. Besides arcane scientific principles and engineering considerations, the successful development of a new biotechnology has become fraught with consideration of numerous ethical, legal, and social issues. These issues can be conveniently lumped together as ELS problems, but a range of other considerations also enter into the calculus of broader "implications," including regulations and trade. The wide variety of terms connected to these non-narrowly technical considerations – risks, defense in depth, safety case, biodiversity, acceptability, etc. – to some extent illustrate how such a broad area of concern is borne out in a correspondingly wide vocabulary. [19][20][21]

5.1. Bioethics in Biotechnological Research

Biotechnology harnesses cellular and biomolecular processes to develop products and technologies. Biotechnological research, however, has largely outpaced biotech policy. Biotech applications can treat certain genetic disorders through gene therapy; gene modification may occur in somatic cells for therapeutic purposes or germ line cells for trait modification. Several policy considerations are discussed. Research and industry expansion increase competitiveness

and sustain market dominance, often at the expense of health and safety. Biotechnology has furthered scientific progression and medical innovation, it has raised ethical concerns about improperly regulating experimental practice. Bioethicists acknowledge the inability to conduct a sound cost-benefit analysis, and typically recommend precautionary regulation; to rationally act, policies must center on full sectoral transparency. Reform efforts have focused on reducing regulatory delays and minor changes rather than reevaluation or harmonization.

Companies are disincentivized to share safety information with regulatory bodies. There is a need to reform the limited regulatory framework, the composition and authority of regulatory bodies must expand to combat scientific advancements and increasingly comprehensive applications; moreover, a more diversified advisory council is necessary to better safeguard public interest. There is also a need for broader international collaboration to exchange information and techniques. Innovation and development of medical devices will benefit from collaborating primarily with others. However, a controversial partnership could place heightened stress on the medical sector, and domestic stakeholders should collaborate to construct advantageous policy for the biotechnology industry, acting in concert to gain maximum benefits from international market liberalization efforts. [22][23][24] [22][23][24]

6. Challenges and Future Directions in Biotechnological Innovations

Though biotechnology seems an altogether modern development, the realization that virtually all foodstuffs, such as bread, cheese, beer, and wine, could be formed by fermentation was known many centuries ago. Startling improvements in genetic and protein engineering now allow for better therapies. More of the newest biopharmaceuticals are peptides, hormones, cytokines, infectious agents, monoclonal antibodies, and the like. Together, biopharmaceuticals account for a steadily increasing share of all money spent on medicines. Drug delivery system offers medication through non-oral and non-injecting routes. Other innovations such as imaging agents, diagnostic kits, therapeutic radiation, and biosensors continue to make significant impacts on medical research, diagnosis, and treatment of diseases. For all other accomplishments, this wealth of knowledge about genomics and proteomics supported by advanced computer technology will bring revolutionary changes to biology, medicine, and indeed all life sciences [2]. Because prospects for biotechnology are increasing at an explosive rate, it is imperative to think systematically about the future. Because it combines advances in the life sciences with parallel developments in the physical sciences, information technology, and engineering, it is especially well positioned to yield dramatic results. The general forecast can be rendered with a high degree of confidence. Enormous improvements in the understanding of cell physiology and pathology will pave the way for such accomplishments as the prompt diagnosis and repair of birth defects, and the eradication of many previously incurable diseases. It is inevitable that biotechnology will foster a host of ethical, social, and legal dilemmas, and the hope is that biotech industry can anticipate and prepare for them in a thoughtful manner. Meanwhile, biotechnological remedies should be promoted, which, among other things, offer a great hope of improvement to developing nations. At the same time, substantial obstacles to the realization of many important gains remain. In addition to the formidable challenge of gathering and assessing biological data that are enormously complex and necessarily incomplete, obstacles of a cultural, political, and economic nature must be overcome. Healing the nations' health will necessitate surmounting resistance to lifestyle changes on the part of individuals, corporations, and governments, and surmounting barriers to infection control on a global scale as well.

6.1. Emerging Trends in Biotechnology

Biotechnology, as a new rapidly emerging capability to understand the molecular mechanisms of the living world, to alter the gene expression of those mechanisms by modifying it either chemically or genetically, and to use the output for safe and sustainable purposes. After conventional technologies that lasted for thousands of years, generally from 10,000 BC when glyphosate was utilized from the Mesopotamia region for the first time, it led to agricultural

revolution and domestication of plants; its operational principle began with recipes for making bread and beer on clay tablets, developed through natural and artificial breeding techniques of the beginning concept, in time, today biotechnology-like bitter genetic improvement has been updated since 10,500 BC. Contemporary biotechnological products have made profound changes in the existence of nature and humans as the benefits could be for the purpose of treatment and medicine or against the intent such as combating and prevention; in the case of the use of biotechnology by modification of the plague bacterium which as a result caused tens of millions people to die in the 14th century. On the contrary, in the following centuries Pizarro and his soldiers when invading Incas sides of Americas had been single instrumented by human smallpox for intentional bioterrorism purpose. Futuristic expectations and probabilities; uncontrolled dosages of X-rays were applied to treat acne to a group of teenage, and one to another group of this procedure used ionizing irradiation to get rid of excessive hair-piercing on the edge of lower lip; the other group inserts physiological saline into the same location. The young woman had—progressive hypertrichosis—excessive facial hairs on a grotesque level at the end of 2nd month in direct proportion of the location that physiologic saline administered from discretion.

7. Case Studies on Biotechnological Innovations in Medicine

Biotechnology involves the exploitation of biological or other scientific techniques and principles in order to create new, innovative products or applications. Over the past few decades, biotechnologies have made a significant impact on a growing focus of importance in medicine and its applications. The development and implementation of biotechnologies have revolutionized many aspects of the healthcare industry, ranging from conventional clinical practices to biopharmaceutical research. Biotechnological innovations have significantly increased the efficiency of the early diagnosis, prevention, and treatment of diseases, and have also contributed to the advancement of the quality of life [1]. In the first decade of the new millennium, political, economic and social concern about healthcare became a topic on the rise. Technological innovation is an important element of the healthcare system, and biotechnological progress is profoundly transforming medicine and the pharmaceutical industry. Many biotechnologies are currently applied in order to develop new therapies and diagnostic tools, and biotechnological innovation refers to several unknown applications that are going to become gradually available, changing medicine and the health sector as a whole. The main biotechnological innovations and their implication in healthcare are discussed with the help of a perspective on this sector gained from a systematic review of literature published until now. The relationship between academic, firm and other organizational actors that is crucial for the development and use of biotechnological innovation in medicine is also discussed, and the accomplishments that Italy has achieved are highlighted, showing how this country stands on the forefront of this field.

7.1. CRISPR-Cas9 in Gene Therapy

After contributing to the double helical model of DNA structure, Nobel Prize laureate James Watson famously stated, "We used to think that our fate was in our stars, but now we know that, in large measure, our fate is in our genes." This sentiment epitomizes the revolution ushered by the field of molecular genetics since its inception. The past several decades have bore witness to significant progress in gene manipulation, gene cloning, and gene expression. This revolution has brought previously unimaginable advancements in biotechnology, pharmaceuticals, and a myriad of basic and applied research arenas. The life sciences community has had little time to adjust to the impacts of these alterations, and already the next frontier in genetic technology is rearing its head. As with much that is transfixing in molecular biology, the next wave of genetic alterations stems from sequencing the Escherichia coli genome [25]. E. coli (lb) is an innocuous strain, typically used by undergraduate biology labs. Nevertheless, lb has high sequence identity to pathogenic E. coli that cause disease in humans. Aside from its genetic identity, the genome demonstrates the likely sources of virulence factors, and metabolic versatility that provide E. coli

with countless ecological niches. Most concerning to health officials is that virulence factors could be accumulated via uptake of pathogenic E. coli genes; an event with precedent in the creation of E. coli strain O157:H7. To the geneticist, however, E. coli just got a lot more interesting for reasons that are just now starting to become clear.

8. Impact of Biotechnological Innovations on Disease Treatment

Biotehnological innovations have a significant impact on the treatment of diseases, provided natural and artificial remedies from plant and microorganisms, a new vaccination method, tissue engineering. Traditional and original biotechnologies are used to produce medicaments suitable for treating diseases various in their nature. Biotechnological products of medicinal purposes may contain natural or modified live elements, such as viruses, microorganisms, cells, tissues, proteins, nucleic acids, etc., as well as blends of material of plant or animal origin [2]. Biotechnologically joined medicinal products may be prepared for the use with suitable carriers by mixing biotechnologically synthesized derivatives and are thus excluded from the present invention by the use of the term “end products”. In the disease treatment field antibiotics and other anti-bacteria drugs as well as in the prevention field vaccination is widely employed to ward off diseases of microorganism origins (bacterial diseases, viral diseases). In the field of biotechnology for medicine of tissue engineering there can be provided a degradable biocompatible scaffold of regenerated tissue was prevented from contraction, and also a method of fabricating the same.

Biotechnology is expected to have an increasing impact on novel drug developments, agriculture and environmental clean-up. Moreover, biotechnology is expected to have a global socio-economic impact based not only on the bio-sciences but also on bio-engineering including material sciences and informatics. A virtual science center in a local area can be utilized by scientists concerned with diseases in ethnic or other genetically distinct communities for drug development. At the same time, this system comes in terms of balanced regional development. Bioinformatics was employed to locate known vaccine epitopes from measles virus proteins. Based on this data, genes were engineered to express T-cell and B-cell epitopes linked to an MHC class II targeting motif. The DNA was transported into a plant expression vector by cloning and using the sequence of the tobacco etch virus coat protein gene [1]. This vector was employed to transform a plant, where it was cloned by homologous recombination into a viral vector for expression of high levels of non-replicating chimeric virus particles presenting an MHC class II targeting motif with a B-cell epitope from the measles fusion protein and an HLA-DR restricted T-cell epitope. The biotechnology treats in-vivo vaccination utilizing toxic materials (native or modified) is stored in fusion with biodegradable polymer membranes which results in in-vivo vaccination when the polymers sent into the body or attached onto the body of the patient thereby useful as a disposable syringe or plaster.

8.1. Cancer Therapies

Successful cancer treatment poses a significant challenge because the disease is highly variable, individual, and characterized by numerous resistant factors [26]. At the same time, the effectiveness of chemotherapy, radiotherapy, hormone therapy, and surgery often does not bring full recovery in many cases, and additionally, they are very toxic to normal tissues. The limits of their efficacy have already been reached at the present level of knowledge. Therefore, there is a necessity for new treatment regimens based on personalized and combined therapy, which will be more effective and much less toxic to the rest of the body. Biological therapy (the so-called “biologicals”) will play an increasingly important role in the treatment of neoplasms.

The development and implementation in practice of this group of drugs is nowadays so widespread that in some cancers has already become the first line of treatment. The future of cancer treatment is comprehensive therapy, which will take into account genetics, epigenetics, and the immune microenvironment. The evolution of cancer therapies would not take place without development of modern molecular biology methods, which allow for a more accurate

understanding of the biology of cancer, finding an appropriate therapeutic target, as well as monitoring therapeutic effects. Thanks to obtaining better bioinformatics methods that allow better data mining of next generation sequences, it is also possible to obtain a perfectly matched drug to a therapeutic target, which in the future will certainly improve the treatment effects. On the example of the most well-known biological therapies, the mechanism of action and the possibilities of use of particular preparations according to their structure will be presented and their major application indications will be discussed in relation to the latest research. Some of the prepared biological therapies are currently still in the experimental phase, and numerous studies are being conducted to prove their safety and efficacy purposes. In the present era many experiments are based on anti-cancer antibodies. There are many ways to modify them, like Restricted Fragment crystallizable of IgG class antibody or to improve its bioavailability. There is also an attempt to manipulate the structure of these molecules to improve the effectiveness of binding, stability, or even the strength of binding to the target molecule. With the technological development within protein engineering, it is now possible to create sites that are able to modify the functionality of the obtained molecule. [27][28][29]

9. Biotechnological Innovations in Drug Development

In an age where considerable advancements in biotechnologies are leading to the very rapid development of new techniques and products, it is challenging to provide a relevant and meaningful examination of some of the most promising innovations. The products resulting from various applications of biotechnologies are continuing to grow at an exponential rate, and the expectations of many is that an even greater percentage of drug development, particularly in industrialized nations, will be in the area of the biologics [1]. In fact, pharmaceutical biotechnology techniques form the basis and are at the core of most methodologies employed today for the discovery and development of both biologics and small molecules. Modern biotechnologies are providing scientists with an ever-widening understanding of human cellular function and the processes of several diseases afflicting humanity, while at the same time, an enormous wealth of additional and innovative biotechnologies have been developed in order to harvest the wealth of primary information found in the human genome.

In the current age of genomic sciences, as well as in the post-genome era, these and other rapidly advancing biotechnologies are allowing scientists and healthcare practitioners of a variety of stripes to peer beyond the threshold of human biology and medicine, providing the first glimpses of many exciting, yet wonderful, vistas. Such advances are expected to provide not only a better understanding of the relationship between genetics and biological function, but are also likely to begin to unravel the underlying causes of many critical diseases, while contemplating the association of genomic variation and drug response. Such information is expected to greatly enhance pharmaceutical research, and is already fueling the discovery and development of new and novel biopharmaceuticals, thereby providing remarkable opportunities for the treatment and potentially even cure treatment of several diseases once considered daunting or impenetrable.

9.1. Biopharmaceuticals

Biopharmaceuticals are a class of products containing mostly therapeutic recombinant proteins that are produced by biotechnological processes. Today, there are many strategic competitive advantages in this market. Consequently, new technological processes are opportunities for increasing production of microorganisms as industrial platforms. Bioprocessing comprises a wide range of techniques which can theoretically increase biopharmaceuticals efficacy, safety, pharmacokinetics, and production rates. An estimated 30% of the top 100 drugs sales are already biotech products, and within the next 5 to 10 years up to 50% of all drugs in development will be biopharmaceuticals. Additionally, antibodies and other new molecules classes are associated with biopharmaceuticals. Biotech blockbusters account for one-third of total pharma market, and some expect this figure could rise to 50% in the short term. Also, biopharmaceuticals based in nucleic acids (e.g. small interfering RNA (siRNA), DNA vaccines, and gene therapy) can

provide very promising strategies and currently these segments have the highest growth rates in the worldwide market. The same gene product can be obtained alternatively by its extraction from animal tissue or even by recombinant DNA techniques; however, the same protein produced by different manufacturers does present different characteristics. This specific topic has been a matter of several generalized quality concerns, which may constrain the desired growth in developing countries. It has been estimated that the cumulative savings for purchase of biosimilars, rather than reference 'innovator' drugs, imported and locally produced, would be many times the costs required for funding the related biotechnology sector. Moreover, localized biosimilar production would favor cumulatively advanced technological skills, up-grading the overall health related biotechnology. Importantly, recent stringent guidelines, as enforced by the ANVISA and corresponding EU directives, should resolve these problems. Now probiotics are allowed only as food additives. Conversely, biodrugs have a therapeutic intention, being ingredients or part of drug delivery systems ([30]). The biopharmaceuticals of food origin are another branch of the emerging biosimilars market, comprising dairy and vegetative high-value products, whose biotechnological advances are still at their infancy.

10. Biotechnological Innovations in Diagnostics

The biotechnologies employed in diagnostics played a pioneering role in promoting the implementation of new biotechnological tools also in modern medicine. The initial contributions of biotechnology to diagnostics can be summarized as follows. It was observed that molecular techniques could significantly improve the performance of conventional diagnostic methods, especially when applied to the isolation of weakly cytotoxic bacteria killed or inhibited by antibiotics. Biotechnological innovations were then used to bring about a drastic change in the diagnostic virology and microbiology practice by providing commercially available reagents for routine isolation and identification procedures. Successively, restriction of laboratory staff's capabilities on the one hand and a conspicuous increase in diagnostic demand associated with the possibility of an early start of adequate chemotherapy stimulated the development of molecular techniques for diagnosis.

In 1983 detecting the unique coding sequences and then the nucleic acids of the agents responsible for infective diseases is a fundamental tool for their diagnosis. Two different families of agents, functioning in a completely opposed way, are responsible for the pathological human infections: (1) exceptionally labile "fast-replicators", generally viruses, causative of acute infections and acute degenerative chronic diseases and (2) "eel-replicators", prokaryotes and protoctists, causative of long latency period chronic infections and/or oncogenetic transformation [31]. Thus it is possible to increase the potential of the molecular biology diagnostics for infective diseases which enable the creation of a sophisticated diagnostic kit for the simultaneous detection of different agents. This is a significant diagnostic step for the clinical management of the patient, providing a diagnostic rather than clinical and therapeutic approach to the disease.

10.1. Point-of-Care Testing

Point-of-care testing encompasses laboratory testing and clinical observations in near-patient settings, permitting rapid reaction to changing patient conditions and thus improving medical outcome. Ideally, test results are available at the point of decision about additional testing, treatment or discharge, providing rapid guidance. To accomplish this, the time span for basic steps of laboratory diagnostics including testing must be minimized while guaranteeing adequate diagnostic safety and accuracy. Point-of-care testing offers short turnaround times in comparison to extensive laboratory testing which makes it suitable for rapidly evolving acute situations and emergencies [32]. The recently improved technological performance is perfectly suited for use in settings such as emergency and intensive care units, emergency medical services, hospital wards, operating and recovery rooms. One large field of applications includes immediate or subsequent clinical situations where classical laboratory testing was deemed inadequate until recently by technical and logistical problems. In this context, the recent development of new miniaturized

instrumentation with high analytical performance and optimized transport systems for sample collection and pretreatment will broaden the scope of point-of-care testing enormously. Rapid immunodiagnostic tests, flow cytometry and gel microdroplet biochemistry have become point-of-care testing techniques in their own right but are not covered in this review. In the future, point-of-care testing will also increasingly focus on follow-up checks and on controlling the efficacy of therapeutic measures. A recent survey among US professionals found that point-of-care testing labs had at least as high yield as central labs.

11. Biotechnological Innovations in Vaccines

Vaccines continue to play a vital role in public health efforts to both prevent the morbidity and mortality associated with infectious diseases. Recent years have witnessed increased investment in the development of innovative vaccine technologies, with the aim of providing improved effectiveness, safety, and cost benefits. Biotechnological advances in the last two decades have led to the development and implementation of new types of vaccines including DNA vaccines, epitope-based vaccines, recombinant vector vaccines, and immunostimulating complexes. Such techniques offer possibilities not only in designing new types of vaccines but also in modifying conventional vaccines to improve their effectiveness [33]. To identify emerging vaccine and reproductive issues and to improve communication and cooperation among agencies, associations and groups, the first GAVI Partners' Forum was convened in Dar es Salaam, Tanzania in December 2003. Forum discussions highlighted a plethora of complex factors that need to be addressed through collective action to reach the shared goals of ensuring global access to affordable, better and more appropriate vaccines, and attaining the full benefits of immunization for children and women, particularly in low-income countries. To enhance access to affordable vaccines for immunization, the International Federation of Pharmaceutical Manufacturers Associations also agreed to establish a consultation mechanism in February 2002 with UNICEF and GAVI, which was maintained in a new Memorandum of Understanding signed in October 2003. In 2002, the Department of Vaccines and Biologicals began developing a Supplemental Position Paper on the new pentavalent DTwP–hepatitis-B–haemophilus influenza type b vaccine for discussion at the November 2003 SAGE meeting. To explore and consolidate approaches to best address emerging vaccine issues, GAVI co-sponsored a Research for Development meeting in New York with the Netherlands' MoH on 13-14 December 2003. Since the cheap vaccine approaches for this meeting were not defined or discussed, they are proposed as the focus for this paper. The policy and other implications are based on the Dar Es Salaam report and discussions at that meeting and in the subsequent partners' forum conference call.

11.1. mRNA Vaccines

Since 2019, the well-established safety and immunogenicity of a number of mRNA-based therapies and vaccines in the clinic have contributed to the observed rapid progress in strategy and delivery. Indeed, clinical trials and subject-enrollment statistics show that genetic vaccines, regardless of the nucleic acid type, are the most common 'first-in-human' agents relative to vector-based vaccines. Clinical data from supported the design of formulations. Of these, was the fastest to launch clinical trials in April 2020, in the USA, based on preclinical optimization, and accumulated robust data by virtue of managing a large volunteer base encompassing a wide range of ethnicities. However, with an expedited trial timeline, safety databases remain relatively small. published a 6-month safety report based on the observation of about 44,000 Covid-19 vaccine recipients 16 years of age or older (73% received the mRNA vaccine and were followed for at least 2 months after injection). Notably, although the observation period for long-term effects is short, the interim review revealed a higher-than-expected number of myocarditis events [34]. In recognition of potential disparity, 's study operations plan includes an external Pediatric Advisory Council (PAC), ensuring constant review while remaining mindful of trial ethics, which likely accounts for the smaller size. Observations that Covid-19 mRNA vaccines cause immune responses different from other vaccines bring a new perspective and call for further

study [35]. Given the expansive nature of vaccine development in the wake of SARS-CoV-2, stringent The United States' Food and Drug Administration (FDA) standards have been relaxed, allowing direct attribution of vaccine-induced signs to mRNA-active composition. In reality, conflating such symptoms with reactions to an infectious agent creates ambiguity surrounding adverse effects and necessitates crucial post-marketing safety surveillances. Recent data indicate that one dose of the vaccine offers little efficacy against the SARS-CoV-2 Delta variant, although protection improves after the second dose. Preliminary data suggest breakthrough infections post immunization with the vaccine due to the Delta variant in 41% of confirmed Covid-19 cases. These data are critical, informing the design of future vaccination campaigns.

12. Biotechnological Innovations in Organ Transplantation

Direct or indirect contact is known to many communities in the form of either an organ transplant or a genetic transplant. For end-stage disease, the organ transplant has been medically examined and has been shown to improve or prolong the patient's quality of life. If the organ or tissue transplantation is used to save the life of the patient or to prevent further deterioration of the patient's quality of life, this procedure can be extremely useful [36]. Over the past two to three decades, rejection of transplantation and the side effects caused by immunosuppressants in regenerated organs and tissues have been a major issue. Other approaches have been developed, such as artificial organs and tissues, as ways to avoid the need for transplantation. Many attempts in the scientific community are being made to improve the techniques of tissue engineering and regenerate medicine. Based on this research, organ and tissue engineering approaches are presented with an overview of current methods of scaffold design. However, the restoration of the damaged tissues and the creation of new tissues have only minor disadvantages. Recent developments in biogenerative engineering have shown that the tissues and organs have improved significantly. One of the most important outputs is that biosynthesis plays a significant role in the scientific community. In general, the three-dimensional bioprinting of tissues and organs is strongly dismissed due to the lack of complete biological post-print accessibility. On the other hand, it has been noted in various studies that the rigorousness of ECM proteins has a direct impact on post-bioprinting cellular attachment. There is less similar work related to the effect of pre-bioprinting on bioink's biological objectivity.

12.1. Organ Printing Technologies

Organ or cell transplantations provide a satisfactory medical technology for end-stage organ failures such as kidney, heart, liver, and pancreas, saving or extending tens/hundreds of thousands of patients' lives each year. However, the unavailability of adequate organs for transplantation is a critical barrier. Of the 80,000 Americans currently awaiting organs, fewer than 20% will eventually receive organ replacements. The development of biogenerative engineering, an aggregation of multifaceted sciences and technologies concerning tissues, medical devices and biomedicines, have the potential to regenerate or repair damaged tissues [36]. Relying on unique therapeutic modalities, look-alike living tissues can be generated in the laboratory with verified biocompatibility and safety which can be implanted into human bodies for clinical applications. Recent years have witnessed major advances in tissue engineering, regenerative medicine, nanotechnology, bioengineering techniques, and biogenerative engineering. Among these advancements, particular progress has been made on three-dimensional bioprinting (also called 3D bioprinting, or just bioprinting) of living tissues and organs. The establishment of the Extracorporeal Life Support Organization (ELSO) international organization, and recent advances in decellularization techniques for organs and tissues, have enabled the generation of a significant number of organs, trachea, esophagus, and other tissues to be created [37]. Bioprinting widely encompasses the deposition of virtually every class of biological polymeric materials as organic skeleton to support cells in maintaining a 3D configuration in the printing area. The equated biomaterials to function as temporary exoskeletons are slowly substituted afterwards by the cellular and extracellular components during the fragile construct maturation process. Bioprinting exhibits essential different features

than that of the classical 3D printing from synthetic materials, and the method choice is properly accounted for them.

13. Biotechnological Innovations in Tissue Engineering

Tissue engineering aims at the in vitro regeneration of diseased tissues. The development of tissue engineered cell-biomaterial constructs, a bioreactor system for their most relevant subsequent cultivation as well as sensor technology, required for a non-invasive online control of the construct properties during the bioreactor cultivation, is depicted. The latter biotechnology promises to profoundly change medical practice in the near future, offering the possibility of regenerating tissues and organs instead of just repairing them.

Bioreactors play a crucial role in supplying the constructs with oxygen, nutrients and biomolecules, and removing waste products. Various bioreactors have been designed and developed to meet the requirements of different engineered tissues in terms of their anatomical structure and function. The bioreactors are artificially designed chambers in which biologic and clinical materials are transplanted to provide a dynamic biochemical and physical environment. Moreover, a distinction has to be made between contact and non-contact sensors. In general, measurements on the cell-biomaterial constructs generally need non-contact sensor devices. The establishment of an in vitro bioreactor system which enables us to simulate the mechanical and biological environment in a healing human wound is firstly described. The bioreactor is used to investigate the suitability of different implant materials for oral tissue regeneration. Appropriate sensor technology for an online control of the bioreactor environment and the cell-material interaction has to be provided. In fact, despite the interesting results that have been obtained so far by the cultivation of a cartilage cell-biomaterial approach in a rotating wall vessel bioreactor, their nature is mainly descriptive and does not allow a deeper insight in the interaction mechanisms between native or engineered and the surrounding environment. [38][39][40][41]

13.1. 3D Bioprinting

Advances in three-dimensional printing technology have transformed many industries, providing new avenues for the fabrication of tailored products with complex architectures. The medical sector is no exception: cutting-edge methods such as three-dimensional bioprinting offer a new approach to creating advanced biomaterials, including models for preclinical trials or dental implants and tissues for transplantation [42]. The fabrication of patient-specific biocomposites relies on medical imagery data to reconstruct individual anatomical structures or tailor scaffold architectures. In principle, such constructs mimic the 3D structure of natural tissues, facilitating a natural attachment and infiltration of living cells, blood vessels and nerves. Moreover, they biodegrade over time, transferring the load to the newly-formed tissue during the regeneration process [43]. As such, they have been proposed for a wide range of biomedical applications, including regenerative repair of cartilage, bones and skin defects. Additional functionalities can be provided by a composition with a controlled release of therapeutics, including anti-inflammatory, antibacterial and anticoagulant agents.

In the space, a fabrication process of large defect-filling porous structures is developed: microstructures with a tunable height and near isotropic stiffness are defined, the optimal arrangement is identified, and a fabrication strategy is evaluated focusing on scaffolds for load-bearing bone defects. Bone tissue, a highly organized combination of organic and inorganic components, undergoes a constant self-renewal process, with an essential balance maintained by the osteoblasts activity and the mesenchymal stem cells differentiation. Several physiologic processes, including disease, trauma or surgical operations, can disturb this balance, leading to nonunion fractures (pseudoarthrosis) or critically-sized cartilage lesions.

14. Biotechnological Innovations in Regenerative Medicine

In spring 2016, the US National Academies of Sciences, Engineering, and Medicine hosted several workshops on the potential uses for gene editing science, examining the scientific and

ethical considerations of human genome editing. It has been suggested that gene editing technologies have the potential to vastly improve our understanding of heritable human biology and genetics, bringing enormous contributions in the fight against cancer, other diseases, and our ability to promote health.

The US National Academy of Medicine, and the US National Academy of Sciences have echoed the call to avoid use of inheritable gene editing until the consequences have been debated for a rather long time with broad societal consent [44]. In 2017 the US National Academy of Medicine called for a globally representative commission to ensure broad societal consensus prior to any clinical use. Moreover, it has been suggested that research of this type should not proceed without further exploration of the technology, ethics, societal engagements, and closer oversight as suggested by international guidelines.

14.1. Stem Cell Therapies

Modern medical technologies, such as improved living conditions, diets, and hygiene, have helped significantly to increase life expectancy. However, increased life expectancy has brought new challenges, especially an increased frequency of chronic diseases, such as neurodegenerative diseases, myocardial infarctions, and arthroses, while these degenerative diseases are a victim of their own success. Novel regenerative therapies are required to meet the need for the ageing population. Stem cell-based concepts are presently widely considered a very promising basis for the development of novel therapeutic strategies. Since the first study applying adult stem cells for cardiac repair was published in 2001, many more reports have appeared although the studies have almost uniformly yielded disappointing results. Largely, outcomes have been plagued by safety concerns without any considerable therapeutic effects. The underlying reasons for the lack of regenerative success are manifold. Firstly, adult stem and progenitor cells generally have a rather restricted culture expansion and differentiation potential. Particularly, it has also been difficult to harness these cells as therapeutic agents organ systems. Although adult stem and progenitor cells have shown very convincing success in regenerative tissues such as blood, skin and cornea, less regenerative organs like brain and heart have so far not exhibited any significant therapeutic effects. Additionally, it has been difficult to achieve efficient targeted genome engineering in adult stem cells at a time when such approaches would have been direly needed. The availability of human pluripotent stem cells provides new exciting opportunities for both basic research and therapeutic development. human pluripotent stem cells comprise embryonic stem cells and induced pluripotent stem cells. ESCs were first isolated from the inner cell mass of mouse blastocysts nearly four decades ago. The generation from human blastocysts was first reported in 1998. Since human ESCs can be maintained in culture indefinitely without losing their pluripotency they have emerged as a very powerful system to study many aspects of embryonic development and differentiation. Although ESCs might herald an entirely new area of medical innovation by enabling the generation of hitherto inaccessible cell lineages, their potential clinical application has been hampered by several concerns. [45] Advanced cell therapeutics are currently changing the landscape of clinical medicine; hence, will mesenchymal stromal cells be a part of it? Over the last 15 years, remarkable advancements in the field of cell therapy have significantly altered strategies for treating patients with otherwise untreatable conditions. This progress has been driven by an unprecedented wealth of knowledge, offering new and often unexpected opportunities for therapeutic interventions, and a broad range of technological innovations. Based on these observations and hypotheses novel cellular therapies are being developed, with potential to dramatically enhance the field of regenerative medicine. These advanced cell therapeutics are expected to significantly broaden the scope of treatment options for patients with recalcitrant clinical conditions, and have thus the potential to significantly alter the clinical landscape. Cell therapies have an ancient history, spanning thousands of years. For instance, it is known that bone marrow transfer was performed long before its description by modern medicine. This old therapy, first reported in 1869, was considered ineffective for more than half a century and hampered by intense research. [46]

15. Biotechnological Innovations in Neurology

Clinical applications in brain science have progressed at a glacial pace compared to other medical disciplines. The anatomical basis for symptoms in the nervous system is much more complex compared to other organ systems, especially when considering the organization of large-scale, distributed brain networks. The diseases are among the most feared because cognition is the defining feature of human beings, and the thought of losing one's cognitive faculties is both frightening and disruptive to relationships with loved ones. The treatments for most neurodegenerative brain diseases are limited, and cure strategies remain underdeveloped. Multiple organizations note that the demographic shift towards an aging population dramatically increases the proportion of people at risk for degenerative brain diseases [47]. This demographic reality further exacerbates pressure to improve clinical outcomes in the neurological sciences. In answering this pressure, technical advances in the field of neuroimaging offer new promise via enhanced characterization of microstructural anatomy, network connectivity, and functional biomarkers of health and disease. The following articles describe cutting-edge applications targeting these outcomes using diffusion tensor imaging, diffusion-based tractography, and positron emission tomography. These techniques are also reviewed in the context of ongoing controversies, methodological challenges, and the societal context of ever-increasing costs for imaging platforms. Finally, the glymphatic system is reviewed as a novel target for future investigation in clinical populations, illustrated through a pilot case study that applies neuroimaging techniques and the beta-amyloid tracer. The mechanisms that keep the brain tumor free are also discussed. The following technologically focused conversation is prefaced by several sections that introduce fundamental concepts in brain science, and techniques used to investigate brain health and disease using the Scalable Brain Atlas.

15.1. Brain-Computer Interfaces

Since the late 1960s, Brain-Computer Interfaces (BCIs) have had various names including brainmachine interfaces, direct neural interfaces, and brain–computer links. Inhabitants with a desire to control some aspects of their interface have used the thoughts in their head as forms of communication for centuries. The idea was to harness the electrical signals coming from the brain and convert those signals into mechanical movement of a studio participant or cursor on a computer monitor. The initial work in BCI was carried out on invasive BCIs, which required the surgical implantation of electrodes into the brain. In the 1990s, advances in electronics, computer processing and excellent neuroimaging technology that lead to non-invasive methods capable of carrying out BCI research made these procedures perpetually contentious. Motivated researchers prefer to make the latest of chance waves of approval in countries where proper ethical standard procedures were lax or non-existent.

Over the years, progress has been made in recognizing and decoding a number of mental, emotional, cognitive states, and events using distinct frequency bands that can be determined from surface brainwaves. Also, non-invasive methods for isolating users from the main field have reduced the problem. More recently, potential contact and high contact electrodes provide greater control options when mining brain signals consistent with better independent component analysis and adaptive factoring of iterative and canonical characteristics. Researchers began to think about the development of CBI systems. After some years the approach to BCIs came together and led to the first EGG-based brain-switch that no longer required staff devices. The potential of BCI technology for social good was realized. Far from curing was a significant social problem and the development of some BCI applications potentially could make an important difference to the quality of life of long-lasting patients.

16. Biotechnological Innovations in Infectious Disease Management

16.1. Novel Antimicrobial Strategies

Even though antibiotics contribute to antimicrobial resistance due to their non-specific mode of

action targeting general prokaryotic cell functions, those strategies must always be applied in the prophylaxis or treatment of infections, possibly augmented with anti-inflammatory or immunostimulatory ways of support. To address the growing problem of resistance to common antibiotics and the unavailability of established and effective treatments for many medical cases, new antimicrobials are being developed and tested for a variety of agents and methods. Here, some classic and new strategies for antibacterial treatment are briefly reviewed. First, we present strategies for small molecule inhibitors of different structures, targeting primary bacterial functions, such as the synthesis of cell wall building units, the enzymes required for their polymerization, and other functions of the cell wall or peptidoglycan. Here, two of the functionally relevant candidate targets and several families of small molecules that have been developed in the last few years are presented: the family of defensins and the C3-secreted 96-amino-acid peptide C3-promoted peptidoglycan degradation.

Due to their broad recognition of microbial structures and their capability to not only directly kill invading pathogens but also affect different arms of the pro- and anti-inflammatory host response, antimicrobial peptides quickly come to the scene as therapeutic tools in viral, bacterial, fungal, and parasitic infections. Antimicrobial peptides are small, cationic, amphiphilic molecules capable of inserting into and disrupting the microbial membrane. Both pathogen-associated molecular patterns and host-derived danger signals activate immune cells, triggering a systemic response, which is not only aimed at eliminating the invading pathogen by efficient phagocytosis and digestion but also at sterile clearance of the released danger signals. Since the first discovery and therefore infection-protective capacity of antimicrobial peptides, this group of molecules has gained increasing interest in the context of novel therapeutic approaches for relevant acute and chronic diseases. As effector molecules of both the innate and the adaptive immune system, these peptides have the required efficiency and tolerability as a scaffold for new drugs.

17. Biotechnological Innovations in Global Health

Recent advances in biotechnology underlie a multitude of innovations poised to transform health care, offering the promise of new treatments, innovative diagnostic tools, and revolutionary therapeutic interventions. Technological ingenuity and creative industrial strategies have combined to produce an exciting stream of new drug, vaccine, and diagnostic products. In addition, similarly novel approaches to the prevention of disease and the management of health care are being developed and commercialized. Unlike advances in many other high-technology industries, however, the vast majority of benefits flowing from recent advances in biotechnology accrue to wealthy industrialized countries. A fortunate few (or the citizens of only a fortunate few nations) enjoy the innovative fruits of research investments made in the basic biomedical sciences over the last several decades of the 20th century. Although the health status of many populations is improving, the health divide between wealthy and marginal societies continues to widen. This introduces a number of innovative drug, vaccine, and diagnostic products conceived and developed with the health care problems of the developing world in mind. The advances become innovations when they demonstrate clinical efficacy, are easy to administer, and significantly reduce costs. Some, such as a patch to deliver measles vaccine and oral bacteria to combat obesity, have only been conceived within the last year and remain in the laboratory and clinical development pipeline. [48] Others, such as new fixed-dose antiretroviral drug combinations to fight the AIDS epidemic in Africa, have been recently introduced to the market and came to fruition through accelerated development track that enabled clinical testing within two years of the original scientific discoveries. Unlike scientific discovery, which is primarily a creative process, scientific advancement in many disciplines can directly lead to innovation, products, or processes that provide some value to society much sooner. This is clearly the case in biotechnology. The problems commodity and generic drugs have in penetrating the market for newer, more advanced products are well known. Similarly, many medical biotechnology companies have suffered from the paradox that developing product details about the safety and

efficacy of a candidate drug, vaccine, or diagnostic can so delay its registration by the health authorities that the competitors have time to ready bioequivalent or even superior follow-on technologies. At the same time, the developing world is extremely diverse; just under one-fifth (440.0 million people) of the world's poorest but live in the populous Middle-Income Countries (MICs) and do not have access to resources. Yet circumstances in these countries are such that they may be particularly suited to innovative solutions. Rigid, stratified, and financially overburdened health systems can be bypassed in favor of decentralized networks emphasizing cost-effective public health interventions. Pharmaceuticals that must be cold-stored might not be appropriate for rural health posts where the electricity supply is erratic or nonexistent; simple, innovative delivery devices can circumvent this problem. Although the benefits of the former far outweigh the latter, even small and relatively harmless adverse reactions have contributed to a greater level of risk aversion by health authorities in developing countries. Given their weak regulatory capacity, this can significantly impede what could otherwise be beneficial innovation. The adoption of conventional medical products is a function of complex, interrelated variables including the socioeconomic level of a country, the level of urbanization, the state of the health care infrastructure, the distribution of the population, levels of pollution, and many others (e.g. out-licensing marketing rights for a drug in a country). It is unlikely that a single determinant will radically alter that country. Though the task is daunting, developing countries are particularly well positioned to adopt innovative solutions, providing the impetus is such that it requires creative technology transfer at the development level from pharmaceutical companies. The benchmarks against which new drug, vaccine, and diagnostic treatments are evaluated in the developed world are the problems to be solved in the developing world. Moreover, the potential markets in the developing world are so gigantic that even a niche pharmaceutical product could yield a substantial return-on-investment (ROI). Therefore, money can also be made by applying a range of strategies, some of which actually mirror the normal drug discovery process (and which is itself a form of innovation), such as target-drug (disease) matching and target-market matching. [49][50]

17.1. Disease Surveillance Systems

A population-based disease surveillance system provides essential data to assess the public health impact of diseases and to develop and monitor programs effectively. Such a system includes the following components: data collectors, data managers, analysts, in-depth researchers, and other professionals who share information about diseases and conditions (including risk factors) and about populations with many diseases. Collected and analyzed information is used by decision-makers to design and evaluate policies and health programs. It also helps professionals to understand conditions better and to answer questions from the public. And by alerting authorities to unusual health events, it lays the groundwork for investigating and controlling them quickly, and for preparing national health systems for bioterrorism [51]. Biological and laboratory surveillance were initiated to notify the authorities of unusual patterns of diseases and to help monitor various campaigns to prevent and control them – disease elimination and eradication. The fight against some major parasitic infections was launched in 1967 on the recommendation of the WHO Expert [52]. The Indian authorities approached this issue, assuming that it was necessary to regularly investigate the population with the parasite. The method proposed by the expert and developed in the USSR was a threshold test of a few drops of blood for the presence of antigens of a parasitic infection. Russia had experience with such a test in disconnected areas and offered to supply it. The population was to be treated if dangerous concentrations of antigens were detected. Thus, such a test of population groups traveled 2-3 times across the country, examining 270 million people at one time for 3-4 months. This was in 1969-1970. Early detection of a dangerous threshold of antigens should stimulate the rapid treatment of people in such areas (negative influence of water after floods, etc.). Treatment – a large-scale field action with visible effect. A prerequisite in this surveillance was the stunning of dangerous antigens in limited areas of Indochina and Burma (not only primates but

also those sick with pathogen populations, as well as a noticeable decrease in the ecological habit noted by observers).

18. Conclusion

Biotechnology is the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services. From its inception, biotechnology has maintained a close relationship with the pharmaceutical industry. Although biotechnology sometimes is defined only in terms of the manipulation of genetic material, as filtered through tools such as recombinant DNA techniques and gene-transfer vectors, it dates back to the initial cultivation of plants, animals, and microorganisms. Biotechnology encompasses the entire spectrum of activities from the downstream processing of drugs and pharmaceuticals to genetic manipulation of micro-organisms in order to develop monoclonal antibodies, recombinant DNA products, biological testing of drugs, and metallic biosorption.

Life on earth ultimately depends on the sun. However, despite this fundamental role, certain forms of its energy, such as UV light, represent a danger for DNA, the molecule that carries the instructions for the organization and reproduction of all living organisms. As a result, during their evolution organisms have acquired various mechanisms to repair this kind of DNA damage. For years, the study of these repair mechanisms has been carried out through direct observation of the processing of damaged DNA by purified repair proteins in biochemical assays. Recently, the development of single molecule techniques that allow the manipulation the observation of individual DNA molecules have made it possible to monitor the dynamics of individual proteins acting on single DNA molecules, providing information that was out of the reach of the previous bulk methods. This paper reviews some of these single DNA manipulation and observation techniques, and presents some of the results obtained that enriched the current views of DNA repair.

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