Deep Science Publishing
https://doi.org/10.70593/978-81-988918-4-6_1

Chapter 1: Unlocking the new frontier of biomedical innovation in disease prevention and treatment

1.1. Introduction to Biomedical Innovation

The advancement of novel biomedical concepts and their applications has ushered in a new era of biomedical innovation. The key categories of biomedical innovation addressed in this chapter include but are not limited to, the large-scale invention and popularization of: (1) rationally designed/engineered molecules, polymers, hydrogels, scaffolds, microcarriers, and matrices; (2) implantable or injectable therapeutics; (3) molecularly targeted or dendritic cell-targeted biomolecules including proteins, RNAi and DNA/RNA therapeutics; (4) high fidelity imaging systems and their implementation in animal models and patients; (5) combinatorial approaches to restoring normal biological and disease functions in patients; and (6) nanoscale systems and devices designed for disease prevention and treatment of cancer and inflammatory, cardiovascular, musculoskeletal, neurological, and infectious diseases and disorders (Issa et al., 2014; Chien et al., 2015; Manero et al., 2022).

The aforementioned concepts are the fruits of progress within the academic and biomedical industry communities combining fundamental knowledge with translational research and technology transfer programs. They are assembled to ultimately achieve patient-ready solutions for chronic and acute diseases and disorders requiring new directions for new discoveries in biomedical innovation. Emphasis is placed on the substantial pioneering contributions from various regions of the globe, particularly the United States because they provide a vast reservoir of expertise and knowledge necessary for assessment and review of future biomedical research initiatives. Creating and managing biomedical innovation programs based on these human factors through appropriate science education and improved technology transfer programs could help at-

risk economies to compete globally using a workforce specializing in biomedical innovation creation and management (Platt et al., 2015; Vavassori et al., 2024).

1.1.1. Overview of Biomedical Innovation Concepts

The conventional approach for biomedical translation and innovation is relatively straightforward. New pharmaceutical or biotechnology technologies, such as novel drugs, vaccine candidates, or diagnostic tools, emerge from basic life, chemical, or physical science either in academic laboratories or within large pharmaceutical companies. These initial candidates are carefully evaluated, tested, and then developed further into effective solutions for important human diseases, medical conditions, or health-related problems, and are released to the market and/or clinic. The regulatory framework and public-private partnership model exist to speed and fund this innovation pipeline to develop public health solutions. Thus, the end goal is to obtain an approved for-profit drug or product. This biomedical supply chain of innovation has traditionally relied upon intellectual property ownership as the incentive for bio-entrepreneurs and companies to develop new products.

Fig 1 . 1 : The Evolving Landscape of Biomedical Innovation

In recent years, several broad and important trends have emerged demonstrating the value and potential of new approaches to biomedical innovation, and hence the need for a more agile and flexible strategy and model for biomedical innovation. Examples of these important trends in global biomedical innovation include the diversification of actors in the biomedical ecosystem, increased funding and access opportunities, the application of new business models, research technologies, data analytics, interconnected innovations, and integration into global health programs and related

activities. These new approaches have been recognized by specialized non-governmental organizations and academic laboratories that are now leading a new “science development” or “last mile” model to fill in the gaps in neglected disease areas by providing “actionable science” for buildable ideas and addressing the innovation-to-access challenge.

1.2. Historical Perspectives in Disease Treatment

Starting with the hunter-gatherers, humans have always had to cope with traumatic injuries and deaths from predation and accidents. Ancient burial sites suggest beliefs in an afterlife and therefore also indicate how important it was for the bereaved to protect the corpse's welfare. Subsequently, in agrarian societies, the developed skills for metallurgy and pottery allowed for more impressive burial sites. Psychological stress in these societies is also reflected in the practice of cranial trepanation, where holes were made in a person's skull. These holes might have provided relief for the associated headaches, seizures, and infections caused by trauma, toxins, and parasites, making it a plausible treatment. However, it might also have provided some form of supernatural control over sanity disorders in some cultures in the past. The discovery of drugs that relieved pain or affected mood likely led to the first known effective treatments, though these might have been seen as magical effects at the time.

With the growth of empires, agricultural production ensured an increased availability of trained shamans, priest-healers, and, later, medical doctors willing to provide services. The development of hospitals by religious groups ensured that the sick received some level of care. The beginnings of rational medicine using herbal remedies were reported by ancient civilizations, while medical schools dedicated to patient care were built in the Greek and later Roman Empires. Rational treatment in holistic belief systems was better established in ancient Indian and Chinese cultures, where practitioners focused on restoring imbalance via herbal preparations.

1.2.1. Evolution of Treatment Modalities Through the Ages

By exploring ancient literature, including the writings of Hippocrates and Galen, as well as Chinese and Indian medical manuscripts, one can gain insight into the historical perspective on disease treatments. For many years, diseases were thought to be caused by supernatural forces or imbalances in biological or humoral systems. Trauma and superficial or localized diseases were treated by specialists such as bone setters, but illnesses, where pathophysiological processes took place in multiple organs, were treated by shamans or priests. The general belief was that only rituals of worship could provide a cure by appeasing or bribing supernatural beings. With the advent of alchemy, plants

with pharmacological properties were used as medicines. Hippocrates believed that diseases were caused by natural forces and prescribed natural remedies including the fasting technique. Galen followed the natural approach and built upon Hippocrates's works by classifying medical knowledge into anatomy, physiology, diagnosis, therapy, and prognosis. In India and China, herbal medicines were used as adjuvant therapies, and acupuncture and surgery were jointly used for various illnesses.

It was during the Renaissance, when there were a lot of developments in all sciences including medicine, with numerous discoveries in anatomy, physiology, and disease pathology, that treatment options advanced. The Age of Enlightenment gave birth to the concept of using physics and chemistry to explore diseases and developed basic principles of chemistry and biology that allowed specialists to focus on individual aspects of molecular pathways to develop novel targeted therapies. The discovery of anesthetic agents allowed major surgical treatments to become feasible. The development of the first synthetic drug targeted towards a specific pathology launched the revolution of modern-day synthetic drugs that would target individual molecular changes to cure diseases, including various antibiotics, and develop novel pharmacological approaches for treating other diseases, including autoimmune diseases, cardiovascular diseases, metabolic diseases, and neurological diseases.

1.3. Current Trends in Biomedical Research

Biomedical research covers a vast collection of areas that extend the knowledge of molecules, cells, tissues, and organs associated with human health and disease. The biomedical research achievements of the last century have benefited the population of developed countries through the eradication of most infectious diseases and the successful handling of many human disorders such as vascular disease, diabetes, cancer, neurological disorders, anesthesiology, surgery-related trauma and recovery, and so on. The future promise of biomedical research for the world population, however, must be more than just the mere extension of the understanding of cellular and molecular processes. It must encompass the use of this information to develop new technologies, products, and processes helpful to disease prevention and treatment. Further, biomedical research must address global and local human health priorities with an emphasis on the research objectives of countries with limited means to fund and also conduct basic and applied biomedical research.

As a radical departure from how the research community has approached biomedical research for the last hundred years, the recent approach to transformative studies seeks large-scale collaborations that leverage theory-building, big data analysis, and prediction, along with the intelligent use of technical advances in delineating the rules and regulations that control increasingly complex biological systems. The ultimate intent

is to bring about a radical change in how we conduct this kind of research with the eventual goal of speeding the pace of biomedical innovators of the future in their quest to apply current and new biomedical technologies to previously unconquerable major disease areas. While the future vision driving the 21st-century approach to systems-related and interdisciplinary biomedical research may differ radically from what has gone before, it is but an extension and acceleration of rationally planned, experimentally driven biomedical research. It is this 21st-century approach to biomedical research that must be embraced by public funding agencies and private philanthropy alike to address the promise and threat of biomedical innovation.

1.3.1. Recent Developments in Life Sciences Research

Since the mid-1990s with the invention of the automated fluorescent sequencer, life sciences have progressed from an empirical science to a high-throughput quantitative science and are now firmly established in the digital science era of today. The Human Genome Project was completed in 2003 and with it, the first version of the Book of Life. Progress continued to advance with developments in DNA technologies, such as next-generation sequencing, single-cell transcriptomics, and T-cell receptor sequencing. The application of these new technologies to translate from genotype to phenotype in a variety of studies in model organisms, across the lifespan in healthy humans, and in research with various diseases has moved forward at an extraordinary pace. The growing understanding of the links among the number of bases in the genome, epigenetics, gene expression in time and space, and human microbiota about the disease is producing revolutionary discoveries in fields as diverse as cancer, cardiovascular disease, neurodevelopment, and neurodegeneration, reproductive and pediatrics, and even infectious diseases.

In addition, the introduction of CRISPR and its family of technologies have now made genome editing accessible to nearly every biology research laboratory in the world. CRISPR applied to a variety of organisms from nematodes to marmosets allows us to address long-standing questions in biology and medicine about the roles of individual genes, the interaction of genes in various pathways, epigenetic modifications, and even microbiota. In parallel, CAR-T cells and other immunotherapies for the treatment of selected cancers and advances in mRNA vaccine technology for the prevention of viral infections have demonstrated the power of biomedical discoveries in affecting the quality of our lives. The creation of the biotech industry by the union of basic research, medical practice, and applications has laid the groundwork for future breakthroughs driven by continuous investment in life sciences research.

1.4. Technological Advances in Disease Prevention

The first function of biomedical innovation, the prevention of diseases, has received extensive attention and investment in recent years, although investment in innovation that targets prevention remains less than investment in drug development. The extraordinary advances in genomic technologies, especially single-cell genomic techniques, and the pervasiveness of wearable health devices are enabling us to rethink and improve innovation that targets disease prevention. The process of discovering how genomic information codes the physiological response to environmental exposures is expected to usher in new technologies that can avert or delay aging and various chronic diseases, such as frailty, sarcopenia, Alzheimer's disease, diabetes, cardiovascular diseases, cancer, and osteoporosis, and infectious diseases. If successful, prevention would be implemented not just once, but through the active engagement of researchers, clinicians, and preventive health practitioners to holistically keep individuals and communities healthy, to entirely prevent or delay the onset of various chronic diseases. There may exist multiple preventive models and strategies involving environmental interventions, treatments, such as vaccines and gene editing technologies or products enhancing genome functionality related to the physiological transition, throughout an individual's life as a result of five factors: epigenetics, the microbiome, stochasticity, exposure to various environmental risk factors, and genome. Independent of the discovery process, the movement to implement precision medicine, starting from the healthy bases of healthy individuals and populations, to improve health and to avert and delay diseases, particularly chronic diseases, among the healthy and pre-symptomatic will create a much larger market for preventive biomedical innovation, than its current size.

1.4.1. Genomic Technologies

Disease prevention is increasingly reliant on developing and deploying advanced technologies to predict genetic predispositions, screen individuals at major risk, monitor health status, and prevent the onset of serious disease. In this domain, the greatest innovation has come from advances in genomic medicine, catalyzed by the completion of the Human Genome Project and subsequent technical advances that have dramatically reduced the cost of genomic sequencing and increased throughput. Genomic technologies are being used to understand the biological dimensions of diseases that have important pathogenetic relationships to pathogen, nutritional, environmental, or other lifestyle exposures. Expectedly, the use of genomic information is beginning to allow for better-targeted prevention strategies designed to block a select disease outcome in a specific person at risk, rather than in the general population, and are slowly moving health systems towards new-age disease prediction, prevention, and personalized

medicine. Extensive international, government, and commercial efforts to decrease genomic sequencing costs and resources have readily made population-based genomic data widely available for a variety of specialty diseases. The rapid uptake of genomic approaches shows the breadth of their applicability. Advanced technologies that once explored rare Mendelian inherited disorders affecting very small population cohorts are now also revealing the role of common variants and epigenomic factors for a diverse set of common complex diseases that collectively affect a majority of the population. Deployment of these noninvasive large set genomic data by various stakeholders will lead to early personalized action, thus adding value to global health systems and populations.

1.4.2. Wearable Health Devices

Biomedical innovation increasingly utilizes wearable health devices that monitor biomarkers associated with health and disease. These devices measure several general health indicators including but not limited to gait and activity level. The use of accelerometers has been widely studied in older populations to identify individual gait and cadence parameters associated with sarcopenia, falls, frailty, risk of morbidity and mortality, or overall aging. They also measure behavioral risk factors such as heart rate, sleep patterns, exercise, mental health, hydration, or diet using various methods. Algorithms are being developed to detect specific diseases or disease-related events, such as when a medication is not taken, a fall happens, or other issues arise. This represents the convergence of the tools of medicine and the tools of technology for innovation in health monitoring. Wearable health devices are beginning to offer accessible long-term monitoring for several costs, diagnostic, and therapeutic problems faced in multiple disease areas around the world.

These devices have the potential to alleviate several issues that our current traditional healthcare monitoring and follow-up systems face. This includes increasing the accessibility of diagnostic and therapeutic monitoring to all patients regardless of their income levels, performing long-term and more frequent assessments of key parameters, reducing the cost associated with hospital or specialist clinic visits, and helping to facilitate improved patient-physician contact and relationship. Specifically, wearable health monitors can also alleviate several limitations of current diagnostic-finding and therapeutic-monitoring endpoints in diseases that affect substantial populations with leading morbidities and mortality worldwide, including cardiovascular disease, metabolic syndrome, chronic obstructive pulmonary disease, neurological disorders, or cancer.

1.5. Innovative Drug Development

Introduction

The pharmaceutical industry has dramatically revolutionized global health outcomes. However, the introduction of innovative medicines has not kept pace with the increasing public health challenges. Medicines remain unavailable to many patients; moreover, almost half of all doctors are unable to fulfill their patients' requests due to the unavailability of efficient therapeutics. Low product diversity is another issue that plagues the pharmaceutical market. Despite advances in genomics and proteomics, the mechanistic elucidation and subsequent drug development of various disease-driven targets remain stagnant. Molecular-based drug design is often inefficient. Drugs targeted for a single disease or even a single interaction are often insufficient for treatment. This chapter discusses our vision for creating next-generation design, development, and manufacture for the pharmaceutical sector. The validation of drug therapy efficacy and potency can take several years and may fail beyond the research phase or after approval due to deleterious side effects on target or off-target tissues because of inadequate potency management, or due to lack of therapeutic efficacy during the patient treatment phase. While research is a key phase for both the private and public sectors, new policies and mechanisms are needed to redirect funding and speed delivery during early drug discovery, preclinical development, and clinical studies to rapidly develop the most effective medicines.

Design Challenges for New Pharmaceuticals: Designing Drug Therapies for Better Outcomes

Difficulties in molecular rational drug development often stem from the lack of sufficient target diversity for obtaining specificity for selective interaction with target proteins/pathways for combination therapies, adjuvant therapies, and next-generation personalized medicines/drugs including both modulatory and cellular reprogramming designed drug molecules. Developing better drugs for efficacy is best accomplished by integrating drugs that target multiple pathways involved in disease mechanism development, and/or by using drugs that exert either lower-off target tissue or higher on-target tissue exertion for better therapeutic index and higher barrier for drug resistance. The creation of multi-target drugs for drug development using rapid analytical methods and sampling from various in vitro assays and cellular systems allows comprehensive R&D knowledge to efficiently design and develop better drugs that the public and health practitioners require. Multi-target drugs also allow possible avoidance of chemical and structural forget in modified selective single-target drugs that induce redundancy via other pathways.

1.5.1. Targeted Therapies

The human body harbors more than 100 trillion cells, the vast majority of which are exposed to the same environment and interact with each other via common resources, such as blood circulation and lymphatic fluid. Phenotypically, the minefield of available cell types is exceptionally rich and diverse and yet composed of epithelial and endothelial cells, connective tissue cells, smooth muscle cells, neurons, macrophages, and lymphocytes. In organs and tissues most prone to non-infectious pathological changes, such as cancer, coronary artery disease, diabetes and its complications, osteoarthritis, and multiple sclerosis, the population of cells responsible for damage or repair are dispersed but occupy well-defined compartments that are in bidirectional communication via excreted factors found in body fluids and the local and systemic immune response. These communication networks help coordinate the activity of cells into functional clusters that define the disease outcome and these are palliated by numerous drugs with varying degrees of efficacy that have been developed for each disease.

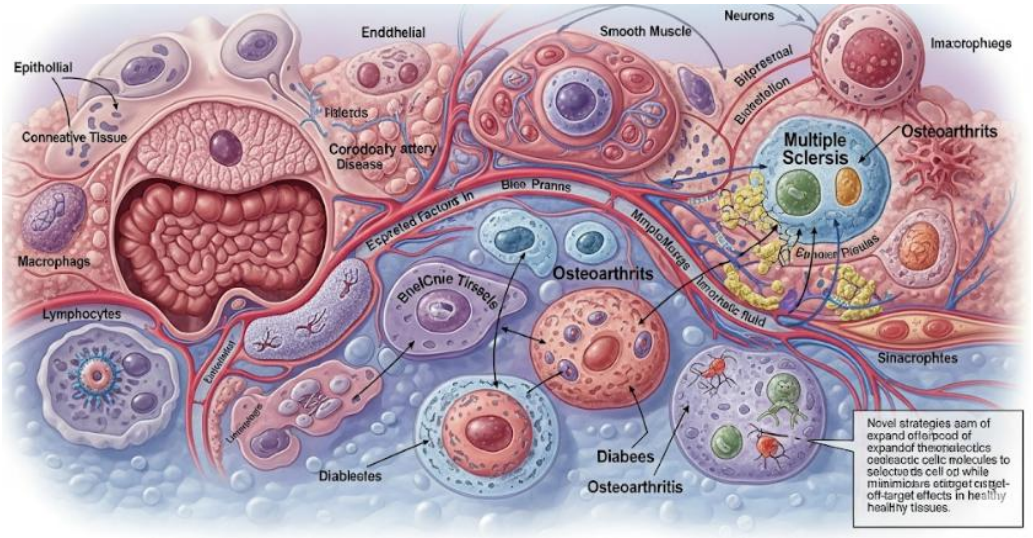

Fig 1 . 2 : Cellular Communication Networks: Orchestrating Disease Outcomes

However, the design of a medicine effective across the millions of healthy and diseased cellular clusters located in different organs and tissues may not induce the desired response and may produce life-threatening effects in some patients. Increasing the pool of available molecules to interact with a single, unique cellular cluster is cumbersome and time-consuming. Targeted therapies employ novel and optimized strategies to expand the pool of available therapeutic molecules. These strategies aim at developing drugs that act on the target cell cluster and minimize drug delivery to healthy tissue unaffected by disease-specific cells. This may increase the drug efficacy without any or

minimal side effects. Although conventional drug delivery systems employ varied techniques to promote the concentration of drugs in diseased organs, their biodistribution across dysfunctional and healthy tissue cells is widely variable, as evidenced in cancer therapy. Targeted drug delivery takes into account local cellular features that may promote selective drug action on diseased tissue cells and avoid off-target effects on healthy tissue cells.

1.5.2. Personalized Medicine

Personalized medicine is a new model involving each patient at the center of the clinical decision process. Personalized medicine may allow for a growing expansion of the classification of favorable responses to specific medicines. Personalization relies on the understanding of the molecular bases of the cellular function of therapeutic targets. The first step to reaching the goal of personalized medicine was the possibility of having non-invasive access to tumor tissue for a molecular study. This period was marked by a studious effort to test the possible predictive role of immune checkpoint inhibitors connected to tumor mutational burden, microsatellite instability, mismatch repair, and PD-L1 or PD-1 expression level, but also the efforts to investigate the possible role of other prognostic markers connected to the host immunity such as T-lymphocyte infiltration.

Efforts to study the heterogeneity of the tumor microenvironment and potential biomarkers in the bloodstream using liquid biopsy have participated in the rapid success of the field in terms of therapeutic implementation, thanks to ongoing and consecutive clinical trials in many different settings, such as neoadjuvant, adjuvant, or advanced disease. Unfortunately, the early clinical response is not sufficient to predict the long-term outcome and, in some cases, it is insufficient to predict the clinical efficacy in the different risk categories, defined as high or low. There were corrected false-positive signals that led to incorrect forward-backward comparisons and unconvincing results. Alongside the limitations in the study of predictive biomarkers, other confounders in the clinical setting are represented by the presence of secondary resistance mechanisms, resulting in the unfortunate evolution towards the progression of patients who have been addressed with the wrong-classified treatment after the early evaluation of the therapeutic response by imaging.

1.6. The Role of Artificial Intelligence in Healthcare

Artificial intelligence is already reshaping the healthcare field and will continue to do so in the coming decades. Potential applications of AI in healthcare abound. They include detection of disease from health information or images, prediction of health status,

predictive modeling of disease progression, drug discovery, diagnostics, disease prevention, personalized medicine, help with treatment choices, treatment delivery, and post-treatment monitoring for efficacy and safety. Many of these areas will have particular importance for innovation in disease prevention and treatment. AI tools allow the analysis and integration of complex, diverse data sets, from genomics to electronic medical records to mobile health applications, that facilitate fully understanding and addressing health problems in a patient or a population. For these reasons, AI already plays an important role, and will increasingly do so, in biomedicine throughout the product development process.

AI systems function by mimicking aspects of human intelligence. Indeed, a large part of the AI system's function is imitation. Supervised learning is the dominant form of training for deep learning systems, with human input provided at some stage to calibrate or refine the initial automated process. But AI machines are not simply functionally mimicking parts of human capability; they search through and learn from vast data sets, typically much larger than a human being could ever hope to process in a lifetime. This allows surprising results even in types of tasks where human intelligence is traditionally assumed to be superior: instant facial recognition in a crowd, defeating humans at games, automated text generation, or self-driving cars.

1.6.1. Data Analysis and Predictive Modeling

The field of healthcare collects vast amounts of data daily. Hospital systems store information on everything from electronic medical records, hospital admissions, lab test results, and discharge reports to outcomes of surgical procedures and treatments. That data can be used in predictive algorithms to assist healthcare providers in predicting which patients are at greater risk for medical issues, preventing readmissions and/or carefully managing disease states, and reducing long-term healthcare costs. Some large healthcare systems have developed advanced research facilities focused solely on the application of predictive analytics to all realms of patient care.

Insurance providers also collect enormous amounts of data related to treatment outcomes, utilization, and costs and have developed significant internal resources for predictive analytics. Solutions continue to evolve, enabling providers to assess patient risk scores, automate care plans, and manage community resources utilizing claims data to reduce costs. Insurance groups are taking a more active role in dictating how treatment plans are structured based on predictive analytics supported by claims data on what would be classified as best practices. Employers interested in lowering costs for employee health plans are utilizing outcomes and utilization information from insurance data to make more informed decisions on their providers, as well. Corporations are also seeking ways to couple insurance claims data with EMR data.

1.6.2. AI in Drug Discovery

The concept of artificial intelligence (AI) encompasses various computational tools and statistical approaches, including graphical models, heuristic search methods, kernel methods, machine learning, natural language processing, robotics, simulation, and time series modeling. AI serves as an umbrella term covering many diverse, yet related, disciplines. The ultimate goal of AI in the biomedical domain is to reproduce basic human cognitive functions, such as language understanding, common sense reasoning, planning, and learning. There is considerable public interest in the special case of using AI for conceptual reasoning, such as image understanding, speech interpretation, decision-making, and robotics. Interest is growing in using AI for drug discovery because of its proven success in automating certain conceptual reasoning tasks.

In addition, there are some unique differences between applying AI to drug discovery, as opposed to imitation or mimicking human cognition. Imitation or mimicry AI can be expected to achieve relatively high accuracy when a sufficient amount of data exists in the field to train the algorithm. In doing so, attempts are made to reproduce the brain activities of highly trained experts who possess sophisticated capabilities. This goes a long way toward accurately reproducing the mental model of cognition underlying the behavior. The focus in fields such as speech recognition, visual interpretation, translation, and text production is to create a highly accurate imitative or mimicry model, while in biomolecular candidate design for drug discovery, the objective is not necessarily the same. The exploration space is extreme, highly diverse, and often poorly characterized.

1.7. Biotechnology in Disease Prevention

Innovative approaches to disease prevention hold great promise for integrated control of infectious or non-communicable diseases in human populations. Such pioneering developments are of special importance at particular times of the year, when humans are more prone to infectious diseases, as the birth of pathogens is making itself noticed. But disease prevention can be envisaged all year round. However, special requests to biotechnological companies or research teams, supporting government policies for the promotion of vaccine development or preemptive gene-editing interventions, should be warranted. Vaccination programs, currently in the implementation phase, are based on virus-like particles or nanoparticle-embedded vaccine formulations that trigger the appropriate type of immune response, which is needed to efficiently neutralize viruses and eradicate infected host cells. Or they are intended to utilize infectious particles or attenuated viral vectors, carrying genes of efficient broadly protective vaccine antigen combinations, which will elicit strong and long-term immunity.

Each adenoviral vector, containing simultaneously two different vaccine genes, could elicit extremely potent anti-virus and anti-infected cell cellular-derived immune responses, which specifically neutralize flu viruses that undergo drastic antigenic changes, as well as destroy virus-infected cells through strong effector cytotoxic T cell activities. Integrated approaches of designing RNA complex nanocarriers for delivering predesigned RNA components of the system into skin cells, combining them with vectors, allowing for systems' repeated application, harboring recently developed systems with the smallest protein, enhance repeated use of predesigned units. Incorporation of anti-bleeding, pro-platelet effects of viral vectors displaying constructs improves the therapeutic efficacy of a combined dose.

1.7.1. Vaccination Innovations

Vaccination is probably one of the most performed, repeated, and exploited procedures. Our society as a whole has protected itself for more than three hundred years against a large variety of infections by vaccinating healthy people –mostly children- with great success. Its widespread adoption facilitated the eradication of smallpox and has significantly reduced several vaccine-preventable diseases. However, we need to recognize a disturbing fact: most of the current vaccines are based on a similar formula: an inactivated or attenuated germ, inactivated bacterial toxins, or vaccine germ-derived antigens administered together with adjuvants in order to boost the immune response. In real terms, over the years despite the enormous knowledge acquired in the immunology and microbiology fields, breakthroughs in vaccine technologies have been rather few. The recent, fast development of mRNA vaccines for COVID-19 opened the question: what opened the gate for rapid implementation of such drastic innovation? Why there has not been previously enough pressure for the development of other vaccine innovations? What implications does it have for the future of vaccines?

Moreover, recent vaccine failures against some important diseases, and the threat of various emerging and re-emerging infectious diseases, stimulate the search for innovative vaccine technology. Apart from a long-desired and long-awaited vaccine against acquired immunodeficiency syndrome, which will hopefully be developed soon, there are already calls for the creation of the so-called "universal influenza vaccine". There are more than 220 candidate HIV/AIDS vaccines in development and more than 30 in clinical evaluation. In this chapter, we present some new class vaccines based on new generating technologies. We will also briefly discuss some additional technologies, and application platforms that we hope will be used additionally for the development of some vaccine innovation.

1.7.2. Gene Editing Technologies

CRISPR, Cpf1, and other RNA-guided nucleases have revolutionized gene editing in all organisms, paving the way for new avenues in genome editing. Gene editing has entered a new phase of innovation following the progress that has been made in the biological tools, on the systems of scientific, ethical, regulatory, economic, and societal assessment and infrastructure that have been established to move the technologies forward, and the legitimacy gained by the pioneer applications in human embryos for both research and clinical objectives and in making designer plants and animals.

Triggered by the innovative gene editing tools, several new avenues of Gene Editing Science and Engineering (GESE) are opening for sustainable health and environmentally friendly bioeconomy. These include using gene editing for functional genomics, population genomics, phylogenomics, and transgenomics. The exploration of the functions of the numerous noncoding RNAs encoded in the genomes, long considered "junk," represents one of the most intriguing challenges of functional genomics. The population genomics of numerous species, including plants, animals, and medical pathogens, by using gene editing to deactivate many genomic loci in pools of genotypes from natural populations and identified by next-generation sequencing is a new challenge. The phylogenomics of microbes and complex plants and animals could be aided by optimizing the techniques to let the microbe, plants, and animals with particular edited traits adapt to specific niches more rapidly.

The power of gene editing can be augmented and engineered into existing biotechnologies, including directed evolution, synthetic biology, microbial and plant consortia, DNA nanotechnology, biocontainment strategies, and diagnostic and therapeutic technologies, among others. For directed evolution, the quantification of numerous traits and the development of genome-wide, saturating gene editing target libraries allow to isolating of the top-performing mutants for diversified directed evolution, an innovative conceptual advance.

1.8. Ethical Considerations in Biomedical Innovation

Although innovation can greatly improve human well-being, it must be context-sensitive and should bring new benefits to those whose medical needs are greatest. Biomedical innovation can also be incredibly expensive and time-consuming, and often, patients, health systems, and insurance companies will foot the bill. For this reason, the inclusion of diverse populations in research and innovation processes forms the bedrock of ethical biomedical innovation. Innovative solutions that do not take into account the population most likely to be affected are built on a shaky foundation. The saying that "the early bird catches the worm" is only half true. The second half is that "the early worm gets eaten."

Additionally, since the potential and consequences of biomedical innovations are so great, the scientific community must maintain a higher standard when investigating and publishing these results. As the saying goes, "With great power comes great responsibility." With research ethics boards, patient advocacy groups, and institutional guidelines, ethical oversight helps prevent the exploitation of marginalized communities and ensures that research has the potential to benefit future patients, particularly from similar groups where the data was initially collected. Furthermore, many current scientists want to ensure that their research benefits society, as a large percentage of cases already donate their medical data to help find cures. With the lines of ethics already blurred, peer reviews and disclosed conflicts of interest act as things to be considered when going through the publication process. However, these additional considerations are an added layer of scrutiny at the end of a long process. If we want to make sure the science we are reading is ethical throughout, the whole research process needs to be assessed and regulated.

1.8.1. Informed Consent

Informed consent is foundational to medical ethics. Implicitly contained within the ethical principle of respect for autonomy, informed consent recognizes that each person is owed the respect necessary to govern his or her own life. Recognition of the individual right to self-determination creates an obligation for the physician and any research investigator to provide all the information necessary for the patient or research subject to make a reasoned and voluntary decision regarding his or her medical treatment or any involvement in biomedical research. This chapter only provides a short overview. Informed consent also made sense in an era of traditional private medicine, where a physician treated a patient because that patient was sick and wanted treatment. Ideally, it means that the physician or researcher has, through the informed consent process, reached full agreement with the patient or research subject on the proposed treatment or research participation. Consent can be the beginning of a meaningful relationship between a researcher and research subject that offers significant benefits to both; however, sometimes consent-based agreements become meaningless.

The solution is not as simple as requiring more information. The informed consent process is very much a negotiation, one in which the researcher seeks permission to carry out a specific set of procedures. Within the domain of clinical trials, the more specific the negotiation, the clearer the boundaries for interpretation of the contract-like relationship. Many words have been used to describe elements of the consent procedure; what these words share is an attempt to describe a process in which subjects are informed about the details of the research activity in which they will (or may) be involved and how the activity pertains to them as individuals. Most importantly, such subjects are

educated about the risks and possible benefits of the research and the procedures that will be followed to protect them from adverse effects. It should also include a discussion about how subject autonomy will be preserved during the research and what recourse will be available if autonomy has been violated.

1.8.2. Equity in Healthcare Access

The second ethical consideration in biomedical innovation deals with equity in healthcare access. 95% of biomedical research funding in the United States comes from private sources; it is then not surprising that pharmaceutical companies prioritize high ROI and seek new models of monetization that make the most of private market incentives. Rapid advances in our understanding of human disease, and formidable technological advances allowing more rapid, less expensive, and more accurate methods of development and testing, along with scientific breakthroughs, offer the promise of a steady stream of new treatments. However, as the recent experience of the pandemic demonstrated, advanced marketplace capitalism can easily impede rapid access to much-needed medical products in a time of crisis. Although enormous investments by private capital led to astonishingly rapid, unprecedented vaccine products that halted the pandemic, these vaccines were only made widely available in the developing world three years after a frantic multinational public and private effort began. Drug and vaccine shortages, wildly inflated prices, and the intellectual property rights granted to the vaccine developers limited the widespread distribution of these lifesaving products.

Equity in healthcare access demands recognition of our shared humanity, of the moral imperative to address the healthcare needs of the poor and underrepresented populations. This moral requirement is undeniable in our relationships and reflected in our professional training. In our daily lives, we strive to be supportive, pleasant, and kind to all. In our professional lives, we are trained to treat all patients regardless of race, nationality, ethnicity, culture, gender, sexual orientation, or disability with dignity and respect. We are trained to provide medical care of the highest quality and to ensure effective communication with patients and caregivers from all backgrounds, using interpreters as needed.

1.9. Conclusion

The past century of advancements in biomedical science offers an unparalleled convergence of knowledge for unexplored translation into clinical applications for

disease prevention and treatment. Here, we have compiled the intellectual foundations to enable the next wave of biomedical innovation, incorporating insights from multiple

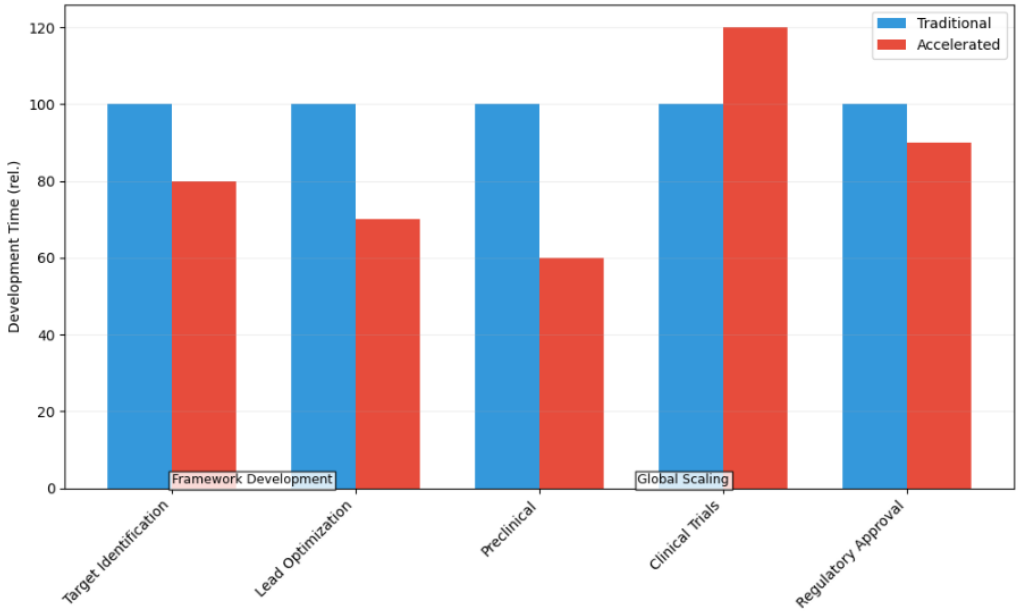

Fig 1 . 3 : Pipeline Stage Acceleration

previous historical eras of significant biomedical discovery and innovation into new integrated frameworks for optimizing product discovery and product-delivery pathway acceleration. By integrating the biological enthusiasm of the pre-modern period with the contextual insights of the modern age into novel human and technological resources, we present the Next-Generation Commitment and Scalable Commitment-Tech frameworks. These two, flexible biomedical innovation foundations offer enhanced pathways to innovative optimization of discovery and delivery pipelines for technical solutions for novel products capable of addressing the major outstanding health-promoting demands of the modern era, such as the global spread of communicable diseases and influence of noncommunicable diseases, such as diabetes, and dietary products characterized as “nutritionally unessential” overconsumption. These two new frameworks also proactively incorporate wider input and ethical queries based on the societal recognition of the major historical drivers of disparities in health outcomes across different regions of our interconnected globe, such as the respective roles of discrimination, nation and caste, and the power of corporate influence on the political process. Recent disruptive technological advances and societal demands for access to just healthcare solutions, especially for combating the spread of new pathogens, enable novel innovations for prevention, treatment, and mitigating the damages incurred during related crises.

1.9.1. Summary and Future Directions in Biomedical Innovation

The unending quest of mankind has always been the quest for a long healthy life. The ancients addressed health needs largely by trial and error, discovering useful herbs, roots, and minerals that brought health and cure. The application of science in disease prevention and treatment has gained importance as lifestyles have become more complex with rapid urbanization and high levels of pollution due to industrialization. Although ancient wisdom passed down through generations has a very important and reliable role in disease prevention and treatment, exploration through scientific observations, testing, development, validation, and application of these findings for the development of clinically efficient and safe drugs or methods have drawn a roadmap for the provision of biomedical innovation for the prevention and treatment of diseases. Biomedical innovations in disease therapy and prevention including drug discovery, vaccines, regenerative medicine, tissue engineering and stem cell therapies, gene and cell therapies, genetic discoveries and enhancements, nanomedicine, bioengineering, and biotechnology have evolved as separate areas maintaining a distance from each other based on individual uniqueness and challenges of the respective discovery, development and clinical application processes.

However, this distance has steadily reduced with the development of novel technologies that created bridges between biomedicine, nanotechnology, biotechnology, bioengineering, and information technology. Novel drug formulations prepared using nanotechnology can now be co-administered with vaccines to facilitate cellular internalization and initiate the vaccine process by stimulating the right immune response. Gene discovery research based on biotechnological products is the backbone of the clinical success of gene and cell therapies. Nanomedicine, Gene and Cell Therapies, Disease Biomarkers and Antibodies, Tissue Engineering and Bone Regeneration, MSC Therapies and Brain Diseases, Stem Cell Banking, Gene Therapy and Eye Diseases, CRISPR Technology and Genetic Disorders, Nanomedicine and Cancer, Brain Machine Interfaces and Neuroprosthesis, Gene Therapy and Infectious Diseases, Gene Delivery and CNS Disorders, Neurogenetics and Rare Diseases. Building resources both in terms of human expertise and technology will require coordinated funding both from the Government Sector as well as the Private Sector.

References

Vavassori, S., Russell, S., Scotti, C., & Benvenuti, S. (2024). Unlocking the full potential of rare disease drug development: Exploring the not-for-profit sector's contributions to drug development and access. Frontiers in Pharmacology, 15, 1441807. https://doi.org/10.3389/fphar.2024.1441807

Issa, N. T., Byers, S. W., & Dakshanamurthy, S. (2014). Big data: The next frontier for innovation in therapeutics and healthcare. Expert Review of Clinical Pharmacology, 7(3), 293–298. https://doi.org/10.1586/17512433.2014.905201

Manero, A., Crawford, K. E., Prock-Gibbs, H., Shah, N., Gandhi, D., & Coathup, M. J. (2022). Improving disease prevention, diagnosis, and treatment using novel bionic technologies. Bioengineering & Translational Medicine, 7(2), e10359. https://doi.org/10.1002/btm2.10359

Platt, R., Carnahan, R. M., Brown, J. S., Chrischilles, E., Curtis, L. H., Hennessy, S., Nelson, J. C., & Selby, J. V. (2015). The next frontier: Fostering innovation by improving health data access and utilization. Clinical Pharmacology & Therapeutics, 97(2), 151–153. https://doi.org/10.1002/cpt.191

Chien, S., Bashir, R., Nerem, R. M., & Pettigrew, R. (2015). Engineering as a new frontier for translational medicine. Science Translational Medicine, 7(281), 281fs13. https://doi.org/10.1126/scitranslmed.aaa4325