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A Review

Biopharmaceuticals and gene therapy: Redefining modern medicine

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Biopharmaceuticals, medicinal products derived from living organisms through advanced biotechnological methods, encompass recombinant proteins, monoclonal antibodies, vaccines, and nucleic acid-based therapies. Gene therapy, a transformative subset of biopharmaceuticals, involves the introduction of genetic material into cells to correct faulty or deficient genes, aiming to treat or prevent disease at its molecular origin. From January 2018 to June 2022, 196 new biopharmaceuticals were approved in the U.S. and/or EU, with monoclonal antibodies dominating the landscape. As of early 2025, the FDA has approved over 30 cell and gene therapies, and industry experts anticipate 30–50 additional approvals by 2030. Gene therapy approaches including gene addition, gene silencing, and genome editing employ viral vectors (AAVs, lentiviruses) and non-viral delivery systems. Clinical applications span genetic disorders, cancers, and infectious diseases, with CAR T-cell therapies and mRNA vaccines marking significant milestones. Despite this progress, high costs, immune responses, and long-term efficacy remain significant barriers. Future directions include AI-driven drug discovery, advanced delivery systems, and expanded manufacturing capabilities. Biopharmaceuticals and gene therapies are poised to redefine modern medicine by offering precise, personalized, and potentially curative treatments.

Keywords: Biopharmaceuticals, CRISPR-Cas9, Gene therapy, Monoclonal antibodies, Viral vectors

Introduction

The pharmaceutical industry has been fundamentally transformed by biopharmaceuticals, complex therapeutic agents produced through biological systems rather than traditional chemical synthesis[1]. These molecules, derived from living organisms such as microorganisms, plants, or animals, encompass a diverse range of therapeutic agents, including recombinant proteins, monoclonal antibodies, vaccines, and gene therapies[2]. The development of biopharmaceuticals involves a multifaceted approach, beginning with a deep understanding of the molecular mechanisms governing health and disease[3]. This knowledge is translated into the design and production of therapeutic proteins or nucleic acids that can modulate specific biological pathways, offering the potential to treat a wide array of diseases, including cancer, autoimmune disorders, and genetic deficiencies[4].

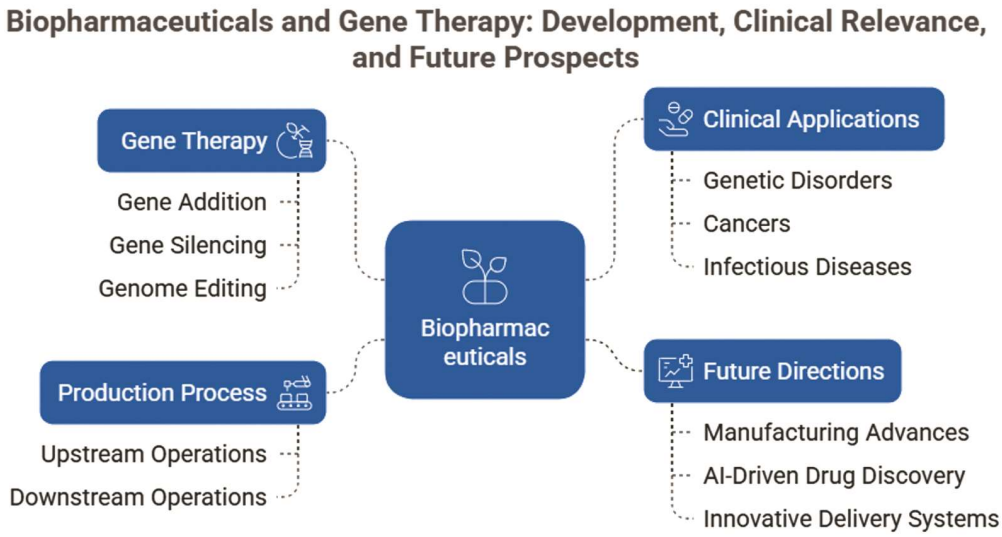
The advent of recombinant DNA technology has been instrumental in propelling biopharmaceutical development, enabling the mass production of therapeutic proteins that were once scarce or impossible to obtain[2]. New drug identification, separation, and characterization have been facilitated by methods including nuclear magnetic resonance, mass spectrometry, high performance liquid chromatography, and Raman spectroscopy[5].

Gene therapy, a subset of biopharmaceuticals, represents a paradigm shift in medicine by directly addressing the genetic roots of disease[6]. This innovative approach involves the introduction of genetic material into cells to compensate for defective genes, correct aberrant gene expression, or introduce new therapeutic genes[7]. Gene therapy holds immense promise for treating a wide spectrum of inherited and acquired diseases, ranging from monogenic disorders like cystic fibrosis and hemophilia to complex conditions such as cancer and neurodegenerative diseases[8]. Active clinical trials are underway targeting a variety of inherited and acquired disorders across different organ systems, showcasing the broad applicability of gene therapy[9]. Despite the remarkable progress, significant challenges remain in manufacturing complexity, regulatory hurdles, and cost considerations. Nevertheless, the potential of these innovative therapies to revolutionize healthcare is undeniable, driving continued research and development.

Biopharmaceuticals

Biopharmaceuticals represent a rapidly expanding field within the pharmaceutical industry, leveraging

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Graphical abstract

biological systems to produce therapeutic agents that address a wide range of diseases[10]. Biotechnology advancements including molecular biology, genetic engineering, and protein engineering have fueled the development of novel biopharmaceutical products[11]. The identification, isolation, and characterization of novel medications have been transformed by recombinant DNA technology, hybridoma technology, and polymerase chain reaction[5]. These technological advancements have enabled the production of complex molecules that were previously difficult or impossible to synthesize using traditional chemical methods[4] (Fig. 1).

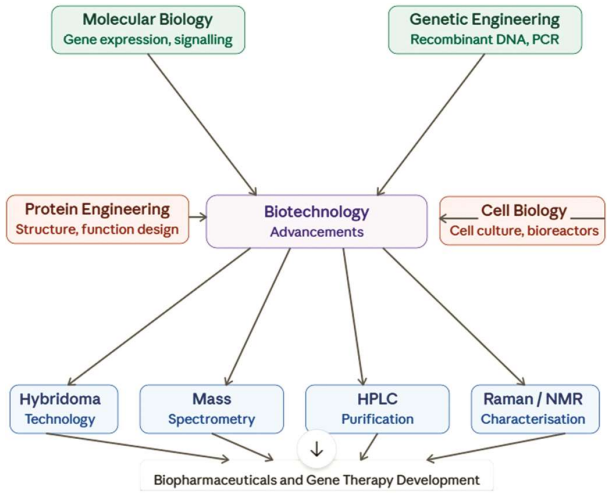


Fig. 1 — Foundational pillars and technologies for the development of biopharmaceuticals and gene therapy process

Recombinant proteins

Recombinant proteins are produced by introducing foreign genes into host cells such as bacteria, yeast, or mammalian cells which then synthesize the desired protein[2]. Mammalian and microbial culture systems have become popular for protein expression[12]. Early examples include insulin, erythropoietin, and growth hormone, all of which transformed the treatment of previously difficult to manage conditions. Recombinant DNA technology enables the precise engineering of host genomes to optimize yield, reduce immunogenicity, and facilitate post-translational modifications essential for therapeutic efficacy.

Monoclonal antibodies

Monoclonal antibodies are highly specific antibodies that target defined antigens, offering precise therapeutic intervention in oncology, autoimmune diseases, and infectious conditions. Their production, typically in Chinese hamster ovary (CHO) cells, allows for reproducible large scale manufacturing. Advances in antibody engineering have given rise to bispecific antibodies, antibody drug conjugates, and fragment based therapies that extend therapeutic versatility.

Nucleic acid-based therapeutics

Nucleic acid-based therapeutics including antisense oligonucleotides, siRNA, and mRNA therapeutics have emerged as promising modalities for treating diseases by targeting gene expression[13]. The success of mRNA vaccines against COVID-19 has catalyzed significant interest in this platform, with applications now

extending to cancer immunotherapy and rare genetic disorders[14]. RNA based therapies offer a flexible platform for targeting either proteins or nucleic acids, representing a shift from single mechanism to comprehensive therapeutic approaches[15].

Cell-based therapies

Cell-based therapies employ living cells often genetically engineered to replace or repair damaged organs or tissues. CAR-T cell therapies, which reprogram a patient's own immune cells to recognize and destroy cancer cells, have produced unprecedented remission rates in specific hematologic malignancies. Synthetic biology further expands this field, enabling biocomputing, therapeutic genome editing, and living biotherapeutics[16].

Production process

The production of biopharmaceuticals involves intricate processes requiring expertise in cell culture, genetic engineering, purification, and formulation[2,12]. The multistep process encompasses understanding molecular mechanisms, synthesis and purification, evaluating product stability and immunogenicity, and clinical trials[3]. These complex molecular structures require significant time to produce, regulate, and test analytically[17].

Upstream processing entails carefully regulating the culture of genetically modified cells in bioreactors. The appropriate cell line must be chosen, and culture parameters including temperature, pH, oxygen levels, and nutrient supply must be optimized to maximize product yield and quality. Scale up from laboratory to industrial production presents significant engineering challenges, including maintaining cell viability and ensuring effective mass transfer[18].

Downstream processing involves a series of purification steps to isolate the desired product from the complex mixture of cellular components and process related impurities. Chromatographic techniques such as affinity chromatography, ion exchange chromatography, and size exclusion chromatography are frequently used[19]. Membrane filtration processes, including ultrafiltration and diafiltration, are utilized to remove contaminants, concentrate the product, and exchange buffers. Approximately 60–80% of total manufacturing costs are frequently attributed to downstream processing[20].

Following purification, the biopharmaceutical product undergoes formulation to ensure stability, efficacy, and appropriate delivery. Lyophilization (freeze drying) is commonly used to improve the stability of protein-based biopharmaceuticals. Strict quality control procedures are required at every stage, including assays for identity, purity, potency, and stability. Process Analytical Technology is increasingly employed to monitor critical process parameters in real time, ensuring consistent product quality and adherence to Good Manufacturing Practice (GMP) (Fig. 2).

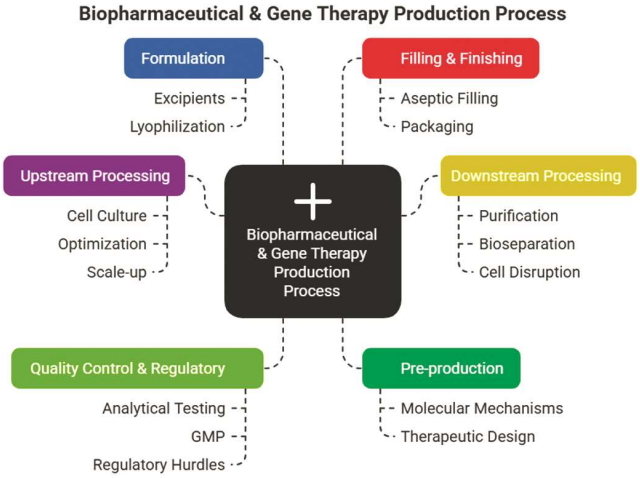


Fig. 2 — Biopharmaceuticals & gene therapy production process

Recent approvals and trends

The biopharmaceutical sector has witnessed considerable expansion and innovation, revolutionizing the treatment landscape for a spectrum of diseases[21]. From January 2018 to June 2022, 196 new biopharmaceuticals were approved in the U.S. and/or EU, with gene and cell therapies representing a growing share. As of early 2025, the FDA has approved over 30 cell and gene therapies, and industry experts anticipate 30–50 additional approvals by 2030.

Several noteworthy trends are shaping the future of biopharmaceuticals. The growing emphasis on precision medicine customizing treatments based on the unique genetic profiles of each patient is particularly notable[22]. CRISPR-Cas9 technology has revolutionized gene editing by enabling precise targeting of specific DNA sequences within the genome[23]. Concurrently, there is increasing interest in non-viral delivery systems including lipid nanoparticles and exosomes as these offer advantages in safety and immunogenicity compared to viral vectors[24].

Gene therapy

Gene therapy, a leading branch of biopharmaceuticals, has emerged as a revolutionary approach for transforming the treatment of genetic disorders, acquired diseases, and certain cancers[25]. Gene therapy places functional genes into cells to replace dysfunctional sequences or to produce a desired protein[26]. The field has witnessed substantial advancements driven by innovations in vector technology, gene editing tools, and a deeper understanding of gene regulation[27]. The first clinical trials were conducted in 1990, and the process involves identifying the correct DNA sequences and cell types, then creating effective delivery methods[28].

Gene therapy is delivered either *in vivo* (directly into the body) or *ex vivo* (cells manipulated outside the body and transplanted back). Viral vectors including lentiviruses, adeno associated viruses (AAVs), and adenoviruses are the most commonly used delivery vehicles due to their efficient cell transduction[5]. Non-viral techniques such as lipid nanoparticles and electroporation are gaining traction, particularly for their reduced immunogenicity and ease of manufacturing[5]. After administration, the therapeutic gene expresses a desired protein, which can restore normal cellular function, target cancer cells, or stimulate an immune response (Fig. 3).

Principles and mechanisms

The primary concept of gene therapy involves injecting genetic material into target cells or tissues to produce a therapeutic effect[29]. It is accomplished through various strategies, including gene augmentation, correction, silencing, and editing[30]. Gene augmentation transfers a functional gene copy into patient cells when a loss of function mutation causes disease, thereby restoring normal function[28]. Gene correction seeks to directly rectify the mutated gene within the cell[31]. Gene silencing suppresses expression of a disease-causing gene, particularly when the abnormal gene product is toxic[32]. Gene editing, using tools such as CRISPR-Cas9, enables precise, targeted modifications to genomic DNA sequences[23].

Vectors for gene delivery

The safe and efficient delivery of therapeutic genes to target cells is a crucial aspect of gene therapy[5]. Adeno-associated viral (AAV) vectors have become especially promising due to their broad tropism,

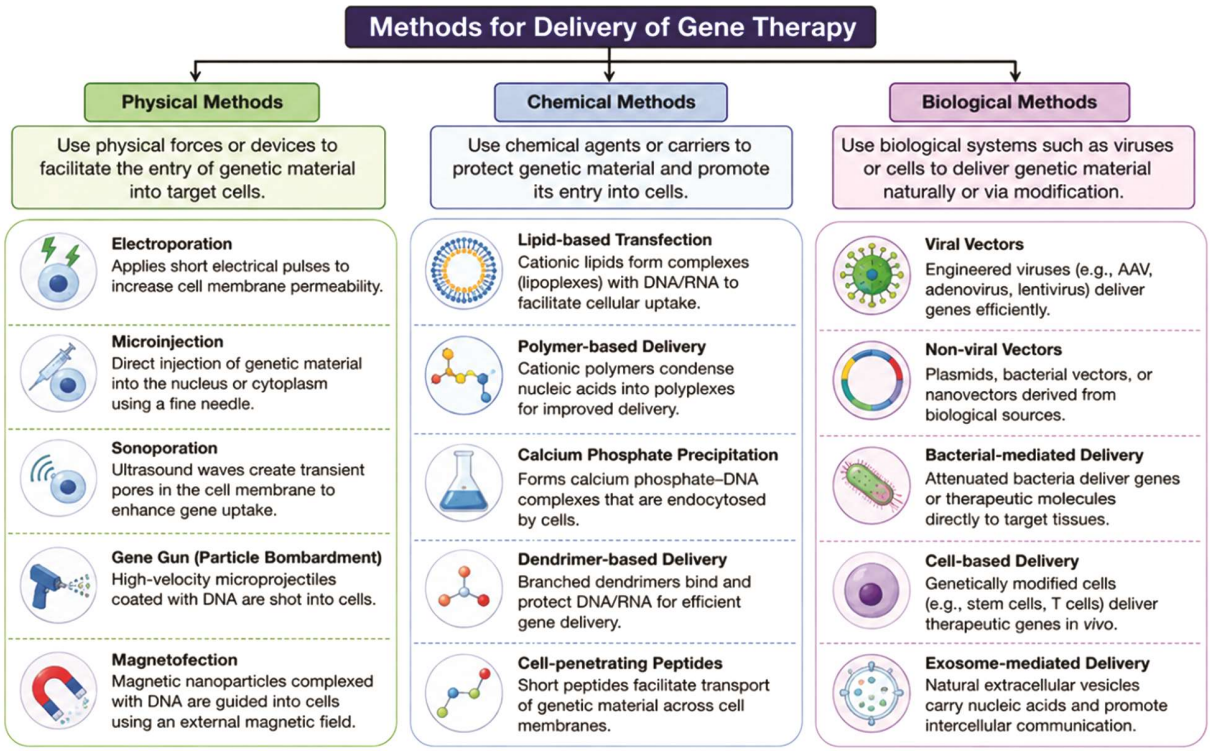


Fig. 3 — Transfection methods of gene transfer. Methods are categorized into: (1) Physical methods: Electroporation, Microinjection, Sonoporation, Magnetofection, Biolistic (gene gun); (2) Chemical methods: Liposomes, Lipid nanoparticles, Calcium phosphate precipitation, cationic polymers; (3) Biological Methods: Viral vectors

minimal immunogenicity, and capacity to drive long-term gene expression[9]. Lentiviral vectors can transduce both proliferating and non-dividing cells, making them appropriate for gene therapy across diverse tissues and organs[33]. Adenoviral vectors, though highly efficient, can elicit significant immune responses; moreover, variable coxsackie-adenovirus receptor expression across tumor types may confer resistance[34].

Non-viral vectors including plasmids, liposomes, and nanoparticles offer advantages of ease of production, low immunogenicity, and the ability to transport large DNA inserts[35]. The selection of a suitable vector depends on the therapeutic gene's size, target cell type, intended duration of gene expression, and immunogenicity potential.

Mechanisms of gene transfer

Different vector types result in different processes of gene transfer. Viral vectors typically enter cells by receptor-mediated endocytosis or direct membrane fusion, releasing their genetic cargo into the cytoplasm and subsequently the nucleus for transcription and translation[36]. Integrating viral vectors, such as lentiviruses, incorporate the therapeutic gene into the host genome, enabling long-term transgenic expression (Fig. 4). Non-viral vectors rely on endocytosis or direct injection, and various strategies including electroporation, sonoporation, and magnetofection have been explored to enhance cellular uptake of DNA[37].

Approved products

Significant advancements in gene-addition strategies and gene editing techniques have been successfully translated to therapeutic applications[23]. A number of gene therapy products have received regulatory approval, marking significant milestones and offering new hope to patients with previously untreatable genetic diseases. The following table summarizes key approved gene therapy products, their type, therapeutic target, and clinical uses (Table 1).

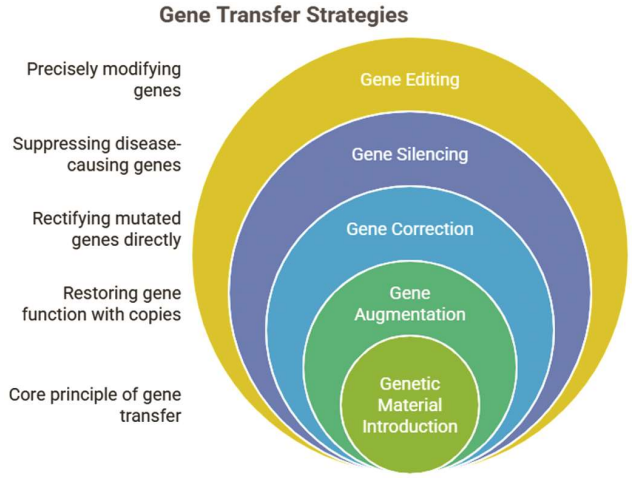


Fig. 4 — Schematic representation of mechanism of gene transfer

Introduction of CRISPR/Cas gene editing technologies, mRNA biotherapeutics, and antisense oligonucleotide medicines has transformed disease treatment. Cells can be taken from the patient, genetically altered in a laboratory, and reintroduced as part of *ex vivo* gene therapy[38]. *In vivo* gene therapy, by contrast, delivers the therapeutic gene directly into the patient's body, typically via systemic or local administration.

Clinical applications and challenges

The therapeutic uses of gene therapy have grown significantly due to advances in vector technology, gene editing tools, and improved understanding of disease pathogenesis[31]. Many clinical trials are currently assessing gene therapy techniques for a wide range of diseases, including infectious diseases, malignancies, ophthalmologic conditions, neurological disorders, and inherited blood abnormalities[9]. The eye is a particularly attractive target due to its immune-privileged status, requiring minimal vector dosages[32]. The skin is another attractive target due to its accessibility[35].

Notable clinical successes include the complete transformation of treatment for severe combined immunodeficiency (SCID, known as 'bubble boy disease') through gene correction of the underlying immune deficiency, and impressive outcomes in spinal muscular atrophy with gene therapy. In oncology, CAR T-cell therapies have achieved unprecedented remission rates in specific leukemia and lymphoma subtypes. CRISPR-Cas9 systems have been effectively applied to inherited blood diseases such as sickle cell anemia[39].

Primary challenges include development of safe and efficient gene delivery vectors[5]. Viral vectors can trigger immune responses or have limited packaging capacity[40]. Non-viral vectors may have lower transfection efficiency (Fig. 5). High cost of gene therapy products remains a major accessibility barrier, particularly in low-resource settings. Long-term safety, including insertional mutagenesis and off-target effects, must be carefully monitored. Equitable access requires collaborative efforts from governments, regulatory agencies, and pharmaceutical companies[41].

Table 1 — FDA/EMA-Approved Gene Therapy Products

Product (Generic Name)	Type of Product	Therapeutic Target	Uses / Indication
Luxturna (voretigene neparvovec)	AAV2-mediated gene addition	RPE65 gene mutation	Inherited retinal dystrophy (Leber congenital amaurosis type 2)
Zolgensma (onasemnogene abeparvovec)	AAV9-mediated gene addition	SMN1 gene	Spinal muscular atrophy (SMA Type 1)
Kymriah (tisagenlecleucel)	CAR T-cell (lentiviral vector)	CD19 antigen	B-cell ALL, DLBCL
Yescarta (axicabtagene ciloleucel)	CAR T-cell (retroviral vector)	CD19 antigen	Large B-cell lymphoma
Tecartus (brexucabtagene autoleucel)	CAR T-cell (retroviral vector)	CD19 antigen	Mantle cell lymphoma, B-cell ALL
Breyanzi (lisocabtagene maraleucel)	CAR T-cell (lentiviral vector)	CD19 antigen	Large B-cell lymphoma
Abecma (idecabtagene vicleucel)	CAR T-cell (lentiviral vector)	BCMA antigen	Relapsed/refractory multiple myeloma
Carvykti (ciltacabtagene autoleucel)	CAR T-cell (lentiviral vector)	BCMA antigen	Multiple myeloma
Skysona (elivaldogene autotemcel)	Lentiviral vector (ex vivo)	ABCD1 gene (hematopoietic stem cells)	Cerebral adrenoleukodystrophy
Zynteglo (betibeglogene autotemcel)	Lentiviral vector (ex vivo)	HBB gene (hematopoietic stem cells)	Beta-thalassemia
Hemgenix (etranacogene dezaparvovec)	AAV5-mediated gene addition	FIX gene	Hemophilia B
Elevidys (delandistrogene moxeparvovec)	AAV rh74 gene addition	Micro-dystrophin gene	Duchenne muscular dystrophy
Casgevy (exagamglogene autotemcel)	CRISPR-Cas9 gene editing (ex vivo)	BCL11A enhancer in HSCs	Sickle cell disease, Beta-thalassemia
Lyfgenia (lovotibeglogene autotemcel)	Lentiviral vector (ex vivo)	HBB gene (HSCs)	Sickle cell disease

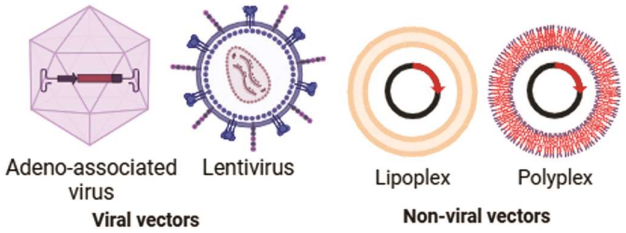


Fig. 5 — Types of viral and non-viral vectors

Future directions

Biopharmaceuticals and gene therapies hold immense promise for treating diseases that were previously incurable[2]. The future of medicine will likely depend on gene products and peptide and protein therapeutics because of their highly specific bioactivity[42]. Several key directions are shaping next-generation development.

CRISPR-Cas9 represents perhaps the most exciting advance in gene therapy, enabling precise and targeted changes to DNA sequences with simplicity, efficacy, and versatility[43]. Preclinical and clinical research has already demonstrated promising results in cancer, infectious diseases, and inherited genetic disorders. Ongoing efforts are focused on increasing specificity through modified guide RNAs and high-fidelity Cas9 variants, as well as improving delivery of CRISPR components via both viral and non-viral systems[44] (Fig.6).

RNA-based therapeutics have experienced significant growth, catalyzed by the licensing of antisense medications for rare diseases and the efficacy of mRNA vaccines against COVID-19[14]. These developments have demonstrated the potential of mRNA platforms for cancer immunotherapy, rare genetic disorders, and infectious diseases. Interest in RNA as a therapeutic molecule continues to accelerate, with novel delivery systems expanding clinical applicability[45].

Artificial intelligence (AI) and machine learning are increasingly being applied to drug discovery, biomarker identification, and personalized medicine frameworks[22]. Non-viral delivery systems, including lipid nanoparticles, exosomes, and engineered bacteria actively targeting tumors, are being refined to improve safety profiles and delivery efficiency[24]. Streamlining manufacturing processes to reduce costs will be essential for improving global access to these therapies.

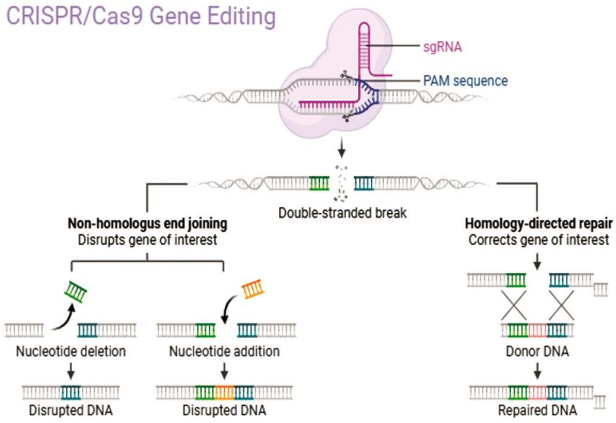


Fig. 6 — Mechanism of CRISPR/Cas9 gene editing

Conclusion

Biopharmaceuticals and gene therapy have emerged as pivotal innovations in modern therapeutics, offering targeted interventions for complex and previously untreatable diseases. This review highlights the evolution of biopharmaceutical modalities including recombinant proteins, monoclonal antibodies, and RNA-based therapeutics and underscores gene therapy's potential in addressing genetic, oncologic, and infectious disorders. Advances in upstream and downstream processing, vector engineering, and formulation strategies have enhanced product efficacy and safety, though challenges in cost, scalability, and long-term outcomes persist.

Future directions point toward integration with artificial intelligence, CRISPR-Cas systems, and non-viral delivery platforms to improve precision, reduce immunogenicity, and expand clinical applicability. Continued research into vector optimization, regulatory harmonization, and equitable access will be essential to realize the full potential of these therapies. The convergence of biopharmaceuticals with personalized medicine frameworks is expected to redefine treatment paradigms, offering curative prospects and improved patient outcomes.

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Conflict of interest

All authors declare no conflict of interest.

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