CRISPR-Based Therapeutics: Molecular Mechanisms of Gene-Targeted Drug Action

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***Abstract*—CRISPR-based therapeutics represent a transformative advancement in molecular medicine by enabling precise, programmable modification of genomic sequences for the treatment of genetic and acquired diseases. Unlike conventional pharmacological interventions that primarily modulate protein function, CRISPR technologies directly target the underlying genetic determinants of pathology, offering the potential for durable or permanent therapeutic effects. This paper examines the molecular mechanisms of CRISPR-mediated gene-targeted drug action, focusing on DNA recognition, cleavage, repair pathways, and emerging gene-editing modalities such as base editing and prime editing. By synthesizing developments in genome engineering, delivery systems, and off-target mitigation strategies, the study evaluates the clinical promise and technical limitations of CRISPR-based interventions. The findings underscore the growing role of gene-editing therapeutics in precision medicine while highlighting ethical, regulatory, and safety considerations that accompany their translational deployment.**

Advances in molecular biology and genomics have progressively shifted the focus of modern medicine from symptomatic treatment toward interventions that address the genetic origins of disease [9]. Among the most significant breakthroughs in this transition is the development of CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)–based genome editing technologies. Initially discovered as a bacterial adaptive immune mechanism, CRISPR systems have been repurposed into versatile tools for precise manipulation of genetic material [2]. Their emergence has fundamentally altered the therapeutic landscape by enabling direct modification of DNA sequences associated with inherited disorders, cancer, and infectious diseases.

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Traditional drug development has largely centered on small molecules and biologics that influence cellular pathways indirectly by interacting with proteins. While these approaches have yielded substantial clinical success, they are often limited by transient effects, drug resistance, and off-target toxicity [8]. CRISPR-based therapeutics introduce a distinct paradigm in which the therapeutic agent acts at the genomic level, potentially correcting pathogenic mutations or modulating gene expression with long-lasting consequences. This shift from protein-centric pharmacology to gene-targeted intervention marks a conceptual evolution in how diseases are understood and treated [10].

At the molecular level, CRISPR-mediated gene editing operates through a programmable nuclease system guided by RNA sequences complementary to target DNA regions. The most widely studied CRISPR-associated protein, Cas9, induces site-specific double-strand breaks that activate endogenous DNA repair mechanisms, primarily non-homologous end joining and homology-directed repair [7]. These repair pathways enable gene disruption, insertion, or correction, depending on the therapeutic objective. Subsequent innovations—including base editing and prime editing—have expanded the precision and versatility of CRISPR technologies by allowing targeted nucleotide substitutions without introducing double-strand breaks, thereby reducing the risk of unintended genomic alterations [1].

The therapeutic potential of CRISPR extends across diverse medical domains. In monogenic disorders, gene editing offers the possibility of permanent correction of disease-causing mutations [4]. In oncology, CRISPR-based approaches are being explored to enhance immune cell targeting of tumors and to investigate tumor-specific genetic vulnerabilities. Infectious disease research has also leveraged CRISPR tools to disrupt viral genomes or engineer host resistance [5]. These applications illustrate the broad adaptability of CRISPR technologies as both therapeutic agents and investigative instruments in biomedical research.

Despite its promise, CRISPR-based therapy is accompanied by significant scientific and ethical challenges. Off-target effects, immune responses to delivery vectors, and limitations in tissue-specific targeting remain active areas of investigation [3]. Furthermore, the prospect of heritable genome modification raises complex ethical and regulatory questions regarding the boundaries of therapeutic intervention. Balancing innovation with safety and societal responsibility is therefore essential for the responsible advancement of gene-editing medicine [6].

This paper explores the molecular mechanisms underlying CRISPR-based therapeutics, emphasizing how programmable gene-editing systems function as targeted drug modalities at the genomic level. By reviewing the biochemical processes of DNA recognition, cleavage, and repair, as well as emerging editing technologies and delivery strategies, the study situates CRISPR within the broader framework of precision medicine. Ultimately, CRISPR-based therapeutics exemplify a shift toward interventions that do not merely treat disease symptoms but aim to rewrite the genetic scripts that give rise to them, redefining the possibilities of modern pharmacological science.

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