Innovations in Pharmacy Planet (iP-Planet)
eISSN: 2348 – 7275

Review

CRISPR-Cas9 in Drug Discovery: Potential Applications and Ethical Considerations

Ashwani Dhingra
Principal, Global Research Institute of Pharmacy,
Yamuna Nagar, Haryana- 135133.

Abstract
CRISPR-Cas9, a groundbreaking genome-editing technology, has revolutionized genetic research and holds immense potential in drug discovery. This review article explores the various applications of CRISPR-Cas9 in drug development, ranging from disease model creation to the identification of novel therapeutic targets. Additionally, the ethical challenges and considerations that arise with its use in drug discovery are discussed. As this technology continues to evolve, it is crucial for scientists, clinicians, and policymakers to address these ethical dilemmas while maximizing the benefits of CRISPR-Cas9 in advancing medical therapeutics.

Keywords: CRISPR-Cas9, Drug Discovery, Potential Applications

Corresponding Author: Mr. Ashwani Dhingra, Principal, Global Research Institute of Pharmacy, Yamuna Nagar, Haryana- 135133
Mail Id- ashwani1683@gmail.com

Introduction

The development of new drugs has traditionally relied on understanding the underlying genetic causes of diseases, and the subsequent identification of targets for therapeutic intervention. The advent of CRISPR-Cas9 technology has dramatically accelerated this process by allowing precise modifications to DNA with unparalleled efficiency and specificity. This technology has already shown transformative potential in both basic and applied sciences, including drug discovery. However, its power raises significant ethical concerns that must be considered in its integration into the clinical and pharmaceutical settings. [1]

Overview of CRISPR-Cas9 Technology

CRISPR-Cas9 was first discovered as a defense mechanism in bacteria, but it has since been harnessed as a genome-editing tool. The system consists of two main components: the Cas9 protein, which acts as molecular scissors to cut DNA, and a guide RNA (gRNA), which directs the Cas9 protein to a specific region of the genome. By exploiting this technology, researchers can induce specific genetic changes, such as gene knockouts, insertions, and corrections, in a variety of organisms, including humans. [2]

Potential Applications of CRISPR-Cas9 in Drug Discovery

Disease Modelling

One of the most significant applications of CRISPR-Cas9 in drug discovery is the creation of genetically modified disease models. Traditional animal models often fail to recapitulate human diseases accurately. CRISPR-Cas9 allows researchers to generate animal models with precise mutations that mimic human genetic disorders, providing a better platform for understanding disease mechanisms and testing potential therapies. For instance, models of neurodegenerative diseases, such as Alzheimer's and Parkinson's, have been generated, enabling researchers to study the progression of these diseases and identify therapeutic targets. [3]

Target Identification and Validation

Target identification is a critical step in drug discovery. CRISPR-Cas9 facilitates the

identification of potential drug targets by enabling researchers to systematically knock out genes and assess the resulting phenotype. This "loss-of-function" approach allows the discovery of genes that are critical for disease progression and could serve as therapeutic targets. Furthermore, CRISPR-Cas9 can be used to validate these targets by creating gene knockouts in cell lines or animal models, confirming their role in disease and providing evidence for their therapeutic potential. [4]

High-Throughput Screening

High-throughput screening (HTS) is a common method for identifying small molecules that can modulate a particular target. CRISPR-Cas9 can be integrated into HTS platforms to create knockout libraries of genes, which can then be screened for phenotypic changes in response to drug treatment. This approach allows for more comprehensive screening, as it can identify not only molecules that affect a specific target but also those that modulate previously unknown pathways. This can open up new avenues for drug discovery, especially for complex diseases where many factors contribute to the pathology. [5]

Gene Therapy

CRISPR-Cas9 holds great promise for gene therapy, particularly in the context of treating genetic disorders. By directly editing the genes responsible for diseases such as cystic fibrosis, sickle cell anemia, and Duchenne muscular dystrophy, CRISPR-Cas9 could offer a permanent solution to these debilitating conditions. Clinical trials are already underway to test CRISPR-based gene therapies, demonstrating its potential to treat genetic diseases at their root cause rather than merely managing symptoms. [6]

Ethical Considerations in CRISPR-Cas9 Drug Discovery

While the potential benefits of CRISPR-Cas9 in drug discovery are vast, there are important ethical considerations that need to be addressed. [7]

Germline Editing and Heritable Changes

One of the most controversial aspects of CRISPR-Cas9 technology is its ability to edit the human germline (sperm, eggs, or embryos), leading to heritable genetic changes. Editing the germline raises concerns about unintended long-term consequences, including off-target effects that could have unforeseen health implications for future generations. In addition, there is the risk of "designer babies," where genetic modifications could be made to enhance traits such as intelligence, physical appearance, or athletic ability. This could exacerbate social inequalities and create ethical dilemmas regarding human rights and genetic diversity. [8]

Off-Target Effects and Precision

Despite its precision, CRISPR-Cas9 is not without its risks. Off-target mutations, where the Cas9 protein cuts unintended sites in the genome, can occur. These mutations could lead to harmful effects, including cancer or other diseases. As CRISPR technology continues to improve, it is crucial that the risks of off-target effects are minimized and thoroughly assessed in drug discovery and gene therapy applications. [9]

Access and Equity

As with many groundbreaking technologies, there are concerns about access to CRISPR-based therapies. These therapies are costly and may only be available to wealthy individuals or developed nations, further widening the gap between socioeconomic groups. In the context of drug discovery, it is essential to ensure that the benefits of CRISPR-Cas9 are equitably distributed and accessible to all populations, especially for those with rare or neglected diseases. [10]

Environmental and Ecological Impact

The use of CRISPR-Cas9 to modify organisms, including plants and animals, could have unintended ecological consequences. For example, genetically modified organisms (GMOs) could disrupt local ecosystems if they are released into the wild. While this is primarily a concern for agriculture and environmental conservation, it could also have implications for drug discovery, particularly if modified organisms are used in drug production or as part of large-scale disease modeling efforts. [11]

Conclusion

CRISPR-Cas9 technology holds immense promise in revolutionizing drug discovery, offering new avenues for disease modeling, target identification, drug screening, and gene therapy. Its ability to make precise genetic alterations opens up possibilities for creating more accurate models of disease, identifying novel drug targets, and developing therapies for previously untreatable genetic disorders. However, as with any powerful technology,

there are significant ethical challenges that must be addressed. These include concerns over germline editing, off-target effects, equitable access, and potential environmental impacts. To fully realize the potential of CRISPR-Cas9 in drug discovery, these ethical considerations must be thoughtfully managed, ensuring that the technology is used responsibly and for the greater good of society.

References

1. Katsila T, Spyroulias GA, Patrinos GP, Matsoukas MT. Computational approaches in target identification and drug discovery. Computational and structural biotechnology journal. 2016 Jan 1;14:177-84.
2. Pope SM. Impact of gene editing tools, like CRISPR/Cas9, on the public health response to disease outbreaks. Disaster medicine and public health preparedness. 2017 Apr;11(2):155-9.
3. Martinez-Lage M, Torres-Ruiz R, Rodriguez-Perales S. CRISPR/Cas9 technology: applications and human disease modeling. Progress in molecular biology and translational science. 2017 Jan 1;152:23-48.
4. Lu Q, Livi GP, Modha S, Yusa K, Macarrón R, Dow DJ. Applications of CRISPR genome editing technology in drug target identification and validation. Expert opinion on drug discovery. 2017 Jun 3;12(6):541-52.
5. Lo CH, Vunnam N, Lewis AK, Chiu TL, Brummel BE, Schaaf TM, Grant BD, Bawaskar P, Thomas DD, Sachs JN. An innovative high-throughput screening approach for discovery of small molecules that inhibit TNF receptors. SLAS DISCOVERY: Advancing Life Sciences R&D. 2017 Sep;22(8):950-61.
6. Khan FA, Pandupuspitasari NS, Chun-Jie H, Ao Z, Jamal M, Zohaib A, Khan FA, Hakim MR, ShuJun Z. CRISPR/Cas9 therapeutics: a cure for cancer and other genetic diseases. Oncotarget. 2016 May 26;7(32):52541.
7. Baumann M. CRISPR/Cas9 genome editing–new and old ethical issues arising from a revolutionary technology. NanoEthics. 2016 Aug;10:139-59.
8. de Araujo M. Editing the Genome of Human Being: CRISPR-Cas9 and the Ethics of Genetic Enhancement. Journal of Ethics and Emerging Technologies. 2017 Jul 1;27(1):24-42.
9. Zischewski J, Fischer R, Bortesi L. Detection of on-target and off-target mutations generated by CRISPR/Cas9 and other sequence-specific nucleases. Biotechnology advances. 2017 Jan 1;35(1):95-104.
10. Fellmann C, Gowen BG, Lin PC, Doudna JA, Corn JE. Cornerstones of CRISPR–Cas in drug discovery and therapy. Nature reviews Drug discovery. 2017 Feb;16(2):89-100.
11. Bortesi L, Zhu C, Zischewski J, Perez L, Bassié L, Nadi R, Forni G, Lade SB, Soto E, Jin X, Medina V. Patterns of CRISPR/Cas9 activity in plants, animals and microbes. Plant biotechnology journal. 2016 Dec;14(12):2203-16

