

CRISPR-Based Cell Line Engineering: Revolutionizing Biomanufacturing and Research

Introduction

CRISPR-based cell line engineering has transformed the way scientists modify and optimize cells for research and biomanufacturing applications. Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) technology, combined with CRISPR-associated (Cas) enzymes, enables precise, efficient, and targeted genome editing. Compared to traditional genetic engineering methods, CRISPR offers greater accuracy, reduced development timelines, and enhanced scalability [1,2]. These advantages have made it a powerful tool for developing high-performance cell lines used in biologics production, gene therapy, and functional genomics.

Discussion

The CRISPR-Cas system functions by introducing site-specific double-strand breaks in DNA, guided by a customizable RNA sequence. Cellular repair mechanisms, such as non-homologous end joining or homology-directed repair, are then exploited to introduce targeted gene knockouts, insertions, or modifications. In cell line engineering, this capability is used to enhance productivity, improve product quality, and increase process robustness.

In biopharmaceutical manufacturing, CRISPR is widely applied to engineer host cells such as Chinese hamster ovary (CHO) cells [3,4]. Targeted gene knockouts can reduce unwanted byproduct formation, eliminate proteases, or suppress apoptotic pathways, leading to higher cell viability and product yield. Gene insertions can improve metabolic efficiency, enhance protein folding, or enable stable expression of complex biologics. CRISPR also allows multiplex genome editing, enabling simultaneous modification of multiple genes in a single step.

Despite its advantages, CRISPR-based cell line engineering presents challenges. Off-target effects remain a concern, requiring careful guide RNA design and thorough screening to ensure genomic stability. Regulatory expectations demand comprehensive characterization of engineered cell lines, including genetic integrity and long-term stability. Ethical considerations and intellectual property issues can also influence technology adoption and development strategies.

Ongoing advancements are addressing these limitations. Improved Cas variants, base editing, and prime editing technologies offer greater precision and reduced off-target activity. Automation and high-throughput screening platforms further accelerate cell line development and selection [5].

Conclusion

CRISPR-based cell line engineering represents a major advancement in biotechnology, enabling precise and efficient genetic modification of production hosts. Its ability to enhance productivity, quality, and robustness makes it invaluable for modern biomanufacturing and research. Although challenges related to safety, regulation, and

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ethics remain, continuous technological innovation is expanding its potential. As genome editing tools continue to evolve, CRISPR-based approaches are expected to play a central role in the future of cell line development and biopharmaceutical production.

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