

Optical genome mapping reveals genomic alterations upon gene editing in hiPSCs

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ABSTRACT Human induced Pluripotent Stem Cells (hiPSCs) hold immense promise for regenerative medicine and disease modeling due to their ability to differentiate into various cell types. Gene editing techniques, such as CRISPR-Cas9, have revolutionized the field by allowing precise modifications to the genome. However, these techniques may also introduce unintended genetic alterations, posing challenges for therapeutic applications. Optical Genome Mapping (OGM) emerges as a powerful tool to comprehensively assess genomic alterations resulting from gene editing in hiPSCs. This article reviews the application of OGM in revealing genomic alterations and discusses its implications for the safety and efficacy of gene editing in hiPSC-based therapies.

INTRODUCTION

Human induced Pluripotent Stem Cells (hiPSCs) have emerged as a valuable resource for regenerative medicine and disease modeling due to their ability to differentiate into various cell types, resembling embryonic stem cells. The advent of gene editing technologies, particularly CRISPR-Cas9, has provided researchers with unprecedented precision in modifying the genome of hiPSCs. These techniques offer the potential to correct disease-causing mutations or engineer desired traits for therapeutic purposes. However, the precise assessment of genomic alterations resulting from gene editing is essential to ensure the safety and efficacy of hiPSC-based therapies. Optical Genome Mapping (OGM) has emerged as a promising tool for comprehensive genome analysis, offering insights into structural variations and unintended genetic alterations. This article aims to explore the application of OGM in revealing genomic alterations upon gene editing in hiPSCs and its implications for therapeutic development [1-5].

Overview of optical genome mapping

Optical genome mapping is a high-throughput technology that provides long-range information about the structure and organization of the genome. Unlike traditional sequencing methods, which rely on short-read sequencing data, OGM utilizes high-molecular-weight DNA molecules that are directly imaged and analyzed. The core principle of OGM involves the linearization of DNA molecules, followed by their imaging using fluorescence microscopy. By labeling specific sequences or motifs along the DNA, OGM enables the detection of structural variations, such as insertions, deletions, inversions, and translocations, at a genome-wide scale. Moreover, OGM facilitates the assembly of complex genomic regions and the identification of chromosomal rearrangements with high sensitivity and resolution [6-8].

Application of OGM in hiPSCs gene editing

The application of gene editing techniques, such as CRISPR-Cas9, in hiPSCs holds great promise for therapeutic interventions. However, the precise characterization of genomic alterations resulting from gene editing is critical for assessing the safety and efficacy of hiPSC-based therapies. OGM offers a comprehensive approach to detect both intended modifications and unintended off-target effects in the hiPSC genome. By analyzing the structural integrity of chromosomes and identifying alterations at the megabase scale, OGM provides valuable insights into the genomic stability of gene-edited hiPSCs.

Genomic alterations revealed by OGM

Several studies have utilized OGM to characterize genomic

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alterations upon gene editing in hiPSCs. These alterations may include large insertions or deletions at the target site, chromosomal rearrangements, Copy Number Variations (CNVs), and structural variations affecting gene expression and function. OGM enables the precise mapping of these alterations, allowing researchers to assess their frequency, size, and impact on the hiPSC genome. Moreover, OGM facilitates the identification of off-target effects, which are unintended modifications occurring at genomic loci with sequence similarity to the target site. By comparing the genome-wide OGM profiles of gene-edited hiPSCs with their parental counterparts, researchers can discern the effects of gene editing on genomic stability and integrity [9,10].

Implications for therapeutic development

The comprehensive assessment of genomic alterations using OGM is crucial for the development of safe and effective hiPSC-based therapies. By identifying potential off-target effects and unintended modifications, OGM helps mitigate the risks associated with gene editing, such as insertional mutagenesis and oncogenic transformation. Furthermore, OGM enables the optimization of gene editing protocols to minimize unwanted genomic alterations while maximizing the desired modifications. The integration of

OGM with other genomic technologies, such as next-generation sequencing and single-cell analysis, enhances our understanding of the molecular mechanisms underlying gene editing in hiPSCs. Ultimately, OGM contributes to the advancement of precision medicine by facilitating the selection of genetically stable hiPSC lines for clinical applications.

CONCLUSION

Optical genome mapping represents a valuable tool for characterizing genomic alterations upon gene editing in hiPSCs. By providing long-range information about the structure and organization of the genome, OGM enables the detection of structural variations and off-target effects with high sensitivity and resolution. The application of OGM in hiPSC-based therapies enhances our ability to assess the safety and efficacy of gene editing protocols, thereby accelerating the translation of hiPSC research into clinical practice. Future studies should continue to refine and expand the utility of OGM in elucidating the genomic landscape of gene-edited hiPSCs and its implications for regenerative medicine and disease modeling.

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