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CRISPR- BASED STRATEGIES FOR TARGETED REMOVAL OF TRISOMY 21

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Down syndrome is a genetic condition affecting one in every 700 births, resulting in an extra chromosome 21. It affects brain and body development and requires screening and diagnostic tests for all pregnant women. Early intervention improves quality of life for children with Down syndrome. Advanced techniques like CRISPR/Cas9 and chromosome silencing are being explored to remove the extra chromosome and correct gene dosage imbalances.

CRISPR/Cas9 is a genome editing tool that precisely targets DNA sequences for modification, potentially correcting chromosomal abnormalities like Down syndrome. It uses a guide RNA to direct the Cas9 enzyme to specific DNA sequences, introducing double-strand breaks that can be repaired. This makes it an effective tool for knocking out or correcting faulty genes. CRISPR is being explored for treating trisomy 21, with strategies focusing on over expressed genes and recognizing extra chromosome 21. However, challenges include delivery methods and potential off-target effects. Ethical concerns include designer babies and consent issues. Despite these, ongoing research holds promise for future applications. Innovations in delivery methods, improved specificity, and regulatory frameworks can mitigate issues. Advances in understanding gene interactions in trisomy 21 could enhance CRISPR strategies' efficacy. Collaborative efforts among geneticists, ethicists, and policymakers are crucial for responsible use of CRISPR technology.

Japanese researchers have developed a method to remove the extra copy of chromosome 21 in Down syndrome patients' cells using allele-specific multiple chromosome cleavage using CRISPR-Cas9. The method specifically targets the M2 allele of chromosome 21, allowing precise removal of only the extra chromosome copy. Researchers have developed a comprehensive allele-specific Cas9 target sequence extraction method that efficiently removes the target chromosome, achieving a chromosome elimination rate of 13.1%. The technique was effective in both dividing and non dividing cells, with 13.9% removal rates observed in differentiated skin fibroblasts. Further research may be needed to evaluate the technique's effectiveness in other cell types. Successful chromosome removal restored normal gene signatures and improved cellular phenotypes, but down regulated genes had higher false discovery rates (FDRs), requiring caution in GO analysis results. While promising, the researchers identified several challenges that need to be addressed prior to potential clinical application, including protecting non target alleles from Cas9-induced double-strand breaks, simplifying the phasing method, and evaluating the approach in clinically relevant cell types like neurons and glial cells."Although a non chromosome-breaking elimination method is desirable, the findings of this study can be used to rescue somatic cells with trisomy," the study authors concluded.