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Gene Editing Using CRISPR in Cystic Fibrosis: A Systematic Review

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ABSTRACT

Introduction: Cystic fibrosis (CF) is a chronic genetic disorder primarily caused by the ΔF508 mutation, leading to defective CFTR protein and mucus buildup, lung damage, and recurrent infections. Current treatments enhance CFTR function but are ineffective for about 10% of mutations, necessitating alternative approaches. CRISPR/Cas9 technology offers promising solutions by precisely modifying the genome to correct disease-associated genes. In CF models, CRISPR/Cas9 has restored normal CFTR function and alleviated physiological defects. Advanced derivatives like base editing and HITI further expand the potential for effective CF therapies. While CF remains a complex disease, gene therapy advancements, especially CRISPR/Cas9, offer hopeful prospects for treatment and potential cure.

Search Strategy: This study adhered to Cochrane systematic review principles and PRISMA guidelines. A comprehensive literature search was conducted using PubMed (Medline), Scopus, Web of Science databases, and Google Scholar up to 2024. The search aimed to identify English-language studies focused on randomized controlled trials applying CRISPR/Cas9 genome editing in CF. Search MeSH terms included “CRISPR/CAS9" "cystic fibrosis", and "CFTR".

Results: Gene editing using CRISPR/Cas9 was explored as means to correct CFTR mutations that led to CF. Since airway cells do not divide, precise non-homologous end joining strategies are required instead of homology-directed repair. CRISPR animal models contribute significantly to CF research, while helper-dependent adenoviral vectors show promise for lung delivery. Current approaches include ex vivo editing of patient cells, CRISPR activation of CFTR expression, and the use of CRISPR/Cas9 in conjunction with adeno-associated virus to replace the CFTR gene in airway stem cells, offering potential for a cure. However, enhancing precision, optimizing delivery methods, and ensuring long-term safety remain critical challenges.

Conclusion and Discussion: CRISPR/Cas9 gene editing presents a promising method for treating CF by directly correcting the underlying genetic defects. While significant advancements have been made in developing various strategies and animal models, challenges related to efficient delivery and precise editing persist. Ongoing research and innovation in these areas are crucial for translating these proof-of-concept studies into effective therapies for CF patients.

Keywords: CRISPR-Cas systems, Cystic Fibrosis, Gene editing