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REVIEWER'S REPORT

Manuscript No.: IJAR-50425 Date: 27-02-2025

Title: CRISPR/Cas9-Mediated Gene Editing: A Novel Approach for Cystic Fibrosis

Recommendation:
Accept as it is……**YES……**
Accept after minor revision……
Accept after major revision ……
Do not accept (*Reasons below*) ……

Rating	Excel.	Good	Fair	Poor
Originality	√			
Techn. Quality		√		
Clarity		√		
Significance			√	

Reviewer's Name: Dr Aamina

Reviewer's Decision about Paper: **Recommended for Publication.**

Comments (*Use additional pages, if required*)
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Reviewer's Comment / Report

Introduction Review:
The introduction effectively presents the historical background of the CRISPR/Cas9 system, tracing its discovery from Escherichia coli to its development as a gene-editing tool. The contributions of Jennifer Doudna and Emmanuelle Charpentier are well-detailed, highlighting their independent research efforts and eventual collaboration. The explanation of the CRISPR mechanism is thorough, covering key components such as Cas9 protein, guide RNA, tracrRNA, and crRNA. The step-by-step breakdown of the gene-editing process, including DNA cleavage, sequence targeting, and gene splicing, provides a strong foundation for understanding the system's functionality. The mention of the PAM sequence and its role in specificity ensures clarity in explaining target site selection.

Mechanism Review:
The description of the CRISPR/Cas9 gene-editing mechanism is comprehensive. The involvement of Cas9 as an endonuclease enzyme, along with the role of guide RNA in targeting specific sequences, is clearly articulated. The process of double-stranded DNA cleavage and its implications for gene editing are well-explained. The distinctions between gene disruption and sequence modification are effectively conveyed, allowing for a clear understanding of CRISPR's applications. The importance of PAM sequences in ensuring accuracy and reducing off-target effects is appropriately emphasized.

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Figure 1 Review:
The inclusion of Figure 1, illustrating the CRISPR/Cas9 gene-editing mechanism, enhances the explanation of the process. The figure description clearly outlines the role of single-guide RNA (sgRNA) in directing Cas9 to create double-strand breaks. The explanation of Non-Homologous End Joining (NHEJ) and Homology-Directed Repair (HDR) is well-structured, contrasting the speed and accuracy of these DNA repair pathways. The distinctions between error-prone NHEJ and precise HDR provide valuable insight into the consequences of CRISPR-induced breaks.

Overall Review:
The section provides a detailed and well-structured overview of CRISPR/Cas9 gene editing and its potential application in Cystic Fibrosis. The historical context, mechanistic details, and explanation of DNA repair pathways are well-integrated, creating a coherent narrative. The scientific terminology is appropriately used, ensuring clarity and accuracy in the discussion. The inclusion of references to key studies and researchers strengthens the credibility of the content.