Harnessing CRISPR-Cas9 Synergy with Metabolic Engineering to Mitigate Antibiotic Resistance in Pseudomonas aeruginosa

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Abstract. The emergence of multidrug-resistant Pseudomonas aeruginosa strains poses a significant threat to global public health. By employing CRISPR-Cas9 technology coupled with metabolic engineering, this study explores a novel approach to suppress resistance mechanisms. We engineered strains with targeted disruptions in critical resistance-conferring genes, leading to enhanced antibiotic susceptibility. The findings demonstrate the potential of integrating gene-editing and metabolic pathways to address antibiotic resistance effectively. This research underscores a promising strategy for future antimicrobial development.

Keywords: CRISPR-Cas9, metabolic engineering, antibiotic resistance, Pseudomonas aeruginosa, genome editing, efflux pumps, metabolic pathways, antimicrobial therapy

Introduction

Antibiotic resistance in Pseudomonas aeruginosa represents a critical challenge in contemporary healthcare, exacerbated by the pathogen's intrinsic and acquired resistance mechanisms. These strains are increasingly recalcitrant to existing therapeutic modalities, necessitating innovative strategies to mitigate this global health concern. CRISPR-Cas9, a powerful genome-editing tool, has emerged as a promising candidate for targeted genetic interventions. Coupled with metabolic engineering, it offers a compelling avenue to disrupt

key resistance pathways in P. aeruginosa. This study investigates the synergistic application of CRISPR-Cas9 and metabolic engineering to attenuate antibiotic resistance in this formidable pathogen. By disrupting genes essential for resistance, particularly those involved in efflux pump regulation and cell wall synthesis, we demonstrate a marked increase in antibiotic susceptibility. Furthermore, metabolic flux analysis reveals alterations in central metabolic pathways, highlighting potential vulnerabilities that can be therapeutically exploited. The results presented here provide a foundation for subsequent research aimed at developing clinically viable solutions. The paper is structured as follows: Section 2 details the materials and methods employed in the study. Section 3 presents the results, followed by a discussion in Section 4 on the implications and limitations of these findings. Section 5 concludes with future perspectives on leveraging gene editing and metabolic modulation in antimicrobial therapy.

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