Disrupting TasA-Induced NF-κB Activation in *Bacillus cereus* Biofilms: A Novel Strategy for Gastric Cancer Prevention

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Abstract

Among the diverse microbial inhabitants of the gastric niche, *Bacillus cereus* long regarded as an environmental and food-associated organism has recently come under scrutiny for its potential involvement in chronic gastric inflammation and early neoplastic changes. This raises a crucial question: How does an environmental organism lead to prolonged inflammatory damage in the stomach? Yet, the mechanisms by which this organism contributes to long-term mucosal damage remain poorly understood, but its ability to form persistent biofilms within the acidic gastric milieu plays a pivotal role. TasA, its major amyloid-like biofilm protein, may aberrantly modulate host inflammatory pathways, thereby prolonging disease processes. Although direct experimental evidence for a TasA-RelA/p65 interaction is lacking, our computational analyses reveal a plausible mechanism by which TasA could sustain NF-κB-mediated inflammation, contributing to the development of gastric cancer. To examine this hypothesis, the TasA protein which lacks a crystal structure was modelled and refined using molecular dynamics simulations, while the available RelA/p65 structure was retrieved for downstream analysis. Protein-protein docking was performed to investigate the TasA-RelA interface potentially responsible for aberrant NF-κB activation and inflammation-associated gastric pathology. Given the absence of therapies that specifically target bacteria-induced dysregulation of host NF-κB signalling, we also examined phytochemical-based interventions. An AI-based virtual screening of bioactive compounds from 14 medicinal plants revealed three plants rich in promising anti-inflammatory agents. These selected compounds were docked against the TasA-RelA complex, and their inhibitory potential was assessed through MD simulations, MM/PBSA, PCA, and ADMET profiling. Together, this *in silico* investigation underscores phytochemicals that can disrupt TasA-mediated NF-κB activation, suggesting a novel approach to mitigate the associated gastric inflammation.

Keywords: Gastric cancer, *B. cereus*, TasA, NF-κB, biofilm, AI-based virtual screening, MDS, PCA.

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