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Immunoinformatics and molecular dynamics studies to predict T-cell-specific epitopes of four *Klebsiella pneumoniae* fimbriae antigens

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ABSTRACT

Klebsiella pneumoniae (*K. pneumoniae*) is a causative agent of severe infections in humans. There is no publically available vaccine for *K. pneumoniae* infections yet. Here, using comprehensive immunoinformatics methods, T-cell-specific epitopes of four type 1 fimbriae antigens of *K. pneumoniae* were predicted and evaluated as potential vaccine candidates. Both CD8+ (class I) and CD4+ (class II) T-cell-specific epitopes were predicted and the epitopes similar to human proteome were excluded. Subsequently, the windows of class-II epitopes containing class-I epitopes were determined. The immunogenicity, IFN-γ production and population coverage were also estimated. Using the 3D structure of HLA and epitopes, molecular docking was carried out. Two best epitopes were selected for molecular dynamics studies. Our prediction and analyses resulted in the several dominant epitopes for each antigen. The docking results showed that all selected epitopes can bind to their restricted HLA molecules with high affinity. The molecular dynamics results indicated the stability of system with minimum possible deviation, suggesting the selected epitopes can be promising candidates for stably binding to HLA molecules. Altogether, our results suggest that the selected T-cell-specific epitopes of *K. pneumoniae* fimbriae antigens, particularly the two epitopes confirmed by molecular dynamics, can be applied for vaccine development. However, the *in vitro* and *in vivo* studies are required to authenticate the results of the present study.

Abbreviations: ANN: Artificial neural network; Comblib: Combinatorial peptide libraries; CPORT: Consensus prediction of interface residues in transient complexes; HLA: Human leukocyte antigen; MD: Molecular dynamics; RMSD: Root mean square deviation; RMSF: Root mean square fluctuation; SMM: Stabilized matrix method; TIP3P: Transferable intermolecular potential with 3 points

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Klebsiella pneumoniae; vaccine; immunoinformatics; type 1 fimbriae; T-cell-specific epitope; molecular dynamics

1. Introduction

Klebsiella pneumoniae is a Gram-negative bacterium that resides in the environment (soil, water, etc.) and the gastrointestinal tract of mammals including humans. In humans, it can cause infection if gains entry to the blood circulation and other sterile tissues (Piperaki et al., 2017).

Various approaches have been tested to combat the antimicrobial resistance related problems in pathogenic bacteria including the recent progress in bioinformatics which has provided novel tools to identify potential drug targets (Miryala et al., 2018; Sugumar et al., 2014). However, the emergence of strains resistant to various antibiotics by presenting several resistance mechanisms as well as the hypervirulent strains greatly narrow down the therapeutic options for *K. pneumoniae* infections. Consequently, this problem has attracted a great attention for vaccine development (Malathi et al., 2019; Miryala et al., 2020; Piperaki et al., 2017).

The development of an effective vaccine would be a great help to control the *K. pneumoniae* infections. Due to the safety concern, whole cell vaccines that consist of multiple proteins are not considered as perfect vaccines. On the other hand, no completely effective single antigen candidate has been found so far for *K. pneumoniae* and attempts for finding a good vaccine candidate are still ongoing.

Four virulence factors of *K. pneumoniae* have been well characterized, namely fimbriae, lipopolysaccharide, capsule, and siderophores. These virulence factors assist this opportunistic pathogen to circumvent the host immune defenses (Paczosa & Mecsas, 2016; Shon et al., 2013). Type 1 and type 3 fimbriae in *K. pneumoniae* facilitate adherence to biotic and abiotic surfaces and mediate epithelial cell invasion and biofilm formation (Piperaki et al., 2017). Type 1 fimbriae composed of a tip fibrillum connected to the rod. Tip fibrillum is composed of a single copy of FimH (the adhesion) and a single copy of FimG (the tip subunit) proteins connected to the

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