Immunoinformatics design of a multi-epitope vaccine against tuberculosis (Research Paper)

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Introduction: Mycobacterium tuberculosis is a pathogen that has been known as a main cause of tuberculosis disease for many years. Although, global BCG vaccination has showed a high reduction in new cases, it has reported variable efficacy (0-80%) among different population. On the other hand, some limitations of live attenuated vaccines, have spurred researchers to develop alternative ones.

Methods: In this study using immunoinformatics tools, the sequences of five Rv0888, Rv2645, Rv3841, Rv3874 and, Rv3875 antigens, as well as Heparin-Binding Haemagglutinin (HBHA) as an adjuvant, were retrieved. Different epitopes were identified employing various databases, and the selected epitopes and adjuvant were linked together using appropriate linkers. Then, allergenicity, antigenicity, solubility and physicochemical parameters of the designed vaccine were analyzed. Moreover, homology modeling, refinement of the 3D model, and their validations were performed. In the next step, molecular docking studies of the designed vaccine with Toll-like receptor 4 (TLR4) proteins as a receptor was done.

Results: A vaccine with a length of 704 amino acids was designed by selecting the high ranked epitope sequences. Allergenicity, antigenicity, solubility and physicochemical parameters studies have shown that the protein is antigenic, non-allergenic, soluble and stable. Also, the comparison of the refined 3D and the original model indicated that the 3D structure was improved and the potential mistakes were minimized. Finally, the best-docked model of vaccine and TLR4 complex was selected. The results showed that vaccine can bind appropriately to TLR4.

Conclusion: The fundamental purpose of this study is to use bioinformatics tools to design an appropriate subunit vaccine. As a result, a subunit vaccine consisting of eight epitopes from five Mycobacterium tuberculosis antigens which was linked to HBHA adjuvant by GPGPG linker was designed. Various evaluations in this study as well as molecular docking between vaccine and TLR-4 showed that the designed vaccine can be a good candidate for