**Designing a novel multiepitope peptide vaccine against melanoma using immunoinformatics approach**

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Malignant melanoma is the most aggressive and life-threaten skin cancer. Nowadays, the prevention and treatment of melanoma are challenging areas for researchers and physicians. Therefore, we implemented an in silico-based approach to design a multi-epitope peptide vaccine for melanoma. This approach consists of immunoinformatics, molecular docking, and dynamic stimulation assessments to identify potent targets. Three most immunogenic melanoma proteins; NEYSO-1, gp-100, and MART-1were considered to predict immunodominant B and T cell epitopes. The prioritized epitopes had significant potential to induce strong humoral and cellular immunity and INF-γ responses without the possibility of allergenicity. To enhance the immunogenic properties of the vaccine, we used adjuvants HBHA, the helper epitope of PADRE, and three segments of the helper epitope from TTFrC. To design the final vaccine construct, appropriate linkers are used to join immunogenic screened-epitopes and also the adjuvants. The physicochemical and immunological properties of the vaccine were evaluated. The designed-vaccine construct was docked to TLR4 to visualize the complex affinity and then conformational dynamics simulation was used to analyze time-dependent interaction behavior. In silico cloning demonstrated that the vaccine can be efficiently expressed in *E.coli*. Therefore, the designed vaccine might have the ability to induce humoral and cellular immune responses against melanoma cancer antigens. This vaccine has a high-quality structure and suitable characteristics such as high stability, solubility, and a high potential for expression in a prokaryotic system. However, these results need the experimental study to ensure the immunogenicity and safety profile of the melanoma candidate vaccine construct.