

Designing of Polyepitopic Vaccine by Targeting E7 Protein Sequences: An Immunoinformatics Approach in Human Papillomavirus 16

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Abstract: Cervical cancer is the fourth common type of cancer among women worldwide. Infection with high-risk human papillomavirus (HPVs) types is necessary for the development of cervical cancer and its precursors. HPV-16 is the most frequently known HPV type in cervical lesions. HPV-16 express E6 and E7 oncoproteins that require for the uncontrolled cellular proliferation. An efficient approach to treat lesions related to HPV infection is based on therapeutic vaccines against tumors induced by HPV. Unlike prophylactic vaccines based on the induction of antibodies, therapeutic anti-tumor vaccines need to induce cell mediated immune responses capable of identifying and eliminating abnormal cells. For this purpose, therapeutic vaccine should be efficiently stimulate innate and adaptive immune system, in particular CD 4⁺ and CD 8⁺ T cells. In the present study we report the design of a recombinant multi-epitope protein containing immunogenic epitopes of HPV-16 E7. To design the vaccine, we assembled a database containing 1070 different sequences of HPV-16 E7 identified worldwide. We then predicted 20 potential HPV-16 E7 epitope using bioinformatics approaches. On the other, we extracted experimental epitopes from IEDB database. Using combination of predicted (theoretical) and experimental epitopes, we achieved potent epitopic construct that can induce both CD 4⁺ and CD 8⁺ T cells efficiently. To increase the magnitude and quality of E7-specific immune response, linkers were inserted between epitopes (AAV used between CD 8⁺ epitopes and GPGPG used between CD 4⁺ epitope). Finally, we developed a therapeutic vaccine candidate employing a recombinant protein consisting of a string of multi-immunogenic T cell epitopes of E7. Although the study requires further in vitro and in vivo screening, it seems this epitope-focused peptide vaccine designing create a potent therapeutic vaccine that can develop alternative approach for the treatment of patients with this cancer.

Keywords: Human Papilloma virus; Therapeutic vaccine E7

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