IDENTIFICATION OF POTENTIAL VACCINE CANDIDATE AGAINST HPV-16 INFECTION IN INDIAN POPULATION USING REVERSE VACCINOLOGY: PART 2

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doi: https://doi.org/10.52458/9789391842109.2022.ch15.eb.asu  Ch.Id:-ASU/EB/ELBDB/2022/15
INTRODUCTION

Human Papilloma viruses (HPV) are a group of hundreds of related viruses that are extremely common worldwide. Amongst these, about 13 of them are cancer causing with HPV-16 and HPV-18 being responsible for about 70 percent of the cervical cancers and precancerous cervical lesions. HPV infection is transmittable through sexual contact and these infections have been studied to be the most important risk factors for cervical cancer. Cervical cancer is the second most common cancer in women worldwide with more than a million women currently being the affected and about 270,000 dying annually worldwide. Majority of these deaths occur in developing countries like India. Despite the fact that it is one of the most preventable forms of cancer, cervical remains the deadliest one, especially in developing countries like India where about 5 percent of women are estimated to be infected with either HPV16 or HPV 18 at a given time and about 69.7 percent women being diagnosed with cervical cancer caused by HPV-16. As per WHO, cervical is one of the most preventable forms of cancer. Since sexual contact is the mode of infection, abstinence and lifetime mutual monogamy are the common preventive strategies known. Although there are barrier methods but sufficient scientific evidences have not yet been established. However, routine screening can help in early detection but for a largely populated developing nation like India, routine screening is difficult to achieve. This calls for the need of effective vaccination against HPV.

Currently, there are two vaccines approved in India against HPV - Gardasil™ marketed by Merck and Cervarix™ marketed by Glaxo Smith Kline. But both of these vaccines are preventive and not therapeutic. This implies that the vaccines will be able to prevent the viral infection by inducing virus-neutralized antibodies but will not be able to protect the cells that are already infected with HPV. Unfortunately, “most people are infected with HPV shortly after the onset of sexual activity” and therefore, we need vaccines that can eliminate this infection before it causes cervical cancer. Therapeutic vaccines are designed to meet this objective of controlling and eliminating the viral infection by priming the antigen-specific immune responses.

Therapeutic vaccines against HPV primarily target two early HPV proteins, namely E6 an E7. These proteins essentially turn out to be the potential vaccine
Identification of potential vaccine candidate against hpv-16 infection in indian population using ……

candidates due to several reasons. One, they are critical for maintenance of malignancy of the infected cells, two, they are encoded by genes that are expressed only in HPV infected cells and not normal cells and three, they are capable of generating T-cell mediated immune responses. There have been several studies, aimed at identification of E6 and E7 based potential vaccine candidates against HPV infection but no Asian population based studies have been performed yet. Due to HLA polymorphism, it becomes essential to develop vaccines that are population specific so as to improve the success rate.

Unlike conventional vaccinology, where the microorganism is first cultured followed by selection of antigens, reverse vaccinology begins with genome sequence analysis, followed by prediction of antigens using bioinformatics tools. The major advantage of employing reverse vaccinology is that vaccine targets can be identified quickly and efficiently. Traditional methods may take decades to unravel pathogens and antigens.

For a global health issue such as HPV and associated cancers, reverse vaccinology is no less than a boon that can accelerate the vaccine development process and reduce the incidence rates significantly. Following are the components of reverse vaccinology:

1. Genome sequences
2. Computer analysis
3. Prediction of epitope/ antigen
4. Candidate vaccine

There are several databases that contain complete genome sequences of various pathogens. The sequences can be extracted from these resources and the bioinformatic tools can then be applied to predict the epitopes, which is the key to vaccine development. Reverse vaccinology overcomes this by predicting and mapping T-cell based specific epitopes. Several studies have been done in this direction to identify E6 and E7 sequences as an MHC-I binding peptide that can elicit CTL responses in HPV 16-induced tumor tissue and clinical trials are going on to test the safety, efficacy and effectiveness of these peptide based vaccines developed using the concept of reverse vaccinology.