# Comprehensive Details on Human Papillomavirus (HPV) Infections and Associated Malignancies: Awareness about Prophylaxis & Treatment Options Available for HPV Infections

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## Dear Editor,

Gul et al.[1] discussed the available treatment options for HPV infections. In the last section they focused on promoting new therapeutic options, but there are a few points that I would like to comment on.

The safety profile and disadvantages of DNA vaccines has not been assessed properly in the paper giving an unfair idea of how DNA vaccines can affect individuals[2]. Even if the DNA vaccines are safer than traditional vaccines; for the DNA vaccines to work, they must enter the nucleus. As a result, when a DNA vaccination is given, the recipients are exposed to foreign DNA that may be incorporated into their genome. Insertional mutagenesis and the potential activation of oncogenes or inactivation of tumour suppressor genes can result from the insertion of foreign genes into the host genome[3].

## Response

Thank you for the fruitful comments. The development and application of DNA vaccines continues to progress. Since the WHO Guidelines for assuring the quality and nonclinical safety evaluation of DNA vaccines were adopted by the Expert Committee for Biological Standardization in 2005 [(5)], many clinical trials of DNA vaccines have taken place and considerable experience in their manufacture and control has accrued. Theoretically, DNA vaccines would be ideal for use in boosting immune responses as they could be used repeatedly (and for different purposes) because they do not generate anti-vector immune responses [5,6,7,8,9,10].

Clearly, the nature of the immune response will depend upon the immunogen expressed and the immunomodulatory elements or formulation of the DNA vaccine, as well as on the method of delivery [11].

In recent researches, development of Cytolytic DNA vaccine that encodes non-structural HCV proteins and a truncated mouse perforin (PRF) produced better outcomes in animal models and Phase I clinical trials. The vaccine was well tolerated, and no toxicity was observed [12]

Furthermore, DNA vaccines have shown considerable promise in clinical trials. Trimble et al. and Kim et al. reported the use of therapeutic DNA vaccines that target human papillomavirus (HPV) 16 and 18 in cervical intraepithelial

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neoplasia (CIN) 2/3 patients [13,14]. Trimble et al. showed that their vaccine (VGX-300) elicited robust CMI responses that resolved persistent HPV infection and prompted regression of cervical lesions in 40% of patients compared to 14% in the placebo group, with similar responses seen in the modified-to-treat group [13]. The study performed by Kim et al. reported a phase I dose escalation study of a therapeutic vaccine (GX-188E) targeting HPV-16 and 18 in CIN3 patients. At 36 weeks after vaccination it was reported that seven out of nine patients cleared persistent HPV infection with complete regression of CIN3 lesions [14]. These studies highlight several important points for DNA vaccines: they can be efficacious in humans, function in a therapeutic manner to resolve persistent viral infection and are safe.

The statement which implies that protein-based vaccines are not specific for MHC, is not entirely correct. Protein-based vaccines also use MHC for antigen presentation, but they contain a broader range of epitopes that can be processed and presented by both MHC class I and MHC class II molecules. Also, the statement that protein-based vaccines promote antibody responses over T cell responses due to MHC II presentation is an oversimplification. While MHC II presentation does promote helper T cell activation and subsequent antibody production, protein-based vaccines can also elicit cytotoxic T cell responses through MHC I presentation[4]. DNA vaccines are undoubtedly the future of vaccines, but they still require empirical evaluation, mentioning a neutral approach. A short essay is not enough for this.

### Response

In answer to the above mentioned highly appreciated comment, this is essential to address that our review is about general awareness of HPV vaccines. We could not provide complete details regarding MHC classifications. Protein based vaccines require epitope-focused for screening MHC class I and MHC class II. Like any new approach, however, many challenges remain in the development and ultimately, the application of epitope-focused vaccines. Considerable research has been performed towards the identification of promiscuous helper T cell epitopes which can be effectively linked to B cell targets in epitope-focused vaccines, and while studies have demonstrated efficacy with these vaccines in inbred mice and rabbits, the application of this approach for human vaccination will require overcoming potential limitations imposed by MHC restriction [15,16].

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