Novel carrier based vaccine delivery systems for mucosal immune responses for HPV L1 capsid protein administered subcutaneously and intra nasally

Muruganandham S 1, Michael A 1,4, Balasubramaniam V 2, Jaganathan S 2

1Department of Microbiology, PSG College of Arts & Science, Coimbatore, India
2Department of Pharmaceutical Biotechnology, Saraswathi College of Pharmaceutical Sciences, Hyderabad, India

ABSTRACT

Human papillomavirus (HPV) vaccines based on L1 capsid protein can prevent genital HPV infection and associated complications after three intramuscular injections. The currently available vaccines for HPV infection are based on capsid protein L1 virus like particles (VLPs) and they are formulated using aluminium adjuvants. The aluminium based vaccines always possess some constrains as they cannot induce the cell mediated immune response and the complete protection is based on the humoral antibodies. Here we have experimented subcutaneous and intranasal immunization of HPV L1 antigen formulated in Niosomes in order to induce both Humoral and Cell Mediated Immune (CMI) response. The Niosomes were formulated with the HPV antigen, with or without Cholera Toxin B (CTB) and immunized in mice. The immune response was studied in both systemic and as well as in mucosal surfaces. The subcutaneous injection elicited an acceptable level of systemic immune response, but failed to produce significant response in mucosal surfaces. The intranasal immunization was effective in eliciting both systemic and mucosal immune responses as tested from serum and vaginal fluids respectively when compared with subcutaneous injection.

Keywords: HPV L1; Intranasal & Subcutaneous Immunization; Niosomes; Serum; vaginal fluid

INTRODUCTION

A high percentage of human cervical tumors contain human papillomavirus (HPV) DNA sequences, mainly HPV type 16 (HPV-16), HPV-18 (3, 9, 20, 30, and 34). The natural history of HPV infection is rather short in the majority of subjects, since clearance of the virus or of low grade cytological and histological lesions occurs in the majority of cases in few months to 1-3 years. However, cervical cancer development is a long process (usually lasting 15 – 20 years). It implies the persistence of infection with a high-risk HPV type in a majority of infected women, leading to pre-cancerous lesions in the minority of infected women, leading to pre-cancerous lesions in the middle term (3-5 years), and eventually to the development of invasive cancer in the long term (>10 years). Although widespread implementation of cytological screening is available in many countries, cervical cancer represents a major cause of morbidity and mortality. Worldwide, cervical cancer is the second most common cause of cancer death in women worldwide with about 80% cases occurring in developing countries (Parkin M et al., 2006).

The development of HPV vaccine is a landmark in the history of immunization, since this is a vaccine primarily directed and considered as an anti-cancer vaccine. The two presently available vaccines in the market prove to be efficacious in the prevention of precancerous lesions. However, they need to extend their protective efficacy for many years, if a substantial impact on HPV-related diseases has to be achieved. With the increasing use of highly purified synthetic peptides in modern vaccinology, appropriate adjuvants are often required to enhance the immunogenicity of these peptides which are generally poorly immunogenic. The development of novel adjuvants is especially important since alum has been reported to be a relatively weak adjuvant for induction of CMI. Concerns about potential toxicity have restricted the widespread use of adjuvants in man since aluminium was first introduced more than 50 years ago which demonstrated better safety & efficacy and approved by USFDA and WHO. However, some adjuvants developed in the recent decades were found to be toxic for clinical use.

The currently available prophylactic vaccines based on non-infectious L1 VLPs have proven to be well tolerated, highly immunogenic and efficient in preventing type specific cervical HPV persistent infection and associated neoplasia. However, these vaccines require multiple intramuscular doses administered over 6 months to be efficient and the primary target groups being pre-adolescent girls, and may decrease the accessibility of the vaccines in developing countries. The