

Plant based HPV pseudovirion production

The technology is an alternative production method for human papilloma virus (HPV) pseudovirion (PsV). A potentially game changing application revolves around recent demonstration that DNA vaccines delivered using HPV PsVs represent an efficient delivery system that can potentially affect the field of DNA vaccine delivery.

Genetic vaccination, in which the antigen is expressed within the host cells, has emerged as a potentially promising approach to generate antigen-specific T-cell-mediated immune responses. The current paradigm for genetic vaccination is to use naked nucleic acid vaccines. This approach has shown great potential in numerous animal models over the last decade, and these vaccines are very stable, simple, inexpensive to manufacture, and thus far safe. However, naked nucleic acid vaccines have generally shown lesser immunogenicity in patients. An emerging mode of delivery for DNA vaccines is the employment of non-replicative viral particles, or PsVs that exploit viral capsids to facilitate the delivery of the vaccine. Recent advances enable the packaging of DNA plasmids into the papillomavirus capsid proteins to generate a 'pseudovirion' that can efficiently deliver the DNA plasmid into the infected cells, resulting in the expression of the encoded gene. Furthermore, because PsVs do not contain the viral genome, they circumvent many of the safety concerns associated with live viral vectors.

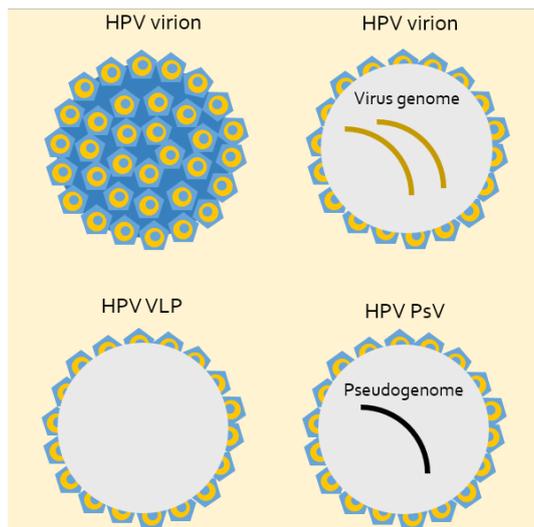


Figure 1: Illustration showing the difference between functional HPV virus particles, virus-like particles; and pseudovirions.

The application of the HPV PsV as a DNA vaccine delivery vehicle would extend beyond cervical cancer. HPV is ubiquitous in cutaneous tissues and hence they are also indicated in other cancers such as skin, throat and lung cancer. Thus the HPV PsV would have application in treatment of most if not all cutaneous cancers.

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HPV, pseudovirion, plant-based, vaccine development

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3 - Proof of Concept

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Recent advances potentially widens the application of HPV PsV as a DNA vaccine delivery vehicle. These studies demonstrate that HPV PsV efficiently delivers nucleic acid vaccines into dendritic cells of patients to trigger cytotoxic T-cell immunity. This would mean that all infections presenting antigens in the blood could potentially be targeted.

Currently, PsVs are only made in mammalian, cancer-derived, cultured cells by transfection of purified DNA. This creates the possibility that the PsVs that are produced could encapsidate oncogenes (cancer-causing genes) from the cell lines, or could be contaminated by mammalian viruses. Our technology obviates this concern.

Benefits

- Recombinant protein expression in plants is a highly scalable process, unlike the cell culture-based method.
- Plant based expression removes the possibility of oncogene or mammalian virus contamination, as the plant virus-derived replicating DNA that is encapsidated in the particles has no possibility of replicating in normal mammalian cells, or of recombining with other mammalian viruses or transposon-like sequences.

Use in vaccine testing

Another application of HPV PsV is in affordable candidate vaccine development and, in particular, inexpensive testing of immune sera. In fact PsV-based neutralisation assay (PBNA), is currently the gold standard for testing candidate HPV vaccines. HPV PsVs therefore have commercial value either as a stand-alone product or as a commercial neutralisation kit which could be sold to companies or to individual researchers to test their candidate HPV vaccines. The luciferase reporter gene has been included, which makes the assay simpler and cheaper compared to the conventional SEAP assay.