NATIONAL CANCER INSTITUTE
Technology Transfer Center

Efficient Cell-Free Production of Papillomavirus Gene Transfer Vectors

Summary

Researchers at the National Cancer Institute (NCI) developed cell free methods for efficiently producing high titer, papillomavirus virus-based gene transfer vectors. These vectors can potentially be used for vaccines and/or cancer therapeutic applications. NCI seeks licensing and/or co-development research collaborations for further development of these vectors.

NIH Reference Number

E-298-2016

Product Type

- Therapeutics

Keywords

- Papillomavirus, virus based gene transfer vectors, vectors, vaccine, therapeutic, cancer, cancer therapeutic, tumor therapy, cell-free production, Schiller

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Papillomavirus pseudoviruses that comprise the L1/L2 capsid proteins can package a wide variety of non-viral DNA plasmids and deliver the packaged genetic material to cells. This function makes them attractive candidates as targeted gene delivery vehicles. Current methods for the efficient production of papillomavirus pseudoviruses require the use of 293TT cells. One key drawback to this production method is SV40 T antigen gene contamination introduced by the 293TT cells. Because T antigen is a known oncoprotein, pseudoviruses generated using this methodology are unsuitable for clinical applications. A second drawback is that intracellular production precludes production of toxin gene-transducing pseudovirions. A third drawback is that intracellular production cannot be used to generate mRNA transducing vectors.

Scientists at the NCI have developed a novel, chemically defined, cell-free, papillomavirus-based vector production system that allows the incorporation of purified plasmid DNA (pseudogenome) or mRNA into high-titer papillomavirus L1/L2 capsids without the use of 293TT cells. Titers as high as 1011 infectious units/mg of L1 were generated. Pseudoviruses were infectious both in vitro and in vivo, and should be compatible with good manufacturing practice (GMP) requirements.

Potential Commercial Applications

- GMP production of papillomavirus-based gene delivery vectors
- Vaccine applications
- Cancer therapeutic applications
- Clinical evaluation of IVP vectors as agents for intravaginal vaccination or cancer treatment

Competitive Advantages

- More suitable for clinical applications compared to standard production methods
- Enables the generation of papillomavirus pseudovirions that can transduce cytotoxic genes
- GMP-grade papillomavirus pseudovirus production
- Chemically defined, cell-free, papillomavirus-based vector production system
- Allows the incorporation of purified plasmid DNA (pseudogenome) or mRNA into high-titer papillomavirus L1/L2 capsids without the use of 293TT cells
- High titer papillomavirus production methods (titers as high as 1011 infectious units/mg of L1)
- Infectious both in vitro and in vivo
- Overcomes the T antigen contamination issues found in current methods for production of papillomavirus based pseudoviruses

Inventor(s)

John Schiller (NCI)

Development Stage

- Pre-clinical (in vivo)

Publications

C. Cerquiera et al. Efficient Production of Papillomavirus Gene Delivery Vectors in Defined In Vitro Reactions. [PMID 28497074]

C. Cerquiera et al. A Cell-Free Assembly System for Generating Infectious Human Papillomavirus 16 Capsids Implicates a Size Discrimination Mechanism for Preferential Viral Genome Packaging. [PMID 26559838]

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/460,640 , Filed 17 Feb 2017

Related Technologies

- E-077-2008

Therapeutic Area

- Cancer/Neoplasm
- Infectious Diseases

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