TECHNOLOGY LICENSING OFFICE
4301 West Markham Street, #831
Little Rock, AR 72205
501.686.6696
email: nmgray@uams.edu

BV 2015-21 - *Compositions and Methods for Generating Reversion Free, Attenuated and/or Replication Incompetent Vaccine Vectors*

APPLICATION:

This invention provides methods for generating reversion free, attenuated and/or replication incompetent vaccine vectors and their use in vaccine compositions and vaccination.

KEY BENEFITS:

- Useful for making vaccine viruses that cannot revert to virulent wild-type virus
- Platform for producing safe, attenuated and replication-incompetent DNA viruses
- Improved means for generating replication-incompetent gene therapy vectors
- Applications for manufacturing herpesvirus vaccines

MARKET SUMMARY:

The *Herpesviridae* family of viruses (herpesviruses) includes large, enveloped viruses with a double-strand DNA genome. Herpesviruses are ubiquitous, and infections can cause morbidity and mortality in livestock, wildlife, and the human population. The nine known human herpesviruses cause a wide range of diseases. Mild infection outcomes include rashes, fever blisters and genital lesions due to herpes simplex viruses. However, human herpesviruses also cause congenital birth defects and potentially lethal diseases such as encephalitis, fulminant hepatitis, and numerous cancers caused by Epstein-Barr virus (EBV) and Kaposi sarcoma-associated herpesvirus.

Herpesviruses and other DNA viruses readily undergo homologous recombination during their productive replication cycles, a property harnessed for decades in the generation of recombinant viruses. However, the recombinogenic nature of the viral genome poses a major problem in efforts to generate replication-defective viruses and potential vaccine strains.

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TECHNICAL SUMMARY:

The propensity of herpesvirus genomes to undergo homologous recombination is a barrier to producing mutant virus stocks that require complementation with a helper gene provided *in trans* . University inventors have developed a method to eliminate complementation of the helper gene with mutant viruses to prevent reversion to wild-type. The result is production of large quantities of mutant herpesviruses (or other DNA viruses) that are replication-incompetent and, therefore, potentially useful for vaccination.

DEVELOPMENTAL STAGE:

Mutant viruses were tested in a SCID mouse model. The infection of immune-deficient SCID mice with mutant, replication-incompetent virus caused no mortality. In contrast, replication competent virus caused 60% mortality in the model.

PUBLICATION:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5347388/

PATENT INFORMATION AND CONTACT:

App Type: PCT
Country: US
Serial No.: PCT/US2017/050229
Patent No.:
File Date: 09/06/2016
Issue Date:
Inventor(s): Craig Forrest, Laurie Krug, Gang Li, Steven Skiena
Tech ID: 1521
Contact: Joe Underwood, Associate Director – Licensing, junderwood@uams.edu