THE SCIENCE WORLD
A Monthly e Magazine
ISSN:2583-2212
Oct, 2023; 3(10), 2724-2728

Popular Article

Vaccinia Viral Vectors and Its applications

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https://doi.org/10.5281/zenodo.10059221

Abstract

Vaccinia virus has been constructed to express foreign genes and used as powerful vectors for production of recombinant proteins. Originating from highly efficacious vaccines securing world-wide eradication of smallpox, vaccinia vectors can be used as delivery system for heterologous genes encoding enzymes, antigens and hormones. Concerns about the safety of vaccinia virus have been addressed by the development of vectors based on attenuated viruses. Amongst them, modified vaccinia virus Ankara (MVA) can be considered as current choice for clinical investigation. As compared to replication competent vaccinia viruses, MVA and NYVAC provides similar levels of recombinant gene expression even in non-permissive cells. However, there are still some concerns regarding the safety and efficacy of vaccinia virus. In this article we have briefly discussed the essential information about vaccinia viral vector including its applications.

Introduction

Vectors are defined as the agents that carry selected genes encoding foreign antigens. The vaccinia virus is antigenically similar to smallpox, both viruses being presumably derived from a common ancestor, that led to its extensive use as a vaccine candidate against smallpox. Nowadays, large number of poxviruses are being used as vector such as fowlpox, raccoonpox and canarypox but vaccinia is one of the most extensively used virus amongst them for the development of vector system (3). It is a large DNA virus that replicates within cytoplasm of susceptible host cells. The virion comprises of a biconcave core, two lateral bodies and the entire

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Published: **30.10.2023**

structure is enclosed within lipid envelope.

Replication cycle

In order to replicate inside the host body, initially the vaccinia virus has to adsorb into susceptible host cells for making its way inside by either direct penetration or viropexis. Following the entry, virus particles are uncoated in a two-step process. During the transcription process, early genes are transcribed first followed by intermediate and late genes. Intermediate genes encode the transcription factors required for transcription of late genes. However, late genes encode virion proteins and early transcription factors that are packaged in virions and used in subsequent rounds of infection. Viral genome replication, transcription and assembly occur at juxtanuclear sites. Finally, the virions are released by budding or exocytosis (5).

Types of vaccinia viral vectors

1) **Modified Vaccinia Ankara Vector (MVA):** The MVA vector was developed by serial passage of vaccinia virus in chicken fibroblast tissue culture during the WHO smallpox eradication campaign. It was thought to be derived from ancestral vaccinia virus Ankara strain which was propagated on the skin of calves and donkeys at the Turkish vaccine institute. Herrlich and Mayr have cultivated this virus on the chorioallantois membrane (CAM) of embryonated chicken eggs and thus, it was named as Chorioallantois Vaccinia virus Ankara (CVA). Because of the high safety associated with attenuated phenotype, MVA is being frequently used for clinical research. Additionally, it has the ability to deliver foreign antigens in a highly immunogenic way, which makes it a suitable vaccine vector (4).
2) **NYVAC Vector:** This is a highly attenuated strain of vaccinia virus. It was derived from a plaque-cloned isolate of the Copenhagen vaccinia strain with the deletion of 18 ORFs that contain virulence factors and human host range replication proteins (6). The ORFs were deleted in a manner that prevent the synthesis of unwanted novel gene products.

Insertion sites and advantages

A number of non-essential loci are available within the genome of vaccinia virus for the insertion of foreign DNA. It includes insertion sites such as thymidine kinase (TK) gene and the BamHI site (2). As a vector it confers many advantages such as cytoplasmic replication, broad host range, large viral genome size, well defined gene architecture, economical, high stability and easy administration.

Applications: It has broad range of applications in various fields such as vaccine production, cell biology exploration, immunology and enzymology. Here, we have briefly described them as

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follows.

1) **Prophylactic vaccine production:** Vaccinia viral vector is the most commonly vector in the formation of potential recombinant vaccine. The premise is to insert a gene encoding an antigen from a heterologous pathogen into Vaccinia. Then, the recombinant virus was used as a live infectious vaccine that can induce an antigen-specific immune response in recipient animals (7). Most of the Vaccinia recombinants used to immunize animals are highly effective at inducing both humoral and cellular immunity (Fig.1).
2) **Cell Biology:** The field of cell biology is one of the most rewarding and promising area for the use of Vaccinia vectors. It has been widely used to express various neuropeptides, growth factors, and receptor proteins. The prime advantage associated with this approach is expression of appreciable (microgram) quantities of protein in biologically active form. Recently, the gene encoding yeast mating-factor protease (KEX2) was recombined in a fully functional form into vaccinia (8).
3) **Immunology:** Vaccinia has provided a new dimension to study the immunological interactions between pathogen and target host organism due to its infectious nature and broad host range. Pathogens such as viruses are complex structures that present an antigenic mosaic to the host immune system; thus, it is often difficult to determine which antigen is relevant to the induction of immunity. This problem can be greatly simplified by use of Vaccinia vectors. For example, in the case of acquired immunodeficiency syndrome (ACID), recombinant Vaccinia strains have been constructed which individually express each of the individual type 1 human immunodeficiency virus (HIV-1) proteins, gpl60, gpl20, tat, and reverse transcriptase (1). These recombinants are being used to determine whether the viral proteins are immunogenic or not.
4) **Basic research:** Vaccinia vectors can be used to express and manipulate any DNA sequence of interest, whether they encode antigens, enzymes, or structural proteins. The cloned sequences within the recombinant vectors work as suitable substrates for site-directed mutagenesis procedure. It is a relatively straightforward procedure to prepare a collection of Vaccinia recombinants expressing different genetically engineered forms of the same protein to address structure-function relationships.

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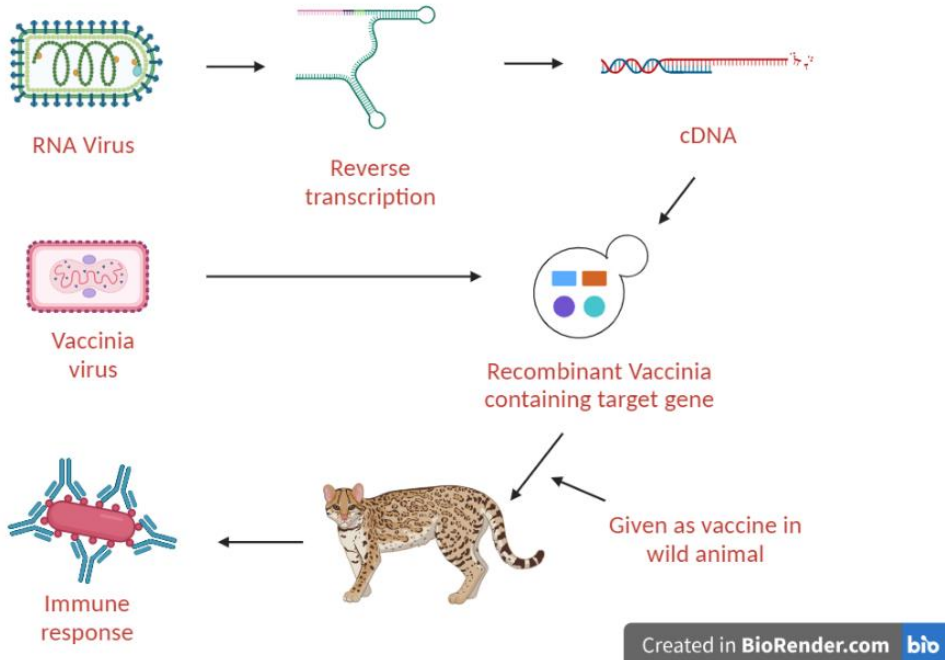

Figure 1. Diagram of Vaccinia viral vector-based vaccine construction

Limitations

Despite having multiple advantages of the Vaccinia viral vectors, the system also has some limitations. It includes lack of large scale and long-term expression capability and additionally, it is of little use to engineer nuclear gene replacements. The use in human population may be less beneficial due to the presence of pre-existing neutralizing antibodies due to its earlier administration as smallpox vaccine.

Conclusions

It is a remarkably powerful experimental vector system. We can easily insert and express any foreign DNA to make recombinants for various studies. Additional information regarding the structure, function and regulation of poxviruses have been widely studied. It is highly likeable that new generations of vaccinia viral vector systems will be developed in near future.

References

Chapman, R., van Diepen, M., Douglass, N., Hermanus, T., Moore, P.L. and Williamson, A.L., 2023. Needle-Free Devices and CpG-Adjuvanted DNA Improve Anti-HIV Antibody Responses of Both DNA and Modified Vaccinia Ankara-Vectored Candidate Vaccines. Vaccines, 11(2), p.376.

Faqih, L., Vallely, P. and Klapper, P., 2023. Genetic stability of SIV Gag/Tat gene inserted into Del-II in modified vaccinia virus ankara after serial passage of recombinant vector in pCEFs cells. Journal of Virological Methods, 312, p.114651.

Kaynarcalidan, O., Moreno Mascaraque, S. and Drexler, I., 2021. Vaccinia virus: from crude smallpox vaccines to elaborate viral vector vaccine design. Biomedicines, 9(12), p.1780.

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Nave, L., Margalit, I., Tau, N., Cohen, I., Yelin, D., Lienert, F. and Yahav, D., 2023. Immunogenicity and Safety of Modified Vaccinia Ankara (MVA) Vaccine—A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Vaccines, 11(9), p.1410.

O'Connell, C.M., Jasperse, B., Hagen, C.J., Titong, A. and Verardi, P.H., 2020. Replication-inducible vaccinia virus vectors with enhanced safety in vivo. PLoS One, 15(4), p.e0230711.

Perdiguero, B., Perez, P., Marcos-Villar, L., Albericio, G., Astorgano, D., Álvarez, E., Sin, L., Gómez, C.E., García-Arriaza, J. and Esteban, M., 2023. Highly attenuated poxvirus-based vaccines against emerging viral diseases. Journal of Molecular Biology, p.168173.

Rocke, T., Streicker, D. and Leon, A., 2023. Management of Vampire Bats and Rabies: Past, Present, and Future. In History of Rabies in the Americas: From the Pre-Columbian to the Present, Volume I: Insights to Specific Cross-Cutting Aspects of the Disease in the Americas (pp. 199-222). Cham: Springer International Publishing.

Vogt, E., Sonderegger, L., Chen, Y.Y., Segessemann, T. and Kunzler, M., 2022. Structural and functional analysis of peptides derived from KEX2-processed repeat proteins in agaricomycetes using reverse genetics and peptidomics. Microbiology Spectrum, 10(6), pp.e02021-22.