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Agricultural Pathogen Becomes a Delivery Vehicle for Vaccines

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Abstract

The Vesicular Stomatitis Virus (VSV), a well-known livestock pathogen and prototypical non-segmented, negative-sense RNA virus, is a member of the *Vesiculovirus* genus and the family *Rhabdoviridae*. Even though the virus is to blame for economically significant epidemics of vesicular stomatitis in cattle, horses, and pigs, molecular biologists and virologists can still use VSV as a useful research tool. In fact, the development of a reverse genetics approach for the recovery of infectious VSV from cDNA altered this virus's functionality and opened the door for its application as a vaccine vector. Many other VSV-based vaccines have been developed, especially for high-consequence viruses. A highly effective VSV-based vaccination against the Ebola virus just got clinical licensure. This review aims to give a comprehensive but succinct understanding of VSV, documenting the virus's transformation into a viable medicinal countermeasure, with a focus on vaccinations, from a persistent agricultural scourge.

Keywords: Vesicular stomatitis virus • Vaccine countermeasure • Ebola virus • Reverse genetics • Medical countermeasure

Introduction

A group of morphologically and genetically related viruses that infect mammals, birds, and reptiles make up the genus *Vesiculovirus* [1]. The term "vesicular stomatitis virus" within this genus refers to a number of closely related viruses that are subdivided into the New Jersey and Indiana serotypes of a single serogroup. While the Indiana serotype is further separated into four different serological complexes, the New Jersey serotype contains the vesicular stomatitis New Jersey virus (VSNJV). Vesicular stomatitis Indiana virus (VSIV) is present in Indiana 1, Cocal virus (COCV) is present in Indiana 2, Vesicular stomatitis Alagoas virus (VSAV) is present in Indiana 3, and Morreton virus is present in Indiana 4. (MORV). In the Americas, all of these VSVs—possibly with the exception of MORV—are to blame for vesicular stomatitis illness in livestock animals (described below) , with VSIV being the most widely acknowledged type species for the genus *Vesiculovirus*. Members of the VSV serogroup will be referred to generally as "VSV," with specific viruses named as required. It should be noted that several additional *vesiculoviruses*, including the Piry virus from South America, the Chandipura virus from South Asia, and the Isfahan virus from Western Asia, can infect mammals and cause sickness, but they will not be discussed in this article [2].

Subjective Heading

Molecular virology and VSV

VSV has been extensively used as a model system to investigate the replication and assembly of mononegaviruses because it is the prototype rhabdovirus. The VSV genome has also been modified so that it can be used as a research tool, a platform for a vaccine, and an oncolytic vector [36]. The VSV reverse genetics system, which enables direct manipulation of the VSV genome via recombinant DNA techniques, is required for the majority of these applications [3].

As with all negative-sense RNA viruses, there are a number of difficulties in producing infectious virus from a cDNA clone of the VSV genome. Negative-sense RNA viruses, like VSV, must first undergo transcription to produce the viral proteins necessary for subsequent rounds of transcription, in contrast to positive-sense RNA viruses, for which the genome is intrinsically contagious. genome replication, too [4]. Additionally, the nucleoprotein is required for the viral RNA polymerase complex to detect both negative-sense genomes and positive-sense antigenomes as templates for transcription and replication. The viral proteins N, P, and L, which together with the RNA genome make up the ribonucleoprotein (RNP) complex, must therefore be supplied in trans in the case of VSV [5].

When the infectious rabies virus, a close member of VSV in the rhabdovirus family, was totally produced from cloned cDNA in 1994, a breakthrough was accomplished. VSV itself was isolated from a full-length cDNA clone by two different labs less than a year later [6]. The key to the rabies virus's and VSV's successful recovery largely depended on the employment of Using plasmids encoding an anti-genomic rather than a genomic RNA counterpart, with the addition of a ribozyme sequence from the hepatitis delta virus (HDV) to produce precise 3′ ends. N, P, and L proteins were made available in trans from so-called "helper" plasmids, and a T7 promoter was used to control expression from each plasmid. The infectious virus was successfully saved when all of the plasmids were transfected into BHK21 cells along with a recombinant vaccinia virus that expressed the T7 RNA polymerase [7].

VSV as a vaccine vector

Many of the characteristics that make VSV an effective platform for a vaccine also make it a useful tool for molecular virology research, including its capacity to express heterologous glycoproteins and multiply at high titers. There is also little pre-existing immunity to the vector due to the low apparent seroprevalence of VSV antibodies in the human population and the fact that the VSV replication cycle only occurs in the cytoplasm of host cells, which eliminates the possibility of viral sequences integrating into the host genome. As a result, rVSV has gained popularity as a vaccine vector over the past few years, and numerous rVSV-based vaccines have proven safe and immunogenic in numerous pre-clinical and clinical trials [8]. The development of VSV-based vaccines has a long and complicated history. Study of dangerous pathogens, particularly the Ebola virus (EBOV). A number of different potential

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vaccines against new and dangerous viruses have now been developed and characterised as a result of the early promise and eventual success of a VSV-vectored EBOV vaccine. The VSV-based EBOV vaccine, for which a wealth of data is available, will be the subject of our discussion below. However, we also discuss other high-risk pathogens for which VSV-based vaccines have been created, such as Marburg virus and other filoviruses, Lassa virus, henipaviruses, and coronaviruses [9].

Discussion

A new vaccine against the Crimean-Congo Hemorrhagic Fever Virus (CCHFV), a bunyavirus spread by ticks that can cause severe hemorrhagic sickness in humans, has just been created using the VSV platform. The CCHFV GPC was substituted for VSV G in Rodriguez et alrVSV, .'s however this virus could only be saved if VSV G was made available in trans. To get over this restriction, the virus was serially passed first through BHK cells that were expressing VSV G and then through BHK cells on their own. The resulting virus, designated here as VSV-CCHFV-GPC, had a number of changes in the GPC that made it capable of replication. STAT-1 knockout mice were immunised with 107 PFU of VSV-CCHFV-GPC, then challenged 35 days later with a lethal dose of 50 PFU CCHFV completely shielded. The complete protection and less severe weight loss were likewise achieved by administering a booster dose 14 days after the prime dose [10].

Conclusion

It is amazing how VSV has progressed from an agricultural disease to a model virus and, eventually, a validated countermeasure since the identification of VSIV in 1925 and the clinical approval of VSV-EBOV in 2019. Reverse genetics is one of the molecular tools that was created to work with VSV and has subsequently been extended and used to study other viruses. VSV has been crucial to our understanding of single-stranded, negative-sense RNA viruses. One of the first clinically authorised EBOV vaccines and a number of other vaccines were developed as a result of the ability to investigate the glycoproteins of high-consequence diseases using VSV as a surrogate thanks to recombinant technologies. VSV is also currently being investigated as an oncolytic vector due to its lytic replication; however that is not covered here. type I interferon-dependent immunological responses: cycle and sensitivity. VSV is a flexible, secure, and productive platform that has already produced useful new countermeasures and holds the possibility of delivering far more in the future.

Acknowledgement

None

Conflict of Interest

None.

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