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Reovirus: Lifecycle, Pathophysiology, and Prospective Therapeutic Uses

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Abstract

Reovirus is a double stranded, non-enveloped RNA virus that is a member of the Reoviridae family. It is well known for its broad host range, which encompasses both people and other animal species. It is also often discovered in the environment. Despite generally being rather innocuous, certain reovirus strains have been linked to serious illnesses in both people and animals. This article gives a thorough introduction to Reovirus, emphasizing its composition, replication process, pathophysiology, clinical relevance, and prospective therapeutic uses. A segmented genome encoding twelve proteins and two concentric protein shells make up the distinctive capsid structure of the Reovirus. Its replication cycle includes viral particle uncoating, host cell receptor attachment, internalization by endocytosis, genome transcription and translation in the cytoplasm. Reovirus has a strong capacity to control cellular functions, including the activation of stress response pathways and manipulation of apoptosis, allowing for effective reproduction and spread inside the host. Reovirus usually causes moderate respiratory or gastrointestinal symptoms in people, particularly in youngsters. However, recent research points to a possible connection between reovirus and more serious conditions including encephalitis, myocarditis, and possibly certain forms of cancer. Further study is needed to completely understand the viral and host components contributing to the pathogenesis of Reovirus induced illnesses since the underlying processes are not yet fully understood. Reovirus has, intriguingly, shown potential as a therapeutic agent in the area of oncolytic virotherapy. Clinical studies investigating the effectiveness of reovirus based therapies, either as monotherapy or in conjunction with other modalities, have shown encouraging results in a variety of cancer types, indicating its potential as an important therapeutic tool. In conclusion, Reovirus is an adaptable viral pathogen that interacts intricately with its host. To further our understanding of viral pathogenesis, create targeted therapies, and take use of Reovirus's special properties for therapeutic applications, it is essential to comprehend the molecular and cellular interactions that drive Reovirus infections. To fully understand this fascinating virus's capabilities and the ramifications for both human and animal health, further study is necessary.

Keywords: Reovirus; Replication process; Viral therapies; Anticancer; Oncolytic viruses

Introduction

The Reoviridae family, of which Reovirus is a member, has several very interesting viral pathogens. The term "respiratory enteric Orphan virus" (or "Reovirus") is an abbreviation for the full phrase "respiratory enteric Orphan virus," which describes the virus since it was first found in the respiratory and gastrointestinal systems and was not previously linked to any disorders [1]. New information, however, shows that it may infect a wide variety of hosts and cause a spectrum of illnesses in both people and animals [2]. Reoviruses are considered to be non-enveloped since they do not have a lipid coat. Instead, its DNA is safeguarded by a protein capsid that is both strong and stable [3]. Reoviruses are distinguished from other viruses by the fact that their viral genome is composed of segmented double stranded RNA (dsRNA). Multiple proteins encoded by the genome's segmentation are essential for viral replication, pathogenicity, and interactions with host cells [4]. In the 1950's, researchers discovered Reovirus from human respiratory and intestinal samples, marking the beginning of the virus's discovery. Early research established that Reovirus was a frequent childhood virus that often manifested as mild respiratory and gastrointestinal symptoms. The genetic variety and clinical importance of Reoviruses have been better understood as a result of recent developments in molecular methods and research strategies [5]. Reovirus has an impressive host range, able to infect mammals, birds, and even reptiles. It is widespread in the environment and may be picked up by sensitive organisms from places including soil, water, and faces [6]. Some strains of Reovirus have been linked to more serious disorders such viral encephalitis, myocarditis, and even malignancy, despite the fact that most Reovirus infections are self-limiting and heal without therapy [7]. Receptor mediated endocytosis is the mechanism through which the virus enters host cells and then releases its genetic material into the cytoplasm of the host cell. After entering a cell, Reovirus relies on the host's machinery for genome replication, protein synthesis, and virus particle assembly [8]. In addition to being

able to successfully replicate and spread, it also has a number of mechanisms that allow it to manipulate host cell processes and avoid being attacked by the immune system [9]. The potential uses of Reovirus in cancer treatment have been widely discussed in recent years. Reovirus has been used in oncolytic virotherapy because of its innate capacity to preferentially infect and proliferate inside tumor cells while sparing normal ones [10]. Evidence from clinical studies of Reovirus based therapies for multiple cancer types is encouraging, opening the door to future investigation and optimization of this therapeutic method [11]. In conclusion, Reovirus is an interesting and adaptable pathogen that may infect a broad variety of hosts and express itself in a wide variety of ways in the body. Research into Reovirus has the potential to advance cancer therapy and give new understanding of viral pathophysiology [12]. In this review article it might be a study about interesting virus and its consequences for both human and animal well-being if researchers keep plugging away at the knotty problems posed by Reovirus and the animals it infects.

Literature Review

Lifecycle of Reovirus

Reoviruses replicate by completing a sequence of well-coordinated stages in the cytoplasm of the host cell. Reovirus particles initiate the replication cycle by binding to receptors on the surface of the host cell and entering the cell. Figure 1 shows the structure of Reovirus [13]. Both the host species and the kind of cell may influence the characteristics of these receptors. Reovirus particles are taken up into the host cell through receptor mediated endocytosis once they have adhered. Reovirus particles go through a process termed uncoating once they are internalized. The viral DNA can only be accessed by removing the protein capsid covering around it. Low pH or proteolytic enzymes in the endosomes are two examples of conditions that might initiate the uncoating process [14]. The transcription and translation of the viral genome take place after the viral DNA has been released into the cytoplasm of the host cell. Segmented double stranded RNA (dsRNA) makes up the Reovirus genome, with each segment encoding a different viral protein [15]. messenger RNAs (mRNAs) are synthesized from the dsRNA segments by the viral RNA dependent RNA polymerase, which is part of the viral core. The machinery of the host cell reads these mRNAs and translates them into viral proteins. Reovirus uses a method called "genome replication through a dsRNA intermediate" to copy its DNA [16]. A replication intermediate known as "panhandle" or "tightly bound" dsRNA is formed when the viral RNA-dependent RNA polymerase produces a complimentary copy of each dsRNA segment. New segments of genomic dsRNA are synthesized using this panhandle dsRNA as a template. Viral particles are assembled from freshly synthesized genomic dsRNA segments and the viral proteins as replication proceeds. Assembly occurs in specialized cytoplasmic inclusions known as piroplasm's [17]. The viral proteins and dsRNA segments assemble within these structures to generate infectious virus particles. Reovirus particles leave the host cell after their assembly is complete. The release process may include cell lysis, which involves the disruption of the host cell membrane, or it may use non-lytic mechanisms like budding or exocytosis. Different Reovirus strains and host cell types may result in a wide variety of release mechanisms [18]. There are many complex interactions between viral components and host cell factors that contribute to the extremely dynamic and controlled nature of the Reovirus replication process. Figure 2 shows the lifecycle of Reovirus. Reovirus is able to efficiently replicate and spread inside its host due to its capacity to regulate host cell processes and control cellular machinery [19].

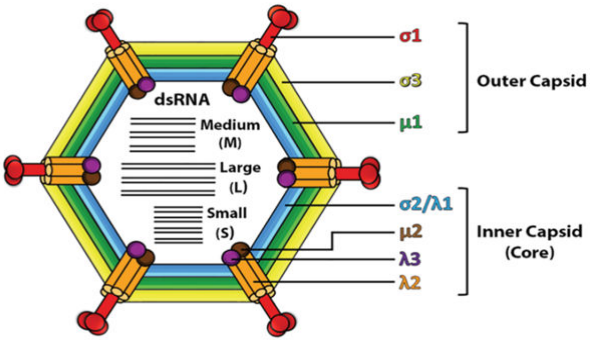

Figure 1: Shows the structure of Reovirus.

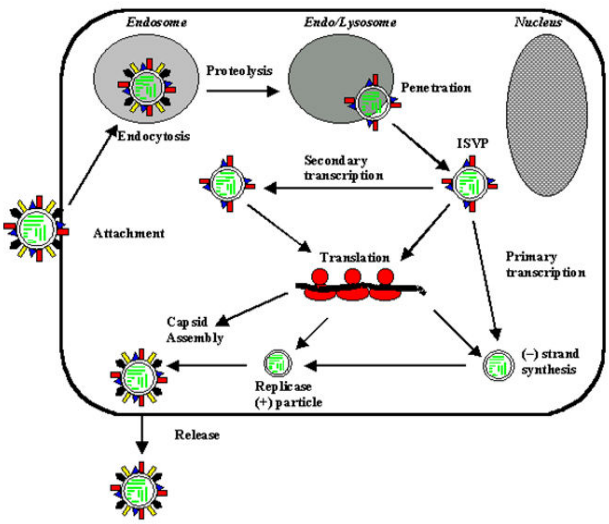

Figure 2: Shows the lifecycle of Reovirus.

Clinical prevalence of Reovirus

The fact that Reovirus can infect both people and animals make it clinically significant. Some strains of the Reovirus have been linked to more severe clinical symptoms, despite the fact that Reovirus infections are often thought to be moderate and self-limiting [20-24]. Some important Reovirus clinical considerations include. Illnesses of the respiratory system and the digestive system as Reovirus is a frequent cause of moderate respiratory and gastrointestinal illnesses in children. Fevers, coughs, runny noses, sore throats, diarrhea and vomiting are all possible side effects. These infections often clear up on their own without any medical intervention [25]. Inflammation of the brain, or viral encephalitis, has been linked to certain Reovirus strains. Fever, headache, altered awareness, convulsions and localized neurological impairments are all possible consequences

of Reovirus encephalitis [26]. Reovirus encephalitis is uncommon, but when it occurs, it may be quite serious and need hospitalization and supportive treatment. Myocarditis is inflammation of the heart muscle and Reovirus has been linked to this condition. Symptoms of Reovirus myocarditis include heart failure, shortness of breath, palpitations and chest discomfort. Hospitalization and heart care specialists may be needed for severe instances [27]. Reovirus has attracted interest as a possible therapeutic agent due to its focus on oncolytic virotherapy. Reovirus is used in oncolytic virotherapy because it may selectively infect and proliferate inside tumor cells, ultimately killing those cells. Multiple forms of cancer, including those of the head and neck, ovaries, and pancreas, have responded well to clinical studies examining Reovirus based therapies, either alone or in conjunction with other modalities [28]. New evidence reveals a relationship between Reovirus and some chronic conditions, such as type 1 diabetes and celiac disease. Reovirus infection may cause immunological responses that aid in the development or progression of various disorders, while the specific pathways are not well known. More research is required to confirm the link and clarify the underlying processes.

Various therapeutic uses of Reovirus

There are a number of promising therapeutic uses for Reovirus. Its capacity to infect and multiply only inside tumor cells, while sparing normal cells, is only one of its distinctive features that makes it a promising therapeutic target. Reovirus has been studied extensively as a potential oncolytic virus for cancer treatments. Viruses are used in oncolytic virotherapy to target and kill only cancer cells. Tumor cells are an easy target for Reovirus, which may multiply inside them, lyse them, and release viral particles, so spreading the infection [29]. Treatments based on reoviruses have been shown to be safe and effective against many different kinds of cancer in clinical studies. Treatments based on Reoviruses may be administered alone or in combination with other modalities like chemotherapy or immunotherapy. Potential adjuvant therapy for cancer treatment using Reovirus. Adjuvants are drugs that boost the body's natural defenses in conjunction with another kind of treatment [30]. Immunogenic cell death caused by Reovirus infection may trigger an immune response against tumors by causing the release of tumor antigens. Chemotherapy and immunotherapy, for example, may be made more effective by this immune response. Research into the potential additive benefits of mixing Reovirus with other therapy methods is now being investigated in clinical studies. Research on vaccines based on Reoviruses has shown promising results in terms of avoiding viral infections and eliciting protective immune responses. Reovirus is a promising vaccine candidate because to its unusual features, such as its capacity to stimulate both innate and adaptive immune responses. Vaccines developed using Reovirus have showed promise in studies against pathogens including Rotavirus, HIV, and influenza. Immune responses against targeted infections or tumor antigens may be elicited using Reovirus vectors as a delivery system. The use of reovirus as a vector for gene therapy has been investigated [31-33]. Therapeutic genes might be delivered to targeted tissues or tumors using Reovirus due to its capacity to infect and proliferate inside target cells. Reovirus vectors have been the subject of research into the delivery of therapeutic genes to target cells for the treatment of cancer, immunological modulation, and other diseases. Reovirus has showed promise as an antiviral agent in the treatment of various viral illnesses. Reovirus has shown antiviral efficacy against a number of other viruses in preclinical research. This includes RSV, HPV and HSV. A strong immune response induced by Reovirus may block the reproduction of these viruses [34]. To determine whether or not Reovirus can be used safely and effectively in clinical settings as an antiviral medication, further study is required. Cancer treatment, vaccine development, gene therapy and antiviral therapy are just few of the areas where Reovirus might be used as a therapeutic agent. Further understanding of the effectiveness, safety and appropriate use of Reovirus based therapeutics in various disease situations is anticipated to emerge through ongoing research and clinical studies [35].

Discussion

Manipulation of apoptosis

Reovirus may use the host cell's programmed cell death mechanism, known as apoptosis, to propagate and survive. To restrict viral replication, Reoviruses may actively inhibit apoptosis by preventing cells from dying too soon [36]. The virus makes use of a number of mechanisms to prevent apoptotic signaling and the activation of pro apoptotic proteins. Reovirus, for instance, may impede the intrinsic apoptosis pathway by blocking the activation of pro apoptotic Bcl-2 family members or by impeding the release of cytochrome c from mitochondria. Reovirus guarantees the survival and sustained infection of host cells by preventing their natural death process, apoptosis. Reovirus has the ability to boost its own reproduction by activating several cellular survival pathways in response to apoptotic signals. One method is the stimulation of the cell survival and anti-apoptosis Phosphatidylinositol 3-Kinase (PI3K)/Akt signaling pathway. By activating PI3K/Akt signaling, reoviruses promote cell survival by preventing the phosphorylation and subsequent deactivation of pro apoptotic proteins like bad and caspase-9. Reovirus may modulate apoptotic signaling by interacting with death receptors including Tumor Necrosis Factor Receptor 1 (TNFR1) [37]. Infection with reovirus has been shown to increase apoptosis induced by TNF Related Apoptosis Inducing Ligand (TRAIL) in several cancer cells. Caspase activation and death may occur in these cells when reovirus infection triggers TRAIL 9. Reovirus typically inhibits apoptosis in order to promote its reproduction, there are circumstances in which the virus actually causes apoptosis. Reovirus infection, for instance, might cause apoptosis by activating both intrinsic and extrinsic apoptotic pathways in some types of cancer cells. There may be interactions between the host cell's genetic and molecular properties and the strain of Reovirus employed to induce apoptosis. When within a host cell, Reovirus may modify apoptotic pathways to ensure its own survival and spread.

Therapeutic agent in oncolytic virotherapy

In the area of oncolytic virotherapy, which employs viruses to selectively infect and destroy cancer cells, reovirus has emerged as a viable therapeutic agent. Invasive cancer cells replicate selectively: Reovirus's capacity to multiply just within cancer cells, sparing healthy ones, is a huge benefit. Cancer cells, which often have an active Ras signaling system, are the virus's preferred host for infection and replication. Oncolysis, the killing of cancer cells without harming healthy tissue, is the result of this kind of targeted replication. Reovirus promotes cell death in tumors via many different pathways. Direct oncolysis is triggered when the virus replicates within cancer cells, killing them and releasing their offspring [38]. When tumor cells are lysed, the released viral particles may infect nearby cancer cells, spreading the infection and increasing the anti-tumor impact. The death of infected cells is immunogenic, resulting in the release of tumor antigens and the activation of the immune system to attack cancer cells, another effect of Reovirus infection. Reovirus infection has been shown to activate anti-tumor immune responses by stimulating the immune system. It initiates and coordinates immune responses against tumors by stimulating innate immunity cells such dendritic cells and Natural Killer (NK) cells. Tumor antigen presentation to immune cells may be improved by Reovirus infection, leading to the activation of tumor specific T lymphocytes. This immune stimulation aids in the destruction of infected and uninfected tumor cells and may produce a permanent memory response to cancer. Reovirus has the potential to improve the effectiveness of cancer treatments when used in conjunction with other medications. When paired with other medicines, such as chemotherapy, radiation therapy, or immunotherapies, it has demonstrated synergistic results. Immune responses, tumor cell killing, and resistance mechanisms may all be enhanced when Reovirus is combined with other therapeutic methods for cancer patients. Clinical investigations using Reovirus have shown a positive safety profile [39]. Most people have been exposed to Reovirus throughout infancy without developing serious symptoms, leading experts to conclude that it is a naturally occurring virus in humans. Due of its low toxicity, Reovirus is an appealing option for use in therapeutic settings. The development of Reovirus based anticancer medicines involves various steps aimed at harnessing the oncolytic properties of the virus and optimizing its therapeutic potential.

Conclusion

Reovirus is a fascinating and adaptable viral pathogen with a broad range of hosts and a variety of clinical symptoms. Reovirus replication is a highly dynamic and controlled process that involves complex interactions between viral and host cell factors. Reovirus infections have a complicated pathophysiology that includes interactions between viral replication, host immune responses, tissue destruction and clinical symptoms. Reovirus has a lot of promise as a therapeutic agent in a variety of medical domains, such as the treatment of cancer, the creation of vaccines, gene therapy and antiviral therapy. Current studies and clinical trials are anticipated to provide further light on the effectiveness, safety and best use of reovirus based treatments in various illness situations. It is crucial to remember that the process of creating anticancer medications based on Reoviruses is continuous and constantly changing. Further understanding of its mechanisms of action, optimization of treatment strategies, and identification of predictive biomarkers are expected to enhance the therapeutic efficacy of Reovirus in the treatment of various types of cancer.

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All the authors equally contributed in completion of this article.

Conflict of Interest

There is no conflict of interest for this article.

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