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ONCOLYTIC VIRUSES: A NOVEL APPROACH TO CANCER TREATMENT

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ABSTRACT

Oncolytic virus therapy is a novel and promising method of treatment, which exploits the use of genetically modified or naturally occurring viruses selectively to infect and destroy cancer cells, sparing normal tissues. Viruses provide two mechanisms of action: direct oncolysis and systemic induction of an anti-tumor immune response. Despite these developments, including genetic engineering to increase the selectivity of the tumor and AI-driven optimizations, challenges in delivery, immune clearance, and regulatory approvals remain. Clinical trials currently under way are increasing the range of cancers treatable with such approaches, while future directions include personalized medicine, innovative design of viruses, and synergistic therapies with immunotherapy and chemotherapy. Ethical and safety considerations, including biosecurity and public perception, will be crucial in ensuring responsible development and widespread clinical application. The integration of these strategies positions oncolytic virus therapy as a transformative tool in modern oncology.

KEYWORDS: Oncolytic viruses, cancer therapy, genetic engineering, immunotherapy, tumor selectivity, viral delivery, artificial intelligence, personalized medicine, clinical trials, biosecurity.

INTRODUCTION

Cancer remains a major cause of death globally and therefore requires new therapeutic approaches. Although surgery, chemotherapy, and radiation therapy are quite effective in many situations, they do not come without the burden of severe side effects and limitations. Recently, biological therapies have emerged as alternatives. Among them, oncolytic virotherapy has received a lot of attention as a novel and potentially revolutionary approach to cancer treatment: the use of genetically modified or naturally occurring viruses to selectively infect and kill cancer cells.[1,2]

Oncolytic viruses (OVs) are viruses that selectively infect, replicate within, and lyse cancer cells without killing normal, healthy cells. Selective cytotoxicity is achieved through either natural or engineered mechanisms that take advantage of the special vulnerabilities of tumor cells. OVs work by multiple mechanisms: direct lysis of cancer cells, activation of the host immune response, and induction of systemic anti-tumor immunity. Among the commonly used oncolytic viruses are adenoviruses, herpes simplex virus (HSV), reovirus, and vaccinia virus, which have unique properties and therapeutic applications.[3,4]

HISTORICAL PERSPECTIVE AND DISCOVERY

This dates back to the early 20th century, when physicians began noticing that patients with cancer could experience regression of their tumors due to viral infections. However, early attempts at using viruses in cancer therapy were limited by concerns over safety and a lack of understanding of both virology and tumor biology. The modern era of oncolytic virotherapy began in the 1990s, following advances in genetic engineering that would allow the production of safer and more effective oncolytic viruses.[5] One of the first notable major successes was the Chinese approval of Oncorine, or H101-an oncolytic adenovirus to treat head and neck cancers in 2005. In 2015, the United States Food and Drug Administration approved talimogene laherparepvec or T-VEC, a modified herpes simplex virus for the

treatment of melanoma. The milestone marked the acceptance of clinical progress for oncolytic virotherapy.[6]

IMPORTANCE AND POTENTIAL OF ONCOLYTIC VIRUS THERAPY IN CANCER TREATMENT

- **Cancer Cells' Targeted Selection:** Oncolytic viruses specifically infect and replicate in cancer cells without harming normal cells, which may improve side effects compared to traditional treatments.[7]
- **Double Mechanism of Action:** Oncolytic virus kills cancer cells by direct oncolysis and also releases antigens specific to tumor cells, which stimulate an overall immune response in the body.[8]
- **Immune Engagement:** Besides its ability to manage the immune environment by stimulating a heightened response in the immune system itself, the oncolytic virus train the body's defenses to recognize and attack cancer in any form, around the clock, with the promise that it could work into the cancer for long-term protection.[8]
- **Prospects of Genetic Support:** They can be custom-tailored for their intended application with the introduction of the therapeutic gene (s) that will further augment their oncolytic potential or application specificity.
- **Incorporate with Other Treatments:** Immunotherapy, chemotherapy, or radiotherapy might also benefit from the effectiveness conferred on oncolytic virus treatments besides reducing drug resistance.[10]
- **Enhanced Use:** Active clinical trial stages involve the use of oncolytic viruses in treating malignancies such as melanoma, malignant glioma, lung cancer, and pancreatic cancer.[11]
- **Minimal Systemic Side Effects:** On a specified level, systemic toxicities are less pronounced compared with chemotherapeutic and therapeutic exposure, reducing the burden of cumulatively low toxicities making it unacceptable in many cases unless the promise of cure outweighs it.
- **Options for Potential Personalized Medicine:** Advances in genetic treatment will allow tailored oncolytic viruses to be produced according to specific genetic mutations and antigen types of patients' tumors.[12]

Classification of oncolytic viruses: Oncolytic viruses can be classified into four types by origin, genetic modification, mode of action, and specificity. Detailed classification is explained as follows.

1. Classification According to Family and Type

- **DNA Viruses**
  - **Adenoviruses:** DNA double stranded oncolytic viruses, modified through genetic techniques for killing specific cancer cells
  - **Herpes Simplex Virus (HSV):** DNA double-stranded viruses. Engineered viruses which can be designed selectively targeting the tumor cell, which induces expression of the immune stimulatory proteins.
  - **Vaccinia Virus:** A large, double-stranded DNA virus that is used in oncolytic virotherapy and can be engineered to selectively target specific cancers.
- **RNA Viruses**
  - **Reoviruses:** Double-stranded RNA viruses that selectively infect and replicate in cells with an activated Ras pathway, which is common in many cancers.
  - **Coxsackievirus A21 (CVA21):** Single-stranded RNA viruses that target cancer cells with high expression of the ICAM-1 receptor.
  - **VSV (Vesicular Stomatitis Virus):** Single-stranded RNA, negative-sense viruses exploiting the defective antiviral response in cancer cells.
  - **POLIOVIRUS (Modified):** A single-stranded RNA virus engineered to attach specifically to tumor associated receptors like CD155.
  - **MEASLES VIRUS:** Single-stranded RNA virus genetically engineered to selectively infect and kill target tumor cells while inducing immune responses.[13,14]

2. Classification Based on Genetic Modification

- **Wild-Type Oncolytic Viruses:** These are natural oncolytic viral strains with intrinsic characteristics for killing cancer cells without the need for modification. For example, reoviridae, which intrinsically embodies the capacity to replicate specifically and effectively in cancer cells that are signaling with Ras mutations.
- **Genetically Manipulated Oncolytic Viruses:** Another group that has been so transgenically mobilized that their ability, specificity, or natural genetic traits are further directed toward oncolysis development or as gene therapy conveyance. For instance, T-VEC, a genetically modified Herpes Simplex Virus designed to immunologically sensitize the patient's body for an anti-melanoma attack.

3. Classification Based on Mechanism of Action

- **Oncolytic Viruses with Immune-Stimulating Properties:** Techniques to modify certain oncolytic viruses so that they will encode cytokines or other stimulants to elicit an immune response against the tumor.
  - Going along with T-VEC (GM-CSF-expressing, HSV- based oncolytic virus).

- **Oncolytic Viruses devoid of Immune-Stimulating Properties:** These are believed to infect and lyse cancer cells using oncolysis as the primary mode of action, not say-taxing too much with the immune response.
  - Reoviruses that are specific to tumors with mutations in specific genetic pathways like their pathway through Ras.

4. Classification Based on Tropism (Specificity for Cancer Cells)

- Oncolytic viruses for broad spectrum: These are good in infecting and destroying so many types of tumors without induction by gene.
  - Example: Vaccinia virus that can be engineered to target any cancer cell type.
- Oncolytic viruses for tumor therapy: These are viruses that are modified or naturally selected for their replication and targeting specificity in the malignant cells with respect to some genetic changes or receptor overexpression.
  - o Example: Coxsackievirus A21 (CVA21) that selectively attacks those cancer cells that have over-expressed receptor for ICAM-1.[15,16]

5. Classification Based on Administration Route

- **Local Administration -- Oncolytic Viruses:** These placed directly into the tumor or the tumor site. This serves as a vehicle to bring highly concentrated levels of the virus onto the very site where the tumor is located, and is generally used in the case of solid tumors.
  - **Example:** T-VEC injected into melanoma tumors.
- **Systemic Administration -- Oncolytic Viruses:** These can be administered intravenously and can reach any part of the body, thereby potentially targeting multiple tumors, including metastatic lesions.
  - **Example:** Systemic administration of Reolysin (reovirus-based) to a variety of cancers, including head and neck cancers.[17,18]

GENETIC ENGINEERING AND ENHANCEMENTS IN ONCOLYTIC VIRUSES

Genetic engineering of oncolytic viruses (OVs) has been critical for their potential elevation in this regard to make them more selective, safe, and efficient therapeutic agents against cancer. These changes would help improve the targeted abilities of these viruses toward tumors with reduced damage to the normal tissue and the elicited robust immune responses against the tumors.

1. Modifications for Improved Tumour Specificity and Safety: Genetic engineering methods are used when making oncolytic viruses with the aim of harnessing the preferential tropism of oncolytic viruses towards cancer cells with minimal impact on normal tissues. Some of these modifications include the following.

- **Targeting Tumor-Specific Receptors:** Viruses can be engineered to attach specifically to those receptors that are overexpressed on cancer cells. This would mean that the virus will preferentially infect tumor cells and avoid healthy cells.
  - **Example**: Certain adenoviruses and coxsackievirus A21 (CVA21) are engineered to attach to receptors like the Coxsackievirus and adenovirus receptor (CAR) or ICAM-1, both of which are overexpressed in some cancers.
- **Inhibition of Viral Replication in Normal Cells**: Oncolytic viruses can be engineered to have genetic alterations that prevent them from replicating in normal, healthy cells but allow them to replicate in cancerous cells. This selective replication is often achieved by exploiting genetic abnormalities present in tumor cells, such as the loss of certain tumor suppressor genes.
  - **Example:** Genetically modified HSV (Herpes Simplex Virus) strains that only replicate in cells with a defective p53 tumor suppressor gene.
- **Use of Tissue-Specific Promoters:** Engineered viruses may be engineered with tissue-specific promoters such that the replication of the virus occurs only in the tumor environment. These promoters are derived from genes which are highly expressed in cancer cells but not found in normal cells.
  - **Example:** In adenovirus-based OVs, it is possible that the viral genome can be engineered to be activated by promoters from genes associated with the tumor, such as E1A for liver cancer.
- **Safety Modifications (Suicide Genes and Self-Limiting Genes):** Some of these oncolytic viruses have suicide genes that can be activated under certain conditions that cause the controlled killing of the virus in case it infects normal tissue. Another approach uses self-limiting genes to make sure that, after reaching a certain level of viral replication, there is no more replication of the virus.
  - **Example:** T-VEC (Talimogene laherparepvec) is genetically modified HSV bearing a gene making the virus unable to replicate in the normal tissues and enhancing its replication inside the tumor cells.[19,20]

2. Enhancements to Boost Immune Responses: Direct killing of cancer cells by oncolytic viruses can stimulate the immune system to recognize and destroy remaining tumor cells. Improvements to oncolytic viruses include increasing the immune responses that would make for better therapy in general.

- **Insertion of Immune-Stimulatory Genes:** Viruses can be engineered to express immune-stimulatory molecules, such as granulocyte-macrophage colony-stimulating factor, which activates dendritic cells and stimulates the immune system. This leads to improved recognition of cancer cells and a more robust systemic immune response.
  - **Example:** T-VEC, the engineered HSV, expresses GM-CSF that activates the immune system against the tumor and the tissues surrounding it.
- **Improvement in Cytokine Production:** The OVs can be genetically engineered to have overexpression of pro-inflammatory cytokines or other immunomodulators such as Interleukins, IL-12, IL-2, among others, to further activate T-cells and other immune cells such as natural killer (NK) cells.

- **Example:** Case in point: Reolysin (Reovirus) among other OVs are genetically engineered for the overexpression of cytokines for enhanced T-cell activation and immune surveillance.
- **Expression of Immune Checkpoint Inhibitors:** Some of the oncolytic viruses are genetically engineered to secrete immune checkpoint inhibitors like PD-L1 or CTLA-4 blockers. These could prevent the evasion of the tumor to immune detection, and enhance the body's immunity to attack cancer cells.
- **Example:** Engineered Vaccinia viruses were modified to produce anti-PD-1 or anti-CTLA-4 antibodies, enhancing the immunogenic response against the tumor.[21,22]

3. Examples of Engineered Oncolytic Viruses: This section will highlight some of the oncolytic viruses that have been tested or are being used in clinical applications with some genetic engineering approaches:

- **T-VEC (Talimogene laherparepvec)**—Modification of Herpes Simplex Virus (HSV). T-VEC was modified to express GM-CSF, an immune-stimulatory cytokine. A deletion in the viral genome allows T-VEC to replicate only in melanoma and tumor cells but not in normal cells; therefore, T-VEC will primarily attack solid tumors. The indication granted by the FDA to T-VEC was melanoma, and there is some promise with T-VEC aiding the immune response against the tumors.
- **Pexa-Vec (JX-594)**—Modified Vaccinia Virus. Expresses GM-CSF to preferentially induce lysis of tumor cells and activate immune response. Pexa-Vec has been administered in trials for liver cancer (hepatocellular carcinoma) and has shown beneficial effects by not just directly targeting tumor cells but also activating the immune response.
- **Oncorine (H101)**—Adenovirus. There was an adenovirus genetically modified to replicate selectively in tumor cells with the defective P53 pathway; it also had enhancements made to increase its efficacy as an oncolytic agent. Approved in China for head and neck cancers Oncorine shows promise as a major step toward genetically-controllable adenovirus therapy in the human malignancies.
- **Reolysin (Reovirus).** Type: Reovirus (double-stranded RNA virus). Modifications: Reolysin has been tailored such that its biological function is activated by pathways mediated by Ras, which are upregulated in cancer cells. The virus is known to lyse cancer cells by itself, but additional effect is brought about via engineering for enhanced oncolysis and immune recognition. Clinical Trials for Reolysin was evaluated in patients with advanced solid tumors as monotherapy.[23,24]

ANTITUMOR IMMUNE RESPONSE INDUCED BY ONCOLYTIC VIRUSES

Oncolytic viruses, in addition to the ability to kill cells through oncolysis, have captured interest because they are able to modulate the immune system. It can elicit innate and adaptive immune responses; thus, OVs can be the ideal candidate for cancer immunotherapy. The immunogenic effect by oncolytic viruses enhances clearance of tumors, elicits an immune memory response, and might also inhibit recurrences of tumors.

1. Innate Immunity Activation: Innate immunity represents the body's initial barrier to infectious diseases, of which viruses are just a small subgroup. Activation of the innate response is therefore the result of the actions of oncolytic viruses in promoting immediate, diffuse immunity as critical in recognizing and eliminating tumour.

- **Pattern Recognition Receptors (PRRs)**: Oncolytic viruses are sensed by various host cell pattern recognition receptors including, but not limited to, Toll-like receptors (TLRs) and RIG-I-like receptors (RLRs), which recognize viral nucleic acids like double-stranded RNA or unmethylated CpG DNA. The signaling of these receptors initiates antiviral immune responses.
- **Type I Interferons (IFN-α/β):** During viral infection, the innate immune system produces type I interferons, IFN-α and IFN-β, which are highly potent in their antiviral effects. IFNs also increase the expression of major histocompatibility complex molecules and enhance the activation of natural killer cells and dendritic cells, which result in the recognition of tumor cells and activation of immunity.
- **Natural Killer (NK) Cells:** These cells are important in the innate immune response. They identify and destroy cells infected with viruses or transformed into cancer cells. Oncolytic viruses increase the activation and recruitment of NK cells to the tumor site. Once recruited, these NK cells can directly kill tumor cells and assist in recruiting other immune cells into the tumor microenvironment.
- **Dendritic Cells (DCs):** OVs activate dendritic cells, a key component that mediates antigen presentation. Activation of the dendritic cells through the oncolytic virus-infected tumor cells helps them recognize such cells, which leads to them taking up tumor antigens they present, their migration to lymph nodes, and activation of T-cells. This initiates the adaptive response.[25,26]

2. Mechanisms Mediating Adaptive Response: This makes the adaptive immune response much more specific and, in fact, tailored, which is mediated by T-cells and B-cells precisely targeting the tumor cells. Oncolytic viruses come into the scene to serve that all-important link between the two facets of immunity: the innate and the adaptive.

- **T-cell Activation:** Oncolytic viruses activate antigen-presenting cells (APCs) like dendritic cells to process and present tumor antigens to CD8+ cytotoxic T lymphocytes (CTLs). Activated CTLs can specifically recognize and kill tumor cells.

Infection of tumor cells by oncolytic viruses generates tumor-associated antigens, which further induces T-cell priming and recruitment to the tumor site.

- **Memory T-cells:** The T-cells activated by oncolytic viruses can result in the generation of memory T-cells which "remember" tumor antigens and mediate long-lasting immunity against rechallenge or metastatic tumors. This can create an immune memory that will result in a fall in tumor size when exposed to the same tumor antigen, followed by the potential prevention of reoccurrence.
- **Humoral Response and B-cells:** Oncolytic viruses can also stimulate B-cells to produce antibodies against tumor-specific antigens. These antibodies may help in opsonizing tumor cells for destruction by macrophages and neutrophils, enhancing the overall anti-tumor immune response.
- **Immune Checkpoint Modulation:** Oncolytic viruses can also modify the tumor microenvironment to be more immunogenic. Through immune stimulation, this can induce upregulation or complementarity with the status of immune checkpoints (such as PD-1/PD-L1 and CTLA-4), which would provide more powerful T-cell responses and improve antigen presentation of tumor cells.[27,28]

3. Role in Promoting Immunogenic Cell Death (ICD): Immunogenic cell death - ICD, in essence, is any kind of programmed cell death which provokes an immune response through the release of damage-associated molecular patterns from the dying cells. Oncolytic viruses are uniquely positioned to induce this form of immunogenic cell death, which in turn enhances their power to induce long-lasting anti-tumor immunity.

- **Releasing Tumor Antigens:** Oncolytic cell death releases tumor-associated antigen into the local environment of the tumor. These antigens, however, undergo processing and presentation by dendritic cells to activate, thus resulting in further specific T-cell activation against that particular tumor cell.
- **DAMPs and Immune Activation:** During the process of oncolysis, tumor destruction leads to the secretion of DAMPs into the tumor microenvironment, including calreticulin, HMGB1 (High Mobility Group Box 1), and ATP. These signals call the immune system into action, heralding that such cell death is immunogenic. These DAMPs are involved in dendritic cell activation and stimulation of the innate and adaptive immune responses that synergize for a better anti-tumor effect.
- **Apoptotic and Necrotic Cell Death:** Oncolytic viruses are thought to generally induce tumor cells to undergo apoptosis, but they may also induce necrosis. Necrotic cell death releases a lot of DAMPs, which can activate immune responses very effectively, rendering necrotic death even more immunogenic than the apoptotic one.
- **Calreticulin Exposure and Phagocytosis:** In ICD, calreticulin translocates to the surface of dying tumor cells where it serves as an "eat me" signal that promotes the phagocytosis of dead cells affected by dendritic cells. This acts in favor of further antigen presentation to T-cells, thus priming the immune system toward targeted action.[29,30]

FDA-APPROVED ONCOLYTIC VIRUSES FOR CANCER THERAPY

A few oncolytic viruses have so far been approved by the FDA for wide clinical application, which represent major steps in the evolution of this new treatment

- **T-VEC (Talimogene laherparepvec)**
- Unmodulated herpes simplex virus **T-VEC** was approved for the treatment of unresectable melanoma by the FDA in 2015, which is why this is considered the world's first Approved Oncolytic Virus. Genetically, T-VEC has been engineered to selectively replicate in the tumor cell and induce tumor lysis. Furthermore, it has been designed to express **GM-CSF** (Granulocyte-Macrophage Colony-Stimulating Factor), a potent adjuvant that augments anti-tumor immunity.
  - The indication for **T-VEC** is in patients where melanoma cannot be surgically removed, alone or in combination with another drug called **pembrolizumab** (Keytruda), which is a **PD-1 inhibitor** that boosts the immune response against the tumor
- **Other Oncolytic Viruses Under Investigation**
  - Officially the first approved OV in the U.S., other oncolytic viruses such as **Reolysin** and **Coxsackievirus A21** are being tested in clinical trials for regulatory approval. Fast track designation by the FDA has been given to some of these, which signifies their promise as novel cancer treatments.[31,32]

CHALLENGES AND LIMITATIONS OF ONCOLYTIC VIRUSES

1. **Pre-existing Immunity:** Natural oncolytic viruses are usually encountered by human beings, and many patients will have had some form of pre-existing immunity against them. This may have been based on prior exposure to the virus or another virus belonging to the same family but of low pathogenicity. Such pre-existing immune responses can, within a very short time, lead to the rapid clearance of the oncolytic virus from the body, thus allowing little time for infecting and killing tumor cells. This observation applies particularly to those types of viruses that are endemic among the human population like **adenovirus and herpes simplex virus (HSV).**
2. **Immune Activation in Normal Tissues:** Activation of the innate immune system through pattern recognition as viral elements may culminate in an unwanted inflammatory response in normal tissues. This very inflammatory response could similarly

trigger further immune clearance, negating any therapeutic effects before the virus can act upon the tumor.

3. **Genetic Diversity of Tumors:** Tumors encompass a diverse population of cells with different mutations, gene expressions, and responses to therapy. It is this **heterogeneity** that indicates that a small subset of tumor cells may become infected by the virus, whereas others resist infection or replication. Moreover, some tumor cells might contain mutations in **viral receptors** or other cellular factors that inhibit viral entry or replication, thus reducing the efficacy of oncolytic viruses for the eradication of the tumor.
4. **Systemic Delivery:** Administering oncolytic viruses using a systemic approach, such as intravenous injection, often results in the loss or dilution of the viral agent before it reaches the tumor location. An oncolytic virus may be cleared by the immune system, treated as a foreign body and removed from circulation by filtration processes located in the liver and spleen, which can effectively hinder the virus's ability to target the tumor.
5. **Local Delivery Issues:** Local delivery methods (i.e., direct injection into tumors) can enhance the concentration of oncolytic viruses at the tumor site. However, difficulty reaching certain tumors, especially those within the deep-seated structures such as brain or pancreas, makes local delivery also a challenge.
6. **Targeting Specificity:** A major concern is that oncolytic virus therapy should affect only tumor cells and spare healthy tissues. There have been suggestions to genetically engineer OVs to recognize some specific tumor marker and/or modified surface receptors, but high target specificity to tumors remains an outstanding challenge. Thus, the non-specific viral replication in healthy tissues can have an adverse effect by causing unwanted inflammation and organ damage.[33,34]
7. **Immunosuppressive TME:** A tumor develops an immunosuppressive environment to prevent immune cell infiltration and decrease the immune response to the virus. Highly expressed **immune checkpoints (e.g., PD-L1)** and **tumor-associated macrophages (TAMs)** are able to suppress immune activation and allow the tumor cells to go undetected. This, therefore, compromises the ability of oncolytic viruses to induce a potent immune response against the tumor.
8. **Neutralizing Antibodies:** After the initial treatment, the body can produce **neutralizing antibodies** against the oncolytic virus that may severely limit the impact of subsequent doses of the virus. The antibodies that neutralize the oncolytic virus will prevent it from infecting and killing cancer cells, thereby reducing the effectiveness of the treatment by increasing in instances of repeated application.

- **Rapid Viral Clearance:** The invading micro-organisms are eliminated very quickly from circulation by host immune guards, especially the **mononuclear phagocyte system (MPS)** that includes the liver and spleen. This quick clearance diminishes the period for the virus to infect tumor cells and perform oncolysis when injected systemically.[35,36]

REGULATORY APPROVAL

The approval and clinical use of oncolytic viruses rely on regulatory frameworks that ensure safety and efficacy but are also cognizant of the public's perception of genetically modified organisms and viral therapies.

- **Regulatory Approval:** Regulatory agencies like the FDA of the United States and EMA of Europe would test oncolytic viruses thoroughly. These bodies ensure that a virus is not harmful, its effectiveness is good, and the risks to the environment are minimum. The pathway of viral therapies to the marketplace must be defined clearly, and the clinical studies have to be performed under regulatory supervision to provide adequate protection for the patients.
- **Ethical Issues:** Ethical issues arise in the use of genetically modified organisms in medicine, especially with regard to equity of access. Oncolytic viruses are expensive to develop and administer, which raises questions about access to these treatments in low-income or underserved populations. Moreover, the possibility of genetic modifications affecting non-cancerous cells raises ethical concerns about unforeseen consequences and long-term effects.[37,38]

CONCLUSION

Oncolytic virus therapy can be the panacea for changing the face of cancer treatment: highly targeted therapy that kills only the cancer cells but, concurrently, provokes the immune system to deliver a broad anti-tumor response. Indeed, even in light of the latest advancement in genetic engineering, design of the virus, and delivery mechanism, the future does seem bright for the therapy-even in the broadening of such a treatment towards other cancers as well, those resistant to treatments through traditional methodologies.

The added potential benefit also includes further combining the oncolytic viruses with immunotherapies, chemotherapy, or even radiation therapy. However, many obstacles will still have to be overcome, including tumor resistance, immune clearance, and limiting delivery. The ethical and safety considerations in the implementation of such therapies are essentially biosecurity and regulatory frameworks that ensure proper use of these therapies. It is assumed that with further advancements in research, artificial intelligence will be integrated and personalized treatment approaches optimized in oncolytic virus therapies to achieve more effective and tailored cancer treatments with improved patient outcomes and expanded therapeutic possibilities in the future.

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