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REVIEW

Measles Virus-Based Genetic Modifications: Progress in Hematological Malignancy Treatment

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Abstract: With the enhancement of public living standards and health awareness, demands for high-quality treatment with hematological malignancies are increasing, correspondingly. However, since significant adverse events have been found associated with chemotherapy, radiotherapy and other traditional anticancer measures, and a considerable number of patients still experience relapse or drug resistance, developing new treatment strategies has become the focus in the field of hematological malignancies. The measles virus vaccine strain, as an oncolytic virus, has been paid special attention to, due to its dual advantages of selectively invading and killing tumor cells and activating anti-tumor immunity. Currently, multiple studies have shown the effectiveness of unmodified measles virus vaccine strains in treating hematological malignancies. However, due to the systemic invasiveness and complexity of hematological malignancies, the concept of genetically engineered measles virus vaccine strain has garnered significant attention. In this article, we reviewed the progress on measles virus vaccine strains in the treatment of hematological malignancies, especially on the application of genetic engineering technology. Meanwhile, we also explored the challenges encountered in current treatments and discussed future design direction for modifying measles virus vaccine strains.

Keywords: measles virus vaccine strain, oncolytic virus, hematological malignancy, genetic engineering, combined therapy

Introduction

Hematological malignancies are a group of malignant diseases originating from the blood and hematopoietic system, mainly including leukemia, lymphoma, and multiple myeloma (MM), which can affect multiple systems and are mostly highly heterogeneous, bringing about difficulties in treatment.[1] Although traditional therapies have improved the survival rate to some extent, a considerable number of patients still experience relapse or drug resistance, resulting in unsatisfactory outcomes.[2] In recent years, the application of targeted and immune cell therapies has made significant progress.[3] However, the inherent adaptability and complexity of hematological malignancies mean that monotherapy is unlikely to conquer cancer completely, and emerging therapeutic approaches are needed to continue to drive comprehensive progress in treatment.[4]

The measles virus (MV) vaccine strain, as an attenuated live vaccine, which has been widely administered globally since the 1960s to prevent measles, has been proved with not only acceptable immunogenicity and safety, but also the ability to selectively invade and directly kill tumor cells through specific surface receptors, or to activate the host's anti-tumor immune system and remodel the tumor microenvironment (TME).[5]

Although the MV vaccine strain has shown promising oncolytic effects against various solid tumor cells, hematological malignancies, as systemic non-solid malignant cells, go to great lengths to avoid viral infection.[6–9] Furthermore, intravenous injection can negatively affect the oncolytic efficacy of the MV vaccine strain. Therefore, genetically engineered MV vaccine strains are necessary to kill tumor cells effectively.[10] In this way, new options can be provided for patients with hematological malignancies, especially those who have not responded to existing treatments.

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MV and MV Vaccine Strains

MV, belonging to the *Paramyxoviridae* family, is a single stranded, nonsegmented, negative-strand RNA virus. Its genome consists of 15894 nucleotides and encodes six structural proteins and two non-structural proteins (Figure 1a and 1b).[11] The surface glycoproteins hemagglutinin (H) and fusion protein (F) mediate receptor binding and cell fusion, respectively, thereby facilitating viral invasion.[12] After entering the cell, MV releases RNA and utilizes the host cell for replication within the cytoplasm. Meanwhile, it triggers cell fusion to form multinucleated giant cells, promoting further viral spread.[13]

In 1954, John Enders and Thomas Peebles successfully isolated the Edmonston strain from the blood of a measles patient named David Edmonston. In the early 1960s, the first generation of MV attenuated live vaccines was successfully developed based on the Edmonston strain. Subsequently, various Edmonston-derived strains and non-Edmonston vaccine strains were developed in different regions.[14] In 1970, a rare case reported an association between natural MV infection and the regression of Burkitt's lymphoma, which sparked further research into the potential relationship between MV vaccine strains and cancer treatment.[15]

MV vaccine strains can selectively invade various tumor cells through membrane cofactor protein (MCP/CD46), in addition to signaling lymphocyte activation molecule (SLAM/CD150) or poliovirus receptor-like protein 4 (PVRL-4/Nectin-4), through which the MV wild-type strains invade cells, while normal cells are not affected due to the lower receptor density below the threshold.[16] The MV vaccine strain can also activate the immune system by providing pathogen-associated molecular patterns (PAMPs), which induce immunogenic cell death (ICD) in tumor cells.[17] After tumor cells lyse, they release damage-associated molecular patterns (DAMPs) and additional PAMPs.[18] These signaling molecules activate pattern recognition receptors (PRRs), promoting the maturation and activation of antigen-presenting cells (APCs).[19] Ultimately, these processes recruit more neutrophils, macrophages, and NK cells, while reducing the proportion of inhibitory immune cells, such as regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs), within the immune cell population (Figure 1c).[20,21] It is worth mentioning that MV vaccine strains are safe enough with little genotoxicity to integrate into the host cell genome or spread among the population.[22]

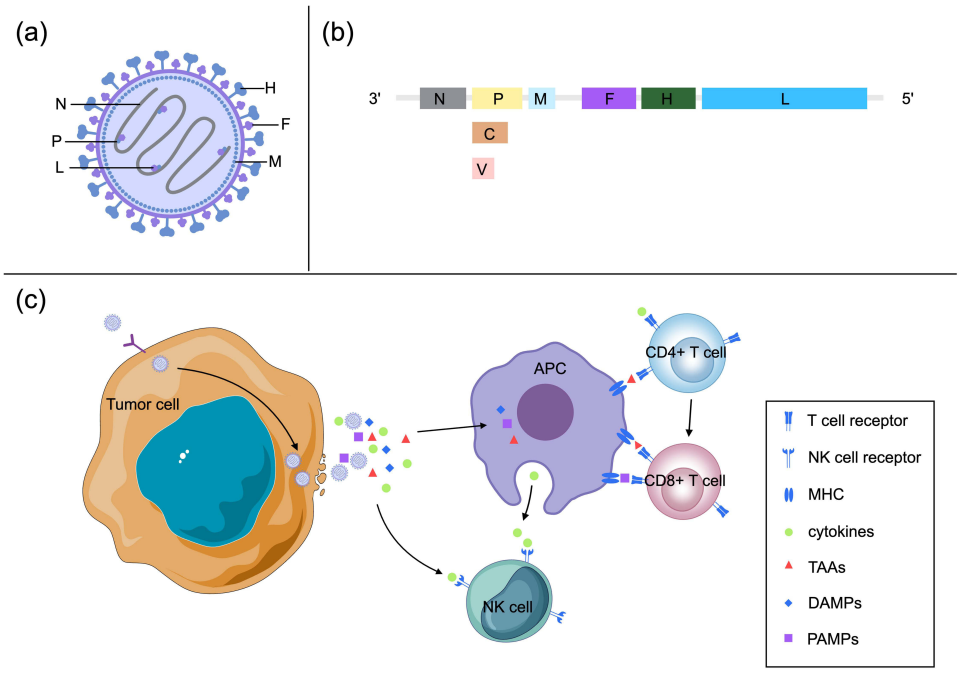

Figure 1 (**a**) Schematic diagram of measles virus (MV) particles. The MV RNA genome is protected by nucleoprotein (N) and binds to RNA-dependent RNA polymerase (L) and its cofactor phosphoprotein (P), forming a ribonucleoprotein (RNP) complex surrounded by membrane protein (M). The surface glycoprotein hemagglutinin (H) and fusion protein (F) mediate receptor binding and cell fusion, respectively; (**b**) Schematic diagram of measles virus genome. The open reading frame encodes six structural proteins, while proteins V and C are non-structural proteins produced by another RNA transcription product of gene P. (**c**) The mechanism of MV-induced immune activation. The MV vaccine strain activates innate immunity and promotes tumor immunogenic cell death (ICD), leading to the release of cytokines, tumor associated antigens (TAAs), damage-associated molecular patterns (DAMPs), and pathogen-associated molecular patterns (PAMPs), followed by recruitment and activation of immune cells, such as antigen-presenting cells (APCs), NK cells, CD4+T cells, and CD8+T cells, resulting in TME remodeling. This figure was created with MedPeer (medpeer.cn).

MV Vaccine Strain Genetic Engineering Platform

In order to treat malignancies with high efficacy, modern oncolytic virus therapy strategies often involve genetic engineering modifications. Through genetic engineering platforms, viruses are modified intentionally to achieve more significant oncolytic effects. The following are the methods of the MV vaccine strain genetic engineering platform.

Enhancing the Specificity of MV Vaccine Strains

In fact, not all tumor cells naturally express viral receptors. In past studies, selected targeting components, such as designed ankyrin repeat protein (DARPin) that targets the epidermal growth factor receptor (EGFR), were fused to the receptor binding site of MV vaccine strains.[23] Leading to retargeting of tumor cell surface molecules, thereby facilitating specific invasion and acceptable oncolytic effects. At the same time, in order to reduce the targeted toxicity to EGFR+ healthy cells, matrix metalloproteinases (MMPs), which are highly expressed in TME, were utilized to enable the virus to encode engineered viral fusion proteins that can be activated by MMPs for additional protease targeting.[24] Dual targeting further enhances tumor selectivity, but compared with non-targeted viruses, the replication rate of dual-targeted viruses is slower, which may affect their efficacy in some tumors and may also result in insensitivity to highly heterogeneous tumor cells.[25] Similarly, by exploiting the differences in molecular levels between normal cells and tumor cells, considering the downregulation of miRNA in tumor cells, miRNA target sites could be inserted into the genome of MV vaccine strains to achieve targeted expression during the post-invasion phase.[26] However, the expression of miRNA may vary significantly among different tumor types or individuals, which could become a barrier to clinical translation.

The engineered MV vaccine strain expresses a bispecific T-cell engager (BiTE) that synergistically binds to CEA +/CD20+ tumor cells and CD3+T cells after invasion, thereby enhancing the specificity of treatment in immune-intact mice with xenograft tumor and promoting contact between T cells and tumor cells.[27] However, intravenous injection may lead to excessively high systemic BiTE levels, causing toxicity in normal tissues, while insufficient BiTE levels within the tumor can compromise therapeutic efficacy. This potentially narrows the therapeutic window of MV-BiTE vaccine strain.[28] Similarly, the MV vaccine strain also faces similar challenges when expressing another type of bispecific connector, such as a bispecific killer engager (BiKE)that synergistically binds to CEA+ tumor cells and CD16A+ NK cells, enhancing the direct cytotoxicity of NK cells against tumor cells.[29] It should be noted that the broad-spectrum antiviral ability of NK cells at the early stage may impair the oncolytic effects, where further research is needed.[30]

Enhancing the Immune Activation Ability of MV Vaccine Strains

The MV vaccine strain can effectively enhance the T-cell-specific response by encoding tumor associated antigens (TAAs) within tumor cells after invasion.[31] An engineered MV vaccine strain that can express Helicobacter pylori-derived neutrophil-activating protein (NAP), a Toll like receptor 2 (TLR2) agonist, in host cells, showed satisfactory oncolytic effects, and an immune activation ability by increasing cytokines such as tumor necrosis factor alpha (TNF -α) and interleukin-6 (IL-6) in host cells.[32] In addition, more powerful oncolytic effects and more persistent protective immune memory were proved in engineered MV vaccine strains which targetedly deliver the genes for IL-12, IL-15, or granulocyte-macrophage colony-stimulating factor (GM-CSF) to tumor cells. The constitutive expression of these cytokines can continuously activate the immune system, thereby enhancing the antitumor immune response.[33,34]

In order to effectively block the binding of cytotoxic T lymphocyte antigen 4 (CTLA-4) to B7 (CD80/CD86), an engineered MV vaccine strain was developed to encode anti-CTLA-4, thereby restoring functions of T cells in immune surveillance and eradication against tumor cells.[35] Similarly, the binding of programmed death-1 (PD-1) and programmed death-1 ligand 1 (PD-L1) could be blocked by engineered MV vaccine strains that encodes anti-PD-1 or anti-PD-L1, leading to increased inflammatory cytokines.[36]

Arming Suicide Genes

The MV vaccine strain can also be used as a vector. It can be modified to carry suicide genes. When the virus infects tumor cells, the suicide gene is expressed inside these cells, producing the corresponding enzyme.[37] This enzyme can convert non-toxic or low-toxic enzyme prodrugs into cytotoxic substances, thereby effectively reducing the damage of the drug to normal tissues.[38] For example, the bifunctional suicide fusion gene (SCD) can encode yeast- derived cytosine deaminase (CD) and uracil phosphoribosyltransferase (UPRT). The combination of MV-SCD vaccine strain and 5-fluorocytosine (5-FC), an enzyme prodrug, can increase sensitivity to drug-resistant tumor cells with lower toxicity.[39] Similarly, MV vaccine strains armed with purine nucleoside phosphorylase (PNP), combined with the prodrug fludarabine (F-ara), have shown significant therapeutic efficacy.[40] Past studies have proved that oncolytic viruses armed with two suicide genes, ie thymidine kinase (TK) and CD, gained more safety and more powerful oncolytic efficacy,[41] providing more directions for the anti-tumor treatment strategy of MV vaccine strains.

Regulating the Expression of Apoptosis Related Genes

An MV vaccine strain with human *BNIP3*, a pro-apoptotic gene, was proved to be able to induce tumor cell apoptosis in vitro.[42] In addition, oncolytic viruses carrying *TP53* gene or *BECN1* gene have displayed high infection efficiency with insignificant damage to normal mononuclear cells.[43,44] An innovative oncolytic virus has been developed, with capsid protein IX which can connect to tumor necrosis factor-related apoptosis-inducing ligand (*TRAIL*), a gene that can induce tumor cell apoptosis and kill surrounding tumor cells through bystander effects. The virus itself can stimulate the expression of *TRAIL* on the surface of APCs. The researchers further encapsulated extra TRAIL on the virus surface, enhancing the viral invasion into tumor cells, and significantly inhibiting tumor growth.[45,46] However, further studies are needed to confirm the potential adverse reactions and immunocompetence of the engineered virus.

Others

For further preclinical and clinical research, MV vaccine strains are encoded with reporter genes through genetic engineering platforms, which facilitates monitoring of virus replication and transmission in vivo. At present, MV vaccine strains are widely used, encoding fluorescent proteins, carcinoembryonic antigen (CEA), or sodium iodide symporter (NIS). Research has found that in situ viral replication of MV-NIS vaccine strains could be imaged by gamma camera after administration of radioactive ^{123}I or ^{131}I. Moreover, the MV-NIS vaccine strain could also be used as radiotherapy to promote the regression of tumor cells.[47]

The genetic engineering platform for MV vaccine strains can also effectively protect the virus from neutralization by acute immunity or inactivation by antiviral factors. Due to the fact that the P gene of MV wild-type strains can avoid the induction of interferon (IFN) and inhibit IFN signaling through the JAK/STAT pathway, thereby combating the innate immune system. The MV Pwt vaccine strain with modified P genes, exhibited significantly improved oncolytic efficacy.[48] It is also possible to recover MV vaccine strains in human cells through the reverse genetics plasmid platform, in order to avoid the virus being inactivated before invasion.[49] In addition, modified oncolytic viruses with E-cadherin expressed could escape from the antiviral activity of NK cells with enhanced transmission between cells.[50] In the future, more innovative insights will be raised into the application of MV vaccine strain genetic engineering platforms to anti-cancer treatment (Table 1).

Application in the Treatment of Hematological Malignancies

Preclinical Trails

Since the beginning of the 21st century, numerous studies have confirmed that MV vaccine strains could specifically kill hematological malignant cells through natural receptor markers. In acute leukemia, MV vaccine strains effectively eradicate leukemia stem cells by targeting the CD46 receptors on their surface and control central nervous system leukemia.[61] Meanwhile, MV vaccine strains display high sensitivity to EB virus-associated diffuse large B-cell lymphoma and EB virus-associated Burkitt lymphoma because these cells highly express CD150/SLAM.[62] Moreover, MM cell lines with *TP53* deficiency showed more satisfactory response to MV vaccine strains, because of the downregulation

Table 1 Summary of MV Vaccine Strain Genetic Engineering Platform

Gene Modification	Mechanisms	Advantages	Limitation	References
DARPin	Targeting EGFR, HER2/neu, or EpCAM	Specificity	Optimize DARPin for tumor types	[23,25]
scFv	Targeting HER2/neu, FRα, CD20 and EGFR, etc.	Specificity	Ensure scFv affinity and stability	[11]
Cytokine targeting	Expressing IL-13 to target IL-13Rα2	Specificity	Tumor IL-13Rα2 levels vary	[51]
CKP	Targeting integrins αvβ3, αvβ5, and α5β1	Specificity	Circulation affects CKP	[52]
miRTS	Allowing MV to be inhibited by miRNA	Specificity	Low MIR-148a needed in TME	[26]
MMP activation	Requiring MMP activation	Specificity	Sufficient MMP activity in TME	[25]
BiTE	Targeting T cells and tumor cells	Specificity and immunostimulation.	Narrow therapeutic window	[27]
BiKE	Targeting NK cells and tumor cells	Specificity and immunostimulation.	NK cells impact infection	[29]
TAA	Expressing NY-ESO-1 or TRP-2	Immunostimulation	Tumor-specific effects	[31,53]
Activate TLR2	Expressing NAP to activate TLR2	Immunostimulation	Immune response variability	[32]
Cytokine immunity	Expressing GM-CSF, IL-12 or IL-15	Immunostimulation	Immune response variability	[33,34]
ICI	Expressing anti-PD-1, anti-PD-L1 or anti-CTLA-4	Immunostimulation	Risk of resistance	[35,36]
IFN	Expressing IFNβ	Immunostimulation	Virus inactivation possible	[54]
SCD	Expressing the enzyme that converts 5-FC to 5-FU	Suicide genes	Individual efficacy differences	[39]
PNP	Expressing the enzyme converting fludarabine	Suicide genes	Individual efficacy differences	[40]
BNiP3	Delivering pro-apoptotic genes	Apoptosis related genes	In vivo studies affected	[42]
Fluorescein	Expressing GFP or mCherry	Long-term	Not quantifiable	[42,55]
Luciferase	Expressing luciferase to react with luciferin	Quantifiable	Not for long-term	[56]
lacZ	Expressing LacZ to react with X-gal	Tissue sections	Not quantifiable	[57]
Lambda protein	Expressing λ to bind with IgG-κ	Monitoring in vivo	Normal cell effects	[58]
CEA	Expressing CEA	Monitoring in vivo	False negatives possible	[59]
NIS	Expressing NIS	In situ imaging	False negatives possible	[47]
Pwt	Replacing with wild-type NPL genes	Protecting virus	Potential toxicity	[48]
HFcdv	Replacing MV HF genes with CDV HF genes	Protecting virus	Requires retargeting	[60]

Abbreviations: HER2/neu, human epidermal growth factor receptor 2; EpCAM, epithelial cell adhesion molecule; FRα, folate receptor α; CKP, cysteine knot proteins; miRTS, miRNA target sequence; NY-ESO-1, New York esophageal squamous cell carcinoma 1 antigen; TRP-2, tyrosinase-related protein-2; ICI, immune checkpoint inhibitors; GFP, green fluorescent protein; lacZ, β-galactosidase gene z; CDV, canine distemper virus.

of CD46 by p53 and their high susceptibility to MV vaccine strains.[63] It is worth mentioning that it is difficult for MV vaccine strains to directly target inherent receptors, in spite of their acceptable oncolytic potential in various hematological malignancies, due to the high heterogeneity and immune escape of hematological malignancies. Flow cytometry analysis showed that hematological malignant cells with SLAM/CD150 expressed were limited to cutaneous T-cell lymphoma (CTCL), a few types of B-cell non-Hodgkin lymphoma, nearly half of chronic lymphocytic leukemia, Hodgkin lymphoma, and multiple myeloma.[64] The differential expression of these surface receptors may ultimately lead to significant differences in the sensitivity and ultimate outcomes of various cells to MV vaccine strains. Fortunately, retargeting technology may be able to solve this problem. It has been reported that, the retargeted MV vaccine strain can effectively invade CD20+/CD30+ lymphoma cells and CD38+ MM cells, with excellent oncolytic effects.[65,66]

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In recent years, research on the combination of MV vaccine strains and drugs is also achieving continuous progress. As mentioned above, MV vaccine strain can directly kill hematological malignant cells due to its inherent oncolytic nature.[67] On the other hand, the suicide gene within the MV vaccine strain can convert the prodrug 5-FC or F-ara into toxic metabolites.[39,40] These metabolites interfere with the DNA synthesis and repair processes in tumor cells, leading to cell death.[68] In addition, cyclophosphamide (CPA) in chemotherapy can kill proliferating lymphocytes, thereby controlling acute immune neutralization and inhibiting the viral inactivation.[69] Exploiting this characteristic, preclinical studies have found that pretreatment with CPA before intravenous administration of the measles vaccine strain results in increased viral RNA copy numbers and prolonged viral spread in mouse and squirrel monkey models.[70] Some studies have revealed that the interaction between viruses and drugs is not a simple one-way effect. Instead, they interact with each other within the body, which is expected to achieve better therapeutic effects with fewer adverse reactions.[71] Some drugs in chemotherapy mainly elicit therapy-induced senescence (TIS) rather than apoptosis at low concentrations.[72] A regimen of low-dose MV vaccine strains combined with gemcitabine at a sub-therapeutic concentration can significantly reduce tumor cells, with no interference with TIS of tumor cells or viral replication.[73] At present, synergistic potential against cancer has been proved in combination of oncolytic viruses and other anti-cancer drugs, such as immune checkpoint inhibitors (Atezolizumab),[74] poly ADP-ribose polymerase inhibitors (Olaparib),[75] multi-targeted tyrosine kinase inhibitors (Sunitinib),[76] BCL-2 inhibitors,[77] and hydrazones.[42]

Clinical Trials and Application

In Phase I clinical trials, the acceptable tolerance and efficacy in treating cancers of MV vaccine strains was first reported in CTCL.[78,79] At the same time, in a phase I/II clinical trial, NCT00450814, with more subjects, the effectiveness of the intravenous MV-NIS vaccine strain was evaluated in treating recurrent and refractory MM. In the phase I trial, a cohort study with different 50% tissue culture infection doses (TCID50), the maximum tolerated dose (MTD) of the MV-NIS vaccine strain (TCID50: 1011) was ultimately determined as the therapeutic dose for the Phase II trial. The most significant adverse events were identified here, including transient chills and fever, gastrointestinal symptoms, and transient blood cell reduction. It was also pointed out that infusion of a MV-NIS vaccine strain at the TCID50 of 1011 within 30 minutes would cause headaches, while the tolerance would be improved when the infusion rate was slower. The regimens in the phase II trial involved cyclophosphamide prior to administration of the MV-NIS vaccine strain.[70] Subsequent studies have shown that MV-NIS treatment significantly increased T-cell responses against specific antigens, such as melanoma associated antigen-A3 (MAGE-A3) and MAGE-C1, and significantly enhanced the TAAs cytotoxic T cell response in MM patients. The long-term complete remission highlighted the potential of MV-NIS combined with other immunomodulators in maintaining persistent tumor remission in MM patients[80] (Table 2).

Table 2 Clinical Trials of Treatment for Hematological Malignancies Using MV Vaccine Strain (March 2025 Clinicaltrials.gov)

Delivery and Assessment Technologies	Tumor Type	Results	Limitations	Phase	Status	ClinicalTrials. Gov Identifier/ References
Systemic administration of MV-NIS	MM	Effective	Small sample size	II	Completed	NCT02192775
Intravenous administration of MV-NIS	MM	Effective	Non-randomized design	I/II	Completed	NCT00450814
PET imaging to evaluate NIS expression	MM	No significant effect	Small sample size	I	Completed	NCT03456908
Intratumoral injection of MV	CTCL	Effective	Small sample size	I	Completed	[79]

MV Vaccine Strain and CAR-T Therapy

Chimeric antigen receptor T-cell (CAR-T) therapy is a cutting-edge immunotherapy in the treatment of hematological malignancies, which involves extracting immune active T cells from the patient, modifying them in vitro to enhance their anti-tumor activity, and finally reintroducing these modified cells into the patient's body to kill tumor cells.[81,82] For the target CD19 on the surface of B cells, CD19 CAR-T has achieved remarkable results in acute B-lymphocytic leukemia and non-Hodgkin lymphoma.[83] However, its therapeutic efficacy is still limited due to the poor permeability, low persistence, and lack of response to "cold tumors".[84] A study has found that combining with oncolytic viruses can enhance the efficacy of CAR-T therapy in B-cell lymphoma.[85] By armed oncolytic viruses with chemokines, CAR-T can be introduced to the vicinity of tumor cells, compensating for the deficiency of T cell in migration.[86] In addition, target viruses can deliver CD19 to tumor cells so as to enhance the activity of CAR-T.[87] On the contrary, some studies have found that IFN induced by oncolytic viruses can limit CAR-T and bring negative therapeutic effects.[88] The combination of MV vaccine strains and CAR-T therapy may be promising, but current research is relatively limited, and more exploration is needed to determine the optimal combined therapy strategy and mechanisms.

MV Vaccine Strains and HSCT

The MV vaccine strain holds promise to help eradicate the malignant cells which contaminate the autologous hematopoietic stem cell transplantation (HSCT) grafts of hematological malignancy patients, without losing normal hematopoietic stem cells, in order to improve the success rate of HSCT.[89] Several mechanisms and related research findings support this hypothesis. First, the MV vaccine strain exhibits selective tropism for tumor cells, destroying them while sparing normal cells. Second, other oncolytic viruses have been reported to effectively reduce the graft versus host diseases (GVHD) caused by allogeneic HSCT.[90] The MV vaccine strain has great potential in the field of HSCT and requires more further study. This suggests that the MV vaccine strain may similarly influence the immune response in autologous HSCT, potentially reducing transplant-related complications. Future studies should focus on validating its efficacy and safety in patients with various hematologic malignancies to enhance overall treatment outcomes.

Challenges and Prospects

As an innovative therapeutic strategy for hematological malignancies, the transformation of the MV vaccine strain from laboratory research to clinical application still faces some obstacles, such as the systemic clearance of the virus by the host immune system and the safety of the virus to the human host. In addition to the MV-Pwt vaccine strain strategy mentioned above, some studies have also used Ruxolitinib, a JAK1/JAK2 inhibitor, to inhibit the IFN response pathway, thereby enhancing the growth of sensitive MV vaccine strains in malignant cells.[55] However, inhibition of IFN may restore the virulence of MV vaccine strains and bring about safety issues.[91] Amino acid substitution was performed at the S-adenosylmethionine (SAM) binding site of L protein, and the results showed that the safety and immunogenicity of MV vaccine strains were improved, providing a new approach for designing safer and more effective MV vaccines.[92] In addition, CPA or histone deacetylase inhibitors can prevent the virus from being neutralized by acute immunity.[70,93] There are also studies that utilized carrier cells or graphene encapsulation to protect MV vaccine strains, and the results showed that the virus replication and spread has been improved and the oncolytic effect has been enhanced.[94,95]

Based on the current clinical trial results, the research direction of future MV vaccine strain genetic modification should be more inclined towards the mechanisms of virus combination with other treatments. When combined with chemotherapy, radiotherapy, and immunotherapy, the appropriate administration route, timing, and dosage will be another challenge in the field of hematological malignancy. Tumor cells may be prematurely destroyed by drugs, which may affect virus replication. However, apoptotic tumor cells may contract and form channel-like structures and gaps, thereby promoting the spread of viruses. Studies have shown that by adjusting the administration timing of 5-FC and MV-SCD vaccine strains, it has been found that early and continuous administration of 5-FC is superior to later or shorter administration in improving oncolytic efficacy.[96] Therefore, further research is needed to determine the optimal combination strategy including MV vaccine strains, where drug interactions may affect the final efficacy.

In summary, the experimental data on multiple MV vaccine strains have shown their broad prospects in the treatment of hematological malignancies. In addition to further mechanism research to fully understand how various therapeutical strategies mediate anti-tumor activity, it is also essential to conduct safety evaluation and preclinical efficacy evaluation of MV vaccine strains early, so as to completely transform MV vaccine strains to be applied to the clinical practice in treating hematological malignancies, and benefit more patients.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

All authors report no conflicts of interest in this work.

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