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Application of mRNA Vaccines in HCC Treatment

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Abstract

The efficiency of mRNA vaccines in COVID-19 prevention has been successfully approved and has been awarded by Nobel prize. However, more potential of such therapeutic approach has not been revealed yet. Developing mRNA vaccines for Hepatocellular Carcinoma (HCC) treatment holds immense potential and significance. These vaccines offer a highly targeted and precise approach to combat this aggressive liver cancer. By encoding antigens specific to HCC cells, mRNA vaccines stimulate the patient's immune system to recognize and attack cancerous cells while sparing healthy tissues, minimizing side effects, and improving the patient's quality of life. mRNA vaccines represent a promising avenue for HCC treatment, offering the potential for more effective, personalized, and less burdensome therapies. Their development could significantly impact the lives of HCC patients by increasing survival rates and reducing the likelihood of cancer recurrence. This article summarizes the potential advantages of applying mRNA vaccines in HCC treatment, to stimulate the enthusiasm for research in this cutting-edge field.

Introduction

Hepatocellular carcinoma (HCC) is the predominant form of liver cancer, accounting for nearly 85% of cases. It ranks as the third-most common malignancy both in terms of occurrence and cancer-related deaths. HCC has witnessed an alarming rise in the United States, with its incidence tripling over the past two decades [1]. While early-stage HCC can be cured through methods like local ablation, surgical resection, or liver transplantation, the disease still exhibits a high recurrence rate, with a five-year survival rate after surgery hovering around 35%. Furthermore, over half of HCC patients receive a diagnosis at an advanced stage, severely limiting the efficacy of available therapeutic approaches. Despite notable progress in HCC treatment, which includes the development of multikinase inhibitors (MKIs) and immune checkpoint inhibitors (ICIs), approved for advanced or metastatic HCC, treatment options for these patients remain constrained. Moreover, a significant proportion of HCC patients continue to grapple with the absence of sustained and optimal clinical benefits, even with the integration of these innovative treatment alternatives [2,3].

The Nobel Prize of 2023 has been awarded for the discovery of developing effective mRNA vaccines against COVID-19 [4]. mRNA vaccines, a groundbreaking approach in the fight against the COVID-19 pandemic, have taken a leading role in global vaccination efforts. These vaccines are meticulously designed to shield against the SARS-CoV-2 virus, which is responsible for COVID-19, harnessing the remarkable potential of messenger RNA (mRNA) technology [4]. Moreover, the mRNA platform has

shown great potential for a broader range of medical applications, including cancer immunotherapy. While mRNA vaccines have not yet been approved specifically for treating hepatocellular carcinoma (HCC), ongoing research in the field of cancer immunotherapy suggests that they could potentially play a role in HCC treatment in the future.

Fundamental characteristics of mRNA vaccines

Harnessing mRNA technology: Traditional vaccines often rely on weakened or inactivated virus forms or viral fragments to trigger an immune response. In contrast, mRNA vaccines, exemplified by the Pfizer-BioNTech and moderna COVID-19 vaccines, steer clear of live virus components. Instead, a minute fragment of synthetic mRNA has been employed [5,6].

Encoding the spike protein: Within these vaccines, the mRNA carries the genetic instructions for a specific segment of the SARS-CoV-2 virus known as the spike protein. This protein plays a pivotal role in the virus's ability to infiltrate human cells. By encoding solely this protein, the vaccine primes the immune system to identify and mount a defensive response [7].

Prompting an immune reaction: Following administration of an mRNA vaccine, the recipient's cells read the mRNA and manufacture spike proteins. These spike proteins, on their own, pose no threat of causing COVID-19. Nonetheless, they trigger the immune system to generate a robust response, including the production of antibodies and the activation of T cells [7].

Building memory cells: Significantly, the immune system retains the ability to recognize the spike protein even after vaccine administration. This immunological memory enables a swift and effective response if the individual encounters the actual SARS-CoV-2 virus later on [5, 6, 7].

High effectiveness: Rigorous clinical trials and real-world data attest to the exceptional effectiveness of mRNA vaccines in preventing COVID-19. They not only lower the risk of infection but also diminish the severity of the disease and reduce hospitalization and mortality rates in vaccinated individuals [8].

Proven safety: mRNA vaccines undergo thorough clinical testing to guarantee their safety. Common side effects, like localized soreness, fatigue, or mild fever, are generally transient and mild. Serious adverse events are exceedingly rare [8].

Rapid development: A standout advantage of mRNA vaccine technology is its capacity for swift development and production. This played a pivotal role in the expeditious creation of COVID-19 vaccines in response to the pandemic [8].

Emergency use authorization: Regulatory agencies in many countries, including the FDA in the United States, granted emergency use authorization (EUA) for mRNA vaccines, permitting their distribution and administration during the pandemic [8].

mRNA vaccines have emerged as a crucial tool in the worldwide endeavor to curb the spread of COVID-19 [8]. They have been administered to millions across the globe, playing a central role in curbing the virus's transmission and mitigating disease severity. Ongoing research and development in mRNA vaccine technology also hold promise for addressing various other infectious diseases and medical conditions in the future [4].

mRNA vaccines for HCC: The potential mechanisms through which mRNA vaccines could effectively combat cancers such as hepatocellular carcinoma (HCC) revolve around harnessing the immune system to target and eliminate malignant cells. Here's a concise overview of these mechanisms.

Antigen presentation: mRNA vaccines carry genetic instructions encoding specific tumor antigens unique to HCC cells. Upon vaccine administration, the body's cells translate this mRNA, leading to the production of these tumor-specific antigens. These antigens are subsequently presented on the surface of antigen-presenting cells (APCs), such as dendritic cells [9].

Immune recognition: APCs showcase these tumor antigens to T cells, pivotal components of the immune system. T cells identify the presented antigens as foreign or abnormal, triggering a tailored immune response directed specifically against HCC cells [9].

Cell activation: T cell activation encompasses the multiplication and specialization of cytotoxic T cells, known as CD8+ T cells. These specialized cells are adept at recognizing and eliminating cells that display the target antigens, including HCC cells in this context [9].

Memory response: Following the initial exposure to the mRNA vaccine, memory T cells are generated. These memory T cells "memorize" the tumor antigens, ensuring a rapid and potent immune response if HCC cells reappear in the future [9].

Immune assault on cancer cells: Activated cytotoxic T cells circulate throughout the bloodstream, infiltrating HCC tumors. They discern and eradicate HCC cells that display the target antigens, effectively mounting an attack against the cancer [9].

Enhanced immune surveillance: The sustained presence of memory T cells maintains vigilant immune surveillance, offering ongoing protection against any residual or recurrent HCC cells and thus diminishing the risk of cancer recurrence [9].

It is vital to acknowledge that while mRNA vaccines hold substantial promise as potential immunotherapies for cancers like HCC, their effectiveness can fluctuate based on several factors, including the selection of tumor-specific antigens, the generated immune response, and the characteristics of the tumor itself. Continuous clinical trials and ongoing research are indispensable to gain a deeper understanding and optimize the utilization of mRNA vaccines in cancer treatment. Furthermore, exploring combination therapies involving mRNA vaccines and other treatments like checkpoint inhibitors and targeted therapies may offer avenues to bolster the anti-cancer immune response [10].

The general processes of developing mRNA vaccines for treating cancer: The design and development of mRNA vaccines aimed at targeting and potentially conquering cancers such as hepatocellular carcinoma (HCC) is a multifaceted and dynamically advancing area of research. Below are the fundamental steps and considerations integral to the creation of mRNA-based cancer vaccines:

Identification of tumor-specific antigens: The initial pivotal step entails the discovery of distinctive antigens or proteins exclusive to HCC cells, absent in healthy cells. These antigens serve as the focal point for the immune response provoked by the vaccine. Researchers employ diverse methodologies, including genomic analysis and molecular profiling, to pinpoint these specific antigens [10].

Selection of antigen-encoding mRNA: Once tumor-specific

antigens are pinpointed, researchers select the mRNA sequences that encode these antigens. These mRNA sequences become the core component of the vaccine, instructing the immune system to identify and mount an assault against HCC cells [11,12].

Formulation and delivery: Ensuring the stability and effective delivery of the mRNA to target cells is paramount. Commonly, lipid nanoparticles and other delivery systems are employed to safeguard and transport the mRNA to its intended destination [11,12].

Preclinical testing: Prior to advancing to human trials, preclinical testing is executed employing animal models to assess the safety and efficacy of the mRNA vaccine. This entails evaluating whether the vaccine can incite an immune response against HCC while not causing undue harm [11,12].

Clinical trials: If preclinical studies exhibit promise, the vaccine proceeds to clinical trials involving human participants. Clinical trials typically encompass several phases: Phase I: This phase evaluates the vaccine's safety and determines the appropriate dosage. Phase II: In this phase, researchers assess the vaccine's effectiveness in a larger cohort of patients and conduct further safety evaluations. Phase III: Large-scale trials are undertaken to substantiate the vaccine's efficacy and safety in a diverse patient population [13,14].

Regulatory approval: Successful completion of clinical trials may culminate in regulatory approval from health authorities such as the FDA in the United States or the EMA in Europe. Approval authorizes the vaccine's application in clinical practice [13,14].

Post-approval monitoring: Even after regulatory approval, continuous monitoring of the vaccine's safety and efficacy persists. This ensures that the vaccine remains effective and safe for HCC patients [13,14].

Combination therapies: mRNA vaccines may be employed in conjunction with other cancer treatments, including surgery, radiation therapy, or chemotherapy, to amplify their effectiveness in addressing HCC [13,14].

Personalized medicine: In certain instances, the design of mRNA vaccines for cancer involves crafting personalized treatments tailored to the specific tumor antigens of individual patients. This strategy is termed personalized or precision medicine.

Continued research: The domain of mRNA-based cancer vaccines remains in constant evolution. Researchers continually explore novel mRNA technologies, delivery methodologies, and combinations with other immunotherapies to enhance outcomes for cancer patients [13,14].

It's crucial to acknowledge that the development of mRNA vaccines for cancer, HCC included, is a protracted and intricate process.

Discussion

The development of mRNA vaccines for cancer treatment holds profound potential and significance. For instance, mRNA vaccines can be meticulously tailored to pinpoint cancer cells exclusively by encoding antigens unique to the tumor. This precision minimizes harm to healthy cells, rendering them a finely targeted form of immunotherapy. In addition, mRNA vaccines activate the patient's immune system, empowering it to recognize and assail cancer cells. This immune response includes the generation of cytotoxic T cells, specialists in obliterating cancerous cells. Moreover, mRNA vaccines can instigate the creation of memory T cells, which retain a recollection of cancer antigens. This guarantees a swift and potent immune response if cancer cells resurface, substantially diminishing the risk of cancer recurrence [8,15]. Also, mRNA vaccines are devoid of live virus components, and the encoded antigens are specific to cancer cells. Consequently, they are generally safe, with fewer unintended effects on non-cancerous tissues compared to conventional treatments like chemotherapy. Furthermore, mRNA vaccines have the potential to be customized for individual patients based on their unique tumor antigens, ushering in the era of personalized or precision medicine in cancer therapy [16,17].

Compared to certain traditional cancer treatments, mRNA vaccines tend to produce fewer and milder side effects. This translates to an improved quality of life for patients during and after treatment [18]. mRNA vaccines can also be synergistically combined with other cancer therapies, such as checkpoint inhibitors or targeted treatments, amplifying their effectiveness and furnishing a multifaceted strategy for combatting cancer. The realm of mRNA-based cancer vaccines is perpetually advancing, with ongoing research dedicated to enhancing their efficacy and broadening their applicability to diverse cancer types [19]. Thus, the successful development of mRNA vaccines for cancer holds the potential to substantially diminish cancer-related mortality rates by introducing innovative and efficacious treatment options, especially for challenging-to-treat malignancies. Additionally, the development of mRNA vaccines for cancer transcends the boundaries of specific cancer types or geographic regions [20]. Its potential impact on cancer treatment extends globally, instilling fresh hope in patients worldwide.

In essence, the potential of mRNA vaccines for cancer treatment lies in their capacity to harness the immune system with surgical precision to target and obliterate cancer cells. Their significance is underscored by the prospect of safer and more potent cancer therapies, reduced adverse effects, and the potential for individually tailored treatments, rekindling optimism for individuals confronting cancer diagnoses. The relentless pursuit of research and clinical trials continues to uncover and unlock the full potential of mRNA vaccines in the ongoing battle against cancer.

Declarations

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