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Review

Lipid Nanoparticle (LNP) Delivery Carrier-Assisted Targeted Controlled Release mRNA Vaccines in Tumor Immunity

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Abstract: In recent years, lipid nanoparticles (LNPs) have attracted extensive attention in tumor immunotherapy. Targeting immune cells in cancer therapy has become a strategy of great research interest. mRNA vaccines are a potential choice for tumor immunotherapy, due to their ability to directly encode antigen proteins and stimulate a strong immune response. However, the mode of delivery and lack of stability of mRNA are key issues limiting its application. LNPs are an excellent mRNA delivery carrier, and their structural stability and biocompatibility make them an effective means for delivering mRNA to specific targets. This study summarizes the research progress in LNP delivery carrier-assisted targeted controlled release mRNA vaccines in tumor immunity. The role of LNPs in improving mRNA stability, immunogenicity, and targeting is discussed. This review aims to systematically summarize the latest research progress in LNP delivery carrier-assisted targeted controlled release mRNA vaccines in tumor immunity to provide new ideas and strategies for tumor immunotherapy, as well as to provide more effective treatment plans for patients.

Keywords: lipid nanoparticles (LNPs); mRNA vaccine; tumor immunity; delivery carrier; review

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1. Introduction

In the field of cancer treatment, the continuous progress of medical science and technology has ushered in unprecedented changes [1–4]. As an innovative therapeutic method, tumor immunotherapy has shown great potential in cancer treatment [5]. Compared with traditional treatments, immunotherapy activates and enhances the body's own immune system to achieve precise effects on tumors, bringing new hope and possibilities for tumor patients [6–9]. However, although tumor immunotherapy has seen remarkable progress in recent years, its application still faces challenges and limitations [10]. One of the main issues is understanding how to improve the effectiveness and specificity of treatment to maximize the inhibition of tumor growth, spread, and recurrence [11–18]. Compared with traditional vaccines, mRNA vaccines have the advantages of fast preparation, strong customization, and of having no need to use live viruses [19]. With the rise in tumor immunotherapy, researchers have been seeking innovative ways to improve the effectiveness and specificity of treatments to better address tumor challenges. mRNA vaccines have attracted much attention as a potential tumor therapy [20]. Their principle is to guide the body's cells to synthesize specific antigen proteins encoded by mRNA sequences; the immune system then produces an immune response against the tumor antigens [21–26]. However, the clinical use of mRNA vaccines is limited by the challenges in delivery and their lack of stability. In this context, lipid nanoparticles (LNPs), which are nanomaterials, have become key to solving the problem of mRNA vaccine delivery [27–30]. The LNP structure is made up

of lipid layers that wrap the mRNA and protect it from degradation. Through specific surface modification and construction schemes, LNPs can achieve the targeted delivery of mRNA and enhance its enrichment in specific cells or tumor tissues, thereby improving its therapeutic effect [31–35]. The construction scheme of LNPs involves many factors, including selecting the lipid composition, regulating its particle size and surface properties, and optimizing the nucleic acid encapsulation rate [36–40]. For example, the stability and targeting of LNPs can be adjusted by rationally designing different types of lipid components. Optimizing the nucleic acid encapsulation rate can improve the delivery efficiency and bioavailability of mRNA vaccines [41]. In addition, surface modifications can enhance the specific recognition and cellular uptake of LNPs by tumor cells using targeted ligands or polymer functionalization. Preventive vaccines are composed of the following types of nanoparticles: Lipid nanoparticles: These consist of lipid bilayers that can be used to enclose mRNA or protein antigens of pathogens. This type of nanoparticle is widely used in mRNA vaccines (COVID-19 vaccines). Protein nanoparticles: The protein antigen surface of a pathogen is fixed to a nanoparticle to enhance the immune system's response to the antigen. These nanoparticles can be made from a variety of materials, such as polymers, metals, or other biocompatible materials. Polymer nanoparticles: These include natural or synthetic polymers that can be used to carry antigens or provide appropriate structural support. Virus-like particles: These are nanoparticles that mimic the structure of viruses and do not contain viral nucleic acids, and VLPs can induce the immune system to produce an immune response similar to that of real viruses.

However, there are some challenges in the clinical application of mRNA vaccines, namely their delivery and lack of stability. In recent studies [42–45], lipid nanoparticles (LNPs) have emerged as an effective mRNA delivery tool. LNPs have excellent biocompatibility and delivery efficiency, can be used as carriers of mRNA vaccines to improve their stability and enhance their targeting, and have shown broad application prospects in tumor immunotherapy.

This review explores the molecular mechanism of LNPs in mRNA vaccine delivery in detail, providing theoretical guidance for the further optimization of LNP design and construction. This information will enhance their effectiveness and safety in tumor immunotherapy and enhance our understanding of the targeted delivery and controlled release mechanism of LNPs, which is helpful in solving the challenges of applying mRNA vaccines in tumor immunotherapy. This study provides a scientific basis for developing more accurate and efficient tumor treatment strategies.

2. mRNA Vaccines and Tumor Immunity

2.1. Principles and Characteristics of mRNA Vaccines in Tumor Immunotherapy

2.1.1. The Basic Working Principle of mRNA Vaccines

As an innovative tumor therapy, mRNA vaccines work by delivering specific mRNA sequences to stimulate the body's immune system and induce an antigenic immune response against tumors [46–50]. The vaccine carries mRNA-encoding tumor-specific antigens that, once injected into the body, are taken up by target cells (such as dendritic cells) and translated into antigenic proteins [51]. These proteins are recognized as exogenous within the cell by the innate immune system and activate antigen-presenting cells (APCs), such as dendritic cells. The APCs present these antigens to T cells and stimulate the T cells to produce a specific immune response [52–56]. The activated T cells will then locate and attack tumor cells that have this specific antigen, enabling targeted tumor immunotherapy.

Lipid nanoparticles (LNPs), as nanoparticle carriers containing mRNA, play an important role in whole-body transport [57–60]. Their superior biocompatibility and efficient intracellular release mechanism make them an ideal drug delivery tool [61–63]. LNPs can effectively protect mRNA, improve its stability, and release mRNA inside cells to promote absorption by the target cells (Figure 1).

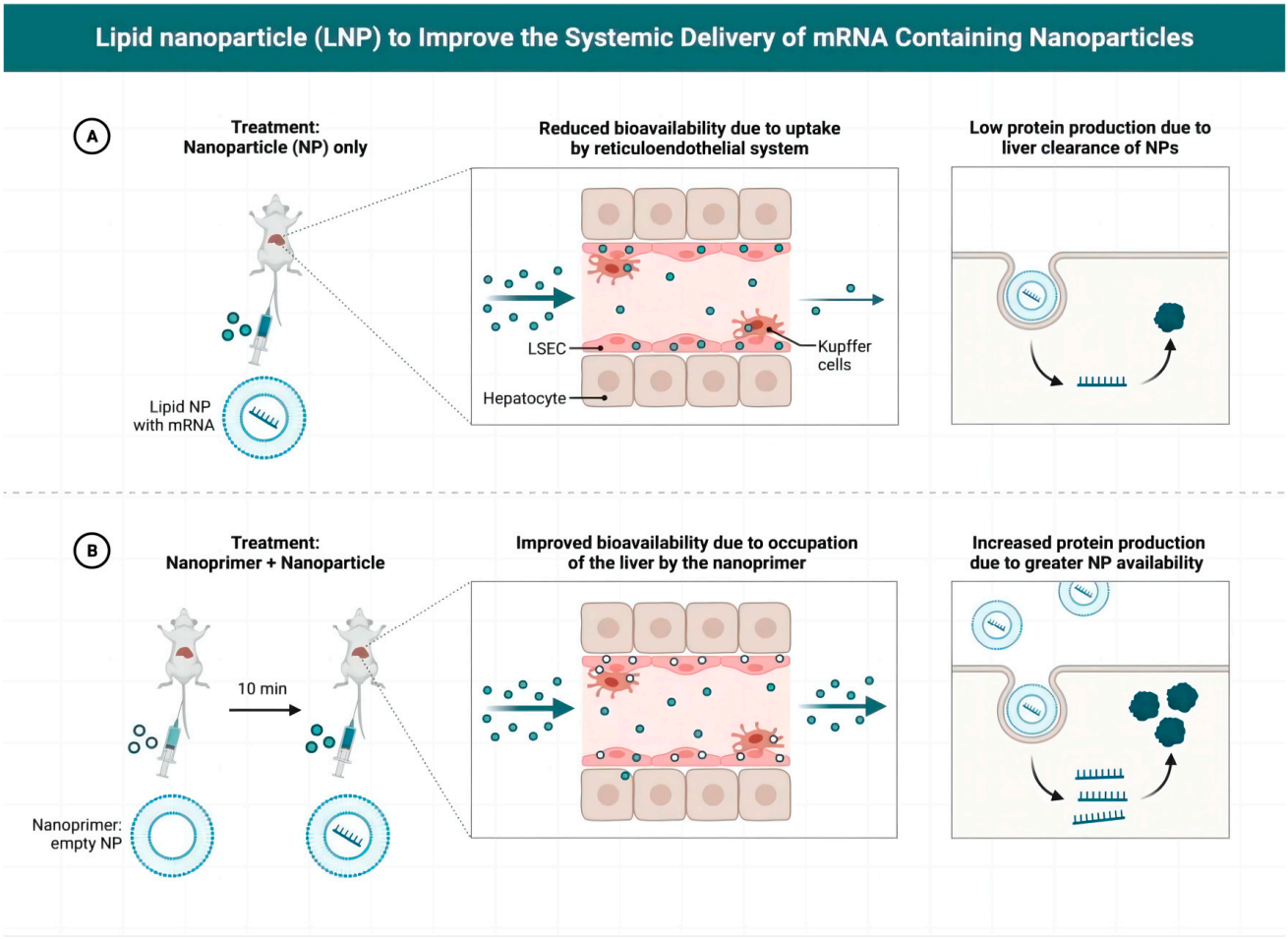

Figure 1. Lipid nanoparticles (LNPs) to improve the systemic delivery of mRNA-containing nanoparticles. (**A**) Treatment with nanoparticle (NP) only; (**B**) treatment with nanoprimer + nanoparticle.

2.1.2. Characteristics and Advantages of mRNA Vaccines

mRNA vaccines have unique characteristics and advantages in comparison to traditional vaccines [64–66]. Their preparation is fast; using modern biotechnology, only the corresponding mRNA sequence is designed, based on the tumor antigen sequence, and there is no need to culture an active virus or prepare a large number of proteins. mRNA vaccines can be highly personalized and can be quickly adjusted to the specific needs of different tumor types or individuals, opening up the possibility of personalized treatment [67–70]. In addition, because mRNA vaccines can encode specific tumor antigens, they have the potential to target specific tumor antigens, which is expected to provide customized immunotherapy for different tumor types [71–74]. In addition, mRNA vaccine preparation is relatively simple, reducing the complexity of traditional vaccine production and improving their production efficiency (Table 1).

Table 1. Analysis of the application of mRNA vaccine types and bionanomaterial carriers.

mRNA Vaccine Type	mRNA Vaccine Carrier Properties	Related Research	Specific Disease Applications	Types of Bionanomaterials Used with mRNA Vaccines
Lipid Nanoparticles [64] (LNP)	High encapsulation, intracellular delivery	Pfizer-BioNTech, Moderna	COVID-19	Liposomes, Polymeric Nanoparticles
Polymeric Nanoparticles [65]	Tunable release, stability	CureVac	COVID-19, Vaccine Development	Polymers, Liposomes

Table 1. *Cont.*

mRNA Vaccine Type	mRNA Vaccine Carrier Properties	Related Research	Specific Disease Applications	Types of Bionanomaterials Used with mRNA Vaccines
Protein–Polymer Nanocomplexes [66]	Targeted, stability	Arcturus Therapeutics	COVID-19, Vaccine Development	Proteins, Polymers
Lipid–Protein Complexes [67–69]	Efficient transfection, mRNA protection	Acuitas Therapeutics	COVID-19, Other Vaccines	Lipids, Proteins
Lipid–Peptide Complexes [70]	Specific targeting, enhanced immunity	Moderna	COVID-19	Lipids, Peptides
Nano-Peptide Particles [71]	Antigen presentation, immune activation	Stanford Research	COVID-19, Cancer Vaccines	Peptides
Magnetic Nanoparticles [72]	Imaging-guided, vaccine delivery	Under Research	Cancer, Vaccine Development	Iron Oxide Magnetic Nanoparticles
Metal–Organic Frameworks (MOFs) [73]	High drug loading, controlled release	Under Research	Vaccine Development	MOFs, mRNA Vaccines
Carbon-Based Nanomaterials [74]	Biocompatibility, delivery efficiency	Under Research	Cancer Immunotherapy	Carbon Nanotubes, Graphene Oxide
Gold Nanoparticles [75]	Efficient transport, immune activation	Under Research	Cancer, Vaccine Development	Gold Nanoparticles, mRNA Vaccines

2.2. Current Status and Challenges of mRNA Vaccines in Tumor Therapy

2.2.1. Existing Clinical Application Cases of mRNA Vaccines

At present, several mRNA vaccines have been clinically tested in the field of tumor therapy [75]. For example, some personalized mRNA vaccines targeting specific tumor antigens have shown some clinical efficacy, prompting the body to produce an immune response against the tumor antigen. Some clinical trials [76–80] have shown that these mRNA vaccines show some therapeutic potential in some tumor types and can stimulate the body's immune system and inhibit tumor growth and spread. However, despite some progress, mRNA vaccines still face some challenges in clinical application [81]. These include stability issues, side effects, and the challenges of generality in different tumor types [82–84]. In addition, the results of some clinical trials have not fully confirmed their efficacy and safety, and further large-scale studies and clinical validations are needed [85]. These challenges limit the widespread use of mRNA vaccines in cancer therapy, and further research is needed to improve their efficacy and reliability for clinical use.

2.2.2. The Challenges of mRNA Vaccines

As an emerging cancer therapy, mRNA vaccines face multiple challenges [86–88]. The stability of mRNA vaccines is a major concern. Because mRNA is easily degraded, its stability in the body is challenged, potentially leading to the degradation and invalidation of vaccines. Therefore, enhancing the stability of mRNA vaccines and prolonging their existence in vivo have become urgent problems to be solved [89]. Immune response regulation is also one of the challenges faced by mRNA vaccines in tumor therapy [90]. The overactivation of the immune system can lead to adverse reactions, such as immune-related toxicity and immunoreactive side effects [91]. Therefore, balancing and regulating the response of the immune system, in order to ensure that the vaccine does not trigger inappropriate inflammation or autoimmune damage when inducing immunity, are key issues in the application of mRNA vaccines. In addition, the versatility of mRNA vaccines across different tumor types and individuals is also a challenge [92–95]. Due to tumor heterogeneity and individual patient differences, it is difficult for a single mRNA vaccine to cover all tumor types. Therefore, it is necessary to develop more widely applicable and scalable mRNA vaccines to meet the therapeutic needs of patients with different tumors. In summary, mRNA vaccines face many challenges in tumor therapy, such as stability, immune response regulation, and versatility.

2.3. Tumor Immune Mechanism Induced by mRNA Vaccines

2.3.1. Immunogenicity and Immune Memory

mRNA vaccines activate the body's immune system by delivering specific mRNA sequences and inducing host cells to synthesize specific tumor antigen proteins [96–98]. These antigenic proteins are presented to T cells by antigen-presenting cells, triggering specific immune responses and promoting the activation and proliferation of CD8+ T cells and CD4+ T cells [99]. mRNA vaccines also contribute to the formation of immune memory, allowing the body to remember and recognize specific tumor antigens in the long term, thereby rapidly generating a specific immune response when exposed to the same antigen again (Figure 2).

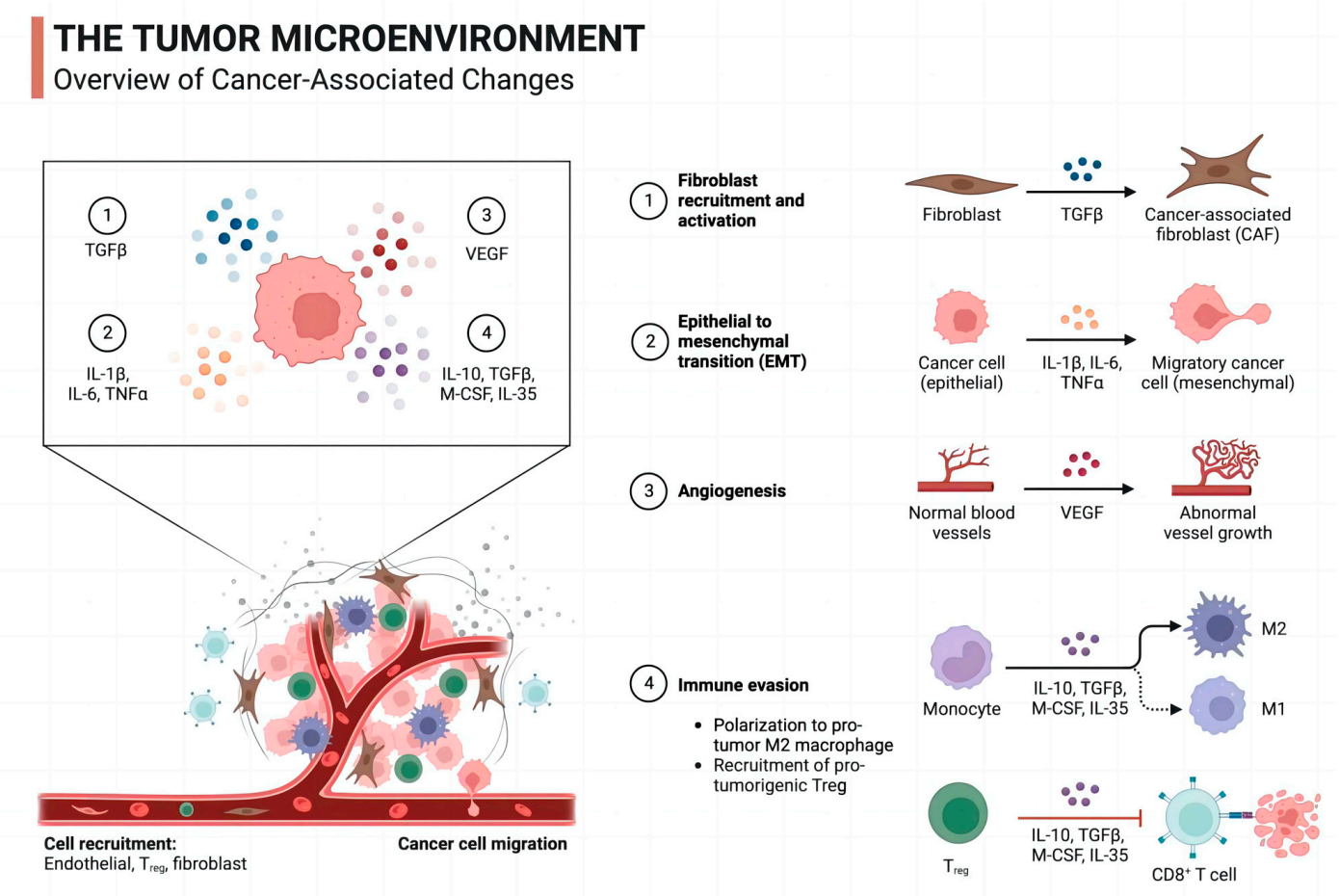

Figure 2. Overview of cancer-associated changes in the tumor microenvironment.

2.3.2. Immune Cells and Tumor Antigens

mRNA vaccines play an important role in tumor therapy by mobilizing immune cells to recognize and attack tumor-specific antigens [100]. These vaccines work by delivering mRNA sequences encoding tumor-specific antigens, driving antigen expression within host cells and promoting immune system activation. Dendritic cells are key cells in the immune system that are able to take up exogenous antigens and present them to T cells to initiate specific immune responses [101–104]. mRNA vaccines activate dendritic cells to take up and present tumor-specific antigens, triggering the activation and proliferation of T cells [105]. CD8+ T cells play a key role in this process. They are activated and transformed into killer effector cells that seek out and attack tumor cells that express tumor-specific antigens. On the other hand, CD4+ T helper cells provide auxiliary support, promote the activation and proliferation of CD8+ T cells, and strengthen the immune response [106–110]. In addition to T cells, NK cells also play an important role [111]. mRNA vaccines promote the activation

of NK cells, which are able to directly recognize and kill tumor cells expressing tumor antigens, enhancing the immune attack against tumors.

mRNA vaccines can induce the expression of tumor-specific antigens by activating dendritic cells and triggering the activation and proliferation of CD8+ T cells, CD4+ T cells, and NK cells to achieve specific immune attacks against tumors [112–114]. An in-depth understanding of this mechanism could help optimize the design of mRNA vaccines and improve their efficacy and safety in tumor immunotherapy.

2.4. Development and Future Prospects of mRNA Vaccines in Tumor Immunotherapy

As cutting-edge tumor therapies, mRNA vaccines have shown broad development prospects [115]. In the future, mRNA vaccines are expected to play an important role in tumor treatment, especially in personalized treatment. Their flexibility and customizability enable them to be precisely designed for specific tumor antigens, providing customized treatment options for all types of tumors [116–118]. mRNA vaccines are expected to show potential advantages in preventing recurrence, treating metastatic tumors, and assisting other therapeutic methods. In addition, mRNA vaccines may become an important part of tumor immunotherapy in the future, combining with immune checkpoint inhibitors or other immunotherapies to form a diversified tumor treatment regimen.

However, mRNA vaccines still face many challenges in tumor immunotherapy [119], such as in improving their stability, enhancing the specificity and persistence of the immune response, and avoiding immune-related adverse reactions [120–122]. The key to addressing these challenges lies in further in-depth research into the design and delivery of mRNA vaccines to enhance their stability and effectiveness in vivo [123–126]. In addition, the combination of new nanotechnology, biomaterials, and cutting-edge technologies, such as gene editing, is expected to provide more effective solutions and provide more reliable support for developing the application of mRNA vaccines in tumor therapy.

3. The Role of Lipid Nanoparticles (LNPs) in mRNA Vaccine Delivery

3.1. Structure and Characteristics of LNPs

As carriers of mRNA vaccines, lipid nanoparticles (LNPs) play an important role in mRNA delivery [127–130]. LNPs are usually composed of hydrophobic lipids, cholesterol, PEG-modified lipids, and ionic surfactants, and they come in different nanomedicine carrier types with different applications, as shown in Table 2. These components form a nanoscale structure whose core is a lipid double layer made of hydrophobic lipids that envelop the mRNA vaccine [131–134]. This structure gives LNPs excellent biocompatibility and stability, helping to protect the mRNA from degradation. In addition, the surfaces of LNPs are often modified with PEG, which can improve their blood circulation time and reduce the chance of them being cleared by the immune system. LNPs have multiple advantages in RNA vaccine delivery [135–137]. Their lipid bilayer structure can effectively encapsulate mRNA vaccines and protect them from degradation by the external environment, which helps to improve the stability of the mRNA. LNPs can improve the biological distribution of mRNA in the body, enhance its cell uptake efficiency, and promote its delivery to target cells, thus enhancing the effectiveness of mRNA vaccines [138–140]. With GeoMx™ spatial analysis, scientists were able to delve deeper into the RNA needed to build lipid nanoparticles (LNPs) to more fully understand their composition and properties (Figure 3).

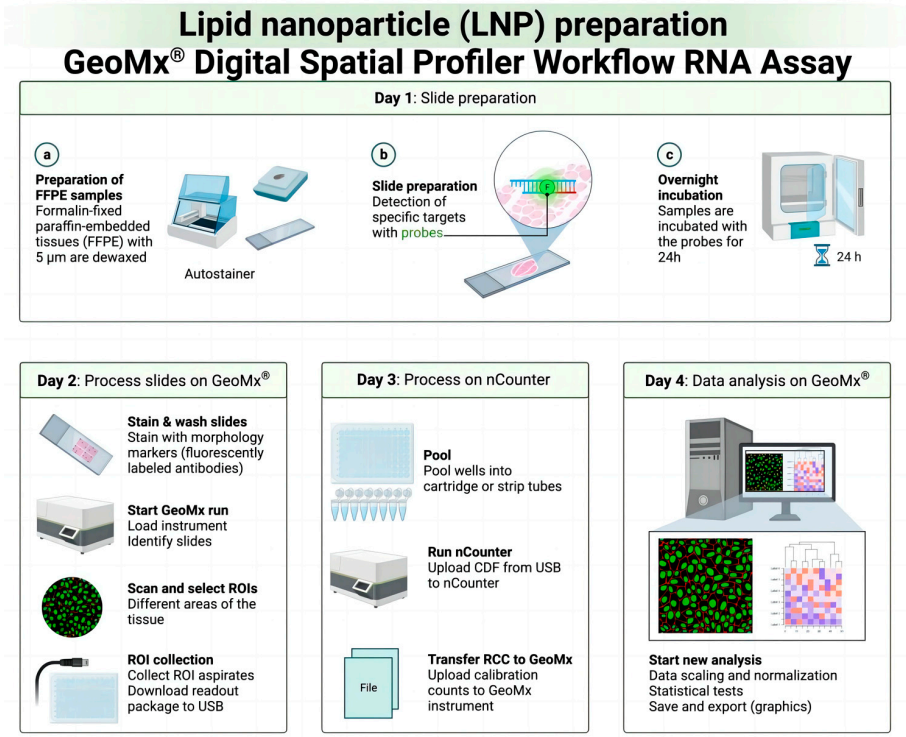

Figure 3. Sequencing technique of the GeoMx™ spatial analysis of RNA in FFPE tissue samples to analyze lipid nanoparticles (LNPs).

Table 2. Induction and analysis of nanomedicine carrier types and applications.

Nanoparticle Carrier Type	Nanomaterial Properties	Related Research	Targeted Tumor	Types of Nanomedicine
Liposomes [127]	Lipid bilayer structure, high encapsulation ability	Doxil, Onivyde	Ovarian cancer, Pancreatic cancer	Chemotherapeutic drug delivery
Polymeric Nanoparticles [128]	Tunable release properties	Abraxane, Genexol-PM	Breast cancer, Gastric cancer	Chemotherapeutic drug delivery
Gold Nanoparticles [129]	Biocompatibility, surface-enhanced Raman scattering	-	Lung cancer, Breast cancer	Tumor photothermal therapy
Iron Oxide Magnetic Nanoparticles [130]	Magnetic properties, imaging functionality	Ferumoxytol	Brain tumors, Breast cancer	Magnetic resonance imaging
Metal–Organic Frameworks (MOFs) [131]	High drug-loading capacity, controlled release	-	Lung cancer, Colorectal cancer	Drug delivery, Imaging
Graphene Oxide [132]	Large surface area, drug-loading capability	-	Lung cancer, Breast cancer	Drug delivery
Carbon Nanotubes [133]	High drug-loading capacity, biocompatibility	-	Lung cancer, Breast cancer	Drug delivery, Photothermal therapy
Protein Nanoparticles [134]	Biocompatibility, specific targeting	Abraxane	Pancreatic cancer, Ovarian cancer	Protein drug delivery
Lipid Nanoparticles [135]	Biocompatibility, high drug-loading capacity	Pfizer-BioNTech mRNA vaccine	Breast cancer, Colorectal cancer	mRNA vaccines
Iron Oxide Nanoparticles [136]	Magnetic properties, imaging functionality	-	Liver cancer, Breast cancer	Magnetic resonance imaging
PLGA Nanoparticles [137]	Biodegradability, controlled release	-	Lung cancer, Breast cancer	Drug delivery
Protein–Polymer Nanocomplexes [138–140]	Targeted, biocompatible	-	Gastric cancer, Colorectal cancer	Protein drug delivery
Phospholipid Nanoparticles [141]	Biocompatibility, stability	-	Gastric cancer, Liver cancer	Drug delivery
Silica Nanoparticles [142]	Tunable morphology, drug-loading capability	-	Liver cancer, Breast cancer	Drug delivery
Polymer Micelles [143]	High drug-loading capacity, solubility	-	Lung cancer, Pancreatic cancer	Chemotherapeutic drug delivery
Nanoemulsions [144]	Drug-carrying capacity, stability	-	Pancreatic cancer, Colorectal cancer	Drug delivery, Treatment

3.2. Delivery Mechanism of LNPs as mRNA Vaccine Carriers

As carriers of mRNA vaccines, lipid nanoparticles (LNPs) play an important role in tumor therapy [141]. Their delivery mechanism mainly manifests in two aspects: targeted delivery and controlled release. LNPs achieve the targeted delivery of mRNA vaccines through their special structural and chemical properties [142–144]. The lipid bilayer structure of LNPs enables them to encapsulate mRNA vaccines, forming stable nanoparticles that help protect the mRNA from degradation [145]. In addition, the LNP surface can be targeted by changing the lipid composition and surface modifications [146]. Tumor-specific surface markers can improve the affinity of LNPs to tumor tissues, promote the enrichment of LNP carriers and their supported mRNA vaccines in tumor cells, and reduce their impact on healthy tissues. LNPs have the characteristic of controlled release, which helps to improve the effect of mRNA vaccines [147–150]. Researchers can achieve the controlled release of mRNA by regulating the lipid composition and structure of LNPs so that the mRNA vaccine can be maintained in the body for a longer time and enhance its therapeutic effect (Figure 4). In addition, LNPs can also promote the intracellular uptake of mRNA so that mRNA vaccines can enter the cell more effectively and initiate the immune response to improve the specific attack ability of tumor cells.

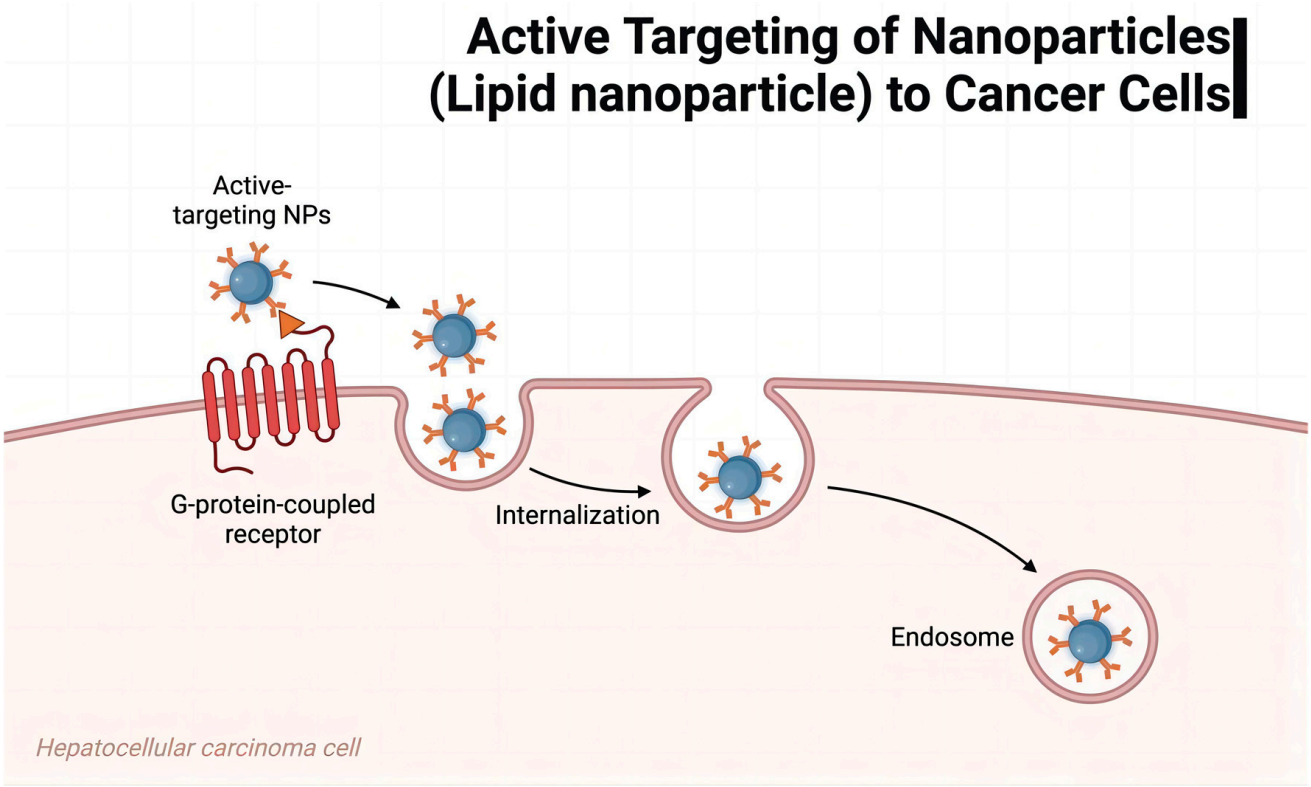

Figure 4. Active targeting of lipid nanoparticles (LNPs) to cancer cells.

As the carrier of mRNA vaccines, lipid nanoparticles (LNPs) can improve the effectiveness of mRNA vaccines in tumor therapy through targeted delivery and controlled release mechanisms [151–153]. Their targeting and controlled release properties make them a potential tumor therapeutic delivery tool, which is expected to lead to more accurate and effective treatment strategies for tumor immunotherapy (Figure 5).

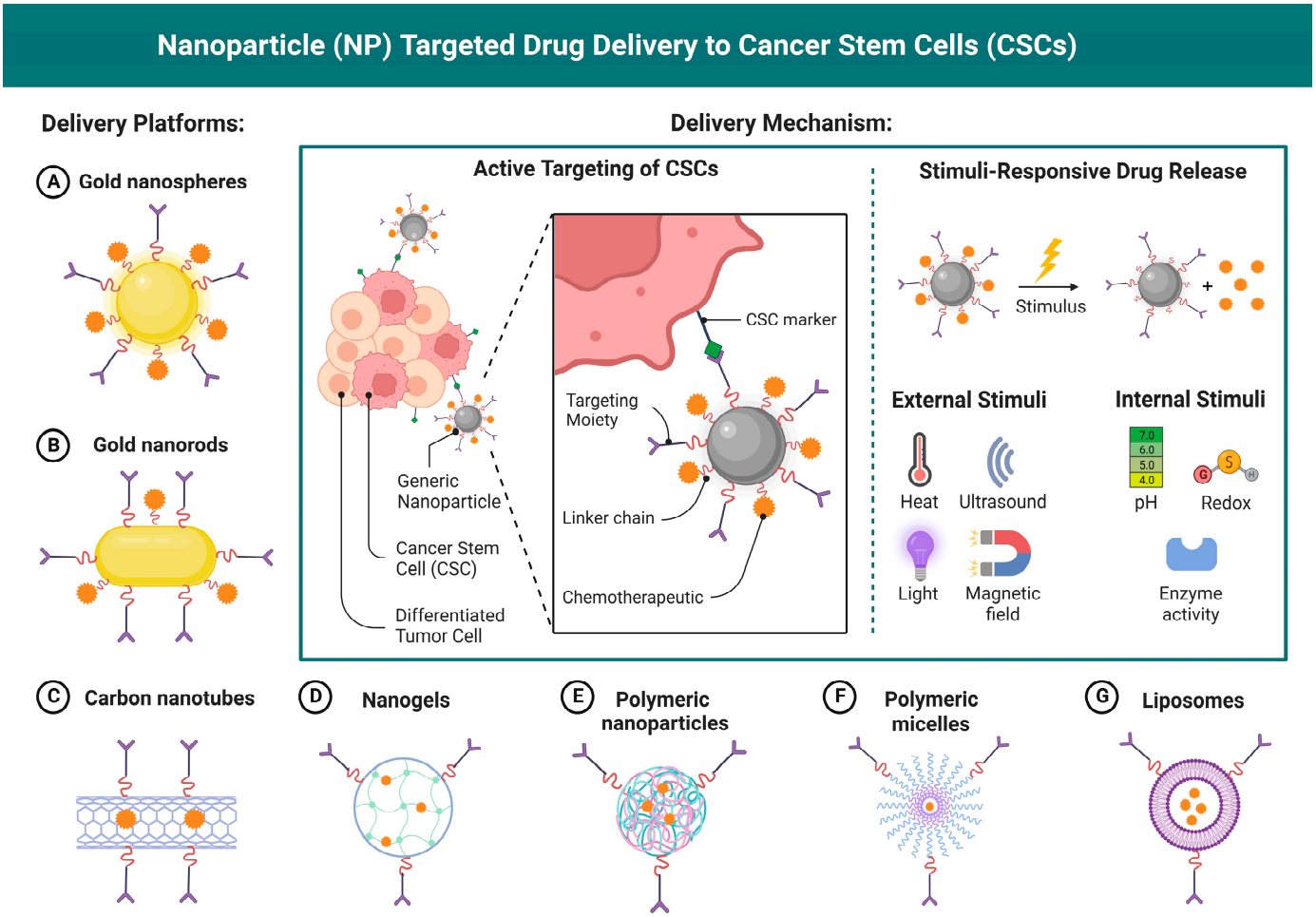

Figure 5. Lipid nanoparticle (LNP)-targeted drug delivery to cancer stem cells.

4. Application of LNP-Assisted mRNA Vaccines in Tumor Immunotherapy

4.1. Progress of Experimental Research

In the field of tumor therapy, the application of LNP-assisted mRNA vaccines has aroused extensive research interest [154]. In past studies [155–160], researchers have achieved a series of encouraging results by using LNP carriers to deliver mRNA vaccines to tumor models (such as liver cancer). Some studies [161–164] have shown that LNP carriers can effectively deliver mRNA vaccines and stimulate tumor antigen-specific immune responses in liver tumor mouse models. For example, some mRNA vaccines targeting tumor-specific antigens delivered through LNP carriers can induce high levels of specific antibodies and cellular immune responses, inhibit tumor growth, and prolong the survival time of mice [165]. In addition, LNP-assisted mRNA vaccines have also been shown to activate CD8+ T cells and enhance immune cell recognition and attacks on tumors, playing an important role in tumor inhibition. Some studies [166–170] have pointed out that LNP carriers can help improve the stability and intracellular uptake efficiency of mRNA vaccines, thus enhancing the biological activity and persistence of mRNA vaccines. These findings provide strong support and evidence for the application of LNP-assisted mRNA vaccines in tumor therapy [171].

However, despite these positive research advances, there remain some challenges and necessary directions for future research [172]. LNP carriers' biological distribution, stability, and interaction with the immune system still need to be further studied to improve their delivery efficiency and reduce any potential toxic effects [173–175]. At the same time, more preclinical studies and clinical trials will help to fully evaluate the potential use of

LNP-assisted mRNA vaccines in tumor immunotherapy, as well as their safety and efficacy (Figure 6).

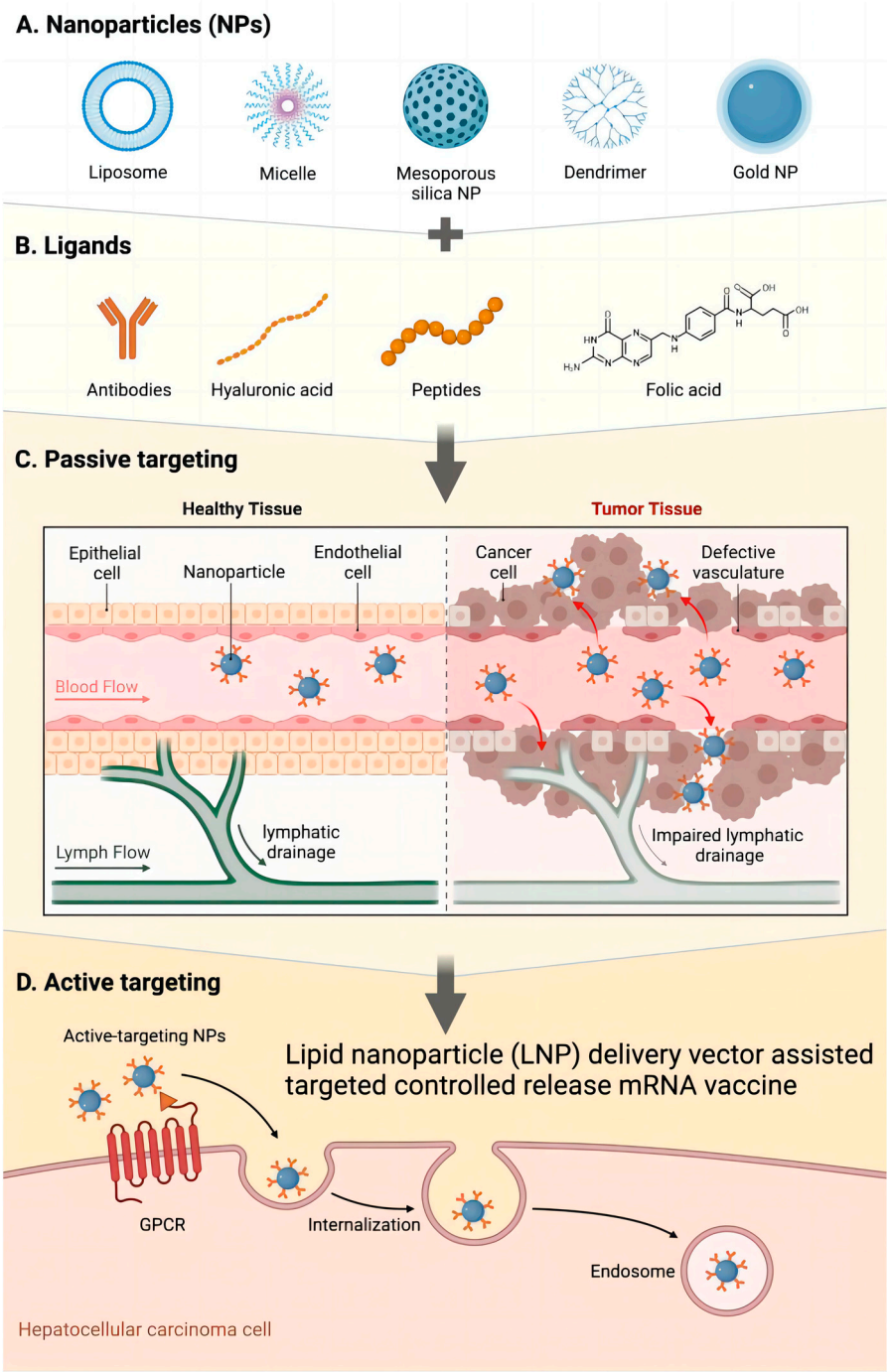

Figure 6. Lipid nanoparticle (LNP) drug delivery systems target liver cancer. (**A**) Nanoparticles (NPs); (**B**) ligands; (**C**) passive targeting; (**D**) active targeting.

4.2. Other Potential Application Areas

LNP auxiliary mRNA vaccines are not limited to single applications in the field of tumor immunotherapy; they also show broad prospects for combined applications, especially in combination with other immunotherapies [176–180]. This combined treatment strategy is expected to improve the effectiveness of tumor therapy, enhance the immune response, and overcome the limitations of a single treatment approach [181–184]. One potential application is the combination of LNP-assisted mRNA vaccines with immune checkpoint

inhibitors. Immune checkpoint inhibitors activate the body's immune system to fight tumors by removing the immunosuppression of tumor cells on T cells [185–188]. LNP auxiliary mRNA vaccines can stimulate and enhance the immune response to tumor-specific antigens [189]. The combined application of the two is expected to be complementary, could improve the effect of tumor immunotherapy, and may expand their application scope [190]. In addition, the combination of LNP-assisted mRNA vaccines with other immunotherapies, such as CAR T cell therapy or tumor vaccines, is also attracting attention [191–194]. This combined application can work synergistically to enhance multiple attacks on tumors. For example, mRNA vaccines can induce the body to produce specific antibodies and T cell immune responses, while CAR T cell therapy works by modifying T cells to directly recognize and attack tumor cells; a combination of the two may achieve more comprehensive and long-lasting tumor treatment effects. However, these combination treatment strategies require more in-depth research to address a number of challenges, including the optimization of treatment protocols, the management of side effects, and the long-term monitoring of treatment effects [195–198]. In addition, the specific mechanisms and interactions of combination therapy also need to be clarified in additional experimental and clinical studies [199].

LNP auxiliary mRNA vaccines have great potential in combination with other immunotherapies, which can provide more comprehensive and effective treatment strategies for tumor immunotherapy and can provide more treatment options for patients.

5. Future Prospects and Challenges

As carriers of mRNA vaccines, LNPs show great potential in tumor immunotherapy, but they still face a series of challenges and development directions [200–205]. The future development trend of LNP carriers in tumor immunotherapy may see a focus on improving their delivery efficiency and accuracy [206–210]. This would include further improving the design of LNPs and optimizing their distribution and stability in vivo in order to improve the delivery efficiency and antitumor effect of mRNA vaccines [211]. At the same time, according to different tumor types and individual patient differences, the development of personalized and customized LNP carriers and mRNA vaccine programs is also an important direction for future development [212–218]. LNP research in tumor immunotherapy will also focus more on safety and on the management of side effects. With the promotion of LNPs in clinical applications, it is necessary to have more in-depth understandings of their metabolic dynamics and toxic reactions in the body, of engaging in the timely detection and remediation of potential safety risks, and of ensuring the safety and controllability of the treatment [219–222]. In addition, in the future, LNP carriers may be combined with emerging technologies, such as nanotechnology and gene editing, in order to explore a variety of new therapeutic strategies [223–226]. For example, novel nanomaterials or carrier technologies can be combined to optimize LNP delivery characteristics [227–230]. Alternatively, gene editing technology and LNP carriers can be combined to achieve the accurate editing and regulation of tumor genes, bringing about more possibilities in tumor treatment [231–236].

However, there are still some challenges in the future development of LNP carriers in tumor immunotherapy [237–240]. This includes improving their delivery efficiency and specificity, overcoming immune-related side effects, exploring more effective targeting strategies, and reducing costs to improve production processes. Addressing these challenges requires interdisciplinary collaboration, the integration of technologies and resources, strengthening of basic research and clinical trials, and the continuous improvement of regulatory policies in order to drive continued innovation in the development of LNP carriers in the field of tumor immunotherapy [241–248].

LNPs have potential as carriers for mRNA vaccines in tumor therapy, but there are still some challenges that need to be overcome to achieve their widespread application [249]. One of the challenges is the stability and immunogenicity of LNPs in vivo [250–252]. LNPs may suffer from protein adsorption and micellar rupture in blood circulation, limiting their

ability to effectively deliver mRNA vaccines. One solution may be to improve the surface modifications of LNPs, using a variety of modifications (e.g., PEG-ification) to improve their stability and blood circulation time and to reduce immune responses [253–255]. Another challenge is the liver enrichment of LNPs. LNPs tend to be concentrated in the liver rather than tumor tissue, which limits their precise delivery to tumors [256–260]. In response to this challenge, we can explore improving the targeting of LNPs, designing specific targeting ligands or functionalized molecules, and making them more inclined to be enriched in tumor tissues in order to improve the therapeutic effect [261]. Lipid nanoparticles (LNP) are a common vaccine delivery system consisting of different lipid components. Typical LNPs include neutral lipids, charged lipids, and pegylated lipids. Neutral lipids are usually composed of phospholipids, such as phosphatidylcholine, which provide structural support for nanoparticles. Charged lipids, such as choline salts, give LNP a charge that helps stabilize and improve the encapsulation efficiency of nucleic acids. Pegylated lipids are used to coat the surface of the nanoparticles, forming a protective layer to slow down the clearance of LNPs by the immune system. These components work together to achieve the efficient delivery of pathogen antigens and trigger immune system responses. By carefully designing these chemical structures, LNPs not only improve the stability and delivery efficiency of the vaccine but also reduce the immune response, providing strong support for vaccine research and development.

In addition, the LNP preparation process, production cost, and scale of production are also challenges [262–265]. To solve these problems, it is necessary to optimize the preparation process, increase the yield, reduce the cost, and promote large-scale production. To address these challenges, interdisciplinary collaboration is essential [266]. Combining expertise in biomedical science, nanotechnology, materials science, and other fields strengthens research cooperation and helps to jointly overcome technical problems [267]. In addition, the guidance and norms of regulatory policies should be strengthened to ensure the safety and effectiveness of LNPs in clinical applications. Notably, some of the vaccine components have been found in the milk of lactating mothers. This finding raises safety concerns that require in-depth discussion and research. In particular, in the presence of vaccine components in the milk of lactating mothers, we need to understand the source, magnitude, and potential impacts these vaccine components have on infant health. When discussing safety, we must consider the importance of breastfeeding in the health of the baby and evaluate it in the context of ensuring their safety [268]. This will help ensure the metabolizing and excretion of the vaccine in lactating mothers and provide a more comprehensive safety assessment for the health of both the mother and child.

In summary, overcoming the challenges faced by LNPs as mRNA vaccine carriers in tumor therapy requires multifaceted efforts and innovation. By continuously improving the stability, targeting, and production technology of LNPs, combined with reasonable research and development strategies, it is believed that LNPs will have broader application prospects in tumor therapy.

6. Conclusions

This study summarized the key role of LNPs as mRNA vaccine carriers in tumor immunotherapy. LNPs can promote the targeted delivery and controlled release of mRNA vaccines, stimulate the immune response, and fight against tumors. The advantages of mRNA vaccines are their rapid preparation, personalized customization, potential for specific tumor antigens, etc. They are expected to become an innovative means of tumor treatment; LNP-assisted mRNA vaccines have achieved encouraging therapeutic effects in tumor models.

In the future, the development prospects of LNP-assisted mRNA vaccines in tumor therapy are broad. The potential for personalized treatment and the application of combined immunotherapy will become an important research direction. However, challenges such as stability, targeting, and the advancing of preclinical and clinical studies still need to be addressed. Further studying LNP structure optimization, targeting strategies, and multidis-

ciplinary cooperation are suggested approaches for improving the effective application of LNP-assisted mRNA vaccines in tumor therapy and promoting their clinical transformation.

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