International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 16, Issue 5, 2024

Review Article

LEVERAGING THE SUCCESS OF MRNA LIPID NANOPARTICLE VACCINE IN COVID-19 TREATMENT: A NARRATIVE REVIEW ON ITS POTENTIAL APPLICATION IN MALARIA TREATMENT

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Received: 16 Mar 2024, Revised and Accepted: 18 Jul 2024

ABSTRACT

Malaria, which is caused by the Plasmodium parasite and transmitted by mosquitoes, continues to be a major global health issue. The worldwide health community continues to work toward finding a conclusive answer to the malaria problem, but it is still elusive. Developing a successful malaria vaccine has proven difficult due to the Plasmodium parasite's complicated life cycle and ability to change and develop resistance to interventions rapidly. Amidst this backdrop, the advent of mRNA Lipid Nanoparticle (mRNA-LNP) vaccines, exemplified by their resounding success in mitigating the Coronavirus Disease 2019 (COVID-19) pandemic, has kindled newfound hope in vaccine development. This review examines the potential of leveraging mRNA technology to induce a robust immune response, thereby potentially revolutionising the landscape of malaria prevention through the development of breakthrough malaria vaccines. The intricate interplay between the efficacy of the mRNA-LNP vaccine against COVID-19 and its prospective utility in addressing malaria is also deliberated upon.

Keywords: Malaria, Vaccine, mRNA, COVID-19, Plasmodium

DOI: https://dx.doi.org/10.22159/ijap.2024v16i5.50885 Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

The Global Technical Strategy for Malaria (2016-2030) aims to reduce 90% of malaria incidence and fatality rates worldwide; thus, fresh, effective preventative antimalarial techniques are required [1]. Malaria is caused by five parasite species, two of which, *Plasmodium falciparum* and *Plasmodium vivax*, pose the greatest threat [2]. Numerous challenges interfere with malaria elimination efforts, encompassing environmental factors, insecticide resistance impeding vector control, high rates of asymptomatic infections, and parasite resistance to various antimalarials [3]. Multiple techniques are currently employed to create vaccines against different phases of parasite growth [4, 5]. Vaccines reduce the risk of infection by working with the body's natural defences to safely develop immunity to disease [6]. Indeed, the number of studies aiming at developing such vaccines has grown exponentially in the past decade [7]; however, they have been hindered by several issues, some of which can be resolved by applying strategies that have been employed to rapidly create vaccines against Coronavirus Disease 2019 (COVID-19) [8]. Therefore, recent vaccine research advancements and identifying promising candidates have stimulated renewed optimism for developing efficacious malaria vaccines [9].

In 2020, the success of mRNA Lipid Nanoparticle (mRNA-LNP) vaccines in COVID-19 treatment made headlines worldwide [10]. This pioneering technology, leveraging messenger RNA to induce an immune response targeted at the Coronavirus, has played a pivotal role in mitigating the spread of the virus during the pandemic [10, 11]. mRNA-LNP vaccines are advantageous in terms of rapid design, production, and flexibility in vaccine development; thus, the application is not limited to COVID-19 alone but to other infectious diseases such as malaria [12, 13]. The complex nature, biology and genetic diversity of the Plasmodium parasite pose significant challenges in treating and managing malaria. Hence, mRNA-LNP vaccines hold promise for effective protection against this malaise [9]. This review examines the potential of leveraging mRNA technology to induce a robust immune response, thereby potentially revolutionizing the landscape of malaria prevention through the development of breakthrough malaria vaccines. The intricate interplay between the efficacy of the mRNA-LNP vaccine against COVID-19 and its prospective utility in addressing malaria is also deliberated upon. Search strategies were employed by querying databases such as PubMed, Scopus and Google Scholar utilising 'malaria', 'vaccine', 'mRNA', 'COVID-19', and 'Plasmodium' as search terms to identify relevant literature published within the last ten years (2014-2024).

Malaria vaccine development obstacles and current state

Despite significant advancements in malaria research, developing an effective vaccine remains challenging [14]. The complex life cycle of the Plasmodium parasite involves multiple stages and interactions with the host's immune system, making it difficult to target effectively with a single vaccine [15, 16]. Additionally, the genetic diversity of the parasite leads to various strains, each requiring distinct immune responses for protection [17, 18]. The traditional approach to vaccine design is expensive and time-consuming, while the conventional approach aims to maximize efficacy and, at the same time, minimize prospective negative effects [19]. Conventional vaccine approaches have struggled to address these complexities, highlighting the need for innovative technologies like mRNA-LNP vaccines [20]. While malaria management efforts have successfully reduced the disease's impact in many areas, a highly effective vaccine remains elusive [21]. Recent advances in malaria vaccine research have brought about several promising candidates in clinical trials [22]. The current malaria vaccine candidates focus on parasites in the pre-erythrocytic, erythrocytic, and sexual stages [23].

RTS, S/AS01 (Mosquirix) [24], and R21/Matrix-M [25] are prominent malaria vaccine candidates [26], with other promising pre-erythrocytic vaccine candidates are in the pipeline [27]. Additionally, several other vaccine approaches are under development, each targeting different stages of the Plasmodium parasite's life cycle, as shown in fig. 1. These candidates offer unique mechanisms of action and advantages, contributing to the diverse strategies employed in malaria vaccine research [28]. RTS, S/AS01E is a subunit vaccine composed of the Circumsporozoite Protein (CSP) antigen from *P. falciparum* combined with the AS01 adjuvant system [29]. The CSP antigen is a key component of the parasite's sporozoite stage, which invades human liver cells during the initial stages of malaria infection [30]. By targeting CSP, the vaccine aims to stimulate an immune response that prevents the parasite from

establishing infection in the liver, thereby reducing the likelihood of clinical malaria [9, 30]. The CSP-based RTS, S was shown to have a statistically significant efficacy against severe malaria in young children. It reduced clinical malaria episodes by around 36% in young African children and about 26% in newborns who got four vaccine doses [7]. The R21/Matrix-M vaccine is also a protein-based subunit vaccine that targets the CSP antigen of the *Plasmodium falciparum* parasite [31]. It combines the R21 antigen with the Matrix-M adjuvant, developed by Novavax, to enhance the immune response [26]. Children aged 5 to 17 mo who were recruited from a highly seasonal malaria transmission scenario in Burkina Faso were reported to be safe and highly immunogenic in a phase 2b trial employing CSP-based R21 with Matrix-M adjuvant, with a protective effectiveness of over 74% [32]. The R21/Matrix-M malaria vaccine represents a significant leap forward in the global fight against malaria, with its high efficacy, affordability, and potential to save countless lives [26].

Limitations of prominent malaria vaccines

Despite the initial success of the RTS, S/AS01ES vaccines, it also faces several limitations [33]. Its efficacy tends to wane over time, and booster doses are needed to sustain long-term immunity. Age-specific variations in vaccine response pose challenges, particularly in children [9]. Moreover, the vaccine does not confer complete protection against malaria; despite its preventive benefits, malaria cases still occur post-vaccination [9, 34], and production and availability remain constrained, particularly in malaria-endemic regions [33]. While the R21/Matrix-M malaria vaccine promises efficacy and safety in clinical studies, it faces several limitations. These include concerns about its generalizability beyond the African populations where it was exclusively tested [35], potential safety issues similar to those observed with the RTS, S/AS01 vaccines, and uncertainties regarding long-term protection and efficacy beyond the 12-month mark [9]. Additionally, limitations in understanding its immune response, the feasibility of a four-dose schedule, and the exclusion of specific age groups from trials raise questions about the vaccine's broader applicability and practical deployment [34].

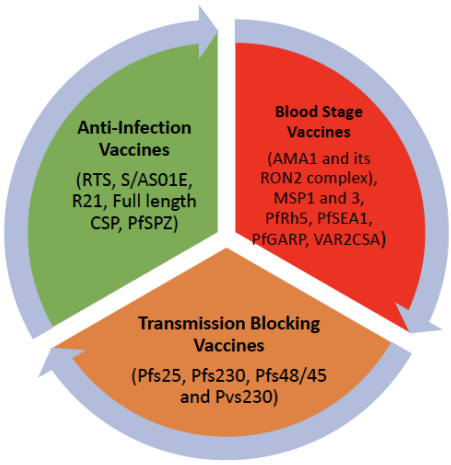

Fig. 1: Malaria vaccines and classification based on their mechanism of action

Pre-erythrocytic vaccines

Several promising vaccine candidates have been identified, focusing on surface antigens on the sporozoites, the infectious form of the malaria parasite transmitted by mosquitoes [36]. Transmission of Plasmodium depends on the completion of its developmental cycle in the mosquito, a process that occurs alongside the digestion of the blood meal and egg development in the mosquito [37]. One of the primary targets for vaccine development is the CSP, which is essential for the parasite's development in both the mosquito and human hosts [38]. RTS, S/AS01, the phase 3 vaccine targeting PfCSP, has limited efficacy and short-lived protection despite World Health Organization (WHO) approval for children. R21, targeting *Pf*CSP, shows improved immunogenicity and protection when combined with the Matrix-M adjuvant [30]. Thrombospondin-related Anonymous Protein (TRAP) is another promising vaccine candidate, eliciting protective immune responses in animal models.

Additionally, co-immunization with multiple pre-erythrocytic vaccine antigens has shown potential for sterile protection in rodent malaria models [39]. The *Pf*SPZ vaccine developed by Sanaria Incorporation uses radiation-attenuated Plasmodium sporozoites to stimulate immune responses against liver-stage parasites [40]. Initial trials have shown promise, but challenges include the need for cold storage and intravenous administration [7]. ChAd63-MVA ME-TRAP, a viral vector vaccine, employs the ChAd63-MVA platform to deliver a key Plasmodium protein. It aims to generate strong T-cell responses and has demonstrated positive results regarding antibody and cellular immune responses [41].

Blood-stage vaccines

The AMA1-C1/Alhydrogel and R32LR AMA-1 vaccines target the Apical Membrane Antigen 1 (AMA1), inhibiting erythrocyte invasion and reducing parasite growth. They have shown efficacy in clinical trials, with the potential to mitigate disease [42]. Several Merozite Surface Proteins (MSP) and invasion complex proteins mediate erythrocyte invasion. It has been found that MSP1 and MSP2 have large levels of genetic variation, which might hamper malaria vaccine development [43]. Another study found that MSP1 includes conserved B-cell epitopes, suggesting that MSP1 might be a good vaccine candidate against *P. vivax* malaria [44].

Transmission-blocking vaccines

*Pf*s25-based vaccines disrupt parasite transmission by inducing antibodies that prevent mosquito development [45]. Various platforms, such as virus-like particles and protein-conjugate vaccines, have been explored, showing promise in preclinical studies [46]. *Pf*s230-based vaccines target a protein crucial for parasite fertilization in mosquitoes, and these vaccines seek to induce antibodies that block parasite development [47]. Although still in the early stages, they can break the malaria transmission cycle [47, 48]. These diverse malaria vaccine candidates offer different strategies to combat the disease, ranging from targeting liver-stage parasites to disrupting transmission, and they contribute to the advancement of malaria vaccine research. By combining these vaccine strategies, malaria control can be approached from multiple angles, potentially increasing the likelihood of successful vaccine development [7, 49].

DNA and viral-vector vaccines

DNA vaccines directly inject the plasmid DNA encoding parasite antigens [50]. These antigens are expressed within host cells, stimulating cellular and humoral immune responses. While DNA vaccines have the benefit of being easy to produce and stable, they have experienced difficulty eliciting robust immune responses in clinical trials, necessitating the development of innovative delivery systems and adjuvants [23]. Adenoviruses and poxviruses have been designed to express malaria antigens and elicit robust immune responses. Viral-vector vaccines can efficiently deliver antigens to target cells, triggering cellular and humoral immune responses [51, 52]. These vaccines often require booster doses to maintain long-lasting immunity. Viral vectors provide a versatile platform for developing vaccines against various stages of the Plasmodium parasite's life cycle [49].

Challenges and the role of innovative technologies

The challenges and limitations associated with traditional malaria vaccine candidates underscore the importance of innovative technologies like mRNA-LNP vaccines. These challenges, ranging from immunogenicity [9], antigenic diversity [7], vaccine delivery [53] and manufacturing scalability [54], have hindered the progress of malaria vaccine development. mRNA-LNP vaccines can address many challenges by providing rapid design, increased immunogenicity, adaptable antigen targeting, simplified delivery, and scalable manufacturing [55]. The advantages of mRNA-LNP

technology open up opportunities to overcome longstanding obstacles in malaria vaccine development and accelerate progress toward effective malaria control and elimination strategies [23]. This adaptability could facilitate the development of combination vaccines that induce broad and durable protection against various stages of the parasite's life cycle [56].

Strategies for combating severe acute respiratory syndrome coronavirus-2 with vaccines

During the COVID-19 pandemic, various strategies were employed to combat Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) [57]. The advancement of genomic sequencing and technology greatly facilitated the creation of COVID-19 vaccines [58]. Vaccine development proved to be a speedy process due to the adaptability and swiftness of the different vaccination technologies available, including those against inactivated viruses, mRNA-based vaccines, live-attenuated vaccines, DNA vaccines, viral-vector-based vaccines, and vaccines targeting protein subunits [59]. Each vaccination platform had unique characteristics that set it apart from others and potentially influenced the safety, efficacy, and duration of the induced protective phase of the vaccine [60].

One of the significant vaccine strategies employed during this period was mRNA-based vaccines [12]. These vaccines relied on quickly translating antigens into the target cells to induce a rapid immune response. However, they were also prone to degradation due to RNases' swift breakdown of their single-stranded mRNA structure [61]. Several ways were explored to increase the capacity of mRNA vaccines to deliver mRNA to the cytoplasm for translation, including using complexing agents based on nanoparticles like lipids and polymers [62]. mRNA vaccines were considered useful because they could resemble real infections and effectively activate the immune system to prevent the spread of the virus [63].

During this time, two notable mRNA-based COVID-19 vaccines were Comirnaty® or BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) [64]. These vaccines were lipid nanoparticle-encapsulated and encoded the complete viral surge of SARS-CoV-2, with the addition of the prefusion conformation bound into two proline mutations (P2S) to trigger antibody reactions that render the virus inactive [65]. The FDA approved the Emergency Use Authorization (EUA) for these vaccines for COVID-19 prophylaxis in December 2020. Subsequently, they were sold as Comirnaty® on August 23, 2021, providing 95% protection against COVID-19 [66]. These vaccination drives aimed to stop the virus's spread and safeguard the general public's health by stimulating and increasing memory T-cells to kill the SARS-CoV-2 virus upon infection (fig. 2). Studies have shown that mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna) reduced the risk of infection by 91% for fully vaccinated individuals [67].

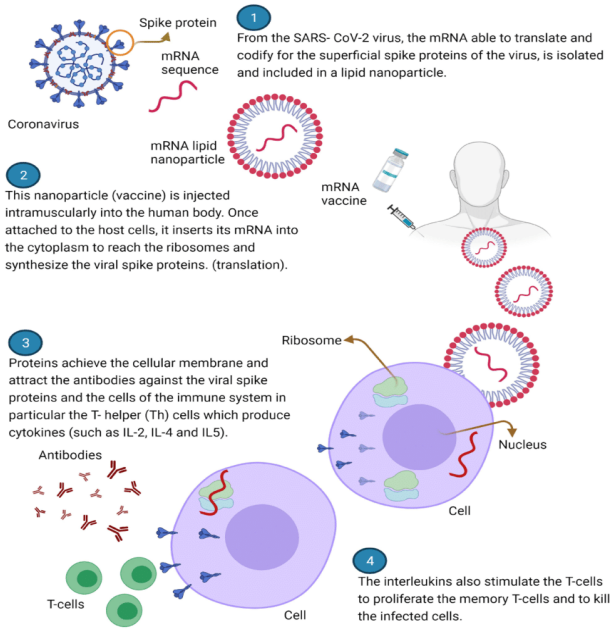

Fig. 2: Mechanism of action of BNT162b2 [68]

mRNA lipid nanoparticle (mRNA-LNP) vaccine

Until recent times, the instability and inefficacy of *in vivo* mRNA distribution have constrained the efficacy of mRNA vaccines. These problems have been mostly resolved by recent technological developments, such as Lipid Nanoparticle (LNP) delivery methods [55]. mRNA-LNP vaccines are composed of various components such as phospholipids, cholesterol, lipids and others that contribute to their effectiveness, as shown in fig. 3 [10]. Ionizable lipids facilitate mRNA delivery into cells by responding to endosomal pH changes, allowing mRNA-LNPs to escape into the cytoplasm for protein translation [69]. Polyethylene glycol provides stability to the nanoparticles, preventing premature mRNA degradation during storage and transport [70]. Liposomes, composed of phospholipids and cholesterol, are recognized as safe and biocompatible carriers for delivery [71]. Cholesterol enhances the structural stability of lipid nanoparticles, maintaining the integrity of the cargo mRNA. Other lipids, such as helper and structural lipids, contribute to the overall stability and encapsulation of mRNA in the nanoparticles [72].

Fig. 3: Nucleic acid-lipid nanoparticle carrier showing the active components, nucleic acid: red coils; cholesterol: yellow circles; helper lipid: brown phospholipid; cationic lipid: green phospholipid; and polyethylene glycol-grafted lipid: blue phospholipid

The mechanism of action of mRNA-LNP vaccines involves the efficient delivery of nucleic acids into host cells, as depicted in fig. 4 [73]. The lipid nanoparticles encapsulate the mRNA, protecting it from degradation and facilitating cellular uptake [74]. Once inside the cell, the ionizable lipids respond to the endosomal pH, promoting the release of mRNA into the cytoplasm [75]. The host cell's machinery then translates the mRNA to produce the target protein, triggering an immune response against the pathogen. This process mimics a natural infection, allowing the immune system to recognize and respond effectively to the pathogen [76].

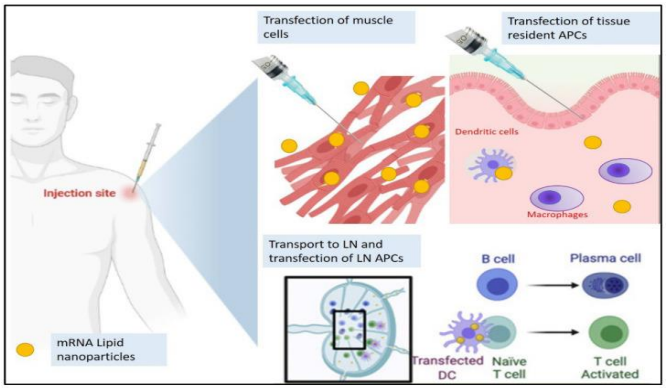

Fig. 4: The mRNA-LNP vaccines' intramuscular delivery and modes of action [73]

Implications for vaccine development

The complex interaction of these components within mRNA-LNP vaccines demonstrates the potential of this technology to revolutionize vaccine development [77]. The design and composition of mRNA-LNP vaccines allow for rapid adaptation to emerging infectious diseases and specific antigens [13]. The stability of these components ensures the integrity of the mRNA cargo, contributing to the vaccine's long shelf life and efficacy [73]. Furthermore, encapsulating and protecting the mRNA payload from premature degradation enhances the chances of a successful immune response [13, 78]. This versatility and efficiency make mRNA-LNP vaccines a promising platform for addressing challenging diseases like malaria, where rapid and specific immune responses are crucial for effective protection [78].

Advantages of mRNA-LNP technology

The advantages of mRNA-LNP technology in vaccine development are multifaceted [79]. mRNA-LNP vaccines can be rapidly designed and produced, allowing for swift responses to emerging infectious diseases, as shown in fig. 5 [80]. Targeting specific antigens on pathogens is another advantage of mRNA-LNP vaccines [81]. Traditional vaccines often use weakened or inactivated pathogens, while mRNA-LNP vaccines can be designed to elicit immune responses against specific proteins, enhancing vaccine efficacy [23, 55]. The surface chemistry of nanoparticles enables the conjugation of targeting compounds, such as antibodies and ligands, facilitating precise interactions with antigens and receptors on target cell surfaces. This capability enhances the targeted delivery of vaccines, allowing for direct administration to specific cells or tissues, thereby potentially improving immune responses while minimizing off-target effects [82].

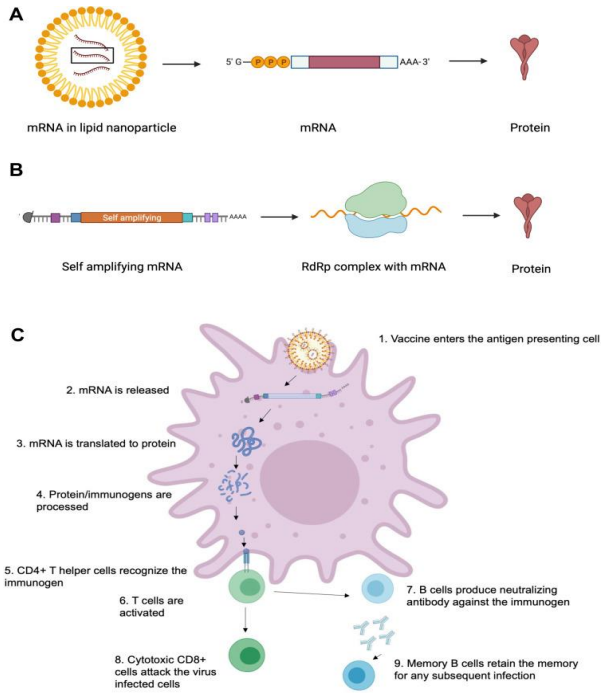

Fig. 5: The mRNA vaccine's mechanisms [80], (A) Translation of a mRNA vaccine in a lipid nanoparticle into a protein to trigger an immune response. (B) *In vivo* response to self-amplifying mRNA by RdRp complexing and subsequent protein translation to trigger an immune response. (C) An immune response is observed due to CD4+T helper cell expression and protein identification, concomitantly stimulating B and CD8+T cells. Neutralizing antibodies are produced by B cells, and memory B cells keep their memory for a future infection

Significance of COVID-19 mRNA-LNP vaccine success revolutionising vaccine development against malaria

The resounding success of mRNA-LNP vaccines against the COVID-19 pandemic marks a pivotal moment in the history of vaccine development [83]. These vaccines, epitomized by Pfizer-BioNTech's Comirnaty® and Moderna's mRNA-1273, represent a paradigm shift in how vaccines are conceptualized, designed, and deployed to combat infectious diseases [84]. The COVID-19 vaccines' efficacy and safety profiles have shown the potential of mRNA-LNP technology to drive similar breakthroughs in addressing other recalcitrant diseases, including malaria [60, 85]. The traditional vaccine development approach, which involves cultivating weakened or inactivated pathogens, is resource-intensive and time-consuming. The mRNA-LNP approach, in contrast, harnesses the power of genetic information to instruct cells to produce antigens, triggering a potent immune response [13]. This strategy's remarkable flexibility facilitates the rapid design and production of vaccines, allowing researchers to pivot swiftly in response to emerging infectious agents [23, 55].

The mRNA-LNP vaccine's significance extends beyond its rapidity as it presents a unique opportunity to tailor vaccines for specific antigens, enhancing their efficacy. In conventional vaccines, broad immune responses may be elicited due to various antigens, leading to suboptimal targeting [86]. The mRNA-LNP technology allows the fine-tuning of vaccines to specifically target the pathogen's key antigens, offering a higher likelihood of inducing robust and targeted immune responses [73]. This precise targeting aligns with the complex challenges posed by diseases like malaria, which demand a multifaceted approach to thwart the complex life cycle of the Plasmodium parasite [16]. The mRNA-LNP vaccines' potential to provide broad protection against diverse pathogen strains is a critical advancement. In traditional vaccines, the evolving nature of pathogens can lead to vaccine-resistant strains emerging over time [54, 56]. The mRNA-LNP-specific protein sequence targeting approach holds the promise of conferring cross-protection against various strains of a pathogen, making it powerful in the fight against diseases marked by high genetic diversity, such as malaria [53].

Transitioning this success from COVID-19 to malaria vaccine development carries profound implications [9, 23]. There are chances to change the course of malaria control by utilizing the flexibility, adaptability, and precision of mRNA-LNP technology [87]. The complexities of the Plasmodium parasite's life cycle and the challenges of achieving broad protection against its various stages are prime targets for the innovation mRNA-LNP vaccines offer [7]. The success of mRNA-LNP vaccines against COVID-19 heralds the potential to accelerate the development of a malaria vaccine by capitalizing on the same technological prowess that has redefined the landscape of pandemic response [23].

Current applications in mRNA-LNP-based malaria vaccine development

The successful development and deployment of mRNA-LNP vaccines against COVID-19 showcase the potential of this technology in responding to global health crises [10, 13]. The rapid response capability during the pandemic could be leveraged for malaria vaccine development, speeding progress toward an effective solution [23]. Due to the complex parasite life cycle, pre-erythrocytic, blood-stage, and transmission-blocking vaccines are three separate types being developed [7]. Vaccines that limit transmission target the female mosquitoes' sexually mature parasites, disrupting the female mosquitoes' sexual life cycle, stopping parasite development, and reducing transmission [88]. It is generally agreed that a vaccine targeting many stages and containing numerous antigen combinations will probably result in a highly effective vaccination to halt malaria transmission [7]. Several recent preclinical studies and animal model trials have demonstrated the immunogenicity and potential transmission-blocking effects of mRNA-LNP malaria vaccines [89]. These studies offer compelling evidence of the technology's effectiveness in inducing protective immune responses. A case study involves mRNA-LNP vaccines targeting the *Plasmodium falciparum* CSP (*Pf*CSP), a critical antigen expressed during the pre-erythrocytic phase of the parasite's life cycle [9, 56]. Preclinical studies in animal models have shown that mRNA-LNP vaccines encoding *Pf*CSP can induce strong immune responses, including producing antibodies and T cells that recognize the protein. These immune responses can potentially prevent sporozoite invasion of liver cells and limit the infection's initial stages [90].

The co-immunization of multiple antigens using mRNA-LNP vaccines has been explored by combining antigens from different stages of the parasite's life cycle, which aims to create vaccines with broader protection [42]. In a recent study, co-immunizing *Pf*CSP and *Pfs*25 mRNA-LNPs demonstrated potential transmission-blocking effects [56]. *Pfs*25 targets the surface 25 protein expressed by mature sexual-stage parasites [91]. The mRNA-LNP vaccine-induced immune responses against both antigens could disrupt the parasite's sexual life cycle and reduce transmission. These properties emphasize the versatility of mRNA-LNP technology in creating multi-antigen vaccines with diverse protective mechanisms [56]. Thus, the mRNA-LNPs vaccine has the potential to confer protective immunity against malaria, and effective strategies to stop the spread of malaria are anticipated to come from a mix of vaccinations that target both the infection stage and the sexual/midgut phases, which is essential for reaching elimination goals [9, 56]. A recent study by Scaria *et al.* [92] demonstrated the efficacy of mRNA vaccines targeting malaria transmission-blocking antigens *Pfs*25 and *Pfs*230D1 by integrating signal peptides and transmembrane domains in mRNA constructs to enhance antigen expression and cellular targeting. Constructs with incorporated GPI anchors or TM domains elicit robust immune responses compared to conventional protein conjugates. Moreover, concurrently delivering multiple antigens within mRNA vaccines enhances their efficacy [92]. Fotaran *et al.* [93] investigated the feasibility of utilising unmodified self-amplifying mRNA (samRNA) vaccines packaged in cationic liposomes for intradermal immunization to target the blood-stage antigen *Pf*RH5. Skin tattooing was employed as the delivery method, and robust dermis antigen production was evidence of efficient delivery and expression. This finding lends credence to the potential inclusion of mRNA-encoded antigens in future vaccine approaches [9, 93].

Challenges of the mRNA-LNP vaccine for malaria

While mRNA-LNP technology is promising, several challenges must be addressed in malaria vaccine development. Optimal vaccination dose is a challenge that could arise in this line of research. There is a need to optimize vaccine dosing and formulation to achieve optimal immune responses and ensure safety [56]. Formulation and administration routes must be identified to produce the necessary immune responses while guaranteeing safety [94]. Long-term research is required to assess the durability and sustainability of vaccine-induced immunity [53]. Rigorous studies in nonhuman primates and, eventually, humans are required to assess safety, efficacy, and potential combination strategies [56]. Moreover, challenges related to scaling up production, cost, and integration into existing malaria control measures must be addressed if the vaccine is ultimately effective [9].

Future directions for research

Based on the findings of current applications in mRNA-LNP-based malaria vaccine development in rodents, future research could focus on conducting similar studies in animals closely related to humans. The resultant finding would help determine the vaccine's safety and efficacy in larger animal models and assess the potential for translation to human trials. Additionally, future studies could explore incorporating other malaria antigens into the vaccine to increase its efficacy and potentially provide broader protection against different parasite strains. Further optimization of mRNA constructs to enhance antigen expression and immunogenicity could be researched. Advancing this research could contribute to developing effective mRNA vaccines for malaria control and elimination. Moreso, optimizing the delivery methods and enhancing antigen presentation of samRNA vaccines for intradermal immunization against malaria. Refining intradermal delivery techniques, such as improving tattooing methods or exploring alternative delivery systems, could significantly enhance vaccine

efficacy while minimizing adverse effects. Additionally, strategies aimed at augmenting antigen presentation, such as incorporating additional adjuvants or targeting specific antigen-presenting cells, hold promise for boosting the immune response elicited by samRNA vaccines.

CONCLUSION

The successful control of the COVID-19 pandemic by mRNA vaccines has shown its efficacy in disease control. mRNA-LNP technology presents a promising avenue for malaria vaccine development. Its ability to facilitate rapid design, target specific antigens, and provide broad protection against diverse strains offers hope for an effective malaria vaccine. By overcoming obstacles and addressing challenges, mRNA-LNP vaccines have the potential to revolutionize malaria control, contributing significantly to global efforts to eliminate malaria and improve public health worldwide. Continued research and investment in mRNA-LNP technology will be critical to advancing malaria vaccine development and realizing the goal of a malaria-free world.

ACKNOWLEDGEMENT

CUCRID is acknowledged for the payment of the article processing charge. CAPIC-ACE is also acknowledged for the scholarship given to Eniola Deborah Adedoyin.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

FUNDING

This work received no funding in terms of grants or other monetary gifts.

AUTHORS CONTRIBUTIONS

FNI: Conceptualisation and Supervision; EDA: Data Aquisation; All authors: Wrote first draft and Approval of final manuscript for submission

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