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Development of a mosaic mRNA vaccine with AI-designed immunogens: A paradigm shift in vaccine science

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Abstract

Rapid mutations in pathogens are a significant challenge in traditional vaccines. Hence, to modify and enhance the efficiency of vaccines, mRNA vaccine technology and AI provide a transformative solution. The technology enables the researcher to design mosaic vaccines that target multiple variants or strains. Hence this review article was designed to explore the intersection of mRNA vaccine technology and AI-design immunogen design, emphasizing the potential of mosaic mRNA vaccine to enhance immunity and broaden the protection against evolving infectious diseases. Here in this study, we discuss the principle of AI design antigen optimization, the architecture of mosaic vaccine, and the critical role of lipid nanoparticles in delivery. Furthermore, we also discuss the current challenges, progress, and future direction in the development of a Mosaic mRNA Vaccine with AI-designed immunogens.

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Introduction

Vaccines are one of the significant strategies against infectious diseases, especially viral infection, and they enhance immunity against pathogenic infection (Pardi and Krammer, 2024; Kumar *et al.*, 2024). However, the development of more effective vaccines against immune-evading pathogens such as HIV is still a big challenge for researchers (Alum *et al.*, 2024). The existing vaccines against some infectious diseases like tuberculosis and malaria have limited efficacy (Hamisi *et al.*, 2024). The vaccine development in past showed slow advancement and limited pan-variant immune responses (Gupta *et al.*, 2024). Furthermore, the limited utility of existing vaccine against rapidly mutating and emerging pathogens such as influenza and Corona-Virus (SARS-CoV-2) also an issue for the researcher (Edalat *et al.*, 2024). Additionally, reactogenic effect can contribute to vaccine uncertainty, further undermining the ability of vaccination campaigns to generate herd immunity (Shukla *et al.*, 2024). Hence these limitations are fuelling the development of novel vaccine technologies to fight more effectively against pathogen (Ugwu *et al.*, 2024). The advancement in sequence technologies and other molecular biology techniques, with addition of AI and Machine learning provide a way to design more effective and advance vaccine against aggressive pathogens like HIV (Dokhale *et al.*, 2024). In recent pandemic (COVID-19), the mRNA vaccine showed significant outcomes, although the antigenic diversity and emerging variants are still existing and need to full fill these gaps (Alzahrani, 2024). Hence, using Molecular biology with addition of AI, this problem could be solved.

Even with the advancement in Biotechnology, immunology and vaccine technologies, the traditional way of vaccine manufacturing still fraught with huge challenges, such as Coast, time, and delay in vaccine availability and development especially in Pandemic (Buckland *et al.*, 2024). Hence, to fight and prevent future pandemic and existing challenges like HIV, still need more effective and advanced technologies (Ugwu *et al.*, 2024). In recent advances in technologies like AI and Machine learning have changed the landscape of vaccine technology, and significantly transformed the development of more effective vaccine (Ali *et al.*, 2024).

These cutting-edge technologies, established opportunities, to design more precise and effective vaccine, immunogen formulations and predict immune response (Vasudevan *et al.*, 2024). The addition of AI and machine learning to vaccine technology introduces a powerful tool for antigen optimization (Bravi, 2024). AI models can predict conserved and immunodominant epitopes across multiple viral strains, generating immunogens that form the basis of mosaic mRNA vaccines (Wang *et al.*, 2024). In Table 1, here we have summarized recent development in mosaic mRNA vaccine around the globe. These vaccines aim to elicit broad and robust immune responses, offering a versatile approach to preventing infectious diseases. This review study was conducted to investigate the Development of Mosaic mRNA Vaccine with AI-Designed Immunogens.

Table 1. Summary of notable mosaic mRNA vaccine candidates

Vaccine candidate	Developer(s)	Target pathogen(s)	Development status	Notes
Mosaic-8 vaccine	California Institute of Technology (Caltech)	Multiple coronaviruses, including SARS-CoV-2 variants	Preclinical studies in animal models	Designed to elicit antibodies against conserved features of sarbecoviruses.
HIV mosaic vaccine	Janssen Vaccines (Johnson & Johnson)	HIV-1	Phase 3 clinical trial (MOSAICO)	Aimed at inducing immunity against multiple HIV-1 strains.
mRNA-1083	Moderna	Influenza and SARS-CoV-2	Phase 3 clinical trial	Combination vaccine targeting both influenza and COVID-19.

Overview of mosaic mRNA vaccine

The knowledge of mosaic mRNA vaccine designing has been emerged more than three decades ago (Pardi and Krammer, 2024). From the last 20 years the vaccine technologies have been advanced significantly and resolved major's health burdens (Danda and Dileep, 2024). Recently the development of nucleoside modified mRNA vaccine for COVID 19 have proven that this platform is easy to developed more effective and precise vaccine on large scale (Fang *et al.*, 2022). The reliable antigen design has enabled mRNA vaccine to entre development for a wide range of pathogen and viruses (Wang *et al.*, 2021; Chaudhary *et al.*, 2021). Hence a detail investigation about the mechanisms such as rotational antigen design, vaccine delivery strategies and vaccination regimens will lily produced potent novel vaccine against a wide range of viruses and other infection. Here we have discussed on overview of Mosaic mRNA vaccine.

Principles of mRNA vaccine technology

From the past several decades the mRNA vaccines have progressed from a lab to clinical reality. During COVID-19 pandemic, the mRNA vaccine has been rapidly synthesized and showed significant outcomes (Hwang, 2024). Furthermore, the mRNA vaccine showed significant results that is we can safely protect patients from infections, although more research is needed in term of mRNA vaccine design optimization, intracellular delivery and applications beyond COVID-19 prophylaxis (Yang *et al.*, 2025; Exposito *et al.*, 2025; Liu and Zhu, 2025; Hejran *et al.*, 2025). According to the principle of mRNA vaccine, the vaccine delivers genetic information which are encoded antigen directly host cells, enhancing the cell mechanisms for protein synthesis (Gao *et al.,* 2024). The antigen is then presented to the immune system, provoking both humoral and cellular immune responses (Huang *et al.*, 2024). The key applications of mosaic mRNA vaccines are, scalability, adaptability and rapid development to variants and other emerging pathogens.

Concept of mosaic vaccine

From the last few decades, remarkably efforts have been done, although the vaccine is significant against some pathogen, but for others, rapid antigenic evolution results in vaccination conferring only short lived or weak protection (Abdaal *et al.*, 2024). Furthermore, due to advances in technology remarkable efforts have been done by targeting the highly conserved region of the pathogen (Universal vaccine) or by making multiple immunological targets within a single vaccine (multiple epitope vaccine) (Xu *et al.*, 2024). Hence the third option which is not explored is a mosaic vaccine (Pérez-Saucedo *et al.*, 2025). Several studies have been conducted recently, on mosaic vaccine which can be delivering to population to achieve better results (Lusso, 2025). The vaccine (Mosaic) could be design on the base of targets (different surface antigen) and immunologically different variants. Here in Table 2 we have summarized key details about mosaic vaccine (Bhaskar *et al.*, 2025).

Table 2. Summarizing key details about a mosaic mRNA vaccine

Feature	Description
Vaccine type	Mosaic mRNA vaccine
Mechanism of action	Encodes antigens with diverse epitopes to stimulate a broad immune response.
Target diseases	HIV, Influenza, and other rapidly mutating pathogens.
Antigen design	Synthetic mosaic antigens generated using computational methods.
Delivery system	Lipid nanoparticles (LNPs) for encapsulation and delivery of mRNA.
Immune response	Induces cellular and humoral immunity targeting multiple viral strains.
Advantages	Broad coverage, quick production, adaptable to emerging variants.
Challenges	Stability, immune tolerance, and scalability of production.
Current status	Preclinical/clinical trials (depending on specific pathogen).
Examples	Mosaic mRNA vaccines developed for HIV and SARS-CoV-2.

Role of AI in immunogen design

The advancement in computational biology, especially AI (Artificial intelligence) have make many possibilities, to change the landscape of many scientific fields, such as medicine, surgery, genetics and molecular biology. Hence in the current study we overview the role of AI in mosaic vaccine design and development.

AI for epitope prediction

AI and machine learning have transformed epitope prediction, an important step in vaccine design and immunotherapy (Xu *et al.*, 2025). The AI and machine learning application manipulate and analyse biological data such as genomic information, the structure of protein, and immunological data (Ali *et al.*, 2025). These technologies analyzed information about B-cell and T cells epitopes, crucial eliciting targeted immune responses (Tenginakai *et al.*, 2025). Artificial intelligence can predict major histocompatibility complex binding affinities, viral strains conserved regions mapping, and stimulate antigen-antibody interactions to optimize the epitope selection for cross-protective immunity (Vaghasia *et al.*, 2025). During the COVID-19 pandemic, the AI rapidly predict immunodominant epitope, due to this quickly vaccine was quickly developed (Mazzocco *et al.*, 2021). Additionally, the AI also provides significant information in cancer diagnosis, by predicting neoepitopes, offering a powerful and scalable approach to tackling diverse health challenges (Boniolo *et al.*, 2021; Zhao *et al.*, 2024). AI algorithm, especially deep learning, and neural network, use to analysed complex genomic and protein data to investigate the conserved epitopes. These epitopes are critical regions on antigen which are recognized by the immune system (Grewal *et al.*, 2024) (Fig. 1).

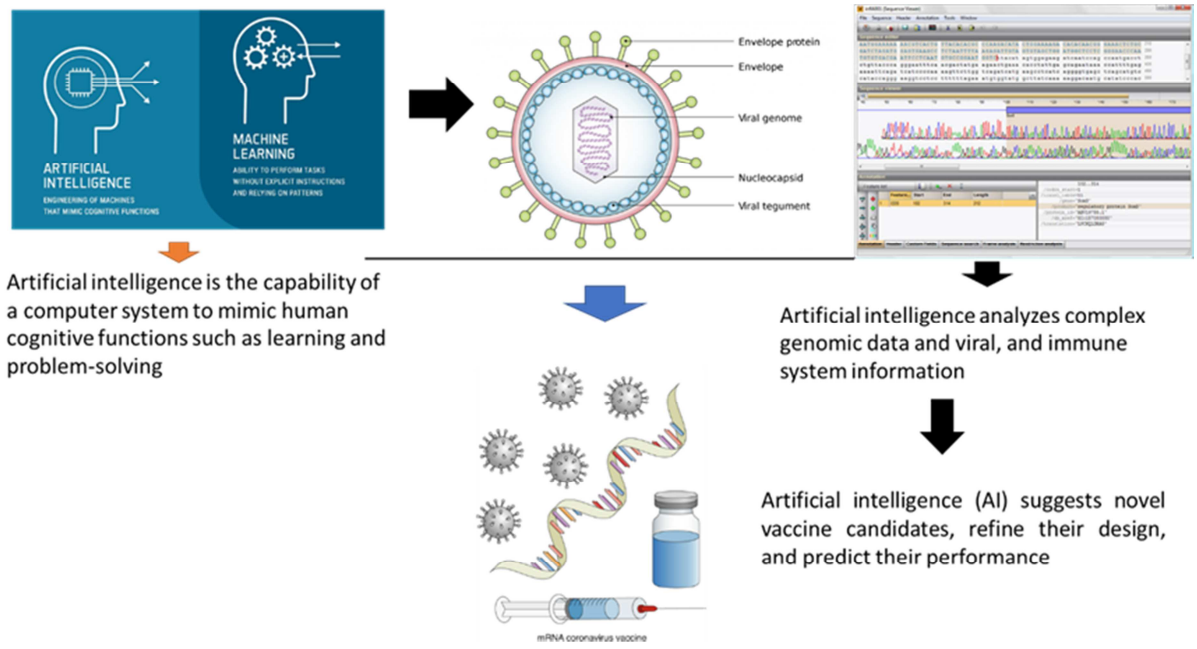

Fig. 1. Schematic representation of the role of AI in mosaic vaccine development. It illustrates how AI integrates diverse pathogen antigen sequences, processes them through reinforcement learning, antigen clustering, and immune simulation modeling, and outputs an optimized mosaic vaccine.

Role of Ai in mosaic immunogens optimization

AI and machine learning have the capability, to analysed genomic information of Viruses, according to that design mosaic immunogens that stimulates the immune responses by triggering the wide range of antigenic components (Nejabat *et al.*, 2024). Researchers use different applications of AI like reinforcement learning, clustering of antigens, and simulation modeling of the immune system (Jamali, 2024). The information gathered from these

techniques is then used for the designing of immunogens that can target a wide range of strains and other pathogens (Ponne *et al.*, 2024). Applications such as reinforcement learning allow AI to significantly improve the immunogen design based on information gathered from predictive models (Olawade *et al.*, 2024). The antigen clustering organizes diverse groups of antigenic elements into meaningful groups, ensuring that the resulting immunogen is representative of the pathogen's variability (Abad *et al.*, 2024). While the immune simulation model is used to predict the response of immunity to the designed vaccine (Morrocchi *et al.,* 2024). These applications provide meaningful information for future vaccine technology, and to rapidly develop more effective vaccines against a wide range of pathogens and viruses.

Using lipid nanoparticle as a delivery system

The LNPs or lipid nanoparticles play an essential role in delivering mRNA vaccines protecting fragile mRNA molecules from the degradation of enzymes, and enhancing their efficient uptake by host cells (Parvin *et al.*, 2024). By creating a biocompatible and stable environment, LNPs ensure the intact function of the mRNA Vaccine until it reaches the targeted host cells. The advancement in lipid nanoparticle formulation, now significantly improved the stability and prolonged storage of mRNA vaccine (Sharma *et al.*, 2024). Additionally, LNPs advancement also enhanced the biocompatibility and reduced the side effects of mRNA vaccines (Wang *et al.*, 2024). Due to improved designing of lipid nanoparticles now used for targeted delivery to antigenic presenting cells, which is crucial for initiating a robust immune response (Jin *et al.*, 2024). Mosaic mRNA vaccine, encoded multiple immunogens, for this vaccine lipid nanoparticle encapsulation is a key factor in ensuring uniform expression of all encoded antigens (Bai *et al.*, 2024). Achieving consistent encapsulation and release kinetics helps maintain the balanced presentation of diverse immunogens, which is vital for eliciting broad and effective immune responses (McBride *et al.*, 2024). These advancements underscore the importance of LNP innovation in advancing the efficacy and scalability of next-generation mRNA vaccines.

The application of mosaic vaccine

Mosaic mRNA vaccine represents a significant advancement in vaccine technology, offering solutions to fight against a wide range of pathogens and viral strains (Weerarathna *et al.*, 2024). Besides this mRNA vaccine is also a key factor in cancer treatment. The mosaic mRNA vaccine has the potential to address several infectious and non-infectious disease (Aleem *et al.*, 2024). Mosaic mRNA vaccines can target the extensive genetic diversity of HIV, incorporating multiple conserved and variable epitopes to stimulate broad neutralizing antibody and T-cell responses (Lusso, 2025). This approach may enhance vaccine efficacy against diverse HIV strains across different regions. By encoding antigens from multiple influenza strains, mosaic mRNA vaccines can improve cross-protection and reduce the need for frequent reformulation (Hsieh *et al.*, 2024).

This could lead to a more universal influenza vaccine capable of combating seasonal and pandemic threats. Mosaic mRNA technology can deliver multiple tumor-associated antigens, enhancing the immune system's ability to target heterogeneous tumor populations (Imodoye *et al.*, 2024). This has implications for creating personalized or universal cancer vaccines. For viruses with high mutation rates or zoonotic origins, such as SARS-CoV-2 variants or other coronaviruses, mosaic mRNA vaccines can incorporate antigens from multiple strains, ensuring broader protection and preparedness for future outbreaks (Fernandes *et al.*, 2024). Mosaic mRNA vaccines can be designed to combat multiple unrelated pathogens in a single shot, simplifying vaccination schedules and increasing global vaccine coverage, particularly in resource-limited settings (Lensch *et al.*, 2024).

Challenges in developing mosaic mRNA vaccines

AI models require extensive datasets for training, which may be limited for newly emerging pathogens. Enhancing data-sharing frameworks and integrating

multi-omics data are essential to improving model accuracy (Vidanagamachchi and Waidyarathna, 2024). Producing mosaic mRNA vaccines involves synthesizing and stabilizing multiple mRNA constructs within a single formulation. Ensuring consistent antigen expression and immunogenicity poses a significant manufacturing challenge (Panday *et al.*, 2025). While mRNA vaccines have demonstrated favorable safety profiles, mosaic formulations with multiple immunogens require rigorous evaluation to prevent adverse immune reactions, such as excessive inflammation or autoimmunity (Bai *et al.*, 2024).

Developing mosaic mRNA vaccines presents several technical and logistical challenges, beginning with the design and selection of immunogens (Chentoufi *et al.*, 2024) Mosaic vaccines aim to encode multiple antigens, often from genetically diverse strains or variants of a pathogen.

Achieving this requires careful computational modeling to identify conserved and variable regions that elicit broad and robust immune responses. Balancing the inclusion of these diverse immunogens while maintaining mRNA stability and efficient translation poses a significant hurdle. Additionally, the risk of immunodominance—where the immune system predominantly targets one antigen over others—must be addressed to ensure a balanced and effective immune response (Chentoufi *et al.*, 2024).

Another challenge lies in the optimization of lipid nanoparticles (LNPs) for delivering mosaic mRNA constructs. Ensuring uniform encapsulation of longer or more complex mRNA sequences, which encode multiple antigens, is critical for consistent expression and immunogenicity. LNPs must also be engineered to maintain stability during storage and transit, particularly in low-resource settings where cold-chain infrastructure may be limited (Pardi and Krammer, 2024). The interplay between the mRNA sequence, LNP composition, and the host immune response adds layers of complexity that require extensive preclinical and clinical testing.

The scalability and cost of production pose significant challenges for mosaic mRNA vaccines.

Manufacturing processes need to be adapted to accommodate the synthesis and purification of large, multi-antigen mRNA constructs while maintaining high yield and quality. Regulatory hurdles also arise from the complexity of mosaic designs, requiring rigorous evaluation of safety, efficacy, and immunogenicity across diverse populations. Addressing these challenges is essential for realizing the full potential of mosaic mRNA vaccines in combating global health threats.

Conclusion

The development of next-generation AI tools, such as generative adversarial networks (GANs) and transformers, holds promise for improving immunogen design. These models can predict immunogenicity and simulate vaccine-induced immune responses with higher accuracy. AI can also enable personalized vaccine design by tailoring immunogens to individual genetic and immunological profiles, potentially improving vaccine efficacy in diverse populations.

Incorporating genomic, proteomic, transcriptomic, and immune repertoire data into AI models will provide a holistic view of host-pathogen interactions, enabling the design of more effective vaccines. The development of mosaic mRNA vaccines using AI-designed immunogens represents a transformative step in combating infectious diseases. By addressing antigenic diversity and enhancing immune coverage, these vaccines offer a promising solution to the challenges posed by rapidly mutating pathogens. Continued advancements in AI, mRNA technology, and delivery systems are poised to unlock the full potential of this innovative approach, paving the way for a new era in vaccine science.

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