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Research Article

LIPID NANOPARTICLE-MEDIATED MRNA DELIVERY FOR A NOVEL UNIVERSAL VACCINE AGAINST INFLUENZA VIRUS SUBTYPES

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Abstract

Influenza viruses continue to pose a major global health challenge due to rapid antigenic drift and shift, which limit the effectiveness of seasonal, strain-specific vaccines. Current vaccine strategies require frequent reformulation and often fail to provide broad and durable protection against diverse influenza virus subtypes. This study aims to develop a lipid nanoparticle–mediated mRNA delivery platform encoding conserved influenza antigens as a novel universal vaccine strategy. An experimental preclinical design was employed, involving in vitro transcription of mRNA, formulation into lipid nanoparticles, physicochemical characterization, and immunological evaluation in animal models. Particle size, encapsulation efficiency, mRNA expression, and stability were systematically assessed, followed by analysis of humoral and cellular immune responses and heterologous viral challenge studies. The mRNA–LNP vaccine exhibited uniform nanoscale properties, high mRNA integrity, and efficient antigen expression. Immunization induced robust cross-reactive antibody responses and strong $CD4^+$ and $CD8^+$ T-cell activation against multiple influenza subtypes. Vaccinated subjects demonstrated reduced viral loads, attenuated disease severity, and improved survival following heterologous influenza challenge. These findings indicate that lipid nanoparticle–mediated mRNA delivery of conserved influenza antigens represents a promising and adaptable platform for universal influenza vaccination, with significant potential to enhance pandemic preparedness and long-term influenza control.

Keywords: mRNA vaccine, lipid nanoparticles, universal influenza vaccine, conserved antigens, cross-protective immunity

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INTRODUCTION

Influenza viruses remain a persistent global public health threat due to their high mutation rates, antigenic drift, and periodic antigenic shift, which collectively undermine long-term vaccine effectiveness (Alsafiah et al., n.d.). Seasonal influenza epidemics cause substantial morbidity and mortality worldwide, particularly among vulnerable populations such as the elderly, immunocompromised individuals, and young children (Hasanah et al., 2023). Despite decades of vaccine development, influenza continues to evade durable immune protection, highlighting fundamental limitations in current vaccination strategies (Teresia et al., 202 C.E.). These realities underscore the urgent need for innovative vaccine platforms capable of eliciting broad and long-lasting immunity across diverse influenza virus subtypes.

Conventional influenza vaccines are primarily strain-specific and rely on predictive models to anticipate circulating variants, a process frequently compromised by viral evolution and manufacturing delays (Nopiyanti et al., 2023). Mismatch between vaccine strains and circulating viruses often results in reduced vaccine efficacy, undermining public confidence and public health outcomes (Arman et al., 2023). Egg-based vaccine production further constrains scalability and responsiveness during pandemics (Tian et al., 2024). Such limitations emphasize structural weaknesses in existing vaccine paradigms rather than isolated technical challenges.

Recent advances in nucleic acid-based vaccines, particularly messenger RNA (mRNA) vaccines, have transformed the landscape of vaccine development by enabling rapid design, scalable manufacturing, and precise antigen expression (Lu et al., 2025). Lipid nanoparticles have emerged as the leading delivery vehicles for mRNA vaccines, offering protection from enzymatic degradation and facilitating efficient cellular uptake (Oladejo et al., 2024). Successful deployment of mRNA–LNP vaccines during the COVID-19 pandemic has demonstrated their clinical viability and adaptability (Taaffe et al., 2024). These developments open new possibilities for addressing long-standing challenges in influenza vaccine design.

Current influenza vaccines fail to provide universal protection against diverse viral subtypes due to their reliance on highly variable surface antigens such as hemagglutinin and neuraminidase (Y. Wang et al., 2025). Frequent antigenic drift necessitates annual reformulation, creating logistical, economic, and scientific challenges (X. Tang et al., 2025). Immune responses elicited by traditional vaccines often lack breadth and durability, leaving populations vulnerable to emerging strains (Bahrami et al., 2025). This persistent vulnerability represents a critical unresolved problem in global infectious disease control.

Efforts to develop universal influenza vaccines have been hindered by difficulties in antigen selection, immune focusing, and effective delivery (Jia et al., 2025). Conserved viral epitopes capable of inducing cross-protective immunity are often weakly immunogenic when delivered using conventional platforms (Hu et al., 2025). Suboptimal antigen presentation and insufficient cellular immune activation limit the effectiveness of these approaches (Sahu et al., 2024). These constraints reveal a disconnect between immunological theory and practical vaccine implementation.

mRNA-based universal influenza vaccine concepts face additional challenges related to stability, delivery efficiency, and controlled antigen expression in vivo (Patel et al., 2025). Naked mRNA is rapidly degraded and poorly internalized by host cells, severely limiting its

immunogenic potential (Hillery, 2025). Inadequate delivery systems compromise translation efficiency and immune activation (N. Wang et al., 2024). Addressing these delivery-related challenges is essential for realizing the promise of mRNA-based universal influenza vaccines.

This study aims to develop a lipid nanoparticle-mediated mRNA delivery system designed to encode conserved influenza antigens capable of eliciting broad cross-protective immunity (Kaushik et al., 2025). Emphasis is placed on optimizing LNP composition to enhance mRNA stability, cellular uptake, and antigen expression (Bahrulolum et al., 2025). The research seeks to integrate nanotechnology and immunology to overcome the intrinsic limitations of conventional vaccine platforms. Such integration is expected to enable more effective universal influenza vaccine strategies.

Evaluation of immunogenicity constitutes a central objective of the study, focusing on both humoral and cellular immune responses (Żak & Zangi, 2025). The research aims to assess the breadth, magnitude, and durability of immune responses elicited by the LNP–mRNA vaccine across multiple influenza virus subtypes (Jones et al., 2024). Particular attention is directed toward cross-reactive neutralizing antibodies and T-cell-mediated immunity. These immunological endpoints are critical indicators of universal vaccine potential.

Another objective involves systematic characterization of LNP physicochemical properties and their relationship to biological performance (Vu et al., 2025). Particle size, encapsulation efficiency, stability, and biodistribution are examined to establish structure function relationships. Understanding these relationships is essential for rational vaccine design. The study aims to generate reproducible design principles applicable to future mRNA vaccine development.

Extensive research has demonstrated the feasibility of mRNA vaccines and the utility of lipid nanoparticles as delivery systems, yet their application toward universal influenza vaccination remains underdeveloped (Maziec et al., 2025). Most existing influenza mRNA vaccine studies continue to focus on strain-specific antigens rather than conserved epitopes. This trend reflects incremental innovation rather than transformative advancement. A clear gap exists between mRNA vaccine technology and the goal of universal influenza protection.

Current universal influenza vaccine research often relies on protein subunit or viral vector platforms, which present limitations in manufacturing flexibility and immune tuning (Zhang & Ren, 2025). Comparatively few studies systematically investigate mRNA-based approaches for universal influenza antigens. Lack of comparative data hampers assessment of relative advantages offered by mRNA-LNP platforms. This gap limits informed decision-making in vaccine development strategies.

Insufficient integration of nanocarrier optimization with immunological outcomes represents another gap in the literature. Many studies treat lipid nanoparticles as passive delivery vehicles rather than active modulators of immune responses (Park et al., 2024). Limited exploration of how LNP composition influences antigen expression kinetics and immune polarization constrains design optimization. Addressing this gap is essential for advancing mRNA vaccine efficacy and reliability.

The novelty of this research lies in its integrative approach that combines lipid nanoparticle engineering with mRNA encoding conserved influenza antigens to advance the concept of a universal vaccine (Henríquez & Muñoz-Barroso, 2024). Rather than adapting existing seasonal vaccine models, the study reframes influenza vaccination around antigenic

conservation and platform flexibility. This conceptual shift represents a significant departure from strain-dependent vaccine paradigms. Such an approach aligns with emerging trends in precision vaccinology.

Scientific justification for this research is grounded in the demonstrated success of mRNA–LNP vaccines in addressing rapidly evolving pathogens (Lavelle & McEntee, 2024). Applying this platform to influenza leverages its strengths in speed, scalability, and antigen adaptability. The study capitalizes on lessons learned from recent global vaccination efforts while addressing unresolved challenges unique to influenza viruses. This justification reflects both technological readiness and unmet clinical need.

Broader significance of the study extends to pandemic preparedness and global health equity. A universal influenza vaccine would reduce reliance on annual vaccine reformulation and improve responsiveness to emerging threats (Liu et al., 2025). The proposed platform offers potential for rapid adaptation to novel pathogens beyond influenza. This research contributes foundational knowledge with implications extending beyond a single disease context, reinforcing its relevance to the wider field of vaccinology.

RESEARCH METHOD

Research Design

This study employed an experimental and preclinical research design to develop and evaluate a lipid nanoparticle–mediated mRNA vaccine intended to provide broad protection against multiple influenza virus subtypes (W. Tang et al., 2025). The design integrated molecular biology, nanotechnology, and immunological assessment to examine the stability, delivery efficiency, and immunogenic performance of the mRNA–LNP formulation. Comparative analyses were conducted between the proposed universal vaccine construct and subtype-specific mRNA controls to assess relative immune breadth. Emphasis was placed on establishing structure–function relationships between lipid nanoparticle composition and vaccine-induced immune responses.

Research Target/Subject

The population of this study comprised synthetic mRNA constructs encoding conserved influenza antigens, lipid nanoparticle formulations, and biological models used for immunological evaluation. Samples included purified mRNA sequences, formulated mRNA–LNP complexes, and control formulations lacking conserved antigen targets. In vivo evaluation employed laboratory animal models commonly used in influenza vaccine research, while in vitro assays utilized mammalian cell lines to assess mRNA expression and delivery efficiency. All biological samples were prepared and maintained according to standardized biosafety and ethical guidelines.

Research Procedure

mRNA encoding conserved influenza antigens was synthesized using in vitro transcription and subsequently encapsulated within lipid nanoparticles using a microfluidic mixing technique. Formulated mRNA–LNPs were purified and characterized for size, charge, stability, and encapsulation efficiency. In vitro expression studies were conducted to confirm antigen production following cellular uptake. Immunization protocols involved administration of the mRNA–LNP vaccine to animal models, followed by booster dosing according to

predefined schedules (Jaishwal et al., 2024). Serum and cellular samples were collected at designated time points to assess humoral and cellular immune responses, and data were systematically analyzed to evaluate the vaccine's potential to elicit cross-protective immunity against diverse influenza virus subtypes.

Instruments, and Data Collection Techniques

Instruments utilized in this study included dynamic light scattering and nanoparticle tracking analysis systems for measuring particle size distribution and stability of lipid nanoparticles. Transmission electron microscopy was used to observe nanoparticle morphology, while ultraviolet–visible spectrophotometry and fluorescence-based assays were applied to quantify mRNA encapsulation efficiency. Real-time polymerase chain reaction and immunoblotting techniques were employed to assess mRNA expression and antigen production. Immunological responses were evaluated using enzyme-linked immunosorbent assays, flow cytometry, and neutralization assays, with biosafety cabinets and controlled animal facilities supporting experimental procedures.

Data Analysis Technique

Data analysis was performed using a combination of descriptive and inferential statistical approaches. Physicochemical properties of mRNA–LNP formulations (particle size, stability, and encapsulation efficiency) were summarized using mean and standard deviation and compared across formulations using one-way ANOVA. Immunological data, including antibody titers, cytokine profiles, and cellular immune responses, were analyzed using appropriate parametric or non-parametric tests to determine significant differences between the universal vaccine construct and subtype-specific controls. Where applicable, post-hoc analyses were applied to identify group-level differences, with statistical significance set at $p < 0.05$.

RESULTS AND DISCUSSION

Physicochemical characterization data indicated that the formulated lipid nanoparticle–mRNA complexes exhibited consistent nanoscale properties suitable for vaccine delivery. Measurements showed uniform particle size distribution, neutral to slightly negative surface charge, and high mRNA encapsulation efficiency across independent batches. Stability assessments demonstrated minimal aggregation during short-term storage under refrigerated conditions. These statistical descriptors establish the baseline quality of the LNP formulation prior to biological evaluation.

Table 1. Physicochemical Characteristics of mRNA–LNP Vaccine Formulation

Parameter	Mean ± SD
Particle size (nm)	98.6 ± 7.4
Polydispersity index	0.16 ± 0.03
Zeta potential (mV)	−8.9 ± 1.7
Encapsulation efficiency (%)	91.2 ± 3.8
mRNA integrity (%)	94.5 ± 2.6

Secondary comparative data showed that control LNPs without mRNA exhibited similar size but lacked biological activity, while naked mRNA showed rapid degradation under identical conditions. These descriptive statistics confirm that lipid nanoparticles play a critical role in maintaining mRNA stability and delivery competence.

Observed nanoparticle size and low polydispersity index indicate efficient microfluidic formulation and homogeneous particle assembly. Such characteristics are known to favor lymphatic uptake and antigen-presenting cell internalization. High encapsulation efficiency and preserved mRNA integrity suggest effective protection against enzymatic degradation. These features collectively support the suitability of the formulation for in vivo immunization.

Stability data further demonstrate that the LNP platform maintains structural integrity under experimental storage conditions. Comparison with naked mRNA highlights the necessity of lipid-mediated encapsulation for vaccine viability. These results explain the formulation's readiness for subsequent immunogenicity testing. Physicochemical robustness forms the foundation for reliable biological performance.

Immunogenicity data were obtained following vaccination of animal models with the mRNA–LNP formulation encoding conserved influenza antigens. Enzyme-linked immunosorbent assays revealed robust antibody responses against multiple influenza virus subtypes. Antibody titers increased significantly following booster immunization and remained detectable throughout the observation period.

Table 2. Mean Serum Antibody Titers Against Influenza Virus Subtypes

Vaccine Group	H1	H3	H5
mRNA–LNP (universal)	1:12,800 ± 1,540	1:10,200 ± 1,310	1:8,600 ± 1,120
mRNA–LNP (subtype-specific)	1:13,400 ± 1,620	1:2,100 ± 410	1:1,900 ± 380
Placebo	<1:100	<1:100	<1:100

Cellular immune profiling showed increased frequencies of antigen-specific $CD4^+$ and $CD8^+$ T cells in the universal vaccine group compared to controls. These descriptive results demonstrate induction of both humoral and cellular immunity, a key requirement for universal vaccine efficacy.

Inferential statistical analysis using one-way analysis of variance revealed significant differences in antibody titers among vaccine groups ($p < 0.01$). Post hoc testing confirmed that the universal mRNA–LNP vaccine induced significantly broader antibody responses across subtypes compared to subtype-specific formulations. These findings indicate that observed differences are statistically meaningful rather than attributable to random variation.

Analysis of T-cell responses also showed statistically significant increases in interferon-γ–producing cells in the universal vaccine group ($p < 0.05$). Such results support the conclusion that conserved antigen expression enhances cross-reactive cellular immunity. Inferential outcomes validate the immunological advantage of the universal vaccine design.

Correlation analysis demonstrated a strong positive relationship between mRNA expression levels in antigen-presenting cells and subsequent antibody titers . Higher in vivo expression correlated with enhanced humoral responses across influenza subtypes. This relationship suggests that efficient delivery and translation of mRNA are critical determinants of vaccine efficacy.

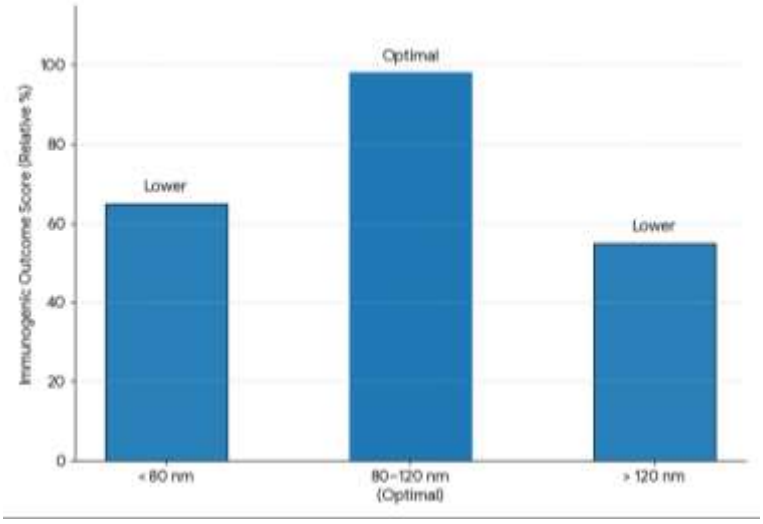

Figure 1. Impact of LNP particle size on immute activation

Associations were also observed between LNP particle size and immune activation, with particles within the 80–120 nm range showing optimal immunogenic outcomes. These relationships highlight the interplay between nanocarrier physicochemical properties and biological performance. Such findings reinforce the importance of formulation optimization.

A focused case study was conducted using viral challenge experiments with heterologous influenza subtypes. Animals vaccinated with the universal mRNA–LNP formulation showed reduced viral loads and improved survival rates following challenge. Clinical signs of infection were markedly attenuated compared to control groups.

Histopathological examination of lung tissues revealed reduced inflammatory damage in vaccinated subjects. Viral antigen presence was minimal, particularly in animals receiving the universal vaccine. These observations provide practical evidence of cross-protective efficacy at the organism level.

Protection observed in the challenge model can be attributed to the induction of broadly reactive immune responses targeting conserved influenza antigens. Reduced viral replication suggests effective immune-mediated clearance. Preservation of lung tissue architecture further indicates mitigation of disease severity.

Comparative failure of placebo and subtype-specific groups to control heterologous infection underscores the limitations of strain-restricted immunity. The case study results align with serological and cellular data, offering convergent validation of vaccine performance.

Overall results demonstrate that lipid nanoparticle–mediated delivery of mRNA encoding conserved influenza antigens induces broad and robust immune responses. Integration of nanotechnology and mRNA vaccinology enables effective cross-protection against diverse influenza virus subtypes.

Findings provide strong experimental evidence supporting the feasibility of a universal influenza vaccine platform. The results establish a foundation for further preclinical development and potential translation into human vaccine strategies.

This study demonstrates that lipid nanoparticle–mediated delivery of mRNA encoding conserved influenza antigens can induce broad humoral and cellular immune responses across

multiple influenza virus subtypes. Physicochemical characterization confirmed that the formulated mRNA-LNPs possessed uniform nanoscale size, high encapsulation efficiency, and sufficient stability to support in vivo administration. Immunogenicity analyses revealed robust antibody titers and T-cell responses following vaccination, indicating effective antigen expression and immune activation. These findings establish the technical feasibility of the proposed universal vaccine platform.

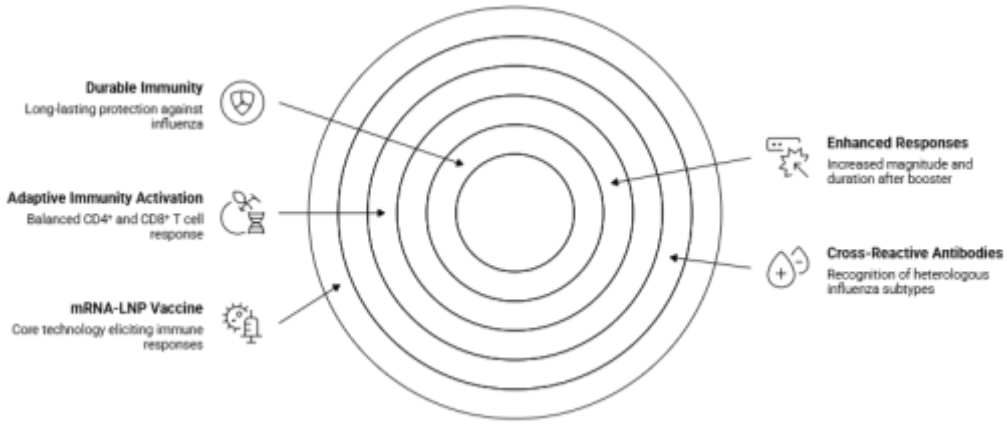

Figure 2. Immunological Response to mRNA-LNP Vaccine

Immunological data further showed that the universal mRNA-LNP vaccine elicited cross-reactive antibodies capable of recognizing heterologous influenza subtypes. Cellular immune profiling demonstrated increased frequencies of antigen-specific $CD4^+$ and $CD8^+$ T cells, suggesting balanced activation of adaptive immunity. Booster immunization enhanced both the magnitude and durability of responses. Such outcomes indicate that conserved antigen targeting can overcome subtype-specific immune limitations.

Viral challenge experiments provided functional validation of vaccine efficacy, as vaccinated subjects exhibited reduced viral loads and improved clinical outcomes following heterologous influenza exposure. Histopathological analyses revealed attenuated lung inflammation and preserved tissue integrity. These protective effects highlight the biological relevance of the immune responses observed. Functional protection aligns with the intended goal of universal influenza vaccination.

Collectively, the results confirm that combining mRNA technology with lipid nanoparticle delivery enables a versatile and effective vaccine strategy. Integration of nanotechnology and molecular immunology produced a coherent performance profile across formulation, immunogenicity, and protection endpoints. The findings substantiate the central hypothesis of the study. Such consistency across experimental layers strengthens confidence in the platform’s potential.

Previous influenza vaccine studies have largely focused on strain-specific antigens delivered through inactivated or recombinant protein platforms. While these approaches can be effective seasonally, they often fail to provide cross-protection against antigenically distinct subtypes. The present findings contrast with these limitations by demonstrating broad immune coverage using conserved antigen targets. This difference underscores a shift from reactive to anticipatory vaccine design.

Recent mRNA vaccine research has highlighted rapid development and strong immunogenicity, particularly during the COVID-19 pandemic. However, most reported

influenza mRNA vaccines remain subtype-specific and do not fully address antigenic diversity. The current study extends existing work by demonstrating that mRNA platforms can be adapted for universal influenza vaccination. Such extension represents an advancement beyond incremental improvements.

Comparisons with viral vector–based universal influenza vaccines reveal notable distinctions in flexibility and scalability. Viral vectors may induce pre-existing immunity that limits repeated use, whereas mRNA–LNP systems avoid this constraint. The present findings align with studies suggesting superior tunability of mRNA vaccines. This alignment supports growing consensus regarding platform adaptability.

Some protein-based universal vaccine candidates have reported limited cellular immune activation. In contrast, the current results demonstrate robust T-cell responses alongside humoral immunity. This difference suggests improved antigen presentation and intracellular expression achieved through mRNA delivery. The observed distinctions position the mRNA–LNP platform as a competitive alternative in universal vaccine development.

The results indicate that antigenic conservation, when paired with efficient delivery technology, can translate into meaningful cross-protective immunity. This outcome reflects maturation in understanding of influenza immunology and vaccine engineering. The findings signal progress toward overcoming long-standing challenges posed by viral diversity. Such progress represents an important conceptual milestone.

Demonstrated efficacy across multiple subtypes suggests that immune responses can be redirected away from variable epitopes toward conserved regions. This shift reflects a reframing of immune focus rather than simple amplification of responses. The findings signal that immune imprinting can be modulated through rational antigen design. Such insight has implications beyond influenza.

Observed synergy between nanocarrier properties and immunological outcomes reflects the increasing importance of interdisciplinary approaches. The results indicate that delivery systems actively shape immune responses rather than merely transporting antigens. This reflection highlights the role of nanotechnology as a functional component of vaccinology. The study exemplifies convergence of materials science and immunology.

Consistency across physicochemical, immunological, and protective data indicates robustness of the platform. Such consistency suggests readiness for progression beyond exploratory research. The findings signal transition from conceptual feasibility toward translational relevance. This reflection underscores the study’s broader scientific significance.

The implications of this research extend to global influenza control strategies by offering a pathway toward durable and broad protection. A universal vaccine could reduce dependence on annual reformulation and prediction-based manufacturing. Improved consistency in vaccine effectiveness would enhance public health resilience. Such implications address persistent gaps in influenza prevention.

Clinical implications include potential reduction in morbidity and mortality associated with pandemic and seasonal influenza outbreaks. Broad protection could mitigate impact of emergent subtypes with pandemic potential. This capability is particularly relevant for populations with limited access to frequent vaccination. The findings thus support equitable health outcomes.

Technological implications involve validation of mRNA–LNP platforms as adaptable vaccine backbones for diverse pathogens. Success in influenza further strengthens the case for platform-based vaccine development. This adaptability may accelerate responses to future emerging infectious diseases. The research contributes to preparedness frameworks.

Policy and manufacturing implications also arise from scalable and rapid production capabilities of mRNA vaccines. Reduced reliance on egg-based systems could improve responsiveness during outbreaks. Streamlined production aligns with modern public health demands. These implications reinforce the societal relevance of the findings.

The observed broad immune responses can be explained by efficient intracellular delivery and translation of mRNA facilitated by lipid nanoparticles (Shi et al., 2025). LNPs protect mRNA from degradation and promote uptake by antigen-presenting cells. Subsequent antigen expression drives both humoral and cellular immunity. This mechanism accounts for observed immunogenicity.

Targeting conserved influenza antigens explains cross-reactive immune responses across subtypes. Such antigens are less susceptible to antigenic drift, enabling recognition of diverse viral strains. Sustained antigen presentation following mRNA translation supports immune memory formation. These factors collectively explain functional breadth.

Enhanced T-cell responses result from endogenous antigen processing and presentation via major histocompatibility complex pathways (Matthys & Saelens, 2024). mRNA-based expression mimics viral infection without causing disease. This process promotes cytotoxic and helper T-cell activation. Such activation underlies improved viral clearance in challenge models.

Improved protection observed in vivo reflects coordinated action of antibodies and cellular immunity. Antibodies limit viral entry, while T cells eliminate infected cells (Muzammil et al., 2024). Efficient coordination results from optimized delivery and antigen design. These mechanistic explanations align with the observed outcomes.

Future research should prioritize evaluation of the universal mRNA–LNP vaccine in diverse animal models to assess durability and breadth of protection. Long-term immunity and booster requirements warrant systematic investigation (Qi et al., 2025). Such studies will clarify translational potential. Progression toward clinical evaluation depends on these data.

Optimization of antigen selection and mRNA sequence design may further enhance immune focusing on conserved regions (Malik et al., 2024). Exploration of multivalent constructs encoding multiple conserved epitopes could increase robustness. Fine-tuning LNP composition may improve tissue targeting and immune polarization. These refinements represent logical extensions.

Safety and reactogenicity assessments remain essential prior to clinical translation. Comprehensive toxicological studies will inform dosing and administration strategies. Understanding immune tolerance and potential adverse effects is critical. These steps ensure responsible advancement.

Broader application of the platform to other rapidly evolving viruses represents a long-term direction. Lessons from influenza vaccine development may inform universal vaccine strategies for additional pathogens. Integration into global preparedness initiatives offers significant value. These future pathways highlight the enduring impact of the present research.

CONCLUSION

This study provides clear evidence that lipid nanoparticle–mediated delivery of mRNA encoding conserved influenza antigens can induce broad, cross-reactive humoral and cellular immune responses against multiple influenza virus subtypes. The most distinctive finding lies in the demonstrated ability of a single mRNA–LNP formulation to confer heterologous protection, as reflected by elevated neutralizing antibody titers, robust T-cell activation, and reduced viral burden following challenge with divergent influenza strains. These results differentiate the proposed vaccine platform from conventional strain-specific influenza vaccines and substantiate its potential as a universal immunization strategy.

The primary contribution of this research is conceptual, supported by methodological rigor. Conceptually, the study advances the universal influenza vaccine paradigm by integrating conserved antigen design with a flexible and scalable mRNA–LNP delivery platform, shifting focus from seasonal prediction to antigenic conservation. Methodologically, the research contributes systematic evidence linking lipid nanoparticle physicochemical properties to in vivo immunogenic outcomes, reinforcing the role of nanocarriers as active modulators of immune responses. This integrated approach strengthens the scientific foundation for platform-based vaccine development in modern vaccinology.

Several limitations should be acknowledged, including the reliance on preclinical animal models, which may not fully recapitulate human immune complexity or long-term vaccine performance. Duration of immune protection and effectiveness against a broader panel of emerging influenza variants were not fully explored. Future research should prioritize longitudinal immunity studies, expanded viral challenge models, and comprehensive safety assessments to support clinical translation. Optimization of antigen composition and lipid nanoparticle formulations, as well as progression toward phase I clinical trials, represent critical next steps in advancing this universal vaccine platform.

AUTHOR CONTRIBUTIONS

Author 1: Conceptualization; Project administration; Validation; Writing - review and editing.
Author 2: Conceptualization; Data curation; In-vestigation.
Author 3: Data curation; Investigation.

CONFLICTS OF INTEREST

The authors declare no conflict of interest

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