

Convergence of Gene Therapy and Vaccine Platforms in the Post-Pandemic Era: A Mini Review

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Abstract

The COVID-19 pandemic accelerated the convergence of vaccine and gene therapy research, demonstrating the potential for gene-encoded platforms to be rapidly reconfigured for both preventive and therapeutic applications. This real-world evaluation validated the principle of adaptable, platform-based molecular medicines. Convergence is facilitated by three key components: Chemically modified nucleotides that reduce innate-immune sensing while maintaining high translation efficiency, lipid nanoparticles refined for targeted and low-toxicity delivery, and viral vectors with adjustable immunogenicity. Emerging technologies, including self-amplifying RNA, selectively targeted lipid nanoparticles, and advanced adenoviruses, have expanded the therapeutic toolkit to include *in vivo* genome editing and personalized neoantigen vaccines. The rapid scale-up of production during the pandemic has had a lasting impact, establishing cGMP manufacturing lines, emergency-use regulatory frameworks, and extensive safety data. However, the field still faces challenges such as context-dependent immunogenicity, the need for thermostable products to improve global distribution, and widening disparities in technology access between high- and low-income regions. Gene-encoded platforms have evolved from a proof-of-concept to a multifaceted therapeutic framework capable of addressing infectious, genetic, and malignant diseases. Their full public health potential will depend on coordinated investment in distributed manufacturing, adaptive regulation, and ethical governance that prioritizes equity alongside technical advancements.

Keywords: Gene therapy, mRNA vaccines, Adenoviral vectors, Platform convergence, Post-pandemic therapeutics, Translational medicine

Introduction

The convergence of gene therapy and vaccine technologies has led to a significant breakthrough in biomedicine, fundamentally changing disease prevention and treatment approaches. Notably, the coronavirus disease 2019 (COVID-19) pandemic accelerated this intersection, resulting in a two-way flow of innovation that transforms therapeutic strategies across various disease areas [1]. While mRNA vaccines against severe acute respiratory syndrome coronavirus 2

(SARS-CoV-2) These developments have received global attention, and the technological synergies between gene-based therapeutics and vaccines have far-reaching implications for infectious and genetic diseases [2,3]. Despite historically distinct goals, the distinction between vaccines and gene therapy has become increasingly blurred, as both fields employ similar molecular tools, including viral vectors, lipid nanoparticles (LNPs), and nucleic acid delivery systems

[1,2,4]. The pandemic accelerated their convergence, demonstrating that platforms delivering immunogenic proteins for vaccination can easily adapt for therapeutic protein replacement, gene editing, and cellular reprogramming [2,3,5].

This convergence occurs at a critical juncture. The disparities in the distribution of the COVID-19 vaccine have highlighted weaknesses in biopharmaceutical manufacturing and distribution systems [6]. However, the success of mRNA vaccines has validated decades of research on gene delivery, proving that adaptable, platform-based treatments are feasible [2,7]. The implications of this convergence extend beyond pandemic preparedness to the treatment of genetic diseases, cancers, and chronic infections resistant to conventional methods [3]. Key technological advances include the development of modified nucleotides that prevent immune reactions while maintaining efficacy, as well as delivery systems that enable the safe introduction of cellular nucleic acids [2,7]. These shared technologies facilitate bidirectional progress. In addition, the regulatory environment was adapted through emergency use authorization pathways, establishing precedents for rapid gene-based therapeutic evaluation while maintaining safety standards [8]. This flexibility, combined with manufacturing scalability, positions gene-based platforms as versatile medical tools. This review examines the current state and future possibilities of vaccine-gene therapy convergence, exploring innovation exchange, underlying scientific principles, limitations, and implications for global health equity and pandemic preparedness.

COVID-19 as a catalyst for gene-based medicine

The global response to SARS-CoV-2 significantly accelerated gene-based therapeutic development, compressing decades of anticipated progress into a period of intense innovation [9,10]. This rapid advancement was facilitated by the convergence of mature platform technologies, flexible regulatory frameworks, and substantial public-private investment [9,10]. The pandemic validated theoretical approaches while exposing critical vulnerabilities in global preparedness [11,12]. Over 40 COVID-19 vaccines were approved within two years, representing a remarkable achievement in translational research [13].

Notably, gene-based vaccines, including mRNA formulations from Pfizer-BioNTech and Moderna, and adenoviral vectors (AdVs) from AstraZeneca and Johnson & Johnson, demonstrated the adaptability and speed of platform technologies [14-17]. These successes were built on decades of foundational research in gene delivery, immunology, and formulation science. The shift from traditional vaccine methods to gene-based immunogen delivery proved transformative. Gene-based vaccines enable recipient cells to produce immunogens, unlike traditional methods, which involve growing and inactivating pathogens or producing recombinant proteins [2]. This approach offers several benefits, including simplified and rapidly scalable manufacturing, straightforward variant adaptation through sequence modification, and the potential for humoral and cellular immunity through endogenous antigen presentation [1-3]. The pandemic has also highlighted the importance of immunological insights, which have broader implications for preventive and therapeutic applications. Balancing beneficial immune activation against harmful inflammation is crucial, and modified nucleotides in mRNA vaccines exemplify this optimization, reducing pattern recognition receptor (PRR) recognition while maintaining translational efficiency [7]. These modifications, initially developed for gene therapy, proved crucial to vaccine success.

The pandemic has also highlighted disparities in global access to vaccines, with far-reaching implications [6,11]. Despite the theoretical benefits of platform manufacturing, cold chain maintenance, technology transfer, and establishment of local manufacturing capacity hinder availability in resource-scarce settings [11]. Vaccination rate disparities between high- and low-income countries emphasize the need for technologies that address both biological efficacy and implementation challenges [6,11]. This recognition is driving innovation in thermostable formulations, simplified delivery devices, and distributed manufacturing models, which will benefit both applications.

The intersection of human immunodeficiency virus 1 (HIV-1) and COVID-19 has introduced complexity in many low- and middle-income countries. Individuals with untreated HIV-1 who are immunocompromised have experienced prolonged SARS-CoV-2 infections, which have led to increased

viral evolution and potentially contributed to the emergence of new variants [18]. This situation highlights the interconnected nature of global health challenges, emphasizing the need for comprehensive approaches that simultaneously address multiple pathogens. New evaluation standards and public acceptance have emerged [12,19]. The administration of billions of mRNA vaccine doses has provided a significant amount of safety data, alleviating concerns about nucleic acid interventions [20]. This real-world evidence, combined with transparent risk-benefit communication, has increased trust in platform technologies [12,19].

Emergency use authorization frameworks emphasize ongoing review and post-market surveillance and offer models for accelerating future development while maintaining safety [8,19,20]. Manufacturing innovations, including large-scale production, have long-term implications [21,22]. These innovations include modular production facilities, specialized reagent supply chains, and optimized quality control, all of which create an infrastructure applicable to diverse gene-based medicines [21-23]. Clinical trial networks, cold-chain systems, and pharmacovigilance programs provide future deployment frameworks [11,24,25].

Evolution and optimization of mRNA platforms

The transformation of mRNA from a biological molecule to a therapeutic platform has led to sustained scientific investment benefits. Following the demonstrations of *in vitro* transcription and functional expression in the 1980s, the field has undergone a series of innovations aimed at addressing challenges in clinical applications [26,27]. The COVID-19 pandemic marked a significant milestone, yet technologies continue to evolve for applications beyond infectious disease prevention [5]. The molecular structure of therapeutic mRNA has improved over the decades through component modifications. Modern synthetic mRNA incorporates sophisticated capping strategies to enhance translation initiation and stability, engineered untranslated regions to fine-tune expression kinetics, codon-optimized open reading frames to maximize efficiency, and controlled poly(A) tail lengths to balance stability with immunogenicity [28–31]. These critical structural modifications and delivery methods are illustrated in **Figure 1**, which visually represents the molecular basis underlying advancements in the mRNA platform.

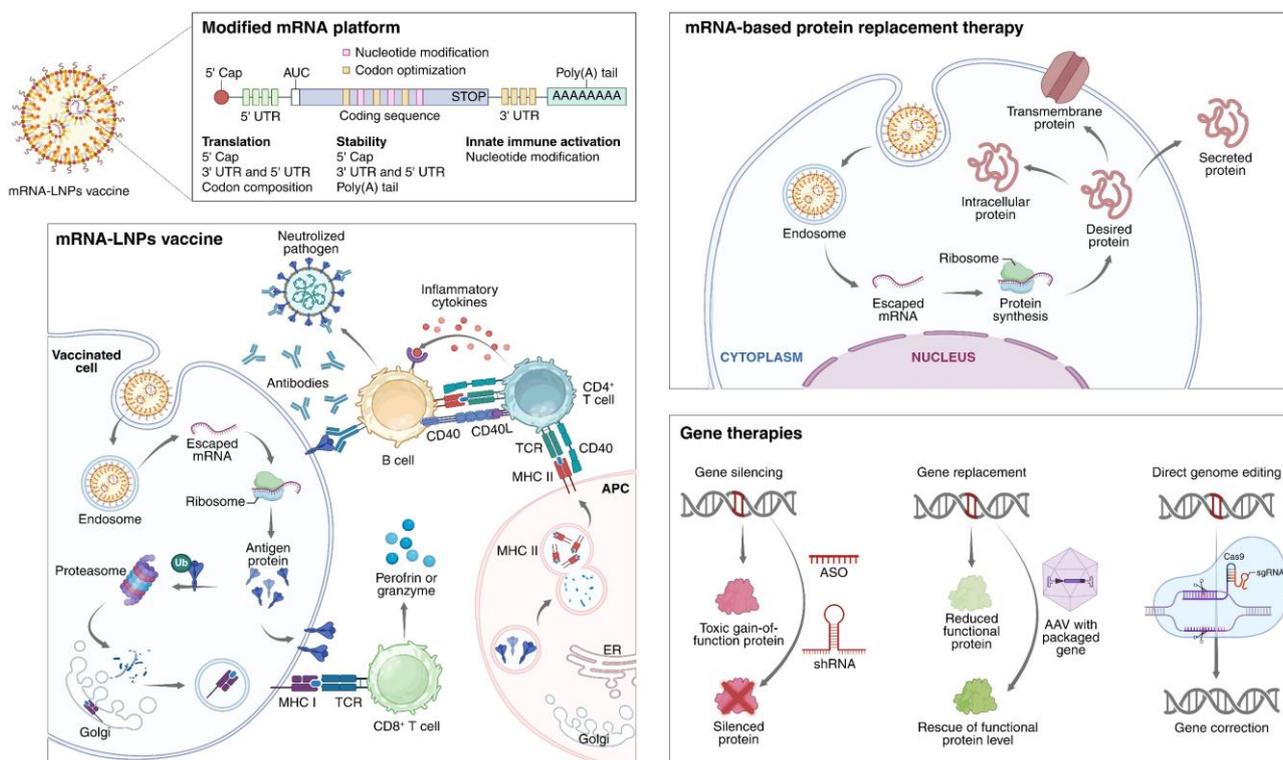


Figure 1 Overview of mRNA and gene-based therapeutic strategies.

The figure provides a detailed illustration of the latest therapeutic methods using mRNA and gene-based technologies, focusing on the structure and modifications of the modified mRNA platform, aiming to enhance translation efficiency and mitigate immune activation. This also explains how mRNA vaccines stimulate the immune system to produce a protective response when combined with lipid particles. Furthermore, the figure describes how mRNA-based treatments enable the production and release of therapeutic proteins inside cells, as well as different gene therapy approaches, including gene silencing, gene replacement, and precise genome editing using CRISPR-Cas9.

This also explains how mRNA vaccines stimulate the immune system. Gene-encoded vaccines elicit protection through a series of innate sensing and adaptive priming steps [29]. In mRNA-LNP formulations, ionizable LNPs are engulfed by antigen-presenting cells (APCs); the acidic endosomal environment then destabilizes the LNP, releasing mRNA into the cytosol, where it is translated into the encoded antigen [2,32,33]. The translated protein is processed and displayed on MHC class I and II

molecules, leading to the stimulation of CD8⁺ cytotoxic T cells and CD4⁺ helper T cells and the maturation of germinal-centre B cells that produce high-affinity antibodies [29]. Nucleoside modifications, such as pseudouridine, dampen excessive PRR signalling while preserving efficient translation, thus balancing adjuvant activity with reactogenicity [34,35]. AdVs naturally stimulate innate immunity because their DNA can activate endosomal DNA sensors such as TLR9, and their tropism for APCs facilitates cross-presentation and strong T-cell priming through CAR/integrin interactions [36,37]. Accordingly, the choice of delivery system and payload chemistry collaboratively shape early innate cues that dictate the magnitude, quality, and durability of the adaptive immune response.

Those mechanistic attributes translated into robust protection observed in randomized phase-3 trials; in symptomatic COVID-19 studies, BNT162b2 achieved roughly 95% vaccine efficacy (VE) in the primary analysis, while mRNA-1273 reached about 94% VE with a comparable 2-dose schedule [14]. For AdV vaccines, interim pooled analyses of ChAdOx1 nCoV-19 from several studies estimated around 70% VE, with the exact figure varying by dosing

schedule [16]. A single-dose Ad26.COV2.S trial reported approximately 67% VE against moderate-to-severe disease beginning 14 days post-vaccination and offered even stronger protection for severe cases [17]. Taken together, these blinded, placebo-controlled trials, anchored to prespecified

primary endpoints, show that both mRNA and adenoviral platforms delivered significant protection in the pre-variant settings of their main assessments. A side-by-side summary of platform characteristics is provided in **Table 1**.

Table 1 Comparison of mRNA-lipid nanoparticle and adenoviral vector vaccine platforms.

Dimension	mRNA-LNP (Pros)	mRNA-LNP (Cons)	Adenoviral vectors (Pros)	Adenoviral vectors (Cons)	Typical applications/notes
Delivery system & payload	Non-viral; transient mRNA payload; no genomic integration risk	Requires LNP for delivery; mRNA is inherently unstable without formulation	Efficient gene delivery with natural APC tropism; strong innate stimulation	Pre-existing/induced anti-vector immunity can reduce efficacy	Both deliver gene-encoded antigens to host cells for <i>in situ</i> expression
Innate sensing/adjuvanticity	Ionizable LNPs and RNA motifs provide tunable innate cues	Over-activation can increase reactogenicity if not optimized	Intrinsic adjuvanticity via DNA sensing; robust T-cell priming	Stronger early reactogenicity in some settings	Choice affects early cytokine milieu and downstream T/B priming
Antigen expression kinetics	Rapid onset; high protein output over a short window (days)	Short duration of expression	Longer expression window (days-weeks)	Expression magnitude can be impacted by anti-vector immunity	mRNA suits rapid priming; AdV suits strong T-cell responses
Adaptive immunity profile	Strong neutralizing antibodies; CD4 ⁺ /CD8 ⁺ responses achievable	CD8 ⁺ magnitude can be formulation-dependent	Potent CD8 ⁺ T-cell priming; good helper responses	Humoral responses may be lower than mRNA for some antigens	Platform choice can be tailored to antibody vs. T-cell emphasis
Anti-vector immunity	No anti-vector immunity; readily boostable	Anti-PEG antibodies can rarely affect reactogenicity/pharmacokinetics	Heterologous vectors or rare serotypes mitigate pre-existing immunity	Homologous boosting is less effective due to anti-vector immunity	Consider baseline seroprevalence and boosting strategy
Booster flexibility	High agility for repeated boosting and variant updates	Reactogenicity can accumulate with frequent boosts in some groups	Single-dose efficacy possible (e.g., Ad26 platforms)	Boosting is limited by anti-vector responses; heterologous boosts are preferred	Heterologous prime-boost can combine strengths
Safety considerations (rare)	No live virus; no replication	Rare myocarditis/pericarditis signals in specific demographics	Replication-incompetent designs; extensive clinical experience	Rare TTS has been reported with some vectors	Risk-benefit varies by age/sex and epidemiology
Manufacturing and scalability	Cell-free IVT; rapid template updates; scalable	LNP formulation and capping chemistry require tight QC	Established bioreactor processes; high yield	Cell-based production; longer lead times for construct changes	mRNA excels for speed; AdV leverages established capacity
Stability/cold chain	Improving stability; lyophilization advances	Often requires a cold/freezer chain (product-specific)	Generally, more tolerant of refrigeration	Still temperature-sensitive; varies by formulation	Match platform to distribution/storage infrastructure

Dimension	mRNA-LNP (Pros)	mRNA-LNP (Cons)	Adenoviral vectors (Pros)	Adenoviral vectors (Cons)	Typical applications/notes
Antigen design agility	Rapid sequence swapping; multivalent mixes feasible	Payload size limits; UTR optimization needed	Multiple inserts are possible with design constraints	Genome packaging limits; recombination checks required	mRNA is ideal for fast variant updates
Representative applications	Respiratory viruses (e.g., SARS-CoV-2, influenza); oncology vaccines	-	Emerging infections (e.g., Ebola, SARS-CoV-2); prime in prime-boost	-	The platform is often chosen by the target pathogen and speed needs

Abbreviations: LNP: Lipid nanoparticle; AdV: Adenoviral vector; APC: Antigen-presenting cell; CAR: Coxsackievirus and adenovirus receptor; UTR: Untranslated region; IVT: *In vitro* transcription; QC: Quality control; TTS: Thrombosis with thrombocytopenia syndrome.

Emerging questions about the long-term genomic integration of vaccine mRNA require a concise review. Mechanistically, non-replicating mRNA vaccines are designed as non-integrating platforms: the RNA stays in the cytosol, lacks reverse-transcriptase activity, and is removed by normal RNA turnover, providing no direct route to chromosomal insertion [38]. Consistent with this, preclinical and clinical data show that mRNA expression is transient and reveals no integration events *in vivo*. An *in-vitro* study in a human hepatoma cell line found reverse-transcribed vaccine-derived sequences only under artificial, high-dose conditions with active LINE-1 elements; these results do not prove chromosomal integration or generalize to *in vivo* situations [39]. In contrast, replication-incompetent AdVs can reach the nucleus but largely exist as episomes, and the risk of insertional mutagenesis for the current vaccine vectors is considered minimal [40]. Overall, the mechanistic and empirical evidence support a non-integrating risk profile for mRNA vaccines and a low insertional risk for AdVs, with continued pharmacovigilance warranted given the scale of use.

Notably, each component is adjusted to meet the specific therapeutic needs of individual patients. Incorporating modified nucleotides represents a pivotal innovation [7,34]. Initial mRNA therapy attempts were hindered by excessive immunogenicity due to strong innate responses triggered by unmodified RNA [34]. The systematic exploration of nucleotide modification, particularly pseudouridine derivatives, has shown that chemical alterations can significantly reduce immune activation while maintaining translational capacity [34].

This discovery has transformed mRNA into programmable therapeutics.

The development of delivery systems has progressed in parallel with mRNA optimization [2,32]. LNPs have emerged as primary platforms after iterative refinement of chemistry, architecture, and formulation. Modern LNPs achieve efficiency through coordinated mechanisms, including cell surface binding, endocytosis, pH-responsive endosomal escape, and cytoplasmic mRNA release [2,33]. Ionizable lipids maintain a neutral physiological pH, minimizing toxicity while protonating in acidic endosomes for membrane disruption [2,32]. The success of COVID-19 vaccines has driven the development of new delivery systems [32,41].

Thermostability remains a challenge for global distribution, and researchers are developing strategies, including lyophilized excipients and alternative lipid compositions, for refrigerator or room temperature storage [42]. Tissue-specific targeting through engineered LNPs incorporating targeting ligands or responsive components enables expansion beyond liver targeting to the central nervous system, lungs, and other tissues [43,44]. Self-amplifying RNA technologies represent a promising evolution through the incorporation of viral replicase machinery, enabling sustained expression at low doses [4,45]. However, complexity poses formulation challenges, driving the need for delivery innovation. The mixed clinical results emphasize the need for comprehensive optimization beyond RNA design [46].

The manufacturing process has undergone significant evolution due to the pandemic, with the establishment of cGMP protocols for large-scale transcription, improved purification methods, and comprehensive analytical techniques transforming mRNA into pharmaceutical products [22]. Platform approaches that produce diverse sequences offer advantages in pandemic preparedness and personalized medicine. Rapid patient-specific synthesis capabilities, validated through vaccine manufacturing, enable the production of individualized cancer vaccines and treatments for rare diseases [22,23]. Alternative delivery methods that go beyond injection are being developed, including inhalable formulations for pulmonary delivery, early-stage oral systems for improved compliance, microneedle patches, and jet injection, which offer thermostability and simplified administration [47-50]. These methods address the challenges of biological and practical implementation in resource-limited settings.

Therapeutic applications of mRNA platforms

The validation of mRNA vaccines has led to significant advancements in therapeutic development, driven by the established safety and efficacy of the technology [5,10,20]. This has resulted in the exploration of previously speculative applications, requiring a re-evaluation of delivery methods, expression patterns, and safety profiles that are more relevant to chronic conditions than to preventing acute infections [5,51].

Protein replacement therapy has emerged as a direct application of fundamental vaccination principles that transform host cells into production facilities [51]. However, this approach poses distinct challenges, particularly in the context of genetic diseases that require sustained, regulated expression without adaptive responses against therapeutic proteins [51,52]. Current programs targeting metabolic disorders navigate these demands through careful optimization [52,53]. Cystic fibrosis exemplifies the potential of this approach and its

complexity. Clinical trials are investigating the use of inhaled mRNA encoding functional cystic fibrosis transmembrane conductance regulator (CFTR) protein to restore chloride channel function, addressing the challenges of large protein delivery and potentially achieving higher local concentrations than systemic administration [54]. However, the lungs pose unique challenges, including mucus barriers, rapid clearance, and the need for repeated administration [55].

The integration of mRNA with gene editing represents an advanced convergence in therapeutic approaches. Rather than replacing proteins, mRNA delivers tools for permanent correction [56,57]. **Figure 2** illustrates the mechanistic overview of these advanced therapeutic strategies, emphasizing the role of LNP-mediated delivery and cellular immune activation. Clinical trials for transthyretin amyloidosis and primary hyperoxaluria demonstrate the co-delivery of CRISPR-Cas mRNA and guide RNAs, combining the manufacturing benefits and non-integrating delivery safety of mRNA with potentially curative effects [56,57]. Temporary expression of editing machinery may reduce off-target effects compared with viral delivery [56]. Additionally, cancer immunotherapy is increasingly adopting mRNA technology, with personalized vaccines encoding patient-specific neoantigens, demonstrating the convergence of high-throughput sequencing, computational prediction, rapid synthesis, and optimized delivery [33]. The combination of multiple neoantigen encoding with inherent adjuvant properties offers advantages over peptide approaches. The initial results show the induction of tumor-specific T-cell responses, which warrant further optimization. Also, cell therapy applications are converging mRNA with advanced therapeutics, offering reduced insertional mutagenesis risk, temporal expression control, and multiple protein capabilities. Chimeric antigen receptor T-cell (CAR-T) manufacturing is increasingly using mRNA electroporation, and *in vivo* reprogramming extension could eliminate complex *ex vivo* logistics [58].

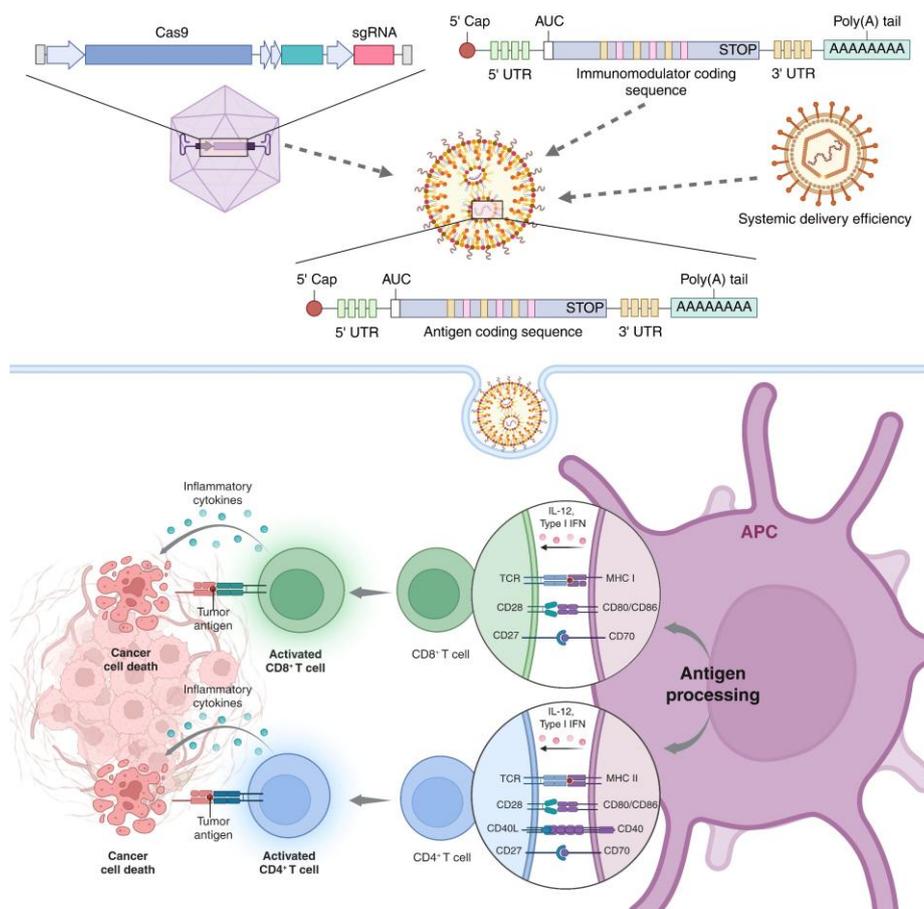


Figure 2 mRNA and CRISPR-based therapeutic strategies for immunotherapy and gene editing. The figure illustrates the use of advanced therapeutic methods that involve lipid nanoparticle systems to deliver modified mRNA encoding therapeutic antigens, immunomodulators, or CRISPR-Cas9 gene-editing constructs throughout the body. Once these agents are taken up by cells, they trigger antigen production and immune activation, resulting in the presentation of antigens by antigen-presenting cells and the stimulation of CD8⁺ and CD4⁺ T cells. This process enables targeted responses, such as the elimination of cancer cells.

Chronic disease applications require a re-evaluation of the safety profile because transient symptoms that are tolerable for infection prevention may be unacceptable for frequent treatment [59]. This drives the development of silent delivery systems that minimize activation while maintaining expression. Targeted systems that concentrate therapeutics in specific tissues address concerns related to long-term administration [43,44]. The development of therapeutic treatments is being influenced by the evolution of regulatory frameworks, enabling the use of streamlined approaches through modular platforms [60]. However, personalized applications are challenging traditional paradigms, and for unlocking the full potential of mRNA technology, frameworks that balance

standardization with flexibility in treatment sequences are essential [60].

Adenoviral vectors: Bridging vaccinology and gene therapy

AdV evolution demonstrates the adaptability of a single technology across various therapeutic areas. Since the 1950s, the discovery and engineering of AdVs have been facilitated by their well-understood biology, large genetic capacity, and ability to deliver genes to both dividing and non-dividing cells, resulting in diverse applications [61,62]. The COVID-19 pandemic highlighted both the potential and limitations of AdVs, while research in gene therapy has informed solutions to the challenges encountered [63-66]. The design of recombinant AdVs balances essential functions with the

capacity to express transgenes [61]. First-generation E1/E3-deleted vectors established frameworks for vaccine and gene therapy applications [61]. However, the distinct requirements of these applications drove the development of different strategies, with vaccines benefiting from immunogenicity and gene therapy requiring minimal activation for persistent expression [63-65]. Consequently, sophisticated designs that modulate responses through selective deletions, immunomodulatory sequences, or shielding strategies were developed [63-66]. The immunological properties of AdVs present context-dependent opportunities and challenges [63,65].

Inherent innate activation through toll-like receptor 9 (TLR9) provides natural adjuvant effects, whereas antigen-presenting cell tropism via CAR receptor and integrin interactions facilitates T-cell priming and presentation [36,67]. These properties enabled the rapid development of COVID-19 vaccines, leveraging existing safety data and incorporating lessons from gene therapy [16,65]. Pre-existing immunity has driven innovation in the development of AdVs, with the creation of rare human serotypes (such as Ad26 and Ad35) and the adoption of non-human adenoviruses (such as chimpanzee and gorilla adenoviruses) exemplifying cross-application solutions [68-70]. The development of ChAdOx1, which emerged from decades of research aimed at circumventing immunity while maintaining favorable properties, accelerated the pandemic response and generated broadly useful vectors [16,70].

Safety concerns during vaccination, particularly thrombotic thrombocytopenia syndrome, emphasize the need for a molecular understanding of AdVs [71-73]. The proposed mechanisms involving vector-platelet factor 4 (PF4) interactions highlight how rare events can emerge during the large-scale deployment of a novel therapeutic approach [74,75]. Findings from these studies inform gene therapy safety assessments and drive the development of improved vector profiles through targeted engineering [76,77].

The evolution of manufacturing processes for AdVs has been driven by dual development, establishing scalable suspension culture production, purification methods that remove contaminants, and comprehensive analytical methods benefiting both vaccine and gene therapy applications [76,78-80].

Pandemic-driven capacity expansion has created gene therapy-applicable infrastructure that addresses translation bottlenecks [81]. Stability and formulation innovations have enabled improved storage and distribution [82].

The expansion of therapeutic applications driven by vaccine development experiences has led to the establishment of safety milestones that prioritize local administration, dose optimization, and careful selection [83]. The development of gutless helper-dependent vectors, which delete viral genes to reduce immunogenicity, has enabled extended expression for chronic diseases [84]. The convergence of vaccine and gene therapy approaches has resulted in the development of novel hybrid strategies [76]. Therapeutic cancer vaccines that deliver tumor antigens combine vaccination principles with gene therapy methods, while vectors expressing immunomodulators alongside antigens are designed to shape responses for therapeutic benefit [85,86]. Replicating oncolytic vectors incorporating delivery and immunotherapy elements [83,86].

Outlook: Convergence and global challenges

The convergence of gene therapy and vaccine technologies is driving significant changes in molecular medicine, extending beyond pandemic responses. This exchange of innovation has created new paradigms where platforms serve as versatile foundations for addressing diverse challenges [1]. Technical, regulatory, and societal factors influence the future development of these technologies [87]. Next-generation platforms will integrate multiple functionalities, including mRNA encoding antigens and immunomodulators, viral vectors with tissue-specific controllable expression, and hybrid systems combining synthetic advantages with delivery efficiency [1,88,89].

Smart systems that respond to physiological cues promise spatiotemporal control and address current limitations [90]. Pandemic preparedness requires comprehensive approaches that go beyond stockpiles and surveillance. The development of plug-and-play platforms demands sustained technology investment, enabling rapid response through molecular tools, manufacturing infrastructure, regulatory frameworks, and distribution networks [87,91,92]. Regional manufacturing hubs in low- and middle-income

countries are essential for ensuring equitable access to manufacturing [93,94]. The effectiveness of these platforms requires acknowledging the variability of pathogens [1].

Although the success of COVID-19 vaccines targeting the stable spike protein may not translate to complex pathogens, such as HIV-1, future success will depend on technological advancement and a deeper understanding of pathogen biology [95,96]. Regulatory environments must accommodate the convergence of these technologies while maintaining standards [97,98]. Although modular platforms facilitate evaluation, combination product complexity challenges existing categories [98,99]. Adaptive frameworks are essential for assessing platform safety independently from applications while overseeing novel combinations. The societal implications of these technologies extend beyond medical benefits to equity, accessibility, and trust [93,100]. As platforms expand to chronic diseases and enhancement, cost and prioritization questions intensify [99]. Sustainable financing, technology transfer, and capacity building are crucial [93]. Transparent communication maintains public trust [100]. Ethics of gene-based intervention require ongoing interdisciplinary dialogue [101].

The current focus on disease treatment may blur with enhanced capabilities as genetic understanding expands. The proactive establishment of an ethical framework guides responsible development [101]. The convergence of these technologies promises a transformation of the therapeutic landscape [102,103]. Accelerated pandemic timelines combined with molecular toolkit expansion present unprecedented opportunities. To realize this potential, sustained research investment, infrastructure development, and capacity building are necessary [92,93]. Maintaining a collaborative spirit is essential for addressing challenges. Learning from successes and failures while fostering innovation and ensuring equitable access can harness the potential of converged technologies to improve global health. The journey from early trials to sophisticated platforms demonstrates the power of persistent inquiry and collaboration, and it promises greater future possibilities as technologies evolve.

Conclusions

Gene-encoded platforms have evolved from specialized experimental tools to versatile molecular tools. This toolkit has rapid reprogramming capabilities for infectious diseases, genetic disorders, cancer immunotherapy, and genome editing *in vivo*. However, this convergence also highlights the shared challenges that need to be addressed, such as managing immunogenicity, ensuring thermostability, obtaining regulatory oversight, and providing equitable access. Future progress will depend on continued technical innovation, including the development of modular lipid nanoparticles, engineered viral vectors, and multifunctional payloads. Coordinated investment, distributed manufacturing, and ethical governance will be crucial in translating laboratory breakthroughs into globally accessible, patient-centered medicines that address both current and emerging health challenges.

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Declaration of Generative AI in Scientific Writing

The authors declare that no generative artificial intelligence (AI) tools were used during the preparation of this manuscript. All authors have reviewed and approved the final version and assume full responsibility for the content and conclusions of this work.

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