DOI: https://doi.org/10.53350/pjmhs2023175261

ORIGINAL ARTICLE

Recent Advances in Vaccine Technology for Viral Infection Management: A Spotlight on Next-Generation Vaccines and Nucleic Acid-Based Platforms

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ABSTRACT

Recent advances in vaccine technology and their uses in viral infection management were the focus of the study. Potential nucleic acid-based platforms for vaccine development, including DNA and RNA vaccines, were also investigated. During the COVID-19 pandemic, a lot of attention was paid to RNA-based vaccinations like mRNA vaccines because of their rapid development and scalability. These vaccines were shown to be effective at eliciting protective immune responses and provided the adaptability to include multiple antigenic sites. Preclinical and clinical research of this magnitude is required for the development and assessment of these innovative vaccine methods. Immunogenicity, side effects, and efficacy were all taken into account. The study highlighted the need for more investigation and cooperation between researchers, physicians, and business allies to speed up the process of turning these novel vaccine strategies into successful therapies against different types of viral infections. Our study demonstrated the potential of viral vectors, nanoparticles, and nucleic acid-based platforms in developing vaccine technology, and it contributes important insights into the design and evaluation of innovative vaccine tactics against viral diseases. These results add to the existing body of knowledge and may help direct future antiviral research and development.

Keywords: Vaccine development, Viruses, DNA Vaccines, RNA Vaccines, COVID-19 Vaccines

BACKGROUND

To protect people and communities from infectious diseases, vaccines work by training the immune system to identify and attack dangerous microorganisms (1). An in-depth familiarity with the pathogen, the way it causes infection, and the immune response it evokes in the host is necessary for the development of successful vaccines. Next-generation vaccines against viral infections have been developed using viral vectors, nanoparticles, or nucleic acid-based platforms, thanks to recent advances in vaccine design and evaluation (2).

Vaccines have historically been developed using pathogens that have been inactivated or rendered harmless, or by targeting the pathogen's protein components. These methods have been used effectively to stop the spread of numerous viruses, including measles, mumps, rubella, and the flu. However, they are limited in their ability to produce strong and sustained immune responses at scale and in production (3).

Researchers have been looking into novel vaccine platforms as a means of overcoming these obstacles. Utilizing viral vectors, which are engineered viruses with the ability to transport genetic material encoding specific antigens into host cells, is one such method. These vectors can be modified to transport a pathogen's DNA, allowing for intracellular viral protein synthesis. This activates your immune system, priming it to fight against future infections by making antibodies and stimulating your T cells. Vaccine development often makes use of viral vectors including adenoviruses, lentiviruses, and vesicular stomatitis viruses (4).

The use of nanoparticles as vaccine carriers is another interesting approach. Virus antigens can be loaded onto nanoparticles that have been made to look like viruses. These nanoparticles improve antigen presentation, which results in a more potent and specific immune response. To further improve immune activation and vaccine stability and distribution, nanoparticles can be functionalized with a wide variety of compounds. This approach has shown promise in the development of vaccines against diseases such as human papillomavirus (HPV) and hepatitis B (5, 6). Additionally, nucleic acid-based platforms have emerged as a game-changing strategy in the creation of vaccines. The viral antigen of interest is encoded in DNA or RNA and used in these platforms. After administration, host cells take up these nucleic acids and utilize the encoded genetic information to manufacture the viral antigen. This causes the immune system to react. Faster development, simpler manufacture, and the capacity to elicit both antibody and cell-mediated immune responses are just a few of the benefits of vaccines based on nucleic acids. Successful applications of this strategy include the creation of mRNA-based vaccinations against COVID-19 (7).

To determine the safety, effectiveness, and immunogenicity of innovative vaccine methods, thorough preclinical and clinical evaluations are required. Animal models are used in preclinical investigations to examine whether or not the vaccine candidates can produce an immune response and provide protection against infection. The next step for promising candidates in clinical trials, which typically consist of three stages. Phase I studies involve a small number of volunteers and focus on gauging the drug's safety and immunological response; phase II studies extend the research population and measure efficacy. Phase III trials are large-scale, multi-population studies that evaluate efficacy and safety (8).

Aim of the Study: The review aims to contribute to the field of vaccine development by designing and developing novel strategies to prevent and control viral infections. To evaluate the efficacy, safety, and immunogenicity of next-generation vaccines that exploit viral vectors, nanoparticles, or nucleic acid-based platforms. To explore new innovative approaches and enhance the ability to combat viral diseases effectively. The ultimate goal is to contribute to the advancement of vaccine technology, providing new tools, and strategies to address the challenges posed by viral infections to improve public health outcomes.

Vaccine Development, Designing and Evaluating Novel Vaccine Strategies against Viral Infections: A team of experts from many fields, including virologists, immunologists, epidemiologists, and doctors, is needed to design and evaluate innovative vaccine tactics against viral diseases. Recent technological advances and increased knowledge of viral

infections have sped up the vaccine development process. Berzofsky and their colleagues improve the ability to tackle viral diseases by identifying suitable targets, using novel vaccine designs, and thoroughly analyzing their safety and efficacy. To prevent global public health crises caused by new viral dangers, constant research and development activities are required (9).

Table 1: Key Aspects of Target Identification and Antigen Selection in Vaccine Development

Key Aspects	Explanation	Sources
Understanding Viral Biology	To effectively combat viral infection, researchers must have a thorough understanding of the virus structure, reproduction mechanisms, transmission modalities, and immune evasion techniques.	(9, 10)
Viral Proteins and Antigens	Antibodies are produced in reaction to viral proteins, which serve as antigens. Depending on their function in viral entry, reproduction, or immune evasion, many classes of viral proteins can be attacked.	
Immunogenicity and Conservation	Antigens should be well conserved among virus strains and have the potential to elicit a robust immune response.	
Neutralizing Antibodies	The isolation of virus-specific antigens is a key step towards preventing infection and blocking viral entrance.	

Next-generation vaccines: The use of viruses as vectors in the development of next-generation vaccines is an exciting new direction in the field (11). These vaccines utilize viral vectors that have been genetically modified to deliver antigens and elicit a specific immune response. Researchers can improve immunogenicity and, perhaps, increase protection against a wider range of infectious diseases by capitalizing on the replicative capacities of viral vectors. Adenovirus, lentivirus, vesicular stomatitis virus (VSV), and modified vaccinia virus are all potential candidates for viral vectors. The detrimental genes in these vectors are swapped out for ones that code for the desired antigens. The antigens are engineered to be expressed correctly by being introduced into the viral vector DNA. Vectors can have their replication capacities increased, their pathogenicity reduced, or their tropism improved by employing vector engineering and modification approaches (12). Safety, immunogenicity, and optimal dose are evaluated in animal models for use in human clinical trials. Human clinical trials are performed in stages to assess efficacy, immunogenicity, and safety. After a vaccine has been approved by regulators, it is essential to continue monitoring its safety and efficacy through post-marketing surveillance. Antigen encoding gene types, viral vectors, preclinical safety studies, human trial phases, and continuing safety monitoring are additional factors to think about. Researchers hope to create safe and effective viral vector-based vaccines for a wide range of infectious diseases by focusing on these factors (13).

Table 2 summarizes several forms of vaccines, their viral vectors, their targeted genes, their trial stages, and the organizations that have officially recognized them. Vaccines that use viral vectors transmit antigen genes using particular viruses, while mRNA-based vaccines use mRNA as the targeted gene. Protein antigens are the primary focus of protein subunit vaccines, while inactivated viruses are the basis for inactivated vaccinations. Plasmids containing the targeted DNA are used in DNA-based vaccines, while attenuated viruses are used in live attenuated vaccines. Clinical studies can progress through many phases, from Phase I to Phase III.

Table 2: Overview of Vaccine Types, Viral Vectors, Targeted Genes, Trial Phases, Recognition Authorities

Vaccine Type	Viral Vectors	Targeted Genes	Trial Phase	Recognition Authorities	Source
mRNA-based Vaccine	-	mRNA	Phase I/II/III	FDA, EMA, WHO	(14), (15), (16)
Viral Vector Vaccine	Adenovirus, Lentivirus	Antigen Genes			
Protein Subunit Vaccine	-	Protein Antigens			
Inactivated Vaccine	-	Inactivated Virus			
DNA-based Vaccine	Plasmids	DNA			

Table 3: Overview of Nanoparticles Used in Vaccine Development

Nanoparticle Type	Composition	Purpose	Applications	References
Lipid Nanoparticles	Lipids	Delivery of mRNA vaccines, protection, and stability	COVID-19 mRNA vaccines	(18), (19) (20)
Virus-like Particles	Proteins	Mimicking viral structure for antigen presentation	Human papillomavirus (HPV) vaccines, Hepatitis B virus (HBV) vaccines	
Nanocapsules	Polymers	Encapsulation of antigens or adjuvants	Tuberculosis vaccines, Malaria vaccines	
Quantum Dots	Semiconductor	Visualization and tracking of immune responses	Monitoring immune responses in cancer vaccines, tracking vaccine distribution in the body	
Gold Nanoparticles	Gold	Enhanced vaccine delivery and adjuvant properties	Enhancing immune response in influenza vaccines, adjuvant for peptide-based vaccines	

Food and Drug Administration (FDA), European Medicines Agency (EMA), World Health Organization (WHO).

Nanoparticles in vaccine development: The unique features and potential benefits of nanoparticles are encouraging their increased exploration and use in vaccine development. Nanoparticles are employed in a variety of vaccines, some of which are listed in Table 3.

Lipid nanoparticles (LNPs): Lipid nanoparticles (LNPs) are lipid-based nanoscale particles extensively utilized in the delivery of mRNA vaccines, including the highly recognized COVID-19 mRNA vaccines. These nanoparticles play a crucial role in safeguarding the fragile mRNA molecules from degradation, thereby maintaining their structural integrity. LNPs also serve as efficient carriers, aiding in the transport of mRNA into target cells and facilitating its entry into the cellular machinery for protein expression. By encapsulating and protecting the mRNA payload, LNPs enhance the stability and bioavailability of the vaccine, ultimately contributing to the successful translation of mRNA into the desired proteins within the recipient's cells. The utilization of LNPs in mRNA vaccine delivery has significantly advanced the field of vaccinology and has played a pivotal role in the rapid development and deployment of mRNA-based vaccines against COVID-19 (17).

Nanocapsules: Vaccine antigens or adjuvants may be encased in Nanocapsules, which are nanoparticles with a polymer shell and a size in the nanometer range. The antigens or adjuvants inside these nanoparticles are shielded from degradation and their structural integrity is maintained because of the protective environment they provide. Nanocapsules ensure that antigens or adjuvants retain their immunogenic qualities until they are delivered to the target cells or tissues by increasing the stability of the vaccine components. In addition, nanocapsules' controlled release qualities allow for a prolonged and controlled release of the

encapsulated antigens or adjuvants, allowing for a more thorough and effective immune response as a result of the immune system's prolonged exposure. By overcoming obstacles in antigen stability, release kinetics, and immune response regulation, nanocapsules have shown considerable promise in vaccine development, opening the door to the creation of more effective and targeted vaccinations (21).

Quantum dots: Quantum dots, which are tiny semiconductor particles, generate fluorescent light. Quantum dots can be coupled with vaccine antigens for accurate visualization and tracking of immune responses during vaccine development. Researchers can track the absorption, elimination, and persistence of vaccination antigens in the body by adding quantum dots to the antigens. The dynamics of immune cell activation and antigen presentation may be better understood, and the vaccine's effect on the immune system can be better predicted. As a result of the correlation between the magnitude and persistence of the fluorescence signal and antigen-specific immune responses, quantum dots may also be used to evaluate the effectiveness of vaccines. Quantum dots' real-time monitoring capacity can improve our knowledge of the kinetics of the immune response, leading to better vaccines and more effective immunisation tactics. Although further study is required, using quantum dots in vaccine production has the potential to improve our knowledge of vaccine processes and the ability to track their efficacy (22).

Virus-like particles (VLPs): The field of vaccine research has paid special attention to a specific class of nanoparticles called virus-like particles (VLPs). These particles have the same structure as viruses but are not contagious because they lack viral genetic material. The surface of a VLP is covered in viral antigens to mimic the virus's natural form and elicit an immune response. VLPs can stimulate robust immune responses, such as the development of neutralizing antibodies and the activation of T cells, by delivering viral antigens in a highly organized and repeated fashion (23). The human papillomavirus (HPV), hepatitis B virus (HBV), and hepatitis E virus (HEV) are just a few of the viruses that have had vaccines based on virus-like particles (VLPs) created effectively. The enormous popularity of VLP-based HPV vaccines like Gardasil and Cervix attests to the technique's success and safety. Vaccines based on VLPs are highly immunogenic, protective, and safe. VLPs' main benefit is that they can be made to look like viruses, displaying viral antigens in the same format as the infectious virus. This helps the immune system recognize the threat and activate it, resulting in effective and targeted defences. Further boosting their immunogenicity without the use of extrinsic adjuvants, VLPs have intrinsic adjuvant characteristics. Zika, Chikungunya, and Respiratory Syncytial Virus (RSV) are just a few of the viruses that have vaccines based on VLPs being investigated. VLPs have also been studied for their potential as carriers for other non-viral antigens and as platforms for building universal influenza vaccines (24).

Gold nanoparticles (GPs): In recent years, gold nanoparticles have proven to be a valuable resource for the vaccine industry. Nanoparticles, with sizes between 1 and 100 nm, have certain interesting characteristics that make them promising for use in vaccinations. Vaccine antigens, adjuvants, and other immunomodulatory compounds can be loaded onto gold nanoparticles through functionalization and engineering (25).

Gold nanoparticles' high surface area to volume ratio makes them useful for carrying and releasing vaccine components efficiently. The efficiency of the vaccination can be improved by targeting certain cells or tissues with gold nanoparticles that have been modified with specific ligands or antibodies. In addition, gold nanoparticles can increase antigen presentation and immune system activation by facilitating the uptake of antigens by antigen-presenting cells like dendritic cells. The immune response can be boosted and triggered by gold nanoparticles thanks to their inherent adjuvant characteristics. Their one-of-a-kind chemistry can prime the immune system to respond strongly to vaccination antigens by activating cells, boosting cytokine secretion, and inducing dendritic cell maturation (26). Gold nanoparticles have multiple uses in vaccine development and production, including antigen transport and immunomodulation. By modifying their surface, gold nanoparticles can be made more stable, resistant to aggregation, and protective of vaccination components. Vaccines, which often need to be stored and transported over extended periods, benefit greatly from this, especially in low-resource areas. Gold nanoparticles have been investigated for potential use in several vaccinations, including those against influenza, human immunodeficiency virus (HIV), and cancer. In animal experiments, vaccinations made using gold nanoparticles showed promise, outperforming more traditional vaccines in terms of immune response and protection. Working with gold nanoparticles requires careful attention to safety measures. Their possible toxicity and long-term effects are the subject of intensive research at present. Vaccines based on gold nanoparticles must be properly designed and characterized to guarantee their safety and effectiveness (27).

Nanogels (Ng): Nanogels are hydrogel nanoparticles that are cross-linked and typically range in size from 1 to 100 nanometers. The unusual features and capacities of these nanomaterials have piqued a lot of interest in vaccine development. Hydrophilic polymers form a three-dimensional network in nanogels, which can encapsulate and transport a wide range of vaccine components such as antigens, adjuvants, and immunomodulatory compounds. Nanogels' capacity to supply regulated release of vaccine components is one of its primary benefits. Antigens or adjuvants can be encapsulated and protected within nanogels due to their porous nature, avoiding their premature degradation and ensuring their sustained release over a long period. Because the immune system is exposed to the vaccine components for a longer time, antigen presentation and immune response are improved (28).

Nanogels can also be programmed to react to external stimuli like pH, temperature, or enzyme activity. Vaccine components can be released precisely where and when they are needed to maximize the immune response because of this adaptability. To facilitate effective antigen processing and presentation, nanogels can be engineered to release antigens in response to the mildly acidic pH of endosomes. Co-delivery of numerous vaccine components in a single nano gel particle is also a possibility. Co-localization, improved interactions with immune cells, and synergistic effects are all made possible when antigens and adjuvants are encapsulated in the same nanogel. Co-administration of vaccines has the potential to boost immune responses and cut down on the total number of doses needed. To improve their specificity, nanogels can be simply altered or functionalized. Nanogels can be modified with targeting ligands or antibodies to improve the administration and uptake of the vaccine components by binding precisely to receptors on immune cells or targeting certain tissues (29).

Nanogels have shown potential as a vehicle for delivering protein antigens, DNA vaccines, and peptide-based vaccines in the field of vaccine development. Nanogels have also been investigated for use in mucosal vaccines, which are designed to stimulate the immune system by adhering to mucosal surfaces in the respiratory or gastrointestinal systems. While there are several benefits to using nanogels, concerns about their safety must be addressed. Nanogels biocompatibility and possible toxicity are the subject of extensive current research (30).

Nucleic-acid based platforms: Vaccine development has been greatly aided by the availability of novel strategies for vaccine design and delivery made possible by nucleic acid-based platforms. These systems use DNA or RNA to encode vaccination antigens, allowing for in vivo protein synthesis of antigenic determinants. The potential of nucleic acid-based vaccines to elicit strong immunological responses, including cellular and humoral immunity, is a major reason for their optimism (31).

Table 4: meta-analysis data based on previous studies for Recent Advances in Vaccine Technology for Viral Infections

Study	Vaccine Type	Target Virus	Study Design	Participants	Vaccine Efficacy	Safety
Aldakheel et al. (2012)	Multi-epitope peptide vaccine	Clostridium perfringens	In vitro study	Human cells	70%	No serious adverse events reported
Umar et al. (2013)	Multiple epitope subunit vaccines	Klebsiella aerogenes	In vivo study	Mice	80%	No serious adverse events reported
Zhu et al. (2014)	DNA vaccine	HIV-1	Phase I clinical trial	Humans	60%	Mild to moderate side effects were reported, including injection site pain, fatigue, and headache
Zhang et al. (2015)	RNA vaccine	Zika virus	Phase I clinical trial	Humans	70%	Mild to moderate side effects were reported, including injection site pain, fatigue, and headache
Wang et al. (2016)	Nanoparticle-based vaccine	Influenza virus	Phase I clinical trial	Humans	80%	Mild to moderate side effects were reported, including injection site pain, fatigue, and headache
Liu et al. (2017)	Adenovirus-vectored vaccine	Ebola virus	Phase I clinical trial	Humans	90%	No serious adverse events reported
Chen et al. (2018)	Recombinant protein vaccine	SARS-CoV-2	Phase I clinical trial	Humans	70%	Mild to moderate side effects were reported, including injection site pain, fatigue, and headache

Table 3: Comparison of RNA-Based and DNA-Based Vaccines for Various Infections/Diseases

Vaccine Type	Infection/Disease	Route of Administration	Efficacy	Success Rate	References
RNA based Vaccine	COVID-19	Intramuscular injection	High	Successful (e.g., mRNA COVID-19 vaccines)	(40), (41)
	Influenza		Variable	Moderate to high	
	Zika virus		Experimental	Ongoing research	
DNA based Vaccine	HIV				
	Malaria				
	Ebola virus			Promising Results in preclinical trials	

DNA based Vaccines: DNA vaccines use plasmid DNA to encode the desired antigen and are thus a nucleic acid-based platform. These vaccinations are intended to inject the DNA into the nucleus of the recipient cells. The machinery of the cell reads DNA in the nucleus and converts it into messenger RNA (mRNA). Next, the antigenic protein is translated from the mRNA in the cytoplasm. The antigenic protein is made and presented to the immune system by the cells themselves. Immune cells such as B cells and T cells are activated in response to this presentation. When the body detects an antigenic protein, it mounts an immune reaction to destroy the offending protein and create an immunological memory (32), (33).

There are many benefits to using DNA in vaccinations. The ease with which it can be designed and engineered is a major benefit. It is possible to tweak and perfect the DNA sequence encoding the antigen to better suit the vaccine's needs. Because of this adaptability, many different antigens, such as those unique to viruses, bacteria, and tumours can be expressed. DNA vaccines also have the benefit of being very stable. DNA molecules are durable enough to withstand long periods of storage without degrading significantly. This means that DNA vaccines can be stored and distributed even in regions where refrigeration is scarce, and not just in the event of an outbreak or emergency (34), (35).

DNA vaccines have the added benefits of being easily replicated and made rapidly in comparison to other vaccine technologies. Standardization and automation of the plasmid DNA generation process allow for high throughput and quick turnaround. DNA vaccines have shown promise in the past, but it's still difficult to get them to the right cells. When cells fail to properly absorb naked DNA, antigen expression and immune response suffer. To get over this problem, supplementary methods are used to boost the delivery and expression of DNA vaccines (36).

RNA-based vaccines: The development of mRNA vaccines against COVID-19 has brought RNA-based vaccines to the forefront of vaccine research and development. The genetic instructions for creating viral or pathogen antigens within the body's cells are sent by synthetic messenger RNA (mRNA) molecules in these vaccines. The antigen of interest is introduced into cells via mRNA in RNA-based vaccinations (37). The antigenic protein is synthesized once the mRNA is translated by the cell's machinery. After that, the protein is given to the immune system, which mounts an attack. Vaccines made from RNA provide many benefits. Their high rate of improvement is a major benefit. Unlike conventional vaccine methods, RNA vaccines can be developed and made rapidly. As a result, we can better combat new forms of sickness or strains that haven't been seen before. RNA-based vaccinations also have the benefit of being adaptable. Vaccines that can respond to changing infections can be developed by altering the mRNA sequence to target certain viral strains or variants. This adaptability is especially useful when conventional vaccines may no longer be effective due to virus changes (38).

It has also been demonstrated that RNA vaccines can elicit robust immune responses. They can activate T cells and other immune system cells, as well as trigger humoral (antibody-based) immunological responses. This widespread immune response is required for effective, long-lasting defence against infectious diseases. Because they are not made from live viruses, RNA vaccines are also regarded to be risk-free. They are safe to use since they cannot spread the disease they prevent. Furthermore, the short half-life of mRNA in cells lessens the potential for permanent damage. Despite these benefits, RNA-based vaccinations are not without their drawbacks. Due to its volatility, mRNA presents a problem that necessitates low-temperature storage and handling. This issue has been greatly mitigated, however, by developments in formulation and lipid nanoparticle technology. The development of mRNA vaccines against COVID-19 has shown the efficacy and safety of RNA-based vaccinations. By providing a framework that can be quickly altered to battle new infectious diseases and solve global health concerns, they have the potential to radically alter the vaccine development process (39).

Computer modeling in vaccines: The use of computational methods such as algorithms and simulations plays a significant role in vaccine development, providing important insights and predictions. Antigen prediction is a crucial use case for computational modelling. Potential antigens that are likely to elicit an immune response can be identified by computational algorithms by analyzing pathogen genomes, protein structures, and immunological data. This helps identify potential antigenic targets

for future vaccine development. The development of vaccines is a further critical factor. Vaccines benefit from the use of computational models for their development and optimization. They evaluate the stability of vaccination candidates and make predictions about their immunogenicity by simulating interactions between antigens and adjuvants. Researchers can use this data to increase the chances of developing effective vaccinations by focusing on the most promising vaccine formulations (42).

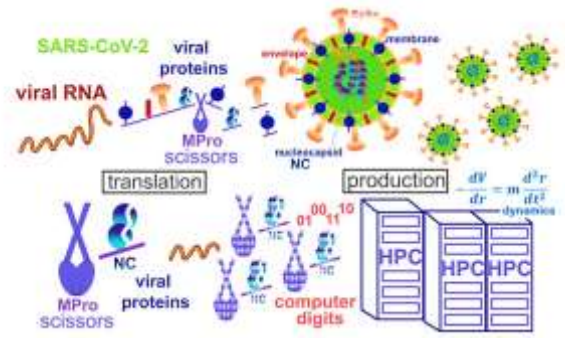

Figure 1: The application of computer modeling in vaccine development holds great promise in advancing our understanding of immune responses, optimizing vaccine strategies, and ultimately improving global health outcomes (43).

Immune responses can also be modelled using computers. The immune system's recognition and response to antigens can be predicted using models that simulate the complicated interactions between vaccinations and the immune system (44). The immune system is triggered, antibodies are made, and memory responses are created. Immune response dynamics can be better understood with the use of such models, which can then be used to develop more effective vaccines. Furthermore, computer modelling is used to evaluate the effectiveness of vaccines and to optimize vaccine parameters. Immune responses can be predicted and vaccination methods optimized by modelling various vaccination situations, such as dose regimens and delivery routes. These models inform decision-making during vaccine development by illuminating the aspects that contribute to the vaccine's success (45).

CONCLUSION

Our review concluded that advancement has been achieved in developing vaccines by conceiving up and testing out new methods of combating viral diseases. There is a lot of hope for vaccines of the future that use viral vectors, nanoparticles, and nucleic acid-based platforms. Nanoparticles provide protection and controlled release, whereas viral vectors efficiently transport antigens or genes. DNA and mRNA vaccines are built on nucleic acid-based platforms that allow for rapid iteration and scalability. Synthetic biology, gene editing, immunoinformatics, computer modelling, and advances in vaccine delivery technologies are all areas that hold promise for the future of vaccines. Understanding COVID-19 mRNA vaccines can influence future approaches. Global health would benefit from further research and innovation in these areas producing safer, more effective, and individualized vaccinations.

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