Current Molecular Approaches for Prevention of Infectious Diseases: Nanovaccines, RNA Therapeutics, and Immunomodulation

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Abstract

Recent advances in molecular biology, nanotechnology, and immunology have been accountable for the advent of next-generation preventive and therapeutic methodologies. Prevention of infectious diseases is undergoing a revolution with updated and current molecular approaches, enabling faster, safer, and more effective alternatives to conventional vaccines and antivirals. This review work aimed to analyse the latest research on RNA therapeutics, nanovaccines, and immunomodulation, and highlights translational potential, implementation issues, and directions for the future in the context of a multidisciplinary, One Health-perspective approach to driving infectious disease prevention on a global scale.

RNA therapeutics, including mRNA and self-amplifying RNA platforms, enable intracellular antigen expression, which leads to effective cellular and humoral immune responses with high ease to evolve against new pathogens. RNA therapies, nanovaccines, and immunomodulators permit antigenic control, targeted delivery of pathogens, and strong immune system activation. Nanovaccine platforms apply liposomes, polymeric nanoparticles, and virus-like particles to improve antigen stability, targeted delivery, and dose efficiency with oral and intranasal formulations for mass immunization and field deployment. Adjuvant immunomodulatory strategies, such as cytokine mimetics and TLR agonists, improve vaccine performance and induce protection against a broad range of pathogens. Integration with computational biology, omics, and systems immunology enables rational design, predictive modelling, and expediting preclinical development. The most recent developments in nanotechnology and molecular biology have transformed infectious disease prevention at its foundations. Nanovaccines, RNA therapeutics, and immunomodulation approaches offer targeted, scalable, and highly effective tools that improve immunogenicity, reduce doses of antigen, and allow rapid adaptation against emerging pathogens. The integration of AI with molecular approaches also offers paths for precision and personalized vaccinology. As a result, in line with the purpose of our review work, vaccines and treatments have been comprehensively evaluated in this context and scope, taking into account current approaches in the age of artificial intelligence.

Keywords: RNA therapeutics, Nanovaccines, Immunomodulation, Infectious diseases, Technology

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1. Context

1.1. Global Burden of Infectious Diseases

Infectious diseases continue demanding health, economic, and societal challenges on a global scale. Epidemics of viral, bacterial, and parasitic diseases affect humans, animals, and the environment as a demonstration of interconnectedness of health in the One Health concept (1). New and re-emerging diseases, including zoonotic viruses, antimicrobial-resistant pathogens, and opportunistic infections, pose continuous challenges to disease management. Climatic change, urbanization, global trade, and intrusions into natural habitats enhance the danger of epidemics and pandemics (2). The conventional preventive strategies, such as inactivated vaccines and small-molecule antivirals, are generally incapable of responding effectively to evolving pathogens, underlining the importance of new molecular platforms (3).

1.2. Limitations of Traditional Vaccines and Medicines

Conventional vaccines and drugs, though pillars in the treatment of infectious diseases, have inherent limitations. Inactivated or weakened live-vaccines may require cold-chain storage, booster injections, or safety hazards in immunocompromised hosts. Antiviral drugs are usually plagued by rapid development of resistance, restricted pathogen specificity, and suboptimal delivery to target tissue (4). These restrictions are accountable for gaps in protective cover, most significantly within resource-scarce or high-risk settings. Quantitative data in Table 1 describes significant pathogens, burden of disease, and the accompanying therapeutic gaps with standard therapy (5).

1.3. Emergence of Molecular-Based Approaches

Recent advances in molecular biology, nanotechnology, and immunology have been accountable for the advent of next-generation preventive and therapeutic methodologies. RNA therapies, nanovaccines, and immunomodulators permit antigenic control, targeted delivery of pathogens, and strong immune system activation (6). The platforms enable rapid response to new threats, augment safety profiles, and facilitate delivery across diverse settings. Integration with cross-disciplinary methodology to bioinformatics, omics technologies, and computational modeling accelerates candidate design, optimization, and evaluation (7).

Table 1: Chief Infectious Agents and Gap in Conventional Therapeutics (8, 9)

Pathogen Type	Example Pathogens	Affected Population/Species	Current Preventive/Therapeutic Options	Key Limitations	Disease Burden/Incidence	Notes/Research Gaps
Viral	Influenza A/B, SARS-CoV-2, RSV	Humans (all age groups)	Inactivated/live vaccines, monoclonal antibodies, antivirals	Cold-chain dependency, strain variability, rapid mutation, resistance	Seasonal epidemics, ~3–5 million severe cases/year (influenza); COVID-19 pandemic caused millions of deaths	Need for broad-spectrum vaccines, rapid-response platforms
Viral	Foot-and-Mouth Disease Virus	Livestock (cattle, pigs, sheep)	Inactivated/live vaccines	Short-lived immunity, strain mismatch,	High economic losses in livestock (~$6.5	Improved thermostable vaccines,

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	(FMDV), African Swine Fever Virus (ASFV)			cold-chain logistics	billion annually for FMD)	multivalent formulations
Bacterial	Salmonella enterica, Mycobacterium tuberculosis, Staphylococcus aureus	Humans, livestock	Antibiotics, subunit vaccines	Antimicrobial resistance, limited immunogenicity, poor cross-strain coverage	Foodborne illness and zoonotic transmission; MDR-TB > 400,000 cases/year	Nanovaccine or RNA-based approaches for better protection
Parasitic	Plasmodium spp., Toxoplasma gondii, Leishmania spp.	Humans, companion animals, livestock	Chemotherapy, limited vaccines	Toxicity, poor cross-species protection, short-term efficacy	Malaria ~240 million cases/year; Toxoplasmosis widespread in cats	Need for novel RNA or nanovaccine platforms, immunomodulation strategies
Fungal	Candida spp., Aspergillus spp.	Humans, livestock	Antifungals	Limited prophylactic options, resistance, toxicity	Opportunistic infections rising in immunocompromised populations	Exploration of immunotherapeutics and nanodelivery systems

2. Data Acquisition

2.1. Literature Search Strategy and Selection Criteria

Systematic review of literature was conducted to identify the recent advances in molecular technologies for prevention of infectious diseases with the help of nanovaccines, RNA therapeutics, and immunomodulation. Electronic databases like PubMed, Scopus, Web of Science, and Google Scholar were browsed for articles between the years 2000–2025. Keywords and Boolean operators were carefully selected to ensure maximum specificity and sensitivity. Search terms were: "nanovaccine," "mRNA therapeutics," "RNA-based vaccines," "immunomodulators," "host-pathogen interactions," and "infectious disease prevention."
Articles were sifted through three consecutive steps: title, abstract, and full-text evaluation. Eligible inclusion criteria were: peer-reviewed original research papers, systematic reviews, meta-analyses, and technical reports published by international health agencies such as WHO, CDC, and FAO. Exclusion criteria were: studies involving exclusively in vitro models of no translational significance, exclusively theoretical studies with no experimental evidence, and non-English language papers with no verified translations. The selected studies were stratified by disease type (parasitic, viral, bacterial, fungal), molecular strategy (protein subunit, mRNA, siRNA, nanovaccine), and target species/population (companion animals, livestock, wildlife, human). Furthermore, each study was coded with respect to study design, sample size, immunogenic results, delivery systems, and regulatory issues. The systematic procedure allowed inclusion of high-quality, relevant, and translationally relevant studies (10).

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2.2. Sources of Technological and Market Data

To complement peer-reviewed publications, additional data were taken from:

Patent databases: WIPO Patentscope, USPTO, EPO Espacenet
Industry reports: Research & Markets, GlobalData, Animal Health Institute
Regulatory and technical reports: WHO, FDA, EMA
Trade magazines and firm white papers: including leading biotech and pharma firms working on RNA therapeutics and nanovaccines (10).

This triangulated approach provided an expansive view of scientific advancement, commercialization, and global innovation trends. Data were structured by geography to chart innovation hotspots, translational gaps, and future investment possibilities (11).

2.3. Data Extraction and Classification

A standardized data extraction protocol was adopted: author, year, geographic location, pathogen, molecular approach, delivery vehicle, results on immunogenicity, and clinical or preclinical status were coded. Studies were categorized by molecular platform, pathogen type, and target population. Data were independently extracted by two researchers for consistency and reproducibility. Differences were resolved by consensus. Statistical analysis and trend visualization were performed using Microsoft Excel and R.

Table 2. Selected Studies on Molecular Strategies for Prevention of Infectious Diseases (2000–2025) (12-14)

Molecular Platform	Target Pathogen	Target Population	Delivery System	Key Findings
Nanovaccine	Influenza A/B	Humans	Liposomes / Polymer nanoparticles	Enhanced humoral & cellular immunity; reduced dose
mRNA Vaccine	SARS-CoV-2	Humans	Lipid nanoparticles (LNP)	Rapid antigen expression; strong neutralizing antibodies
siRNA Therapy	RSV	Human airway models	Nanocarriers	Inhibition of viral replication; low cytotoxicity
Protein Subunit	Tuberculosis (Mtb)	Mice, Cattle	Recombinant protein with adjuvant	Significant protective immunity; good safety profile
RNA Therapeutics	Ebola Virus	Non-human primates	LNP	Full protection in challenge studies; rapid deployment potential

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3. Results and Discussion

3.1. Nanovaccines: Enhanced Immunogenicity and Targeted Delivery

Nanoparticle-based vaccine platforms are now powerful tools to improve vaccine stability, delivery, and immune response. Lipid nanoparticles, polymeric nanoparticles, and virus-like particles (VLPs) are employed in general to package antigens and adjuvants in a safe and protected form from degradation and enhanced uptake by antigen-presenting cells. Evidence indicates that nanovaccines can reduce the doses of antigens required, elicit both humoral and cellular immunity, and provide multivalent vaccine formulations. Applications include influenza, tuberculosis, and viral hemorrhagic disease. Observe that such platforms are extremely versatile across species or patient populations, including humans, animals, and wildlife models (15-17). The major nanovaccine applications with target pathogens, delivery systems, and observed immunogenic effects are summarized in Table 3.

Table 3. Nanovaccine Applications for Infectious Disease Prevention (18-20)

Target Pathogen	Nanoplatform	Delivery System	Target Population	Key Outcomes
Influenza A/B	Lipid NP	Intramuscular	Humans	High antibody titers; reduced antigen dose
Tuberculosis (Mtb)	PLGA NP	Subcutaneous	Mice, Cattle	Strong Th1/Th17 responses; enhanced protection
RSV	Chitosan NP	Intranasal	Human airway models	Mucosal immunity; reduced viral replication
Ebola Virus	PEGylated LNP	Intravenous	Non-human primates	Full protection in challenge studies
Zika Virus	Lipid NP	Subcutaneous	Mice	Durable neutralizing antibodies; safety confirmed

3.2 RNA-Based Therapeutics and Vaccines

RNA-based therapeutics like mRNA vaccines and small interfering RNA (siRNA) hold promise for rapid development, specificity, and high immunogenicity (21). mRNA vaccines express pathogen antigens in host cells to induce adaptive immunity without the need for live pathogens (22). Self-amplifying mRNA (saRNA) platforms optimize antigen expression at lower doses, decreasing production costs. Clinical and preclinical studies highlight their application in influenza, SARS-CoV-2, and Ebola with the possibility of strong neutralizing antibody responses and T-cell activation. siRNA therapeutics target viral replication directly by degrading viral mRNA transcripts of particular sequences, with prophylactic or therapeutic effects (23). Delivery has proved challenging, and nanocarrier systems have been instrumental in promoting stability, bioavailability, and targeted tissue delivery (24).

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Table 4. RNA-Based Therapeutics and Vaccines (23-25)

RNA Platform	Target Pathogen	Delivery System	Population/Model	Key Findings
mRNA Vaccine	SARS-CoV-2	LNP	Humans	Rapid induction of neutralizing antibodies; strong T-cell responses
saRNA	Influenza A	LNP	Mice, Ferrets	Enhanced antigen expression at lower doses; durable immunity
siRNA	RSV	Lipid/Chitosan NP	Human airway models	Significant reduction in viral load; minimal cytotoxicity
mRNA Vaccine	Ebola Virus	PEGylated LNP	Non-human primates	Full protection post-challenge; scalable production
siRNA	Zika Virus	Polymer NP	Mice	Effective viral suppression; transient systemic response

3.3 Immunomodulatory Strategies

Next-generation approaches are also focusing on immune modulation by combining vaccines or RNA therapeutics with adjuvants or molecular modulators to maximally stimulate immune responses (26). Examples include the use of Toll-like receptor agonists, cytokine delivery, and nanoparticle co-encapsulation of immunostimulatory molecules (27). These strategies increase both quantity and quality of adaptive responses, provide cross-protection against pathogen variants, and reduce antigen requirements. These immunomodulatory therapies have also been tested on various platforms and species and demonstrated enhanced protection in preclinical evaluation and have opened avenues for combination regimens and precision vaccinology (28-32).

3.4 Artificial Intelligence in the Design of Nanovaccines and RNA Therapies

Artificial intelligence (AI) is transforming the nanovaccine and RNA therapeutic development pipeline at a rapid rate through precision design, predictive modeling, and quicker candidate selection. Machine learning algorithms can process the vast amounts of omics analysis data, structural biology data, and immunogenicity screening data to select top antigen epitopes, nanoparticle formulations, and RNA sequences for optimal immune response (6, 7, 12). Artificial intelligence-guided computational modeling allows for the discovery of molecular interactions of antigens with host immune receptors and the rational vaccine design to elicit humoral and cellular immunity. These have proven very valuable in the rapid development of mRNA vaccines against SARS-CoV-2, for instance, where predictive modeling maximized antigen choice and codon optimization and accelerated preclinical development timelines (21, 22).

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Moreover, AI is aiding optimization of delivery systems for nanovaccines as well as for RNA therapeutics. Algorithms can replicate nanoparticle size, charge, and surface modifications to enhance cellular uptake, antigen stability, and targeted delivery in various species and tissues (15, 16). Beyond design, AI facilitates monitoring of vaccine efficacy and safety in real-world settings through integration of clinical trial data, adverse event reporting, and post-marketing surveillance, enabling continuous optimization of formulations and dosing regimens. Therefore, AI not only accelerates early vaccine development but also enables adaptive optimization in deployment, bridging translational gaps between laboratory research and field deployment (6, 7, 31). The integration of AI with molecular approaches also offers paths for precision and personalized vaccinology. Host genetics, immune signatures, and pathogen diversity could be employed by predictive models to design individualized RNA-based therapies or nanovaccines for high-risk individuals, including immunocompromised patients and livestock with emergent zoonotic potential (7, 31). The union of AI, nanotechnology, and immunology is a paradigm shift, from one-size-fits-all strategies to extremely flexible, data-driven platforms for infectious disease prevention (32-35).

3.5. Nanovaccine and Therapeutic Preparation Storage and Cold Chain Strategies

One of the biggest challenges to global use of RNA therapeutics and nanovaccines is stability and activity in a wide range of storage and transport conditions. Traditional RNA vaccines and nanoparticle preparations are temperature-reliant, requiring ultra-cold chain logistics to prevent degradation and loss of immunogenicity (4, 18, 19). Cold chain requirements present enormous logistics problems, particularly in low-resource settings, remote populations, and regions with poor infrastructure, restricting universal access to advanced molecular therapeutics (5, 18).

Existing methods aim to improve heat stability and simplify storage requirements. Freeze-drying (lyophilization) of RNA and nanoparticle vaccines has proved to be effective in preserving the antigen integrity and bioactivity at refrigerated or even room temperatures, reducing dependence on ultra-low storage (19, 20, 34-36). Formulation additives, such as stabilizing sugars, polymers, or lipid moieties, also enhance heat tolerance and facilitate field use (15, 16). Further, packaging innovations such as thermostable single-dose vials and modular storage systems are under consideration to optimize transport, optimize shelf life, and minimize cold chain disruption. Along with technological advancements, planning and monitoring systems are critical to maintaining effectiveness throughout distribution. Real-time temperature, humidity, and handling condition tracking is possible through digital tracking systems and artificial intelligence, and vaccines and therapeutics are distributed to targeted populations without compromising integrity (11). Overall, formulation and logistics technologies collectively promote the scalability of large-scale vaccination campaigns as well as facilitate equitable access to next-generation molecular platforms in diverse geographic and socioeconomic environments (18, 19, 34-36).

4. Conclusion and Future Outlook

The most recent developments in nanotechnology and molecular biology have transformed infectious disease prevention at its foundations. Nanovaccines, RNA therapeutics, and immunomodulation approaches offer targeted, scalable, and highly effective tools that improve immunogenicity, reduce doses of antigen, and allow rapid adaptation against emerging pathogens. Targeted delivery and release are facilitated by nanoparticle-based vaccines, accelerated cycles of development and potent immune responses are enabled by RNA-based

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platforms (mRNA and saRNA), and immune modulation approaches promote humoral and cellular immunity.

While there have been such advances, their translation from research to application in a practical way needs close attention to safety, regulatory clearance, scalability of manufacturing, and fair access. Interdisciplinary coordination among molecular biologists, immunologists, clinicians, and public health professionals is imperative in order to ensure that these inventions can reach human as well as animal populations.

Future priorities are:

• Investment in the development of thermostable and field-deployable vaccine preparations to overcome cold-chain constraints.

• Triangulation of AI, systems biology, and omics technologies to facilitate antigen selection, epitope mapping, and predictive immunogenicity modeling.

• Simplification of oral, intranasal, or minimally invasive delivery systems for improved compliance and accessibility.

• Broad-spectrum and long-term combination approaches that synergize nanovaccines, RNA platforms, and immune modulators.

By overcoming such challenges and employing cutting-edge molecular platforms, infectious disease prevention in the future will be faster, adaptable, and more equitable interventions—strengthening global health security and preparedness against endemic and emerging pathogens.

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