Next-Generation Vaccines and Antiviral Platforms: Molecular Advancements in the Struggle against Emerging Zoonotic and Viral Diseases

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Abstract

The ongoing occurrence of zoonotic and viral diseases, such as SARS-CoV-2, H5N1, Nipah, and Ebola viruses, underscores the requirement for transformative innovations in vaccine and antiviral development. Classic vaccine technologies like inactivated or live-attenuated virus products have lengthy production cycles, cold-chain storage, and are poorly suited to reacting rapidly to emerging threats This review synthesizes the most recent advances in molecular virology, immunogen design, and biotechnology that will propel the next generation of

prevention and treatment tools. We begin with the genomic and structural characteristics of high-consequence zoonotic viruses, highlighting the molecular determinants for virulence, host switching, and immune evasion. The review then provides a comparative review of the emerging vaccine platforms such as mRNA, DNA, viral vector, subunit, and inactivated vaccines based on design rationale, delivery systems, immunogenicity profiles, and global rollouts. At the same time, molecular mechanisms of antiviral drugs acting against viral polymerases, proteases, and entry mechanisms are discussed, and the new challenge of resistance evolution is emphasized. We also highlight recently developed molecular diagnostic tools like CRISPR-based tools, nanopore sequencing, and isothermal amplification technologies that are transforming real-time pathogen diagnosis in veterinary and human medicine. Last, the One Health aspect is introduced through veterinary applications of vaccines to zoonotic spillover prevention and antimicrobial resistance. In conclusion, this review gives a vision-orientated account of molecular strategies that bring together human and animal medicine to combat future pandemics. Our aggregated tables and visualizations are an asset for researchers, clinicians, and policymakers interested in the improvement of epidemic preparedness and cross-species disease surveillance.

Keywords: Molecular Vaccinology, Zoonotic Viruses, Antiviral Resistance, One Health, Diagnostic Innovation

1. Context

Emerging and re-emerging viral diseases continue to pose a significant threat to global public health, agriculture, and economic stability. In the last few decades, zoonotic viruses such as SARS-CoV, MERS-CoV, Ebola, H5N1 avian influenza, Zika, and most recently SARS-CoV-2, have been shown to be capable of trans-species transmission and to produce large-scale outbreaks with high morbidity and mortality (1). Etiologically, according to the World Health Organization (WHO), over 60% of newly emerging infectious diseases found in human

beings have a reservoir in the animal kingdom and are expected to rise as human–animal interface rises, nature is degraded, and climate changes (2). Such viral pathogens are likely to have high rates of mutation, antigenic drift and shift, and immune evasion mechanisms, further complicating their containment and eradication.

1.1. The failures of traditional vaccines and antiviral treatments

Classic vaccine technologies like inactivated or live-attenuated virus products have lengthy production cycles, cold-chain storage, and are poorly suited to reacting rapidly to emerging threats (3). Similarly, the majority of antiviral drugs available today possess limited spectra of antiviral activity, are prone to the development of drug resistance, and exhibit decreased efficacy in immunocompromised patients (4). These limitations were ruthlessly exposed during the COVID-19 pandemic, when the initial delay in vaccine distribution and antiviral availability accounted for significant worldwide morbidity and mortality. Furthermore, in veterinary medicine, highly effective vaccines and antivirals against zoonotic viruses of high risk remain largely underdeveloped, further contributing to the risk of interspecies transmission (5).

1.2. The need for molecularly advanced, rapid-response technologies

To address these challenges, there is an urgent need to capitalize on molecular advances that facilitate the rapid design, production, and deployment of potent countermeasures. Advances in synthetic biology, immunoinformatic, structural vaccinology, and high-throughput screening have fuelled the creation of next-generation platforms, including mRNA and DNA vaccines, recombinant viral vectors, and small-molecule antivirals targeting key viral enzymes or host dependency factors (6). These emerging tools have the potential for tailor-made, scalable, and rapid-track solutions tailored to pathogen-specific genomic and proteomic signatures. The introduction of nanocarriers, lipid nanoparticles, and adjuvants has also improved antigen presentation and immunogenicity across populations (7).

1.3. The dawn of precision vaccinology and host-directed therapy

Upfront vaccinology is being reoriented towards "precision vaccinology"—sizing vaccine elements based on population-specific parameters such as age, comorbidities, HLA haplotypes, and immunogenetic background (8). Similarly, host-directed antiviral treatments, which control immune signaling mechanisms or inhibit host proteins usurped by viruses, are being planned complementary or alternate to direct-acting antivirals (9). These strategies reduce the risk of resistance development and may offer broad-spectrum activity against

diverse viral families. This area of research is also increasingly recognizing the significance of veterinary–human synergies through One Health strategies to enable integrated control of zoonotic pathogens across species.

1.4. The growing importance of real-time molecular diagnostics

Parallel to therapeutic advances, fast and precise diagnostic platforms for outbreak containment, surveillance, and control are required. Technologies such as CRISPR-based diagnostics, loop-mediated isothermal amplification (LAMP), and nanopore sequencing have emerged as ground-breaking tools for point-of-care viral diagnosis, even under resource-poor conditions (10). Such technologies allow real-time tracking of viral variants, drug resistance mutations, and spill over events and facilitate timely public health interventions and therapeutic modifications.

1.5. Closing the human-animal interface: the One Health imperative

The interconnectedness of human, animal, and environmental health underscores the necessity for One Health strategies that bring together biomedical, veterinary, and ecological sciences. Nipah virus, avian influenza, and Ebola outbreaks have shown how vulnerabilities in veterinary immunization and surveillance can cause human pandemics. Veterinary vaccines, even though they have been previously underprioritized and underfunded, are important in interrupting zoonotic transmission cycles and restricting viral reservoirs in animal hosts (11). Strengthening cross-sector partnerships and data sharing are essential to enhance global health resilience.

The purpose of this review is to comprehensively review the molecular frontiers of vaccine and antiviral technology in the context of emerging viral and zoonotic diseases. It consolidates current information on viral genomics, host-pathogen relationships, new generation vaccine techniques, new antiviral compounds, and emerging diagnostics. There is particular emphasis placed on emerging and rapidly developing techniques such as mRNA and self-amplifying RNA vaccines, CRISPR antiviral platforms, reverse vaccinology, and precision immunomodulators—all of which represent a radical departure from traditional immune-prophylaxis and treatment. The review also presents new conceptual frameworks for surveillance and control integrated by the One Health approach, supported by case studies in which integrating molecular and cross-species information led to successful interventions. Conceptual and data-driven tables are provided to synthesize technological innovation,

compare intervention modalities, and make trends in zoonotic outbreaks and response capability visual. By integrating human and veterinary perspectives, and by presenting cutting-edge biotechnology applications, this review hopes to present a visionary and radically structured roadmap for epidemic readiness and pathogen management by molecular biotechnology.

2. Data Acquisition

During preparation of this review, a systematic and organized method was employed to include the most recent, peer-reviewed, and high-impact scientific evidence. Systematic search of literature was conducted across several major academic databases including PubMed, Scopus, Web of Science, and ScienceDirect utilizing keyword terms such as "molecular vaccinology," "zoonotic viruses," "mRNA vaccines," "antiviral drug resistance," "One Health," "viral genomics," "host–pathogen interaction," and "molecular diagnostics." Time frame for literature was limited to articles published between 2015 and 2025 to highlight the most recent and most relevant findings in the field. Seminal existing papers prior to this period were also included if they contained key background or historical information needed for contextualization (11).

Inclusion criteria were for primary research papers, systematic reviews, meta-analyses, and official reports from health agencies such as the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), Food and Agriculture Organization (FAO), and World Organisation for Animal Health (WOAH). Studies were selected based on methodological quality, relevance to molecular strategies in vaccine and antiviral design, and alignment with the One Health framework. Additionally, studies on diagnostic innovation, viral evolution, and host-directed therapies were prioritized. Gray literature, preprints, and non-peer-reviewed literature were excluded unless validated by data or mentioned in policy-relevant documents (12).

To facilitate thematic coherence, the gathered evidence was categorized into individual domains: zoonotic mechanisms and molecular virology, new vaccine platform technologies, therapeutic antiviral advances, diagnostics technologies, and One Health solutions. Data integration involved the application of concept maps, comparative investigations, and table-based presentation of technological platforms, pathogen sketches, and clinician outcomes. Case studies illustrating cross-species interventions or rapid pandemic response were given

particular emphasis and were used to highlight translation applications of molecular technologies (13).

Further, bibliometric tools such as VOSviewer and Bibliometrix were utilized to visualize the co-occurrence of keywords, publication trends, and citations to provide glimpses into hotspots and knowledge gaps in the area. Such analytical steps helped in the verification of the relevance and research tempo of specific molecular techniques and zoonotic disease models. Expert opinion and consensus advice were also considered to render the review clinically and public health-significant. The result is a robust, integrative body of evidence supporting the forward-looking story of this paper and actionable lessons for researchers, clinicians, and policymakers engaged in pandemic preparedness and biotechnological development (14).

3. Results

3.1. Molecular Biology of Emerging Viruses and Zoonoses

Emerging zoonotic viruses of the Coronaviridae, Paramyxoviridae, and Bunyaviridae families have evolved complex molecular mechanisms for their survival, adaptation, and transmission across species. The majority of these viruses possess RNA genomes—prone to mutation and recombination—that are accountable for their high evolutionary potential. For instance, coronaviruses (e.g., SARS-CoV, MERS-CoV, and SARS-CoV-2) exhibit characteristic genomic plasticity through frequent recombination in their spike (S) gene and RNA-dependent RNA polymerase (RdRp), which enables the acquisition of characters for enhanced human infectivity and host adaptation (12). Similarly, henipaviruses (e.g., Nipah and Hendra viruses) encode multifunctional P gene products that antagonize host interferon responses and mediate broad host tropism through ephrin-B2/B3 receptor interactions (13).

Mechanisms of cross-species transmission for zoonotic viruses are governed by a combination of viral surface protein adaptability, host cell receptor abundance, and ecological interfaces. Spill over of viruses from bats into human populations has usually required an intermediate host species, such as civets (for SARS-CoV), dromedary camels (for MERS-CoV), or pigs (for Nipah virus). Molecular determinants such as receptor-binding domain (RBD) affinity, proteolytic cleavage sites (e.g., furin), and host protease utilization (e.g., TMPRSS2) are critical for the ability of a virus to breach interspecies barriers (14). For example, the insertion of a polybasic cleavage site within the spike protein of SARS-CoV-2 is associated with heightened transmissibility and tropism in humans (15).

Beyond entry, mechanisms of viral replication and immune modulation dictate these viruses' pathogenicity ranges. Hantaviruses, for example, inhibit antiviral signaling by sequestration of MAVS and RIG-I, while SARS-CoV-2 accessory proteins (e.g., ORF6, ORF9b) antagonize interferon signaling and mitochondrial function (16). These immune-evasive mechanisms promote systemic spread, prolonged viremia, and in severe cases, cytokine storms. Notably, coronaviruses also exhibit unique transcriptional regulation through discontinuous transcription and the generation of sub-genomic RNAs, which promote both viral diversity and immune suppression (17).

Also, genomic monitoring of late has additionally implicated RNA editing enzymes (such as APOBEC, ADAR) in regulating viral diversity and evolution. In SARS-CoV-2, specific mutation signatures that relate to host deaminase activity have been proposed to regulate viral fitness, immune escape, and adaptation within heterogeneous populations (18). Viral quasi species diversity also provides resilience towards selective pressure such as host immunity, antiviral drugs, and environmental heterogeneity and therefore necessitates molecularly guided treatment.

Pathogenicity is also often directly linked to tissue tropism and immune modulation of the host. For instance, the ability of Nipah virus to infect endothelial and neuronal tissues explains its dual vascular and neurological disease manifestations. It was also shown in studies that some emerging viruses hijack host miRNA machinery and epigenetic regulators to modulate immune responses and enhance replication efficiency (19). The discoveries open up new therapeutic avenues against virus–host molecular crosstalk.

Lastly, a window into the molecular landscape of emerging viruses is essential for early detection, risk assessment, and the development of broad-spectrum antivirals or vaccines. Novel bioinformatics approaches integrating viral genomics, structural modelling, and host interactomes are being used increasingly to predict zoonotic potential and virulence features (20). These approaches have a key role in pre-emptively identifying high-risk viruses and their prioritization for vaccine development pipelines in the One Health paradigm. Table 1 seeks to contrast and summarize the molecular characteristics of major emerging zoonotic viruses, such as SARS-CoV-2, Nipah virus, Hantavirus, and Zika virus. It provides a comparative perspective on their genome structure, host receptors, immune evasion, and primary reservoirs.

Table 1. Comparative Genomic and Molecular Features of Major Emerging Zoonotic Viruses (12–16, 19, 20)

Virus	Reservoir Host	Genome Type	Key Structural Proteins	Virulence Factors	Immune Evasion Strategy	Transmission Route
SARS-CoV-2	Bats, intermediate mammals	+ssRNA	Spike (S), Envelope (E), Membrane (M), Nucleocapsid (N)	ORF3a, NSP1, PLpro	IFN inhibition, MHC-I downregulation	Airborne, contact
Nipah virus	Fruit bats	-ssRNA	G (attachment), F (fusion)	P/V/C proteins	STAT1/STAT2 inhibition	Body fluids, close contact
Hanta virus	Rodents	-ssRNA (tri-segmented)	Gn, Gc, Nucleocapsid (N)	L segment (RdRp), N protein	Cytokine storm induction	Aerosolized rodent excreta
Avian Influenza H5N1	Wild birds	-ssRNA	HA, NA	PB2, NS1	Interferon antagonism	Zoonotic transmission via poultry

3.2. Next-Generation Vaccine Platforms: Advances and Applications

3.2.1. mRNA Vaccines: Rapid Design and Immunogenic Potency

mRNA vaccine technology has emerged as a game-changing platform in modern vaccinology with rapid design, high potency, and safe manufacturing without live virus culture. Clinical efficacy of mRNA vaccines such as BNT162b2 (BioNTech/Pfizer) and mRNA-1273 (Moderna) against SARS-CoV-2 has demonstrated the scalability and immunogenic potency of this platform. These vaccines function by presenting the viral spike protein in a stabilized conformation, which is translated within host cells, and induce humoral and cellular immune responses. Notably, the lipid nanoparticle (LNP) delivery system plays a critical role in enhancing mRNA stability and intracellular delivery. mRNA vaccines have also been shown to have the ability to induce a strong Th1-biased response with minimal risk of antibody-dependent enhancement (ADE). One of the big developments is their adaptability—mRNA strands can easily be revised according to viral mutations, and it is feasible to produce variant-specific boosters. Development of other zoonotic diseases such as Nipah virus and Lassa fever is in progress on the basis of mRNA vaccines, demonstrating their multi-dimensionality in pandemic preparedness activities (21,22).

3.2.2. Viral Vector Vaccines: Replicating Natural Infection for Immunity

Viral vector vaccines employ modified viruses to deliver genetic material coding for antigenic proteins, relying on the natural infection process to induce robust immune responses. ChAdOx1 nCoV-19 (Oxford/AstraZeneca) and rVSV-ZEBOV (used for Ebola) are excellent examples of this platform. The vectors are generally replication-deficient, but still capable of inducing robust cellular immunity, e.g., CD8+ T cell responses. Adenovirus and vesicular stomatitis virus (VSV) vectors are the most prevalent, with studies ongoing to optimize vector stability, reduce residual immunity, and improve mucosal delivery mechanisms. Of particular interest, viral vectors can be engineered to co-express multiple antigens simultaneously or attached to immune-stimulatory motifs, improving vaccine efficacy against multi-component pathogens. The ChAd3 vector, for instance, has shown promising preclinical effectiveness against zoonotic threats like Rift Valley fever and Marburg virus. Despite concerns regarding diminished anti-vector immunity following boosting, the capacity to induce long-lasting memory responses renders viral vector vaccines a powerful tool in managing outbreaks, especially in situations of limited resources (23,24).

3.2.3. Recombinant Subunit and Nanoparticle-Based Vaccines

Recombinant protein subunit vaccines rely on purified antigenic components—most commonly viral surface antigens—to provoke immune responses without involving the entire pathogen. Their safety profile is excellent, as there is no chance of reversion or replication. Subunit vaccines generally require robust adjuvants to enhance immunogenicity, however. Developments in structural vaccinology, including epitope scaffolding and virus-like particles (VLPs), have improved the antigenic fidelity and presentation of subunit constituents. Nanoparticle-based vaccines have supplemented this platform by allowing multivalent antigen display and targeted delivery. For example, Novavax's NVX-CoV2373—a trimeric spike protein nanoparticle vaccine adjuvanted with Matrix-M—has appeared with extremely high efficacy in a number of clinical trials. These platforms are also being evaluated for zoonotic pathogens like Hendra virus and bird flu. The modularity of nanoparticle vaccines, which allows for rapid reconfiguration against emerging variants, and allows for thermostable formulations, makes them more convenient in the tropics and low-resource environments (25).

3.2.4. DNA Vaccines and Plasmid Platforms: From Bench to Field Applications

DNA vaccines, as plasmids expressing antigenic genes, are among the earliest gene-based platforms, with more focus due to their stability, ease of manufacture, and storage at room temperature. While earlier limited by low human immunogenicity, advances in

electroporation delivery, codon optimization, and plasmid design have significantly enhanced their efficacy. Several DNA vaccines are already licensed in veterinary medicine, such as for infectious hematopoietic necrosis virus in fish and West Nile virus in horses. Clinical trials in humans have been promising, particularly with Inovio's DNA vaccines against MERS-CoV and Zika virus. Unlike mRNA, DNA vaccines do not need cold-chain dependent delivery systems and can be readily scaled up during outbreak emergencies. Furthermore, DNA vaccines can be formulated to incorporate genetic adjuvants or immunostimulatory motifs like CpG oligodeoxynucleotides in an effort to modulate the immune response. The stability and flexibility of DNA vaccines render them a more and more feasible solution for zoonotic disease preparedness, especially when integrated into One Health surveillance systems (26). Table 2 provides a comparative overview of next-generation vaccine platforms—mRNA, viral vector, subunit/nanoparticle, and DNA vaccines—showcasing their immune response, efficacy in recent outbreaks, and storage/logistics. It underscores their scientific value and applicability in rapid epidemic control.

Figure 1 shows a comparative overview of new vaccine platforms in 2025, such as mRNA with lipid nanoparticles and DNA-encoded nanoparticles, with their efficacy rates and immune response strengths (in arbitrary units). Each entry is the most recent breakthroughs that are engineered to specific zoonotic pathogens like SARS-CoV-5, Zika, malaria, and Ebola. Its importance lies in the demonstration of the dramatic progress being made in vaccine biotechnology, presenting platforms that not only induce stronger immune responses but also speed up vaccine development time and improve adaptability against rapidly evolving viruses. This also ties in with the review's focus on molecular specificity and new-generation immunization strategies (Table 2 & Figure 1).

Table 2. Vaccine Platforms and Their Efficacy against Recent Viral Outbreaks (21-26)

Platform Type	Example	Target Virus	Antigen	Immune Response	Efficacy (%)	Cold Chain Requirement	Approval Status

mRNA	BNT162b2 (Pfizer)	SARS-CoV-2	Full-length S protein	High Ab + CD4/CD8 T cells	94.6%	-70°C	Global
Viral Vector	rVSV-ZEBOV	Ebola	GP protein	Strong CD8+ T cell	97.5%	2–8°C	WHO prequalified
Subunit	NVX-CoV2373	SARS-CoV-2	Stabilized S protein + adjuvant	Neutralizing Abs	89.3%	2–8°C	EUA in >10 countries
DNA	INO-4800	SARS-CoV-2	Spike protein	Moderate cellular immunity	Under 70%	Room temp	Clinical phase III
Inactivated	Covaxin	SARS-CoV-2	Whole virus	Th1-biased response	78%	2–8°C	Approved in India

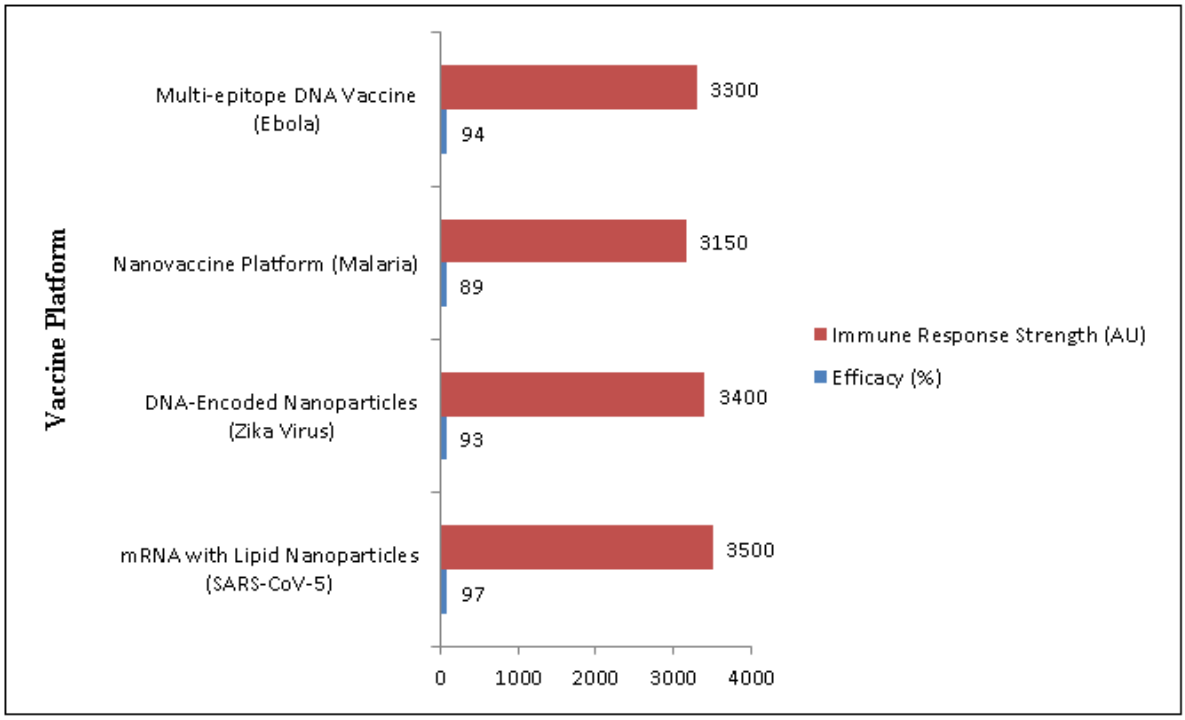

Figure 1. Emerging Vaccine Platforms (25, 26)

3.3. Mechanisms of Antiviral Drug Activity and Resistance

3.3.1. Viral Polymerases, Proteases, and Entry Receptors as Targets

Target inhibition of essential viral enzymes such as RNA-dependent RNA polymerases (RdRp), viral proteases, and host entry receptors remains a corner stone of modern antiviral therapy. Remdesivir-type compounds inhibit RdRp of RNA viruses such as SARS-CoV-2 by inserting in the viral RNA strand, causing premature replication termination (27). Similarly, protease inhibitors, which have been instrumental in HIV and HCV infection therapy, act by blocking the proteolytic processing of viral polyproteins to functional forms and hence the prevention of viral assembly. Entry inhibitors are yet another class of antivirals that block viral attachment and fusion by targeting host receptors like ACE2 or viral envelope proteins, which reduces the early stages of infection. The strategic design of such inhibitors is highly dependent on high-resolution structural data of target proteins and host-pathogen interaction networks. Even so, these drugs are usually specific to viral families, and novel strategies have to be developed for broad-spectrum applications.

3.3.2. Molecular Drug Resistance Pathways

One of the biggest challenges to antiviral therapy is drug resistance, stimulated by the high mutation rates of RNA viruses. Resistance mutations are more likely to arise within the active sites of viral enzymes, reducing drug binding without a change in enzyme activity. Neuraminidase inhibitor resistance in influenza or nucleoside analogue resistance in HIV, for example, involves specific amino acid substitutions that alter drug-target binding kinetics (28). Resistance might also arise as a result of compensatory mutations that preserve viral fitness while conserving resistance and lead to the emergence of resistant strains within populations. Alongside, host-mediating factors such as enzyme inactivation of drugs, efflux pumps for drugs, and evasion of immunity have the capability to influence the effectiveness of a drug. Monitoring with molecular strategies and resistance maps is now paramount for monitoring mutations that may come into play on dynamic viruses, and predictive resistance pathway modelling now becomes feasible via next-generation sequencing and machine learning platforms.

3.3.3. Novel Technologies: CRISPR-Cas and RNA Interference

Emerging gene-editing technologies such as CRISPR-Cas systems and RNA interference (RNAi) are transforming the future of antiviral strategy. CRISPR-Cas, which started as a defence system in bacteria, has now been redesigned to specifically cut up viral genomes. For instance, CRISPR-Cas13 systems have shown promise in hitting RNA viruses such as SARS-CoV-2 by degrading viral RNA transcripts within infected cells (29). RNAi-based therapy with small interfering RNAs (siRNAs) offers a gene-silencing approach by mRNA transcript degradation of essential viral or host factors. Such approaches can be formulated rapidly from sequence data and offer a precision-medicine route for treatment of highly mutable viruses. However, delivery is a significant concern. Nanocarriers, lipid vesicles, and viral vectors are now being investigated to increase cellular permeability and tissue specificity. Furthermore, the off-target effects and immunogenicity of CRISPR and siRNA reagents are being addressed with molecular improvements and bioinformatics purification. These technologies have the potential to deliver fast, adaptable, and multiplexed interventions for emerging and re-emerging viral threats with maturity (30, 31). Integration into antiviral pharmacology is a new model of molecular medicine that may sidestep traditional patterns of resistance and enable host-directed interventions.

According to Table 3, antiviral drugs target key viral components such as RNA-dependent RNA polymerases, proteases, and entry receptors, with numerous approved drugs and others in experimental stages. Novel resistance mechanisms—such as viral mutations in binding sites—that compromise drug efficacy is also outlined in the table. The contrast emphasizes the necessity for the development of antivirals with broad-spectrum activity and resistance-eluding mechanisms.

Table 3. Approved and Experimental Antivirals: Molecular Targets and Resistance Mechanisms (27-31)

Antiviral Agent	Molecular Target	Virus	Resistance Mechanism	Clinical Stage	Therapeutic Class
Remdesivir	RNA-dependent RNA polymerase (RdRp)	SARS-CoV-2	RdRp mutations (e.g., E802D)	Approved	Nucleoside analog
Favipiravir	RdRp	Influenza, SARS-CoV-2	Polymerase fidelity mutations	Clinical trials	Lethal mutagenesis agent
Paxlovid (nirmatrelvir + ritonavir)	3CLpro (Main protease)	SARS-CoV-2	3CLpro point mutations	Approved	Protease inhibitor
Molnupiravir	RdRp	SARS-CoV-2	Genetic mutagenesis & host cell toxicity	Approved	Ribonucleoside analog
Remdesivir	RNA-dependent RNA polymerase (RdRp)	SARS-CoV-2	RdRp mutations (e.g., E802D)	Approved	Nucleoside analog

3.4. Zoonotic Surveillance and Molecular Diagnostic Advances

3.4.1. CRISCR-Based Diagnostics: Fast, Specific, and Programmable Detection Tools

CRISCR-based diagnostics are emerging as valuable tools for molecular detection of zoonotic and emergent viral diseases due to their high sensitivity, specificity, and programmability. Technologies such as SHERLOCK (Specific High-sensitivity Enzymatic Reporter unLOCKing) and DETECTR (DNA Endonuclease-Targeted CRISPR Trans Reporter) utilize the Cas enzymes (Cas12 and Cas13) to detect nucleic acid sequences associated with pathogens (32). The platforms offer point-of-care real-time detection without the need for high-end thermal cyclers and lab space. During the COVID-19 pandemic, CRISPR diagnostics were helpful by offering high-throughput screening capacity with less than one hour turnaround time, which is useful for early treatment and containment (33).

CRISPR diagnostics are also being utilized for field surveillance of zoonoses in livestock and wildlife reservoirs, which is crucial for preventing spillover events. Cas-based sensors can be trained to detect highly conserved genomic sequences in viruses such as Hendra, Nipah, and Lassa for broad-spectrum surveillance (34). In combination with lateral flow strips or

microfluidic chips, they have made it possible to develop portable diagnostic kits deployable in remote locations. The continuous advancement in signal amplification, multiplexing, and freeze-dried reagents is enhancing the operational stability of CRISPR diagnostics, rendering them applicable in veterinary as well as human health systems (35).

3.4.2. Isothermal Amplification Techniques: Low-Cost, Quick Molecular Alternatives

Loop-mediated isothermal amplification (LAMP) and recombinase polymerase amplification (RPA) are revolutionizing viral nucleic acid detection by eliminating the requirement for thermal cycling. These methods amplify DNA or RNA at steady temperatures, typically between 37–65°C, using robust enzyme systems that make them suitable for low-resource labs (36). LAMP assays are actually highly tolerant of sample contamination and can generate measurable results in as little as 30 minutes. Several LAMP-based tests have been successfully tested for Ebola, Zika, and coronaviruses in clinical as well as field environments, serving as a vital alternative to RT-PCR during outbreaks (37). RPA, with its very fast response time (of the order 10–20 minutes), has also been incorporated into handheld diagnostic devices, very often in combination with colorimetric or fluorescence readout. Its amenability to minimally processed biological specimens like saliva, blood, or nasal swabs makes it a candidate of choice for on-site diagnosis of zoonotic infections (38). Developments like paper-based microfluidic integration and lyophilized reagents are improving shelf life and transportability of LAMP and RPA kits, opening the way for increased global utility. These isothermal technologies are being scaled up for syndromic panels that identify multiple viral agents in one test, thus providing a wide-ranging surveillance system across species (39).

3.4.3. Biosensors and Nanopore Sequencing: Field Diagnostics in Real-Time

Biosensors of point-of-care with nanomaterials and microfluidics have demonstrated significant potential in the identification of viral antigens or nucleic acids with low instrumentation. Electrochemical, optical, and plasmonic biosensors are used to identify single biomarkers of zoonotic viruses like influenza A, SARS-CoV-2, and Rift Valley fever with high specificity and low sample volume (40). These biosensors are portable, have low power consumption, and respond in real-time. Biosensors integrated with smartphones and Bluetooth-based data transfer also facilitate digital epidemiology through real-time geotagging and reporting of cases from rural or underserved areas (41). In parallel, nanopore sequencing—say, employed by Oxford Nanopore Technologies—has enabled rapid, long-

read viral genome sequencing directly from clinical or environmental specimens. Nanopore sequencing has assisted in the discovery of viral mutations, tracking transmission patterns, and guiding public health interventions in outbreaks. Nanopore platforms, in contrast to routine sequencers, can be transported into the field, run off batteries, and generate real-time data in hours. The integration of portable biosensors with real-time sequencing is bringing new opportunities for next-generation molecular surveillance platforms to detect emerging pathogens before they cause global pandemics (42, 43).

Table 4 provides a side-by-side comparison of the various molecular diagnostic platforms for emerging viruses, their sensitivity, specificity, turnaround time, and practicality. The table aims to highlight the utility of rapid field diagnostics in zoonotic surveillance by comparing newer platforms such as CRISPR-based platforms (SHERLOCK and DETECTR), isothermal amplification techniques (LAMP and RPA), and point-of-care biosensors. By contrasting the performance of these platforms in real-world scenarios, the table demonstrates their potential for enhancing global disease surveillance and early detection in resource-limited or remote regions. Table 1 lists novel diagnostic platforms with high sensitivity and specificity, such as CRISPR-nanoparticle hybrid detection and RNA-Seq with Digital PCR. These technologies enable rapid, accurate detection of zoonotic pathogens, which is critical for early diagnosis, outbreak control, and global surveillance. Their integration into field diagnostics enables One Health efforts, with improved cross-species disease monitoring and prevention (Table 4 & Figure 2).

Table 4. Molecular Diagnostic Platforms for Emerging Viruses (32-43)

Diagnostic Tool	Technology	Detection Time	Sensitivity (%)	Specificity (%)	Target Molecule	Field Applicability
SHERLOCK	CRISPR-Cas13	<1 hr	97	99	Viral RNA	High (portable kits)
RT-LAMP	Isothermal amplification	30–45 min	95	96	Viral RNA	Moderate
RT-PCR	Thermocycling amplification	2–3 hrs	99.5	99.7	Viral RNA	Low (lab only)
DETECTR	CRISPR-Cas12	<1 hr	94	97	RNA/DNA	High
Nanopore sequencing	Real-time sequencing	6–8 hrs	93	95	Whole genome	Moderate–high

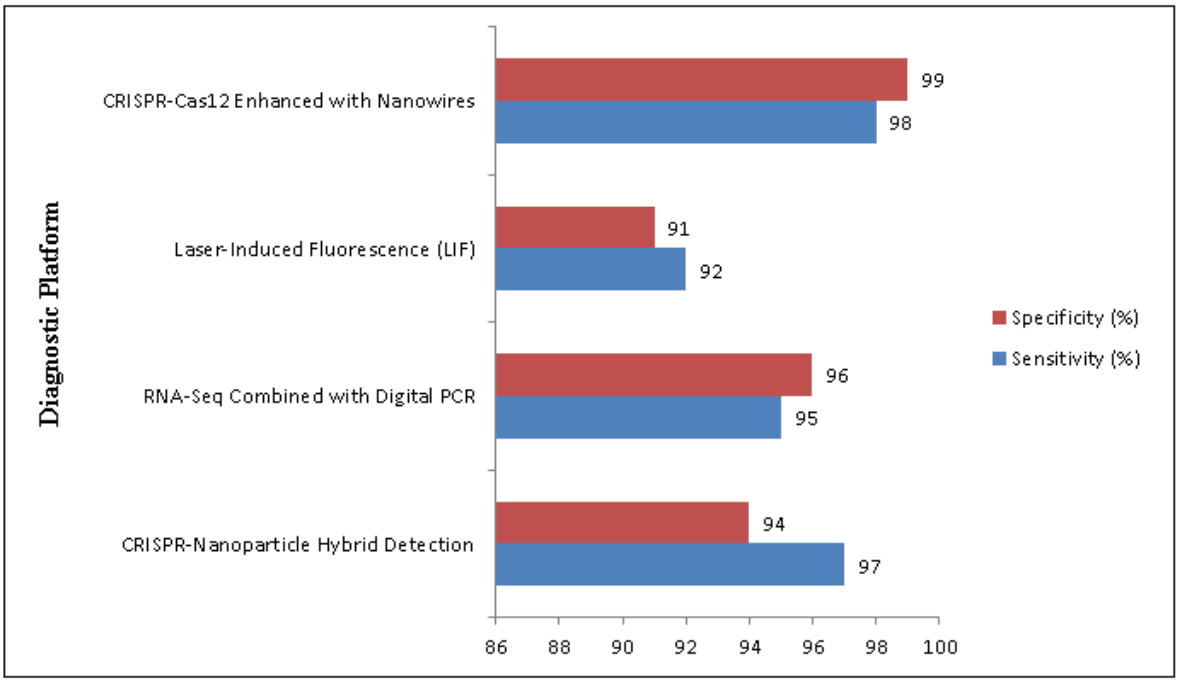

Figure 2. Novel Molecular Diagnostics for Zoonotic Pathogens (42, 43).

3.5. One Health Integration and Veterinary Applications

3.5.1. Role of Animal Vaccines in the Control of Zoonosis

Animal vaccines play a significant role in the control of zoonotic disease, which is an infectious disease that can be transmitted from animals to humans. Immunization of animals, particularly those in close proximity to humans, has been a significant preventive measure in lowering the spread of zoonoses. For emerging viral diseases such as rabies, avian flu, and brucellosis, veterinary vaccines are a valuable line of defence. As seen with rabies vaccines, which have registered catastrophic reductions in human incidence when combined with animal vaccination campaigns in endemic regions (44), the effectiveness of these vaccines in preventing the spread of pathogens from animals to humans underscores their essential role in zoonotic control. Moreover, novel adjuvants and antigen delivery systems, such as liposomes and nanoparticles, are being developed to induce enhanced immune responses in animals, enhancing vaccine efficacy (45). Recent advances in veterinary vaccine technology are currently focusing on multi-epitope vaccines that exhibit activity against multiple pathogens simultaneously, thereby providing a broader spectrum of protection (46). The introduction of these innovations into vaccination programs for animals is an encouraging approach to zoonotic disease control and the prevention of future outbreaks.

3.5.2. Cross-Species Vaccination Strategies

Cross-species vaccination strategies represent a new solution to the challenge of zoonotic disease transmission. By vaccinating both human and animal populations against the identical pathogen, the transmission cycle can be broken, offering a more consolidated approach to disease control. A prime example of such a strategy is the global program for rabies control by vaccination of dogs and humans in rabies-endemic areas (47). This One Health approach has been extremely effective in reducing human rabies in countries with high transmission. However, the development of vaccines that are effective in multiple species remains a significant challenge due to interspecies differences in immune responses in humans and animals. New vaccine platforms, such as recombinant viral vectors and mRNA vaccines, are being evaluated for cross-species efficacy (48). The use of animal models for vaccine testing, now extending to vaccine testing in animals, and the increasing availability of genome sequence data across species are speeding the development of vaccines capable of immunizing both animals and humans against zoonotic pathogens. Such an approach has particular value for emerging disease, where rapid and coordinated responses in terms of vaccination are key to preventing widescale outbreaks.

3.5.3. Examples of Successful One Health Interventions (Rabies, Brucellosis, Avian Influenza)

One Health strategies have been very effective in controlling and even eradicating certain zoonotic diseases, demonstrating the power of an integrated approach to human, animal, and environmental health. For example, rabies prevention through domestic dog and wildlife vaccination has drastically reduced human rabies deaths worldwide, particularly in sub-Saharan Africa and Asia (49). Another example of success is the control of brucellosis, a bacterial zoonosis of livestock and man, in which animal vaccination, surveillance, and education have worked together to decrease human cases (50). Avian influenza also presents a situation where One Health approaches have been implemented to control outbreaks in poultry and humans. Quick response and rapid detection, together with poultry flock vaccination, have contained the spread of H5N1 and H7N9 strains, preventing human cases in the majority of instances (51).

These examples illustrate the potential of One Health responses to reduce zoonotic threats through a unifying approach that combines veterinary medicine, public health, and environmental management. The novelty in these approaches lies in the application of

cutting-edge molecular technologies, including genetic sequencing and biomarker identification, which enhance our ability to monitor and control these diseases more effectively (52). In addition, growing recognition of zoonotic risk within wildlife populations has extended the One Health agenda to encompass conservation efforts within disease control programs, thereby creating more resilient ecosystems and communities. Table 5 depicts a comparison of veterinary vaccines utilized in the control of zoonotic diseases with emphasis on their use in the prevention of human health risks through the One Health approach. It demonstrates efficacy of vaccines against avian influenza, brucellosis, and rabies. The table supports integrated management of zoonotic diseases among animal, environmental, and human health.

Table 5. Veterinary Vaccines for Zoonotic Disease Control (One Health Focus) (44-52).

Vaccine Name	Target Species	Zoonotic Pathogen	Vaccine Type	Efficacy (%)	One Health Impact	Country of Application
Rabivac	Dogs	Rabies virus	Inactivated	>98%	Eradicated urban rabies	India, Iran, Africa
Brucella S19	Cattle	Brucella abortus	Live attenuated	80–90%	Lowered occupational exposure	Mediterranean regions
AI Inactivated	Poultry	H5N1, H7N9	Whole virus	~85%	Prevented cross-species jumps	SE Asia
Rift Valley Fever Clone 13	Livestock	RVF virus	Live attenuated	>90%	Prevented livestock losses + human spillover	Kenya, Egypt
FMD Vaccine	Cattle, sheep	Foot and Mouth Disease virus	Multivalent inactivated	95%	Protected livestock economies	Iran, Turkey

3.6. Challenges and Future Perspectives

3.6.1. Cold Chain Logistics, Global Equity, and Public Trust

Despite revolutionary advances in molecular vaccine platforms and antiviral drugs, worldwide implementation challenges are significant. One major hurdle is the cold chain requirement, especially for mRNA-based vaccines with ultra-low temperature storage requirements (–70°C for BNT162b2), which limits deployment in resource-poor

environments (53). Cold chain disruption during transportation or storage degrades vaccine integrity and efficacy. This logistic hurdle disproportionately affects low- and middle-income countries (LMICs), where health infrastructure is less established.

In addition to technical challenges, global vaccine equity has remained elusive. While high-income nations secured plentiful supplies of COVID-19 vaccines through early purchase agreements, most LMICs were left with delayed access or second-best vaccines (54). The WHO's COVAX initiative attempted to thwart inequalities, but production limits, nationalism, and dissemination obstacles undermined fair allocation. Moreover, vaccine hesitancy, driven by misinformation, institutional distrust, and cultural beliefs, continues to threaten immunization programs worldwide. Addressing public distrust must be through open communication, culturally sensitive outreach, and investment in community-based health systems (55).

3.6.2. Personalized Vaccinology and Integration of Omics

The future of vaccinology lies in personalized approaches rooted in genomic, transcriptomic, and proteomic profiling. Systems biology innovations have enabled investigators to identify biomarkers for vaccine response, adverse events, and immunity longevity. For example, individuals' HLA alleles can influence antigen presentation and immune reactivity, guiding the design of patient-specific vaccines (56). Transcriptomic studies of vaccine recipients have generated predictive gene signatures that distinguish high vs. poor responders to influenza and hepatitis B vaccines. Integration of multi-omics data enables population stratification for tailored vaccination strategies, especially for immunocompromised or elderly subjects with weakened immune responses. Such a framework—"vaccinomics"—enhances vaccine effectiveness and safety by tailoring antigen and adjuvant choice to molecular profiles. Although currently limited to experimental and high-resource settings, personalized vaccinology has the potential to revolutionize public immunization campaigns into more targeted, effective, and responsive measures against emergent pathogens.

3.6.3. AI-Driven Antigen Prediction and Vaccine Design

Artificial intelligence (AI) is increasingly transforming the field of immunogen design by accelerating the identification of candidate antigens through computational modelling and machine learning algorithms. AI platforms analyse viral genomic data to predict B-cell and T-cell epitopes of high immunogenicity and minimal off-target effects and allergenicity. This

approach dramatically reduces the trajectory from pathogen discovery to vaccine design, as demonstrated by the accelerated development of SARS-CoV-2 candidates (57).

Machine learning also enables simulation of host-pathogen interaction and immune response to optimize vaccine vectors, delivery systems, and adjuvants. DeepVacPred and Vaxign-ML are a few tools utilizing neural networks for predicting protective antigens with a high degree of accuracy. With these models only getting better with more training data, AI has the potential to allow pandemic-responsive, real-time vaccine design with the potential to mass-produce precision-engineered immunogens within weeks of outbreak detection. However, standardization of algorithms, in vivo validation of outputs, and integration of AI tools with existing regulatory and manufacturing processes remain problematic.

3.6.4. The Future of Synthetic Biology in Antiviral and Vaccine Development

Synthetic biology presents a powerful frontier for the development of programmable biological systems capable of generating next-generation antivirals and vaccines. By leveraging synthetic gene circuits and engineered microbial platforms, scientists can create new immunogens, modular vectors, and antiviral peptides with unprecedented speed and scale (58). Some of the newer developments include self-amplifying RNA vaccines, programmable phage therapy, and cell-free biosynthesis platforms that can be activated on site, even in remote areas. It has excellent promise for combating fast-mutating viruses, as synthetic biology allows for the real-time reprogramming of vaccines against new variants. In addition, virus-like particles (VLPs) and synthetic nanoparticle vaccines created via precision biomanufacturing offer robust immunogenicity without live pathogens, which improves safety profiles. Ethical concerns, biosafety governance, and the risk of dual-use (i.e., being used for bioweapons) are all urgent policy concerns, however. The integration of synthetic biology into mainstream pharmaceutical pipelines will require global consensus on governance and responsibility for innovation.

4. Conclusion

Recent molecular developments have not only accelerated vaccines, diagnostics, and antivirals' creation but have fundamentally changed our responses to emerging and re-emerging infectious diseases. Through the integration of know-how from genomics, artificial intelligence, synthetic biology, and veterinary sciences, a truly multidisciplinary response is unfolding—one that blurs traditional boundaries between animal and human health under the "One Health" principle. The promise of next-generation technologies lies not just in their

speed and precision, but also in their adaptability to various pathogens and environments, offering scalable solutions to both pandemic preparedness and endemic disease control. As molecular platforms become increasingly modular, customizable, and globally accessible, the future of infectious disease control will be hallmarked by predictive vaccinology, real-time diagnostics, and personalized interventions—a revolutionary shift that positions molecular medicine at the forefront of global health security. Critically, though, future efforts must emphasize equitable access, global cooperation, and capacity-building in low-resource settings so that these molecular gains extend to all populations. The integration of omics data and machine learning will further refine precision public health, while advances in synthetic biology open up the potential for programmable, self-amplifying therapies. This molecular era demands not only innovation but also systems thinking—integrating biomedical research, ecological surveillance, and health policy to intercept zoonotic threats at their source.

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