STM JOURNALS

International Journal of
Vaccines

Volume 1, Issue 2, 2024
July–December
DOI (Journal): 10.37591/IJV

https://journals.stmjournals.com/ijv

Review IJV

Innovative Vaccine Technologies: Current Landscape and Future Prospects in Preventive Medicine

Satish Kumar Sarankar[1,*], Santosh Ojha[1], Brajesh Rajak[1], Sushma Somkuwar[2]

Abstract

This review article presents a comprehensive analysis of recent advancements and emerging trends in vaccine development, offering insights into the dynamic landscape of preventive medicine. Delving into a spectrum of infectious diseases, including influenza, HIV/AIDS, malaria, tuberculosis, respiratory syncytial virus (RSV), Group B Streptococcus (GBS), norovirus, and chikungunya, the review highlights innovative approaches and breakthroughs in vaccine technology. It explores efforts to develop universal influenza vaccines, long-awaited HIV vaccines, and next-generation malaria and tuberculosis vaccines. Additionally, the review examines ongoing clinical trials for RSV, GBS, norovirus, and chikungunya vaccines, emphasizing the importance of targeting vulnerable populations and addressing global health challenges. Furthermore, the review discusses the implications of precision vaccinology, immunoengineering, and equitable vaccine distribution in shaping the future of public health. By synthesizing diverse perspectives and recent research findings, this article contributes to the discourse on vaccine innovation and underscores the critical role of vaccines in disease prevention and global health security.

Keywords: Vaccine, mRNA, Viral Vectors, Immunoengineering, Infectious Disease

INTRODUCTION

In the aftermath of the COVID-19 pandemic, there was an extraordinary hastening in the development and dissemination of vaccines, sparking a revitalization in vaccine technology [1]. However, the advancements in vaccine technology extend far beyond the realm of pandemic response, encompassing a diverse array of innovative approaches aimed at combating a spectrum of infectious diseases and even extending to novel applications in oncology and immunotherapy. Recent developments in vaccine technology have not only revolutionized preventive healthcare but have also paved the way for groundbreaking discoveries in the fields of immunology, molecular biology, and bioengineering [2].

***Author for Correspondence**
Satish Kumar Sarankar
E-mail: satish.sarankar@gmail.com

[1]Professor and Principal, Faculty of Pharmacy, Mansarovar Global University, Sehore, Madhya Pradesh, India
[2]Associate Professor, Faculty of Pharmacy, Mansarovar Global University, Sehore, Madhya Pradesh, India
[3]Assistant Professor, Faculty of Pharmacy, Mansarovar Global University, Sehore, Madhya Pradesh, India
[4]Associate Professor, School of Pharmacy, LNCT University, Bhopal, Madhya Pradesh, India

Received Date: March 20, 2024
Accepted Date: March 21, 2024
Published Date: March 30, 2024

Citation: Satish Kumar Sarankar, Santosh Ojha, Brajesh Rajak, Sushma Somkuwar. Innovative Vaccine Technologies: Current Landscape and Future Prospects in Preventive Medicine. International Journal of Vaccines. 2024; 1(2): 7–15p.

One of the most notable breakthroughs in vaccine technology is the advent of mRNA vaccines, exemplified by the highly successful Pfizer-BioNTech and Moderna COVID-19 vaccines [3, 4]. These vaccines represent a paradigm shift in vaccine design, leveraging the body's own cellular machinery to produce specific antigens and stimulate robust immune responses. The unprecedented speed with which mRNA vaccines were developed and deployed underscores the transformative potential of this technology, offering a blueprint for rapid response to emerging infectious threats [5].

In addition to mRNA vaccines, viral vector vaccines have emerged as a potent tool in the fight

against infectious diseases. By genetically modifying harmless viruses to express target antigens, viral vector vaccines can elicit strong and durable immune responses. The Oxford-AstraZeneca COVID-19 vaccine, based on a chimpanzee adenovirus vector, exemplifies the versatility and scalability of this approach [6]. Moreover, ongoing research aims to refine viral vector platforms, enhance immunogenicity, and broaden their applicability to a diverse range of pathogens.

Beyond conventional vaccine platforms, innovative strategies such as virus-like particles (VLPs), protein subunit vaccines, and recombinant DNA vaccines are also driving advancements in vaccine technology. VLPs mimic the structure of viruses without containing genetic material, offering a safe and highly immunogenic platform for vaccine development. Similarly, protein subunit vaccines utilize specific protein components of pathogens to induce immune responses, circumventing the need for live or inactivated viruses. Furthermore, recombinant DNA vaccines harness genetic engineering techniques to introduce antigen-encoding DNA sequences into host cells, triggering potent immune responses [7–9].

The convergence of bioinformatics, structural biology, and computational modeling has facilitated the rational design of vaccines, accelerating the identification of antigenic targets and the optimization of vaccine formulations. Furthermore, advances in manufacturing technologies, such as cell culture-based production systems and synthetic biology approaches, are enhancing vaccine scalability, affordability, and global accessibility. In addition to infectious disease prevention, vaccine technology is poised to revolutionize other fields of medicine, including cancer immunotherapy and personalized medicine. Cancer vaccines, designed to stimulate the immune system to recognize and destroy tumor cells, hold promise for improving outcomes in various malignancies. Moreover, emerging platforms such as neoantigen vaccines, which target tumor-specific mutations, offer a tailored approach to cancer treatment, potentially transforming the landscape of oncology [10–12].

Recent developments in vaccine technology represent a convergence of scientific ingenuity, technological innovation, and global collaboration. From mRNA vaccines to viral vectors and beyond, these advancements are reshaping the landscape of preventive healthcare and opening new frontiers in disease control and eradication. As we continue to navigate the challenges of infectious diseases and explore the therapeutic potential of vaccines, the future holds immense promise for further breakthroughs and transformative discoveries.

RECENT BREAKTHROUGHS: NEWLY DEVELOPED VACCINES FOR DIVERSE DISEASES

COVID-19 Vaccines

- *Pfizer-BioNTech COVID-19 vaccine:* Utilizes mRNA technology to trigger an immune response against the spike protein of the SARS-CoV-2 virus.
- *Moderna COVID-19 vaccine:* Similar to the Pfizer-BioNTech vaccine, it also employs mRNA technology to induce immunity against the spike protein of the virus.
- *Johnson & Johnson COVID-19 vaccine:* Uses a viral vector (adenovirus type 26) to deliver genetic instructions for producing the spike protein, prompting an immune response [13].

mRNA vaccines encode a portion of the virus's genetic material (in this case, the spike protein of SARS-CoV-2) within lipid nanoparticles, which are injected into the body to prompt an immune response. These vaccines are delivered via intramuscular injection. The Pfizer-BioNTech vaccine necessitates two doses, spaced 21 days apart, while the Moderna vaccine mandates two doses, with an interval of 28 days between administrations [14]. High efficacy rates reported in clinical trials, exceeding 90% in preventing COVID-19 infection and severe illness for these vaccines. Viral Vector COVID-19 Vaccine utilizes a non-replicating adenovirus vector (adenovirus type 26) to deliver genetic instructions for producing the spike protein of SARS-CoV-2 and administeredas single-dose intramuscular injection [15]. It demonstrated high efficacy in preventing severe COVID-19 illness and hospitalization, with slightly lower overall efficacy compared to mRNA vaccines.

Ebola Virus Vaccine

- *Merck's rVSV-ZEBOV vaccine:* Utilizes a recombinant vesicular stomatitis virus (rVSV) vector to deliver Ebola virus glycoprotein, eliciting an immune response against the Ebola virus.

Recombinant vesicular stomatitis virus (rVSV) vector carrying the Ebola virus glycoprotein gene, triggering an immune response against Ebola virus, administered as intramuscular injection as single dose regimen [16]. It demonstrated efficacy in preventing Ebola virus infection during outbreaks in Africa, with high levels of protection observed in clinical trials.

Human Papillomavirus (HPV) Vaccine

- Gardasil 9 offers defense against nine types of HPV, encompassing those linked to cervical, vulvar, vaginal, and anal cancers, along with genital warts.

Virus-like particles (VLPs) composed of viral capsid proteins that resemble HPV, inducing an immune response against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58. It is administered as intramuscular injection, typically administered as a two- or three-dose series, depending on age at initial vaccination. It exhibits high effectiveness in preventing HPV infection and the related cancers, providing safeguarding against genital warts, as well as cervical, vulvar, vaginal, and anal cancers [17, 18].

Zika Virus Vaccine

- *VLA1601:* Developed by Valneva SE, is an inactivated vaccine against Zika virus, designed to prevent Zika virus infection and associated complications.

This inactivated vaccine comprises entire Zika virus particles that have undergone chemical or physical inactivation to render them non-infectious. It is administered via intramuscular injection, and the dosage regimen may vary depending on clinical trials and recommendations [19–20]. Its efficacy data may vary depending on clinical trials and development stage.

Dengue Fever Vaccine

- *Dengvaxia (CYD-TDV):* Developed by Sanofi Pasteur, it's the first licensed vaccine for dengue fever, providing protection against all four dengue virus serotypes [21, 22].

Live attenuated vaccine containing weakened forms of all four dengue virus serotypes, administeredas subcutaneous injection typically three-dose series at six-month intervals. It offers protection against all four serotypes of the dengue virus, with differing levels of effectiveness against each serotype.

Malaria Vaccine

- *RTS,S/AS01 (Mosquirix):* Developed by GlaxoSmithKline, it's the first malaria vaccine approved for use, targeting the Plasmodium falciparum parasite, which causes the deadliest form of malaria.

The subunit vaccine consists of the RTS,S antigen, comprising a segment of the Plasmodium falciparum circumsporozoite protein fused with a hepatitis B surface antigen [23, 24]. As intramuscular injection, typically it is administered as a four-dose series, with an initial dose followed by three booster doses. It has moderate efficacy in preventing clinical and severe malaria, particularly in young children.

Shingles Vaccine

- Shingrix, created by GlaxoSmithKline, is a recombinant subunit vaccine designed to offer robust protection against shingles (herpes zoster) in individuals aged 50 and above.

Recombinant subunit vaccine composed of glycoprotein E (gE) antigen and an adjuvant system (AS01B) to enhance immune response [11]. It is administered through intramuscular injection in a two-dose series, with the second dose typically given 2 to 6 months following the initial dose. It has high efficacy in preventing shingles and related complications, with long-lasting protection.

Typhoid Fever Vaccine

- *Typbar TCV:* Developed by Bharat Biotech, it's a typhoid conjugate vaccine (TCV) that offers longer-lasting immunity and requires fewer doses compared to older typhoid vaccines.
- Conjugate vaccine composed of Vi capsular polysaccharide of Salmonella Typhi conjugated to a carrier protein, administered as intramuscular injection in single-dose regimen. It has high efficacy in preventing typhoid fever, with long-lasting protection [25–26].

These examples demonstrate the diversity of vaccine technologies and their applications in preventing a wide range of infectious diseases, from viral infections like COVID-19 and Ebola to bacterial diseases like typhoid fever.

VACCINE DEVELOPMENT TECHNOLOGIES: AN OVERVIEW

mRNA-based Vaccines (Such as those Developed by Pfizer-BioNTech and Moderna for COVID-19)

Messenger RNA (mRNA) vaccines work by introducing genetic material (mRNA) into cells, instructing them to produce a protein that triggers an immune response. For COVID-19 vaccines, the mRNA carries instructions for producing the spike protein found on the surface of the SARS-CoV-2 virus. Lipid nanoparticles encapsulate the mRNA, facilitating its delivery into host cells [27]. After entering the cells, the mRNA is translated into the spike protein, prompting the immune system to generate antibodies targeting the virus.

Viral Vector-based Vaccines (Like the Johnson and Johnson COVID-19 Vaccine)

Viral vector vaccines utilize a benign virus, acting as a vector, to transport genetic material containing the desired antigen. In this instance, adenovirus vectors are altered to contain the gene responsible for the spike protein of SARS-CoV-2. Once inside host cells, the adenovirus vector delivers this genetic material, directing the cells to manufacture the spike protein. Recognizing the spike protein as foreign, the immune system initiates a response, offering defense against potential future encounters with the virus [28].

Recombinant Vesicular Stomatitis Virus (rVSV) Vector Vaccine (Merck's rVSV-ZEBOV Ebola Vaccine)

This vaccine uses a live, attenuated vesicular stomatitis virus (VSV) as a vector to deliver the Ebola virus glycoprotein gene. The VSV vector has been modified to be non-pathogenic in humans. Once administered, the VSV vector expresses the Ebola virus glycoprotein, prompting the immune system to generate protective antibodies against Ebola virus infection [29].

Inactivated Vaccines (VLA1601 Zika Virus Vaccine)

Inactivated vaccines comprise virus particles that have been deactivated or rendered inactive, preventing them from causing illness. These vaccines typically induce an immune response against the whole virus. The Zika virus is grown in cell culture and then chemically or physically inactivated to create the vaccine [30]. Upon administration, the inactivated virus triggers the immune system to generate antibodies targeting the Zika virus.

Recombinant Subunit Vaccine (Shingrix Shingles Vaccine)

Recombinant subunit vaccines contain specific protein subunits of a pathogen rather than the whole organism. These vaccines are formulated to elicit an immune response against crucial antigens. Shingrix, for example, contains recombinant glycoprotein E (gE) derived from the varicella-zoster virus, which is responsible for causing shingles [31]. The purified protein is combined with an adjuvant to enhance the immune response when administered.

Conjugate Vaccine (Typbar TCV Typhoid Fever Vaccine)

Conjugate vaccines link a polysaccharide antigen from a pathogen to a carrier protein, enhancing the immune response, especially in infants and young children. Typbar TCV is a conjugate vaccine where

the Vi polysaccharide antigen of Salmonella typhi, the bacterium that causes typhoid fever, is conjugated to a carrier protein [32]. This linkage improves the immune response and increases the vaccine's efficacy [Table 1]..

Table 1 : A summary of some technologies that pharmaceutical and vaccine companies are currently working on:

Technology	Description
mRNA vaccines	Utilizes messenger RNA (mRNA) to instruct cells to produce viral proteins, triggering an immune response against specific pathogens.
Viral vector vaccines	Uses modified viruses as vectors to deliver genetic material encoding antigens, stimulating immune responses against targeted pathogens.
Protein subunit vaccines	Utilizes purified proteins or fragments of pathogens to induce an immune response without the risk of causing disease.
DNA vaccines	Administers DNA encoding antigens directly into cells, prompting the production of antigenic proteins and subsequent immune responses.
Live attenuated vaccines	Contains weakened or attenuated forms of pathogens that can still replicate but are less virulent, leading to the induction of strong and long-lasting immune responses.
Inactivated vaccines	Comprises pathogens that have been killed or inactivated, unable to cause disease but still capable of eliciting an immune response.
Nanoparticle vaccines	Utilizes nanoparticles as carriers to deliver antigens, enhancing vaccine stability, immunogenicity, and targeted delivery to immune cells.
Virus-like particle (VLP) vaccines	Mimics the structure of viruses without containing genetic material, offering a safe and highly immunogenic platform for vaccine development.
Recombinant vector vaccines	Employs non-replicating viruses or bacteria as vectors to deliver antigen-encoding genes, triggering immune responses against targeted pathogens.
Conjugate vaccines	Links antigens from pathogens to carrier proteins, enhancing the immune response, particularly in infants and young children.
Adjuvanted vaccines	Includes adjuvants, substances that enhance the body's immune response to antigens, thereby improving vaccine efficacy and duration of protection.

ADVANCEMENTS IN VACCINE DEVELOPMENT ACROSS MULTIPLE INFECTIOUS DISEASES

There are ongoing endeavors aimed at transforming vaccine development for a wide range of infectious diseases. A universal influenza vaccine is in development, aiming to confer long-lasting immunity against multiple strains of influenza viruses, thus obviating the need for annual flu shots. Similarly, scientists are diligently working on an effective vaccine against HIV, the causative agent of AIDS, with several candidate vaccines progressing through preclinical and early clinical trials, seeking to elicit broad and enduring immune responses against HIV [33]. In the realm of malaria prevention, ongoing research is focused on enhancing the efficacy and durability of existing vaccines like RTS,S/AS01 (Mosquirix), while also pursuing the development of next-generation vaccines targeting various stages of the malaria parasite's lifecycle [34]. New tuberculosis vaccine candidates are also being developed to overcome the limitations of the current Bacille Calmette-Guerin (BCG) vaccine, with the aim of providing enhanced protection against pulmonary and extrapulmonary forms of TB [35]. Clinical trials for respiratory syncytial virus (RSV) vaccines are underway, particularly targeting vulnerable populations such as infants, young children, and older adults, who are at heightened risk of severe RSV infections.

Furthermore, efforts are being dedicated to developing a vaccine against Group B Streptococcus, a major cause of sepsis and meningitis in newborns, with a focus on pregnant women to safeguard both mothers and infants. Research into a norovirus vaccine is also ongoing, given its role in gastroenteritis outbreaks worldwide, especially in confined settings like cruise ships and healthcare facilities [36]. Additionally, vaccine candidates against chikungunya virus, responsible for fever and debilitating joint pain, are progressing through preclinical and clinical stages, with the aim of preventing outbreaks in regions where the virus is endemic or emergent. These collaborative efforts highlight the persistent

drive towards innovative solutions in combating infectious diseases and enhancing global public health outcomes.

INSIGHTS INTO THE POTENTIAL ADVANTAGES OF NEW VACCINE TECHNOLOGIES AND DEVELOPMENTS

1. *Enhanced efficacy:* Advances in vaccine design and technology may lead to vaccines with improved efficacy, providing better protection against target pathogens. This could include vaccines that induce broader and longer-lasting immune responses, reducing the risk of breakthrough infections [37].
2. *Increased safety profiles:* New vaccine platforms and manufacturing techniques may result in vaccines with improved safety profiles, minimizing adverse reactions and side effects. Enhanced safety features could increase public confidence in vaccination and reduce hesitancy [38].
3. *Reduced dosing schedules:* Novel vaccine formulations and delivery methods may allow for reduced dosing schedules, such as single-dose vaccines or vaccines requiring fewer booster shots. Streamlined vaccination schedules could improve convenience and compliance, especially in resource-limited settings.
4. *Improved stability and storage:* Innovations in vaccine formulation and stabilization technologies may lead to vaccines that are more stable at various temperatures and storage conditions. Improved stability could aid in the distribution and storage of vaccines, especially in areas lacking adequate refrigeration or cold chain infrastructure.
5. *Broader coverage against variants:* Vaccine designs that target conserved regions of pathogens or induce cross-reactive immune responses may offer broader protection against emerging variants of concern. This could mitigate the impact of viral mutations and reduce the need for frequent vaccine updates [39].
6. *Customized vaccines for specific populations:* Advancements in personalized medicine and vaccine development techniques may enable the creation of vaccines tailored to specific populations, such as age groups, immunocompromised individuals, or individuals with genetic predispositions. Customized vaccines could optimize immune responses and improve outcomes in vulnerable groups [40].
7. *Novel therapeutic applications:* Beyond infectious disease prevention, new vaccine technologies may have therapeutic applications in areas such as cancer immunotherapy, autoimmune disorders, and chronic diseases. Therapeutic vaccines have the potential to provide precise treatment alternatives with reduced side effects when compared to conventional therapies.
8. *Global health equity:* Efforts to develop affordable, accessible, and scalable vaccine technologies may contribute to greater equity in global health, ensuring that life-saving vaccines reach underserved communities worldwide. Increased accessibility could help address disparities in healthcare and reduce the burden of infectious diseases in low-resource settings.

These potential advantages highlight the transformative impact that ongoing research and innovation in vaccine development may have on public health outcomes, disease prevention, and healthcare delivery in the years ahead.

FUTURE TECHNOLOGY AND ADVANCEMENT EXPECTATIONS IN VACCINES

The future of vaccine technology holds great promise, with several exciting advancements on the horizon. Here are some expectations for future technology and advancements in vaccines:

1. *Next-generation vaccine platforms:* Researchers are exploring innovative vaccine platforms beyond mRNA and viral vectors, such as DNA vaccines, nanotechnology-based vaccines, and virus-like particles (VLPs). These platforms offer unique advantages, including improved immunogenicity, stability, and ease of manufacturing.
2. *Universal vaccines:* Initiatives are in progress to create universal vaccines that can offer extensive protection against various strains or entire categories of pathogens. For instance, universal influenza vaccines target conserved sections of the virus, aiming to provide enduring immunity across a range of strains and diminishing the necessity for yearly vaccine adjustments.

3. *Precision vaccinology:* Progress in genomics, proteomics, and bioinformatics is propelling the advancement of personalized vaccines customized to individual genetic profiles, immune reactions, and susceptibilities to diseases. Personalized vaccine approaches hold the potential to optimize vaccine efficacy, minimize adverse reactions, and improve outcomes in diverse populations [41].
4. *Targeting emerging infectious diseases:* With the increasing threat of emerging infectious diseases, there is a growing focus on rapid-response vaccine platforms capable of quickly adapting to novel pathogens. Flexible vaccine technologies, such as modular vaccine platforms and synthetic biology approaches, enable rapid antigen design and production, facilitating timely responses to emerging threats [42].
5. *Immunoengineering and immunomodulation:* Immunoengineering strategies aim to enhance vaccine efficacy by precisely tuning immune responses, optimizing antigen presentation, and modulating immune pathways. Novel adjuvants, immune stimulants, and delivery systems are being developed to enhance vaccine potency, durability, and breadth of protection [43].
6. *Innovative delivery systems:* Advances in vaccine delivery systems, including microneedle patches, oral and intranasal vaccines, and implantable devices, offer alternative routes of administration, improved patient compliance, and enhanced mucosal immunity. These technologies enable needle-free vaccination and facilitate targeted delivery to mucosal surfaces, where many pathogens enter the body [44].
7. *Combination vaccines and therapeutic vaccines:* Combination vaccines that target multiple diseases simultaneously or provide both preventive and therapeutic benefits are gaining traction. Therapeutic vaccines for chronic infectious diseases, cancer, and autoimmune disorders harness the immune system to treat existing conditions, offering potential breakthroughs in disease management and treatment [45].
8. *Global access and equity:* Efforts to improve vaccine accessibility, affordability, and distribution worldwide are ongoing, with initiatives focused on advancing vaccine manufacturing capacity, supply chain logistics, and equitable distribution mechanisms. Effective collaboration among governments, pharmaceutical companies, and international organizations is essential to guaranteeing worldwide access to vaccines that save lives.

In general, the trajectory of vaccine technology is marked by innovation, collaboration, and a dedication to tackling global health obstacles. With continued research, investment, and collaboration, vaccines will remain indispensable tools in preventing infectious diseases, improving public health, and advancing human well-being worldwide.

REFERENCES

1. Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., Huang, B., Shi, W., Lu, R., Niu, P., Zhan, F., Ma, X., Wang, D., Xu, W., Wu, G., Gao, G. F., & Tan, W. (2020). A novel coronavirus from patients with pneumonia in China, 2019. New England Journal of Medicine, 382(8), 727–733.
2. Gully, P. R. (2020). Pandemics, regional outbreaks, and sudden-onset disasters. Healthcare Management Forum, 33(4), 164–169.
3. Ball, P. (2021). The lightning-fast quest for COVID vaccines-and what it means for other diseases. Nature, 589(7841), 16–18.
4. WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation. (2021). Placebo-controlled trials of Covid-19 vaccines-why we still need them. New England Journal of Medicine, 384(2), e2.
5. Fu, W., Sivajohan, B., McClymont, E., et al. (2022). Systematic review of the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnant and lactating individuals and their infants. International Journal of Gynaecology and Obstetrics, 156, 406-417.
6. Donders, G. G. G., Grinceviciene, S., Haldre, K., et al. (2021). ISIDOG Consensus Guidelines on COVID-19 Vaccination for Women before, during and after Pregnancy. Journal of Clinical Medicine, 10, 2902.

7. Global Preparedness Monitoring Board. (2019). A World at Risk: Annual Report on Global Preparedness for Health Emergencies. Geneva, Switzerland: World Health Organization. Licence: CC BY-NC-SA 3.0 IGO.
8. Alvim, R. G., Itabaiana, I. Jr., & Castilho, L. R. (2019). Zika virus-like particles (VLPs): stable cell lines and continuous perfusion processes as a new potential vaccine manufacturing platform. Vaccine, 37, 6970–6977.
9. He, L., De Val, N., Morris, C. D., Vora, N., Thinnes, T. C., Kong, L., et al. (2016). Presenting native-like trimeric HIV-1 antigens with self-assembling nanoparticles. Nature Communications, 7, 1–15.
10. Lu, L., Duong, V. T., Shalash, A. O., Skwarczynski, M., & Toth, I. (2021). Chemical conjugation strategies for the development of protein-based subunit nanovaccines. Vaccines, 9, 563.
11. Stphen, S. L., Beales, L., Peyret, H., Roe, A., Stonehouse, N. J., & Rowlands, D. J. (2018). Recombinant expression of tandem–HBc virus-like particles (VLPs). In C. Wege & G. Lomonossoff (Eds.), Virus-Derived Nanoparticles for Advanced Technologies (pp. 97–123). Humana Press.
12. Uddin, M. N., Henry, B., Carter, K. D., Roni, M. A., &Kouzi, S. S. (2019). A novel formulation strategy to deliver combined DNA and VLP based HPV vaccine. Journal of Pharmacy & Pharmaceutical Sciences, 22, 536–547.
13. Rosenblum, H. G., Hadler, S. C., Moulia, D., et al. (2021). Use of COVID-19 vaccines after reports of adverse events among adult recipients of Janssen (Johnson & Johnson) and mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna): update from the Advisory Committee on Immunization Practices—United States, July 2021. MMWR. Morbidity and Mortality Weekly Report, 70, 1094–1099.
14. Wang, W., Huang, B., Zhu, Y., Tan, W., & Zhu, M. (2021). Ferritin nanoparticle-based SARS-CoV-2 RBD vaccine induces a persistent antibody response and long-term memory in mice. Cellular & Molecular Immunology, 18, 749–751.
15. Zak, M. M., & Zangi, L. (2021). Lipid nanoparticles for organ-specific mRNA therapeutic delivery. Pharmaceutics, 13, 1675.
16. Claude, K. M., Underschultz, J., & Hawkes, M. T. (2018). Ebola virus epidemic in war-torn eastern DR Congo. The Lancet, 392, 1399–1401.
17. Burley, M., Roberts, S., & Parish, J. L. (2020). Epigenetic regulation of human papillomavirus transcription in the productive virus life cycle. Seminars in Immunopathology, 42, 159–171.
18. Diamos, A. G., Larios, D., Brown, L., Kilbourne, J., Kim, H. S., Saxena, D., et al. (2019). Vaccine synergy with virus-like particle and immune complex platforms for delivery of human papillomavirus L2 antigen. Vaccine, 37, 137–144.
19. Garg, H., Mehmetoglu-Gurbuz, T., & Ruddy, G. M., Joshi, A. (2019). Capsid containing virus like particle vaccine against Zika virus made from a stable cell line. Vaccine, 37, 7123–7131.
20. Vouga, M., Musso, D., Goorhuis, A., Freedman, D. O., & Baud, D. (2018). Updated Zika virus recommendations are needed. The Lancet, 392(10150), 818-819.
21. Paixao, E. S., Teixeira, M. G., & Rodrigues, L. C. (2018). Zika, chikungunya and dengue: The causes and threats of new and re-emerging arboviral diseases. BMJ Global Health, 3, e000530.
22. Prompetchara, E., Ketloy, C., Thomas, S. J., &Ruxrungtham, K. (2020). Dengue vaccine: Global development update. Asian Pacific Journal of Allergy and Immunology, 38, 178–185.
23. Lee, D. H., Chu, K. B., Kang, H. J., Lee, S. H., Chopra, M., Choi, H. J., et al. (2019). Protection induced by malaria virus-like particles containing codon-optimized AMA-1 of Plasmodium berghei. Malaria Journal, 18, 1–12.
24. Janitzek, C. M., Peabody, J., Thrane, S., Carlsen, P. H., Theander, T. G., Salanti, A., et al. (2019). A proof-of-concept study for the design of a VLP-based combinatorial HPV and placental malaria vaccine. Scientific Reports, 9, 5260.
25. Yousafzai, M. T., et al. (2019). Ceftriaxone-resistant Salmonella Typhi outbreak in Hyderabad City of Sindh, Pakistan: High time for the introduction of typhoid conjugate vaccine. Clinical Infectious Diseases, 68, S16–S21.

26. Andrews, J. R., et al. (2019). Typhoid conjugate vaccines: A new tool in the fight against antimicrobial resistance. The Lancet Infectious Diseases, 19, e26–e30.
27. Baden, L. R., et al. (2021). Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. New England Journal of Medicine, 384, 403–416.
28. Zellweger, R. M., Wartel, T. A., Marks, F., Song, M., & Kim, J. H. (2020). Vaccination against SARS-CoV-2 and disease enhancement - knowns and unknowns. Expert Review of Vaccines, 19, 691–698.
29. Liu, C.-H., Hu, Y.-T., Wong, S. H., & Lin, L.-T. (2022). Therapeutic strategies against Ebola virus infection. Viruses, 14(3), 579.
30. Shehu, N. Y., Shwe, D., Onyedibe, K. I., Pam, V. C., Abok, I., Isa, S. E., & Egah, D. Z. (2018). Pathogenesis, diagnostic challenges and treatment of Zika virus disease in resource-limited settings. Nigerian Postgraduate Medical Journal, 25(2), 67-72.
31. Low, J. M., Gu, Y., Ng, M. S. F., et al. (2021). Codominant IgG and IgA expression with minimal vaccine mRNA in milk of BNT162b2 vaccinees. NPJ Vaccines, 6, 105.
32. Klemm, E. J., et al. (2018). Emergence of an extensively drug-resistant Salmonella enterica serovar Typhi clone harboring a promiscuous plasmid encoding resistance to fluoroquinolones and third-generation cephalosporins. mBio, 9, e00105–18.
33. D'Souza, M. P., & Frahm, N. (2010). Adenovirus 5 serotype vector-specific immunity and HIV-1 infection: A tale of T cells and antibodies. AIDS, 24, 803–809.
34. van Riel, D., & de Wit, E. (2020). Next-generation vaccine platforms for COVID-19. Nature Materials, 19, 810–812.
35. Dhanasooraj, D., Kumar, R. A., &Mundayoor, S. (2016). Subunit protein vaccine delivery system for tuberculosis based on hepatitis B virus core VLP (HBc-VLP) particles. In M. S. Islam (Ed.), Methods in Molecular Biology (pp. 377–92). Humana Press Inc.
36. Hall, A. J., et al. (2013). Norovirus disease in the United States. Emerging Infectious Diseases, 19, 1198–1205.
37. Gatti-Mays, M. E., Redman, J. M., Collins, J. M., &Bilusic, M. (2017). Cancer vaccines: Enhanced immunogenic modulation through therapeutic combinations. Human Vaccines &Immunotherapeutics, 13, 2561–2574.
38. Heath, P. T., et al. (2021). Safety and efficacy of NVX-CoV2373 Covid-19 vaccine. New England Journal of Medicine, 385, 1172–1183.
39. Van Oosten, L., et al. (2021). Two-component nanoparticle vaccine displaying glycosylated spike S1 domain induces neutralizing antibody response against SARS-CoV-2 variants. mBio, 12(4), e01813-21.
40. Aurisicchio, L., Pallocca, M., Ciliberto, G., & Palombo, F. (2018). The perfect personalized cancer therapy: Cancer vaccines against neoantigens. Journal of Experimental & Clinical Cancer Research, 37, 86.
41. Berlanda Scorza, F., Tsvetnitsky, V., & Donnelly, J. J. (2016). Universal influenza vaccines: Shifting to better vaccines. Vaccine, 34, 2926–2933.
42. Bremer, P. T., et al. (2016). Combatting Synthetic Designer Opioids: A Conjugate Vaccine Ablates Lethal Doses of Fentanyl Class Drugs. AngewandteChemie International Edition, 55, 3772–3775.
43. Guo, J., et al. (2019). Immunogenicity of a virus-like-particle vaccine containing multiple antigenic epitopes of Toxoplasma gondii against acute and chronic toxoplasmosis in mice. Frontiers in Immunology, 10, 592.
44. Lorenzer, C., Dirin, M., Winkler, A. M., Baumann, V., & Winkler, J. (2015). Going beyond the liver: Progress and challenges of targeted delivery of siRNA therapeutics. Journal of Controlled Release, 203, 1–15.
45. Gatti-Mays, M. E., Redman, J. M., Collins, J. M., &Bilusic, M. (2017). Cancer vaccines: Enhanced immunogenic modulation through therapeutic combinations. Human Vaccines &Immunotherapeutics, 13, 2561–2574.

