Perspective

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Comparative Immunogenicity of mRNA and Viral Vector Vaccines in Preventing SARS-CoV-2 Reinfection

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Introduction

Since the onset of the COVID-19 pandemic, vaccination has been the cornerstone of global public health efforts to curb the spread of SARS-CoV-2. Among the various vaccine platforms, mRNA-based vaccines (such as Pfizer-BioNTech's BNT162b2 and Modern's mRNA-1273) and viral vector vaccines (such as AstraZeneca's ChAdOx1 nCoV-19 and Johnson & Johnson's Ad26.COV2.S) have demonstrated remarkable efficacy in reducing infection rates, hospitalizations, and deaths. However, as new variants emerge and population immunity evolves, understanding the comparative immunogenicity of these vaccine platforms is critical to optimizing booster strategies and predicting long-term protection. Immunogenicity encompasses both humoral and cellular immune responses, which together determine vaccine-induced protection against reinfection [1].

Description

mRNA vaccines represent a novel class of immunization technology that delivers lipid nanoparticle-encapsulated messenger RNA encoding the SARS-CoV-2 spike protein. Once inside host cells, this mRNA is translated into spike antigen, triggering robust immune activation. Studies have shown that mRNA vaccines elicit higher neutralizing antibody titers compared to viral vector vaccines, particularly against early variants such as Alpha and Delta.

Moreover, these vaccines induce potent germinal center reactions, leading to the generation of high-affinity, long-lived plasma cells and memory B cells. The mRNA platform also promotes a strong $CD4^+$ T-cell response, particularly Th1-type cytokines such as IFN-γ and IL-2, which are crucial for antiviral defense. However, mRNA-induced immunity tends to wane over time, necessitating booster doses to maintain protection against emerging variants like Omicron [2].

Viral vector vaccines, by contrast, employ non-replicating adenoviruses to deliver DNA encoding the spike protein, resulting in both humoral and cellular immune activation. Although antibody titers from viral vector vaccines are typically lower than those from mRNA vaccines, they generate stronger $CD8^+$ cytotoxic T-cell responses, which are essential for eliminating infected cells and conferring cross-variant protection. This difference may explain why viral vector vaccines maintain moderate efficacy even against variants that partially escape antibody neutralization. Additionally, viral vectors may induce innate immune stimulation through Pattern Recognition Receptors (PRRs), providing an adjuvant-like effect [3].

However, pre-existing immunity to the vector (such as adenoviruses) can attenuate vaccine efficacy, and concerns over rare adverse effects, including Vaccine-Induced Thrombotic Thrombocytopenia (VITT), have prompted more cautious use. These challenges have accelerated the shift toward next-generation platforms that minimize vector-related limitations.

Comparative studies suggest that heterologous vaccination combining an mRNA and a viral vector vaccine can achieve superior immunogenicity, providing the advantages of both platforms. This mixed approach enhances both neutralizing antibodies and T-cell responses, offering broader and more durable protection. As SARS-CoV-2 continues to evolve, understanding the immunological profiles of these vaccine types will guide booster strategies, inform variant-specific vaccine updates, and strengthen pandemic preparedness [4,5].

Conclusion

Both mRNA and viral vector vaccines have proven effective in preventing severe COVID-19, yet they differ in their immunogenicity profiles. mRNA vaccines induce strong antibody-mediated immunity, while viral vector vaccines elicit more pronounced T-cell responses. Together, these complementary immune mechanisms have shaped global vaccine strategies. Continued surveillance of immune responses, particularly in the context of reinfection and variant evolution, remains vital.

Acknowledgement

None

Conflict of Interest

None

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