CHAPTER

5

Recent and advanced nano-technological strategies for COVID-19 vaccine development

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1 Introduction

The coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is one of the most difficult health crises that humanity has faced in recent years. The pandemic has affected millions of people across the globe causing harm to humans as well as the economies of nations. Several public health strategies such as the use of masks, social distancing, regular washing of hands as well as contact tracing, have been employed since the beginning of the outbreak to curtail the spread of the virus. However, these practices have not been able to completely prevent the widespread of the pandemic (Young, Thone, & Jik, 2021). Despite the tireless efforts of researchers and scientists all over the world, there is as of now, still, no cure for COVID-19, although the United States Food and Drugs Administration (FDA) recently approved the use of remdesivir for treatment, especially in severe cases of viral infection (Campos et al., 2020). The outbreak of the pandemic has stretched the limits of healthcare systems and challenged the management of the situation using conventional tools in the development

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virulence genes. The mutants lose their pathogenicity property in the host cells but can replicate to a limited extent. Several genes possessed by coronaviruses are not required for replication and these genes can be deleted, leading to attenuation in vivo. Various non-structural proteins and structural E proteins can be deleted to yield vaccine strains of several coronaviruses. Deletion of the E protein leads to attenuation and generation of an efficacious vaccine strain (Almazán et al., 2013; Netland et al., 2010). There can be a problem of reversion of the attenuated strain to the virulent strain (Jimenez-Guardeño et al., 2015). Therefore, the deletion of virulence genes may provide a more effective mechanism of attenuation.

Codon deoptimization is another efficient approach to viral attenuation. The nucleic acid sequence is modified to use suboptimal codon pairs to encode the wild-type amino acid sequence, which considerably slows the translation of the viral protein during infection. This approach can produce a replication-competent but highly attenuated strain in vivo (Mueller et al., 2020). The recoded virus has an antigenic property similar to that of its pathogenic parents. Consequently, the attenuated viruses induce immune responses that are identical to those of virulent strains (Mueller et al., 2020).

The inability of the attenuated strain to revert genetically to become pathogenic is an important consideration in the generation of a live attenuated vaccine. Coronaviruses are known to often recombine in nature and this makes the development of an attenuated live vaccine against SARS-CoV-2 challenging. The attenuated strain could recombine with other wild coronaviruses resulting in a fully virulent strain. One of the drawbacks of live attenuated viruses is the use of exhaustively long cell or animal cultures in their development. Also, pre-existing cross-reactive immunity resulting from natural exposure with other human coronaviruses could limit the efficacy of SARS-CoV-2 vaccines developed using this platform. Another disadvantage of this technique is that attenuated vaccines cannot be given to immune-compromised persons since the attenuated agent would find a niche to multiply uncontrollably and, on rare occasions, revert to a wild-type phenotype, resulting in severe disease. As a result of these drawbacks, only two live attenuated SARS-CoV-2 vaccine candidates have reached clinical trials as seen in Table 1 (World Health Organization, 2021).

4.2 Inactivated pathogen vaccines

Viruses inactivated through physical and chemical means have been used successfully in human vaccines against hepatitis A, polio, and influenza (Murdin, Barreto, & Plotkin, 1996; Vellozzi et al., 2009). In this platform, a dead form of the pathogen is used, thus ensuring a better safety profile than live attenuated vaccines. During the inactivation process using chemicals, heat, or radiation, some of these vaccine strains lose their immunogenicity making this platform less efficient than live attenuated pathogen immunization. Moreover, inactivated pathogen vaccines are poor inducers of cytotoxic $CD8^+$ T cells, which are necessary for an effective COVID-19 vaccine. Inactivated viral vaccines require an adjuvant which are compounds that enhance and amplify the immune responses to the presence of an