

Next Generation Vaccine Development

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DESCRIPTION

The mRNA vaccine has a protective effect of 90% or more against COVID-19. The underlying mechanism involves the introduction of the spike protein into the host cell, suggesting that an immune response to spike protein may provide effective protection. However, the mutagenicity of spike protein raises questions about the duration of vaccination protection and future vaccine efficacy. D614G (102), Cluster 5, B.1.1.7 "N501Y.V1" that appeared in late January 2020 after the start of the COVID-19 epidemic discovered in Mink, Denmark from June to August 2020. The species was discovered as "B.1.351" 501Y.V2 "(104), which was reported in the United Kingdom on December 14, 2020. With the exception of cluster 5, the remaining three mutants significantly increased the infectivity of the virus. Studies impaired the ability of convalescent sera to neutralize B.1.351, but mutant B.1.1.7 remained sensitive to neutralizing antibodies induced by the hereditary spike vaccine. Concerns remain as to whether first-generation vaccines can provide adequate protection against 4,444 mutants. Serums of recipients vaccinated 3 weeks after the initial dose of PfizerBioNTech's BNT162b2 vaccine showed reduced neutralization titers for the entire set of spike mutations present in mutant B.1.1.7. (108). The ability to neutralize sera vaccinated with mRNA1273 (latest) against mutants was also tested using a pseudo-virus-based neutralization assay.

The results showed that the neutralizing ability of the serum inoculated with mRNA 1273 did not show a significant change in B.1.1.7, but decreased in B.1.351. The recombinant subunit vaccine NVXCoV2373 showed a protective effect of 89.3% in a phase 3 clinical trial conducted in the United Kingdom, and about 50% of infected recipients were positive for the B.1.1.7 mutant. Further analysis of UK clinical data showed that NVXCoV2373 was 95.6% of old strains and 85.6% of UK 4,444 mutants. However, the effectiveness of South African recipients has dropped to 60. We found that 90% of these recipients were positive for the B.1.351

variant. Many other companies are currently testing the ability of vaccine sera to neutralize various strains. This is also a very important consideration in vaccine evaluation.

Developers and manufacturers need to focus on viral mutations and propose strategies for developing next-generation vaccines to combat mutants. The next generation COVID19 vaccine will need to be re-encoded and manufactured according to the circulating mutant sequence. Alternatively, immunogenetically conserved viral proteins, linear B cell epitopes and MHC I / II restricted T cell epitopes are screened by a bioinformatics approach to combat persistent viral mutations. It may provide new virus ideas for next-generation virus design. The vaccine manufacturing process varies from platform to platform. Recombinant nucleic acid vaccines and recombinant viral vectorized vaccines enter cells to express antigens to stimulate the immune system. These types of vaccines can be created by introducing new antigen sequences into the genome and creating them using existing manufacturing facilities. Vaccines can, in principle, be redesigned and synthesized as long as new sequence information is available. The speed of design and synthesis, as well as the excellent immunogenicity of the mRNA vaccine, make it an excellent platform for the urgent development of the COVID19 vaccine. However, the uniqueness of the technology limits the research and development of many companies. Compared to mRNA vaccines, the process of producing recombinant subunit vaccines is relatively complex and requires *in vitro* transcription to produce immunogenic proteins. Customizing the manufacturing process to produce a mutant protein is not so easy, and the introduction of mutations can change the immunogenicity of the protein. Inactivated vaccines require isolation of the new mutant strain at the BSL3 laboratory before being amplified and inactivated to develop a vaccine for the new mutant strain. High level production equipment and master resources are the main constraints.

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