Nanotechnology-Enabled COVID-19 mRNA Vaccines

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COVID-19 mRNA vaccines contain synthetic mRNA sequences encoded for the Spike proteins expressed on the surface of SARS-CoV-2, and utilize the host cells to produce specific antigens that stimulate both humoral and cellular immunities. Lipid nanoparticles are essential to facilitate the intracellular delivery of the mRNA to its action site, the ribosome, to fully exert its effect.

Keywords: mRNA vaccine ; lipid nanoparticles ; intracellular delivery ; endosome escape

In December 2019, a new contagious disease, later known as the coronavirus disease-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported [1]. Since then, COVID-19 has rapidly spread across the globe, causing devastating medical, social, and economic consequences. In March 2020, the World Health Organisation (WHO) declared it a pandemic. There was a strong consensus that reliable vaccines are the most promising strategy to control the pandemic. Within a year after the disease outbreak, two messenger ribonucleic acid (mRNA) based vaccines became the first two vaccines to gain Emergency Use Authorisation (EUA) from the U.S. Food and Drug Administration (FDA), bringing hope to billions of people on the planet. Two mRNA vaccines, BNT162b2 (Comirnaty®) and mRNA-1273, developed by Pifzer/BioNTech and Moderna, respectively, set the milestone in scientific history as the first-ever approved mRNA vaccines and opened a new era of mRNA-based approaches to prevent various diseases [2][3][4]. Never before have vaccines been developed and distributed in such a short period of time. A few more mRNA-based vaccines have reached various clinical stages of development (**Table 1**).

Table 1. Examples of mRNA vaccines against COVID-19 at various stages of development (updated on 4 August 2021).

Vaccine Name	Developer (s)	Formulation [5]	Stage of Development (Timeline)
CVnCoV mRNA	CureVac, Germany	LNP-mRNA	Phase IIb/III NCT 04652102 (December 2020–May 2022)
ARCT-021	Arcturus Therapeutics/Duke-NUS Medical School, USA and Singapore	LUNAR® (pH-sensitive LNP-mediated delivery of saRNA)	Phase II NCT04668339 (January 2021–April 2022) NCT04728347 (January 2021–June 2022)
LNP-nCoVsaRNA-02	Imperial College London, UK	LNP-saRNA(proprietary, cationic, PEGylated)	Phase I NCT04934111 (September 2021–August 2022)
ARCoV	PLAAMS */ Walvax Biotech, China	LNP-mRNA	Phase Ib ChiCTR2000034112 (June 2020–December 2021) ChiCTR2000039212 (October 2020–December 2021)

* PLAAMS: People's Liberation Army Academy of Military Sciences.

The lightning-fast success of these mRNA vaccines are not only built on the extensive research in mRNA therapeutic application during the last decades, but also the major technical innovations in nanotechnology for intracellular delivery and advances in nanomedicine production. In this entry, we will first introduce the principles of the mRNA vaccines against COVID-19, followed by a detailed discussion on the roles of nanoparticles, in particular lipid nanoparticles (LNPs), in

assisting the transportation of mRNA into the acting site of host cells to exert its effects. The manufacturing and storage requirements of these are also briefly outlined.

References

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