The basic principle of mRNA therapeutics involves delivery of in vitro transcribed mRNA into a target cell, where cellular machinery translates the mRNA into a functional protein. In vaccine applications, an mRNA encoding a viral protein will elicit a protective immune response, whereas in therapeutic applications, an mRNA encoding an absent (or dysfunctional) protein in a patient provides functional protein expression. Thus, mRNAs can be widely used in vaccine development, protein replacement therapy, and the treatment of genetic diseases.

ADVANTAGES:
- Enables druggability of intracellular, transmembrane, and secreted proteins.
- Restores gene expression without risk of genomic integration.
- Druglike behavior: ability to repeat dose and adjust dose/dose interval.
- Endogenous post-transcriptional modifications increase probability of correct folding, glycosylation, and trafficking of the protein and decrease risk of immunogenicity.
- Minimal changes to the manufacturing process for multiple targets.
- Rapid development from target gene selection to product candidate.

CHALLENGES:
- Stability: mRNA is susceptible to degradation.
- Delivery: LNPs must be tissue-specific and biodegradable.
- Immunogenicity: risk of activating the immune system via Toll-like and retinoic acid-inducible gene–like receptors.
- Manufacturing: difficult to achieve high quality and highly pure mRNA with scalable manufacturing processes.

APPLICATIONS:
Because of the central role of mRNA in protein expression, mRNA technology has broad applicability in the treatment or prevention of disease. Two mRNA-based coronavirus disease 2019 (COVID-19) vaccines have Emergency Use Authorization, demonstrating the clinical validation of this revolutionary approach.

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Lipid nanoparticles (LNPs) are the most common delivery system being developed to effectively deliver mRNA medicines for many therapeutic indications, protecting the mRNA from degradation. The LNPs are customized for delivery to specific tissues, focusing on optimal size, surface charge, and lipid composition. Significant progress has been made in developing safe mRNA therapeutics for a number of disease indications.

**Declaration of interests**
The authors have no interests to declare.

**Literature**
4. Weide, B. et al. (2008) Results of the first phase I/II clinical vaccination trial with direct injection of mRNA. *J. Immunother.* 31, 180–188

mRNA replacement therapy for genetic diseases is being developed for lung and liver diseases (inhaled and intravenous delivery).

Immuno-oncologic approaches can leverage the intrinsic immune adjuvant effects of mRNA.