MRNA Vaccine Trend

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The world is in the middle of a pandemic, making it imperative to develop our immunity. Most conventional vaccines against viruses are developed from viruses that are grown in chicken eggs or mammalian cells. The entire conventional vaccine process takes months to process and develop and is complex. With the ongoing pandemic, there is an urgency to develop a vaccine at the earliest and conventional vaccine will slow down the process of development. The scientists and researchers globally have focused on mRNA vaccine.

Messenger RNA or mRNA is an interim step between the translation of DNA and protein production by ribosomes in the cytoplasm. It is produced by transcribing a DNA template synthesized from the known genetic sequence encoding the immunogen dispersed worldwide.

The plan and production of mRNA-based vaccines on a clinical scale is conceivable within weeks from the time the antigenic sequence becomes accessible. The mRNA production is cell-free and employs in vitro transcription procedure. In the laboratory both the template and transcript can be created by using resources that are readily accessible.

Various studies were carried out to find an alternative to the conventional vaccines. In 1990, the first successful study was published by J.A. Wolff et.al, where they were successfully transcribed in vitro mRNA in animals by injecting reporter mRNAs into mice. In the year 1992, another study demonstrated a physiological response in rats after administering vasopressin-encoded mRNA in hypothalamus. Although these results were promising but it failed to generate any significant investment in developing therapeutics based on mRNA. This is due to the instable nature of mRNA, ineffectual in vivo delivery and high characteristic immunogenicity.

Major technological advancement, innovation and research in the past decade facilitated mRNA therapeutics and making it a promising tool in the field of protein replacement therapy and vaccine development. One of the key features of mRNA which makes it desirable is its safety, efficacy and production. There is no possibility of infection or insertional mutagenesis as mRNA is a non-integrating and non-infectious platform. Furthermore, normal cellular processes can degrade mRNA and the in vivo half-life is controlled via use of delivery methods. The immunogenicity of mRNA can be tempered to increase the safety profile.

Several alterations make mRNA more stable and translatable by making mRNA into carrier molecules which expresses in the cytoplasm. There are two types of RNA which are being studied currently – non-replicating and virally derived mRNA and self-amplifying RNA. The conventional mRNA-based vaccines encrypt the antigen of interest and contain 5' and 3' untranslated regions whereas self-amplifying RNAs encrypts the antigen of interest and viral encoding technology which enables intracellular RNA amplification and protein expression.

Numerous mRNA vaccines have been developed in recent years and its immunogenicity and efficacy were authenticated. Synthetic mRNA has become more translatable than before due to engineering of RNA sequence. Successful development of competent and non-toxic carriers allowing prolonged antigen expression in vivo have been observed. Some vaccine designs contain new adjuvants, while others elicit effective responses in the absence of identified adjuvants.

Since mRNA can be produced by in vitro reactions with recombinant enzymes, ribonucleotide triphosphates and a DNA template, thus shows that it is simple and easy to produce as compared to traditional protein subunit and conventional vaccine manufacturing platforms. The rapid production of mRNA in a small GMP facility is possible due to its simplicity and reaction yield. Even though the manufacturing process is independent of the sequence and is determined by the length of RNA, nucleotide and capping chemistry and purification of the product, it is still possible to encounter certain sequence properties related problems. However, the process can be made consistent to manufacture any encoded protein immunogen; thereby making it apposite for quick response to evolving infectious diseases.

Pharmaceutical companies are working to develop a formulation of mRNAs to make it stable at higher temperatures as most products are required to be stored at -70°C presently for early phase of studies. This would make mRNA more suitable for vaccine distribution. Few published studies show that steady refrigerated or room temperature formulations can be made. A study showed that the RNActive platform was active after lyophilization and storing it at 5–25°C for 3 years and at 40°C for 6 months; whereas another study established that freeze-dried naked mRNA is steady for at least 10 months under frozen settings. The study by Probst J. et.al, shows that mRNA can be

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stabilized by improving packaging within nanoparticles or by co-formulation with RNase inhibitors. Although lipid-encapsulated mRNA was observed to be stable for at least 6 months but long-term storage of mRNA–lipid complexes in an unfrozen form has not yet been reported.

Since the vaccines are administered by healthy individuals, the safety requirement of prophylactic vaccines is very strict. As mRNA manufacturing process does not require any toxic chemicals or contaminated cell cultures, production of mRNA evades the risks associated with other vaccine platforms. Additionally, the rapid manufacturing time for mRNA provides few prospects to introduce contaminated microbes. The hypothetical risks of integration of the vector into DNA of the host cell are not a concern for mRNA in vaccinated people. For these reasons, mRNA vaccines are considered a safe vaccine format.

There is a burst in academic and clinical research for mRNA therapeutics. There have been preclinical and clinical studies indicating the efficacy of the mRNA vaccine. Even those most of early studies were on cancer applications of the vaccine, recent studies have established the effectiveness, flexibility, and adaptability of mRNA to protect against a wide variety of infectious pathogens, including influenza virus, Ebola virus, Zika virus, Streptococcus sp., T. gondii and more recently COVID-19.

The future of mRNA vaccines is therefore extremely bright. The rapidity with which mRNA-based vaccines were developed during this ongoing pandemic along with mass production of the vaccine and clinical use to confront the COVID-19 pandemic, provides evidence that mRNA vaccines offer a promising proposition to immunization.

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Declaration of patient consent : The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's parents have given their consent for patient images and other clinical information to be reported in the journal. The patient's parents understand that his names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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