COMMENTARY

Nano-mRNA Therapeutics for Improved Cancer Immunotherapy

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INTRODUCTION

The global approval of two messenger RNA (mRNA) vaccines (BNT162b2 and mRNA-1273) in late 2020 has demonstrated the extraordinary effectiveness of mRNA therapeutics combined with lipid Nano formulation technology in defending people against COVID-19 pandemic. This novel and intriguing dual approach involving Nano formulations and mRNA therapeutics is thought to be a hopeful model in future tailored cancer immunotherapy. Recent developments in Nano formulation technologies have played a significant part in the adaptation of the mRNA platform in cancer therapy. Present the biologic principles and developments of mRNA technology, as well as the chemistry basics of interesting mRNA transport Nano formulations, in this overview. The most potential Nano-mRNA therapeutics for improved cancer immunotherapy through modulation of particular immune cell subtypes. Dendritic Cells (DCs) in peripheral lymphoid organs initiate mRNA cancer vaccine-mediated antigen specific immunotherapy, and DCs, Natural Killer (NK) cells, cytotoxic T cells, or numerous immunosuppressive immune cells in the Tumour Microenvironment (TME) reverse immune escape. The emphasise the clinical progress of advanced Nano-mRNA therapeutics in tailored cancer treatment and the revolutionary integrated technology's future paths towards clinical application. The authorised use and rising global vaccination rate of two effective and safe mRNA-based vaccines (BNT162b2 and mRNA-1273) against COVID-19 have successfully reduced coronavirus transmission and deadly illness, making extraordinary contributions to assisting people in surviving the difficult pandemic. The success of these COVID-19 vaccines based on lipid Nano formulation and mRNA has given useful insights into the treatment. By bringing tumour antigen-encoding Nano-mRNA technology to cancer patients.

In 1989, described the effective *in vitro* protein expression of mRNA delivered by a synthetic cationic Lipid Nanoparticle (LNP). In 1990, study successfully showed *in vivo* transfection of reporter firefly protein by direct infusion of naked mRNA into rodents. The administration of mRNA expressing vasopressin into rodents showed the biological reaction of mRNA platforms for the first time in 1992, though the biological function was short-lived. Liposome-mRNA expressing influenza virus protein induced antigen specific Cytotoxic T Lymphocytes (CTLs) against virus-infected cells in rodents in 1993, showing immunogenic properties of mRNAs. The first cancer mRNA vaccine expressing carcinoembryonic antigen was developed in 1995. Antigen-specific antibody immune reaction protected rodents from tumour challenge. Despite these early encouraging findings, the creation of mRNA therapies was not well funded at the time, owing to a lack of mRNA biology expertise and weak control over mRNA stability, intrinsic immunogenicity, and *in vivo* transport methods. When a pathogen invades, the innate immune system recognises it by detecting pathogen-associated molecules (such as RNA), coordinating an adaptive immune reaction. It took decades to get from RNA detection to licenced mRNA products for human use. TLRs (such as TLR3, TLR7, and TLR8) of Antigen-Presenting Cells (APCs) were discovered detecting RNA molecules in the early twenty-first century, but it was unclear how APCs can differentiate pathogen RNA. Until 2005, self-RNA was derived from dead self-cells. It was found that RNA modifications such as base substitutions and pseudo uridine incorporation could inhibit RNA-mediated activation of TLRs 3, 7, and 8, decreasing immunomodulatory function. This important discovery revealed the process by which innate immune cells detect non-self RNA molecules and fueled research into RNA modifications and related receptor-based immune recognition.

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