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COMMENTARY

Positive aspects of the mRNA platform for SARS-CoV-2 vaccines

Khalid Hajissa [a,b] and Ali Mussa [c]

[a]Department of Medical Microbiology & Parasitology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Malaysia; [b]Department of Zoology, Faculty of Science and Technology, Omdurman Islamic University, Omdurman, Sudan; [c]Department of Biology, Faculty of Education, Omdurman Islamic University, Omdurman, Sudan

ABSTRACT

The unprecedented need to acquire a safe and effective vaccine for the long-term control of coronavirus disease 2019 (COVID-19) is a global imperative. Researchers have been working urgently and collaboratively to develop vaccines against the causative agent of COVID-19. The use of messenger RNA (mRNA) vaccine platform offers new opportunities for the development of effective vaccines. The first use of COVID-19 mRNA vaccines for individuals outside the clinical trials raised concerns over their safety and future efficacy. In social media, particularly in developing countries, widely shared false claims allege that the current mRNA-based COVID-19 vaccines potentially integrate into the host genome and thus may genetically modify humans. These vaccines are also assumed to lack efficacy due to the emergence of new strains. Such misinformation cause people to hesitate about receiving vaccination against COVID-19. This commentary aimed to outline the structure, mechanism of action and the major motive for the use of COVID-19 mRNA vaccine, with a focus on scientifically addressing challenges associated with conspiracy theories and dispelling misinformation around vaccination.

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Introduction

Since its discovery in Wuhan, China, in December 2019, coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a prime public health threat and prompted widespread concern around the world.[1] The virus has rapidly spread to other parts of the world, and the number of cases has dramatically increased. Globally, the number of cases continued to surge with a widespread community transmission, marking COVID-19 as the most rapidly growing pandemic in modern times.[2]

The lack of specific and effective treatment highlights the importance of infection control measures to limit the effects of virus spread[3] Accordingly, a range of public health interventions and restrictive measures have been implemented globally to mitigate the impact of COVID-19 pandemic.[4] However, such measures can significantly contribute to the slowdown of COVID-19 transmission, but they do not eliminate the virus. This problem is reflected by the progressive resurgence in COVID-19 cases in various parts of the world (second wave) that eased restrictions. Thus, the virus will continually emerge at regular intervals following premature relaxation of preventive measures because these strategies prevent individuals from being infected with SARS-CoV-2 but fail to provide them with proper immunity, leaving them susceptible to additional waves of infection. The return to prepandemic normalcy is improbable until a safe and effective vaccine strategy becomes available, and a global vaccination program is implemented successfully.

The urgent need for vaccines prompted an unprecedented level of solidarity, with extensive scientific collaboration between governments, industry and scientific community, to accelerate the development of potential COVID-19 vaccines. Vaccine development efforts have progressed swiftly, and several major vaccine platforms have provided vaccines that are efficacious in preventing disease. The use of messenger RNA (mRNA) vaccine platform offers new opportunities to acquire effective vaccines. The mRNA vaccine platform is used by two frontrunners in the race for COVID-19 vaccine development (Pfizer-BioNTech and Moderna).[5,6] Although both vaccines have been licensed, the first use of mRNA vaccines on individuals outside clinical trials initiated the spread of misconceptions and conspiracy theories. This situation can fuel skepticism among populations and cause people to hesitate about undergoing vaccination. The inoculation of entire populations with COVID-19 vaccine is largely impeded by the false claim that mRNA can integrate into the human genome and alter a person's genetic material. Another false assumption is that COVID-19 vaccine can potentially lack efficacy particularly after the emergence of new SARS-CoV-2 strains. This condition also resulted in the reluctance and concern of numerous people, including those with high risk of infection, regarding immunization against coronavirus. Furthermore, health-care providers lack technical knowledge to address the questions and concerns of individuals about COVID-19 mRNA vaccine. This knowledge gap is considered an important factor that creates mistrust between people and health-care providers.

In this context, sharing scientific information regarding the nature of mRNA vaccine may play an important role in COVID-19 vaccination programs by effectively reducing public panic about this novel vaccination technology. Thus, scientific communities should collaborate to dispel myths and misinformation around COVID-19 vaccine. This commentary

CONTACT Ali Mussa alimaha1341989@gmail.com Department of Biology, Faculty of Education, Omdurman Islamic University, Omdurman, Sudan.

aimed to outline the structure and mechanism of action and address the major concerns surrounding COVID-19 mRNA vaccine. This review may play a major role in the development of a general understanding of this vaccine platform.

COVID-19 mRNA vaccine

For decades, scientists have explored the possibilities of mRNA. The efforts to apply the scientific promise of mRNA into medical reality have started with COVID-19 vaccine. The mRNA vaccine is noninfectious and a non-integrating platform with almost no potential risk of insertional mutagenesis.[7] The development of a mRNA-based vaccine against COVID-19 constitutes a rapid and versatile platform that will enable quick response to this pandemic. The technology has been around for a while. However, Pfizer/BioNTech and Moderna are the first to introduce a mRNA vaccine that completed all stages of clinical trials and was given a license for human use. Clinical trials for mRNA vaccines against viral diseases, including Zika, dengue, *Ebola, cytomegalovirus*, influenza and rabies infection, proved the capability of this novel approach to elicit potent and broadly protective immune responses.[8] This platform empowers vaccine development programs due to its flexibility and capability to mimic the structure and expression of any antigen, as observed in the course of natural infections.[5]

The mRNA vaccine combines the desirable advantages of live-attenuated vaccines, such as endogenous antigen expression and T cell induction with the outstanding safety profile of killed or subunit vaccines. The core principle behind mRNA vaccine is to deliver synthetic mRNA encoding one or more antigens into the host cell cytoplasm, where its expression generates sufficient quantity of the translated protein.[9] The antigen will then appropriately present to the immune system.

Although mRNA vaccines are clinically efficacious and safe, the key advantage of this platform is its capability for scalable production within an extremely short period. Thus, mRNA vaccines are an attractive response option for the COVID-19 pandemic. In addition, new targets requiring multi-antigen approaches will benefit from the speed at which mRNA can render multiple constructs. The licensure of two COVID-19 mRNA vaccines for human use demonstrates mRNA vaccination as potential tools in controlling global pandemic and public health threat. These licensed vaccines include BNT162b1 (Pfizer/BioNTech) and mRNA-1273 (Moderna TX, Inc.), which are composed of synthetic modified mRNA that encodes the trimerized receptor-binding domain (RBD) of the spike protein (S) and the prefusion stabilized S protein of SARS-CoV-2, respectively. The mRNA encapsulated in lipid nanoparticles ensures the efficient and safe delivery to the cytoplasm of host cells. The two vaccines have shown the potential to elicit a highly S-protein-specific antiviral response. However, various issues, misinformation, and conspiracy theories arose with regard to the safety and effectiveness of COVID-19 mRNA vaccines in the future. These issues include the potential genome integration and the possible inefficiency due to the emergence of new strains. These allegations are scientifically untrue. No interaction occurs between cytosolic mRNA and the genome, and mRNA vaccines remain outside the cell nucleus. Thus, mRNA vaccines are incapable of human genome integration and genetic modification. In addition, gene silencing is unlikely to occur because protein expression is independent of the promoter. Following the entry to human cells, the mRNA quickly degrades, reducing the risk of long-term expression.

The emergence of contagious new SARS-CoV-2 variants (SARS-CoV-2 VUI 202012/01) and possibly new strains in the future raises additional questions about the capability of the new virus variants to alter the efficacy of the current vaccine candidates. All viruses, including SARS-CoV-2, change over time, but most of these mutations or changes exhibit no direct influence on vaccine performance. However, further laboratory investigations are required to fully understand the effect of specific mutations on the effectiveness of vaccines. The new variants have spike protein mutations targeted by the currently licensed vaccines. However, vaccines produce antibodies against most regions in spike proteins. Thus, a single change will not lessen the effectiveness of the vaccine. In addition, no evidence indicates that the current vaccines will be less effective against VUI 202012/01 mutation. Still, over time, as additional mutations occur, mRNA alterations can be performed to increase the stability of these vaccines. The nature of mRNA platform allows rapid reformulation to efficiently adapt to sudden changes in the virus strains.

Conclusion

The recent advancement in mRNA technology allows the novel design and production of safe and effective COVID-19 vaccines. The approach has the potential to streamline vaccine discovery and facilitate rapid response to emerging infectious diseases. Being non-integrative and noninfectious, mRNA vaccines allow for direct clinical applications without the need for laborious and time-consuming screening of integrated oncogenes or viral component. The current COVID-19 mRNA vaccines show no potential to integrate into the host genome nor cause genetic modification in humans.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

ORCID

Khalid Hajissa http://orcid.org/0000-0002-1725-6702
Ali Mussa http://orcid.org/0000-0002-1116-7362

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