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Fight against COVID-19 with mRNA vaccines and interaction with Dermal fillers

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The current coronavirus disease 2019 (COVID-19) outbreak has created a huge demand for rapid and high-volume vaccine manufacturing. Several new platform technologies and traditional manufacturing approaches are being used to meet this demand. Among them, the mRNA vaccine platform technology holds great promise for obtaining an emergency use authorization to facilitate immunization against SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), which causes the respiratory illness COVID-19. However, this is a new technology, which means that there is significant uncertainty about possible production at a large scale and speed. Vaccines of mRNA work by providing our cells with the genetic code to make viral proteins. Once proteins that do not cause any disease are produced, the body triggers an immune response against the virus, allowing them to develop immunity. mRNA can be used to make any protein theoretically. Still, it is much easier to produce than the proteins themselves or the inactivated and attenuated versions of viruses commonly used in vaccines, which makes this technique attractive, says mRNA specialist Norbert Pardi, at the University of Pennsylvania.

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The idea of using mRNA to make useful proteins to fight against viral disease has been around for many decades. However, so far, no vaccine using this special technology has made it that far in clinical trials. The success of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines is great for the RNA field because there were only a handful of persons who trust mRNA vaccines until recently. Now we have great chances to prove this fact (their usefulness) in a real pandemic situation.

The approval of the U.S. Food and Drug Administration (FDA) of two highly effective COVID-19 vaccines in December 2020 marks a major milestone in the fight against the pandemic for Americans. Pfizer BioNTech's 2-dose COVID-19 vaccine regimen, administered on days 0 and 21, was 95% effective in preventing symptomatic COVID-19 infection measured 7 days after the second dose. The vaccine has proven to be equally protective for all age groups and racial and ethnic groups. The Moderna two-dose COVID-19 vaccine regimen, given on days 0 and 28, was 94% effective in preventing symptomatic COVID-19 measured 14 days after the second dose. The Moderna vaccine was slightly less effective in people aged 65 and over, but it was equally effective in different racial and ethnic groups [1].

Most recipients of Moderna's COVID-19 vaccine (NSDQ: MRNA) have experienced

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mild side effects such as fatigue, temporary facial swelling, headache, and pain at the injection site. Temporary facial swelling can be another side effect for mRNA vaccine recipients who have previously received dermal fillers. During the third phase of the Moderna study, three people developed swelling of their face or lips after being vaccinated, FDA Medical Officer Dr. Rachel Zhang said in today's Advisory Committee on Vaccines and Allied Biologicals on the Moderna COVID-19 vaccine. Two of these patients had dermal fillers in their cheeks within the 6 months before vaccination. Another received a dermal filler in his lip 2 days after vaccination [2].

The FDA has classified two cases of facial swelling as serious side effects for patients who dermal filler, although the incidents have resolved. The agency determined that the lip swelling incident was medically important but not a serious side effect. A patient with lip swelling has reported similar swelling in the past years after receiving cold or flu vaccinations. In these cases, all patients experienced swelling and inflammation in the area where the filler was injected. A couple of patients received a cheek filler 6 months before the vaccine, and one patient received a dermal filler 2 days after the vaccination. All were dosed with steroids and antihistamines, and all of their reactions resolved.

COVID-19 and other viral infections on their own can cause such immunogenic reactions in people who have recently received dermal fillers. The FDA concluded in a white paper that the localized dermal filler in these cases may be caused by an inflammatory response due to the interaction between the immune response after vaccination and the dermal filler. This phenomenon has been reported following natural infection (e.g., after flu-like illness) [3,4].

In an early proof of concept for using gene therapy to make proteins needed to fight against disease, published in 1990, scientists reported that cells in mice successfully produce proteins encoded by injected RNA or DNA. This method was potentially revolutionary: in theory, it could create any protein the body needs to boost immunity against pathogens and fight diseases such as cancer and rare genetic disorders.

Despite its promises, working with mRNA is problematic. Normal mRNA only produces low levels of proteins, and the molecule degrades too quickly within the body to make it useful as a therapeutic agent. Also, RNA can trigger an immune response that is unique to the protein it encodes. If you inject foreign RNA into humans or animals, you can cause a very serious inflammatory reaction, and this is our body's defense mechanism against viruses that can use RNA or DNA to store their genetic information.

Because of these problems, adoption of this technology has been slow, and many scientists have chosen to focus mRNA instead on developing vaccines with DNA that is more stable and easier to work with, says Margaret Liu, chairman of the board of the International Plant Protection Society Vaccines and the pioneer of gene vaccines [5]. (Margaret Liu is on the scientific advisory board for the Jenner Institute at Oxford University, which developed the AstraZeneca vaccine for COVID-19.)

Why these mRNA vaccines seem to be so authentic, while previous attempts to control other pathogens did not seem promising, remains an open mystery. One of the simple reasons may be the sheer number of resources that have been invested in their development. Margaret Liu also suggests that one explanation for the high efficacy levels is that vaccines may elicit a nonspecific inflammatory response to mRNA, which may enhance its specific immune response, given that the modified nucleoside technique reduced inflammation but did not eliminate it. On the other hand, it could also explain intense reactions such as pain and fever that have been reported in some recipients of the SARS-CoV-2 mRNA vaccine. Others have suggested that lipid nanoparticles are responsible for these serious but temporary side effects, which have been reported by some of the trial participants [6].

After all, it is too early to tell why these vaccines work so well. "These are intermediate results so far. They remain unpublished. Furthermore, we still need extensive security databases related to these products," Jackson says. Some issues need to be addressed, such as concerns about the need to store vaccines in freezers, especially in the case of the Pfizer/BioNTech vaccine, which needs to be stored at -70°C. Another SARS-CoV-2 mRNA vaccine developed by the German company CureVac, can be stored at 5°C. This vaccine, based on unmodified mRNA, is undergoing clinical trials phase I [2,5].

About 2 decades after the first successful *in vivo* introduction of mRNA, mRNA vaccines promise to be a revolutionary technology platform for developing vaccines for both therapeutic and prophylactic purposes. Today, the scientific community is eagerly awaiting the first clinical efficacy data. However, there is still a wide field for further development/improvement of mRNA-based vaccines. As discussed, the format and uptake of mRNA are critical parameters for efficient antigen expression, which can be influenced by new

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RNA constructs and the composition and introduction of mRNA. However, any changes in these parameters can have serious consequences for mRNA production and its interaction with RNA sensors and should be carefully considered early [7].

However, at an early stage, this would increase the complexity of the vaccine and treatment regimen, making development more difficult. Collectively, mRNA represents a promising vaccine vector in terms of flexibility, efficacy, and safety. Consequently, it could become a "revolutionary technology" for cancer immunotherapy and vaccination, prophylactic or therapeutic, against infectious diseases.

Now that mRNA vaccines have unleashed their potential, many more vaccine manufacturers are likely to take an interest in the technique, and others predict that it will usher in a new era for mRNA applications for infectious diseases, especially those that are fast response platforms to help manage outbreaks.

Covid-19 and other viral infection could possibly induce immunologic reactions particularly who has received recently dermal fillers, it concluded that localized swelling is due to inflammatory proliferation response after dermal filler and occasional late-onset of inflammatory response. This has been reported as a natural infection for instance after Influenza-like illness. It has been noted that it was resolved by following treatment with steroids or antihistamines, it was only localized, and there were no symptoms of systematic disease observed.

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