COVID-19 mRNA Vaccines

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How are mRNA vaccines unique compared to other commonly administered vaccines (such as a live-attenuated or inactivated virus), and are there differences in how mRNA vaccines are evaluated for safety/efficacy?

Many common vaccines contain inactivated (“killed”) viruses or live-attenuated viruses. Live-attenuated virus vaccines are composed of genetically manipulated viruses that are incapable of causing disease in healthy individuals. In contrast, mRNA vaccines encode a viral protein. Upon delivery into the cell, the mRNA is translated into a viral protein which is typically expressed on the surface of these cells. This elicits an immune response against the viral protein, ultimately leading to protection against future infection. The COVID-19 vaccines developed by Pfizer/BioNTech and Moderna use this technology to deliver mRNA into cells that encode for the SARS-CoV-2 spike protein.1,2

Although the process of development and approval of COVID-19 vaccines was expedited, the standards used to evaluate the safety and efficacy of SARS-CoV-2 mRNA vaccines in clinical trials were largely the same as commonly administered vaccines. The accelerated COVID-19 vaccine development process was facilitated by modifications in how vaccines are reviewed: “rolling reviews” by regulators in real-time, rather than regulators waiting until the end of the trial to review all data. Companies were also willing to assume increased funding risks for these large clinical trials due to the urgent need for COVID-19 vaccines globally. Although mRNA vaccines had not been approved for widespread human use before this pandemic, they have been studied in humans for more than a decade against viruses such as influenza, Ebola, and Zika.3 Clinical trials have also been performed to evaluate mRNA vaccines as treatments for specific forms of cancer, including melanoma7 and prostate cancer.8

With the possibility of virus mutation, what factors might impact vaccine efficacy, and do you think current vaccines will offer the same level of protection from novel strains of COVID-19?

Since the current COVID-19 mRNA vaccine encodes only the spike protein, mutations that result in antigenic changes to the spike could influence vaccine efficacy. When tested against the UK variant (B.1.1.7), the mRNA vaccine showed no significant reduction in antibody responses.4,5 However, reduced spike binding by antibodies was observed when
the vaccines were tested against the South Africa (B.1.351) and Brazil (P.1) variants. It is not entirely clear the extent to which reductions in antibody binding influence vaccine effectiveness. While most current studies have focused on antibody-mediated responses, T cell response must also be considered. Preliminary studies suggest that T cell responses are much less impacted by variants than antibody responses, indicating that they may still provide sufficient protection despite reduced antibody binding. Another important factor to take into account when evaluating vaccine efficacy is that immunity is not binary. A vaccine that does not completely protect against symptomatic infection may still be very effective at preventing severe disease. These trials were extremely rare. The general public is not familiar with the vaccine evaluation and approval process, leading many to believe the accelerated approval of COVID-19 vaccines somehow compromised safety evaluation. An important way we can address vaccine hesitancy is by explaining how this process was expedited without compromising safety. By conveying reliable scientific information to the public in an accessible way, scientists and politicians can provide reassurance that the protective benefits of these highly effective vaccines outweigh the minimal associated risks.

What may explain vaccine hesitancy/pushback from the public and in your opinion, how could scientists and/or politicians better address these concerns?

In our modern, virtual world dominated by social media, there is a plethora of misinformation circulating about vaccine safety and efficacy. It can be difficult for non-experts to untangle this web of misinformation, so it is critical to help the public determine how to identify credible sources of information. The safety profile of COVID-19 mRNA vaccines is excellent. Participants in clinical trials for both mRNA vaccines displayed the same types and general frequencies of acute reactions typically experienced after administration of common vaccines that have been approved for years/decades (i.e., pain/swelling at the injection site, fatigue, etc.). Any severe adverse effects seen in

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References:
1. Polack F, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine. N Engl J Med. 2020 Dec;383(27):2603-2615.
2. Baden L, El Sahy H, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021 Feb;384(5):403-416.
3. Pardi N, Hogan M, Porter F, Weissman D. mRNA vaccines — a new era in vaccinology. Nat Rev Drug Discov. 2018 Jan;17:261–279.
4. Liu Y, Liu J, Xia H, Zhang X, Fontes-Garfias CR, Swanson KA, et al. Neutralizing Activity of BNT162b2-Elicited Serum — Preliminary Report. N Engl J Med. 2021.
5. Wu K, Werner AP, Koch M, Choi A, Narayanan E, Stewart-Jones GBE, et al. Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine — Preliminary Report. N Engl J Med. 2021.
6. Tarke A, Sidney J, Methot N, Zhang Y, Dan JM, Goodwin B, et al. Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+ T cell reactivity in COVID-19 exposed donors and vaccinees. bioRxiv. 2021.
7. Weide B, Carralot JP, Reese A, Scheel B, Eigentler TK, Hoerr L, et al. Results of the first phase II clinical vaccination trial with direct injection of mRNA. J Immunother. 2008 Feb;31(2), 180-8.
8. Kongsted P, Borch TH, Ellebaek E, Iversen TZ, Andersen R, Met Ø, et al. Dendritic cell vaccination in combination with docetaxel for patients with metastatic castration-resistant prostate cancer: A randomized phase II study.