

PERSPECTIVE

Why Do We Still Lack a COVID-19 Vaccine? Searching for the Missing Pieces

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According to a recent newspaper report, two Israeli companies, namely MigVax Corp. and the Israel Institute for Biological Research in Ness Ziona, have made progress on their own coronavirus vaccines (28 July, 2020; <https://www.jpost.com/health-science/coronavirus-vaccine-what-protection-might-be-available-to-israelis-soon-636639>).

They are on the front line in this field because they had already developed an in-house vaccine to fight a coronavirus infection that appeared 4 years ago, causing tracheobronchitis in poultry (www.migal.org.il/7010). As the chicken coronavirus exhibits a high homology (80%) with severe acute respiratory syndrome" (SARS) coronavirus-2 (SARS-CoV-2) <https://www.migal.org.il/en/coronavirus-vaccine-project>, responsible for the current pandemic in humans, the chicken vaccine might also work in humans with a few modifications (www.jpost.com/HEALTH-SCIENCE).

The SARS-CoV coronavirus, responsible for the 2002 SARS outbreak, affecting 8000 people in China, also has a high (at least 90%) homology with the spike region (receptor-binding domain) of SARS-CoV-2 [1]. Thus, the experience gained from 2002 in developing a SARS-CoV-2 vaccine could be very useful under the current circumstances. Indeed, several attempts have been made to develop a SARS-CoV vaccine [2] and promising results have been obtained, including an antibody response in vaccinated monkeys [3, 4] and the demonstrated safety of a formaldehyde-inactivated virus in 36 Chinese volunteers [5]. However, extended data concerning phase I (safety) trials in humans were never reported. Whether this was because the vaccine was ineffective in eliciting antibodies in larger human trials or because of the development of side effects, or both, is unknown. Nonetheless, unpublished, even negative, data should be shared, as this kind of information may also be very useful in accelerating the preparation of a vaccine targeting SARS-CoV-2. Alternatively, as the SARS epidemic was over by 2003, there occurred the erroneous belief that there was no longer a need for a vaccine; however, these research funds may have been redirected in China. In this case, at least in China, new government rules aimed at modifying behaviors and traditions regarding wet markets and the handling and slaughter of wild animals could reasonably be expected, given that these practices seem to be major causes of interspecies coronavirus spill-over along with the occurrence of virus natural mutation, as recently suggested [6].

Whatever the reasons, we were impressed to see that Israeli scientists already have a vaccine to fight a poultry coronavirus infection that started 4 years ago, while a SARS-CoV-specific vaccine that caused a serious outbreak 18 years ago is not yet available even for phase II trials.

Since vaccine development is a lengthy process, we are in a race against time. In recent months, many attempts have been and are being made to develop a safe and effective coronavirus vaccine and new therapeutic options for COVID-19 treatment are available [7-9]. Since March 2020, only two coronavirus vaccines have entered phase III trials; one produced by Moderna (Palca, Joe (27 July 2020), "COVID-19 vaccine candidate heads to widespread testing in U.S." NPR. Retrieved 27 July 2020), and one developed by the University of Oxford and drugmaker AstraZeneca ("Investigating a Vaccine Against COVID-19". *ClinicalTrials.gov*. Retrieved 14 July 2020). Nonetheless, even if a COVID-19-specific vaccine will shortly be available, its potential long-term side effects will still be unknown at the time when mass vaccination campaigns will start.

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