Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to Editors

Passive inhaled mRNA vaccination for SARS-Cov-2

Dear Editor,

The world is currently facing an unprecedented outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes the Coronavirus Disease 2019 (COVID-19) in humans. At the time of writing, more than 38 million persons have been infected with the virus, with more than a million recorded COVID-related deaths [1]. Scientists are urgently trying to develop a safe and efficacious vaccine for SARS-CoV-2, which must also be produced in large quantities to protect vulnerable populations against SARS-CoV-2.

To achieve this, we propose the massive and passive immunization of the at-risk population via cohorting with individuals who have recently contracted SARS-CoV-2, but are deemed non-infectious albeit reverse transcription-polymerase chain reaction (RT-PCR)-positive. Testing RT-PCR positive would imply the continued spread of non-viable mRNA particles into the surroundings [2].

Multiple studies have noted that individuals who has had SARS-CoV-2 for more than 10 days were non-infectious, though they remained RT-PCR-positive [3,4]. The above finding is in line with current US Centers for Disease Control and Prevention (CDC) guidance that "persons with mild to moderate COVID-19 remain infectious no longer than 10 days after symptom onset" and persons with "more severe to critical illness or severe immunocompromise likely remain infectious no longer than 20 days after symptom onset" [5].

Messenger RNA (mRNA) as a means for passive immunization has been extensively studied for years. Early studies since the 1990s showed that exogenous mRNA could direct protein expression *in vivo*, cementing mRNA as a promising drug platform technology [6,7]. Several studies later demonstrated the utility of mRNA in vaccine development and conferring protection against cancers [8] and infectious diseases [9,10]. Moreover, passive mRNA immunization also experiences fewer safety issues due to its non-integrative and transient nature [11], the latter of which contributes to better and/or easier control of protein expression.

The potential role of mRNA vaccination in the fight against SARS-CoV-2 is evidenced by ongoing COVID-19 Phase I vaccine trials conducted by several pharmaceutical companies, including Moderna Therapeutics' mRNA-1273 vaccine [12,13], which has yielding promising results. The feasibility of inhaled RNA for passive transfection has also been proven in a number of studies [14]. On a mechanistic level, the inhaled RNA may lead to passive synthesis of non-infectious spike proteins using cell transfection machinery, hence leading to immunization of the individual.

Though there are no conclusive or ongoing large scale clinical studies yet to prove the above hypothesis, we believe this proposal is worth exploring in our battle against COVID-19, given the significant number of already recovered individuals and the natural shedding of nonviable SARS-CoV-2 particles in the environment.

Contributions

Wee Song Yeo conceived the original idea for the study. Qin Xiang Ng and Wee Song Yeo carried out the study, and the relevant data analysis and interpretation. All authors contributed to the data analysis and interpretation. All authors discussed the results, contributed to the writing of the paper and approved the final manuscript.

Role of funding source

None.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Wee Song Yeo[a], Qin Xiang Ng[b,*]
[a] *Mount Elizabeth Hospital, 3 Mount Elizabeth, Singapore 228510, Singapore*
[b] *MOH Holdings Pte Ltd, 1 Maritime Square, Singapore 099253, Singapore*

[*] Corresponding author.
E-mail address: ng.qin.xiang@u.nus.edu (Q.X. Ng).