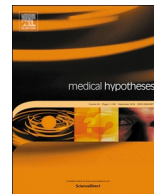




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## Is a COVID-19 vaccine developed by nature already at work?

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### ARTICLE INFO

#### Keywords:

SARS-CoV-2  
COVID-19  
Coronavirus  
Vaccine  
Immunity

### ABSTRACT

The COVID-19 positive cases are increasing at an alarming rate across the world. On the contrary, the morbidity and mortality are showing decreasing trend as time progresses. The most intriguing part is the rise in asymptomatic Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) positive cases in the population, which made us speculate some kind of gradual development of immunity in the population. To date, no attention has been given to the accumulation of killed/inactivated/degenerated SARS-CoV-2 associated molecular particle patterns (SAMPPs). In this paper, we introduced the concept of SAMPPs and its existence on inanimate objects is quite conceivable due to the size of SARS-CoV-2 and exuberant shedding of the virus in respiratory secretions. SAMPPs can come into the contact with mucosal surfaces and thereof associated antigen-presenting dendritic cells. Thus, we hypothesized the existence of SAMPPs mediated the development of immunity against SARS-CoV-2 infection, which has caused an increase in the incidence rate of asymptomatic cases and a decrease in mortality rate. To understand the existence of SAMPPs associated natural immunity against SARS-CoV-2, future population based serological testing are recommended to investigate serum antibody levels against various molecular particles associated with SAMPPs.

### Introduction

In a widespread Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) pandemic, numerous views and ideas about interventions including pharmaceutical and non-pharmaceuticals have emerged [1]. Numerous drugs are being used empirically according to experience and availability with varying degrees of adverse effects [2]. Among the pharmaceutical interventions, major candidates are in the form of vaccines and drug-based interventions. In recent times, promising and interesting data have accumulated on the rDNA technology-based RNA and DNA vaccines towards SARS-CoV-2 [3]. Fig. 1.

The SARS-CoV-2 positive cases are increasing at an alarming rate with the average daily increase in cases of about 2,55,441 (7-day moving average calculated on 5th August 2020) [4]. On the contrary, the morbidity and mortality are showing decreasing trend as time progresses. During the initial periods, the case fatality rate (CFR) was 15% (6 of 41 patients) [5]. As time progressed, the CFR decreased to between 4.3% and 11% [6,7] and later to 3.4% [8]. The rate reported outside China in February was even lower (0.4%; two of 464) [9]. Above all, the most intriguing part is the rise in asymptomatic SARS-CoV-2 positive cases in the population, which made us speculate

gradual development of some kind of immunity in the population. Despite the advancement in the pathogenesis of COVID-19 infection, till date the convincing reason for the decrease mortality rate and symptomatic cases has not been reported in the literature.

Notwithstanding the future role of these pharmaceutical interventions, we have ignored the contribution made by nature in the form of accumulation of killed/inactivated/degenerated SARS-CoV-2 associated molecular particle patterns (SAMPPs). The existence of SAMPPs on inanimate objects is quite conceivable due to exuberant shedding of the virus in respiratory secretions and the ease of settlement due to the size of the virus. In support of this contention, SARS-CoV-2 RNA has been detected in the samples collected from the object surfaces as well as from the air [10–12]. In this paper, we introduced the concept of SAMPPs and its mechanism in development of adaptive immunity with sound scientific background and justifications.

### Hypothesis

The action of factors such as soaps, detergents, sanitizers or other spraying chemicals on SARS-CoV-2 leads to the formation of SAMPPs. SAMPPs are present on the inanimate objects and are present in

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<https://doi.org/10.1016/j.mehy.2020.110335>

Received 18 August 2020; Received in revised form 17 September 2020; Accepted 2 October 2020

Available online 07 October 2020

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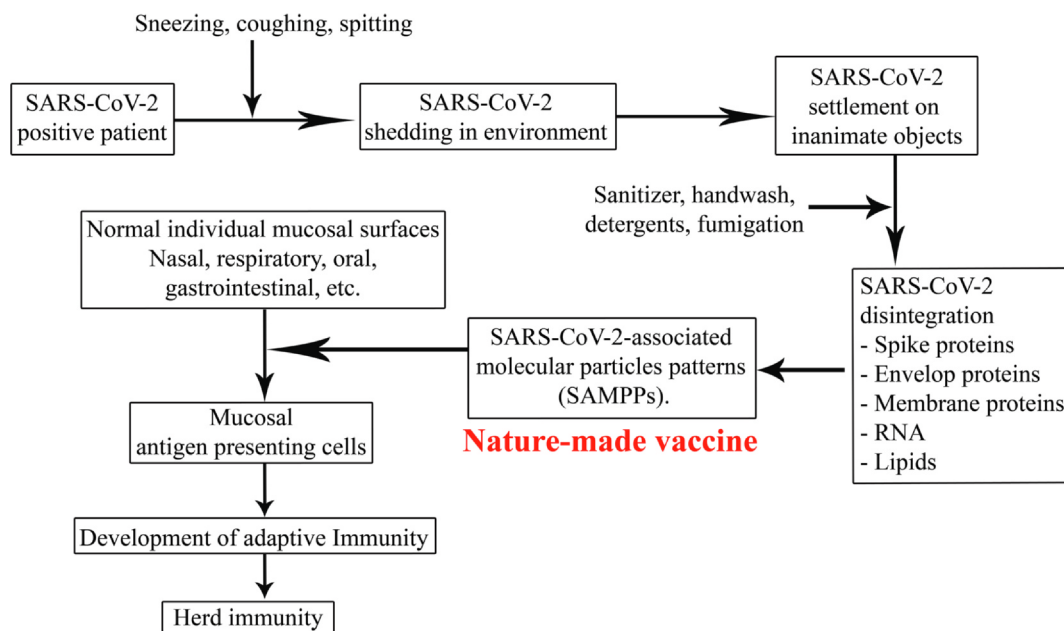


Fig. 1. Flowchart depicting mechanism of SARS-CoV-2 associated molecular particles pattern as a nature made vaccine.

abundance in COVID-19 affected areas of the community. After mucosal contact, SAMPPs are recognized by the antigen-presenting cells (mostly dendritic cells) by the virtue of their pattern recognition receptors. Further immunological events lead to the development of antibodies possibly against various constituents' molecular units of SAMPPs. Repeated exposure of SAMPPs to antigen presenting cells acts like a booster dose and prevent the waning of immunity against SARS-CoV-2. Thus, we hypothesized the existence of SAMPPs mediated development of immunity against SARS-CoV-2 infection, which has caused an increase in the incidence rate of asymptomatic cases and a decrease in mortality rate. We also propose the significance of this mechanism in achieving naturally developed herd immunity against SARS-CoV-2.

### SAMPPs as nature created COVID-19 vaccines

At global levels, non-pharmaceutical interventions including soaps/detergents/sanitizers/other-spraying chemicals are immensely helpful to halt the transmission of SARS-CoV-2 [13]. Besides that, reusable facemasks are recommended by WHO for protective measures. These reusable facemasks are treated by soaps/detergents/sanitizers/other spraying chemicals and this may also serve as a point for the accumulation of inactivated/killed SARS-CoV-2 and its molecular particles [14]. We hereby take this opportunity to coin the terms for this entity as SAMPPs.

By the virtue of coughing and sneezing, nasopharyngeal secretions are the major source for the contributions to the SAMPPs. However, saliva has also been reported to harbor SARS-CoV-2 and is projected as potential medium for the diagnostic test using RT-PCR [15]. With this information, we envisaged that all the activities wherein saliva comes in contact with inanimate objects such as eating and drinking can potentially contribute to the formation of SAMPPs.

In fact, soaps, detergents, sanitizers and other spraying chemicals are highly alkaline in nature. Three major building blocks for SARS-CoV-2 are lipids, RNA genetic materials and proteins including glycoproteins such as SPIKE proteins, which are responsible for the attachment to the target cells [16]. There are well-established facts that show the instability of RNA materials including the genome from prokaryote and eukaryote systems. Data suggests that alkaline conditions hydrolyze the virus RNA genome from the biological samples [17]. Similar possibilities are expected in case of influenza viruses that contain RNA

genome. The generation of nature-based vaccines may be attributed to the observed immunity among the target human populations in a due course of several decades. It is important to note that the most infective SARS-CoV-2 protein is SPIKE protein that is a type of glycoprotein. There is appreciable data that show that glycoproteins are highly stable even in alkaline conditions compared to the biological molecules such as RNAs and lipids of several types of viruses [18,19].

The support for nature created vaccines that contribute to the development of immunity can be substantiated from the fact that the trend of morbidity and mortality due to SARS-CoV-2 not showing any correlation with the incidence rate. We speculate that nature created vaccine may be the major source in the form of direct or indirect exposure of the SAMPPs during the non-pharmaceutical interventions including the use of soap/detergents/sanitizers and many more other chemicals. The nature and composition of the SAMPPs will be dynamic and heterogenous in nature. However, it is very difficult to predict the composition of the SAMPPs, theoretically, it would be composed of various components of virus and their sub-units such as envelope (E), spike (S), membrane (M), and nucleocapsid (N).

The authors opine that non-pharmaceutical interventions based on SARS-CoV-2 components including antigenic SPIKE glycoproteins may enter the host body system by various routes including eye, oral, respiratory, nose, genital and gastrointestinal tract. Interesting to note that these entry points for SAMPPs including antigenic SPIKE glycoproteins may be a potential source for the antigen-presenting cells residing within these tissue systems and can contribute towards humoral and cellular-based immune responses among the exposed patients. Due to constant presence of SAMPPs on inanimate objects, repeated exposure is expected which will act as a booster dose, that will help in preventing the waning of immunity against SARS-CoV-2. Moreover, multiple antigenic exposures derived from SAMPPs might provide a more comprehensive antibody response against SARS-CoV-2. This is very well depicted in an increasing number of asymptomatic cases and decreased mortality in recent times. We also believe that proposed contention would also be responsible for development of natural herd immunity against SARS-CoV-2.

### Potential limitations with RNA/DNA based vaccines

In recent years, rDNA technology has enabled the design of RNA/

DNA based vaccines against many viruses including influenza and SARS-CoV-2 viruses [3]. Despite the accumulating data on the potential generation of the immune response to mRNA-based vaccines, there is a possibility that mRNA or DNA based vaccines may be genetically modified or edited by the host cellular system. In this way, an undesirable effect and non-responsiveness due to genetic heterogeneity among the target populations can be expected. More frequent doses of such mRNA or DNA based vaccines may be required during the life-time of target populations. A limitation in the form of bioavailability is also possible during the parental administration of RNA/DNA based vaccines among the host patients and such issues may be heterogeneous among the populations. Another limitation will be for the availability of required doses of vaccines for more than 7.8 billion population that need to be vaccinated within a short time frame.

If the existence of SAMPPs mediated immunity in a host is proved with appropriate experimentations, then it will sabotage the need for the expensive RNA/DNA based vaccines. The other way round, only patients without any evidence of SAMPPs mediated immunity can be targeted for a vaccination with any form of human-made vaccines.

### Hypothesis testing

To prove the hypothesis, it is paramount importance to prove the existence of SAMPPs on inanimate objects. This can be achieved through analysis of swab samples with comprehensive high-resolution mass spectrometry. Moreover, more specific identification and confirmation of various SARS-CoV-2 particles on inanimate objects can be done using real time reverse transcription polymerase chain reaction. Already in the literature studies confirmed the presence of SARS-CoV-2 RNA on various object surfaces as well as in atmosphere [10,11]. Most of the touchable surfaces in the designated hospital for COVID-19 are heavily contaminated with virus [12], suggesting that the environment is a potential medium of presence of SAMPPs.

To understand the existence of SAMPPs associated natural immunity against SARS-CoV-2, future population-based studies are recommended to investigate serum antibody levels against various molecular particles associated with SAMPPs. This can specifically include Spike protein, small envelope glycoprotein, membrane glycoprotein, and nucleocapsid protein, and also several accessory proteins. To bring further depth into research, antibody production against the domains and subdomains of each of the aforementioned proteins can be investigated. The presence of these antibodies in SARS-CoV-2 negative or asymptomatic SARS-CoV-2 positive patients will strengthen the proposed hypothesis.

Recently, there is rapid increase in the seroprevalence studies in the literature to identify the anti-SARS-CoV-2 antibodies in different population settings. A systematic review on similar ground reported higher seroprevalence rate for close contacts and high-risk healthcare workers 22.9% (95% CI: 11.1–34.7%) and 14.9% (4.8–25.0%) respectively. However, the detection rate was slightly low in low-risk healthcare workers and general population of 5.5% (4.6–6.4%) and 6.3% (5.5–7.1%), respectively [20]. Although this data supports the proposed hypothesis, we recommend future studies on similar ground to further strengthen the proposition.

### Funding Source

The author received no specific funding for this work.

### 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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