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

Protective effects of vaccinations and endemic infections on COVID-19: A hypothesis

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Dear Editor,

Severe acute respiratory distress syndrome (SARS) – coronavirus (CoV) 2 (COVID-19) infection is in the pandemic state with inter-country variations in the occurrence and case fatality. We believe that the low occurrence/fatality of **COVID-19** may be due to the existing vaccination status and endemicity of other infections which might have enhanced their immune system to face the challenges of COVID-19. We would like to highlight on possible reasons and the extended evolutionary synthesis (EES) to support our views.

Existing vaccination

A few vaccines including Bacille Calmette-Guerin (BCG) vaccination offer non-specific immune effect [1] and this trained immunity gives protection against several other pathogens [2,3] and reduces viremia, it's virulence, sepsis and mortality [4,5]. So, a clinical trial has been initiated to ascertain the above fact [6]. Interestingly, BCG produces persistent conformational changes in innate and adaptive immune cells and increases interleukin-1B secretion, which enhances anti-microbial immunity [7–9]. Also, antibodies generated against live attenuated measles vaccine provide neutralising effect on SARS-CoV and also induce antibodies against SARS-CoV antigen [10]. Since BCG and measles vaccines may provide some non-specific protection against COVID-19, these may be considered at least for the susceptible population before the development **COVID-19** specific vaccine.

Endemic infections

Countries with a high prevalence of infections with dengue, chikungunya, malaria etc., have a low occurrence of COVID-19 makes one to hypothesize that endemic infections may protect through interferon which retard subsequent illness/disease through viral interference [11,12]. This viral interference happens via multifactorial manners such as immune response, cellular response, RNA interference and defective interfering particles or genomes of the host [13]. The concept of cross-protection offered by previous herpetic infections against vaccinia lesions [14] was first brought to light by Edward Jenner two centuries ago. Previous experimental studies have revealed that beta coronaviruses are capable of inducing immune responses against one another by way of generating neutralizing antibodies which cross-react against other SARS-CoV viruses [15,16]. Based on the above, we believe that the above principles may apply for the less occurrence of COVID-19 in regions where other viral infections are prevalent.

Extended evolutionary synthesis (EES)

Overall the organisms and individuals based on previous exposure to vaccines and infections come from the environment, internal sensors, memorized experience, and genome prefer to develop pathways in a goal-directed manner and improve the behavioural traits and phenotypic variability so as to protect and survive from infectious agents. All these are considered under EES by Pigliucci and Müller [17] and EES brings out the hidden morphogenetic capabilities and protect the organisms/cells.

Points to ponder

Cross immunity though helps, the questions to be considered are: "will cross-immunity enhance career status for COVID-19 and make the disease endemic or contribute to mutations of viruses and hamper vaccine research/vaccination against COVID-19?", "will the low levels of cross-immunity produced from the other beta coronaviruses make SARS-CoV-2 to die out, and/ or will it contribute to a resurgence of the same after a few years [18]?". Further studies are warranted to answer the above. Till then, we accept that Nature and Science strengthen the immune system through repeated infections and vaccinations respectively, and prepares living organisms to face the challenges of existing, emerging and re-emerging infections. During this process, infectious agents may mutate, and attack the living organisms differently. All are aware that we can't fight against Nature, but live in a symbiotic/harmonious manner with other infectious agents as much as possible with and/ or without vaccinations.

Thus, the successful one survives and life propagates forever.

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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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2020.109849.

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