Preventive and Therapeutic Strategies to Fight COVID-19

SUMMARY
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), COVID-19, rapidly spread in the world in 2019. It may lead to multi-organ failure and death. The primary findings showed that the virus infects host cells through binding to ACE2 and CD147 and triggers a pathogenesis cascade. However, to design an effective COVID-19 therapeutic, it is necessary to have enough information about cell signalling cascades following virus attachment and entrance. Due to the multi-faceted nature of this disease, different stages have been considered for it and the treatment in each stage is different from the other stage. In the initial phase, the body's defense against the virus is very important, and in the next phase, it is important to prevent the cytokine storm and its complications. In this thematic issue, we uncover some important biomolecules involved in COVID-19 virulence and propose some preventive and therapeutic strategies to combat virus and diseases.

INTRODUCTION
In December 2019, China witnessed an acute respiratory syndrome that led to death. After a while, the disease quickly spread around the world and became to be known as COVID-19. However, later, clinical symptoms showed the involvement of other organs, as well. As a known cause of this disease, coronavirus had shown severe pathogenicity some years ago by SARS-CoV and MERS-CoV viruses in 2002 and 2012. This time the SARS-CoV-2 virus is pandemic, and as of 26 March 2021, 126 million cases infected by the virus, while 2.76 million cases died. Despite many efforts to eradicate the virus and treat the patients, there is no successful therapeutic strategy to combat the virus. An important reason is the virus's unknown mechanisms and its mutation that frequently changes virus genotype and disease symptoms.

The first step in designing effective therapeutics for COVID-19 is to have enough information about its pathogenesis and the mechanisms involved. SARS-CoV-2 attaches through its spike glycoproteins to host cell receptors, including ACE2 and CD147. However, it is possible to the virus has other unknown receptors, as well. Following attachment to its receptor, spike cleavages into S1 and S2 by a serine protease TMPRSS2 [1]. It was demonstrated that TMPRSS2 is more critical than cathepsin L for virus virulence. The virus enters host cells by S2 and upon C-terminal domain cleavage of ACE2 using the TNF-alpha-converting enzyme (TACE), TNF-α is produced and triggers a cascade leading to cytokine storm.

In this issue, it is demonstrated that six conserved miRNAs encoded by the virus mediate SARS-CoV-2 virus pathogenesis through the modulating of cell proliferation, differentiation, and immune responses leading to cytokine storm. Therefore, targeting these miRNAs is of value [2]. Moreover, others mentioned the major role of oxidative stress in respiratory diseases, including COVID-19. They proposed antioxidant agents such as vitamin C, lipophilic vitamins, Zinc, melatonin, quercetin, polyphenols, etc., as a supplement therapy for COVID-19 [3]. However, Torabi-Rahvar et al. believed that two arms of anti-viral and anti-inflammatory therapeutics in the form of combination therapy are necessary [4]. Noticeable stage of the disease will define the type of therapeutics. Since, at the early stage, the body needs to combat the virus, anti-inflammatory medications may worsen the symptom.

In this thematic issue, we have emphasized the preventive and therapeutic strategies to combat COVID-19. Preventive strategies are in the range of simple hand hygiene to vaccination. Alshammery et al. in a cross-sectional study of 627 participants, showed that women were significantly far better than men who have COVID-19 knowledge and practicing behaviour in Saudi Arabia. In other words, women are more concerned about hand hygiene, staying at home, and sneezing into the elbow [5]. Although hygiene is crucial, the use of vaccines is inevitable due to the numerous viral mutations, transmission rate and pathogenicity. Tavakol et al. proposed several strategies for efficient vaccine designing and development. Cell-based immune enhancement should be considered in vaccine development for COVID-19. To this end, a short sequence of spike and not a whole spike sequence would be preferred to avoid adverse immune reactions. They believed that since nanoparticles act as adjuvant and passive targeting agents with higher cellular up-take potential than the antigens’ soluble form, incorporating antigens and segments of the target biomolecule into nanoparticles will enhance the vaccine’s efficacy [6].

Despite numerous warnings about social distance, the use of masks, etc., many people are still infected with the virus. Therefore, therapeutic strategy is an essential mechanism to combat the virus in patients. Cytokine storm is the major pathogenesis mechanism of SARS-CoV-2 in patients with the final fate of death. Therefore, therapeutics that prevent this cascade are of interest. Interestingly, clinical studies always are not in line with pre-clinical studies. Although it theoretically seems that a humanized interleukin-6 receptor-inhibiting monoclonal antibody successfully combats the COVID-19, clinical findings showed that tocilizumab combined with other drugs has the benefit just for the moderate case of COVID-19 and it has no efficacy in severe patients [7]. Tian et al. summarized the anti-viral agents and anti-cytokine storm syndrome agents with clinical evidence such as arbidol, remdesivir, favipiravir, Meplazumab, Anakinra, Camostat, nafamostat, etc. [8].

Beside synthetic drugs, Shoaib et al. demonstrated that the administration of natural compounds of ethnomedicinal plants such as Lyco-rosis radiata, Artemisia annua, Pyrois lingua, and Lindera aggregate as a promising therapeutic strategy. These natural compounds show therapeutic efficacy through the interaction with viral proteins and lys353 and lys31 hotspot binding pockets [9]. Cannabis sativa is another natural compound showing pre-clinical anti-viral efficacy [10]. Furthermore, ACE2 inhibiting phenolic compounds such as quercetin, cuminum and gallic acids are proposed to decline COVID-19 pathogenesis [11]. It is crucial to keep in mind that the baseline level of ACE2 is necessary to avoid tissue damages while reducing the C-terminal cleavage of ACE2 decreases COVID-19 pathogenesis by blocking the cytokine storm.

REFERENCES

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Prof. Alexander Marcus Seifalian
and Dr. Shima Tavakol
Guest Editors:
Nanotechnology and Regenerative Medicine Commercialization Centre (NanoRegMed Ltd),
London BioScience Innovation Centre, London, United Kingdom
E-mails: a.seifalian@gmail.com
shima.tavakol@yahoo.com