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.

Stem Cell Research 55 (2021) 102468

Contents lists available at ScienceDirect

Stem Cell Research

journal homepage: www.elsevier.com/locate/scr

Editorial

COVID-19

ARTICLE INFO

Keywords
COVID-19
SARS-CoV-2
Stem Cell
Furin
ACE2
Sex
Infection
Risk Factor
Antiviral
Immune

COVID-19, which was first reported in Wuhan, China in late 2019, has quickly become a pandemic worldwide. As of July 17, 2021, more than 190 million laboratory-confirmed cases and over 4 million deaths of COVID-19 have been notified to WHO. There has been tremendous amount of basic and clinical research on SARS-CoV-2 and COVID-19. Although it is impossible to cover all aspects of COVID-19 research by a few articles, we have carefully chosen 9 review papers which are presented in this special issue of *Stem Cell Research* that covered the possible evolution of this virus, infection routes, organ susceptibility, risk factors, pathological phenotypes, structural bases for viral infection and drug design, drug screening, antiviral antibodies and therapies. Moreover, stem cell transplantation as a potential therapy has been discussed in several papers.

Despite great efforts by many scientists, the origin of COVID-19 is yet unknown. It is presumed to arise through zoonotic transmissions, similar to previous SARS and MERS outbreaks caused by two related coronaviruses. However, there is a hypothetical theory that this SARS-CoV-2 was engineered through some kind of gain-of-function research and leaked due to a lab accident. Wu and Zhao examined the seemingly unusual furin cleavage site that is inserted into the coding region of the spike protein which is critical for SARS-CoV-2 to bind to the ACE2 receptor of the host cells. Interestingly, they found that it has occurred multiple times in coronaviruses before. This is another important evidence for the natural occurrence theory of SARS-CoV-2 although it does not rule out the remote possibility that the increased infection rate of SARS-CoV-2 after addition of this furin cleavage site was a result of some kind of molecular recombination experiments in the lab.

There is growing evidence indicating aged males are more prone to COVID-19. Li et al. have reviewed the previous studies regarding the risk factors and lethality associated with COVID-19. Indeed, males and females are different in inflammatory response. Furthermore, females exhibit higher antiviral immune reaction. The *ACE2* gene as well as the genes encoding a few key immune regulatory proteins are located on X chromosome which is subject to random X chromosome inactivation and sex hormone regulation. These can partly account for the sex-dependent differences in immune response and lethality observed in the patients infected with SARS-CoV-2.

It is important to find out which tissues or cell types that are susceptible to SARS-CoV-2 infection in humans. Human pluripotent stem cells (PSCs) can be used for studying SARS-CoV-2 infection mechanisms and host responses after they are differentiated through monolayer cell cultures or organoids. It can be also used for antiviral drug screening. The human organs such as lung, heart, kidney, liver, pancreas, brain and eye are expected to be all susceptible to SARS-CoV-2 infection based on these organoids derived from human PSCs. These platforms can be used for screening potential drugs or other treatment options against SARS-CoV-2. In the subsequent review articles, Shao and the colleagues examined the effects on heart and lung upon SARS-CoV-2 infection; Jin and the colleagues analyzed the viral receptor expression in the eye and potential effects of SARS-CoV-2 on human ocular tissues and diseases after infection; Yan and the colleagues discussed about how the reproductive systems may be infected by SARS-CoV-2 and its potential effect after transmission through the reproductive systems.

There is urgent need to find suitable antiviral drugs since this virus may continue to circulate in human populations for the years to come. Wang and the colleagues provide a detailed overview about 3D structures of the viral proteins of SARS-CoV-2. These may benefit the rational design of the potential drugs against S protein, Mpro and RdRp that are essential for membrane fusion, protein processing and RNA amplification of SARS-CoV-2, respectively. These structures may also help to

https://doi.org/10.1016/j.scr.2021.102468

Available online 17 July 2021

develop therapeutic antibodies which are also reviewed by Min and the colleagues in their review paper of this special issue. The RBD domain of the viral S protein is required for ACE2 receptor binding during infection. It has been proposed to be a good target for neutralizing antibodies against SARS-CoV-2. Min and the colleagues have also discussed about the approaches for screening and identification of the neutralizing antibodies. Besides antiviral drugs and neutralizing antibodies, mesenchymal stem cells (MSCs) may be applied to improve the health of the patients recovering from SARS-CoV-2 infection that is extensively reviewed by Musial and Gorska-Ponikowska. MSCs have been used for cell transplantation therapies in other diseases such as ischemic cardiomyopathy and autoimmune diseases. They can also secrete a number of cytokines that have immunomodulatory functions. These may be beneficial for COVID-19 patients since their immune systems exhibit elevated inflammatory responses and share some features with autoimmune diseases too.

Rapid development of a few effective vaccines has enabled almost half of the people in the US to be vaccinated and protected from the infection by SARS-CoV-2. As a result, the newly infected patients in the US have been steadily decreasing until the Delta variant is becoming the dominant SARS-CoV-2 virus in the US. It is the similar case for Israel whose population is almost fully vaccinated, and yet the new cases have started to climb from the recent very low levels. Given the high infection rates and mutation rates of SARS-CoV-2, it is likely that COVID-19 will not go away anytime soon, especially in developing countries whose populations have rarely been vaccinated yet. We do hope that there will be some effective drugs or therapies available for COVID-19 patients in the near future. These will help to keep the spreading and potential damage by SARS-CoV-2 to the minimum, together with the eventual vaccination of entire populations of the world. We would like to thank Dr. Thomas Zwaka, the former Editor-in-Chief for *Stem Cell Research*, for giving us the great opportunities to work with many good scientists in the field for this special issue on COVID-19. We also appreciate the tremendous help from the editorial staff during the review processes. We would like to extend our good wishes to the future success of the journal under the leadership of current Editor-in-Chief Dr. Alessandro Prigione.

Xiajun Li*
School of Life Science and Technology, ShanghaiTech University, Shanghai 201210, China

Albert Jiarui Li
Edgemont High School, 200 White Oak Lane, Scarsdale, NY 10583, USA

Bin Du*
State Key Laboratory of Rare, Complex and Critical Diseases, Medical ICU, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Sciences, 1 Shuai Fu Yuan, Beijing 100730, China

* Corresponding author.

* Corresponding author.
E-mail address: lixj1@shanghaitech.edu.cn (X. Li).
E-mail address: dubin98@gmail.com (B. Du).