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Stem Cell Modelling in COVID-19

Rajeev Nagpal[1*], Akriti Srivastava[2] and Victor Ekuta[3]

[1]Brandeis University, Boston, Massachusetts, USA.
[2]University of Connecticut Health Centre, Farmington, Connecticut, USA.
[3]Massachusetts Institute of Technology, Boston, USA.

Authors' contributions

This work was carried out in collaboration among all authors. Authors RN and AS designed the study and wrote the first draft of the manuscript. Authors RN, AS and VE managed the analyses of the study. Authors AS and VE managed the edits and literature searches. All authors read and approved the final manuscript.

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Opinion Article

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ABSTRACT

The ability of stem cells to differentiate into any desired cell type can make them an indispensable tool in COVID-19 modelling studies. Stem cells derived from patients with preexisting conditions or derived from vulnerable populations such as children, can also assist scientists in understanding the unique contributions of these diverse factors to variations in COVID-19 infection responses. Innovative approaches are urgently needed to adequately address the global impact of COVID-19. Stem cell based strategies offer such an approach.

Keywords: Stem cell; modelling; COVID-19.

1. INTRODUCTION

The discovery of stem cells changed the face of biomedical research. The ease with which stem cells can be isolated and the unique ability of stem cells to form any desired cell type renders them extremely important for understanding human physiology under normal as well as pathological conditions [1,2,3]. With the advent of 3D organoid systems, research has taken a safer

**Corresponding author: E-mail: rajeevnagpal@brandeis.edu;*

and faster approach in understanding disease mechanisms and pathogenesis [4].

While previous epidemics, such as Ebola and Middle East Respiratory Syndrome Coronavirus, exposed the world, to some extent, to the threat posed by newly emerging viruses, never before have world economies, life, and health been disrupted as severely as in the case of coronavirus disease-19 (COVID-19) [5]. Each country has reacted differently to the public health measures imposed during Covid 19 which has to a large extent governed the severity of the disease spread and outcomes in all these nations [6]. With stem cells serving as successful disease models in several distinct areas of research, it would be interesting to explore a similar role for these cells in modeling COVID-19.

2. POSSIBILITIES FOR STEM CELLS IN COVID-19 MODELLING

Owing to the ethical constraints associated with using animal models for research purposes, various guidelines were laid down globally. Therefore, stem cell-based models emerged as a potential strategy for avoiding the ethical pitfalls surrounding animal research. Stem cells can be easily derived from a normal individual or a patient through minimally invasive procedures and have the potential to almost completely mimic the in vivo system in a dish. Over the years, progress in this field has been reported in both developed and developing nations, highlighting the use of stem cells as a viable alternative to animal models [7]. This particular trait of stem cells could prove highly advantageous for research on SARS-CoV-2. While COVID-19 causing viral strains have been identified and isolated, the mechanisms through which these strains manifest their damaging effects over the various organ systems of the body remain elusive. Consequently, a reliable model system to investigate these mechanistic underpinnings is extremely important. Stem cell modelling appears to be a safe technique that can be easily leveraged to mimic the organ systems of the body in the form of organoids. In fact, some research groups have already leapt into action with this concept.

To clearly elucidate the phenomenon of tissue tropism in SARS-CoV-2, various research groups have employed organoid approaches as the method of choice. Recently, Penninger and colleagues reported the ability of SARS-CoV-2 to directly infect human induced pluripotent stem cell (iPSC) derived capillary organoids as well as kidney organoids. These observations might aid in understanding the kidney dysfunction associated with SARS-CoV-2 infection and how it spreads in the body of affected individuals [8]. In another study, Zhou and colleagues utilized the first organoid culture derived from the epithelium of bat intestines. The cells that are derived from this epithelial layer and propagated in the form of enteroids precisely recapitulate the multicellular structure and composition of the epithelium present in bat intestines. This could be a promising model and a significant step towards the study of the microbial infections present in the intestine of bats that have the ability to infect the human population [9].

In addition, stem cell models can be derived from patients with various underlying conditions, such as cardiovascular or respiratory disease, to understand differences in coronavirus infection and to evaluate the safety and response of possible COVID-19 therapies in patients with preexisting conditions. Several research groups have already launched novel efforts to explore how cardiac disease impacts COVID-19 and to assess the cardiac effects of COVID-19 targeted therapeutics [10]. Similarly, SARS CoV2 can cause various illnesses, ranging from asymptomatic to mild or even to severe presentations. Stem cell modelling might enable researchers to tease apart underlying genetic variants that could explain observed differences in disease severity among different populations [10]. Likewise, stem cell modelling may elucidate the reasons for differences in how COVID-19 impacts vulnerable populations, such as young children and the elderly. Early on, a widespread misconception that children were not affected by COVID-19, ultimately stymied research and clinical efforts to uncover the unique effects of the disease on this population. However, studies across the world have now shown that COVID-19 can have significant effects on children [11,12]. Due to ethical concerns associated with testing vulnerable populations like children and the elderly, stem cell modelling may provide a mechanism for accelerating studies of COVID-19 in these populations, while lessening ethical concerns.

3. THERAPEUTIC IMPLICATIONS OF STEM CELLS IN COVID 19

Although very limited data exists presently regarding the therapeutic applications of stem cells in Covid 19, some studies are underway to

explore the same. As per a few studies, mesenchymal stem cells have been found effective in relieving Acute Respiratory Distress Syndrome (ADRS) by modulating the adaptive and immune responses through their paracrine signalling. Some clinical trials are also being carried out to prove the potential of these stem cells from a therapeutic point of view in ADRS. Since respiratory stress is a major hallmark of SARS CoV2 mediated Covid 19 the researchers hope mesenchymal stem cells could be a potential remedial measure against the disease. However, it's still too early to comment on it concretely but there surely is hope [13,14].

Recently a group of Chinese researchers also described a possible vaccine derived from engineered human mesenchymal stem cells which showed some positive response [15]. The study is still in its infancy on a large scale, however it can lead to further newer developments and possible approaches for stem cell based vaccine against COVID 19.

4. CONCLUSION

The ability of stem cells to differentiate into any desired cell type can make them an indispensable tool in COVID-19 modelling studies. The fibroblast cells taken either from COVID-19 patients or from healthy individuals can further be converted to induced pluripotent stem cells. These cells can then be differentiated into cell types and organ systems affected by the virus and converted into 3D organoids. The 3D modelling of these differentiated iPSCs can then be used to model the effects the COVID-19 virus has on various organ systems of the body to understand the disease mechanism and manifestation. Stem cells derived from patients with preexisting conditions or derived from vulnerable populations such as children, can also assist scientists in understanding the unique contributions of these diverse factors to variations in COVID-19 infection responses. Now, more than ever, innovative approaches are urgently needed to adequately address the global impact of COVID-19. Stem cell based strategies offer such an approach.

5. LIMITATIONS

Currently, there are no approved stem cell-based approaches for the prevention and treatment of COVID-19 infection. Lack of literature dealing with these technical issues with respect to COVID19 is one of the limitations of this article. However, further discussions and dissemination on this idea may prepare us for future pandemic scenarios.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Laurenti E, Göttgens B. From haematopoietic stem cells to complex differentiation landscapes. Nature. 2018; 553(7689):418-26.
2. Sangeetha P, Maiti SK, Divya M, Shivaraju S. Mesenchymal Stem Cells Derived from rat boné marrow (rBM MSC): Techniques for isolation, expansion and differentiation. Journal of Stem Cell Research & Therapeutics. 2017;3(3):00101.
3. Srivastava A, Singh S, Pandey A, Kumar D, Rajpurohit CS, Khanna VK, Pant AB. Secretome of differentiated PC12 cells enhances neuronal differentiation in human mesenchymal stem cells via NGF-like mechanism. Molecular Neurobiology. 2018;55(11):8293-305.
4. Varkey JB, Ribner BS. Preparing for serious communicable diseases in the United States: What the Ebola virus epidemic has taught us. Emerging Infections 10. 2016:39-52.
5. Dutta D, Heo I, Clevers H. Disease modeling in stem cell-derived 3D organoid systems. Trends in Molecular Medicine. 2017;23(5):393-410.
6. Nagpal R, He Y, Goyal N, Radia H, Kumanan M. Comparison between India, USA and China on the basis of rigidity of public health measures with case count and mortality rate during COVID-19. Current Journal of Applied Science and Technology. 2020:127-32.
7. Singh S, Srivastava A, Srivastava P, Dhuriya YK, Pandey A, Kumar D, Rajpurohit CS. Advances in stem cell research-a ray of hope in better diagnosis and prognosis in neurodegenerative

diseases. Frontiers in Molecular Biosciences. 2016;3:72.
8. Clevers H. COVID-19: Organoids go viral. Nature Reviews Molecular Cell Biology. 2020;1-2.
9. Zhou J, Li C, Liu X, Chiu MC, Zhao X, Wang D, Wei Y, Lee A, Zhang AJ, Chu H, Cai JP. Infection of bat and human intestinal organoids by SARS-CoV-2. Nature medicine. 2020;1-7.
10. Stem Cells as Tools to Identify COVID-19 Treatments [Internet]; 2020. Available:https://www.closerlookatstemcells.org/2020/06/06/stem-cells-as-tools-to-identify-covid-19-treatments/ [Cited 2020 Jun 29]
11. Mehta NS, Mytton OT, Mullins EWS, Fowler TA, Falconer CL, Murphy OB, et al. SARS-CoV-2 (COVID-19): What do we know about children? A systematic review. Clinical Infectious Diseases; 2020.
12. Zhang C, Gu J, Chen Q, Deng N, Li J, Huang L, et al. Clinical and epidemiological characteristics of pediatric SARS-CoV-2 infections in China: A multicenter case series. PLOS Medicine. 2020;17(6).
13. Tsuchiya A, Takeuchi S, Iwasawa T, Kumagai M, Sato T, Motegi S, Ishii Y, Koseki Y, Tomiyoshi K, Natsui K, Takeda N. Therapeutic potential of mesenchymal stem cells and their exosomes in severe novel coronavirus disease 2019 (COVID-19) cases. Inflammation and Regeneration. 2020;40(1):1-6.
14. Orleans LA, is Vice H, Manchikanti L. Expanded umbilical cord mesenchymal stem cells (UC-MSCs) as a therapeutic strategy in managing critically ill COVID-19 patients: the case for compassionate use. Pain physician. 2020;23:E71-83.
15. Liu J, Jiao H, Yin X. Engineered human mesenchymal stem cells as new vaccine platform for COVID-19. bioRxiv; 2020.

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