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Can stem cells be plausible biologics against COVID-19?

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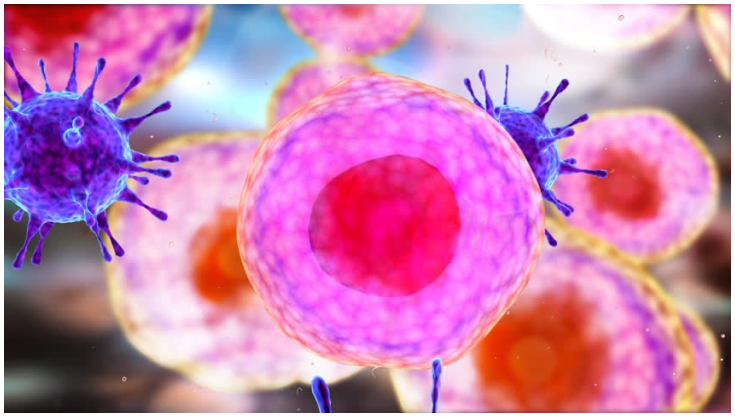
How about killing the virus and replacing the dead lung cells back so that oxygen absorption starts?



COVID-19 is indeed spreading faster than one would imagine. In the absence of tangible alternatives, governments across the world are taking difficult, arduous and economy crippling quarantine route to contain spread of the virus.

However, what about the people who have been already known to be affected or those who are passive carriers of the virus, in whom the virus is lurking to show up again and again at an opportunistic moment.

Medical fraternity is groping with this problem. At present, there are no proven drugs to vanquish the virus. Anti-malarial drugs like hydroxychloroquine (HCQ) or chloroquine are no answer, as they are not known to kill the virus. They may, at best, do not allow virus to invade healthy cells of affected humans. Known antivirals like remdesivir, favipiravir may work on containing the virus but it is yet to be proven beyond doubt. Moreover, toxicity issues with medications like anti-viral drugs exists. Under these conditions out-of-the-box thinking is required.

We know that novel corona virus affects lungs mainly, leading to breathing problems and in severe cases death. Patients affected with the virus have difficulty in breathing as the virus affects outer layer of cells of the lungs that take oxygen from air and transfer it into the blood to be sent across our body. The virus latch on these crucial cells and kill them thereby affecting breathing. Specifically, the mortality in COVID-19 patients are associated with onset of acute respiratory distress syndrome (ARDS) due to its cytokine storm phenomenon resulting in uncontrolled systemic inflammatory response from the release of pro-inflammatory cytokines (IFN-?, IFN?, IL-1?, IL-6, IL-12, IL-8, IL-33, TNF-?, TGF-?) and chemokines (CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL-10 etc). This causes edema, dysfunction of the air exchange, acute respiratory distress syndrome, acute cardiac injury and the secondary infections, which may lead to death.

How about killing the virus and replacing the dead lung cells back so that oxygen absorption starts. How about using one's own cells, produced somewhere else, to do this work.

We think that answer could lie in use of Stem Cells available elsewhere to treat the affected lungs thus make the patient normal again.

What are stem cells? Stem cells are ubiquitous undifferentiated cells, which have the capability to grow into organs in which cells do defined jobs. For example, stem cells produced in bone marrow can grow into cells of the lung. In principle, if lung cells of a particular organ die translocating stem cells into that place can restore the cells and thus save the organ. Among stem cells, the Mesenchymal Stem Cells (MSCs) found in bone marrow have homing ability, immune-regulatory nature, anti-inflammatory effects, and multilineage differentiation potential.

In recent years, the art of cellular therapy has revolutionized the field of regenerative medicine towards natural healing cascade. In the context of COVID19, there is a possibility of treatment of patients by transplanting stem cells. The cellular therapy induces cellular proliferation, chondrogenesis, angiogenesis and rejuvenation of degenerated lung tissue to attain micromolecular homeostasis.

Doctors and scientists working on a few severely ill COVID-19 patients in China reported encouraging results with stem-cell therapy. The results, though of preliminary, are highly encouraging.

Specifically, in a collaborative effort between the groups lead by Dr. Kunlin Jin, M.D., Ph.D. Professor, Department of Pharmacology and Neuroscience, University of North Texas Health Science Center, USA and Professor Robert Chunhua Zhao, Ph.D. (in Medicine) School of Life Sciences, Shanghai University, Shanghai, China and Institute of Basic Medical Sciences Chinese Academy of Medical Sciences, Beijing, China came together to treat critically ill and aged COVID-19 patients with MSCs. Within two days, the patients showed significant improvement. The researchers published the results in recently released issue of the journal *Aging and disease* (2020, Vol. 11, Issue number 2, pages 216-228).

Similarly, the results from a collaborative efforts between Professor Bing Liang, Department of Critical Care Medicine, Baoshan People's Hospital, Baoshan, China, Professor Chuanyun Qian, Emergency Department of the First Affiliated Hospital of Kunming Medical University, Kunming, China, Professor Min Hu, Intervention and Cell Therapy Center, Peking University Shenzhen Hosptial, Shenzhen, China has revealed that the stem cell therapy is effective for treatment of critically ill and aged COVID19 patients. In this case researchers employed stems cells derived from human umbilical cord (Ref Advanced article chinaXiv:202002.00084v1; *yet to be peer reviewed*) .

It appears, the MSCs attenuates cytokine storm and improvise lung compliance and curb off the disease. Since the doctors use the stems cells produced and available elsewhere in the patient's own body to treat the disease, there are no chemotherapy related toxicity issues and there are no compatibility, contamination or rejection related issues.

This therapeutic option of treating critically ill COVID-19 patients with MSCs is relatively non-invasive and inexpensive. The cellular therapy against severe COVID-19 is likely to restore normal breathing by addressing the inflammatory response, maintain functional alveoli microenvironment, promote endogenous regeneration and repair, and natural resistance against the virus with no or minimal side-effects.

Moreover, rapidly expanding COVID-19 patient pool in India provides an opportunity to perform clinical and scientific studies on the patients with South-Asian gene-pool. Although, research in the stem-cell therapy for treating COVID19 is at a nascent stage, there is enormous opportunity and potential to initiate this type of study. Research, in future, will move towards preservation of stem cells at the time of birth, in cell-banks, to be retrieved and used against such devastating and dilapidating diseases, especially for treatment of that individual. Needless to note, and imperative that due ethical consideration must be made while undertaking such a study.

Overall, COVID-19 pandemic, spreading like wildfire compels us to address it through the promising stem cell and regenerative medicine therapy. It demands a focused inter-departmental team to put stem cell therapy into clinical practice to combat this pandemic. We advocate for conducting studies in larger cohort and randomized controlled trials to adduce this novel modality of treatment in combating COVID-19 infection and its complication.

Sooner the better!

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