Received: 27 February 2020 | Accepted: 21 March 2020
DOI: 10.1002/sctm.20-0083

STEM CELLS TRANSLATIONAL MEDICINE

LETTER TO THE EDITOR

Mesenchymal stem cells as a potential treatment for critically ill patients with coronavirus disease 2019

To the Editor,

We read with interest the article by Abraham and Krasnodembskaya regarding mesenchymal stem cells (MSCs)-derived extracellular vesicles for the treatment of acute respiratory distress syndrome (ARDS).[1] Since December 2019, the outbreak of coronavirus disease 2019 (COVID-19) in Wuhan, China, has drawn worldwide attention. As of February 26, 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had infected more than 82 000 people and had led to 2800 deaths from acute lung injury (ALI) and ARDS worldwide. Unfortunately, the numbers of both infected patients and fatalities are still growing and no effective drugs are clinically approved.

Similar to two other lethal coronaviruses, SARS-CoV and MERS-CoV, SARS-CoV-2 induces excessive and aberrant host immune responses that are always accompanied by cytokine storms (CS) and subsequent ALI or even ARDS, resulting in multiple organ failure and death.[2] Even in patients who were treated in intensive care units for CS, persistent inflammation led to serious sequelae of lung fibrosis, causing lung dysfunction and reduced quality of life.[3] Although corticosteroid given to reverse catabolism in critical illness decreased the mortality after SARS and MERS infection, the clinical application of corticosteroid has been restricted in COVID-19, considering its delay in virus clearance and complications in survivors. There is an urgent need for advancing therapeutic interventions with both functions for CS suppression and lung reparation in critical patients.

MSCs have been found to be capable of modulating immune responses, thereby reducing inflammation as well as immunopathology and protecting alveolar epithelial cells during ALI and ARDS.[4-7] More importantly, MSCs were efficacious in reducing the nonproductive inflammation and in promoting lung generation in a phase 2 clinical trial (NCT03608592), as well as in patients with ALI and ARDS in clinical

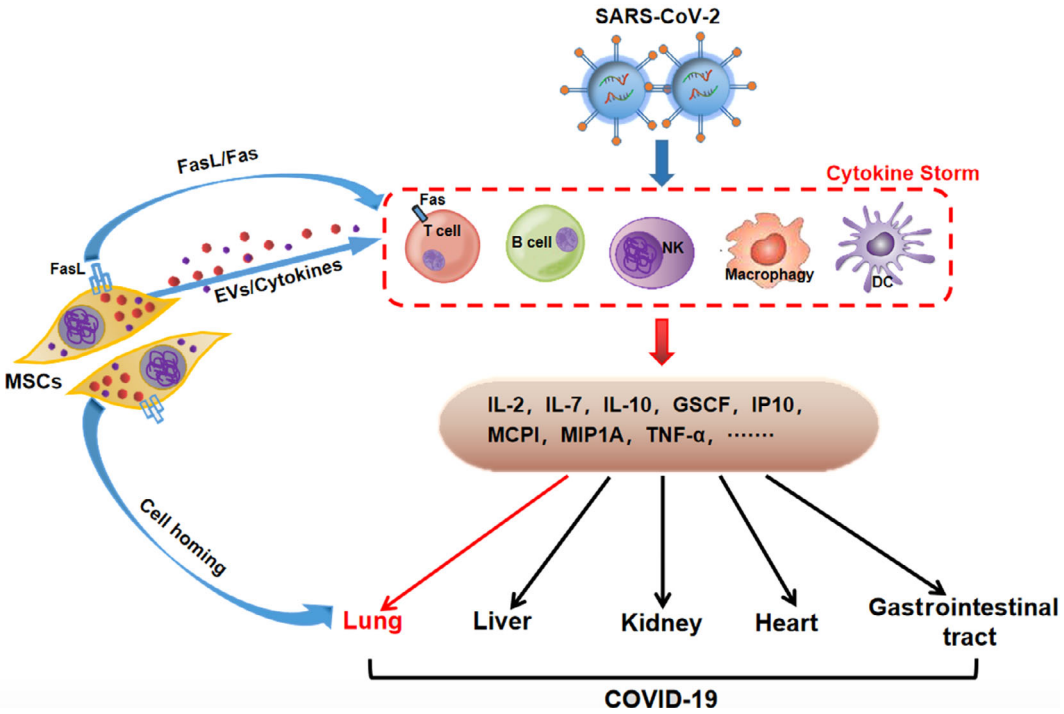

FIGURE 1 Potential mechanism of MSCs in the treatment of severe COVID-19

practice.[8-10] As a result, MSCs may alleviate the SARS-CoV-2-derived CS and ARDS, and have a potential effect on the treatment of subsequent chronic respiratory dysfunction and lung fibrosis.

To alleviate acute respiratory disease and reverse pulmonary fibrosis in intensive-care SARS-CoV-2-infected patients, three curative properties of MSCs have emerged (Figure 1): (a) directly inducing the apoptosis of activated T cells to relieve the aberrant and excessive immune responses, (b) homing toward specific injuries of lung to maintain homeostasis as well as promote regeneration, and (c) releasing cytokines to diminish inflammation and extracellular vesicles (EVs) to stimulate tissue reparation.[1] Notably, it has been proved that MSC-released cytokines can potently inhibit neutrophil intravasation and enhance the differentiation of macrophages.[5,6] Moreover, these MSC-released EVs can deliver microRNA, mRNA, DNA, proteins, and metabolites into host cells in specific injuries of the lung to promote lung repair as well as regeneration and restore lung function.[1]

As the continuing epidemic threat of SARS-CoV-2 to global health and the fast-growing number of fatalities, advancing new therapeutic development becomes central or primary to minimize the death and sequelae from SARS-CoV-2 infection. Thus, MSCs should be considered as a potential treatment for these critical patients. A recent clinical trial (NCT04252118) is expected to verify its efficacy and safety.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest.

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