

COVID-19 Embryonic Stem Cell Transplantation

Zuangrong Sheepsattayakorn

Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

***Corresponding Author :** Zuangrong Sheepsattayakorn, Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Received : August 18, 2023 ;

Accepted : August 19, 2023 ;

Published : September 21, 2023 ;

Editorial

Mesenchymal stem cell (MSC) populations that possess comparable potential for multi-lineage differentiation have been isolated in vitro from a variety of bone marrow (BM) and non-BM tissues, such as the placenta, adipose tissue, amniotic fluid, umbilical cord, and peripheral blood [1–10]. Ten to one hundred Colony-Forming Unit-Fibroblast (CFU-F) per 10⁶ Marrow Mononuclear Cells (MNCs) make up the clonogenic BM-human MSC fraction [11]. Human leukocyte antigen (HLA)-DR expression, multipotency (i.e., chondrogenic, osteogenic, and adipogenic), positive expression of surface antigens CD73, CD90, and CD105, and adherence to plastic are the characteristics of BM-human MSCs [11]. By 2000, physicians' interest in intravenously administered MSC treatment had grown [12]. A prior work showed that both human and murine MSCs can cause immunological suppression by drawing in and eliminating auto-reactive T cells through FasL, which in turn promotes macrophage production of TGF- β and the development of regulatory T cells [13]. The connection between MSC-induced Monocyte Chemoattractant Protein-1 (MCP-1) secretion and dying T cells triggers macrophages to release TGF- β , which in turn activates regulatory T cells and enhances immunological tolerance [14]. The therapeutic importance of MSCs was emphasised by their ability to promote wound healing and differentiate and engraft in vivo [15–21].

The recommendations for MSC characterization were developed in 2006 by the International Society for Cellular Therapy.

They aim to standardise information regarding the biology, definition, isolation, and characterization criteria of MSCs, their significance in vivo, and institutional and ethical laws related to their clinical usage [11]. Several studies have been studied in China since the COVID-19 pandemic. For example, the following ClinicalTrials.gov identifiers are being used to fight against severe COVID-19 or COVID-19 pneumonia: NCT04252118, NCT04273646, NCT04276987, NCT04293692, NCT04302519, NCT04288102, etc. [22–27]. MSCs can help regulate the immune system and help patients return to normal, especially the elderly [28]. They can also reduce the overabundance of inflammatory chemicals and the overproduction of immune cells brought on by the COVID-19 [28].

In conclusion, clinical investigations have shown that human MSCs are safe and are presently being considered as a stem cell treatment for several disorders, including severe COVID-19. However, more research is urgently required to examine and refine several aspects of the human MSC culture environment through the creation of a bioprocess that can be run in compliance with Good Manufacturing Practises (GMP).

References

1. Williams AR, Hare JM. Mesenchymal stem cells: biology, pathophysiology, translational findings, and therapeutic implications for cardiac disease. *Cir Res* 2011; 109 (8): 923-940.
2. Lee OK, Kuo TK, Chen WM, Lee KD, Hsieh SL, Chen TH. Isolation of multipotent mesenchymal stem cells from umbilical cord blood. *Blood* 2004; 103 (5): 1669-1675.
3. Wang HS, Hung CS, Peng ST, Huang CC, Wei HM, Guo YJ, et al. Mesenchymal stem cells in the Wharton's jelly of the human umbilical cord. *Stem Cells* 2004; 22 (7): 1330-1337.
4. Tondreau T, Meuleman N, Delforge A, Dejeneffe M, Leroy R, Massy M, et al. Mesenchymal stem cells derived from CD133-positive cells in mobilized peripheral blood and cord blood : proliferation, Oct4 expression, and plasticity. *Stem Cells* 2005; 23 (8): 1105-1112.

5. Vellasamy S, Sandrasaigaran P, Vidyadaran S, George E, Ramasamy R. Isolation and characterization of mesenchymal stem cells derived from human placenta tissue. *World J Stem Cells* 2012; 4 (6): 53-61.
6. Anker PS l't, Scherjon SA, Kleijburg-van der Keur C, Noort WA, Claas FH, Willemze R, et al. Amniotic fluid as a novel source of mesenchymal stem cells for therapeutic transplantation. *Blood* 2003; 102 (4): 1548-1549.
7. De Coppi P, Bartsch Jr G, Siddiqui MM, Xu T, Santos CC, Perin, et al. Isolation of amniotic stem cell lines with potential for therapy. *Nat Biotechnol* 2007; 25 (1): 100-106.
8. Zuk PA, Zhu M, Ashjian P, De Ugarte DA, Huang JI, Mizuno H, et al. Human adipose tissue is a source of multipotent stem cells. *Mol Biol Cell* 2002; 13 (12): 4279-4295.
9. Gimble J, Guilak F. Adipose-derived adult stem cells: isolation, characterization, and differentiation potential. *Cytotherapy* 2003; 5 (5): 362-369.
10. Zvaifler NJ, Marinova-Mutafchieva L, Adams G, Edwards CJ, Moss J, Burger JA, et al. Mesenchymal precursor cells in the blood of normal individuals. *Arthritis Res* 2000; 2 (6): 477-488.
11. Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, Krause D, et al. Minimal criteria for defining multipotent mesenchymal stromal cells, the International Society for Cellular Therapy position statement. *Cytotherapy* 2006; 8: 315-317.
12. Horwitz EM, Gordon PL, Koo WK, Marx JC, Neel MD, McNall RY, et al. Isolated allogeneic bone marrow-derived mesenchymal cells engraft for cell therapy of bone. *Proc Natl Acad Sci* 2002; 99: 8932-8937.
13. Akiyama K, Chen C, Wang D, Xu X, Qu C, Yamaza T, et al. Mesenchymal stem cell-induced immunoregulation involves Fas ligand/Fas-mediated T cell apoptosis. *Cell Stem Cell* 2012; 10 (5): 544-555.
14. Choi H, Lee RH, Bazhanov N, Oh JY, Prockop DJ. Anti-inflammatory protein TSG-6 secreted by activated MSCs attenuates zymosan-induced mouse peritonitis by decreasing TLR2/NF-Kb signaling in resident macrophages. *Blood* 2011; 118: 330-338.
15. Karp JM, Leng Teo GS. Mesenchymal stem cell homing: the devil is in the details. *Cell Stem Cell* 2009; 4 (3): 206-216.
16. Sivanathan KN, Gronthos S, Rojas-Canales D, Thierry B, Coates PT. Interferon-gamma modification of mesenchymal stem cells : implications of autologous and allogeneic mesenchymal stem cell therapy in allotransplantation. *Stem Cell Rev* 2014; 10 (3): 351-375.
17. Nemeth K, Keane-Myers A, Brown JM, Metcalfe DD, Gorham JD, Bundoc VG, et al. Bone marrow stromal cells use TGF-beta to suppress allergic responses in a mouse model of ragweed-induced asthma. *Proc Natl Acad Sci* 2010; 107 (12): 5652-5657.
18. Ren G, Zhang L, Zhao X, Xu G, Zhang Y, Roberts AI, et al. Mesenchymal stem cell-mediated immunosuppression occurs via concerted action of chemokines and nitric oxide. *Cell Stem Cell* 2008; 2 (2): 141-150.
19. English K, French A, Wood KJ. Mesenchymal stromal cells: facilitators of successful transplantation? *Cell Stem Cell* 2010; 7 (4): 431-442.
20. Murphy MB, Moncivais K, Caplan AI. Mesenchymal stem cells: environmentally responsive therapeutics for regenerative medicine. *Exp Mol Med* 2013; 45: e54.
21. Tyndall A. Mesenchymal stem cell treatments in rheumatology: a glass half full? *Nat Rev Rheumatol* 2014; 10 (2): 117-124.
22. Beijing 302 Hospital, China. ClinicalTrials.gov Identifier: NCT04252118. Mesenchymal stem cell treatment for pneumonia patients infected with 2019 novel coronavirus. Available at: https://clinicaltrials.gov/ct2/show/NCT04252118?show_xprt=Y (accessed on March 28, 2020).
23. Wuhan Union Hospital, China. ClinicalTrials.gov Identifier: NCT04273646. Study of human umbilical cord mesenchymal stem cells in the treatment of novel coronavirus severe pneumonia. Available at: https://clinicaltrials.gov/ct2/show/NCT04273646?show_xcprt=Y (accessed on March 28, 2020).

24. Ruijin Hospital, China. ClinicalTrials.gov Identifier: NCT04276987. A pilot clinical study on inhalation of mesenchymal stem cells exosomes treating severe novel coronavirus pneumonia. Available at: https://clinicaltrials.gov/ct2/show/NCT04276987?show_xprt=Y (accessed on March 28, 2020).
25. Puren Hospital Affiliated to Wuhan University of Science and Technology, China. ClinicalTrials.gov Identifier: NCT04293692. Therapy for pneumonia patients infected by 2019 novel coronavirus. Available at: https://clinicaltrials.gov/ct2/show/NCT04293692?show_xprt=Y (accessed on March 28, 2020).
26. CAR-T (Shanghai) Biotechnology Co., Ltd., China. ClinicalTrials.gov Identifier: NCT04302519. Novel coronavirus induced severe pneumonia treated by dental pulp mesenchymal stem cells. Available at: https://clinicaltrials.gov/ct2/show/NCT04302519?show_xprt=Y (accessed on March 28, 2020).
27. Beijing 302 Hospital, China. ClinicalTrials.gov Identifier: NCT04288102. Treatment with mesenchymal stem cells for severe coronavirus disease 2019 (COVID-19). Available at: <https://clinicaltrials.gov/ct2/show/NCT04288102> (accessed on March 28, 2020).
28. Liying Z. China.org.cn. Mesenchymal stem cell therapy shows promise in treating COVID-19. Published online on March 7, 2020. Available at: www.china.org.cn/china/2020-03/07/content_75785868.htm (accessed on March 28, 2020).