

Editorial

# Stem Cells Therapy in General Medicine

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## **Editorial Article**

Regenerative medicine is much of intense interest among scientists and clinicians. This is a comparatively new field and needs further developments in use. To date, more than 355K in PubMed and almost 3M in Google Scholar, different articles, studies, protocols, and reports related to stem cells indexed and published. In this editorial, we briefly explored the current status and the perspectives of stem cell therapy in general medicine.

Stem cells are the cells with the ability to self-renewal and capable of regenerate the damaged/injured cell types of organs and tissues (1). They are divided into two groups being embryonic and non-embryonic (known as adult stem cells). According to differentiation potential stem cells are divided into 5 types: totipotent, pluripotent, multipotent, oligopotent and unipotent (2). Totipotent stem cells can differentiate into embryonic as well as to extraembryonic cell types. Pluripotent stem cells give rise to any cell types of endoderm, mesoderm and ectoderm, whereas multipotent stem cells differentiate to any cell type of mainly closely related cell family. Oligopotent and unipotent stem cells have differentiation potential towards few cell types and only one type of the cells, respectively.

Due to immunogenicity and ethical issues, embryonic stem cells which are derived from embryonic blastocysts are mostly restricted to in vitro experimental use, therefore clinical applications and the efficiency of these types of cells in therapy needs further research. In comparison, adult stem cells as hematopoietic and mesenchymal stem cells are widely used and reported in many clinical applications. These types of cells exist in mature tissues and can generate different cell types and even regenerate organs. Currently, there are no ethical restrictions on adult stem cells and it was recently shown that autologous adult stem cells have shown therapeutic prevalence in heart disease treatment and other diseases (3-6). The main areas of general medicine, (except onco-hematology, cancer, and systemic diseases), where treatment with stem cell became in common use are depicted in **Figure 1**.

According to the International Society for Cellular Therapy, mesenchymal stem cells are redefined as multipotent mesenchymal stromal cells (7) which has a potency of differentiation into osteoblasts, adipocytes, chondroblasts and potentially many other cell types. However, there is no accepted more precise description of these two types of mesenchymal cells to distinguish, and mostly mesenchymal stem cell (MSC) as a term is used for both types of cells nowadays. MSC cells are widely used in animal models as well as in human diseases, as diabetes, nephropathy (8, 9). Usage of adult stem cells are progressed in gene therapy by being genetically engineered human adult stem cells and has a promising future.

It was reported that MSCs have a potential to reduce or suppress T cell response (10-12) and have shown positive and promising results in the treatment of inflammatory and immunological diseases (13, 14). There are differences in usage of MSCs in clinical applications. The majority reports use bone marrow-derived MSCs (BM-MSCs) which are expanded in vitro before in vivo applications (15, 16), whereas other reports show where they used stem cells bypassing selection step in animal and human studies (17-19) and there are studies where stem cells were selected by using surface markers prior to use (20, 21). In vitro expansion of stem cells prior injection can reduce the quality of treatment, because

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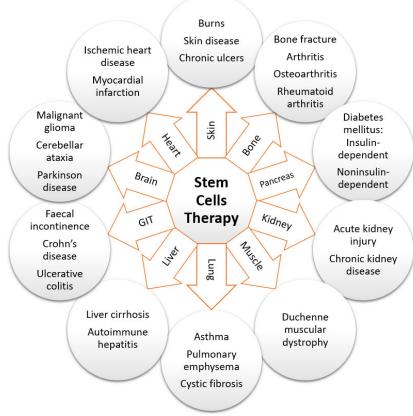


Figure 1: Stem cells therapy in general medicine

of the prolonged culturing period and limited functional potential (22). In comparison, non-expanded stem cell populations would have more repair potential, enough number of cells, although comparative studies needed.

BM-MSCs could contain multiple cell populations, which have the same ancestral cell, and the number and potential of these cell populations may vary in reparation (22). Therefore, pooled samples containing various populations may not be efficient in therapy due to the inhibition of less efficient population by more efficient ones. Besides, there are no currently available reports showing the optimal dosage and route of administration of stem cells neither in human nor in animal models. Nevertheless, the most common route of interventions conducted via intraarterial or intravenous infusions to provide systemic delivery to damaged organs/tissues and via local applications for treatment of local external surgical diseases such as burns, ulcers, and wounds (3, 6, 18, 23).

Nowadays, scientists and pharmaceutical industries are developing and manufacturing commercially available stem cells for pre-clinical trials and practical use (24-27). However, these are allogeneic stem cells, collected from different sources or donors, and their immunogenicity mostly debated comparing to autologous stem cells (28). Allogeneic MSCs have hypoimmunogenic property and might be transplanted between HLA-incompatible donors, which bypass the concerns regarding transplant rejection issues (29). Although, MSCs reported as low-immunogenic and immune-evasive cells (30), and clinical advantage of autologous MSCs over allogeneic MSCs has not been demonstrated to date. Even so, patients who underwent treatment with allogeneic stem cells should be screened for panel reactive antibody and donor-specific antibody, if the information was provided, and be aware of high sensitization before organ transplantation in the case of necessity. Further studies should be addressed to these issues, along with long-term outcomes and malignancy.

In conclusion, stem cell therapy is the future of regenerative medicine and the more insight research is needed to understand the exact biology and the therapeutic potential of stem cells. Stem cell-based treatment is exciting and very promising, that most likely benefit the human health. New editorial board of Electronic Journal of General Medicine welcomes all authors worldwide, to submit their valuable studies in the area of stem cells treatment and regenerative medicine for further consideration and publication.

# REFERENCES

- 1. Odorico JS, Kaufman DS, Thomson JA. Multilineage differentiation from human embryonic stem cell lines. Stem Cells. 2001;19(3):193-204. https://doi.org/10.1634/stemcells.19-3-193
- 2. Hans R. The potential of stem cells: An inventory. Human biotechnology as Social Challenge, England, Ashgate Publishing, Ltd. 2007;28.
- Strauer B, Brehm M, Zeus T, Gattermann N, Hernandez A, Sorg R, et al. Intrakoronare, humane autologe Stammzelltransplantation zur Myokardregeneration nach Herzinfarkt. DMW-Deutsche Medizinische Wochenschrift. 2001;126(34/35):932-8. https://doi.org/10.1055/s-2001-16579-1
- 4. Rakhimbekova GA, Tuganbekova SK, Askarov MB, Zhusupova AS, Krivoruchko NA, Akshalova GA, et al. Autologous hematopoietic stem cell transplantation in systemic sclerosis. J Clin Med Kaz. 2013;3(29):7-10.
- Gaipov A, Taubaldiyeva Z, Askarov M, Turebekov Z, Popova N, Tuganbekova S. Impact of autologous bone marrow-derived stem cells to markers of renal deterioration in type 1 diabetes mellitus with nephropathy. Nephrology Dialysis Transplantation. 2015;30(suppl 3):iii534-iii. https://doi.org/10.1093/ndt/gfv195.10
- Dzholdasbekova A, Fedotovskikh G, Askarov M, Komsabakova B, Baigenzhina A, Kairatova A, et al. Systemic administration of autologous mononuclear precultured bone marrow stem cells in heart failure. J Clin Med Kaz. 2015;3(37):14-8.
- 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(4):315-7. https://doi.org/10.1080/14653240600855905
- Gaipov A, Turebekov Z, Serebrennikova D, Kozina L, Askarov M, Tuganbekova S. Autologous bone marrow-derived stem cells transplantation in type I diabetes mellitus. Nephrology Dialysis Transplantation. 2016;31(suppl 1):i217i. https://doi.org/10.1093/ndt/gfw169.03
- Tuganbekova S, Gaipov A, Turebekov Z, Saparbayev S, Shaimardanova G, Popova N, et al. Fetal Renal Stem Cell Transplant in Nephrotic and Nonnephrotic Glomerulonephritis with Stage 2-4 Chronic Kidney Disease: Potential Effect on Proteinuria and Glomerular Filtration Rate. Exp Clin Transplant. 2015;13 Suppl 3:156-9.
- 10. Sato K, Ozaki K, Oh I, Meguro A, Hatanaka K, Nagai T, et al. Nitric oxide plays a critical role in suppression of T-cell proliferation by mesenchymal stem cells. Blood. 2007;109(1):228-34. https://doi.org/10.1182/blood-2006-02-002246
- 11.Le Blanc K, Ringden O. Immunomodulation by mesenchymal stem cells and clinical experience. J Intern Med. 2007;262(5):509-25. https://doi.org/10.1111/j.1365-2796.2007.01844.x
- 12. Keating A. How do mesenchymal stromal cells suppress T cells? Cell stem cell. 2008;2(2):106-8. https://doi.org/10.1016/j.stem.2008.01.007
- 13. Aksu AE, Horibe E, Sacks J, Ikeguchi R, Breitinger J, Scozio M, et al. Co-infusion of donor bone marrow with host mesenchymal stem cells treats GVHD and promotes vascularized skin allograft survival in rats. Clin Immunol. 2008;127(3):348-58. https://doi.org/10.1016/j.clim.2008.02.003
- 14. Tian Y, Deng YB, Huang YJ, Wang Y. Bone marrow-derived mesenchymal stem cells decrease acute graft-versushost disease after allogeneic hematopoietic stem cells transplantation. Immunol Invest. 2008;37(1):29-42. https://doi.org/10.1080/08820130701410223
- 15. Abdallah BM, Kassem M. Human mesenchymal stem cells: from basic biology to clinical applications. Gene Ther. 2008;15(2):109-16. https://doi.org/10.1038/sj.gt.3303067
- 16. Brooke G, Cook M, Blair C, Han R, Heazlewood C, Jones B, et al. Therapeutic applications of mesenchymal stromal cells. Semin Cell Dev Biol. 2007;18(6):846-58. https://doi.org/10.1016/j.semcdb.2007.09.012
- 17. Crovace A, Lacitignola L, De Siena R, Rossi G, Francioso E. Cell therapy for tendon repair in horses: an experimental study. Vet Res Commun. 2007;31 Suppl 1:281-3. https://doi.org/10.1007/s11259-007-0047-y
- 18. Beeres SL, Lamb HJ, Roes SD, Holman ER, Kaandorp TA, Fibbe WE, et al. Effect of intramyocardial bone marrow cell injection on diastolic function in patients with chronic myocardial ischemia. J Magn Reson Imaging. 2008;27(5):992-7. https://doi.org/10.1002/jmri.21081
- 19. Bartsch T, Brehm M, Zeus T, Strauer BE. Autologous mononuclear stem cell transplantation in patients with peripheral occlusive arterial disease. J Cardiovasc Nurs. 2006;21(6):430-2. https://doi.org/10.1097/00005082-200611000-00003

- 20. Schafer R, Wiskirchen J, Guo K, Neumann B, Kehlbach R, Pintaske J, et al. Aptamer-based isolation and subsequent imaging of mesenchymal stem cells in ischemic myocard by magnetic resonance imaging. Rofo. 2007;179(10):1009-15. https://doi.org/10.1055/s-2007-963409
- 21. Jin HJ, Bae YK, Kim M, Kwon SJ, Jeon HB, Choi SJ, et al. Comparative analysis of human mesenchymal stem cells from bone marrow, adipose tissue, and umbilical cord blood as sources of cell therapy. Int J Mol Sci. 2013;14(9):17986-8001. https://doi.org/10.3390/ijms140917986
- 22. Charif N, Li YY, Targa L, Zhang L, Ye JS, Li YP, et al. Aging of bone marrow mesenchymal stromal/stem cells: Implications on autologous regenerative medicine. Biomed Mater Eng. 2017;28(s1):S57-S63. https://doi.org/10.3233/BME-171624
- 23. Tuganbekov T, Askarov M, Ashimov N, Saipiyeva D. Stem Cells Therapy of Lower Extremity Ulcers. J Clin Med Kaz. 2013;4(30):14-20.
- 24. Kayupov B, Saparbayev S, Ualiyeva S, Kassymova Z, Oralbay A, Zhakupova A, et al. Development of lyophilized drug of human hepatocytes for the liver failure treatment. J Clin Med Kaz. 2013;4(30):70-6.
- 25. Tabatabaei FS, Samadi R, Tatari S. Surface characteristics of three commercially available grafts and adhesion of stem cells to these grafts. Bio-medical materials and engineering. 2017;28(6):621-31. https://doi.org/10.3233/BME-171700
- 26. Davies BM, Smith J, Rikabi S, Wartolowska K, Morrey M, French A, et al. A quantitative, multi-national and multistakeholder assessment of barriers to the adoption of cell therapies. J Tissue Eng. 2017;8:2041731417724413. https://doi.org/10.1177/2041731417724413
- 27. Abbasalizadeh S, Pakzad M, Cabral JMS, Baharvand H. Allogeneic cell therapy manufacturing: process development technologies and facility design options. Expert Opin Biol Ther. 2017;17(10):1201-19. https://doi.org/10.1080/14712598.2017.1354982
- 28. Li Pira G, Biagini S, Cicchetti E, Merli P, Brescia LP, Milano GM, et al. Immunoselection techniques in hematopoietic stem cell transplantation. Transfus Apher Sci. 2016;54(3):356-63. https://doi.org/10.1016/j.transci.2016.05.012
- 29. Le Blanc K, Tammik C, Rosendahl K, Zetterberg E, Ringden O. HLA expression and immunologic properties of differentiated and undifferentiated mesenchymal stem cells. Exp Hematol. 2003;31(10):890-6. https://doi.org/10.1016/S0301-472X(03)00110-3
- 30. Ankrum JA, Ong JF, Karp JM. Mesenchymal stem cells: immune evasive, not immune privileged. Nat Biotechnol. 2014;32(3):252-60. https://doi.org/10.1038/nbt.2816

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