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Dates: **Received:** 30 December, 2015; **Accepted:** 31 December, 2015; **Published:** 31 December, 2015

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www.peertechz.com

ISSN: 2641-3000

Editorial

Mesenchymal Stem Cell as a Vector for Gene and Cell therapy Strategies

Editorial

Stem cells are undifferentiated biological cells that able to maintain undifferentiated state through cell division and give rise to any mature cell type. They are almost divided into embryonic (ESC) and adult stem cells (ASC). ASCs have lineage restriction in compare to ESCs which they cannot differentiate into all 3 layers (ectoderm, mesoderm and endoderm) [1,2].

The most characterized ASC population in bone marrow is hematopoietic (HSC) and mesenchymal stem cells (MSC). HSC was transplanted in many blood related diseases like as leukemia and HIV infection [3-6]. In addition to bone marrow transplantation, MSCs have ability to specifically target tumor tissue and pathological condition such as organ fibrosis [7,8]. It is provided alternative therapeutic approaches -cell and/or gene therapies- by unique self-renewal and multi lineage differentiation capability of stem cells [9-11], like as MSCs. They originate from mesoderm and in addition to chondrocytes, osteocytes and adipocytes, they can differentiate into ectodermic and endodermic cells [12]. There are three criteria to detect which cells are MSCs: 1) they must be plastic-adherent 2) Expression of mature stromal cell marker like as CD105, CD73, CD90 and lack of CD45, CD34, CD14, CD19 and HLA-DR molecules expression at their surfaces 3) in vitro differentiation into osteoblasts, adipocytes and chondroblasts [13].

It is demonstrated that MSCs are responsible for growth, wound healing and replacing cell during pathological condition. So, they have critical role in the repairment of tissue injury and degenerative disease and may be perfect vectors for handling the anti-tumor or anti-fibrotic factors. Liver regeneration in cirrhosis and hepatitis B patients is provided by MSCs [14,15]. This tissue engineering technology is showed in treatment of patients with deep skin burns, diabetic critical limb ischemia and bone damages caused by osteonecrosis [16-18]. Also, MSCs can regulate immune response and provided first based-stem cell drug that treat GVHD and crohn`s disease [19,20]. MSC therapy in Osteoarthritis patients improves pain and function [21]. Clinical efficacy is obtained in Rheumatoid Arthritis after 3 month by MSCs [22]. It is showed ALS patients enhanced level of immune-modulatory factors, such as VEGF and TGF-β, after MSCs administration [23]. In MI, transplantation of MSCs in ischemic region enhanced cardiovascular function [24]. Genetic modification and MSCs therapy is applied in renal failure disease [25,26].

As mentioned above, MSCs have critical roles in immune and non-immune disease treatment. But dosage, time, route of administration and events after MSCs infusion are the major questions up to now [20]. In addition, stability in karyotypes of MSCs is observed before 10 passages by genomic mutation and do not undergo malignant transformations [27].

In gene and cell therapy strategies by stem cells, almost target gene is transferred by viral vectors that cause immune stimulation while MSCs administration as a vector in addition to suppress the immune system by inhibition of T cell proliferation and cytokines (IFNγ) can emerge in inflammation tissue specific sites [28,29]. Novel approaches to improve clinical efficacy suggest that combination therapy provide by pre-conditioning of MSCs with licensing stimuli like as IFNγ and TNFα or chemokines [30,31].

As well as, the clinical studies showed autologous/allogeneic MSC transplantation has not any adverse or side effects yet [32]. So, they can be a suitable vector for targeted genes in refractory disease treatment and cancer therapy [33,34]. By the way, autologous modified MSCs return to patient and GVHD, HLA-matching problems are not observed [32].

Altogether, specific immune-modulatory feature of MSCs attract the interest to know them as a vector for safe and effective treatment in many refractory disease by plasticity. Non-tumorigenic and several mesoderm cell type differentiation confirms them for cell therapy and tissue engineering strategies even by gene modification. As a vector, some viral and non-viral showed immune stimulation and non-stability during cell division. In addition they have restricted capacity to carry out target genes or associated with target cells. Repeat in injection of viral and non-viral vector is another limitation. But MSCs removed some restrictions. Immune modulation, multi lineage differentiation, rapid proliferation and short time length between culture and clinical application are the features that bold them as a vector for treatment strategies.

It is not known exactly which sources, doses of administration in special diseases are needed and what is contraindication in clinical use. For example, although in cancer therapy MSCs were applied successfully but they can provide rejection because of immune suppression features while one of the purposes in cell therapy for tumor genesis is immune stimulation against proliferation of cancer cells.

References

1. Wei X, Yang X, Han ZP, Qu FF, Shao L, et al. (2013) Mesenchymal stem cells: a new trend for cell therapy. Acta Pharmacologica Sinica 34: 747-754.
2. Salem HK, Thiemermann C (2010) Mesenchymal stromal cells: current understanding and clinical status. Stem Cells 28: 585-596.
3. Hutter G, Nowak D, Mossner M, Ganepola S, Mussig A, et al. (2009) Long-term control of HIV by CCR5 Delta32/Delta32 stem-cell transplantation. N Engl J Med 360: 692-698.
4. Tebas P, Stein D, Tang WW, Frank I, Wang SQ, et al. (2014) Gene editing of CCR5 in autologous CD4 T cells of persons infected with HIV. N Engl J Med 370: 901-910.
5. Esmaeilzadeh A, Farshbaf A (2015) Novel Approaches Based on Autologous Stem Cell Engineering and Gene-Modification; Evidence for the Cure of HIV/AIDS. Genetic Syndromes & Gene Therapy 6: 1.
6. Esmaeilzadeh A, Farshbaf A, Erfanmanesh M (2015) Autologous Hematopoietic Stem Cells transplantation and genetic modification of CCR5 m303/m303 mutant patient for HIV/AIDS. Medical Hypotheses 84: 216-218.
7. Konala VB, Mamidi MK, Bhonde R, Das AK, Pochampally R, et al. (2015) The current landscape of mesenchymal stromal cell secretome: A new paradigm for cell-free regeneration. Cytotherapy S1465-3249(15)01101-9.
8. Zomer HD, Vidane AS, Goncalves NN, Ambrosio CE (2015) Mesenchymal and induced pluripotent stem cells: general insights and clinical perspectives. Stem Cells Cloning 8: 125-134.
9. Erfan Manesh M, Esmaeilzadeh A, Hajikhan Mirzaei M (2015) IL-24: A Novel Gene Therapy Candidate For Immune System Up-Regulation in Hodgkin's Lymphoma. Journal of Medical Hypotheses and Ideas 9: 61-66.
10. Hajikhan Mirzaei M, Esmaeilzadeh A (2014) Overexpression of MDA-7/IL-24 as an anticancer cytokine in gene therapy of thyroid carcinoma. Journal of Medical Hypotheses and Ideas 8: 7-13.
11. Piri Z, Esmaeilzadeh A, Hajikhanmirzaei M (2012) Interleukin-25 as a candidate gene in immunogene therapy of pancreatic cancer. Journal of Medical Hypotheses and Ideas 6: 75-79.
12. Dezawa M, Ishikawa H, Itokazu Y, Yoshihara T, Hoshino M, et al. (2005) Bone marrow stromal cells generate muscle cells and repair muscle degeneration. Science 309: 314-317.
13. Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, et al. (2006) Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. Cytotherapy 8: 315-317.
14. Peng L, Xie DY, Lin BL, Liu J, Zhu HP, et al. (2011) Autologous bone marrow mesenchymal stem cell transplantation in liver failure patients caused by hepatitis B: short-term and long-term outcomes. Hepatology 54: 820-828.
15. Kharaziha P, Hellstrom PM, Noorinayer B, Farzaneh F, Aghajani K, et al. (2009) Improvement of liver function in liver cirrhosis patients after autologous mesenchymal stem cell injection: a phase I-II clinical trial. European Journal of Gastroenterology and Hepatology 21: 1199-1205.
16. Rasulov MF, Vasilchenkov AV, Onishchenko NA, Krasheninnikov ME, Kravchenko VI, et al. (2005) First experience of the use bone marrow mesenchymal stem cells for the treatment of a patient with deep skin burns. Bulletin of Experimental Biology and Medicine 139: 141-144.
17. Yamada Y, Ueda M, Hibi H, Baba S (2006) A novel approach to periodontal tissue regeneration with mesenchymal stem cells and platelet-rich plasma using tissue engineering technology: A clinical case report. International Journal of Periodontics and Restorative Dentistry 26: 363-369.
18. Lu D, Chen B, Liang Z, Deng W, Jiang Y, et al. (2011) Comparison of bone marrow mesenchymal stem cells with bone marrow-derived mononuclear cells for treatment of diabetic critical limb ischemia and foot ulcer: a double-blind, randomized, controlled trial. Diabetes Res Clin Pract 92: 26-36.
19. Kebriaei P, Isola L, Bahceci E, Holland K, Rowley S, et al. (2009) Adult human mesenchymal stem cells added to corticosteroid therapy for the treatment of acute graft-versus-host disease. Biol Blood Marrow Transplant 15: 804-811.
20. Mannon PJ (2011) Remestemcel-L: human mesenchymal stem cells as an emerging therapy for Crohn's disease. Expert Opin Biol Ther 11: 1249-1256.
21. Koh YG, Jo SB, Kwon OR, Suh DS, Lee SW, et al. (2013) Mesenchymal stem cell injections improve symptoms of knee osteoarthritis. Arthroscopy 29: 748-755.
22. Wang L, Wang L, Cong X, Liu G, Zhou J, et al. (2013) Human umbilical cord mesenchymal stem cell therapy for patients with active rheumatoid arthritis: safety and efficacy. Stem Cells Dev 22: 3192-3202.
23. Kim HY, Kim H, Oh KW, Oh SI, Koh SH, et al. (2014) Biological markers of mesenchymal stromal cells as predictors of response to autologous stem cell transplantation in patients with amyotrophic lateral sclerosis: an investigator-initiated trial and in vivo study. Stem Cells 32: 2724-2731.
24. Kim J, Shapiro L, Flynn A (2015) The clinical application of mesenchymal stem cells and cardiac stem cells as a therapy for cardiovascular disease. Pharmacology and Therapeutics 151: 8-15.
25. Morigi M, Imberti B, Zoja C, Corna D, Tomasoni S, et al. (2004) Mesenchymal stem cells are renotropic, helping to repair the kidney and improve function in acute renal failure. J Am Soc Nephrol. 15: 1794-1804.
26. Held PK, Al-Dhalimy M, Willenbring H, Akkari Y, Jiang S, et al. (2006) In vivo genetic selection of renal proximal tubules. Mol Ther 13: 49-58.
27. Wang Y, Zhang Z, Chi Y, Zhang Q, Xu F, et al. (2013) Long-term cultured mesenchymal stem cells frequently develop genomic mutations but do not undergo malignant transformation. Cell Death Dis 4: e950.
28. Han Z, Jing Y, Zhang S, Liu Y, Shi Y, et al. (2012) The role of immunosuppression of mesenchymal stem cells in tissue repair and tumor growth. Cell Biosci 2: 8.
29. Uccelli A, Moretta L, Pistoia V (2008) Mesenchymal stem cells in health and disease. Nature Reviews: Immunology 8: 726-736.
30. Duijvestein M, Wildenberg ME, Welling MM, Hennink S, Molendijk I, et al. (2011) Pretreatment with interferon-gamma enhances the therapeutic activity of mesenchymal stromal cells in animal models of colitis. Stem Cells 29: 1549-1558.
31. Chen H, Min XH, Wang QY, Leung FW, Shi L, et al. (2015) Pre-activation of mesenchymal stem cells with TNF-alpha, IL-1beta and nitric oxide enhances its paracrine effects on radiation-induced intestinal injury. Scientific Reports 5: 8718.
32. Robert M (2014) safety in mesenchymal stem cell transplantation. biolmedical research and therapy 1: 21-24.
33. Rath P, Shi H, Maruniak JA, Litofsky NS, Maria BL, et al. (2009) Stem cells as vectors to deliver HSV/tk gene therapy for malignant gliomas. Curr Stem Cell Res Ther 4: 44-49.
34. Loebinger MR, Sage EK, Janes SM (2008) Mesenchymal stem cells as vectors for lung disease. Proc Am Thorac Soc 5: 711-716.

Citation: *Esmaeilzadeh A, Farshbaf A (2015) Mesenchymal Stem Cell as a Vector for Gene and Cell therapy Strategies. Stud Stem Cells Res Ther1(1): 017-018.*