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

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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


