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Letter to the editor

The advantages and limitations of mesenchymal stem cells in clinical application for treating human diseases

Recently, Hong et al. [1] reported the application of human umbilical cord blood derived mesenchymal stem cells (hUCB-MSCs) on bone regeneration in ovariectomized rats with femoral defects. In this study, the bone regeneration was comparable to nonosteoporotic bone regeneration and it was concluded that hUCB-MSCs could be used in alternative stem cell therapy.

MSCs, which possess characteristics like self-renewal and differentiation potential, have been isolated from a variety of tissue sources including bone marrow, peripheral blood, umbilical cord blood, adipose tissue, fetal liver and lung, dental pulp, skeletal muscle, and synovium [2]. Particularly, the hUCB-MSCs have been proposed as a potential source of MSCs for cell therapy for bone diseases like osteoporosis, instead of bone marrow-derived MSCs (BM-MSCs) or adipose tissue-derived MSCs, owing to its multiple advantages including easy harvesting, immunosuppressive potential, and a stronger capacity to differentiate into osteoblasts than other MSC sources [3].

For the past several years, MSCs including hUCB-MSCs have been applied in animal models or human clinical trials for various disease treatments such as osteoarthritis, graft-versus-host disease (GVHD), multiple sclerosis, spinal cord injury, and liver diseases [2]. In fact, a number of phase I/II trials were processed to identify safety issues and viability of clinical MSC therapy in humans. Recent several studies reported that the clinical application of both autologous and allogenic MSCs did not show severe adverse effects in several animal experiments. Therefore, MSC therapy is expected to find clinical application in human diseases [2].

However, there are some critical issues that need to be addressed before MSCs can be used for clinical therapy in humans, most important of which is the safety issue. Tumor support or the suppression effect of MSCs has been reported and the potential tumorigenicity of MSC-based therapy was recently presented [4]. Despite many clinical results and ongoing clinical trials, there is, as yet, no clear report regarding the long-term safety of MSCs including hUCB-MSCs in humans. In addition, putative profibrogenic potential of MSCs, as shown in liver fibrosis induced by human BM-MSCs [5], poses another obstacle in their therapeutic use. Furthermore, MSCs are mostly a heterogeneous mix of different cell populations that are defined by cell surface phenotypes and/or functional ability to differentiate into multiple cell lineages including osteoclast, chondrocyte, adipocyte, or skeletal myocyte lineages. Heterogeneity may exist within and between MSC populations from diverse sources including donors, tissue, clonal subpopulations and single cells, according to age, sex, genetics, environmental conditions, aging, and epigenetic modifications [6]. Recently, it was reported that the angiogenesis capacity of hUCB-MSC for peripheral artery disease therapy depended on the donor [7].

Although these serious constraints in the therapeutic use of MSCs need to be resolved, the use of MSCs in regenerative medicine remains promising due to their attractive advantages including anti-inflammatory and immunomodulatory features. MSCs may be able to treat a broad range of diseases from repair of skeletal diseases to treatment of GVHD. Thus, more rigorous clinical trials and animal studies are necessary to make MSC therapy a safe and effective therapeutic approach for multiple diseases.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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