



Editorial

Mesenchymal stem cell in wound healing and regeneration



As the regeneration technologies developing, stem cell therapy has been a promising and attractive way to enhance tissue regeneration and problem wound healing. Stem cells are characterized by their multipotency and capacity for self-renewal, and their ability to secrete proregenerative cytokines, making them a promising choice for the tissue regeneration.¹ Currently, stem cell therapy has been tested in preclinical and clinical trials in several different fields with positive clinical outcomes.² Prochazka et al. showed in a study of 96 patients with critical limb ischemia that treatment with autologous mesenchymal stem cells (MSCs) could reduce the frequency of major limb amputation within the first 120 days of follow-up.² In addition, Kirana et al. found that transplantation of bone marrow derived stem cells in the treatment of limb ischemia induced chronic tissue ulcers of diabetic foot patients was safe and feasible, and the improvement in microcirculation could lower the amputation rate.³ Although ethical issues remain unresolved and controversial, stem cell research continue to play an increasing role in the growing need for replacement organs and tissues.⁴

Candidate cell populations for therapeutic application include adult MSCs, embryonic stem cells and induced pluripotent stem cells.¹ As compared with embryonic-derived tissues, adult MSC sources avoid the ethical concerns regarding fetal tissue harvest. MSCs have been isolated from bone marrow, umbilical cord blood, and adipose tissue, and the tissue origin of mesenchymal stem cells seems to be a major determinant of progenitor characteristics.^{5–7} Adipose tissue-derived MSCs have been successfully used in regenerative applications in animal models, such as rabbit condylar defect model and murine calvarial defect model, which have been shown to facilitate chondrogenesis and their osteogenic potential.⁸ Bone marrow derived MSCs are also able to differentiate into a wide variety of nonhematopoietic cells and produce a number of growth factors and cytokines that are important for tissue repair and remodeling and are currently being used in clinical trials for the treatment of chronic obstructive pulmonary disease (COPD) with varying inclusion criteria (different stages of COPD).⁹ Actually, current therapeutic therapies of MSCs include the regeneration of the myocardium lost as a result of ischemic heart disease, stroke

and tendon defect,¹⁰ and therefore, it is interesting to investigate the roles of MSCs transplantation in the repair of large uterine defects presented by Dr. Ho and colleagues in the *Journal of the Chinese Medical Association*.¹¹

Dr. Ho and colleagues demonstrated the differentiation of MSCs to uterine myometrium in mice model.¹¹ The authors examined the roles of MSCs transplantation in the repair of large uterine defects, made in both uterine horns of female rats by a punch instrument, followed by injection of bone marrow-derived MSCs into the myometrium around the defect.¹¹ It was interesting that the transplanted MSCs were detected in the uterine horn with no signs of rejection at day 4 after transplantation, and 70–80% uterine wound closure was achieved. Furthermore, the paracrine signaling effect of MSC conditioned medium, which was abundant in cytokines and chemokines, such as plasminogen activator inhibitor-1 (PAI-1), macrophage migration inhibitory factor (MIF), and IL-6, could stimulate resident stem cells near the injured tissue to repair the defect.¹¹ Therefore, MSCs and MSC-conditioned medium may be applied to promote healing of large uterine defects in laparoscopic removal of huge intramural masses. Although these findings are interesting, the question is raised—why the authors did not use the endometrial MSCs for regenerative medicine? A recent publication showed that the endometrium might be a better source of MSCs for generative medicine,^{12,13} since the sampling of endometrium might be more easier compared with others, including bone marrow-derived MSCs. In addition, is there any difference of MSCs derived from the different resources? For example, MSCs derived from the uterine fibroid tissue are more sensitive to bisphenol A.¹⁴ Finally, although it is not confirmed, it is highly possible to have a success if we use MSCs obtained from the same organ in the repair of defect of the organ itself.

In conclusions, stem cell therapy is flourishing as an exciting field encompassing several organ and tissue system. The challenge is to investigate when to deliver these stem cells of regeneration, where, and by what delivery apparatus or mechanism can directly determine their efficacy. With the continued refinement of stem cell research, the future of stem cell therapy is exciting and promises to provide novel regeneration technology.

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Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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