EDITORIAL

http://dx.doi.org/10.5125/jkaoms.2013.39.2.41
pISSN 2234-7550 · eISSN 2234-5930

Dental tissues as adult stem cell source

Bong-Wook Park, D.D.S., Ph.D.

Division of Oral and Maxillofacial Surgery, Department of Dentistry, School of Medicine, Gyeongsang National University, Jinju, Korea

Multipotent stem cells are the most crucial factor in tissue engineered regeneration procedures. Although bone marrow has been most widely studied and used as mesenchymal stem cell (MSC) source, several attempts have recently been made to obtain multipotential stem cells from more easily accessible sources, including skin, fat, periosteum and dental tissues[1-5]. In previous studies, skin has been shown as an excellent adult stem cell source, which differentiated into osteogenic and neural cells *in vitro* and enhanced bone formation in the maxillary sinus floor and nerve regeneration *in vivo*[5,6]. Further, stem cells derived from fetus differentiated into primordial germ cell and oocyte, and exhibited similar characteristics compared to embryonic stem cells[7,8]. However, harvesting skin tissue also involves an invasive procedure, and stem cells from the skin of older donors possess less stemness and regenerative potential than that of younger donors[4,5].

Dental tissues from extracted teeth could be used as alternative sources of adult stem cells. Dental stem cells were firstly isolated from the pulp tissues of removed third molars (dental pulp stem cell, DPSC), and showed similar characteristics with bone marrow derived MSC[1,2]. After then, some researchers have succeeded in the isolation of stem cells from the pulp tissues of human exfoliated deciduous teeth (SHED)[9] or mesiodens[10]. Subsequently, other dental tissues, such as periodontal ligament[11], root apical papilla[12], and tooth follicle[13], have been explored as adult stem cell sources. MSC-like characteristics of dental stem cells with plastic adherent growth and colony formation, expression of MSC-specific cell surface markers, and multilineage *in vitro* differentiation ability were similar to those of MSCs from skin or bone marrow[14]. However, interestingly, different dental tissues from same donor showed varying stem cell characteristics, including transcription factor expression levels and *in vitro* differentiation potential[15]. Stem cells from root papilla showed the highest expression level of transcription factors and cell surface markers[15]. However, dental follicle derived cells showed enhanced osteoblast-specific genes and ectopic bone formation after *in vivo* transplantation[14], indicating dental follicle is the powerful stem cell source in bone tissue regeneration. Dental pulp is expected to harbor the pools of undifferentiated precursor cells for nerve or vascular tissue regeneration.

The most powerful advantage of dental tissues as stem cells source is that primitive and multipotent tissues could be obtained around age 20, a later age compared to that of other stem cell sources, such as umbilical cord blood or matrix. If these dental tissues are preserved for long time without losing their stemness, they could be used as autologous stem cell source for demanding applications in regenerative medicine. A recent study reported the successful isolation of stem cells from long-term cryopreserved dental pulp tissues of deciduous teeth using a cryoprotectant, 90% fetal bovine serum (FBS) and 10% dimethyl sulfoxide[16]. However, FBS is xenogenic material for human tissue and cells and may alter tissue's properties, and not suitable for long-term preservation of human tissues. Interestingly, an efficient and safe dental tissue cryopreservation method using sucrose and ethylene glycol has been developed, and further analyses are being proceeded for its clinical application (data not published). In near future, the dental tissues, follicle, pulp and root papilla, of extracted wisdom teeth could be cryopreserved for later use as autologous stem cells sources.

References

1. Gronthos S, Mankani M, Brahim J, Robey PG, Shi S. Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. Proc Natl Acad Sci U S A 2000;97:13625-30.
2. Gronthos S, Brahim J, Li W, Fisher LW, Cherman N, Boyde A, et al. Stem cell properties of human dental pulp stem cells. J Dent Res 2002;81:531-5.
3. Lindroos B, Mäenpää K, Ylikomi T, Oja H, Suuronen R, Miettinen S. Characterisation of human dental stem cells and buccal mucosa fibroblasts. Biochem Biophys Res Commun 2008;368:329-35.
4. Toma JG, Akhavan M, Fernandes KJ, Barnabé-Heider F, Sadikot A, Kaplan DR, et al. Isolation of multipotent adult stem cells from the dermis of mammalian skin. Nat Cell Biol 2001;3:778-84.

5. Kang EJ, Byun JH, Choi YJ, Maeng GH, Lee SL, Kang DH, et al. In vitro and in vivo osteogenesis of porcine skin-derived mesenchymal stem cell-like cells with a demineralized bone and fibrin glue scaffold. Tissue Eng Part A 2010;16:815-27.
6. Park BW, Kang DH, Kang EJ, Byun JH, Lee JS, Maeng GH, et al. Peripheral nerve regeneration using autologous porcine skin-derived mesenchymal stem cells. J Tissue Eng Regen Med 2012;6:113-24.
7. Shen W, Park BW, Toms D, Li J. Midkine promotes proliferation of primordial germ cells by inhibiting the expression of the deleted in azoospermia-like gene. Endocrinology 2012;153:3482-92.
8. Park BW, Shen W, Linher-Melville K, Li J. Deleted in azoospermia-like enhances in vitro derived porcine germ cell formation and meiosis. Stem Cells Dev 2013;22:939-50.
9. Miura M, Gronthos S, Zhao M, Lu B, Fisher LW, Robey PG, et al. SHED: stem cells from human exfoliated deciduous teeth. Proc Natl Acad Sci U S A 2003;100:5807-12.
10. Huang AH, Chen YK, Lin LM, Shieh TY, Chan AW. Isolation and characterization of dental pulp stem cells from a supernumerary tooth. J Oral Pathol Med 2008;37:571-4.
11. Seo BM, Miura M, Gronthos S, Bartold PM, Batouli S, Brahim J, et al. Investigation of multipotent postnatal stem cells from human periodontal ligament. Lancet 2004;364:149-55.
12. Reynolds AJ, Jahoda CA. Cultured human and rat tooth papilla cells induce hair follicle regeneration and fiber growth. Differentiation 2004;72:566-75.
13. Morsczeck C, Götz W, Schierholz J, Zeilhofer F, Kühn U, Möhl C, et al. Isolation of precursor cells (PCs) from human dental follicle of wisdom teeth. Matrix Biol 2005;24:155-65.
14. Park BW, Kang EJ, Byun JH, Son MG, Kim HJ, Hah YS, et al. In vitro and in vivo osteogenesis of human mesenchymal stem cells derived from skin, bone marrow and dental follicle tissues. Differentiation 2012;83:249-59.
15. Song JH, Park BW, Byun JH, Kang EJ, Rho GJ, Shin SH, et al. Isolation and characterization of human dental tissue-derived stem cells in the impacted wisdom teeth: comparison of dental follicle, dental pulp, and root apical papilla-derived cells. J Korean Assoc Oral Maxillofac Surg 2010;36:186-96.
16. Ma L, Makino Y, Yamaza H, Akiyama K, Hoshino Y, Song G, et al. Cryopreserved dental pulp tissues of exfoliated deciduous teeth is a feasible stem cell resource for regenerative medicine. PLoS One 2012;7:e51777.