EDITORIAL

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Dental stem cells as a cell source for tissue engineering

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Dental stem cells (DSCs) have been isolated from dental follicles, pulps, root apical papillae, and periodontal ligaments of extracted teeth, and all have exhibited multipotential, self-renewal, and mesenchymal stem cell (MSC) characteristics[1,2]. However, DSCs from different sources vary in their differentiation properties: stem cells from dental follicles or root apical papillae of wisdom teeth showed superior osteogenic differentiation potential, whereas dental pulp stem cells demonstrated remarkably enhanced *in vitro* and *in vivo* neurogenic differentiation ability[1-3]. Importantly, a new tissue cryopreservation protocol has developed for use as an autologous stem cell source[4]. In previous reports, MSCs were successfully isolated from long-term cryopreserved dental tissues (follicles, pulps, and root apical papillae)[4,5]. MSCs from cryopreserved dental tissues showed identical characteristics to those from fresh dental tissues, including stemness, *in vitro* differentiation potential, and cell proliferation rate[4,5]. This tissue cryopreservation method makes it possible to safely store dental tissues after tooth extraction for a long time, allowing them to be used as an autologous stem cell resource. Cells from autologous source may reduce unexpected side effects, such as various immune reactions, when they were *in vivo* transplanted.

In one previous report, MSCs from cryopreserved and fresh dental follicles showed excellent osteogenic regeneration potential and immunomodulatory properties through suppression of the T-helper cell-mediated adaptive immune response, when they were transplanted *in vivo* transplanted into mandibular bone defects[3]. In addition, DSCs from follicles or pulps of extracted wisdom teeth successfully differentiated into cardiomyocyte- and hepatocyte-like cells *in vitro*[5,6]. More importantly, dental pulp-derived stem cells (DPSCs) were distinguished as one of the most powerful cell sources for neurogenic differentiation *in vitro* and *in vivo*[2,7,8]. Previously, DPSCs were shown to exhibit remarkable neurogenic differentiation potential, in terms of expression of neuron-specific markers and having higher Na^+ and K^+ current with the expression of synaptic markers[2]. According to one hypothesis, the origin of dental pulp from the neural crest allows it to more easily differentiate into neuronal cells, compared to other cell lines[7]. Moreover, because of their immunomodulatory effect, DPSCs can activate microglia/astroglia in the host microenvironment, which will enhance the Wallerian degeneration and macrophage invasion, accelerating peripheral nerve regeneration[2]. Interestingly, *in vivo* transplantation of DPSCs to treat sciatic nerve defects in experimental rats increases motor nerve function with histologically abundant regeneration of axonal fibers[8]. Moreover, recent work revealed that DPSCs exhibit higher cholinergic neuronal differentiation potential with acetylcholine production *in vitro* (unpublished data).

Taken together, stem cells from dental tissue, including pulps, apical papillae, and follicles, are shown to be excellent sources for tissue regeneration, with immunomodulatory properties. Stem cells from root apical papillae and follicles demonstrated superior osteogenic differentiation and regeneration potential *in vitro* and *in vivo*. Whereas stem cells from dental pulp revealed excellent *in vitro* neurogenic differentiation and *in vivo* peripheral nerve regeneration potential. In addition, the new method for long-term cryopreservation of dental tissues after tooth extraction can safely preserve them for use as an autologous stem cell source for patients in need,

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which would create a new business model in dentistry.

Conflict of Interest

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

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