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Application of dental stem cells in three-dimensional tissue regeneration

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Abstract

Dental stem cells can differentiate into different types of cells. Dental pulp stem cells, stem cells from human exfoliated deciduous teeth, periodontal ligament stem cells, stem cells from apical papilla, and dental follicle progenitor cells are five different types of dental stem cells that have been identified during different stages of tooth development. The availability of dental stem cells from discarded or removed teeth makes them promising candidates for tissue engineering. In recent years, three-dimensional (3D) tissue scaffolds have been used to reconstruct and restore different anatomical defects. With rapid advances in 3D tissue engineering, dental stem cells have been used in the regeneration of 3D engineered tissue. This review presents an overview of different types of dental stem cells used in 3D tissue regeneration, which are currently the most common type of stem cells used to treat human tissue conditions.

Key Words: Dental stem cells; Dental pulp stem cells; Stem cells from human exfoliated deciduous teeth; Periodontal ligament stem cells; Stem cells from apical papilla; Dental

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Core Tip: Dental stem cell seeding in three-dimensional (3D) engineered scaffolds that mimic the human tissue microenvironment is an emerging technology for regenerative medicine. Dental pulp stem cells, stem cells from human exfoliated deciduous teeth, periodontal ligament stem cells, stem cells from apical papilla, and dental follicle progenitor cells have been used for tissue regeneration utilizing 3D approaches. The analytical results of this literature review reveal many basic and preclinical studies that support the hypothesis that the application of dental stem cells is a feasible approach for translational medicine and is an applicable method for 3D tissue regeneration.

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INTRODUCTION

The multipotent properties of stem cells make them excellent sources of material for tissue repair. Five dental-derived cell types have been isolated and characterized as dental stem cells[1]. Dental pulp stem cells (DPSCs), stem cells from human exfoliated deciduous teeth (SHEDs), periodontal ligament stem cells (PDLSCs), stem cells from apical papilla (SCAP), and dental follicle progenitor cells (DFPCs) are different types of dental stem cells involved in different stages of tooth development (Figure 1). Considering their differentiation potential, dental stem cells have been introduced to regenerate damaged or lost tissue. Dental stem cells are not restricted to use in dental tissue repair but can also participate in neural, adipose, bone, and cartilage tissue regeneration[2,3]. Recently, three-dimensional (3D) tissue engineering has been applied to therapeutic medicine. Cells are seeded in 3D engineered scaffolds to mimic the human tissue microenvironment during cell differentiation. The cell morphology and gene expression of the cells cultured under 3D conditions are more consistent with those of cells observed in native tissue[4]. The use of customized 3D tooth implants with dental stem cells seeded in suitable scaffolds as replacements for lost teeth is a promising approach in dentistry. In addition to tooth repair, there is growing interest in the concept of 3D tissue regeneration with dental stem cells.

Here, we searched databases to identify the literature on dental stem cells used in 3D tissue regeneration. The literature searches and data mining were performed by customized scripts with the "easyPubMed" and "PubMed.mineR" packages in R for use with the PubMed database[5-7]. The keywords used in the queries included "pulp stem cells", "exfoliated deciduous teeth stem cell", "periodontal ligament stem cell", "apical papilla", "dental follicle cells", "3D", "tissue", "regeneration" and "engineering". The search results were output with the "abstract" format in the "easyPubMed" package and were analyzed by the "PubMed.minR" package. A total of 88 papers were found with the aforementioned criteria. After review, only one-third of the papers articulated original research on dental stem cells in 3D tissue regeneration. In this review, we aim to provide a clear point of view on each type of dental stem cell used in combination with 3D tissue scaffolds, such as microspheres, hydrogels, or 3D printed scaffolds, to regenerate into teeth, neurons, bone, blood vessels and cartilage (Figure 1 and Table 1).

DPSCS

DPSCs located in the soft connective tissue inside the dental crown were first identified in 2000 (Figure 1)[8]. DPSCs exhibit MSC-like properties, including a high proliferation rate, multilineage potential, and immunomodulatory properties[8,9]. Even though DPSCs exhibit features similar to those of BMSCs, their characteristics of

Table 1 List of dental stem cells used for three-dimensional tissue regeneration

Dental stem cells	Biomaterials	Addition of materials/growth factors/cells	Type of tissue regeneration	Ref.
DPSCs				
DPSCs	CaP porous granules, NF-gelatin/MgP	No	Odontogenic differentiation	Nam <i>et al</i> [24], and Qu <i>et al</i> [30]
	SS-PLLA-b-PLYS, pNIPAAm, NF-PLLA	No	Pulp-dentin regeneration	Kuang <i>et al</i> [16], Itoh <i>et al</i> [17], and Soares <i>et al</i> [18]
	Coll/HA/PLCL, ABM/ABM-P-15, PVA/PU	No	Bone tissue	Mohanram <i>et al</i> [13], Cooke <i>et al</i> [19], and Akkouch <i>et al</i> [21]
	OMMT/PVA	No	Neuro-like cells	Ghasemi Hamidabadi <i>et al</i> [47]
	Matrigel	No	Endotheliocytes and pericytes	Luzuriaga <i>et al</i> [51]
	Collagen gel	SDF1, bFGF BMP7	Dental pulp tissue	Suzuki <i>et al</i> [23]
DPSCs with growth factors	Ti6Al4V	Poly-L-lys coating	Osteoblastic differentiation	Galli <i>et al</i> [32]
	Porous silk fibroin	bFGF	Dental pulp tissue	Yang <i>et al</i> [26]
	PCL	VEGF, BMP2	Vascularized bone tissue	Park <i>et al</i> [39]
	HP hydrogel	bFGF	Spinal cord	Luo <i>et al</i> [48]
DPSCs with other cells	Matrigel and collagen gel	Human normal oral epithelial cells	Epithelium invagination-like structure	Xiao and Tsutsui[35]
	PCL/PLDLA	Endothelial cells	Vascularized bone tissue	Jin and Kim[36]
	PLLA/PLGA	Human neonatal dermal fibroblasts	Spinal cord	Guo <i>et al</i> [50]
DPSCs in 3D printed scaffolds	HA/TCP	Apical papilla (SCAP)	Pulp-dentin regeneration	Hilkens <i>et al</i> [40]
	PCL	Platelet-rich plasma	Calvaria bone	Li <i>et al</i> [27]
	Alg-Gel		Bone	Yu <i>et al</i> [38]
	PLAS		Neural differentiation	Hsiao <i>et al</i> [42]
	AMP/ECM		Craniomaxillofacial bone	Dubey <i>et al</i> [41]
SHED				
SHED with growth factors	No	EGF, FGF	Spinal cord	Feng <i>et al</i> [58]
	No	SHED-conditioned medium	Sciatic nerve	Sugimura-Wakayama <i>et al</i> [59]
SHED in 3D formed scaffolds	Polylactoglycolide, SHED aggregated hemisphere		Bone tissue	Laino <i>et al</i> [56], and Vakhrushev <i>et al</i> [57]
PDLSCs				
PDLSCs	Hydroxyapatite/ β -tricalcium phosphate (HA/ β -TCP)		Periodontal tissue	Kim <i>et al</i> [66]
	GelMA/PEG		PDLSC proliferation	Ma <i>et al</i> [80]
PDLSCs with growth factors	PLGA	CTGF, BMP-7, BMP-2	Periodontal tissue	Cho <i>et al</i> [73]
	Platelet-rich fibrin	Aspirin	Periodontal tissue	Du <i>et al</i> [76]
PDLSCs with other cells	Collagen/Chitosan	Somatic MSCs and DPSCs	Odontogenic differentiation	Ravindran <i>et al</i> [79]
	No	HUVECs	Periodontal tissue	Kramer[77]
	PLGA-PEG-PLGA thermal hydrogel	PDLSCs overexpressing PDGF-BB	Alveolar bone tissue	Pan <i>et al</i> [78]

SCAP				
SCAP with growth factors	PLLA nanofibrous microspheres (NF-MS)	BMP-2	Pulp-dentin regeneration	Wang <i>et al</i> [86]
	No	BMP-2, SDF-1 α	Odontoblast differentiation	Xiao <i>et al</i> [87]
	Alg-Dent hydrogel	Dentin ECM	Pulp-dentin regeneration	Athirasala <i>et al</i> [95]
DFPCs				
DFPCs	Coll-nano-HA/OPS		Bone tissue	Salgado <i>et al</i> [102]

DFPCs: Dental follicle progenitor cells; SCAP: Stem cells from apical papilla; PDLSCs: Periodontal ligament stem cells; SHED: Human exfoliated deciduous teeth; DPSCs: Dental pulp stem cells; SDF1: Stromal-derived factor-1 α ; bFGF: Basic fibroblast growth factor; BMP-7: Bone morphogenetic protein-7; Ti6Al4V: Titanium-6-aluminum-4-vanadium; Poly-L-lys: Poly-L-lysine; CaP: Calcium phosphate; OECs: Human normal oral epithelial cells; PLCL: Collagen (Coll)/hydroxyapatite (HA)/poly(l-lactide-co- ϵ -caprolactone); NF-gelatin/MgP: Gelatin/magnesium phosphate; VEGF: Vascular endothelial growth factor; BMP-2: Morphogenetic protein-2; EGF: Epidermal growth factor; FGF: Fibroblast growth factor; PCL: Polycaprolactone; NF-SMS: Nanofibrous spongy microspheres; SS-PLLA-b-PLYS: Star-shaped poly(l-lactic acid)-block-poly(l-lysine); PLDLA: Poly-L/D-lactide; ECs: Endothelial cells; HA/TCP: Hydroxyapatite/tricalcium phosphate; OMMT/PVA: Chitosan-intercalated montmorillonite/poly(vinyl alcohol); PRP: Platelet-rich plasma; pNIPAAm: Poly-N-isopropylacrylamide gel; HP: Heparin-poloxamer hydrogel; NF-PLLA: Nanofibrous poly(l-lactic acid) scaffolds; Alg-Gel: Alginate/gelatin hydrogel; 3DP-PLASs: Polylactic acid scaffolds; ABM: Bone mineral; ABM-P-15: Biomimetic collagen peptide; PVA: Polyvinyl alcohol; PU: Polyurethane; AMPs: Amorphous magnesium phosphates; ECM: Extracellular matrix; PLLA: Polylactoglycolide scaffolds; NF-MS: Nanofibrous microspheres; SDF-1 α : Normal cell-derived factor-1 α ; GelMA: Gelatin methacrylate; PEG: Poly(ethylene glycol); dimethacrylate; PLGA: Poly(lactic-co-glycolic acids); CTGF: Connective tissue growth factor; HUVECs: Human umbilical vein endothelial cells; Coll-nano-HA/OPS: Collagen-nanohydroxyapatite/phosphoserine.

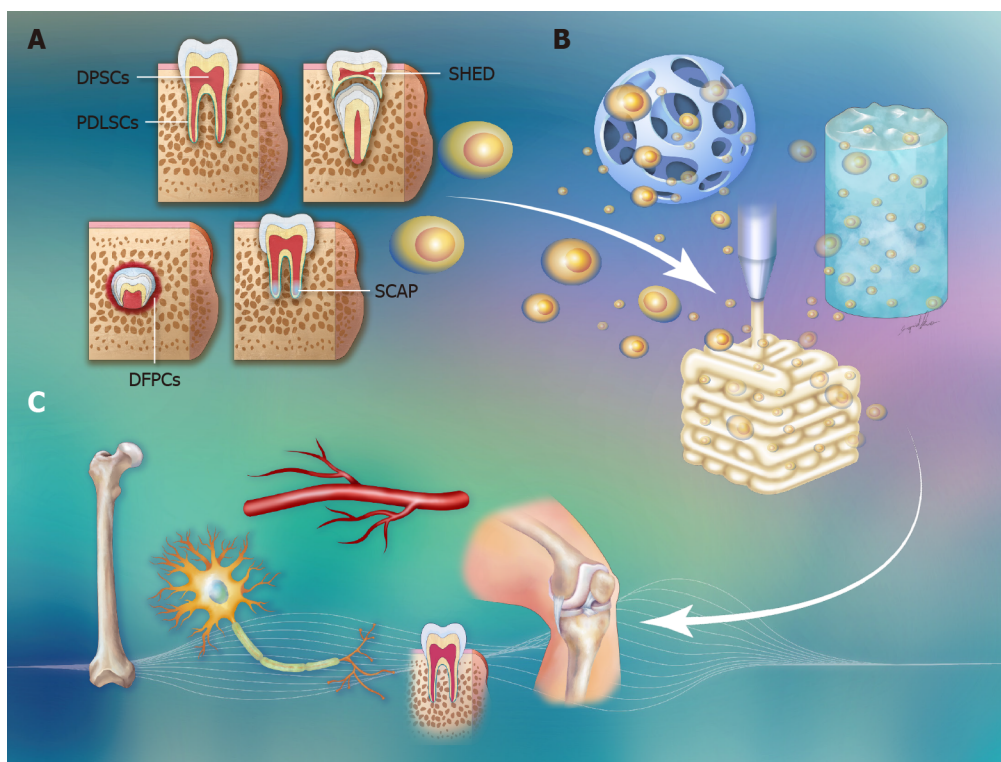


Figure 1 Schematic illustration of dental stem cells in three-dimensional tissue regeneration. A: Five different types of dental stem cells are harvested during different tooth developmental stages; B: Dental stem cells are incorporated with various forms of three-dimensional (3D) biomaterials (microspheres, hydrogels, or 3D printed scaffolds) to generate 3D engineered tissue; C: Dental stem cells are induced to differentiate into different types of tissue, such as teeth, neurons, bone, blood vessels and cartilage.

causing little morbidity at the donor site, a higher proliferation rate, and multipotency make DPSCs better stem cell sources for tissue regeneration[10]. DPSCs cocultured with apical bud cells (ABCs) exhibited more active odontogenic differentiation ability than BMSCs cocultured with ABCs[11]. The neural differentiation of IMR-32 cells was significantly enhanced when treated with secretomes derived from DPSCs compared to BMSCs[12]. The assessment of neurogenic potential on the secretome of DPSCs and BMSCs indicated that DPSCs presented better potential for neural differentiation[12]. Most DPSC studies have focused on dental pulp and bone tissue regeneration.

Compared to bone marrow stem cells, DPSCs have a higher proliferation rate and better osteogenic capacity when seeded in a scaffold of bone mineral (ABM) coated with a biomimetic collagen peptide (ABM-P-15), even generating a more organized collagenous matrix 8 wk after *in vivo* implantation[13]. Moreover, different gene expression patterns have been found in the transcriptome profiles of DPSCs compared to those of bone marrow stem cells, indicating unique gene expression patterns within DPSCs[14].

Application in 3D tissue regeneration

In addition to conventional tissue regeneration approaches with cells loaded on two-dimensional scaffolds, DPSCs have been cultured on 3D biomaterials for the development of tissue constructs. A bioink containing human DPSCs and fibrinogen incorporated with polycaprolactone (PCL) was designed for the production of dentin pulp complex structures[15]. Nanofibrous spongy microspheres made from star-shaped poly(L-lactic acid)-block-poly(L-lysine) (SS-PLLA-b-PLYS) were seeded with DPSCs for dental pulp tissue regeneration[16]. Poly-N-isopropyl acrylamide (pNIPAAm) gel containing DPSCs was made in a rod shape to fill in the root canal for pulp tissue regeneration[17]. Simvastatin and nanofibrous poly(L-lactic acid) (NF-PLLA) scaffolds[18] and a mixture of polyvinyl alcohol (PVA) and polyurethane (PU) [19] were combined with DPSCs to investigate the potential of tissue regeneration. Self-assembling peptides, with structures similar to the extracellular matrix (ECM), are among the smart materials used for 3D culture[20]. A 3D scaffold composed of collagen (Coll), hydroxyapatite (HA), and poly(L-lactide-co- ϵ -caprolactone) (PLCL) increased the adhesion and viability of DPSCs and enhanced bone regeneration compared to a PLCL-only scaffold[21]. DPSCs grown in a peptide-based scaffold presented RGD- and vascular endothelial growth factor (VEGF)-mimetic peptide epitopes and exhibited better survival and angiogenic and odontogenic differentiation [22].

With increased knowledge of the function of growth factors, an increasing number of studies have introduced growth factors into different types of tissue regeneration. In 2011, human DPSCs were placed on the surface of 3D collagen cylinders and cultured with the addition of stromal-derived factor-1 α , basic fibroblast growth factor (bFGF), and bone morphogenetic protein-7 (BMP-7) for dental pulp regeneration[23]. Seeding DPSCs on 3D calcium phosphate (CaP) porous granules promoted odontogenic differentiation by increasing the gene expression of dentin sialophosphoprotein (*DSPP*) and dentin matrix protein 1 (*DMP1*)[24]. Porous silk fibroin scaffolds fabricated with bFGF, which has been reported to facilitate pulp regeneration[25], were used to fill the root canal space for tooth repair[26]. Platelet-rich plasma (PRP) containing various growth factors along with DPSCs was added to 3D printed PCL mesh for bone regeneration in a rat calvaria defect model[27].

In addition to growth factors, metal ions have also been confirmed to contribute to cell differentiation[28]. Magnesium (Mg) is involved in the process of biomineralization during bone and tooth development[29]. Qu *et al*[30] incorporated Mg into nanofibrous gelatin biomaterials to develop 3D gelatin/Mg phosphate (NF-gelatin/MgP) scaffolds seeded with DPSCs, and odontogenic proliferation and differentiation were enhanced. The materials used for dental implants, such as titanium-6-aluminum-4-vanadium (Ti6Al4V), are also used as 3D scaffolds for tissue regeneration. Their properties of low corrosion and smooth metal surfaces prevent stem cells from colonizing this biomaterial[31]. Coatings of poly-L-lysine (poly-L-lys), which carries positive charges, induced focal adhesion kinase activation and increased the osteoblastic differentiation of hDPSCs[32]. A coculture system not only provides intercellular factors but also enables communication between two types of cells, which is critical for the development and arrangement of the ECM[33,34]. DPSCs cocultured with human normal oral epithelial cells harvested from gingival tissue were inoculated into 3D Matrigel to form an epithelium invagination-like structure, a key feature of early tooth development[35]. Poly-L/D-lactide (PCL/PLDLA) porous microspheres were loaded with DPSCs and human endothelial cells to promote osteogenesis and angiogenesis for vascularized bone tissue regeneration[36].

3D printing techniques can print cells, growth factors, or biomaterials in the desired location to achieve more complicated multicell tissue structures[37]. In contrast to cultures in 2D alginate/gelatin hydrogel (Alg-Gel) scaffolds, 3D Alg-Gel scaffolds can be printed in a seven-layer coin shape and loaded with DPSCs. These DPSC-loaded 3D printed scaffolds achieved higher cell proliferation, odontoblastic differentiation, and bone mineralization, suggesting that a 3D environment is more suitable for cell proliferation and differentiation[38]. In addition, Park *et al*[39] designed the printing of DPSCs with VEGF in the central zone and bone morphogenetic protein-2 (BMP-2) in

the peripheral area of the 3D-printed construct to fabricate vascularized bone structures. A cone-shaped scaffold was printed with hydroxyapatite/tricalcium phosphate (HA/TCP) powder that was polymerized by an ultraviolet (UV) photoinitiator. DPSCs and SCAP were mixed with collagen gel and loaded into the 3D printed HA/TCP scaffold for dental pulp regeneration[40]. 3D PCL mesh supplemented with PRP containing various growth factors along with DPSCs was custom printed to fit rat calvarial defects for bone regeneration[27]. PRP containing various growth factors, along with DPSCs, was added to 3D printed PCL mesh for bone regeneration in a rat calvaria defect model[27]. A novel DPSC-loaded bioink containing a mixture of amorphous Mg phosphates and ECM increased the bone density during craniomaxillofacial bone regeneration[41]. With the 3D printing technique, the shape, pore size, and gap size can be precisely controlled to study their microenvironmental effects on cell proliferation and differentiation. Polylactic acid scaffolds (PLASs) were printed in different gap sizes, and it was discovered that smaller gaps in 3D PLASs presented with different cellular orientations[42].

In addition to their osteogenic and odontoblastic potential, the chondrogenic potential of DPSCs has been investigated. Zhang *et al*[43] successfully induced DPSCs to undergo a chondrogenic differentiation process, and their synthesis of sulfated glycosaminoglycans was confirmed. DPSCs formed into 3D pellets were subjected to chondrogenic potential investigation, resulting in the enrichment of collagen I deposition. The content of glycosaminoglycan or collagen type II was not enhanced even with the addition of chondroinductive growth factors, suggesting that the chondrogenic lineage of DPSCs favors differentiation into fibrous cartilage rather than hyaline cartilage[44]. DPSCs, derived from cranial neurons, can differentiate into neuron-like cells for axon regeneration and are potential cell sources for neuron regeneration[45,46]. DPSCs were seeded within chitosan-intercalated montmorillonite/poly(vinyl alcohol) (OMMT/PVA) nanofibrous mesh, and they differentiated into neuron-like cells[47]. A thermosensitive heparin-poloxamer hydrogel with DPSCs and bFGF enhanced motor and sensory functional recovery after spinal cord injury repair[48]. Chitosan scaffolds have been demonstrated to enhance neuronal cell survival and differentiation. Zheng *et al*[49] incorporated bFGF into chitosan scaffolds and found that it promoted DPSC differentiation into neuronal cells but did not affect cell survival. Human adipose microvascular endothelial cells were coseeded in a PLLA/poly(lactic-co-glycolic acids) (PLGA) scaffold with DPSCs to fabricate a prevascularized scaffold, which promoted revascularization, axon regeneration, myelin deposition, and sensory recovery in a rat complete spinal cord transection model[50]. Moreover, DPSCs seeded in Matrigel were able to differentiate into endotheliocytes and pericytes in serum-free culture media and secrete VEGF[51].

SHED

SHED cells, first isolated in 2003, present with positive expression of embryonic stem cell markers, such as OCT4 and NANOG, stage-specific embryonic antigens (SSEA-3 and SSEA-4), and mesenchymal stem cell markers (STRO-1 and CD146)[52-54]. Compared to DPSCs, SHEDs showed higher levels of osteocalcin expression and alkaline phosphatase activity[55]. SHEDs were confirmed to be more immature than DPSCs, allowing them to be “osteoblast-like” and “odontoblast-like”, expressing osteocalcin and RUNX-2 markers[53]. Moreover, when SHEDs were cultured in medium with dexamethasone, they differentiated into adipocytes. After *in vitro* culturing for 2 wk in osteogenic medium, extracellular mineralized matrix started to be secreted by the SHEDs. This multilineage potential makes SHEDs alternative sources of dental stem cells[56].

Applications in 3D tissue regeneration

SHEDs cultured *in vitro* for 7 d were found to aggregate together, and they started to form a 3D ossification hemisphere after 36 d[56]. This mineral matrix was identified by alizarin red staining within the self-formed 3D woven bone tissue. SHEDs can be applied in a 3D polylactoglycolide scaffold fabricated by a surface-selective laser sintering device. The expression of osteocalcin was elevated in SHED-loaded polylactoglycolide scaffolds, suggesting that SHEDs are promising cell sources for scaffold populations in tissue bone engineering[57]. In addition to bone regeneration, SHEDs may be a source of neurons. When they were incubated in neurodifferentiation medium supplemented with epidermal growth factor (EGF) and fibroblast growth factor (FGF), SHEDs showed increased expression of neuron markers, such as β III-

tubulin, microtubule-associated protein 2, tyrosine hydroxylase, and Nestin[58]. These results confirmed the neurogenic potential of SHEDs. In spinal cord injury, a supply of SHEDs rescues hindlimb locomotor function[52]. Furthermore, SHED-conditioned medium was demonstrated to regenerate peripheral nerves in sciatic nerve defects in a rat model. The rat static nerve defects at the mid-thigh level were covered with silicon conduits containing SHED-conditioned medium and resulted in an increase in Schwann cells, axon density and the number of regenerated myelinated fibers[59]. Injection of SHEDs into the brain at the site of perinatal hypoxia-ischemia (HI) injury improved the survival rate of HI-injured mice through inhibition of the expression of proinflammatory cytokines[60]. Although SHEDs have multidifferentiation potency and fewer limitations in terms of ethical concerns in their clinical application, only a few studies have investigated the application of SHEDs in 3D-printed scaffolds for tissue regeneration. It is possible that the collection, treatment methods, and storage of harvested SHEDs have not been standardized or popularized.

PDLSCS

Periodontitis is a very common oral disease resulting in periodontal tissue destruction and, more seriously, tooth loss[61]. Many periodontal regeneration treatments have been performed to restore the damaged periodontium. PDLSCs were isolated from mature periodontal ligaments and found to express the stem cell markers CD105, CD90, and CD73[62-64]. Seo *et al*[63] successfully isolated PDLSCs from human third molars, and the expression of the stem cell markers STRO-1 and CD146/MUC18 was found in PDLSCs. In addition to the expression of stem cell markers, the osteogenic and adipogenic potential of PDLSCs was also identified[65], which makes PDLSCs alternative cell sources for tissue regeneration. The regeneration steps of periodontal tissue were demonstrated by PDLSCs incorporated with hydroxyapatite/ β -tricalcium phosphate (HA/ β -TCP) as carriers[66]. First, the proliferation of PDLSCs was increased, and collagen matrices were formed. Subsequently, the collagen fibers started to assemble, and cemental-like tissue was observed. Mineralization was present in the cemental-like tissue, and along with the presence of Sharpey's fibers, mature collagen fibers were present. Later, the maturation of cemental-like tissue was identified by the expression of cemental tissue genes, such as α -smooth muscle actin antibody, collagen type XII (ColXII), osteoblast specific factor-2/periostin, and aspirin/PLAP-1[67].

Application in 3D tissue regeneration

A 3D collagen scaffold was fabricated with precise control of the pore size, pore wall alignment, and percolation diameter to investigate the effect of the scaffold structure on periodontal tissue regeneration. The results suggested that a larger percolation diameter increased PDLSC cell elongation and directionality, whereas the pore size influenced cell invasion and cell distribution[68]. In addition to the manipulation of the scaffold structure, the addition of growth factors also promoted the capacity of tissue regeneration. During cemental tissue formation, connective tissue growth factor (CTGF) was found to promote the differentiation of periodontal ligament fibroblasts during the process of osteogenesis[69]. BMP-7, expressed in the cementum, alveolar bone, and periodontal ligament, induces cementogenic differentiation by acting as a progenitor for cementoblasts[70,71]. The expression of BMP-2, localized only in alveolar bone, was also involved in cementogenic differentiation by increasing the expression of cementum attachment protein (CAP)[72]. Since CTGF, BMP-7, and BMP-2 are beneficial for periodontal ligament formation, Cho *et al*[73] compared the effect of these three growth factors by incorporating them into 3D printed PLGA microspheres, and the results indicated that BMP-7 triggered thicker cementum-like layers, better integration with the dentin surface and higher expression of cementum protein 1[73]. In addition to supplying growth factors to promote tissue regeneration, inhibition of inflammatory reactions can also improve tissue formation. For instance, Liu *et al*[74] demonstrated that reductions in tumor necrosis factor- α and interferon- γ levels by the introduction of BMMSCs enhanced bone regeneration. Cao *et al*[75] demonstrated that aspirin promoted BMMSC-based calvarial bone regeneration. Thus, platelet-rich fibrin-containing PDLSCs were treated with aspirin, a non-steroidal anti-inflammatory drug, which increased periodontal bone formation[76].

Instead of providing a direct supply of factors that are required for tissue regeneration, human umbilical vein endothelial cells (HUVECs) were cocultured with PDLSCs to form 3D cell sheet constructs, which were wrapped around human tooth

roots for implantation into the subcutaneous layer of mice. The HUVEC and PDLSC coculture group exhibited the thickest PDL ligament-like arrangement compared to the PDLSC-only group, suggesting that HUVECs contributed to regulating the thickness of the periodontal compartment[77]. Another strategy for improving the supply of vasculature to bone regeneration is the introduction of genetically modified PDLSCs. A lentiviral construct containing platelet-derived growth factor BB (PDGF-BB), an angiogenic gene, was introduced into PDLSCs to overexpress PDGF-BB. A PLGA-PEG-PLGA thermal hydrogel seeded with PDLSCs overexpressing PDGF-BB promoted bone formation in alveolar bone defects[78]. To investigate the possibility of incorporating somatic MSCs in tissue regeneration, a mixture of PDLSCs, somatic MSCs, and DPSCs was cocultured within 3D collagen/chitosan scaffolds for odontogenic differentiation[79]. The results indicated that many growth factors, transcription factors and signaling molecules involved in odontogenic differentiation were significantly promoted in the group mixed with somatic MSCs. In addition to the application of periodontal tissue regeneration, 3D PDLSC-loaded constructs were applied to study the effect of the growth microenvironment on PDLSC differentiation. PDLSCs were seeded in a customized 3D cell-laden hydrogel array with a gradient of gelatin methacrylate (GelMA) and poly(ethylene glycol) (PEG) dimethacrylate compositions to study the response of PDLSCs to ECM[80]. The higher the ratio of PEG was, the better the performance of the PDLSCs in cell proliferation and cell spreading, indicating that the composition of the ECM influenced the behavior of the PDLSCs.

SCAP

SCAP is only present at the tip of the developing tooth root before the tooth erupts. Although SCAP shares some similar characteristics with DPSCs, there are still some differences between these two types of stem cells[8]. In contrast to DPSCs, which are the sources of replacement odontoblasts, SCAP is the primary source of odontoblasts involved in the formation of root dentin[81]. Comparing their *in vitro* osteo/odontogenic differentiation potential with DPSCs, SCAP presents stem cell markers (STRO-1, CD146, and CD34) similar to those of DPSCs but with a significantly higher proliferation rate and mineralization potential during dental formation[82]. Other MSC markers, CD73, CD90, and CD105, were also identified in SCAP[40]. Liu *et al*[83] found that CD24 was exclusively expressed in SCAP, not in DPSCs. SCAP are comparatively easy to isolate from the tips of developing roots. They are digested with a cocktail of collagenase to isolate single-cell suspensions, which are grown under routine cell culture conditions[84].

Application in 3D tissue regeneration

In addition to using residual dental pulp in dentin regeneration, SCAP with osteogenic potential obtained from dental roots have been applied for dentin regeneration[85]. Injectable PLLA nanofibrous microspheres (NF-MS) with the ability to controllably release BMP-2 were encapsulated in SCAP for dentin regeneration[86]. More mineralization and osteodentin formation were observed in NF-MS with controlled BMP-2 release microspheres, suggesting their potential for dental tissue repair. In addition to BMP-2 release, SCAP cotreated with stromal cell-derived factor-1 α , which is able to promote odontoblast differentiation of dental pulp cells, were shown to undergo odontogenic differentiation-related gene and protein expression[87]. PDGF-BB is known to promote angiogenesis during tissue regeneration[88,89]. The addition of PDGF-BB promoted the proliferation of SCAP and improved new bone formation and mineralization in a rat calvaria defect model[90].

The growth factor TGF β 3 was shown to be involved in tissue regeneration[91]. Somoza *et al*[92] observed that TGF β 3 secretion by SCAP was elevated when they were grown in a 3D microenvironment regardless of the materials used for the scaffold. Thus, SCAP were applied and incorporated into a 3D scaffold for tissue regeneration. Considering the secretion properties of SCAP, Na *et al*[93] developed a 3D scaffold-free stem-cell sheet-derived pellet (CSDP) by culturing a large amount of SCAP on a culture dish to form a cell sheet that enriched the secreted ECM. CSDP exhibited the odontogenic/osteogenic potential to form dental pulp-like and dentine-like tissue after implantation into the subcutaneous layer in immunodeficient mice. Dental ECM was reported to enhance cell proliferation and mineralization[94]. A novel SCAP-loaded bioink was developed by applying dental ECM to printable alginate to form dentin-derived bioink, in which soluble dentin molecules significantly enhanced odontogenic

differentiation[95].

DFPCS

The dental follicle is the connective tissue surrounding the enamel organ and dental papilla that forms a vascular fibrous sac. In 2005, Morsczech *et al*[96] isolated DFPCs from the dental follicle of human third molar teeth, which were found to express the stem cell markers Notch and Nestin. Their potential for osteogenic, adipogenic, chondrogenic, and neural differentiation was further confirmed[97]. Subsequently, DFPCs were applied for tissue regeneration, such as the regeneration of the salivary glands, dental roots, and bone tissue[98-100].

Application in 3D tissue regeneration

Among the applications of dental stem cells in tissue regeneration, only a few studies have introduced DFPCs to 3D tissue regeneration. DFPCs cultured in a 3D rotatory culture system displayed many follicle markers, such as CD44, CD90, CD146, CD31, CD34, and CD45Ag[101]. Furthermore, their differentiation potential was increased when DFPCs were cultured in a 3D dynamic culture system. For the generation of 3D tissue constructs, DFPCs were seeded in 3D porous scaffolds of collagen-nanohydroxyapatite/phosphoserine (collagen-nano-HA/OPS) biocomposite cryogels and implanted into the subcutaneous layer of *nu* mice. These 3D DFPC-loaded collagen-nano-HA/OPS constructs exhibited greater osteogenic differentiation with higher levels of osteopontin secretion[102].

CLINICAL APPLICATIONS OF DENTAL STEM CELLS

The use of dental stem cells for autologous or allogeneic transplantation has been introduced into clinical practice. The biological safety of dental stem cells requires strict regulation. Standard examinations for viruses, pathogenic microorganisms, or any sources with animal origins are necessary[103-105]. Due to the immune response, a same-species origin of the stem cell culture system is recommended for cell therapy [106]. According to the Clinical Gov website, there are fewer than 10 cases of the use of dental stem cells in clinical applications, implying a gap in the application of dental stem cells between basic research and clinical practice. There is a scarcity of data for the use of decellularized biological membranes for preparing 3D dental regenerative constructs, which is a crucial approach for regenerative dentistry. Indeed, dental stem cells are not the most suitable stem cell choice for tissue regeneration due to harvest contamination, small cell amounts available per patient and invasive harvesting approaches. However, the regenerative potential of dental stem cells is still supported by several clinical results. A clinical study reported that most clinical trials based on the use of DPSCs cells were performed for bone regeneration, periodontitis, and dental pulp regeneration, whereas trials involving the use of periodontal PDLSCs were conducted to study periodontal disease treatment. No clinical trials that used DFPCs were found[107]. Overall, dental stem cells are not commonly used to treat human diseases. Identical to the original issues hindering stem cell therapy, ethical concerns and cell sources are the main obstacles. Moreover, the survival of grafted dental stem cells exhibited different results after long-term follow-up observations. Autologous PDLSCs were detected after 8 wk in an ovine periodontal defect model, whereas donor PDLSCs implanted into recipient mice were untraceable two weeks after implantation [108]. Whether autologous or allogeneic stem cell sources affect the survival rate of transplanted cells remains to be further investigated.

CONCLUSION

Dental-derived stem cells with mesenchymal stem cell properties are promising cell sources for tissue regeneration. Comparisons among these five types of dental-derived stem cells showed that DPSCs, SHEDs, and PDLSCs present a higher growth potential than BMSCs[109]. Moreover, SCAP and DPSCs showed weaker adipogenic differentiation than BMSCs[84]. Regardless of whether the different types of dental stem cells have osteogenic or odontogenic potential, each cell type presents unique differentiation potentials in the corresponding tissue type. Although dental stem cells present

differentiation potential for adipogenesis, chondrogenesis, and neurogenesis, most of their clinical utility lies in the field of regenerative dentistry. With the trend of 3D tissue engineering, the application of dental stem cells to 3D tissue reconstruction has been emphasized. In this review, many basic research and preclinical studies were presented to support the idea that dental stem cells can be applied in a feasible approach to translational medicine and are available resources for 3D tissue regeneration.

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REFERENCES

- 1 **Bojic S**, Volarevic V, Ljubic B, Stojkovic M. Dental stem cells--characteristics and potential. *Histol Histopathol* 2014; **29**: 699-706 [PMID: 24446280 DOI: 10.14670/HH-29.699]
- 2 **Ercal P**, Pekozer GG, Kose GT. Dental Stem Cells in Bone Tissue Engineering: Current Overview and Challenges. *Adv Exp Med Biol* 2018; **1107**: 113-127 [PMID: 29498025 DOI: 10.1007/5584_2018_171]
- 3 **Yao L**, Flynn N. Dental pulp stem cell-derived chondrogenic cells demonstrate differential cell motility in type I and type II collagen hydrogels. *Spine J* 2018; **18**: 1070-1080 [PMID: 29452287 DOI: 10.1016/j.spinee.2018.02.007]
- 4 **Knight E**, Przyborski S. Advances in 3D cell culture technologies enabling tissue-like structures to be created in vitro. *J Anat* 2015; **227**: 746-756 [PMID: 25411113 DOI: 10.1111/joa.12257]
- 5 **Fantini D**. Easypubmed: Search and retrieve scientific publication records from pubmed. R package version 2.13. 2019. [cited 3 April 2021]. In: CRAN.R-project [Internet]. Available from: <https://CRAN.R-project.org/package=easyPubMed>
- 6 **Rani J**, Shah AB, Ramachandran S. pubmed.mineR: an R package with text-mining algorithms to analyse PubMed abstracts. *J Biosci* 2015; **40**: 671-682 [PMID: 26564970 DOI: 10.1007/s12038-015-9552-2]
- 7 **Team RC**. R: A language and environment for statistical computing. R foundation for statistical computing, vienna, austria. 2020. [cited 3 April 2021]. In: R-project [Internet]. Available from: <https://www.R-project.org/>
- 8 **Gronthos S**, Mankani M, Brahimi 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**: 13625-13630 [PMID: 11087820 DOI: 10.1073/pnas.240309797]
- 9 **Mortada I**, Mortada R. Dental pulp stem cells and osteogenesis: an update. *Cytotechnology* 2018; **70**: 1479-1486 [PMID: 29938380 DOI: 10.1007/s10616-018-0225-5]
- 10 **Shi S**, Robey PG, Gronthos S. Comparison of human dental pulp and bone marrow stromal stem cells by cDNA microarray analysis. *Bone* 2001; **29**: 532-539 [PMID: 11728923 DOI: 10.1016/s8756-3282(01)00612-3]
- 11 **Yu J**, Wang Y, Deng Z, Tang L, Li Y, Shi J, Jin Y. Odontogenic capability: bone marrow stromal stem cells vs dental pulp stem cells. *Biol Cell* 2007; **99**: 465-474 [PMID: 17371295 DOI: 10.1042/BC20070013]
- 12 **Kumar A**, Kumar V, Rattan V, Jha V, Bhattacharyya S. Secretome Cues Modulate the Neurogenic Potential of Bone Marrow and Dental Stem Cells. *Mol Neurobiol* 2017; **54**: 4672-4682 [PMID: 27422132 DOI: 10.1007/s12035-016-0011-3]
- 13 **Mohanram Y**, Zhang J, Tsiridis E, Yang XB. Comparing bone tissue engineering efficacy of HDPSCs, HBMSCs on 3D biomimetic ABM-P-15 scaffolds *in vitro* and *in vivo*. *Cytotechnology* 2020; **72**: 715-730 [PMID: 32820463 DOI: 10.1007/s10616-020-00414-7]
- 14 **Kim SH**, Kim YS, Lee SY, Kim KH, Lee YM, Kim WK, Lee YK. Gene expression profile in mesenchymal stem cells derived from dental tissues and bone marrow. *J Periodontol Implant Sci* 2011; **41**: 192-200 [PMID: 21954424 DOI: 10.5051/jpis.2011.41.4.192]
- 15 **Han J**, Kim DS, Jang H, Kim HR, Kang HW. Bioprinting of three-dimensional dentin-pulp complex with local differentiation of human dental pulp stem cells. *J Tissue Eng* 2019; **10**: 2041731419845849 [PMID: 31205671 DOI: 10.1177/2041731419845849]
- 16 **Kuang R**, Zhang Z, Jin X, Hu J, Shi S, Ni L, Ma PX. Nanofibrous spongy microspheres for the delivery of hypoxia-primed human dental pulp stem cells to regenerate vascularized dental pulp. *Acta Biomater* 2016; **33**: 225-234 [PMID: 26826529 DOI: 10.1016/j.actbio.2016.01.032]
- 17 **Itoh Y**, Sasaki JI, Hashimoto M, Katata C, Hayashi M, Imazato S. Pulp Regeneration by 3-dimensional Dental Pulp Stem Cell Constructs. *J Dent Res* 2018; **97**: 1137-1143 [PMID: 29702010 DOI: 10.1177/0022034518772260]
- 18 **Soares DG**, Zhang Z, Mohamed F, Eyster TW, de Souza Costa CA, Ma PX. Simvastatin and nanofibrous poly(l-lactic acid) scaffolds to promote the odontogenic potential of dental pulp cells in

- an inflammatory environment. *Acta Biomater* 2018; **68**: 190-203 [PMID: [29294374](#) DOI: [10.1016/j.actbio.2017.12.037](#)]
- 19 **Cooke ME**, Ramirez-Garcia Luna JL, Rangel-Berridi K, Park H, Nazhat SN, Weber MH, Henderson JE, Rosenzweig DH. 3D Printed Polyurethane Scaffolds for the Repair of Bone Defects. *Front Bioeng Biotechnol* 2020; **8**: 557215 [PMID: [33195122](#) DOI: [10.3389/fbioe.2020.557215](#)]
 - 20 **Rubert Pérez CM**, Stephanopoulos N, Sur S, Lee SS, Newcomb C, Stupp SI. The powerful functions of peptide-based bioactive matrices for regenerative medicine. *Ann Biomed Eng* 2015; **43**: 501-514 [PMID: [25366903](#) DOI: [10.1007/s10439-014-1166-6](#)]
 - 21 **Akkouch A**, Zhang Z, Rouabhia M. Engineering bone tissue using human dental pulp stem cells and an osteogenic collagen-hydroxyapatite-poly (L-lactide-co-ε-caprolactone) scaffold. *J Biomater Appl* 2014; **28**: 922-936 [PMID: [23640860](#) DOI: [10.1177/0885328213486705](#)]
 - 22 **Xia K**, Chen Z, Chen J, Xu H, Xu Y, Yang T, Zhang Q. RGD- and VEGF-Mimetic Peptide Epitope-Functionalized Self-Assembling Peptide Hydrogels Promote Dentin-Pulp Complex Regeneration. *Int J Nanomedicine* 2020; **15**: 6631-6647 [PMID: [32982223](#) DOI: [10.2147/IJN.S253576](#)]
 - 23 **Suzuki T**, Lee CH, Chen M, Zhao W, Fu SY, Qi JJ, Chotkowski G, Eisig SB, Wong A, Mao JJ. Induced migration of dental pulp stem cells for *in vivo* pulp regeneration. *J Dent Res* 2011; **90**: 1013-1018 [PMID: [21586666](#) DOI: [10.1177/0022034511408426](#)]
 - 24 **Nam S**, Won JE, Kim CH, Kim HW. Odontogenic differentiation of human dental pulp stem cells stimulated by the calcium phosphate porous granules. *J Tissue Eng* 2011; **2011**: 812547 [PMID: [21772958](#) DOI: [10.4061/2011/812547](#)]
 - 25 **Galler KM**, Hartgerink JD, Cavender AC, Schmalz G, D'Souza RN. A customized self-assembling peptide hydrogel for dental pulp tissue engineering. *Tissue Eng Part A* 2012; **18**: 176-184 [PMID: [21827280](#) DOI: [10.1089/ten.TEA.2011.0222](#)]
 - 26 **Yang JW**, Zhang YF, Sun ZY, Song GT, Chen Z. Dental pulp tissue engineering with bFGF-incorporated silk fibroin scaffolds. *J Biomater Appl* 2015; **30**: 221-229 [PMID: [25791684](#) DOI: [10.1177/0885328215577296](#)]
 - 27 **Li J**, Chen M, Wei X, Hao Y, Wang J. Evaluation of 3D-Printed Polycaprolactone Scaffolds Coated with Freeze-Dried Platelet-Rich Plasma for Bone Regeneration. *Materials (Basel)* 2017; **10** [PMID: [28773189](#) DOI: [10.3390/ma10070831](#)]
 - 28 **Liu YJ**, Su WT, Chen PH. Magnesium and zinc borate enhance osteoblastic differentiation of stem cells from human exfoliated deciduous teeth *in vitro*. *J Biomater Appl* 2018; **32**: 765-774 [PMID: [29119879](#) DOI: [10.1177/0885328217740730](#)]
 - 29 **Wiesmann HP**, Tkotz T, Joos U, Zierold K, Stratmann U, Szuwart T, Plate U, Höhling HJ. Magnesium in newly formed dentin mineral of rat incisor. *J Bone Miner Res* 1997; **12**: 380-383 [PMID: [9076580](#) DOI: [10.1359/jbmr.1997.12.3.380](#)]
 - 30 **Qu T**, Jing J, Jiang Y, Taylor RJ, Feng JQ, Geiger B, Liu X. Magnesium-containing nanostructured hybrid scaffolds for enhanced dentin regeneration. *Tissue Eng Part A* 2014; **20**: 2422-2433 [PMID: [24593189](#) DOI: [10.1089/ten.TEA.2013.0741](#)]
 - 31 **Tognarini I**, Sorace S, Zonefrati R, Galli G, Gozzini A, Carbonell Sala S, Thyron GD, Carossino AM, Tanini A, Mavilia C, Azzari C, Sbaiz F, Facchini A, Capanna R, Brandi ML. *In vitro* differentiation of human mesenchymal stem cells on Ti6Al4V surfaces. *Biomaterials* 2008; **29**: 809-824 [PMID: [18022689](#) DOI: [10.1016/j.biomaterials.2007.10.043](#)]
 - 32 **Galli D**, Benedetti L, Bongio M, Maliardi V, Silvani G, Ceccarelli G, Ronzoni F, Conte S, Benazzo F, Graziano A, Papaccio G, Sampaolesi M, De Angelis MG. *In vitro* osteoblastic differentiation of human mesenchymal stem cells and human dental pulp stem cells on poly-L-lysine-treated titanium-6-aluminum-4-vanadium. *J Biomed Mater Res A* 2011; **97**: 118-126 [PMID: [21370441](#) DOI: [10.1002/jbm.a.32996](#)]
 - 33 **Mittelbrunn M**, Sánchez-Madrid F. Intercellular communication: diverse structures for exchange of genetic information. *Nat Rev Mol Cell Biol* 2012; **13**: 328-335 [PMID: [22510790](#) DOI: [10.1038/nrm3335](#)]
 - 34 **Manz BN**, Groves JT. Spatial organization and signal transduction at intercellular junctions. *Nat Rev Mol Cell Biol* 2010; **11**: 342-352 [PMID: [20354536](#) DOI: [10.1038/nrm2883](#)]
 - 35 **Xiao L**, Tsutsui T. Three-dimensional epithelial and mesenchymal cell co-cultures form early tooth epithelium invagination-like structures: expression patterns of relevant molecules. *J Cell Biochem* 2012; **113**: 1875-1885 [PMID: [22234822](#) DOI: [10.1002/jcb.24056](#)]
 - 36 **Jin GZ**, Kim HW. Co-culture of Human Dental Pulp Stem Cells and Endothelial Cells Using Porous Biopolymer Microcarriers: A Feasibility Study for Bone Tissue Engineering. *Tissue Eng Regen Med* 2017; **14**: 393-401 [PMID: [30603495](#) DOI: [10.1007/s13770-017-0061-2](#)]
 - 37 **Mironov V**, Boland T, Trusk T, Forgacs G, Markwald RR. Organ printing: computer-aided jet-based 3D tissue engineering. *Trends Biotechnol* 2003; **21**: 157-161 [PMID: [12679063](#) DOI: [10.1016/S0167-7799\(03\)00033-7](#)]
 - 38 **Yu H**, Zhang X, Song W, Pan T, Wang H, Ning T, Wei Q, Xu HHK, Wu B, Ma D. Effects of 3-dimensional Bioprinting Alginate/Gelatin Hydrogel Scaffold Extract on Proliferation and Differentiation of Human Dental Pulp Stem Cells. *J Endod* 2019; **45**: 706-715 [PMID: [31056297](#) DOI: [10.1016/j.joen.2019.03.004](#)]
 - 39 **Park JY**, Shim JH, Choi SA, Jang J, Kim M, Lee SH, Cho DW. 3D printing technology to control BMP-2 and VEGF delivery spatially and temporally to promote large-volume bone regeneration. *J Mater Chem B* 2015; **3**: 5415-5425 [PMID: [32262513](#) DOI: [10.1039/c5tb00637f](#)]
 - 40 **Hilkens P**, Bronckaers A, Ratajczak J, Gervois P, Wolfs E, Lambrechts I. The Angiogenic Potential

- of DPSCs and SCAPs in an *In Vivo* Model of Dental Pulp Regeneration. *Stem Cells Int* 2017; **2017**: 2582080 [PMID: 29018483 DOI: 10.1155/2017/2582080]
- 41 **Dubey N**, Ferreira JA, Malda J, Bhaduri SB, Bottino MC. Extracellular Matrix/Amorphous Magnesium Phosphate Bioink for 3D Bioprinting of Craniomaxillofacial Bone Tissue. *ACS Appl Mater Interfaces* 2020; **12**: 23752-23763 [PMID: 32352748 DOI: 10.1021/acsami.0c05311]
 - 42 **Hsiao D**, Hsu SH, Chen RS, Chen MH. Characterization of designed directional polylactic acid 3D scaffolds for neural differentiation of human dental pulp stem cells. *J Formos Med Assoc* 2020; **119**: 268-275 [PMID: 31155229 DOI: 10.1016/j.jfma.2019.05.011]
 - 43 **Zhang W**, Walboomers XF, Shi S, Fan M, Jansen JA. Multilineage differentiation potential of stem cells derived from human dental pulp after cryopreservation. *Tissue Eng* 2006; **12**: 2813-2823 [PMID: 17518650 DOI: 10.1089/ten.2006.12.2813]
 - 44 **Longoni A**, Utomo L, van Hooijdonk IE, Bittermann GK, Vetter VC, Kruijt Spanjer EC, Ross J, Rosenberg AJ, Gawlitta D. The chondrogenic differentiation potential of dental pulp stem cells. *Eur Cell Mater* 2020; **39**: 121-135 [PMID: 32083715 DOI: 10.22203/eCM.v039a08]
 - 45 **Arthur A**, Rychkov G, Shi S, Koblar SA, Gronthos S. Adult human dental pulp stem cells differentiate toward functionally active neurons under appropriate environmental cues. *Stem Cells* 2008; **26**: 1787-1795 [PMID: 18499892 DOI: 10.1634/stemcells.2007-0979]
 - 46 **Askari N**, Yaghoobi MM, Shamsara M, Esmaeili-Mahani S. Human Dental Pulp Stem Cells Differentiate into Oligodendrocyte Progenitors Using the Expression of Olig2 Transcription Factor. *Cells Tissues Organs* 2014; **200**: 93-103 [PMID: 25966902 DOI: 10.1159/000381668]
 - 47 **Ghasemi Hamidabadi H**, Rezvani Z, Nazm Bojnordi M, Shirinzadeh H, Seifalian AM, Joghataei MT, Razaghpour M, Alibakhshi A, Yazdanpanah A, Salimi M, Mozafari M, Urbanska AM, Reis RL, Kundu SC, Gholipourmalekabadi M. Chitosan-Intercalated Montmorillonite/Poly(vinyl alcohol) Nanofibers as a Platform to Guide Neuronlike Differentiation of Human Dental Pulp Stem Cells. *ACS Appl Mater Interfaces* 2017; **9**: 11392-11404 [PMID: 28117963 DOI: 10.1021/acsami.6b14283]
 - 48 **Luo L**, Albashari AA, Wang X, Jin L, Zhang Y, Zheng L, Xia J, Xu H, Zhao Y, Xiao J, He Y, Ye Q. Effects of Transplanted Heparin-Poloxamer Hydrogel Combining Dental Pulp Stem Cells and bFGF on Spinal Cord Injury Repair. *Stem Cells Int* 2018; **2018**: 2398521 [PMID: 29765407 DOI: 10.1155/2018/2398521]
 - 49 **Zheng K**, Feng G, Zhang J, Xing J, Huang D, Lian M, Zhang W, Wu W, Hu Y, Lu X, Feng X. Basic fibroblast growth factor promotes human dental pulp stem cells cultured in 3D porous chitosan scaffolds to neural differentiation. *Int J Neurosci* 2021; **131**: 625-633 [PMID: 32186218 DOI: 10.1080/00207454.2020.1744592]
 - 50 **Guo S**, Redenski I, Landau S, Szklanny A, Merdler U, Levenberg S. Prevascularized Scaffolds Bearing Human Dental Pulp Stem Cells for Treating Complete Spinal Cord Injury. *Adv Healthc Mater* 2020; **9**: e2000974 [PMID: 32902147 DOI: 10.1002/adhm.202000974]
 - 51 **Luzuriaga J**, Irurzun J, Irastorza I, Unda F, Ibarretxe G, Pineda JR. Vasculogenesis from Human Dental Pulp Stem Cells Grown in Matrigel with Fully Defined Serum-Free Culture Media. *Biomedicines* 2020; **8** [PMID: 33182239 DOI: 10.3390/biomedicines8110483]
 - 52 **Sakai K**, Yamamoto A, Matsubara K, Nakamura S, Naruse M, Yamagata M, Sakamoto K, Tauchi R, Wakao N, Imagama S, Hibi H, Kadomatsu K, Ishiguro N, Ueda M. Human dental pulp-derived stem cells promote locomotor recovery after complete transection of the rat spinal cord by multiple neuro-regenerative mechanisms. *J Clin Invest* 2012; **122**: 80-90 [PMID: 22133879 DOI: 10.1172/JCI59251]
 - 53 **Miura M**, Gronthos S, Zhao M, Lu B, Fisher LW, Robey PG, Shi S. SHED: stem cells from human exfoliated deciduous teeth. *Proc Natl Acad Sci U S A* 2003; **100**: 5807-5812 [PMID: 12716973 DOI: 10.1073/pnas.0937635100]
 - 54 **Kerkis I**, Kerkis A, Dozortsev D, Stukart-Parsons GC, Gomes Massironi SM, Pereira LV, Caplan AI, Cerruti HF. Isolation and characterization of a population of immature dental pulp stem cells expressing OCT-4 and other embryonic stem cell markers. *Cells Tissues Organs* 2006; **184**: 105-116 [PMID: 17409736 DOI: 10.1159/000099617]
 - 55 **Koyama N**, Okubo Y, Nakao K, Bessho K. Evaluation of pluripotency in human dental pulp cells. *J Oral Maxillofac Surg* 2009; **67**: 501-506 [PMID: 19231772 DOI: 10.1016/j.joms.2008.09.011]
 - 56 **Laino G**, Graziano A, d'Aquino R, Pirozzi G, Lanza V, Valiante S, De Rosa A, Naro F, Vivarelli E, Papaccio G. An approachable human adult stem cell source for hard-tissue engineering. *J Cell Physiol* 2006; **206**: 693-701 [PMID: 16222704 DOI: 10.1002/jcp.20526]
 - 57 **Vakhrushev IV**, Antonov EN, Popova AV, Konstantinova EV, Karalkin PA, Kholodenko IV, Lupatov AY, Popov VK, Bagratashvili VN, Yarygin KN. Design of tissue engineering implants for bone tissue regeneration of the basis of new generation polylactoglycolide scaffolds and multipotent mesenchymal stem cells from human exfoliated deciduous teeth (SHED cells). *Bull Exp Biol Med* 2012; **153**: 143-147 [PMID: 22808514 DOI: 10.1007/s10517-012-1663-2]
 - 58 **Feng X**, Xing J, Feng G, Sang A, Shen B, Xu Y, Jiang J, Liu S, Tan W, Gu Z, Li L. Age-dependent impaired neurogenic differentiation capacity of dental stem cell is associated with Wnt/ β -catenin signaling. *Cell Mol Neurobiol* 2013; **33**: 1023-1031 [PMID: 24043508 DOI: 10.1007/s10571-013-9965-0]
 - 59 **Sugimura-Wakayama Y**, Katagiri W, Osugi M, Kawai T, Ogata K, Sakaguchi K, Hibi H. Peripheral Nerve Regeneration by Secretomes of Stem Cells from Human Exfoliated Deciduous Teeth. *Stem Cells Dev* 2015; **24**: 2687-2699 [PMID: 26154068 DOI: 10.1089/scd.2015.0104]

- 60 **Yamagata M**, Yamamoto A, Kako E, Kaneko N, Matsubara K, Sakai K, Sawamoto K, Ueda M. Human dental pulp-derived stem cells protect against hypoxic-ischemic brain injury in neonatal mice. *Stroke* 2013; **44**: 551-554 [PMID: [23238858](#) DOI: [10.1161/STROKEAHA.112.676759](#)]
- 61 **Zhu W**, Liang M. Periodontal ligament stem cells: current status, concerns, and future prospects. *Stem Cells Int* 2015; **2015**: 972313 [PMID: [25861283](#) DOI: [10.1155/2015/972313](#)]
- 62 **Iwasaki K**, Komaki M, Yokoyama N, Tanaka Y, Taki A, Kimura Y, Takeda M, Oda S, Izumi Y, Morita I. Periodontal ligament stem cells possess the characteristics of pericytes. *J Periodontol* 2013; **84**: 1425-1433 [PMID: [23240762](#) DOI: [10.1902/jop.2012.120547](#)]
- 63 **Seo BM**, Miura M, Gronthos S, Bartold PM, Batouli S, Brahimi J, Young M, Robey PG, Wang CY, Shi S. Investigation of multipotent postnatal stem cells from human periodontal ligament. *Lancet* 2004; **364**: 149-155 [PMID: [15246727](#) DOI: [10.1016/S0140-6736\(04\)16627-0](#)]
- 64 **Liu W**, Konermann A, Guo T, Jäger A, Zhang L, Jin Y. Canonical Wnt signaling differently modulates osteogenic differentiation of mesenchymal stem cells derived from bone marrow and from periodontal ligament under inflammatory conditions. *Biochim Biophys Acta* 2014; **1840**: 1125-1134 [PMID: [24231680](#) DOI: [10.1016/j.bbagen.2013.11.003](#)]
- 65 **Deng C**, Sun Y, Liu H, Wang W, Wang J, Zhang F. Selective adipogenic differentiation of human periodontal ligament stem cells stimulated with high doses of glucose. *PLoS One* 2018; **13**: e0199603 [PMID: [29979705](#) DOI: [10.1371/journal.pone.0199603](#)]
- 66 **Kim YT**, Park JC, Choi SH, Cho KS, Im GI, Kim BS, Kim CS. The dynamic healing profile of human periodontal ligament stem cells: histological and immunohistochemical analysis using an ectopic transplantation model. *J Periodontol Res* 2012; **47**: 514-524 [PMID: [22308979](#) DOI: [10.1111/j.1600-0765.2011.01463.x](#)]
- 67 **Horiuchi K**, Amizuka N, Takeshita S, Takamatsu H, Katsuura M, Ozawa H, Toyama Y, Bonewald LF, Kudo A. Identification and characterization of a novel protein, periostin, with restricted expression to periosteum and periodontal ligament and increased expression by transforming growth factor beta. *J Bone Miner Res* 1999; **14**: 1239-1249 [PMID: [10404027](#) DOI: [10.1359/jbmr.1999.14.7.1239](#)]
- 68 **Ansari S**, Diniz IM, Chen C, Sarrion P, Tamayol A, Wu BM, Moshaverinia A. Human Periodontal Ligament- and Gingiva-derived Mesenchymal Stem Cells Promote Nerve Regeneration When Encapsulated in Alginate/Hyaluronic Acid 3D Scaffold. *Adv Healthc Mater* 2017; **6** [PMID: [29076281](#) DOI: [10.1002/adhm.201700670](#)]
- 69 **Duan X**, Ji M, Deng F, Sun Z, Lin Z. Effects of connective tissue growth factor on human periodontal ligament fibroblasts. *Arch Oral Biol* 2017; **84**: 37-44 [PMID: [28941713](#) DOI: [10.1016/j.archoralbio.2017.09.010](#)]
- 70 **Thomadakis G**, Ramoshebi LN, Crooks J, Rueger DC, Ripamonti U. Immunolocalization of Bone Morphogenetic Protein-2 and -3 and Osteogenic Protein-1 during murine tooth root morphogenesis and in other craniofacial structures. *Eur J Oral Sci* 1999; **107**: 368-377 [PMID: [10515202](#) DOI: [10.1046/j.0909-8836.1999.eos107508.x](#)]
- 71 **Kémoun P**, Laurencin-Dalicieux S, Rue J, Farges JC, Gennero I, Conte-Auriol F, Briand-Mesange F, Gadelorge M, Arzate H, Narayanan AS, Brunel G, Salles JP. Human dental follicle cells acquire cementoblast features under stimulation by BMP-2/-7 and enamel matrix derivatives (EMD) in vitro. *Cell Tissue Res* 2007; **329**: 283-294 [PMID: [17443352](#) DOI: [10.1007/s00441-007-0397-3](#)]
- 72 **Pitaru S**, Pritzki A, Bar-Kana I, Grosskopf A, Savion N, Narayanan AS. Bone morphogenetic protein 2 induces the expression of cementum attachment protein in human periodontal ligament clones. *Connect Tissue Res* 2002; **43**: 257-264 [PMID: [12489168](#) DOI: [10.1080/03008200290001276](#)]
- 73 **Cho H**, Tarafder S, Fogge M, Kao K, Lee CH. Periodontal ligament stem/progenitor cells with protein-releasing scaffolds for cementum formation and integration on dentin surface. *Connect Tissue Res* 2016; **57**: 488-495 [PMID: [27215800](#) DOI: [10.1080/03008207.2016.1191478](#)]
- 74 **Liu Y**, Yang R, Shi S. Systemic infusion of mesenchymal stem cells improves cell-based bone regeneration via upregulation of regulatory T cells. *Tissue Eng Part A* 2015; **21**: 498-509 [PMID: [25159486](#) DOI: [10.1089/ten.TEA.2013.0673](#)]
- 75 **Cao Y**, Xiong J, Mei S, Wang F, Zhao Z, Wang S, Liu Y. Aspirin promotes bone marrow mesenchymal stem cell-based calvarial bone regeneration in mini swine. *Stem Cell Res Ther* 2015; **6**: 210 [PMID: [26519141](#) DOI: [10.1186/s13287-015-0200-4](#)]
- 76 **Du J**, Mei S, Guo L, Su Y, Wang H, Liu Y, Zhao Z, Wang S. Platelet-rich fibrin/aspirin complex promotes alveolar bone regeneration in periodontal defect in rats. *J Periodontol Res* 2018; **53**: 47-56 [PMID: [28862325](#) DOI: [10.1111/jre.12485](#)]
- 77 **Kramer JL**. Decreasing the organ donor shortage. *Am J Forensic Med Pathol* 1995; **16**: 257; author reply 259-257; author reply 260 [PMID: [7495271](#) DOI: [10.1111/jre.12405](#)]
- 78 **Pan J**, Deng J, Luo Y, Yu L, Zhang W, Han X, You Z, Liu Y. Thermosensitive Hydrogel Delivery of Human Periodontal Stem Cells Overexpressing Platelet-Derived Growth Factor-BB Enhances Alveolar Bone Defect Repair. *Stem Cells Dev* 2019; **28**: 1620-1631 [PMID: [31663419](#) DOI: [10.1089/scd.2019.0184](#)]
- 79 **Ravindran S**, Huang CC, George A. Extracellular matrix of dental pulp stem cells: applications in pulp tissue engineering using somatic MSCs. *Front Physiol* 2014; **4**: 395 [PMID: [24432005](#) DOI: [10.3389/fphys.2013.00395](#)]
- 80 **Ma Y**, Ji Y, Huang G, Ling K, Zhang X, Xu F. Bioprinting 3D cell-laden hydrogel microarray for screening human periodontal ligament stem cell response to extracellular matrix. *Biofabrication*

- 2015; **7**: 044105 [PMID: [26696269](#) DOI: [10.1088/1758-5090/7/4/044105](#)]
- 81 **Huang GT**, Sonoyama W, Liu Y, Liu H, Wang S, Shi S. The hidden treasure in apical papilla: the potential role in pulp/dentin regeneration and bioroot engineering. *J Endod* 2008; **34**: 645-651 [PMID: [18498881](#) DOI: [10.1016/j.joen.2008.03.001](#)]
 - 82 **Bakopoulou A**, Leyhausen G, Volk J, Tsiftoglou A, Garefis P, Koidis P, Geurtsen W. Comparative analysis of *in vitro* osteo/odontogenic differentiation potential of human dental pulp stem cells (DPSCs) and stem cells from the apical papilla (SCAP). *Arch Oral Biol* 2011; **56**: 709-721 [PMID: [21227403](#) DOI: [10.1016/j.archoralbio.2010.12.008](#)]
 - 83 **Liu C**, Xiong H, Chen K, Huang Y, Yin X. Long-term exposure to pro-inflammatory cytokines inhibits the osteogenic/dentinogenic differentiation of stem cells from the apical papilla. *Int Endod J* 2016; **49**: 950-959 [PMID: [26383494](#) DOI: [10.1111/iej.12551](#)]
 - 84 **Nada OA**, El Backly RM. Stem Cells From the Apical Papilla (SCAP) as a Tool for Endogenous Tissue Regeneration. *Front Bioeng Biotechnol* 2018; **6**: 103 [PMID: [30087893](#) DOI: [10.3389/fbioe.2018.00103](#)]
 - 85 **Kitamura C**, Nishihara T, Terashita M, Tabata Y, Washio A. Local regeneration of dentin-pulp complex using controlled release of fgf-2 and naturally derived sponge-like scaffolds. *Int J Dent* 2012; **2012**: 190561 [PMID: [22174717](#) DOI: [10.1155/2012/190561](#)]
 - 86 **Wang W**, Dang M, Zhang Z, Hu J, Eyster TW, Ni L, Ma PX. Dentin regeneration by stem cells of apical papilla on injectable nanofibrous microspheres and stimulated by controlled BMP-2 release. *Acta Biomater* 2016; **36**: 63-72 [PMID: [26971664](#) DOI: [10.1016/j.actbio.2016.03.015](#)]
 - 87 **Xiao M**, Qiu J, Kuang R, Zhang B, Wang W, Yu Q. Synergistic effects of stromal cell-derived factor-1 α and bone morphogenetic protein-2 treatment on odontogenic differentiation of human stem cells from apical papilla cultured in the VitroGel 3D system. *Cell Tissue Res* 2019; **378**: 207-220 [PMID: [31152245](#) DOI: [10.1007/s00441-019-03045-3](#)]
 - 88 **Battegay EJ**, Rupp J, Iruela-Arispe L, Sage EH, Pech M. PDGF-BB modulates endothelial proliferation and angiogenesis *in vitro* via PDGF beta-receptors. *J Cell Biol* 1994; **125**: 917-928 [PMID: [7514607](#) DOI: [10.1083/jcb.125.4.917](#)]
 - 89 **Lange S**, Heger J, Euler G, Wartenberg M, Piper HM, Sauer H. Platelet-derived growth factor BB stimulates vasculogenesis of embryonic stem cell-derived endothelial cells by calcium-mediated generation of reactive oxygen species. *Cardiovasc Res* 2009; **81**: 159-168 [PMID: [18806276](#) DOI: [10.1093/cvr/cvn258](#)]
 - 90 **Deng J**, Pan J, Han X, Yu L, Chen J, Zhang W, Zhu L, Huang W, Liu S, You Z, Liu Y. PDGFBB-modified stem cells from apical papilla and thermosensitive hydrogel scaffolds induced bone regeneration. *Chem Biol Interact* 2020; **316**: 108931 [PMID: [31874163](#) DOI: [10.1016/j.cbi.2019.108931](#)]
 - 91 **Penn JW**, Grobbelaar AO, Rolfe KJ. The role of the TGF- β family in wound healing, burns and scarring: a review. *Int J Burns Trauma* 2012; **2**: 18-28 [PMID: [22928164](#)]
 - 92 **Somoza RA**, Acevedo CA, Albornoz F, Luz-Crawford P, Carrión F, Young ME, Weinstein-Opppenheimer C. TGF β 3 secretion by three-dimensional cultures of human dental apical papilla mesenchymal stem cells. *J Tissue Eng Regen Med* 2017; **11**: 1045-1056 [PMID: [25690385](#) DOI: [10.1002/term.2004](#)]
 - 93 **Na S**, Zhang H, Huang F, Wang W, Ding Y, Li D, Jin Y. Regeneration of dental pulp/dentine complex with a three-dimensional and scaffold-free stem-cell sheet-derived pellet. *J Tissue Eng Regen Med* 2016; **10**: 261-270 [PMID: [23365018](#) DOI: [10.1002/term.1686](#)]
 - 94 **Salehi S**, Cooper P, Smith A, Ferracane J. Dentin matrix components extracted with phosphoric acid enhance cell proliferation and mineralization. *Dent Mater* 2016; **32**: 334-342 [PMID: [26777093](#) DOI: [10.1016/j.dental.2015.11.004](#)]
 - 95 **Athirasala A**, Tahayeri A, Thiruvikraman G, França CM, Monteiro N, Tran V, Ferracane J, Bertassoni LE. A dentin-derived hydrogel bioink for 3D bioprinting of cell laden scaffolds for regenerative dentistry. *Biofabrication* 2018; **10**: 024101 [PMID: [29320372](#) DOI: [10.1088/1758-5090/aa9b4e](#)]
 - 96 **Morsczeck C**, Götz W, Schierholz J, Zeilhofer F, Kühn U, Möhl C, Sippel C, Hoffmann KH. Isolation of precursor cells (PCs) from human dental follicle of wisdom teeth. *Matrix Biol* 2005; **24**: 155-165 [PMID: [15890265](#) DOI: [10.1016/j.matbio.2004.12.004](#)]
 - 97 **Liu J**, Yu F, Sun Y, Jiang B, Zhang W, Yang J, Xu GT, Liang A, Liu S. Concise reviews: Characteristics and potential applications of human dental tissue-derived mesenchymal stem cells. *Stem Cells* 2015; **33**: 627-638 [PMID: [25447379](#) DOI: [10.1002/stem.1909](#)]
 - 98 **Xu QL**, Furuhashi A, Zhang QZ, Jiang CM, Chang TH, Le AD. Induction of Salivary Gland-Like Cells from Dental Follicle Epithelial Cells. *J Dent Res* 2017; **96**: 1035-1043 [PMID: [28541773](#) DOI: [10.1177/0022034517711146](#)]
 - 99 **Chen G**, Chen J, Yang B, Li L, Luo X, Zhang X, Feng L, Jiang Z, Yu M, Guo W, Tian W. Combination of aligned PLGA/Gelatin electrospun sheets, native dental pulp extracellular matrix and treated dentin matrix as substrates for tooth root regeneration. *Biomaterials* 2015; **52**: 56-70 [PMID: [25818413](#) DOI: [10.1016/j.biomaterials.2015.02.011](#)]
 - 100 **Tsuchiya S**, Ohshima S, Yamakoshi Y, Simmer JP, Honda MJ. Osteogenic differentiation capacity of porcine dental follicle progenitor cells. *Connect Tissue Res* 2010; **51**: 197-207 [PMID: [20053131](#) DOI: [10.3109/03008200903267542](#)]
 - 101 **Steimberg N**, Angiero F, Farronato D, Berenzi A, Cossellu G, Ottonello A, Kaigler D, Mazzoleni G. Advanced 3D Models Cultured to Investigate Mesenchymal Stromal Cells of the Human Dental

- Follicle. *Tissue Eng Part C Methods* 2018; **24**: 187-196 [PMID: 29327669 DOI: 10.1089/ten.TEC.2017.0428]
- 102 **Salgado CL**, Barrias CC, Monteiro FJM. Clarifying the Tooth-Derived Stem Cells Behavior in a 3D Biomimetic Scaffold for Bone Tissue Engineering Applications. *Front Bioeng Biotechnol* 2020; **8**: 724 [PMID: 32671055 DOI: 10.3389/fbioe.2020.00724]
- 103 **Healy L**, Hunt C, Young L, Stacey G. The UK Stem Cell Bank: its role as a public research resource centre providing access to well-characterised seed stocks of human stem cell lines. *Adv Drug Deliv Rev* 2005; **57**: 1981-1988 [PMID: 16290151 DOI: 10.1016/j.addr.2005.07.019]
- 104 **Washio K**, Iwata T, Mizutani M, Ando T, Yamato M, Okano T, Ishikawa I. Assessment of cell sheets derived from human periodontal ligament cells: a pre-clinical study. *Cell Tissue Res* 2010; **341**: 397-404 [PMID: 20632035 DOI: 10.1007/s00441-010-1009-1]
- 105 **Gombold J**, Karakasidis S, Niksa P, Podczasy J, Neumann K, Richardson J, Sane N, Johnson-Leva R, Randolph V, Sadoff J, Minor P, Schmidt A, Duncan P, Sheets RL. Systematic evaluation of *in vitro* and *in vivo* adventitious virus assays for the detection of viral contamination of cell banks and biological products. *Vaccine* 2014; **32**: 2916-2926 [PMID: 24681273 DOI: 10.1016/j.vaccine.2014.02.021]
- 106 **Osathanon T**. Transplantation of cryopreserved teeth: a systematic review. *Int J Oral Sci* 2010; **2**: 59-65 [PMID: 20737931 DOI: 10.4248/IJOS10021]
- 107 **Yamada Y**, Nakamura-Yamada S, Konoki R, Baba S. Promising advances in clinical trials of dental tissue-derived cell-based regenerative medicine. *Stem Cell Res Ther* 2020; **11**: 175 [PMID: 32398041 DOI: 10.1186/s13287-020-01683-x]
- 108 **Menicanin D**, Mrozik KM, Wada N, Marino V, Shi S, Bartold PM, Gronthos S. Periodontal-ligament-derived stem cells exhibit the capacity for long-term survival, self-renewal, and regeneration of multiple tissue types in vivo. *Stem Cells Dev* 2014; **23**: 1001-1011 [PMID: 24351050 DOI: 10.1089/scd.2013.0490]
- 109 **Tatullo M**, Marrelli M, Shakesheff KM, White LJ. Dental pulp stem cells: function, isolation and applications in regenerative medicine. *J Tissue Eng Regen Med* 2015; **9**: 1205-1216 [PMID: 24850632 DOI: 10.1002/term.1899]



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