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The Sliding of Pulp Stem Cells

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Editorial

Pulp stem cells take origin from multipotent bone marrow stromal cells (BMSCs). They have the potential to differentiate into osteoblasts, chondrocytes, adipocytes, myelosupportive fibrous-stroma, and even muscle and neural tissues.

Dental pulp tissue is derived from migrating neural crest cells during development, and harbor various populations of multipotential stem/progenitor cells. *In vitro*, neural differentiation studies of rat and human adult dental pulp cells (DPCs) and stem cells from human exfoliated deciduous teeth (SHEDs) demonstrated that these stem/precursor cell populations are able to differentiate into neurons based on cellular morphology and the expression of early neuronal markers. This shed lights on potential therapy.

Bone Marrow stromal cells (BMSCs)

The classical definition of a stem cell implicates two properties:

1) The ability to self-renew and
2) The ability to differentiate

- Self-renewal: implies the ability to go through numerous cycles of cell division while maintaining the undifferentiated state.
- Potency: the cells have the capacity to differentiate into specialized cell types. In the strictest sense, these stem cells are either totipotent or pluripotent. They are able to give rise to any mature cell stem cells, although multipotent or unipotent progenitor cells are sometimes referred to as stem cells. These properties allow clinical implications.

Mesenchymal Stem Cells (MSCs)

Isolated from bone marrow represent a very small fraction, 0.001–0.01% of the total population of nucleated cells in marrow [3]. They are pluripotent, and underwent self-renewal cells. They display adhesion to the plastic of culture dishes. In addition:

Asymmetric division or/and symmetric division play role in the biology of stem cells: After pre-differentiation, they are involved in terminal differentiation into osteoblasts/odontoblasts, chondrocytes, adipocytes, myoblasts and neurones.

Stem cells arise inside niches. Distinct lineages are underlined either as Embryonic and Foetal stem cells (ESC)n, or as adult stem cells/postnatal (ASCs).

Renewal and Healing Due to Stem Cells

Mesenchymal stem cells (MSC) are at the origin of bone (osteoblasts), cartilage (chondrocytes), fat tissue (adipocytes), tendon (tenogenic), muscle cells and also stroma of bone marrow. Colony forming units-fibroblastic (CFU-f) allows an estimate of the number of MSC in patient bone marrow.

New born: 1/10.000

Teen 1/100.000

30 years 1/250.000

50 years 1/400.000

80 years 1/2000.000

Mesenchymal stem cells are multipotent cells found in several adult tissues. The concept emerged that mesenchymal stem cell (MSC), act as single cell capable of forming bone, cartilage, and other mesenchymal tissues.

Five Types of Human Dental Stem Cells

Have been Identified in pulp and Peripulpal tissues. Different phenotypes of dental and Peridental stem cells have been isolated and characterized. They are implicated in pulp therapies and tissue regeneration.

1.	Stem cells of the Dental pulp (DPSCs), including permanent teeth (Post Natal Pulp SC) and/or human exfoliated deciduous teeth deciduous teeth (SHED)
2.	Apical papilla stem cells (SCAP)
3.	Periodontal ligament stem cells (PDLSCs)
4.	Dental stem cells from the follicular sac (DFPCs)
5.	BMMSCs Odontogenic, Osteogenic, Adipogenic, Chondrogenic, Myogenic, and Neurogenic SC.

The dental stem cells can be used as progenitors and they play role in pulp regeneration. Many reports emphasis these therapeutic possibilities. Obviously, dental pulp SC may contribute to the coronal pulp chamber regeneration. In case of carious lesion and pulp necrosis, regeneration may occur either as odontoblasts lining the periphery of root canals (Tertiary Dentin); or they may contribute to the re-formation of root canals even after a total necrosis (Closure of the radicular pulp located inside root canals).

Stem cells are scarce and may recolonize the whole endodont, both the coronal and radicular pulp. The ratio of STEM cells versus pulp cells is about 5% [1,2].

Age-related parameters in early-passage BM hMSC from different donor groups.

Age of donor ‘	**‘Young” (7–18)**	**“Adult” (19–40)**	**“Aged” (>40)**
Cell size	276± 34	306 ±61	376±55

Due to the scarcity of stem cells after implantation of transcription factor, adult pulp Stem Cells (ASCs), may de-differentiate and regress in order to become embryonic stem cells (ESCs). These IPS are not stable and may de-differentiate into embryonic stem cells [3,4,6].

6- Induced pluripotent stem cells (IPS) Expression of transcription factors *(Oct-3/4, Sox, 2 (OKMS), c-Myc, Klf4 et NANOG)*. Adult stem cells may underwent regression and become embryonic cells.

Human SCs represent only about 1 out of every 30,000 cells (0.003%) in the bone marrow. The niche where they are issued consists of a local tissue microenvironment, capable of housing and maintaining one or more stem cells. Distinct “stromal” cell types initially guide niche morphogenesis and continue to directly contact and signal to resident stem cells.

We can consider the possibility of use of stem cell populations and their technology for future clinical applications, displaying ability to cure diseases like parkinsonism, juvenile diabetes, certain forms of cancer, muscular dystrophy, spinal injuries and heart problems (Myocardial Infarction). This is the property of coronal pulp. In contrast, this is not the case for cells located in the apical papilla (SCAP) that seem to be pre-progenitors [7,8,9].

Electron microscopy and immunostaining analysis showed that pulpal cells are linked by desmosome-like junctions and gap-junctions, forming a syncytium moving from the apical part (SCAP) toward the crown. Cells slide and are transported from the apex to the coronal part. The extracellular matrix was composed of thin collagen fibrils and implicate amorphous ground substance associated with Glycosaminoglycans favoring cell mobility. These data suggest that the syncytium-like structure formed by pulp radicular cells is a pre-request for plithotaxis, a collective cell migration process. This emergent mechanism governs pulp healing and regeneration after a dental lesion.

To conclude, the new emergent and dynamic concept highlights the sliding of pulp cell in the pulp. Two steps regulate the dynamic transport of SC within the dental pulp.

1. Firstly, inside the root canal, SCAP cells are moving from the center of the pulp to the periphery of the dental pulp. At this location, they contribute to the formation of parietal dentin, beneath a calciotraumatic line, associated with the narrowing of the radicular pulp. SCAP cells are sliding from the apex of the tooth to the center of the pulp and afterward, from the center of the pulp chamber toward the pulp periphery in the crown. Linked by gap junctions and desmosomes, and in association with tight junctions the cells reach the outer cell coronal layers, subjacent to odontoblasts.

2. Secondly, migration may be due to the sliding of SCAP cells located in the apical part of the root toward the crown. This approach shed lights on the apical niches of stem cells present in immature molars, and they provide new tools for future regenerative pulp therapies. Stem cells are incorporated into the odontoblast layer, or they underwent apoptosis.

The dynamic sliding of stem cells inside the pulp, leading to dentin generation or re-generation is a major event in the pulp healing. Clinical implications lead the cell dynamic contributing to cell renewal and potential pulp therapies [5,10].

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