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## Short Communication

# Regenerative medicine, stem cells and pulp repair

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### Introduction

The biological basis for regenerative therapies was established long ago by Spallanzani's observations in the early 1760. He showed that the tail and limb of salamander regenerate after surgical removal. The demonstration was completed by Trembley (1740), reporting that a bisected hydra may give rise to two completely formed individuals [1-2]. It comes out from such experiments that the regeneration of part of the body is possible after surgery and beneficial to regenerate a member.

During early embryonic formation, stem cells are derived from the inner mass of mouse blastocyte. They are qualified to express ameloblast-specific proteins such as ameloblastin, amelogenin and/or odontoblast-related mRNA. This is actually the case for molecules such as DSPP and dentin matrix acid phosphoprotein-1 when they are cultured in suitable conditioned mediums [3].

In adults, mesenchymal stem cells display odontogenic potential and they express odontogenic genes such as Pax9, Msx1, Lhx7, DMP1 and DSPP. Stem cells may be isolated from human exfoliated deciduous teeth (SHED) and/or postnatal human stem cells (DPSCs) [4-5]. SCAP cells are derived from the apical part of the papilla of growing tooth roots

[6-8]. STEM cells slide from the central part of the pulp to the lateral sub-odontoblastic boundaries. They move from the root toward the coronal part of the crown [9]. DPSCs, SHEDs, SCAPs differentiate into odontoblasts and adipocytes. Dental follicle (DFSCs), and periodontal ligament-like of permanent tooth (PDLSCs) may also contribute to regenerative medicine [10-13].

The biology of dental stem cells has an important impact in the context of regenerative dentistry [14]. Populations of DPSCs possesses (1) generic mesenchymal stem cells-like properties (MSCs) ; (2) colony forming ability; and (3) were shown to express *in vitro* osteoblastic, adipogenic, chondrogenic or even neuronal markers. Dental stem cell populations also express different panels of surface markers such as 3G5, STRO-1, CD44, CD106, CD146, CD90 and Sca-1 used to characterize hematopoietic stem cells.

Human embryonic stem cells express positive marker expression [Oct-4, Nanog, Rex-1 (transcription factor), and SSEA-3 and SSEA-4 (stage specific embryonic antigen), TRA-1-60 and TRA-1-81]. The expression of these markers is maintained in subclones obtained from these cells. They can be induced to undergo uniform differentiation into smooth and skeletal muscles, neurons, cartilage and bone under chemically defined culture conditions. They have been characterized *in vitro* and *in vivo*:

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*In vitro* characterization of DPSCs: These cells possess dentinogenic potential, adipogenic and neurogenic differentiation capacities and they express the respective gene markers.

*In vivo* characterization of DPSCs: Mixed with hydroxyapatite/tricalcium phosphate, they form dentin-pulp-like complex in immunocompromised mice. Expressing DSPP, a dentin-like structure is deposited on dentin surface.

Following transplantation, DPSCs are clonogenic cells, capable of self-renewal and multilineage differentiation. DPSCs are able to regenerate a dentin-pulp-like complex composed of mineralized matrix, with tubules lined by odontoblasts and an arrangement similar to the dentin-pulp complex found in normal teeth. Pulp cells express bone markers such as bone sialoprotein, alkaline phosphatase, type I collagen and osteocalcin.

Members of the TGF $\beta$  super family and cytokines regulate their differentiation. They are similar to bone marrow stromal stem cells (BMSSCs) and display potential to develop into osteoblasts, chondrocytes, adipocytes, myelo-supportive fibrous-stroma, muscle and neural tissues. They respond to specific environment signals, generate new stem cells and/or select a particular differentiation program.

The phenotypical analysis evidenced that DPSCs were highly positive for CD29, CD44, CD90 and HLA I. They were negative for CD34, CD45, CD71, and HLA II. Postnatal dental pulp contains cells that are clonogenic, highly proliferative, and capable of regenerating a tissue. Hence, these properties define them as stem cells, implicated in regenerative medicine [15].

**Table 1:** Types of dental pulp stem cells and their properties

*Stem cells permanently present in adult tooth (DPSCs):	*Dental stem cell properties	*Signaling inputs for reparative dentin formation
*Dental pulp stem cell (DPSCs).	Self-renewal They are able to enter in mitosis in response to appropriate signals and to differentiate toward odonto/osteogenic cells.	**Tooth injury may promote stem cell recruitment Local secreted factors : bioactive extracellular matrix molecules
*Periodontal ligament stem cells (PDLSCs)	Long-term survival and maintenance of reparative capacity	Ca <sup>2+</sup> release
*Apical papilla stem cells (SCAPs)	Distinct subpopulations expressing markers of mesenchymal stem cells of the bone marrow Stro-1, CD44, CD106, 3G5, CD146, CD90, Sca-1	Mechanical inputs changes in matrix elasticity
*Stem cells present in deciduous tooth (SHEDs)		Diffusible signals emanating from stromal, inflammatory, circulating cells.
<ul style="list-style-type: none"> <li>• Exfoliated deciduous teeth stem cells (SHEDs)</li> <li>• Stem cells present during crown formation (DFSCs) : Dental follicle stem cells</li> </ul>		

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