Available online at www.sciencerepository.org

Science Repository

Short Communication

Regenerative medicine, stem cells and pulp repair

Michel Goldberg*

Paris Cité University, Faculty of Fundamental and Biomedical Sciences, INSERM UMR-S 1124. 45 rue des Saints Fathers 75006 France, Paris

ARTICLE INFO

Article history:
Received 23 March, 2018
Accepted 16 April, 2018
Published 15 May 2018

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 hematopoetic 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:*

* *Correspondence to: Michel Goldberg, Paris Cité University, Faculty of Fundamental and Biomedical Sciences, INSERM UMR-S 1124. 45 rue des Saints Fathers 75006 France, Paris*
Tel: +0662676709; Email: mgoldod@gmail.com

http://dx.doi.org/10.31487/j.RGM.2018.10.003

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 TGFβ 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** Self-renewal	***Signaling imputs for reparative dentin formation**
***Dental pulp stem cell (DPSCs)**.	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 recruitement Local secreted factors : bioactive extracellular matrix molecules
***Periodontal ligament stem cells (PDLSCs)**	Long-term survival and maintenance of reparative capacity	Ca^{2+} 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.
• **Exfoliated deciduous teeth stem cells (SHEDs)** • **Stem cells present during crown formation (DFSCs) :** Dental follicule stem cells		

REFERENCES

1. Trembley A (1744) Memoirs to serve as the story of a group of freshwater polyps with horn-shaped arms. Leiden, J & H Verbeek.
2. Spallanzani, L. (1768), Prodromo di un opera da impnmersi sopra /a riproduzioni animali, Nella Stamperia di Giovanni Montanari, Modena. English translation by Matthew Maty as An Essay on Animal Reproductions. T. Becket and P.A De Hondt, London, 1769
3. Baudry A, Uzunoglu E, Schneider B, Kellermann O, Goldberg M (2016) From pulpal stem cells to tooth repair: an emerging field for dental tissue engineering. *Evidence-Based Endodontics* 1: 2-5.
4. Gronthos S, Mankani M, Brahim J, Robey PG, Shi S (2000). Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. *Proc Natl Acad Sci USA* 97: 13625-13630. [Crossref]
5. Miura M, Gronthos S, Zhao M, Lu B, Fisher LW, et al. (2003) SHED: Stem cells from human exfoliated deciduous teeth. *Proc Natl Acad Sci U S A* 1000: 5807-5812. [Crossref]
6. Sonoyama W, Liu Y, Fang D, Yamaza T, Seo B, et al. (2006). Mesenchymal stem cell-mediated functional tooth regeneration in swine. *PLoS ONE* 1: 79. [Crossref]
7. Sonoyama W, Liu Y, Yamaza T, Tuan RS, Wang S, et al. (2008) Characterization of apical papilla and its residing stem cells from human immature permanent teeth—a pilot study. *J Endod* 34: 166-171. [Crossref]
8. Huang G T-J, Sonoyama W, Liu Y, Liu H, Wang S, et al. (2008) The hidden treasure in apical papilla: the potential role in pulp/ dentin regeneration and bioroot engineering. *J Endod* 34: 645–51. [Crossref]
9. Hirata A, Dimitrova-Nakov S, Djole SX, Ardila H, Baudry A, et al. (2014) Plithotaxis, a collective cell migration, regulates the sliding of proliferating pulp cells located in the apical niche. Connect Tissue Res. 55 Suppl 1: 68–72. [Crossref]
10. Seo BM, Miura M, Gronthos S, Barthold PM, Batouli S, et al. (2004) Investigation of multipotent postnatal stem cells from human periodontal ligament. *Lancet* 364: 149-155. [Crossref]
11. Morsczeck C, Gotz W, Schierholz J, Zeilhofer F, Kuhn U, et al. (2005) Isolation of precursor cells (PCs) from human dental follicle of wisdom teeth. *Matrix Biol* 24: 155-165. [Crossref]

12. Honda MJ, Immaizumi M, Tsuchiya S, Morsczeck C (2010) Dental follicle stem cells and tissue engineering. *J Oral Sci* 52: 541-552. [Crossref]
13. Harichane Y, Hirata A, Dimitrova-Nakov S, Granja I, Goldberg M, et al. (2011) Pulpal projenitors and dentin repair. *Adv Dent Res* 23: 307-312. [Crossref]
14. Dimitrova-Nakov S, Harichane Y, Goldberg M, Kellermann O (2013) Dental stem cells: Progress and perspectives. *World J Stomatol* 2: 35-39.
15. Goldberg M (2017) Stem cells: Tools for dental tissues regeneration. *J of Dental Health, Oral Disorders & Therapy* 6: 00208.