Adipose-Derived Adult Stem Cells: Available Technologies for Potential Clinical Regenerative Applications in Dentistry

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ABSTRACT: Tissue homeostasis depends closely on the activity and welfare of adult stem cells. These cells represent a promising tool for biomedical research since they can aid in treatment and promote the regeneration of damaged organs in many human disorders. Adult stem cells indefinitely preserve their ability to self-renew and differentiate into various phenotypes; this capacity could be promoted in vitro by particular culture conditions (differentiation media) or spontaneously induced in vivo by exploiting the biochemical and mechanical properties of the tissue in which the stem cells are implanted. Among the different sources of adult stem cells, adipose tissue is an attractive possibility thanks to its ready availability and the standard extraction techniques at our disposal today. This review discusses the isolation, characterization, and differentiation of human adipose-derived adult stem cells, as well as regeneration strategies, therapeutic uses, and adverse effects of their delivery. In particular, since oral disorders (e.g., trauma, erosion, and chronic periodontitis) often cause the loss of dental tissue along with functional, phonetic, and aesthetic impairment, this review focuses on the application of human adipose-derived adult stem cells, alone or in combination with biomaterials, in treating oral diseases.

KEY WORDS: dentistry, adipose-derived adult stem cells, biomaterials, dental tissue regeneration, bone

I. INTRODUCTION

In recent years, postnatal stem cell biology has aroused considerable interest in the possibility of exploiting the regenerative potency of adult stem cells for different clinical applications. Although the human body is, in general, able to promote self-regeneration, some tissues are less able to heal or tackle the requirements entailed in regeneration. By definition, stem cells are able to promote self-renewal and can differentiate along multiple lineage pathways; they thus represent a very attractive tool for clinical applications to promote the regeneration of damaged tissues.[1]

Undifferentiated stem cells can undergo 2 different types of cell division, ensuring their self-renewal: One type gives rise to a symmetric division, which produces 2 identical daughter cells of the same lineage as the progenitor cell. The second type of division entails an asymmetrical procedure, which generates one stem cell plus one transit amplifying cell with limited self-renewal potential, since it divides a

0278–940X/14/$35.00

finite number of times and then terminally differentiates.[1,2]

In terms of their regenerative and differentiation potency, among the hierarchy of stem cells, embryonic stem cells are the most effective source; they are responsible for tissue development during histogenesis and are theoretically able to differentiate into any body tissue.[3] There are, however, considerable limitations on their use with regard to both cell regulation and ethical considerations. Conversely, adult stem cells maintain a moderate ability to differentiate into different tissues, and technical procedures for their cultivation and differentiation now are established. Moreover, to our knowledge, no ethical restrictions limit dealing with adult stem cells. Another important issue in favor of using adult stem cells for clinical applications concerns immune reactivity; they can be collected directly from the patient, reducing immunological side effects related to the use of cells that are transplanted from others.[4]

II. ISOLATION OF ADIPOSE-DERIVED ADULT STEM CELLS

A number of studies have analyzed the PLA population via biochemical and molecular approaches to demonstrate its stem cell content; all have shown that surface molecules expressed by hASCs are numerous and that they change over time, depending on the number of passages and plastic adhesion.[5]

Many standard methods have been developed to guarantee this capacity for multilineage in vitro differentiation of hASCs. They use specific stimuli, such as growth factors, drugs, and/or hormones, to test the differentiation ability of each lineage functionally. Each of these molecules is capable of recognizing its own cellular receptor and can transduce differentiation signals into the target cells (Table 2).

Cells committed to becoming adipogenic are generally maintained in a monolayer for about 2 weeks in the presence of a medium containing 10% fetal bovine serum, insulin 10 μM, isobutilmethilxantine 0.5 mM, dexamethasone 10^{-6} M, and indomethacin 200 μM.[22] Conversely, the osteogenic differentiation capacity of hASCs is achieved by cultivating cells for about three weeks in a medium containing 10% fetal bovine serum, ascorbic acid 5×10^{-6}M, dexamethasone 10^{-8}M, and β-glycerophosphate 10^{-2}M.[10]

TABLE 1: Expression Markers of Human Adipose-Derived Adult Stem Cells.

Common Markers	Uncommon Markers
CD29	CD49e
CD44	CD54
CD73	CD146
CD90	α−Smooth muscle actin
CD105	Collagenase type 1
	Osteonectin
	Osteopontin
	Fibroblast growth factor-2

A. hASC-Biomaterial Composites for Bone Regeneration

Since the multipotency of adipose-derived hMSCs was discovered, research has made substantial progress toward using hASCs as a cell source in tissue engineering, in combination with biodegradable scaffold biomaterials (Fig. 1). These scaffolds provide support for cell adhesion, spread, and proliferation and can promote differentiation and, eventually, tissue organization. A current research strategy for bone tissue engineering is based on using lipoaspiration-selected hASCs either in the expansion of the in vitro population or for in vivo delivery within scaffolds or a matrix configured to generate new functional bone.

III. CONCLUSIONS

The use of hASCs for regenerative purposes in the dental field has very good prospects. These cells are easily obtainable, thanks to the accessibility and abundance of adipose tissue, and posses the potential to overcome several current limitations in many fields of regenerative medicine. However, despite the

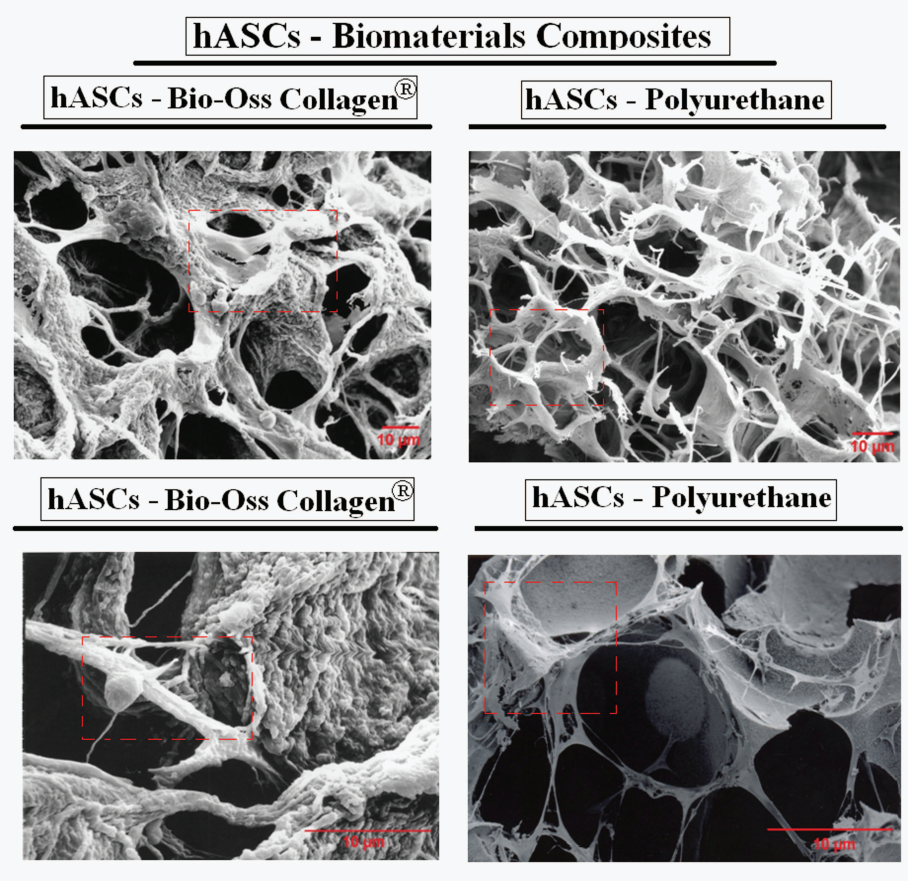

FIG. 1: Scanning electron microscopy images of some human adipose-derived adult stem cell (hASC)-biomaterial composites.

demonstrated properties, as yet there is no standard protocol for their use in clinical settings, especially when used in combination with biomaterials. As a consequence, further experimental studies and larger randomized controlled trials must be performed to ensure the safety and efficacy of hASCs, in accordance with the guidelines of the European Medicines Agency and the U.S. Food and Drug Administration, to treat disorders for which current medical and surgical therapies are neither effective nor practical.

ACKNOWLEDGMENT

This work was supported by the Italian Ministry for University and Research (PRIN 2010-2011: 20102ZNJ5_006 to A.C. and B.A).

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