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# Stem Cells in Aesthetic Procedures

## Art, Science, and Clinical Techniques

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# Contents

# 6 Adipocytes and Osteoblasts from Human Adipose Tissue Mesenchymal Stem Cells for the Production of Compatible and Safe Biomaterial Crucial in Cosmetic, Reconstructive, and Regenerative Medicine

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## 6.1 Introduction

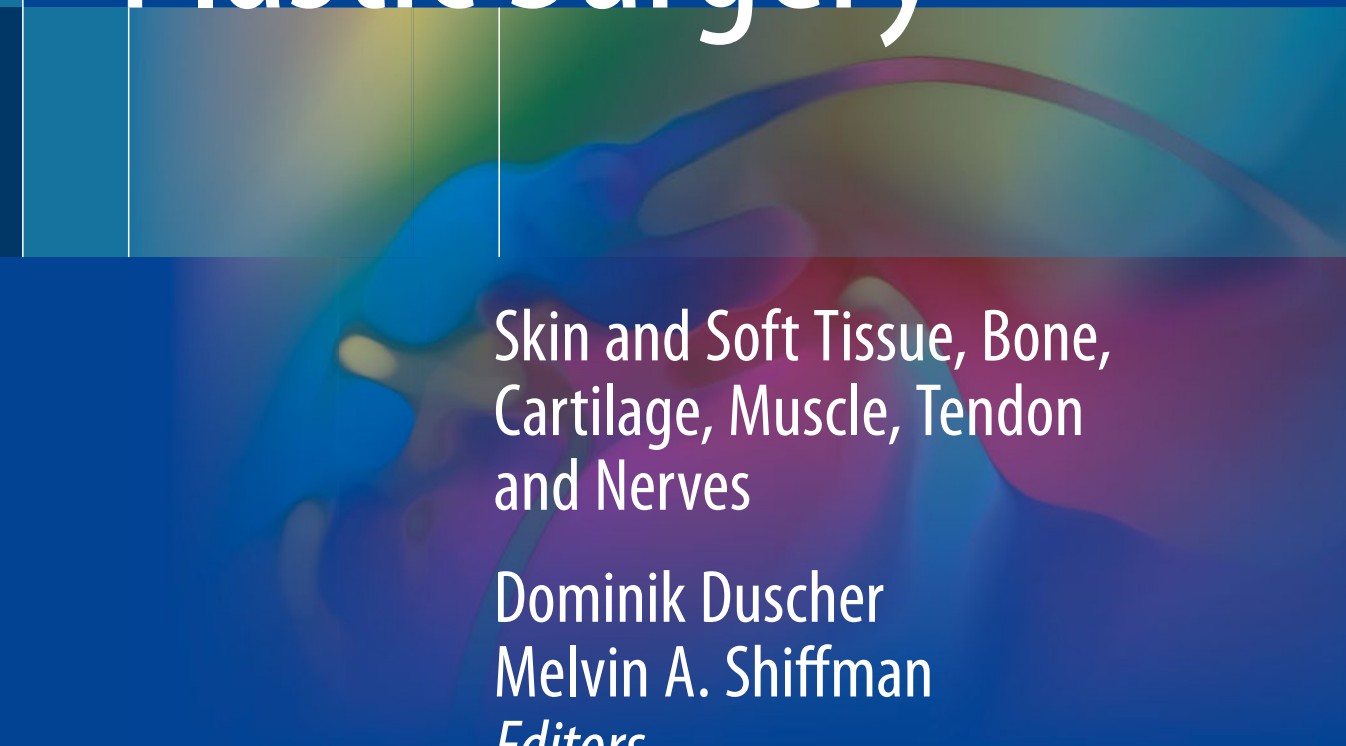
Several published works have confirmed the possibility to obtain a population of stem cells from adipose tissue that share similar features and morphogenetic profile of MSCs from known sources such as BM, UCB, amniotic fluid, scalp tissue, placenta, and synovial tissue [1–13]. A common pattern of all MSC cultures in vitro is a combination of specific and homogeneous traits including the formation of uniform colonies with a typical fibroblast spindle-like shape, self-renewal capacity, high viability, and multilineage ability such as osteoblasts, adipocytes, keratinocytes, cardiomyocytes, chondrocytes, hepatocytes, and tenocytes [4–6, 14–18]. In general, they do not express definite markers of hematopoietic cell surface phenotype and are positive for integrins and adhesion molecules, positive for matrix receptors, and positive for few very specific markers such as CD13 (APN), CD28, CD166 (ALCAM), CD44, CD73, CD90, CD105 and CD166, vimentin, desmin, Runx2, osterix (OX), and HLA class I [4, 10, 11, 14, 15, 19, 20].

One of the most intriguing traits of MSCs is their immune-modulatory capacity that is of relevant clinical importance as they may be transplanted without the need of HLA matching between donor and recipient which is strictly required in allogeneic adult stem cell procedures, in BM transfusion, or in organ transplants [3, 21–26]. While each MSC subgroup shows an identical immune-phenotypic profile, each set clearly expresses remarkable quantitative and qualitative differences, revealing a sort of heterogeneity linked to a specific genetic set that control different activities within the system [5, 11, 13, 18, 25]. The possibility to obtain MSCs from different sources other than the more classic ones like BM and UCB is of vital importance in the field of regenerative medicine and may provide the opportunity to avoid unnecessary invasive procedures or to explore a better sustainable therapeutic strategy which is based on multiple possible choices considered on a case-by-case basis [13, 18, 26–28]. Adipose tissue, like marrow, is of mesoderm origin; it starts to form during the last trimester of intrauterine life and contains a variety of stromal cells that group into microvascular endothelial cells, smooth muscle cells, and MSCs that can be isolated by enzymatic digestion and centrifugation [18, 24, 29, 30]. Adipose tissue is to be considered a complex structure that performs on multiple levels as an energy store and as an endocrine organ capable of producing and secreting a large number of molecules including leptin, adiponectin, and resistin which control endothelial functionality and may influence the vascular system [29, 31, 32]. Data from our study, in line with published research, have confirmed that fat tissue compared to BM contains more MSCs. From 1 g of tissue, you may collect $5 \times 10^{4-5}$ MSCs which is 500-folds larger than 1 g of MSCs obtained from BM [24, 33, 34]. hATMSCs, as their respective equivalent, have the ability to differentiate into diverse cell lines such as myoblasts, chondroblasts, cardiomyocytes, hepatocytes, adipocytes, and osteoblasts maintaining a unique plasticity typical of all MSCs [13, 19, 24, 30, 35, 36]. This study, in line with edited data, has demonstrated that hATMSCs, at least in vitro culture, behave in a similar manner and are able to home in a bone-like environment such as sea coral scaffold [10, 19, 27].

In line with other studies and with our previously published work, the authors have tried to establish a method that allows the use of these cells in combination with bio-scaffolds to be used in the reconstruction of hard tissue such as bone and in scaffolds in repairing damaged soft tissue and semihard tissues such as cartilage and intervertebral disk bulbs [10, 37, 38]. Therefore, the first task was to use hATMSCs and adipocytes and osteoblasts seeded onto marine coral *Porites lutea* to generate a hard structure bio-scaffold; the second task was to generate a soft scaffold using a fibrin gel seeded with human adipocyte cells to generate a soft structure scaffold. The fibrin gel has been generated by using autologous patient's blood; from this sample, fibrinogen and thrombin have been isolated and then mixed in unique solution in a ratio of 1:1 [37–40].

However, despite the promising results from preliminary clinical trials, our concern is about the possible contribution of hATMSCs in vivo as an active player in the process of vascular

# Regenerative Medicine and Plastic Surgery



## Skin and Soft Tissue, Bone, Cartilage, Muscle, Tendon and Nerves

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**Part III Cartilage Regeneration**



**Part IV Muscle and Tendon Regeneration**

**Part V Nerve Regeneration**

# 13 Innovative Scaffold Solution for Bone Regeneration Made of Beta-Tricalcium Phosphate Granules, Autologous Fibrin Fold, and Peripheral Blood Stem Cells

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## 13.1 Introduction

Diseases, trauma, and surgical procedures can be the cause of bone paucity and defects. Due to the complexity of bone anatomy and physiology bone tissue degeneration and diseases can pose a big threat to doctors and physicians. However, modern bone tissue biomedical engineering has been considered as a valid substitute solution for these conditions [1]. Procedures applied to repair defects or

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degeneration need the use of proper biomaterials with the right dimensions and anatomy shape that can fit into the damaged area. The cases of larger and more difficult defects need highly osteogenic scaffolds to promote and improve the bone tissue formation and regeneration [2].

The majority of scaffolds made of ceramics and metals or from polymers showed a weak osteogenic capability. Bone grafts are currently available in many different forms, such as allogeneic/autologous demineralized bone matrix or implants, growth factor-loaded microbeads, or bio-derivate as calcium hydroxyapatite, gels, ceramic derivate, sea corals, and metals [2, 3]. The main target is to reduce the incidence of collateral complications such as rejection, infection and inflammation, and donor-site morbidity and of course reduce the overall costs and related expenses such as frequent hospitalization [3–5]. Breakdowns, such as partial ruptures or complete collapse, are the major issues related to synthetic implants, generally due to quality of the material and subtle autoimmune responses that may also create ideal conditions for bacterial growth, inflammation, and rejection [6–9]. Metal implants, for example, may cause malfunction due to aseptic loosening with specific inflammatory and immune responses to metal-wear particles released during bio-corrosion which intensify the osteolytic activity of osteoclasts at the bone-implant interface, leading to a progressive loss of fixation [8, 9]. Therefore, an optimal biomaterial should possess specific bio-characteristics and qualities that should be biodegradable, tolerable, and safely absorbed by the body. This should happen without causing any kind of damaging event such as an inflammation or an immune reaction, capable of carrying and supporting tissue growth and proliferation, thus allowing bone regeneration [5, 9].

The latest generations of bio-implants have been created with the precise intent of functioning as cell carriers capable of reproducing human bone formation process. The newest generation of these types of scaffolds has been developed with materials that possess specific mechanical and structural properties that are compatible with the anatomical site into which they are to be inserted, with enough volume fraction and high surface area to carry an enough number of cells within the scaffold and the surrounding host tissues. This allows ingrowth and vascularization [5]. Therefore, the new bio-implants tend to replicate the process of the formation of new bone development or which physiologically takes place after an injury [10].

An inflammatory response takes place after an implantation of a biomaterial as a consequence of host immune response [10]. During this phase monocytes differentiate to tissue macrophages. However, presence of MSCs promotes an immune-modulatory activity on macrophage M1/M2 balance towards M2 commencing a favorable cascade of events where interleukins such as IL-10, IL-4, IL-13, and IL-6 and prostaglandin E2 initiate the first step of the repairing process [11–14]. Bone plays a key role in well functioning of immune system and it is the site that immune cells are created. In fact, autoimmune disorders often induce bone tissue damages and degeneration, an event that has been confirmed by an experiment where macrophage ablation leads to intramembranous bone defection and inhibiting of the healing process [14].

In effect, previous studies have shown that some biomaterials due to high similarity with human tissues are able to trigger physic-chemical signals leading to stem cell differentiation towards diverse cell phenotypes as osteoblasts [15, 16]. Results have shown that biomaterials based on calcium phosphate (CaP), a major constituent of native bone tissue, induce naïve stem cells towards osteogenic differentiation promoting in vivo bone tissue formation and augmentation [16, 17].

However, though CaP is quickly absorbed in vivo, the process often occurs preceding the formation of new bone tissue that results in an incongruence between the host's new bone and scaffold. Conversely, β-TCP seems to be better compatible as the absorption rate is slower with a steady release of both calcium ($Ca^{2+}$) and sulfate ($SO_4^{2-}$) ions [18].

In line with our published study, we can confirm that hPB contains the right amount of different subsets of pluripotent and multipotent stem cells such as MSCs, HSCs, NSCs, and ESCs capable of differentiating into cells of different lineages such as osteoblasts [19]. In this current study, we have noted that part of hPB-SCs were induced to differentiate to active osteoblasts under the direct influence of β-TCP granules within a period of 7–10 days without the need of