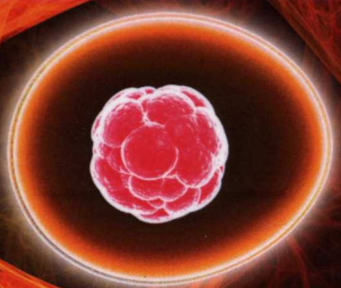
Stem Cells - Laboratory and Clinical Research

Adipose-Derived Stem Cells (ASCs)

Clinical Applications, Biological Characteristics and Therapeutic Potential in Regenerative Medicine



Yunfeng Lin
Guo Li • Jinfeng Liao
Editors

NOVA

Adipose-derived stem cells (ASCs) exist in adipose tissue and can differentiate into different embryonic layer cells and tissues in specific inductive conditions. The amount of ASCs in adipose tissue is much higher than that of bone marrow-derived stem cells. The adipose tissue is abundant in the subcutaneous tissue and easy to obtain. So, ASCs are considered a rich source of adult stem cells. In addition, ASCs do not express the major histocompatibility complex, Class II, suggesting that ASCs not only are suitable for autologous transplantation, but also have potential in allogeneic transplantation. Due to the rich origins, multilineage differentiation potential and immune tolerance, ASCs have been playing a significant role in the development and application of tissue engineering in recent years. In this book, the authors focus on the biological characteristics, clinical applications and therapeutic potential in regenerative medicine of ASCs, including: (1) the culturing methods, markers, secreted cytokines and multi-lineage differentiation potential of ASCs; (2) the current knowledge related to the effects of biophysical stimuli, especially the substrate stiffness and topography, on the differentiation of stem cells and their potential mechanisms; (3) the nanostructures and nanoparticles' applications on ASCs, as well as their dominating roles in regulating the proliferation, adhesion, migration, and differentiation of ASCs; (4) the process of ASC osteogenic differentiation, such as the methods of induction and verification, related genes, and signaling pathways; and (5) the therapeutic potential and clinical applications of ASCs in the cardiovascular system, wound-healing, anti-aging, and plastic surgery.

The authors sincerely hope that this book will provide further insight for basic and applied researchers as well as clinicians involved in regenerative medicine, thus contributing to further advances in the regenerative medicine of ASCs.

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PREFACE

Adipose-derived stem cells (ASCs) exist in adipose tissue and can differentiate into different embryonic layer cells and tissues in specific inductive conditions. The amount of ASCs in adipose tissue is much higher than that of bone marrow-derived stem cells. The adipose tissue is abundant in the subcutaneous tissue and easy to obtain. So, ASCs are considered a rich source of adult stem cells. In addition, ASCs do not express the major histocompatibility complex, Class II, suggesting that ASCs not only are suitable for autologous transplantation, but also have potential in allogeneic transplantation. Due to the rich origins, multilineage differentiation potential and immune tolerance, ASCs have been playing a significant role in the development and application of tissue engineering in recent years. In this book, the authors focus on the biological characteristics, clinical applications and therapeutic potential in regenerative medicine of ASCs, including: (1) The culturing methods, markers, secreted cytokines and multi-lineage differentiation potential of ASCs; (2) the current knowledge related to the effects of biophysical stimuli, especially the substrate stiffness and topography, on the differentiation of stem cells and their potential mechanisms; (3) the nanostructures and nanoparticles' applications on ASCs, as well as their dominating roles in regulating the proliferation, adhesion, migration, and differentiation of ASCs; (4) the process of ASC osteogenic differentiation,

such as the methods of induction and verification, related genes, and signaling pathways; and (5) the therapeutic potential and clinical applications of ASCs in the cardiovascular system, wound healing, anti-aging, and plastic surgery.Therapeutic Potential in Regenerative Medicine Adipose-derived stem cells (ASCs) exist in adipose tissue and can differentiate into different embryonic layer cells and tissues in specific inductive conditions. The amount of ASCs in adipose tissue is much higher than that of bone marrow-derived stem cells. The adipose tissue is abundant in the subcutaneous tissue and easy to obtain. So, ASCs are considered a rich source of adult stem cells. In addition, ASCs do not express the major histocompatibility complex, Class II, suggesting that ASCs not only are suitable for autologous transplantation, but also have potential in allogeneic transplantation. Due to the rich origins, multilineage differentiation potential and immune tolerance, ASCs have been playing a significant role in the development and application of tissue engineering in recent years. In this book, the authors focus on the biological characteristics, clinical applications and therapeutic potential in regenerative medicine of ASCs, including: (1) The culturing methods, markers, secreted cytokines and multi-lineage differentiation potential of ASCs; (2) the current knowledge related to the effects of biophysical stimuli, especially the substrate stiffness and topography, on the differentiation of stem cells and their potential mechanisms; (3) the nanostructures and nanoparticles' applications on ASCs, as well as their dominating roles in regulating the proliferation, adhesion, migration, and differentiation of ASCs; (4) the process of ASC osteogenic differentiation, such as the methods of induction and verification, related genes, and signaling pathways; and (5) the therapeutic potential and clinical applications of ASCs in the cardiovascular system, wound healing, anti-aging, and plastic surgery.

The authors sincerely hope that this book will add further insight into basic and applied researchers as well as clinicians involved in regenerative medicine, thus contributing to further advances in the regenerative medicine of ASCs.

Chapter 1 - Adipose-derived stem cells (ASCs), an important type of postnatal adult stem cells, are thought to be one of the most promising stem cell types, as human adipose tissue is ubiquitous and easily obtained in large quantities with minimal donor site morbidity and patient discomfort. The use of autologous ASCs for both research and cellular therapeutic treatments is feasible and has been shown to be both safe and efficacious in preclinical and clinical studies of various injuries and diseases. In this chapter, the authors review many studies associated with ASCs and summarize the different classifications of adipose tissues, as well as the basic characteristics, culturing methods, markers, secreted cytokines, multi-lineage differentiation potential, and applications of ASCs for a more systematic and broader understanding of ASCs.

Chapter 2 - Cardiovascular diseases are the leading cause of death worldwide. The loss or dysfunction of cardiomyocytes is associated with many forms of heart disease. With increasing awareness of the shortcomings of heart transplantation and left ventricular assist devices, cardiovascular surgeons have to consider alternative methods of treatmentfor heart diseases. With much progress made in stem cell research, the transplantation of stem cells has attracted tremendous attention from basic scientists and clinicians as a promising strategy for improving the outcomes of patients with cardiovascular diseases. Adipose-derived stem cells (ASCs) have extensive proliferative capacity in cell culture conditions and are able to differentiate into several lineages, including into endothelial cells, smooth muscle cells, and cardiomyocytes. Additionally, ASCs can secrete many growth factors and cytokines, which have angiogenic, anti-apoptotic, and immunoregulatory functions. The differentiation ability and paracrine function of ASCs have made them an optimal candidate for repairing damaged tissues, such as the ischemic or infarcted heart.

Chapter 3 - Stem cells are undifferentiated cells with important properties for self-renewal and differentiation. Adipose-derived stem cells (ASCs) have many advantages, such as accessibility and abundance, compared to other kinds of stem cells. Regeneration therapies using ASCs have received much attention in the treatment of various dermatological

diseases. In previous studies, ASCs were shown to have antioxidant, whitening, and wound-healing effects in the skin through secretion of various growth factors and by activating fibroblasts. There is an abundance of literature supporting the efficacy of ASCs in both aesthetic and reconstructive cases. In dermatology, there are also many studies on the effective application of ASCs, such as improved retention in autologous fat transplantation, antioxidant action, and whitening effects. In this chapter, the authors will summarize the therapeutic potential and clinical applications of ASCs in wound healing, anti-aging, and plastic surgery.

Chapter 4 - Adipose-derived stem cells (ASCs) naturally residing in the stromal-vascular fraction of adipose tissue have properties of self-renewal and are one of multipotent mesenchymal stem cells that can be applied in cell therapy because of their potential to differentiate into a wide range of specialized cell lineages, including osteoblasts, chondrocytes, myocytes, cardiomyocytes, and endothelial cells. Compared to bone marrow-derived stem cells (MSCs), ASCs are a more promising resource for cell therapy owing to their accessibility, abundance, and low immunogenicity. The secretion of paracrine factors affects the differentiation of ASCs to repair and regenerate damaged tissue via many approaches. In the local microenvironment, several stimuli significantly affect the maintenance and survival of ASCs. The majority of signaling molecules interact with ASCs at the nanoscale level. Thus, scaffolds with surface nanostructures have potential applications for ASCs and in the field of regenerative medicine. Nanostructures created by natural, synthetic, or composite polymeric biomaterials provide artificial templates of the extracellular matrix (ECM). With the properties of high surface area to volume ratio, porosity with beneficial mechanical properties, and a biomimetic platform to attract ASCs and induce differentiation, nanostructures can assist in tissue function. In this chapter, the authors review the characteristics of ASCs and nanotechnology, the various nanostructure and nanoparticle applications of ASCs as well as their dominating roles in regulating the proliferation, adhesion, migration, and differentiation of ASCs. A comprehensive understanding of the effects of nanostructures and nanoparticles on ASCs' behaviors is significant and

helpful to enhance the therapeutic potential and clinical applications of ASCs in regenerative medicine.

Chapter 5 - Autologous adipose-derived stem cells (ASCs) isolated from subcutaneous adipose tissue were applied and proven to be effective in treating bone defects. ASCs could be considered as a potent cell source for bone regenerative medicine. This chapter summarizes the process of ASC osteogenic differentiation, analyzes the related genes and signaling pathways, reviews the methods of induction and verification, discusses the main factors and their mechanisms, elucidates the ASC-related bone regeneration, and proposes a future research direction. ASC osteogenic differentiation is a complex process involving multiple genes, protein interactions, and signaling pathways including Runx2, Osterix, Wnt, bone morphogenetic protein, Notch, fibroblast growth factors, cyclic adenosine monophosphate/protein kinase A, and Hedgehog mitogen activated protein kinase, all of which have played an important role in the osteogenic differentiation process.

Chapter 6 - With the outstanding advantages of easy access and ability to differentiate into multiple cell types, adipose-derived stem cells are a promising cell source for tissue engineering. However, precise control of differentiation remains challenging. The interaction between a cell and the extracellular matrix (ECM) may be critical in the regulation of cellular behavior. Biomaterials mimicking physical properties or microstructure of ECM have shown potential value in the control of stem cell differentiation lineages. This chapter summarizes the current knowledge related to the effects of biophysical stimuli, especially substrate stiffness and topography, on the differentiation of stem cells and their potential mechanisms.

CONTENTS

Preface		**vii**
Chapter 1	Basic Characteristics, Secretion, Differentiation, and Applications of Adipose-Derived Stem Cells *Shiyu Lin, Guo Li, Qi Zhang, Tao Zhang, Sirong Shi, Changyue Xue, Dan Zhao, Qiang Xie and Yunfeng Lin*	**1**
Chapter 2	Adipose-Derived Stem Cells: Therapeutic Potential in Cardiovascular System *Dan Zhao, Guo Li and Jinfeng Liao*	**39**
Chapter 3	Therapeutic Potential of Adipose-Derived Stromal Cells in Wound Healing, Anti-Aging, and Plastic Surgery *Changyue Xue and Guo Li*	**77**
Chapter 4	Nanotechnology and Adipose-Derived Stem Cells Applied to Tissue Engineering *Sirong Shi, Shiyu Lin, Guo Li, Tao Zhang, Changyue Xue, Dan Zhao, Qiang Xie and Yunfeng Lin*	**111**

Chapter 5 Adipose-Derived Stem Cells: Therapeutic Potential in Bone Regenerative Medicine **147**
Qiang Xie, Anchun Mo and Xiaoxiao Cai

Chapter 6 Biophysical Regulation in the Differentiation of Adipose-Derived Stem Cells **195**
Tao Zhang, Taoran Tian, Shiyu Lin, Sirong Shi and Xiaoxiao Cai

Index **215**

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Chapter 1

BASIC CHARACTERISTICS, SECRETION, DIFFERENTIATION, AND APPLICATIONS OF ADIPOSE-DERIVED STEM CELLS

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ABSTRACT

Adipose-derived stem cells (ASCs), an important type of postnatal adult stem cells, are thought to be one of the most promising stem cell types, as human adipose tissue is ubiquitous and easily obtained in large

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quantities with minimal donor site morbidity and patient discomfort. The use of autologous ASCs for both research and cellular therapeutic treatments is feasible and has been shown to be both safe and efficacious in preclinical and clinical studies of various injuries and diseases. In this chapter, we review many studies associated with ASCs and summarize the different classifications of adipose tissues, as well as the basic characteristics, culturing methods, markers, secreted cytokines, multi-lineage differentiation potential, and applications of ASCs for a more systematic and broader understanding of ASCs.

Keywords: adipose-derived stem cell, characteristics, marker, cytokine, differentiation, application

1. INTRODUCTION

Stem cells are self-renewing, possess long-term viability, and have multi-lineage differentiation potential. These properties make them useful as seeding cells for regenerative medicine. However, stem cells need to meet the following criteria to be used in clinical practice: (1) easy availability. (2) multi-lineage differentiation potential in a regulated and reproducible manner. (3) convenient collection process. (4) safety and efficacy in the host [1].

Stem cells are usually divided into embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs), and postnatal adult stem cells. ESCs are capable of extensive self-renewal, expansion, and multipotent differentiation, and have potential for future use. However, their use has been restricted owing to ethical and potential immune-rejection constraints [2]. iPSCs are derived from differentiated cells by inducing pluripotency with several transcription factors involved in reprogramming [3]. iPSCs are phenotypically and functionally indistinguishable from ESCs. However, the safety and effectiveness of iPSCs in clinical practice and in the long term are unclear.