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Alexander Birbrair *Editor*

Stem Cells Heterogeneity - Novel Concepts

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Stem Cells Heterogeneity - Novel Concepts

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Preface

This book's initial title was *Stem Cells Heterogeneity*. However, due to the current great interest in this topic, we were able to assemble more chapters than would fit in one book, covering stem cell biology under distinct circumstances. Therefore, the book was subdivided into three volumes entitled "Stem Cells Heterogeneity - Novel Concepts," "Stem Cells Heterogeneity in Different Organs," and "Stem Cells Heterogeneity in Cancer."

This book, *Stem Cells Heterogeneity - Novel Concepts*, presents contributions by expert researchers and clinicians in the multidisciplinary areas of medical and biological research. The chapters provide timely detailed overviews of recent advances in the field. This book describes the major contributions of stem cells to the biology of different organs in physiological and pathological conditions. Further insights into the biology of stem cells will have important implications for our understanding of organ development, homeostasis, and disease. The authors focus on the modern methodologies and the leading-edge concepts in the field of stem cell biology. In recent years, remarkable progress has been made in the identification and characterization of stem cells in several tissues using state-of-the-art techniques. These advantages facilitated identification of stem cell subpopulations and definition of the molecular basis of stem cells' role within different organs. Thus, the present book is an attempt to describe the most recent developments in the area of stem cell heterogeneity which is one of the emergent hot topics in the field of molecular and cellular biology today. Here, we present a selected collection of detailed chapters on what we know so far about the stem cells in various tissues and under distinct pathophysiological conditions. Eleven chapters written by experts in the field summarize the present knowledge about stem cell heterogeneity in distinct circumstances.

Alice Jouneau from INRA discusses the heterogeneity in epiblast stem cells. Ricardo Pardal and colleagues from Sevilla University describe stem heterogeneity in the adult carotid body. Salvetti Alessandra and Leonardo Rossi from the University of Pisa compile our understanding of stem cell heterogeneity in planaria. Wa Xian and colleagues from the University of Texas Health Science Center update us with what we know about Barrett's esophagus stem cells. Kiyoshi Ohnuma and colleagues from Nagaoka University of Technology summarize current knowledge on

pluripotent stem cell heterogeneity. Jiri Hatina and colleagues from Charles University address the importance of sarcoma stem cell heterogeneity. Elio A. Prieto González from the Interamerican Open University focuses on heterogeneity of adipose-derived stem cells. Ganokon Urkasemsin and Joao N. Ferreira from Mahidol University introduce our current knowledge about salivary gland stem cells. Weiqiang Wang and Zhong Chao Han from Tianjin Institute of Health and Stem Cells talk about the heterogeneity of human mesenchymal stem cells. Sujit K. Bhutia and colleagues from the National Institute of Technology Rourkela focus on mitochondrial heterogeneity in stem cells. Finally, Dario Pisignano and colleagues from the University of Bari give an overview of the heterogeneity of renal stem cells and their interaction with bio- and nano-materials.

It is hoped that the articles published in this book will become a source of reference and inspiration for future research ideas. I would like to express my deep gratitude to my wife Veranika Ushakova and Mr. Murugesan Tamilsevan from Springer, who helped at every step of the execution of this project.

This book is dedicated to the memory of my grandfather Pavel Sobolevsky, PhD, a renowned mathematician, who passed away during the creation of this piece.



My grandfather Pavel Sobolevsky z"l, PhD (March 26, 1930–August 16, 2018)

New York, NY, USA
Belo Horizonte, MG, Brazil

Alexander Birbrair

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Chapter 1

Stem Cells Heterogeneity



Alexander Birbrair

Abstract Adult endogenous stem cells are crucial to maintain organ homeostasis due to their particular capacity to originate more specialized cell populations in a coordinated manner based on the body necessity. Extensive studies in a variety of tissues have highlighted the importance of stem cells for the functioning of our organism, including the skin, intestine, stomach, skeletal muscle, bone marrow, and others. Although significant progress has been made in our understanding of stem cell biology, our knowledge about these cells still remains limited due to their complexity and their dynamics. The advancement of our knowledge on these essential cells will have substantial implications in our understanding of tissue homeostasis and disease. Importantly, not all stem cells are alike even within the same tissue. They differ in their cell cycle status, surface marker expression, response to various extrinsic molecules, and distinct lineage outputs after transplant. The expanding literature which backs heterogeneity within stem cells is presently of great interest and brings questions as how stem cell subpopulations are generated, why they exist, and whether stem cells heterogeneity influences disease progression or therapy options. In more recent years, the combination of fluorescent and confocal microscopy with genetic state-of-art techniques, such as fate lineage tracking and single-cell RNA sequencing, enabled remarkable advance in the discovery of multiple novel essential functions for stem cell subpopulations in health and disease, before unexpected. This book provides an overview on our knowledge of stem cell subtypes in different organs under physiological and pathological conditions and discusses the possible origins and consequences of stem cells heterogeneity. This book's initial title was Stem Cells Heterogeneity. However, due to the current great interest in this topic, we were able to assemble more chapters than would fit in one book, covering stem cell biology under distinct circumstances. Therefore, the book

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was subdivided into three volumes entitled: *Stem Cells Heterogeneity—Novel Concepts*, *Stem Cells Heterogeneity in Different Organs*, and *Stem Cells Heterogeneity in Cancer*. Here, we offer a selected compilation of comprehensive chapters on what we know so far about heterogeneity within stem cells. More than 30 chapters written by scientists in the field outline our present knowledge on stem cells heterogeneity.

Keywords Stem cells · Heterogeneity · Plasticity · Regeneration · Microenvironment · Niche

Adult endogenous stem cells are crucial to maintain organ homeostasis due to their particular capacity to originate more specialized cell populations in a coordinated manner based on the body necessity [1]. Extensive studies in a variety of tissues have highlighted the importance of stem cells for the functioning of our organism, including the skin [2], intestine [3], stomach [4], skeletal muscle [5], bone marrow [6], and others [7]. Although significant progress has been made in our understanding of stem cell biology, our knowledge about these cells still remains limited due to their complexity and their dynamics. The advancement of our knowledge on these essential cells will have substantial implications in our understanding of tissue homeostasis and disease. Importantly, not all stem cells are alike even within the same tissue. They differ in their cell cycle status, surface marker expression, response to various extrinsic molecules, and distinct lineage outputs after transplant. The expanding literature which backs heterogeneity within stem cells is presently of great interest and brings questions as how stem cell subpopulations are generated, why they exist, and whether stem cells heterogeneity influences disease progression or therapy options. In more recent years, the combination of fluorescent and confocal microscopy with genetic state-of-art techniques, such as fate lineage tracking and single-cell RNA sequencing, enabled remarkable advance in the discovery of multiple novel essential functions for stem cell subpopulations in health and disease, before unexpected. This book provides an overview on our knowledge of stem cell subtypes in different organs under physiological and pathological conditions and discusses the possible origins and consequences of stem cells heterogeneity.

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