

Preface

The field of regenerative medicine is searching for stem cells that can be safely and efficiently employed in the regeneration of damaged organs. The ideal stem cell type would be pluripotent stem cells, which, according to their definition, have a broad potential to differentiate into cells from all three germ layers (meso-, ecto-, and endoderm). However, true pluripotent/multipotent stem cells in adult tissues are extremely rare and are still waiting to be tested in the clinic. In the meantime, various types of stem cells isolated from adult tissues are being employed in several *in vivo* experiments and in clinical trials aimed at regeneration of damaged organs (e.g., myocardial infarction, liver damage, ischemic kidney failure, or stroke). There is also mounting evidence that stem cells secrete a variety of growth factors, cytokines, chemokines, and bioactive lipids that regulate their biology in an autocrine/paracrine-manner and orchestrate interactions with the surrounding microenvironment. In addition to soluble factors, cells also secrete microvesicles (MVs), which are small, spherical membrane fragments shed from the cell surface or secreted from the endosomal compartment that seem to play an important and underappreciated role in improving the function of damaged organs. Such cell-derived paracrine signals may explain why the final therapeutic benefits are similar when applying different types of stem cells.

This book is focused on stem cells isolated from adult tissues and the various potential mechanisms involved in their therapeutic effects. The first chapter provides a general overview of the various stem cells isolated from embryonic and adult tissues that are endowed with pluri/multipotential differentiation potential and their advantages and limitations in clinical applications. In Chapter 2, we describe the potential mechanisms involved in the therapeutic effects of adult stem cells, with special emphasis on a population of very small embryonic-like stem cells. Human umbilical cord blood is a promising source of stem cells, and this topic will be reviewed in the third chapter. Dr. Ewa Zuba-Surma et al. discusses various types of stem cells that are present in this promising source of cells for therapeutic applications. It has been postulated for many years that hematopoietic stem/progenitor cells express the CD34 antigen. Dr. Sonoda et al. focuses on a population of CD34-negative cells that possess broader hematopoietic potential, and, as his group pro-

poses, is a population of the most primitive hematopoietic stem cells. The full hematopoietic potential of these cells is revealed after intra-bone injection. For more than forty years, hematopoietic stem cells isolated from bone marrow and, more recently, mobilized peripheral blood or umbilical cord blood have been employed to treat patients suffering from several malignant and non-malignant hematological and metabolic disorders. In the footsteps of hematologists, cardiologists have also tried to employ various types of cells to treat patients suffering from heart infarct or chronic heart insufficiency. This important issue is discussed by Dr. Wojciech Wojakowski et al. in Chapter 5.

In the following chapter, Dr. Ahmed Abdel-Latif and coauthors discuss important mechanisms involved in the trafficking of stem cells during heart infarct, with special emphasis on the role of bioactive lipids such as sphingosine-1-phosphate (S1P) and ceramide-1-phosphate (C1P) in the mobilization of stem cells from hematopoietic tissues and their homing to injured myocardium. Another important clinical area with a research focus on stem cells is neurology. Dr. Cesario Borlognan presents an overview of the potential applications of various types of stem cells in neurology. Moreover, recent evidence indicates that changes in trafficking of stem cells may also be involved in some psychiatric disorders, and this novel and exciting field is presented by Dr. Jerzy Samochowiec et al. Another important clinical area for stem cell therapies is dermatology, particularly in patients that are suffering from extensive skin burns. Dr. Justyna Drukala explores the involvement of local epidermal stem cells and mobilized stem cells circulating in peripheral blood.

An important clinical area for potential stem cell therapies is prematurely born neonates. In these youngest of patients, a potential source of stem cells is their own umbilical cord blood. This novel application of stem cells in neonatology is presented by Dr. Boguslaw Machalinski. In the past few years, it has been proposed that ovaries contain stem cells that are the precursors of oocytes. Dr. Deepa Bhartiya et al. examine the concept that ovarian surface epithelium contains a population of very small embryonic-like stem cells that are precursors of oocytes. Next, Dr. Dong-Myung Shin addresses the molecular mechanisms that explain the quiescent state of very small embryonic-like stem cells. Reversal of this state is an important issue in broadly applying these cells in the clinic. Dr. Giovanni Camusi and Dr. Peter Quesenberry discuss the potential role of membrane-derived microvesicles in cell-to-cell communication and their potential involvement in organ regeneration. Besides soluble factors, cell membrane-derived vesicles are responsible for several beneficial effects of stem cell therapies. The final chapter presented by Dr. Jerzy Kawiak et al. is focused on changes in the profile of circulating stem cells during systemic sepsis. The number and profile of the phenotypes of various types of stem cells that are mobilized into peripheral blood in this stress situation as well as a profile of some factors that affect their trafficking may be of novel prognostic value.

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