PREFACE

Stem cells can be considered the antithesis of aging and, indeed, stem cells are defined by their immortal self-renewing properties. The fertilized egg is the ultimate stem cell, being the predecessor of the hundreds of billions of cells that comprise the body. During very early embryonic development, individual cells in the blastocyst (embryonic stem cells) retain their ability to generate the entire body. At later times in development, multi-potent stem cells become more restricted and eventually each tissue harbors populations of progenitor cells that have the capability of forming mainly the cell types that comprise that specific tissue. For example, in the nervous system, neural progenitor cells give rise to glia and neurons, whereas in the bone marrow, stem cells give rise to the many different types of blood cells including lymphocytes and macrophages. The present volume of *Advances in Cell Aging and Gerontology* covers the cellular and molecular mechanisms regulating stem cell fate in relation to aging and age-related disease.

The book begins with a chapter by Thomas Smithgall, which describes the fundamental properties of embryonic stem cells with a focus on mechanisms regulating their self-renewal and differentiation capabilities. It is human embryonic stem cells that are the subject of current controversy from the standpoint of the ethics of using these cells to generate new organs and to treat various diseases. It is already becoming clear that embryonic stem cells have considerable potential for replacing dysfunctional or dead cells in an array of age-related diseases including diabetes, cardiovascular disease and neurodegenerative disorders.

The next three chapters focus on bone marrow stem cells. Gary Van Zant and colleagues discuss intriguing findings suggesting that there is genetic control on the self-renewing capability of bone marrow, and that there is a relationship between lifespan of the species and the functional capabilities of hematopoietic stem cells. Amelia Globerson discusses the role of hematopoietic stem cells in the aging thymus. It has long been known that the size of the thymus progressively decreases with aging, and an understanding of the stem cell populations that have the potential to re-populate the thymus is of considerable interest in understanding immunological decline during aging. Karen Chandross and Eva Mezey discuss the exciting findings concerning the possibility that progenitor cells in one tissue in the adult are capable of forming cells of other tissue types when placed in the proper environment. They focus on the plasticity of adult bone marrow stem cells and the signaling mechanisms that regulate their differentiation into either blood cells or cells of other tissue such as the brain.

Two chapters discuss aging and neural stem cells. It is now clear that the adult brain contains populations of stem cells capable of dividing and differentiating into neurons, astrocytes and oligodendrocytes. An increasing knowledge of the molecular regulation of these neural stem cells is leading to an understanding of their role in adult brain plasticity, for example, in learning and memory. In addition, pre-clinical studies and in some cases clinical studies are in progress to establish whether transplantation of embryonic or neural stem cells into patients with disorders such as Parkinson's disease

and stroke can be effective in restoring brain function. Jingli Cai and Mahendra Rao discuss molecular and cellular mechanisms regulating neural stem cell fate, and my colleagues and I discuss neural stem cells in the context of neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease and Huntington's disease.

Ken Boheler and Anna Wobus present a chapter describing exciting findings on the role of stem cells in myocardial development and aging. There have rapid advances in understanding of the regulation of heart development and in developing stem cell-based therapies for repairing damaged heart tissue and promoting re-growth of blood vessels. Adult skeletal muscle contains populations of stem cells that likely play a major role in regeneration of damaged muscle. Patrick Seale and Michael Rudnicki discuss basic aspects of the cell and molecular biology of skeletal muscle regeneration, and exciting findings suggesting that myogenic stem cells also have the potential to differentiate into other cell types and can even reconstitute the hematopoietic system when administered intravenously. These findings further emphasize the plasticity of stem cells in the adult. In the final chapter, Robert Jilka and Michael Parfitt provide an overview of the role of stem cells in bone formation and remodeling in the adult. A decline in bone strength is a major problem among the elderly and an understanding of how stem cells contribute to bone development may provide new avenues for the prevention and treatment of bone disorders of aging.

Collectively the chapters in this book provide the reader with a concise, yet comprehensive, view of stem cell, molecular and cellular biology in the context of aging and age-related disease. It is hoped that this cross-disciplinary approach will foster new research that will lead to a better understanding of the role of alterations in stem cells during aging and in age-related disease, and to the development of novel approaches for manipulating stem cells in ways that promote successful aging and a longer healthspan.