
Preface

As the world population ages, health care costs are expected to escalate as a result of the increase in age-related, degenerative diseases. Regenerating the failing cells and organs associated with these diseases would preserve quality of life and help curtail the increase in health care costs. Medical scientists today are faced with the challenge of developing new and innovative regenerative therapies to meet this need. A major focus of this research is to identify sources of cells and tissues that can be used in regenerative therapies. Stem cells, by definition, can self-replicate and, under the right conditions, differentiate into mature cell phenotypes. Stem cells are a potential source of cells for regenerative medical therapies, and research on defined stem cell populations will facilitate the study of organ development *ex vivo*. Understanding stem cell growth and development will shed light on the biological process of tissue/organ development and likely lead to novel regenerative therapies.

Although all stem cells have a limited capacity for self-replication and differentiation, some stem cells are capable of differentiating into multiple cell types, a property known as plasticity. Embryonic stem (ES) cells are derived from the early blastocyst and contain stem cells capable of generating all adult tissues. This makes ES cells the most pluripotent, or plastic, of the available stem cells. Recently, ES cell lines were derived from animal and human blastocysts. These cell lines are capable of self-replication and can be expanded in culture to provide a renewable source of cells. Human ES cell lines are an invaluable research tool for the study of human development *in vitro*. In addition, human ES cells have the potential for direct use in therapies; thus, these cell lines represent a major advance in cell biology that will have a broad impact on subsequent medical research.

The study of stem cell biology is likely to have profound effects for the near future, affecting the current equilibrium in medical research. The evolution of science and medicine is punctuated by events that are clearly so significant that they alter the future course of scientific and medical discovery. The derivation of human ES cell lines, in my mind, is clearly such an event. Human ES cell lines, along with other stem cell lines, will have broad and long-lasting effects on developmental biology and translational research. However, the fundamental importance of ES cell lines does not necessarily imply that ES cells will become

the cell source for regenerative medicine. The appropriate stem cells will need to be evaluated for each disease system that may benefit from regenerative therapy.

Many disease processes stand to benefit from regenerative medical therapies, including disorders of the central nervous system, cardiovascular, gastrointestinal, and hematologic systems. Currently, some of these disorders can be treated using whole organ transplantation. However, whole organ transplantation is limited to a small percent of patients because of the scarcity of organs for donation and the need for broad spectrum immunosuppressive therapies. As opposed to other systems, degenerative disorders of the endocrine system can currently be treated using exogenous hormonal therapies. These therapies, however, are frequently inadequate, resulting in significant morbidity and mortality to patients. The difficulty in treating endocrine disorders is developing a therapy that mimics the natural feedback mechanisms inherent to functional endocrine organs. Most current exogenous endocrine therapies fail to mimic the precise metabolic control of endogenous hormone release, resulting in under- or overtreatment and thereby leading to complications. This is clearly illustrated by the persistent complications of diabetes in patients on exogenous insulin therapy. Replacing endocrine organ function with functionally responsive cells will allow for the precise regulation of hormone release through natural feedback and should dramatically improve medical care. The recent success of islet transplantation indicates the potential for cell therapies to improve medical care for patients with diabetes. Again, the major drawback is the lack of tissue available for these procedures. The shortage of islets and other endocrine tissues could be overcome by developing alternative tissue sources such as the use of stem cells. Endocrine diseases, in particular diabetes, are therefore prime targets for stem cell therapeutics.

The objective of this text is to provide a primary source of information on basic stem cell biology and the application of stem cell research to endocrine diseases. As such, this book should be useful for both clinical endocrinologists and endocrine researchers alike. The information in this book is divided into two main sections: first, a basic stem cell biology section and second, translational stem cell research with endocrine applications. In the basic science section, each of the major sources of stem cells are discussed, including embryonic, cord blood, germ line, and adult stem cells tissues. Because it is not clear which stem cell types will eventually be used for endocrine therapies discussing all stem cells allows a side-by-side comparison of the different stem cell types and a full understanding of the pros and cons of each. The second section explores how stem cells may be employed to develop endocrine-related cells or tissues. This includes discussions on directed differentiation using transgenes and development of endocrine-specific phenotypes including β -cells, hepatocytes, bone, and sperm. Because

many endocrine disorders are autoimmune mediated, we also include a discussion of stem cell therapy for the treatment of autoimmune disorders. In the future, stem cell therapies for thyroid and other endocrine disorders may be available, but these areas are not discussed given the limited amount of research currently available.

In closing, I would like to thank all the contributing authors for taking time from their research efforts to share their thoughts and ideas in this book. Their collective expertise provides an excellent starting point for the endocrine researcher, illuminating the complexity and potential of stem cell research in endocrinology. I also want to thank Drs. Laura Andrews and Brian Nauert for their thoughts, editorial comments, and efforts in my research lab while I was working on this project. Finally, I would like to thank Dr. Lynn Loriaux for his ongoing support of stem cell research at Oregon Health and Sciences University and my family, for enduring cold dinners and late nights with few complaints. I could not flourish without their support and encouragement. My accomplishments are clearly a reflection of all those around me.

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