Preface

Stem cells, characterized by the ability to both self-renew and to generate differentiated functional cell types, have been derived from the embryo and from various sources of the postnatal animals and human. The recent advances in stem cell research have led to a better understanding of self-renewal, maintenance, and differentiation of both embryonic and somatic stem cells. This has significantly increased our knowledge of cellular and developmental biology in general and will certainly continue to do so for a long time to come. Moreover, given their role in maintaining and replenishing tissues, stem cells represent a potential means of restoring tissue function and thereby treating the root cause of degenerative disease. Therefore, in parallel, we need to improve our cognizance of the challenges involved in applying stem cells in clinical settings. The current chapters highlight both of these aspects: that of understanding the “actual” and that of developing the “possible.”

In recognition of the growing excitement and potential of stem cells as models for both the advancement of basic science and future clinical applications, I felt it timely to edit this book in which forefront investigators would provide new findings for the use of stem cells to study various lineages and tissue types and some applications. We are pleased to provide *Trends in Stem Cell Biology and Technology*, a broad-scaled series of cutting-edge chapters that have already been shown to have, or will soon have, tremendous utility with stem cells and their differentiated progeny. The authors have put together recent advances and perspectives in important fields of stem cell research: embryonic stem (ES) cells, somatic stem cells, and stem cell therapy, which deal with embryonic and somatic stem cells and their potential therapeutic applications.

Embryonic stem cells are pluripotent cells with the capacity to give rise to every somatic cell type. The nature, characteristics, and potentials of human ES cells are described in the article by Bongso and Fong. In addition, Eckardt and McLaughlin describe the generation of ES cells from gamete-derived uniparental embryos, which can be patient-derived and potentially histocompatible with the gamete donor. They also address evaluation of the integrity of the lines generated, an essential criterion in interpreting differentiation assays in vivo and in vitro. Also, Ragina and Cibelli explain the derivation of parthenogenetic embryonic stem (PGES) cells from the inner cell mass of parthenogenetic embryo at the blastocyst stage. These pluripotent stem cells offer an easily obtainable pool of stem cells that can be used as a source for derivation of autologous tissues, albeit limited to females in reproductive age. PGES cells' derivation does not require destruction of a viable embryo and therefore bypasses the ethical debates surrounding the use of naturally fertilized embryos. Moreover, Zuccotti and coworkers summarize the advancement in nuclear reprogramming and in cell reprogramming by cell fusion, using amphibian eggs or egg extracts, with cell extracts, with synthetic molecules, or by induced expression of specific genes and production of induced pluripotent stem cells. In contrast, Mardanpour et al. describe general considerations regarding molecular and cellular aspects of reprogramming of germ cells at different developmental stages to stem cells compared with their counterpart, ES cells. Moreover, epigenetic modifications, such as covalent modifications of histones and DNA methylation, are extremely important control mechanisms for self-renewal, cell fate, and cloning which describe by Andollo et al. and Balbach et al. Production of genetically manipulated mice by genetic manipulation of mouse ES cells is one of the premier tools for the study of genetic diseases. Matthaei describes his methods to produce these animals that have proven to be highly reliable as well as give exceptionally high rates of germline transmission with all strains of ES cells that he has used. Moreover, in just the past few years amazing progress has been made in germ cells differentiation from stem cells in vitro, which is review by Marqués-Mari et al.

Several chapters summarize the current state of knowledge in the somatic stem cell field. De Rooij reviews recent developments in the field of spermatogonial stem cells (SSCs). These cells are important for male fertility and recently it has been shown that at least mouse SSC are able to transform into multipotent stem cells capable of differentiation into various other cell lineages. Moreover, Olive and coworkers describe recent experimental results, including data from their laboratory, regarding gene expression profile of the SSC population. The chapter focuses on both up- and down-regulated protein coding transcripts and several differentially expressed microRNAs, which are increasingly being implicated in stem cell functions, such as pluripotency. In their article, Abdallah et al. describe mesenchymal stem cells, which occur in bone marrow stroma and in the stroma of diverse organs. They can give rise to, for example, osteoblasts, adipocytes, and chondrocytes and are currently being introduced into the clinic for the treatment of a variety of diseases.

Stem cells and their application in therapeutic replacement strategies are described in six articles focusing on heart failure, deafness, diabetes, and corneal injury. Stamm and coworkers summarize the basic research background of cardiac regenerative medicine and give a critical appraisal of the current efforts to translate the experimental approaches into the clinical setting. Moreover, Saric et al. critically review the current literature on use of fully undifferentiated ES cells for cardiac repair, elaborate on the tumorigenic risk of ES cells and pluripotent cells in general, and summarize strategies for elimination of this threat as an important step toward translation of ES cell–based therapies to clinic. This discussion is also highly relevant for clinical applicability of newly developed autologous ES cell–like stem cells, so-called induced pluripotent stem (iPS) cells, which circumvent ethical and, to some extent, immunological concerns linked to the use of blastocyst-derived ES cells, but still possess high tumorigenic potential. Trachoo and Rivolta review several protocols used to generate neural precursors from human ES cells, including initial attempts to establish otic placodal precursors. They discuss their potential application in the development of a new therapy for deafness.

Franceschini and coworkers describe recent experimental results, including data from their laboratory, regarding the first evidence that transplanted stem cell that migrate to the neurolfactory mucosa may contribute to neuroepithelium structure restoration with resumption of the sensorineural olfactory loss. Moreover, diabetes is a degenerative pathology that has different causes. Roche et al. summarize the key work that has been performed in the bioengineering of both ES cells and adult stem cells toward insulin-secreting cells to treat diabetes. The adult corneal epithelium is continuously regenerated from stem cells under both normal conditions as well as following injury and is located at the basal layer of the corneoscleral limbus. These stem cells simultaneously retain their capacity for self-renewal and maintain a constant cell number by giving rise to fast-dividing progenitor cells. Kolli and coworkers discuss corneal epithelial anatomy, corneal epithelial stem cell biology, and the application of this biology in the field of regenerative medicine.

Moreover, in an interesting review, Hosseinkhani and Hosseinkhani review the application of scaffolding materials together with stem cell technologies for applications in tissue regeneration. Conventional in vitro models to study differentiation of stem cells are freshly isolated cells grown in two-dimensional cultures. Clinical trails using in vitro stem cell culture can be expected only when the differentiated stem cells mimic the tissue regeneration in vivo. Therefore, the design of an in vitro three-dimensional model of biodegradable scaffolds that mimics the in vivo environment is needed to effectively study its application for regenerative medicine. Tissue engineered scaffolds have a significant effect on stem cells proliferation and differentiation. Moreover, Wolf and Mofrad describe the significance of processes that convert mechanical signals into a cascade of biochemical signals that affect the phenotype of stem cells, a process called cellular mechanotransduction. Mechanotransduction, in combination with other experimental techniques, may provide new insights into the operations that occur at the cellular level. Understanding cellular mechanotransduction can also prove useful in understanding the overall effect on biological systems resulting from a change in just a few small variables. To elucidate the particular roles that stem cells play in healing during the adult stages, a role for stem cells that is still poorly understood as compared to what is known about them in an embryonic environment, experimental approaches must combine both mechanical and biochemical observations.

Collectively, these chapters should prove a useful resource not only to those who are using or wish to use stem cells to study specific applications, but also to those interested in stem cell biology advances. We hope this book will also serve as a catalyst to spur others to use stem cells for both the fundamental understanding of stem cells and their potential utility.

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Finally, I hope that the book will achieve the intent that I had originally imagined: that it will prove to be a book with something for both experts and novices alike, and that it will serve as a launching point for further developments in stem cells.

Hossein Baharvand Ph.D
Department of Stem Cells
Royan institute
and
Department of Developmental Biology
University of Science and Culture
Tehran, Iran

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