Patients suffering from a wide variety of diseases may benefit from cell-based therapies. Transplantation of nonimmunogenic cells may be able to functionally repair or replace damaged tissue or missing cells with important roles. However, currently available cell-based therapies are limited in scope and have almost exclusively relied on autologous and allogenic sources of transplantable cells. Further prohibiting their widespread use, donor-limited cells can be difficult to obtain, have inadequate expansion capabilities, and may result in graft-versus-host disease. Due to their inexhaustible capability to expand and wide-ranging differentiation potential, human embryonic stem cells (hESCs) and the less ethically controversial induced pluripotent stem cells (iPSCs) hold great promise in serving as alternative cell sources for regenerative medicine and may offer many advantages over currently available cell-based therapies. They may help treat diseases such as atherosclerosis, diabetes, stroke, liver, kidney disease as well as a variety of hematologic and neurologic disorders. This special issue focuses on the promise and therapeutic potential of hESC/iPSCs in a wide variety of diseases. It highlights important advances as well as common problems that must be resolved before the therapeutic potential of hESC/iPSCs becomes clinical reality.

One of the biggest safety considerations hindering clinical application of hESC- and iPSC-based products is the risk of tumor formation. Pluripotent cells like hESCs and iPSCs harbor an intrinsic ability to divide and self-renew without undergoing senescence. Many hESC-/iPSC-based therapies are based on derivatives of the cells that are no longer pluripotent, yet the risk of a surviving pluripotent cell possibly contaminating the therapeutic cell preparation is a major safety issue. Inefficient differentiation and incomplete maturation top the list of hurdles that need to be overcome in order to bring hESC-based therapies to the clinic. As many articles in this special issue illustrate, directing the in vitro differentiation of hESCs into therapeutically useful cell types is a complex and often difficult process. From altering cytokine cocktails and media formulations to using scaffolds and 3-dimensional matrices, researchers have applied many different strategies to increase the efficiency of producing the desired cell types from hESCs and iPSCs. Also hampering iPSC research, reprogramming efficiencies, and quality of the resulting iPSC lines vary greatly and need to be optimized before iPSCs can routinely be used to generate patient-specific therapeutic cells. While these issues are being resolved in cell culture labs, hESC-/iPSC-based therapies will also have to undergo rigorous preclinical testing in suitable animal models of disease. As the reader will discover in the ensuing articles, some hESC-/iPSC-based therapies are already being examined in animal models and showing signs of therapeutic utility.

Beginning with a review article on tissue engineering, the reader of this special issue will first learn about the use of hESCs to generate chondrocytes, osteocytes, and mesenchymal stromal cells for bone and vascular disease therapies. The next two articles review cell-based therapies to treat hematologic disorders and type 1 diabetes, respectively. The first paper describes how hESCs/iPSC derivatives may
be able to substitute for red blood cells, platelets, and various subpopulations of immune surveying white blood cells. The second article focuses on how hESC/iPSCs can be used to generate insulin-producing islet cells and may be able to functionally replace cells of a failing diabetic pancreas. Next, the reader will learn about cardiovascular disease, ischemia, and life-threatening damage to the heart muscle. Two back to back review articles focus on how hESCs and more specifically iPSCs can be used to generate cardiomyocytes and how these powerful cells can improve the function of a heart weakened by tissue damage. Highlighting the far-reaching application of hESC-/iPSC-based therapies, the next two articles move away from the heart and into the brain. The first article introduces the reader to a broad range of neurologic disorders including those with degenerative, developmental, genetic, or metabolic roots. It describes how patient-specific iPSCs can be used in disease models and help develop new therapies. The second paper is a primary research article that examines the therapeutic utility of hESC-derived motor neuron progenitors in rodent models of spinal muscular atrophy, amyotrophic lateral sclerosis, and spinal cord injury. Capping off the broad therapeutic topics covered in this special issue, the eighth and final paper is a primary research article that brings us back to hESCs themselves and their initial derivation. Ethical considerations surrounding the destruction of human embryos provided not only the impetus for the development of iPSCs but also, as this final paper discusses, new derivation methods that avoid the destruction of viable human embryos. From the diverse collection of papers in this special issue, the reader should gain a better understanding of why proponents of hESC/iPSC research lobby so hard for continued research and development. In the face of rising health care costs and widespread clinical need, hESCs and/or iPSCs may one day provide a cost-effective means for large-scale production of therapeutic cells and revolutionize the field of regenerative medicine.

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