Preface

The stem cell field has captured the imagination of the therapeutic community. Stem cells are defined as those cells that can give rise to a vast array of cell types ("pluripotency") as well as to other stem cells ("self-renewal"). The most primordial stem cell is that obtained from the inner cell mass of the blastocyst; these are termed "embryonic stem cells" and can theoretically give rise to all of the cells of the developing organism. By a series of developmental steps, these embryonic stem cells are presumed to give rise to cells with similar stem-like qualities, but that come to populate the various emerging organs of the embryo and fetus. These cells, termed "tissue-resident" or "tissue-derived stem cells, retain stem-like features, but somehow have "learned" their address within the body. They are postulated to exist not only in the embryo and fetus where they participate in specific organogenesis, but to persist into adulthood, possibly to maintain homeostasis or to mediate self-repair or regenerative processes. The tissue-resident stem cell that has been most extensively explored is the hematopoietic stem cell. It made sense that such a cell should exist because cells of the blood are constantly turning over. That stem cells could similarly reside in solid organs, however, was a revelation. Stem cells from the nervous system, neural stem cells (NSCs), were the first solid organ stem cell identified, isolated, expanded and grown in culture, characterized, transplanted, and employed in animal models. First "unveiled" by developmental biologists, the NSC has come to capture the imagination of the neuroregeneration community. Furthermore, because it was the first solid organ stem cell employed, and because there has grown such a rich knowledge of its behavior and therapeutic potential over the past 15 years, the NSC has come to serve as a prototype for understanding and exploiting stem cell biology within most other solid organs throughout the body. Because it was also the first solid organ stem cell to be abstracted from human material, it has shown the therapeutic community what potential might exist. Therefore, a book such as this will hold interest for all readers interested in the biology and therapeutic promise of the stem cell. Though the field is moving quickly, much work still needs to be done.

In the last few years, rapidly advancing NSC research has been providing encouraging evidence that such cells can serve as novel tools for repairing/restoring central nervous system anatomy and perhaps function damaged by acquired (e.g., from trauma) and neurodegenerative (e.g., genetically based) disorders. Scientists are exploring differences between different sources of embryonic, fetal, and adult stem cells and trying to understand their fundamental biological properties and functional characteristics that may determine the appropriateness of various cell sources for specific clinical applications. At present there has been a considerable amount of data gathered on multipotential NSCs as a source of transplantable progenitors for CNS repair. Their fundamental properties, such as proliferation and differentiation under specific culture conditions, have been described in a variety of mammalian species including humans. Their ability to join developmental programs within the recipient's brain as well as to participate in restoring missing enzymes or genetic information, or simply replacing lost/damaged cells in the diseased or injured brain, has become obvious. Here we have tried to outline the most important basic issues of NSC research with a primary focus on the translational aspects of the NSC field. Because the utilization of human embryonic and/or fetal tissue, though the "gold standard" for stem cell efficacy and safety, is alloyed with ethical and logistical considerations, researchers have begun the search for alternative yet equivalent sources of stem cells. The jury is still out as to whether they exist for the nervous system. (For example, it remains unclear whether stem cells derived from one tissue can "change addresses" and commitments to take on the identity of another.)

The promising area of stem cell research as it applies to nervous system dysfunction is still in its infancy and it may be quite premature to predict when it will generate cell therapies for patients.

Neural Stem Cells for Brain and Spinal Cord Repair is divided into three main sections. The first section "Stem Cells for and from the CNS: fundamental properties" summarizes potential sources of stem cells and their prospective advantages in cellular transplantation therapies, as well as their enormous plasticity to generate diverse cell types inside and outside of the original germ layer.

The second section: "In vitro and/or in vivo Manipulations of Stem/Progenitor Cells for the CNS" contains chapters illustrating the signaling pathways that regulate stem cell division and differentiation. Further chapters define methods of NSC expansion and propagation, neuromorphogenesis, factors determining cell fate both in vitro and *in situ*, and the induction of self-reparative processes within the brain.

While in the first two parts, the reader is given a detailed view of the fundamental biology of stem cells in the CNS; the third section, "Stem/progenitor Cells in Representative Therapeutic Paradigms for the CNS" gives the reader material on strategies that may lead to fruitful clinical therapeutic applications in the near future. It is intriguing to recognize that the same stem cell may play a therapeutic role by a number of mechanisms, at times simultaneously. These may include replacement of degenerated, dysfunctional, or maldeveloped cells, as well as the provision of factors (either produced intrinsically by the cells or induced to do so following genetic engineering) that may protect, correct, recruit, promote self-repair in, or mediate connectivity of host cells.

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