Foreword

Almost everything we know about cell transplantation dates to the end of World War II. It was found that mice could be protected against otherwise lethal irradiation by an injection of spleen or marrow cells. At first it was hypothesized that the protection was caused by a humerol factor in the spleen or marrow preparations. That the protection might be caused by living cells seemed to be ruled out by several experiments. However, cytogenetic and skin transplant studies made it clear that the cellular hypothesis rather than the humoral hypothesis was the explanation for the irradiation protection phenomenon.

The early investigators recognised that there must be some kind of seed cell or cells in the spleen or marrow preparations that generated the repopulated marrow. These cells came to be called stem cells, but the search for the elusive stem cell became a long and complicated one. There followed thousands of experiments in inbred mice that clarified the requirements for successful cell transplants and described the immunological phenomena involved. The dog became a model for bridging the gap of knowledge between inbred mice and outbred species. As is often the case, physicians were driven to attempt to alleviate human disease by the application of knowledge gained from studies of animal systems. Application of this knowledge to human marrow transplantation began to produce results in patients with fatal disorders such as immunodeficiency disease, leukemia, and aplastic anemia. By the end of the twentieth century, transplantation of hematopoietic cells from marrow, blood, or cord blood had taken its place in the therapeutic armamentarium against an ever-increasing number of diseases.

As work continued, stem cells were isolated and characterized. Despite many studies, the expansion of human stem cells by *in vitro* culture proved to be difficult. Gene therapy of human stem cells remained an attractive but elusive goal. It had long been assumed that hematopoietic stem cells would produce only hematopoietic cells, but intriguing data began to suggest that marrow stem cells might generate other tissues such as a liver, a heart, or even a central nervous system. These and other tissues and organs seemed to have their own stem cells, and these stem cells might not be lineage specific. The plasticity of stem cells, or transdifferentiation, became a major subject of study. Techniques for obtaining stem cells form embryonic tissues were developed and seemed to offer even greater utility. Application of these stem cells to a variety of otherwise incurable human diseases became a possibility.

Thus, at the beginning of the twenty-first century, the stage was set for this work, *Handbook of Stem Cells*. This two-volume book is a much-needed attempt to bring together the cumulative work of many investigators in widely diverse aspects of stem cell studies. Clearly, this field is a work in progress. Much more work will be needed to fulfill the exciting promise of stem cell research. This handbook provides essential information for those who undertake this challenge.

E. Donnall Thomas, (Hon)