

Preface

Adult/Postnatal stem cells provide for life-long cell replacement in tissues and organs. They have an inherent ability for self-renewal and differentiation into multiple cell types that are characteristic of their tissue of origin, and have been identified in an increasing number of tissues/organs even in brain and myocardium in which cell turnover was reputedly absent. In addition, many stem cells have inherent homing abilities that are instrumental in therapeutic applications. Stem cells are also the driving force of cancer, where genetic/epigenetic alterations culminate in uncontrolled self-renewal and tumorigenesis either in tissue stem cells or in some of their progenitor/differentiated derivatives. As a rare subset of the tumor, cancer stem cells are the only drive of tumor initiation/propagation and, upon transplantation, have been shown to recapitulate the hierarchical clonogenic differentiating/differentiated organization of the original tumor cell population. Stem cells are thus the key targets of 1) long-term gene therapy and broad/synergistic transient regenerative/epigenetic gene therapy for both inherited diseases and acquired/aging disorders on their autologous side, and 2) effective anti-cancer therapy on their dark side.

Autologous stem cells have been instrumental in the first unequivocal successes for gene therapy (2000–2004), whereby *ex vivo* retrovirally corrected hematopoietic stem cells have been returned to the patients. Such a stem cell gene therapy achievement that relies on random integration of therapeutic transgenes into host chromosomes is presented together with emerging experimental approaches aimed at eliminating random integration oncogenic hazards through site-specific integration or gene targeting. Breakthrough endonuclease-boosted gene targeting for gene correction (inherited diseases) or targeted integration of therapeutic transgene (other pathologies), culminating in an efficiency compatible with clinical correction of a disease gene, is one of the highlights of the book. Other highlights include the pioneering transplantation of adult pluripotent stem cells as a substitute for tissue-specific stem cells, thereby pinpointing the breakthrough potential of such autologous cells able to contribute to all three germ

layers both for multi-systemic diseases and for the development of a universal stem cell gene therapy platform. The autologous side is thus discussed in terms of magnifying stem cell therapeutic homing/regenerative capabilities through transient regenerative gene therapy, and in terms of tackling most pathologies (including mitochondrial DNA diseases and aging disorders) through stem cell repopulation dynamics into appropriate niches (long-term engraftment) and tissues (cell turnover). Regarding the dark side, focus is on both the increasing number of identified tissue-specific cancer stem cells as the ultimate targets for recurrence-free cancer therapy and on the development of armed stem cells as tumor-homing vectors for targeted anti-cancer stem cell gene therapy.

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