

Preface

In the last few decades, stem cell research has developed groundbreaking technologies to both study and treat diseases. This research has proven fruitful for the field of ophthalmology, especially in recent years. With its relative immune privilege, the eye has proven an ideal testing ground for stem cell therapies.

This book describes just a few of these developing treatments. The authors of this book describe a wide range of possible applications, from oculofacial plastic surgery to the restoration of sight lost by degenerative disorders and glaucoma, to cancer research. Indeed, stem cell research seems to have reached a critical mass in ophthalmology. As recently as 2011, the FDA approved trials for stem cell-based treatments for macular degeneration; other clinical trials may follow, as discussed in the last chapter of this book.

These changes have not happened overnight. From a scientific standpoint, several discoveries have made stem cells a viable treatment source for humans. In 1981, when embryonic stem cells were first synthesized in the laboratory, it became possible to imagine generating graft tissues or animal models to test drugs from stem cells. Fifteen years later, the Yamanaka research group discovered that mouse skin samples could be reprogrammed through gene therapy into induced pluripotent cells. Both ES and iPS cells are pluripotent, or reprogrammable. Moreover, iPS cells are autologous, meaning they are derived from the subject's own tissue. By modifying cell culture media or performing gene therapy, researchers have been able to generate many types of tissues using ES cells and iPS cells.

Autologous tissues can also be generated using the progenitor cells which exist naturally inside the body. Unlike pluripotent stem cells, progenitor cells can differentiate into a limited number of tissues. These "local" cells can be adapted to replace and repair diseased tissue. Promising progenitor cells include: adipose tissue stem cells, ciliary stem cells, mesenchymal stem cells, corneal stem cells, and lens stem cells.

A significant area of stem cells research has been the retinal degenerative disorders. These conditions all involve degeneration of the retinal pigment epithelium, a tissue that sustains living photoreceptors. Researchers have hoped to restore this tissue with differentiated stem cells. To date, several studies have found visual

rescue in mice treated with stem cell-derived RPE and photoreceptors. Intricate new surgical techniques have had to be developed to perform these transplant procedures.

Transplant surgeries can be used to replace many kinds of damaged tissue. Recently, adipose tissue-derived stem cells have attracted interest as source of tissue for oculo-facial surgeries such as facial reconstruction, wound healing, and skin rejuvenation. The ease of gathering these autologous stem cells makes them particularly advantageous for plastic surgeries.

Stem cell-derived tissues such as lens and corneal tissue may be suitable for transplant. Media outlets have already begun reporting on the potential that severe corneal epithelial diseases may be treatable with corneal stem cells. Successful efforts have also been made to generate lens progenitor cells and lentoid bodies from ES stem cells.

Research on mesenchymal (or, marrow) stem cells may allow treating vascular disorders of the eye. Recent findings suggest that these can be transplanted into the eye to improve angiogenesis. Bone marrow cells may have potential for treating ischemic retinal diseases, and perhaps even some non-ischemic retinal diseases.

The treatment of glaucoma may involve special challenges. It has recently been discovered that transplantation of stem cells into the retina can potentially replace damaged neurons, or provide neurotrophic factors to surviving neurons. These may be useful for treating glaucoma, providing that neurons are able to integrate. A number of signaling and transcription factors are currently being studied to this end.

Gene therapy has continued to evolve alongside stem cell therapy. New gene therapy techniques using gene addition, or enhancing gene replacement, have improved the efficiency of directly treating disease-causing genes. These gene therapy methods minimize the risk of mutagenesis and may be used along with stem cells to replace diseased patient cells with new disease-free cells.

Finally, stem cell research has improved our understanding of the pathogenesis of eye diseases. The mechanisms leading to various types of cancer are still unknown. This book contains a discussion of the evidence that cancer stem cells can lead to uveal melanoma.

Stem cell research never stops changing and growing. There may come a time when the research discoveries of today alter the landscape of ophthalmologic practice. The last chapter of this book describes the types of safety trials that may be used to assess stem cell-based treatments' viability. In the meantime, these cells of great potential continue to offer challenges to researchers and hope to patients with serious eye pathologies.



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