The human brain’s ability to sense and interpret acoustic events taking place in remote or nearby locations in the external environment is mediated by highly specialized and extremely sensitive sensory hair cells located in the inner ear. These cells transduce acoustic information from the environment into a pattern of neural activity that can be interpreted by sophisticated neural networks located at multiple levels of the central nervous system. It has long been known that hair cell loss in mammals due to aging, ototoxic drugs, acoustic trauma, infection, or genetic factors results in permanent hearing loss or balance problems. Over the past 50 years, efforts to find a cure for deafness have focused on hardware and engineering solutions. While much effort has been made to use electronic means to improve hearing, the next giant step toward restoring hearing to the profoundly deaf will involve regenerating the damaged biological structures in the inner ear, in particular the hair cells and spiral ganglion neurons. The major clinical advances in hearing and balance that will occur in the 21st century will involve biologically based medical innovations that were set into motion during the past few decades by the discovery of hair cell regeneration and by the recognition that stem cells exist in many regions of the nervous system, including the inner ear.

These discoveries, and the potential for helping people with hearing loss, are the focus of this volume. In Chapter 1, Salvi reviews the history of studies on hair cell regeneration and provides an overview of current knowledge as well as new technologies to promote regeneration and repair. The recognition that hair cell regeneration can occur in nonmammals gave way to ground breaking studies using gene therapy to simulate hair cell regeneration in mammals. The history of the field, as well as what is known about the morphology associated with regeneration and repair of sensory hair cells, are the focus of Chapter 2 by Meyers and Corwin. One of the fundamental issues examined is whether regenerated hairs arise from repair of damaged cells, conversion of support cells to hair cells, or proliferation of support cells that differentiate to either hair cells or replacement support cells.

One of the most important areas that stimulated studies of damage, regeneration, and repair has been in the avian auditory system. In Chapter 3, Salvi and Saunders describe the remarkable recovery of function of the avian auditory system following acoustic trauma and ototoxic insult. Physiological studies show significant recovery, with only minor deficits except for cases in which the
supporting cells are destroyed. In Chapter 4, Dooling, Dent, Lauer, and Ryals go into considerable detail about actual recovery of hearing function following loss of hair cells. Behavioral measures of hearing, the gold standard, show almost complete recovery of function on simple measures such as threshold as well as highly sophisticated measures that involve discrimination of complex vocalizations.

The mechanisms involved in proliferation, differentiation, and regeneration are discussed in detail by Oesterle and Stone in Chapter 5. The roles that growth factor, intercellular signaling, intracellular signaling and differentiation factors play in proliferation, conversion, and repair are carefully considered. In Chapter 6, Forge and Van De Water consider ways to protect sensory hair cells from damage so that regeneration is not needed. The modes of cell death are reviewed and various strategies for blocking cell death such as antioxidants, inhibition of apoptosis, and small molecules that block genes or enzymes in the cell death pathway are considered. Finally, in Chapter 7, Rivolta and Holley discuss new experimental approaches that may aid in understanding cell death, cell repair, proliferation, and differentiation. The use of gene array technologies and inner ear cell lines may provide more efficient and comprehensive methods for understanding apoptosis, repair, and regeneration.

As is often the case, new volumes in the Springer Handbook of Auditory Research amplify and extend materials discussed in earlier volumes in the series. While the current volume concerns regeneration and repair, engineering methods have been quite successful in dealing with deafness. In particular, cochlear implants have been a widely used approach and this was covered in depth in Vol. 20 of the series, Cochlear Implants (edited by Zeng, Popper, and Fay). The genetics of the ear and of hearing loss was discussed in detail in Vol. 14, Genetics and Auditory Disorders (edited by Keats, Popper, and Fay). While the current volume focuses on hair cells, Vol. 23, Plasticity of the Auditory System (edited by Parks, Rubel, Fay, and Popper), includes chapters that consider overall plasticity at many levels of the auditory system. Mechanisms of damage to the auditory system is considered at length in in Vol. 31, Auditory Trauma, Protection, and Repair (edited by Schacht, Popper, and Fay). Finally, the physiology and function of sensory hair cells is discussed in many chapters of Vol. 27, Vertebrate Hair Cells (edited by Eatock, Fay, and Popper).

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