Interactions Between Mechanosensory Hair Cells and Support Cells of the Zebrafish Lateral Line During Development, Death, and Regeneration: Is Taking Your Sox(es) Off a Key to Mechanosensory Hair Cell Regeneration?

Nicholas Coley, University of California, Davis

Half or more of individuals over age 60 years will experience some form of hearing impairment stemming from loss of mechanosensory hair cells of the inner ear cochlea. The zebrafish lateral line is a sensory organ along the midline of the fish that uses mechanosensory hair cells analogous to those of the cochlea to detect currents and predator/prey movements. Whereas loss of human cochlear hair cells is irreversible and results in deafness, zebrafish can continually regenerate lateral line hair cells from an underlying population of supporting cells representing a stem cell niche. Thus, studying the genetic similarities and differences between cochlear and lateral line hair cell development, death, and regeneration can potentially elucidate factors that facilitate lateral line hair cell regeneration and preclude cochlear regeneration. Here, we demonstrate divergence in regulation of two key hair cell development transcription factors, Atoh1 and Sox2, between the cochlea and lateral line that may underlie the zebrafish’s capacity to regenerate hair cells. In the cochlea, Sox2 acts upstream of Atoh1 in development to promote supporting cell fate, and later Sox2 inhibits Atoh1 expression. Conversely, Atoh1 prompts the adoption of cochlear hair cell identity. Through morpholino-mediated antisense decay and mutation analysis, we demonstrate that Sox2 expression requires Atoh1 gene function in lateral line development, differing from the cochlea. Also in contrast to the cochlea, we show that the regenerating lateral line transiently loses Sox2 expression in supporting cells concurrent with Atoh1 expression. After the death of cochlear hair cells, surviving supporting cells strongly and tonically express Sox2 and never express Atoh1. Thus, we postulate that the deafened cochlea’s inability to regenerate hair cells may stem from tonic Sox2 expression in supporting cells that inhibits Atoh1 expression and subsequent hair cell regeneration. Currently, we are using a heat shock-inducible Sox2-GFP transgenic line of zebrafish to test this hypothesis.

© American Society for Clinical Pathology

Am J Clin Pathol 2015;144:A017