Title
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Journal
Annals of the New York Academy of Sciences, 1170(1)

ISSN
0077-8923

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Publication Date
2009-07-01

DOI
10.1111/j.1749-6632.2009.04108.x

Symposium Overview

Stem Cells in Sensory Epithelium Development and Regeneration

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Many adult tissues are renewed throughout life via processes that are either known or thought to rely on a population of tissue-specific stem cells. For example, studies of both skin and brain have identified local stem cells that have complex interactions with their niche environment, leading to regulated cell genesis. The senses of both smell and taste are well known to be mediated by sensory epithelia that are also continually replaced, although the mechanisms that govern renewal are less well understood. In this symposium, we showcased some recent advances in development of the taste and olfactory periphery, with the hope of shedding light on potential mechanisms governing adult renewal of these sensory epithelia. These chemical senses presentations were bookended by talks pertaining to regeneration and maintenance of auditory and skin epithelia in adults. The purpose here was to highlight potential parallels in our understanding of molecular and cellular mechanisms regulating auditory hair cells and skin with cell renewal in chemosensory epithelia.

Neil Segil (House Ear Institute, Los Angeles) began with an overview of his work on the development and potential for regeneration of auditory hair cells. In vertebrates, hair cells of the inner ear are delicate mechanoreceptors that transduce pressure waves into electrical signals interpreted by the nervous system. In many species, including birds, amphibians, and fishes, these hair cells can be generated in the event of injury or to accommodate growth; however, mammals appear to have lost this regenerative capacity during evolution. Thus, the mechanisms that restrict regeneration in mammals are of great interest to both developmental neurobiologists and clinicians. One exciting idea explored by Dr. Segil is that under certain conditions mammalian auditory epithelium may be able to regenerate. Specifically, as is the case in birds, a population of mammalian auditory support cells, located adjacent to hair cells, may be able to reactivate the potential to give rise to new hair cells by altering levels of key cell cycle inhibitors and through alteration of signaling through the Notch pathway.

After this introduction to key concepts in sensory epithelium differentiation, Shoba Thirumangalathu (University of Colorado Denver, School of Medicine) discussed development of the taste epithelium, focusing on her studies to identify the embryonic cell population that gives rise to adult taste buds. She employed inducible and tissue-specific molecular genetic mouse models to label the developing tongue epithelium as the first taste structures—the taste placodes—form, and to follow these cells and their progeny through to adult stages. Although it has long been assumed that taste placodes represent taste papillae, which in turn

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International Symposium on Olfaction and Taste: Ann. N.Y. Acad. Sci. 1170: 5–6 (2009).
doi: 10.1111/j.1749-6632.2009.04108.x

give rise to taste buds within a subregion of each papilla, Dr. Thirumangalathu showed that in fact, taste placodes only contribute cells to taste buds, and not to the surrounding taste papilla.

Early development of taste buds and papillae in the lingual epithelium has recently been found to rely extensively on signaling through the Wnt pathway. While the cells responsive to Wnts have been identified through a reporter system, the specific Wnt ligand involved (from among 19 family members) has not been identified. Hong-Xiang Liu (University of Michigan, School of Dentistry) explored the role of Wnt5a in tongue and taste bud development via use of a mouse line in which this gene had been knocked out. Interestingly, while tongue development was dramatically reduced in the mutant, taste bud patterning was not affected, suggesting that other Wnt ligands need to be tested for their role in taste bud genesis.

The two talks dedicated to the taste periphery were followed by a pair of presentations on development of the olfactory system in mice. Shimako Kawauchi (University of California, Irvine) presented her findings pertaining to the molecular regulation of olfactory epithelium development. Her discussion focused on the impact of several secreted factors, growth and differentiation factor 11 (GDF11), follistatin (FST), and fibroblast growth factor 8 (FGF8), through interaction with a transcriptional regulator, FoxG1, on olfactory neuron progenitor specification and subsequent differentiation. Altogether, her talk concluded that tissue-specific intrinsic factors, such as the transcriptional regulator FoxG1, can act to modulate the effects of extrinsic signaling molecules in controlling morphogenesis and neurogenesis in the olfactory epithelium.

Diego Rodriguez-Gil (Yale University, School of Medicine) completed the discussion on the olfactory system with an exploration of the onset of olfactory receptor protein expression with respect to the developmental state of the olfactory receptor neurons (ORNs). Overall, he found that receptor-protein expression began in ORNs as early as embryonic day 11.5 in mice, and as late as postnatal day 0. Despite the broad range for expression onset, with respect to the small subset genes examined, a receptor was typically expressed 1 day before an ORN sprouts an axon, 2 days before the axon contacts its central target, the olfactory bulb, and roughly 4 days prior to the expression of proteins involved in the olfactory transduction cascade.

Finally, Dr. Maranke Koster (University of Colorado Denver, School of Medicine) provided an overview of her work on the development and maintenance of skin, and in particular, the complex role of the p63 transcription factor in these processes. p63 has several functions and numerous splice variants, which influence p63 activities, several of which have been explored by Dr. Koster. In mice engineered to lack p63, null embryos die at birth as the skin fails to initiate the stratification program, and thus these pups lack a barrier to the external environment and quickly desiccate. Interestingly, Dr. Koster showed that the lingual and palatal epithelia of $p63^{-/-}$ mice also lack stratification, and that the pattern of fungiform papillae appears to be disrupted. Thus, this presentation came full circle by implicating a key transcriptional regulator of skin development in the embryogenesis of the lingual taste epithelium.

Conflicts of Interest

The authors declare no conflicts of interest.