Chem. Senses 27: 567, 2002

Mechanisms of Differentiation and Migration of Olfactory Progenitors: An Overview

H. Baker and F.L. Margolis[1]

The Burke Medical Research Institute, White Plains, NY 10605 and [1]Department of Anatomy and Neurobiology, University of Maryland School of Medicine, Baltimore, MD 21201, USA

Correspondence to be sent to: Harriet Baker, The Burke Medical Reasearch Institute, An Affiliate of Weill Medical College, Cornell University, 785 Mamaroneck Avenue, White Plains, NY 10605, USA. e-mail: habaker@med.cornell.edu

A current focus of research in neurobiology is to define the mechanisms by which neurons reach their final destination and acquire their differentiated phenotype. An ideal model for these studies is the olfactory system, where nasal placodally derived gonadotropin-releasing hormone (GnRH) neurons, olfactory receptor neurons and interneurons of the olfactory bulb (OB) show unique migratory behaviors and phenotypic regulation.

Peripheral olfactory receptor cells and OB interneurons, both granule and periglomerular cells, are continuously generated even in adult animals, permitting the comparison of migratory and differentiation phenomena in developing and adult animals. Recent advances in defining the molecular mechanisms directing appropriate targeting and differentiation of both GnRH neurons and OB interneurons were the subject of a symposium at the 23rd annual AChemS meeting.

The following four reviews summarize presentations that addressed the intrinsic and extrinsic regulation of pathfinding, cell division and phenotype in migrating progenitor cells. Susan Wray posits that GnRH cells derive from an area of the nasal placode associated with the respiratory system—not, as previously assumed, with the region generating olfactory neuroepithial cells. She also presents data demonstrating a role for the recently identified factor, nasal embryonic luteinizing hormone-releasing hormone factor, in the derivation and migration of GnRH-expressing cells from the olfactory epithelium into the preoptic area and hypothalamus during early gestation. Stewart Anderson addresses issues related to the early derivation of cortical and OB interneurons, including granule and periglomerular cells. OB interneurons derive from the anterior subventricular zone (SVZa) and migrate through the rostral migratory stream (RMS) to populate the granule and glomerular cell layers. Genes required for neuronal fate determination of bulbar and cortical interneuron precursors are identified. Data are also presented to support the hypothesis that early telencephalic dorsal/ventral expression of the signaling molecules, bone morphogenic proteins (BMPs), retinoids and sonic hedgehog pattern the expression of transcription factors that determine neurotransmitter phenotype in the cortex and OB. Aldo Fasolo describes glia- and neuron-associated molecules in the RMS required for directed migration of cells into the OB. Data presented from different species suggest that during early postnatal development glial tubes are not required for appropriate migration of progenitors through the RMS. The authors conclude that glia in the RMS may be implicated in the compartmentalization of a microenvironment necessary for persistent neurogenesis and migration in adults. Molecules regulating the dynamics of stem cell proliferation and diffentiation in the SVZa and in the RMS are the focus of the contribution by Marla Luskin. Specifically discussed is the role of BMP signaling in regulating the cell cycle inhibitor $p19^{INK4d}$. The latter is expressed at highest levels in regions where proliferation is low—specifically, in the ventricular ependymal zone, in more anterior aspects of the RMS and in the OB. In sum, the data described in these reviews address current concepts on a broad range of issues related to olfactory system development.

Acknowledgements

This work was supported in part by National Institutes of Health Grants AG09686 (H.B.) and DC03112 (F.L.M.).