Development of the *Drosophila* Olfactory System

Veronica Rodrigues and Thomas Hummel*

Abstract

The olfactory system throughout the animal kingdom is characterized by a large number of highly specialized neuronal cell types. Olfactory receptor neurons (ORNs) in the peripheral sensory epithelium display two main differentiation features: the selective expression of a single odorant receptor out of a large genomic repertoire of receptor genes and the synaptic connection to a single type of relay neuron in the primary olfactory CNS target area. In the mouse olfactory system, odorant receptors themselves play a central role in the coordination of both types of ORN differentiation. The olfactory system of *Drosophila*, although similar in structural and functional organization compared to mammals, does not seem to involve odorant receptors in the selection of OR gene expression and target cell recognition, suggesting distinct developmental control mechanisms. In this chapter we summarize recent findings in *Drosophila* of how gene networks regulate ORN specification and differentiation in the peripheral sensory organs as well as how different cellular interactions and patterning signals organize the class-specific axonal and dendritic connectivity in the CNS target area.

Introduction

An essential function of the nervous system is to receive vital information about the environment through different sensory channels. To create a faithful internal representation of the external world in the brain, the highly selective incoming information must be organized in a meaningful manner, which requires that presynaptic inputs be matched to appropriate postsynaptic outputs. A well-studied example of neuronal sensory and synaptic specificity is the olfactory system. Molecular cloning of olfactory receptors (ORs) in vertebrates has provided valuable insights into the functional and anatomical organization of the olfactory system, including the projection of olfactory receptor neurons (ORNs) from the olfactory epithelium to the primary synaptic target in the CNS, the olfactory bulb (OB). In mice, the olfactory epithelium contains about 1000 different classes of ORNs defined by a unique OR expression. ORNs of a given sensory specificity intermingle with those of different OR classes in the olfactory epithelium, but send their axons to a distinct primary synaptic target unit in the olfactory bulb brain region. Although it is now well established that in mice ORs function in ORN axon-axon segregation in a local, contextual fashion, the mechanism underlying terminal axon sorting remains obscure. The results of two recent studies have integrated the role of ORs and classical neuronal adhesion molecules in explaining how discrete identities of ORNs are converted into a spatial map of axonal connections.

The adult olfactory system of *Drosophila* displays the same degree of sensory and synaptic specificity compared to vertebrates (Fig. 1), but with a reduced numerical complexity making it

*Corresponding Author: Thomas Hummel—Institut fuer Neurobiologie, Universitaet Muenster, Badestrasse 9, D-48149 Muenster, Germany. Email: hummel@uni-muenster.de

an excellent experimental model to determine developmental control mechanisms. The recent flurry of research on Drosophila olfactory system development and function has been catalyzed by the discovery and analysis of odorant receptor genes by the laboratories of Leslie Vosshall, John Carlson and Andrew Chess (reviewed in Laiissue and Vosshall, this issue and references there-in).

Figure 1. Organization of the Drosophila adult olfactory system. A) Whole mount preparation of the developing adult Drosophila brain, showing the projections of olfactory receptor neurons (ORNs) from the antenna (ANT) through the antennal nerve (AN) into the antennal lobe (AL), which is localized just ventrally to the mushroom body (MB) neuropil. The position of the lateral horn (LH) and the optic lobe (OL) is indicated. The inset indicates the position of the two olfactory appendages, the antenna (ANT) and the maxillary palp (MP). (B, B') Schematic drawing of the neuronal circuitry in the olfactory system: 1) Antennal ORN project their axons, associated with different types of glial cells (GCs), into the ipsi-lateral AL and axons converge into glomeruli according to the OR expression (red and green ORN class). B') Inside each glomerulus, ORN axon terminal branches interact with dendrites of Projection Neurons (PNs, mostly uni-gglomerular projections) and Local Interneurons (LNs, multi-gglomerular projections). 2) Most ORN classes send a projection across the commissure to innervate the corresponding glomerulus in the contra-lateral AL. 3) PNs transmit the olfactory information along their axons onto the MBs and neurons of the LH. Glial cells (GCs) cover the surface of the AL and send processes into the synaptic AL. C) Organization of ORN projections into three main fascicles in the third antennal segment. D) Subdivision of the AL neuropil into glomerular synaptic units (Glo), which can be individually recognized based on their position, size and shape. E) Distribution of two ORN classes (47b and 88a) across the antennal surface. ORN47b and ORN88a are localized together in the same sensillum (F) and project to neighboring glomeruli in the AL (G). H, I) Multi-gglomerular innervation of LN dendrites (red) in the AL (dotted line). ORN axon terminals (green) occupy a region inside the glomerulus different from LN dendritic branches (red). J) A group of three glomeruli is shown, occupied by two classes of PNs (red, dotted lines) and a non-overlapping innervation by an ORN class (green). Red labeling: N-Cadherin (A, D), CD2 (E-I), 22C10 (C); Green labeling: GFP (A-J).