This Week in The Journal

● Cellular/Molecular

OR Genes and Axonal Projections in Zebrafish

Yuki Sato, Nobuhiko Miyasaka, and Yoshihiro Yoshihara

(see pages 1606–1615)

Thanks to Buck and Axel and colleagues, most neuroscientists are aware of the precise topographical map of the mouse olfactory nerve projection in which each olfactory sensory neuron (OSN) expresses a single odorant receptor (OR), and OSNs expressing a given OR converge on a set of glomeruli in the olfactory bulb. This week, Sato et al. mapped the zebrafish axonal projection using a bacterial artificial chromosome transgene. The transgene contained a cluster of 16 OR genes, two of which (*OR111–7* and *OR103–1*) were replaced with yellow and cyan membrane-targeted reporters. Distinct sets of OSNs were fluorescently labeled, whereas their axons targeted the same cluster of glomeruli. For the *OR111* subfamily, each OSN expressed a single OR, but a few OSNs coexpressed *OR111* and *OR103* subfamily members, and *OR103–1* was always coexpressed with *OR103–2/103–5*. Such dual receptor expression has also been seen in *Drosophila*. Maybe fish are a bit more like flies than mice in this case.

The image shows the medial view of the projection of zebrafish OSNs to the olfactory bulb (center of image). A specific population of OSNs were labeled with fluorescent reporters and identified by immunoreactivity (brownish red in image). See the article by Sato et al. for details.

▲ Development/Plasticity/Repair

NGFI-A and Epigenetic Programming

Ian C. G. Weaver, Ana C. D'Alessio, Shelley E. Brown, Ian C. Hellstrom, Sergiy Dymov, Shakti Sharma, Moshe Szyf, and Michael J. Meaney

(see pages 1756–1768)

To the list of things for which we should thank our mothers, add epigenetic programming. Adult offspring of rat moms who provide high licking and grooming behavior (High LG mothers) have lower stress responses and increased glucocorticoid receptor (GR) expression. This week, Weaver et al. provide further evidence for the underlying mechanism. The GR promoter contains a response element for the transcription factor nerve growth factor-inducible protein A (NGFI-A), and binding of NGFI-A increases in offspring of High LG mothers. Increased maternal care is also associated with demethylation of a 5′ CpG dinucleotide site within this response element. The authors show that NGFI-A binding activated GR gene expression, whereas DNA methylation reduced NGFI-A binding and transcriptional activity. Because the 5′ CpG dinucleotide is hypermethylated at birth, the authors propose that early maternal care triggers epigenetic reprogramming of the GR promoter via an NGFI-A-dependent cascade.

■ Behavioral/Systems/Cognitive

"Liking," "Wanting," and Hedonic Hotspots

Kyle S. Smith and Kent C. Berridge

(see pages 1594–1605)

This week, Smith and Berridge investigated the interaction of two so-called hotspots for hedonic impact ("liking") and incentive motivation ("wanting") responses associated with compulsive behaviors. These 1 mm^3 hotspots reside in the shell of the nucleus accumbens and in the ventral pallidum and are reciprocally connected. To test the interaction between hotspots, the authors used a sucrose stimulus and tested rats for changes in Fos expression and for behavioral "liking" and "wanting" responses. Injection of the μ-opioid receptor agonist D-Ala2-*N*-Me-Phe^4-glycol^5-enkephalin (DAMGO) at either hotspot increased Fos expression locally and at the distant hotspot. DAMGO injections at either site also increased "liking" responses such as tongue protrusions and "wanting" behavior such as food consumption. However, injection of an opioid antagonist, naloxone, at one site and DAMGO at the other revealed a difference. Both hotspots were required for opioid enhancement of "liking" responses, but stimulation of the NAc hotspot was sufficient to trigger "wanting."

♦ Neurobiology of Disease

Getting ADAM10 to the Membrane

Elena Marcello, Fabrizio Gardoni, Daniela Mauceri, Stefano Romorini, Andreas Jeromin, Roberta Epis, Barbara Borroni, Flaminio Cattabeni, Carlo Sala, Alessandro Padovani, and Monica Di Luca

(see pages 1682–1691)

Amyloid precursor protein (APP) takes one of two major processing routes: either it is cleaved by β-secretase and γ-secretase to form amyloid β (Aβ), or it is cleaved by α-secretase. The latter cleaves within the Aβ sequence, thus avoiding the production of amyloidogenic fragments. In this week's *Journal*, Marcello et al. report that the putative α-secretase ADAM10 (a disintegrin and metalloproteinase 10) interacts directly with synapse-associated protein-97 (SAP97), a membrane-associated guanylate kinase (MAGUK) involved in trafficking of glutamate receptors. The interaction, via the SH3 domain of SAP97, was required for ADAM10 localization at postsynaptic membranes. Glutamate receptor activation increased SAP97-mediated membrane trafficking of ADAM10 and increased APP cleavage at the α-secretase site. Because the α-secretase activity attributed to ADAM10 occurs in the membrane compartment, the results indicate a possible link between synaptic function and APP processing.