This Week in The Journal

● Cellular/Molecular

TAG-1 Traffics Internalized Neuropilin-1

Puneet Dang, Elizabeth Smythe, and Andrew J. W. Furley

(see pages 10370–10382)

Growing axons are guided by attractive and repulsive molecules that are detected by receptors on growth cones. How axons respond to a given cue depends not only on what receptors they express, but also on what auxiliary proteins and downstream effectors are present. Repulsion of sensory axons by semaphorin 3a (Sema3a), for example, requires expression of the cell adhesion molecules L1 and TAG-1, as well as the Sema3a receptor complex that includes neuropilin-1. Dang et al. propose that L1 is required for Sema3a-induced internalization of neuropilin-1, and TAG-1 is required to segregate neuropilin-1 from L1 after internalization. Sema3a treatment of mouse sensory neurons increased both L1 endocytosis and colocalization of neruopilin-1 with L1 and TAG-1. Although internalized neuropilin-1 initially colocalized with L1, this colocalization quickly decreased, whereas colocalization of neuropilin-1 with TAG-1 remained elevated. In neurons lacking TAG-1, neuropilin-1 did not dissociate from L1 after internalization and downstream signaling by the Sema3a receptor complex was impaired.

▲ Development/Plasticity/Repair

Dendritic Growth Pattern Varies across Bipolar Cell Types

Felice A. Dunn and Rachel O.L. Wong

(see pages 10306–10317)

In the mouse retina, every cone photoreceptor contacts at least 10 types of cone bipolar cell, thus initiating parallel processing of visual information from each point in the visual field. Bipolar cell types differ in the extent of their dendritic fields—and hence the number of cones they may contact—as well as in their axonal arborization patterns and responses to light (ON or OFF). Dunn and Wong found that the process of dendritic development differed across three types of ON cone bipolar cells. The dendritic arbors of all three classes showed periods of growth and retraction during postnatal development, and all grew exuberant branches that were later pruned. During this developmental period, whereas the number of contacts type 6 bipolar cells made with cones only increased, the number made by type 7 and 8 bipolar cells increased and then decreased, indicating that some contacts were later retracted.

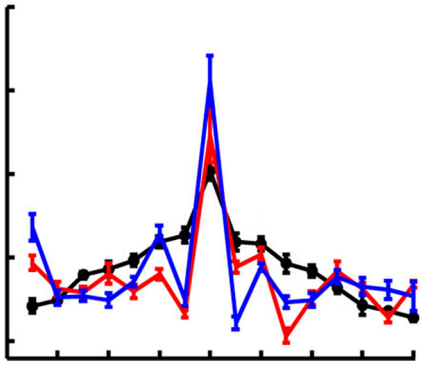
■ Behavioral/Systems/Cognitive

Cholinergic Inputs Sharpen Olfactory Tuning

Ming Ma and Minmin Luo

(see pages 10105–10116)

Cholinergic inputs from the basal forebrain to the main olfactory bulb (MOB) of rodents facilitate behavioral odor discrimination and learning, but the neuronal basis for this facilitation is unclear. Some studies have suggested that cholinergic inputs inhibit MOB mitral cells (the main output neurons of the bulb), but others suggested that acetylcholine excites mitral cells, possibly by inhibiting GABAergic interneurons. To resolve this question, Ma and Luo expressed channelrhodopsin in cholinergic projection neurons, thus enabling selective optical activation of these inputs while recording from morphologically identified neurons in the MOB. Activation of cholinergic inputs reduced spontaneous activity of mitral cells, as well as of GABAergic granule and periglomerular cells. In addition, cholinergic activation often sharpened the olfactory tuning of mitral cells by enhancing responses to odors that initially evoked relatively strong responses and suppressing responses to less effective odorants. Furthermore, cholinergic activation broadly enhanced odor-evoked responses in granule and periglomerular cells.



Optical stimulation of a mitral cell at 10 Hz (red trace) or 50 Hz (blue trace) increased or decreased its firing rate (*y*-axis) in response to different odors (*x*-axis), resulting in sharper olfactory tuning. See the article by Ma and Luo for details.

◆ Neurobiology of Disease

PPARγ Agonist Promotes Aβ Uptake by Glia

Shweta Mandrekar-Colucci, J. Colleen Karlo, and Gary E. Landreth

(see pages 10117–10128)

Two features of type II diabetes—insulin resistance and hyperinsulinemia—are also associated with cognitive impairment, accumulation of β-amyloid (Aβ), and increased risk for Alzheimer's disease (AD). Common diabetes treatments, including peroxisome proliferator-activated receptor-γ (PPARγ) agonists, show promise in treating AD. How PPARγ, a transcription factor that activates genes involved in lipid metabolism, affects AD pathogenesis is poorly understood, but some of its effects likely stem from its induction of liver X receptor, which in turn induces expression of apolipoprotein E (ApoE). ApoE is an essential lipid-transport protein that is produced by glia, binds to and promotes degradation of Aβ, and is strongly linked to AD risk. Mandrekar-Colucci et al. found that the PPARγ agonist pioglitazone increased *apoe* expression in mouse glia and increased degradation of Aβ by wild-type, but not *apoe*-null glia. Pioglitazone also induced *apoe* expression and reduced levels of Aβ in mice harboring AD-linked mutations, apparently by stimulating Aβ uptake by both astrocytes and microglia.