This Week in The Journal

● Cellular/Molecular

Optical Stimulation of Olfactory Cilia

Hiroko Takeuchi and Takashi Kurahashi

(see pages 766–775)

A novel technique for studying sensory transduction in olfactory sensory cilia is described this week by Takeuchi and Kurahashi. The binding of odorant molecules to olfactory receptors leads to activation of adenylyl cyclase and increased cAMP concentration in the cilium. cAMP, in turn, activates calcium channels, which, together with calcium-dependent chloride channels, depolarizes the cell. To study these transduction mechanisms more closely, Takeuchi and Kurahashi used laser-scanning confocal microscopy to locally release caged cyclic nucleotides (in 1 μm spots) in the cytoplasm of dissociated olfactory cells, while simultaneously obtaining whole-cell electrical recordings. Although these studies did not discriminate between the contribution of calcium and chloride channels, they did reveal that the transduction channels are distributed throughout cilia, with a higher channel density proximally. In addition, responses to stimuli at different points along a cilium summed linearly. And different cilia on the same cell responded similarly to the same stimulus.

▲ Development/Plasticity/Repair

Regulation of Opsin Expression in Cones

Hong Liu, Paige Etter, Susan Hayes, Iwan Jones, Branden Nelson, Byron Hartman, Douglas Forrest, and Thomas A. Reh

(see pages 749–756)

The transcription factor NeuroD1 is known to play a role in photoreceptor development, but its precise role in genesis, specification, and/or maintenance is not clear. Liu et al. now report that NeuroD1 helps to specify medium-wavelength M-opsin cone photoreceptors by activating the thyroid hormone receptor TRβ2 via an intron control region. Like TRβ2 knock-outs, NeuroD1$^{-/-}$ knock-out mice had as many cones as wild type, but all the cones expressed short-wavelength S-opsin, and none expressed M-opsin. TRβ2 expression was reduced 10-fold in NeuroD1$^{-/-}$ mice but was restored by transfecting the mutant retinas with NeuroD1. Furthermore, mutation of a sequence in the intron control region prevented induction of TRβ2 by NeuroD1. Both the roles of NeuroD1 and the regulation of opsin expression are more complicated than described here, however. NeuroD1 by itself cannot induce TRβ2 (and thus M-opsin) expression, and photoreceptor degeneration occurs in NeuroD1, but not TRß2 knock-outs.

■ Behavioral/Systems/Cognitive

Somatosensory Processing of Orientation Information

Sliman J. Bensmaia, Peter V. Denchev, J. Frank Dammann, James C. Craig, and Steven S. Hsiao

(see pages 776–786)

The neural processing that allows us to feel the orientation of a bar resembles that involved in seeing the orientation, according to experiments on somatosensory processing reported by Bensmaia et al. in this issue. Many neurons recorded in macaque somatosensory cortex (areas 3b and 1) fired preferentially when bars were presented in a particular orientation, regardless of stimulus amplitude (how hard the stimulus was pressed) or motion (whether or how fast the bar was scanned along the finger). The firing pattern of these neurons suggested that they receive input primarily from slow-adapting type 1 mechanosensory afferents (which do not themselves show orientation selectivity). Based on their firing patterns, orientation-selective neurons could discriminate between angles that differed by >15°—a slightly smaller difference than humans perceived in psychophysical studies. Modeling the receptive fields of orientation-sensitive neurons suggested that they, like visual receptive fields, have an excitatory center and inhibitory surround.

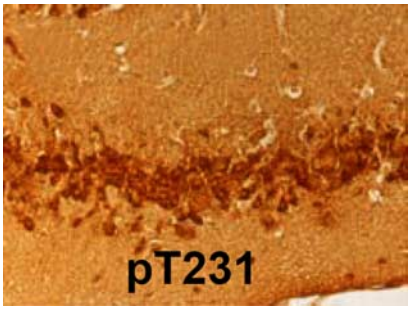
◆ Neurobiology of Disease

Tau Aggregation Forms Persistent Neurofibrillary Tangles

Maria-Magdalena Mocanu, Astrid Nissen, Katrin Eckermann, Inna Khlistunova, Jacek Biernat, Dagmar Drexler, Olga Petrova, Kai Schönig, Hermann Bujard, Eckhard Mandelkow, Lepu Zhou, Gabriele Rune, and Eva-Maria Mandelkow

(see pages 737–748)

Tauopathies are neurodegenerative diseases that involve dysfunction of the microtubule-associated protein Tau. For example, hyperphosphorylated Tau forms the paired helical filaments (PHFs) found in Alzheimer's disease. Tauopathies could potentially result from disruption of axonal transport or from abnormal expression, phosphorylation, and/or aggregation of Tau. Support for the last possibility is presented by Mocanu et al. They isolated the effects of aggregation by creating transgenic mice that expressed proaggregation or anti-aggregation forms of the Tau repeat domain, which is involved in PHF formation but lacks most of the phosphorylation sites involved in tauopathy and does not bind well to microtubules. Neurofibrillary tangles (NFTs), neurodegeneration, and synapse loss were all observed in the proaggregation, but not the antiaggregation, mouse lines. Endogenous Tau colocalized with mutant Tau in NFTs and became hyperphosphorylated in proaggregation lines. Surprisingly, NFTs containing endogenous Tau persisted even after mutant Tau expression was turned off and disappeared from NFTs.



Immunostaining reveals that endogenous Tau is phosphorylated and missorted to the somatodendritic compartment in the hippocampus of mice expressing a proaggregation mutant Tau. See the article by Mocanu et al. for details.