This Week in The Journal

Cellular/Molecular

Identification of a Ca^{2+}-Activated Cl^- Channel in Photoreceptors

Heidi Stöhr, Julia B. Heisig, Peter M. Benz, Simon Schöberl, Vladimir M. Milenkovic, Olaf Strauss, Wendy M. Aartsen, Jan Wijnholds, Bernhard H. F. Weber, and Heidi L. Schulz

(see pages 6809–6818)

Calcium-activated chloride currents in photoreceptor synaptic terminals are hypothesized to fine-tune synaptic transmission. Full understanding of the physiological role of this current requires molecular identification of the responsible channel, and Stöhr et al. might have accomplished this task. In a screen for genes involved in normal retinal physiology, the authors identified TMEM16B, a member of a family of transmembrane proteins, which is highly expressed in retina. Because recent studies identified TMEM16A as a putative calcium-activated chloride channel in other tissues, the authors examined whether TMEM16B plays this role in photoreceptors. TMEM16B was expressed predominantly in photoreceptor terminals, colocalized with a presynaptic protein complex in which it interacts directly with PSD95. Overexpression of TMEM16B in human embryonic kidney cells introduced a calcium-activated, outwardly rectifying anion conductance that had a reversal potential near that of chloride and was reduced in low-chloride media.

Development/Plasticity/Repair

Transient Tonotopic Reorganization in Birds

Dexter R. F. Irvine, Mel Brown, Marc R. Kamke, and Edwin W Rubel

(see pages 6871–6882)

Auditory neurons are classified by their characteristic frequency—the sound frequency to which they are most sensitive—but most respond to a wide range of frequencies if the sound pressure level (SPL) is high enough. Mammalian auditory cortex is organized tonotopically by characteristic frequency, but if hair cells are lost, the representation of nearby frequencies expands into the deprived region. Irvine et al. investigated whether similar frequency reorganization occurs in birds, whose hair cells regenerate. Antibiotic treatment killed hair cells responding to high frequencies, and regions of the avian homolog of auditory cortex that normally represent these frequencies subsequently responded only to lower frequencies. Unlike in mammals, however, the SPL required to activate these neurons was much higher than normal, suggesting that the neurons did not change their sensitivity to lower frequencies, but simply continued to respond to these frequencies at high SPL. After hair cell regeneration, normal tonotopy was restored, but sensitivity remained somewhat elevated, possibly resulting from hair-cell morphological abnormalities.

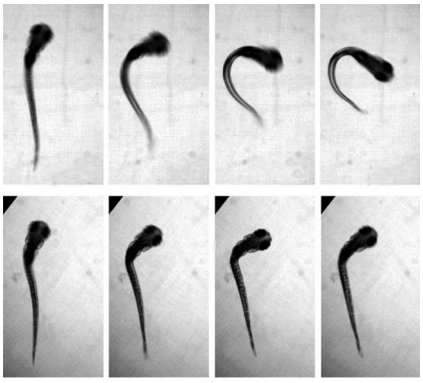
Behavioral/Systems/Cognitive

Role of Inhibitory Neurons in Fish Startle Reflex

Chie Satou, Yukiko Kimura, Tsunehiko Kohashi, Kazuki Horikawa, Hiroyuki Takeda, Yoichi Oda, and Shin-ichi Higashijima

(see pages 6780–6793)

The fast escape reflex in fish is useful for studying reticulospinal motor control networks. Sounds activate auditory nerves, which directly activate two hindbrain Mauthner cells, which form monosynaptic connections with motor neurons, causing a C-shaped bend that precedes escape swimming. When a stimulus activates both Mauthner cells, commissural local (CoLo) inhibitory neurons are essential for efficient escape, as demonstrated by Satou et al. CoLos are electrically coupled to Mauthner cells and form short-latency inhibitory synapses onto contralateral motor neurons. Bilateral ablation of CoLos prevented formation of the C-shaped bend in response to some auditory stimuli, and instead appeared to cause bilateral contraction—which would be expected if both Mauthner cells were activated. Such abnormal bends were eliminated when one Mauthner cell was ablated along with the CoLos. Thus, rapid activation of CoLos by one Mauthner cell appears necessary to suppress opposing motor commands if the second cell fires soon afterward.



Escape responses in normal zebrafish (top row) and fish in which CoLos were ablated caudal to the seventh segment. The C shape is not formed in the ablated fish. See the article by Satou et al. for details.

Neurobiology of Disease

Inverse Correlation Between apoE and Amyloid Levels

Kelly R. Bales, Feng Liu, Su Wu, Suizhen Lin, Deanna Koger, Cynthia DeLong, Jeffrey C. Hansen, Patrick M. Sullivan, and Steven M. Paul

(see pages 6771–6779)

In the brain, apolipoprotein E (apoE) transports lipids and cholesterol, which are important for neuronal growth and repair. Three isoforms of apoE are present in humans. The $\varepsilon 4$ allele increases one's risk of late-onset Alzheimer's disease (AD) and other neuropathologies, whereas the $\varepsilon 2$ allele reduces AD risk. Proposed explanations for these effects include: ApoE4 is less stable than other isoforms, it is less effective in promoting repair, and it increases two hallmarks of AD, β-amyloid (Aβ) plaque formation and tau hyperphosphorylation. Bates et al. examined the relationship between *Apoe* genotype and Aβ deposition in transgenic mice that expressed mutant amyloid precursor protein along with human *Apoe* alleles. Soluble apoE levels were highest, and toxic Aβ levels were lowest in $\varepsilon 2$ mice, whereas $\varepsilon 4$ mice had low apoE levels, more Aβ, and more amyloid plaques. The correlation between brain apoE and Aβ levels suggests increasing apoE levels might protect against AD.