This Week in The Journal

● Cellular/Molecular

OFF Ganglion Cells Express Low-Voltage-Activated Ca^{2+} Channels

David J. Margolis, Andrew J. Gartland, Thomas Euler, and Peter B. Detwiler

(see pages 7127–7138)

ON and OFF retinal ganglion cells (RGCs) fire in response to light onset and offset, respectively. To optimize their encoding of light increment and decrement, ON and OFF RGCs of a given morphological and functional class exhibit different response dynamics and spatial integration. Margolis et al. suggest that the ability of one type of mouse OFF RGC to precisely encode light offset results from dendritic expression of low-voltage-activated (LVA) calcium channels, which are not expressed in ON RGCs of the same class. Whereas both ON and OFF RGCs responded to depolarization or changes in illumination with calcium influx through high-voltage-activated channels, only OFF RGCs showed an increase in calcium influx after hyperpolarization. As in other neurons, LVA calcium channels in OFF RGCs were inactivated near resting membrane potentials, were deinactivated by hyperpolarization, and contributed to rebound spiking after termination of hyperpolarization, which likely occurs as a result of decreased inhibitory input at light offset.

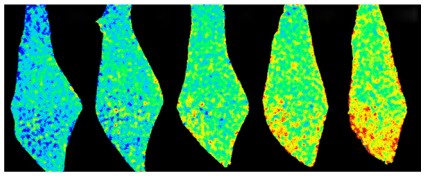
▲ Development/Plasticity/Repair

Calmodulin-Activated Adenylate Cyclase Mediates Antirepellent Effects

Hong Xu (徐洪), Sarah G. Leinwand, Alison L. Dell, Emma Fried-Cassorla, and Jonathan A. Raper

(see pages 7423–7433)

Axonal growth cones encounter many environmental cues that promote growth, collapse, or turning and thus guide axons to their targets. Whether and how a growth cone responds to a cue depends on the combination of receptors it expresses. In zebrafish, for example, expression of CXCR4, a receptor for the chemokine SDF1, allows retinal ganglion cell (RGC) axons to grow through environments containing the repellent slit2, if SDF1 is also present. The antirepellent effect of SDF1 is mediated by calcium–calmodulin and requires cAMP. Xu et al. report that the signaling cascade activated by SDF1 also includes the calmodulin-activated adenylate cyclases ADCY8 and ADCY1, which are expressed in zebrafish RGC axons when they cross the midline. Knockdown of ADCY8 did not affect axon growth when cultured with SDF1 or slit2 alone, but when both molecules were present, axons lacking ADCY8 grew less than wild-type. ADCY8 knockdown caused pathfinding errors at the optic chiasm *in vivo*.



A cAMP sensor based on fluorescence resonance energy transfer shows increases in cAMP levels in cultured retinal ganglion cells after SDF1 application. Images were taken at ~5 min intervals. See the article by Xu et al. for details.

■ Behavioral/Systems/Cognitive

Inferior Frontal Sulcus Is Involved in Audiovisual Decisions

Uta Noppeney, Dirk Ostwald, and Sebastian Werner

(see pages 7434–7446)

Studies on perceptual decision making about single-modality sensory stimuli have led to the hypothesis that increases in neural activity in specific brain regions reflect accumulation and integration of information about the stimuli, and that once a threshold level of activity is reached, a decision is made. But when identifying and classifying objects in the world, we often consider information from multiple sensory modalities, e.g., vision and hearing. This requires us to distinguish stimuli related to the object from unrelated stimuli—a task that becomes more difficult as environmental noise increases. Noppeney et al. asked whether specific brain regions accumulate and integrate multimodal information to make perceptual decisions, and if so, how the process is affected by unrelated stimuli. To do so, they examined brain activity in subjects viewing video clips that had congruent or incongruent audio tracks. Their analyses led them to propose that the left inferior frontal sulcus is important for integrating audiovisual information.

♦ Neurobiology of Disease

Histone Methylation Regulates NMDA Receptor NR2B Subunit

Yan Jiang, Mira Jakovcevski, Rahul Bharadwaj, Caroline Connor, Frederick A. Schroeder, et al.

(see pages 7152–7167)

In the nucleus, DNA is wrapped around histone proteins. Posttranslational modifications of histones, including methylation and acetylation, alter protein interactions with DNA and thus regulate transcription. Regulation of these modifications contributes to gene expression changes during cell fate determination, differentiation, and plasticity. Although the roles of histone acetylation in neurons have been widely studied, relatively little is known about the regulatory targets of methylation. Jiang et al. found that the histone methyltransferase Setdb1 associates with a small percentage of chromatin in mouse neurons, including that of *Grin2b*, the gene encoding the NMDA receptor subunit NR2B. Overexpression of Setdb1 increased histone methylation associated with *Grin2b* and reduced NR2B expression. Like mice treated with NR2B antagonists or antidepressants, mice overexpressing Setdb1 showed increased sucrose consumption, more mobility during tail suspension, and quicker recovery from learned helplessness than wild-type mice. Whether these effects resulted from downregulation of NR2B or of other genes targeted by Setdb1 is uncertain.