This Week in The Journal

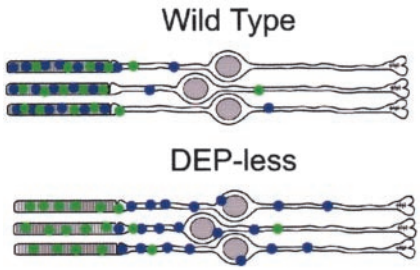
● Cellular/Molecular

Delivering RGS9 to the Rod Outer Segment

The DEP Domain Determines Subcellular Targeting of the GTPase Activating Protein RGS9 *In Vivo*

Kirill A. Martemyanov, Polina V. Lishko, Nidia Calero, Gabor Keresztes, Maxim Sokolov, Katherine J. Strissel, Ilya B. Leskov, Johnathan A. Hopp, Alexander V. Kolesnikov, Ching-Kang Chen, Janis Lem, Stefan Heller, Marie E. Burns, and Vadim Y. Arshavsky
(see pages 10175–10181)

Nowhere is targeting of proteins more critical than in the super-specialized outer segment of rod photoreceptors. In this issue, Martemyanov et al. investigate a potential targeting role of the DEP (for Disheveled, EGL-10, Pleckstrin) homology domain in RGS9, a GTPase-activating protein that regulates the lifetime of activated transducin, and thus the light response. RGS9 forms a complex with a G-protein β subunit (Gβ5) that is then membrane anchored by R9AP. The 70 aa DEP domain appears in a number of signaling molecules and may be involved in protein targeting. The authors created a transgenic mouse in which the DEP domain of RGS9 was deleted. DEP-less mice had normal amounts of RGS9, but it was no longer segregated to the outer segment. Photoreceptors in these mice had markedly slowed recovery after a light flash similar to RGS9−/− neurons. In the DEP-less mice, R9AP was normally segregated to the outer segment, suggesting that DEP binding to R9AP is necessary for targeting.



The distribution of RGS9 (blue) and R9AP (green) at their respective locations in rods of wild-type and DEP-less mice.

▲ Development/Plasticity/Repair

Dorsal Column Input and Somatotopy in Somatosensory Cortex

Patterned Activity via Spinal Dorsal Quadrant Inputs Is Necessary for the Formation of Organized Somatosensory Maps

Neeraj Jain, Pamela S. Diener, Jacques-Olivier Coq, and Jon H. Kaas
(see pages 10321–10330)

As with other sensory systems, the organization of the somatosensory cortex (S1) depends strongly on sensory input during early critical periods. For example, complete loss of sensory input by limb amputation, whisker removal, or nerve transactions disrupts the formation of histologically defined modules (barrels) in S1. This week, Jain et al. used a spinal lesioning procedure dubbed "overhemisection" to examine the contribution of different sensory tracts to the organization of S1. On postnatal day 3, the time at which barrels usually appear in the forelimb region of S1, they hemisected the rat spinal cord in the upper cervical region and transected the contralateral dorsal funiculus. As a result, S1 contralateral to the hemisection lost all uncrossed dorsal column inputs but retained input from the crossed spinothalamic pathway. Six months later, they examined the functional and anatomical organization of S1. The modules in S1 for the forepaw and hindpaw (i.e., areas with sensory input below the spinal lesion) were lost. Neurons in those regions of S1 were also abnormal, either not responding to skin stimulation or only responding to upper arm afferents that enter the spinal cord above the lesion. Thus spinothalamic input, with its largely overlapping cortical receptive fields, was insufficient to support normal development of modules in S1.

■ Behavioral/Systems/Cognitive

The Rewards of the βarrestin Knock-Out

Enhanced Rewarding Properties of Morphine, but not Cocaine, in βarrestin-2 Knock-Out Mice

Laura M. Bohn, Raul R. Gainetdinov, Tatyana D. Sotnikova, Ivan O. Medvedev, Robert J. Lefkowitz, Linda A. Dykstra, and Marc G. Caron
(see pages 10265–10273)

μ-Opioid receptors (μOR) as well as dopamine receptors desensitize when they are phosphorylated and subsequently bind βarrestins, thus preventing receptor–G-protein coupling. Mice lacking βarrestin-2 (βarr2) are more sensitive to the antinociceptive effects of morphine, presumably because receptor desensitization is reduced. Now Bohn et al. use βarr2 knock-out mice to determine whether the reinforcing and psychomotor effects of morphine are likewise enhanced. By comparing morphine and cocaine, the authors separated effects on actions on opioid and dopamine receptors. Both drugs increase dopaminergic activity in the mesolimbic system, but cocaine acts directly on dopamine handling, whereas morphine works indirectly through the μOR. In response to morphine, βarr2 knock-out mice released more dopamine in the striatum than wild-type (WT) mice, and they also showed increased conditioned place preference. Cocaine treatment did not differ between WT and knock-out animals. Thus the rewarding as well as antinociceptive behaviors in βarr2 knock-out mice are mediated through the μOR rather than dopamine receptors. Whereas the μOR appears to be selective for βarr2, βarr1 may be sufficient to desensitize dopamine receptors. Unexpectedly, morphine caused less enhancement of locomotor activity in βarr2 knock-out mice; the authors propose that coactivation of serotonin pathways may dampen the opioid-induced hyperactivity.