This Week in The Journal

Cellular/Molecular

Hikaru genki Clusters Drosophila *Acetylcholine Receptors*

Minoru Nakayama, Fumiya Matsushita, and Chihiro Hama

(see pages 13872–13877)

The extracellular matrix of synaptic clefts contains proteins that help cluster neurotransmitter receptors. This week we learn that Hikaru genki (Hig) is one such protein. Hig is a secreted protein localized to some synaptic clefts in *Drosophila* CNS, and it is required for normal locomotion and longevity. Nakayama et al. extend previous studies to show that Hig localizes specifically to cholinergic synapses, where it helps cluster acetylcholine receptors (AChRs). Expression of AChR subunits was reduced in *hig* mutants and as a result, the mutants were more resistant to a lethal AChR agonist. Interestingly, the longevity phenotype of *hig* mutants was rescued not only by expressing wild-type *hig* selectively cholinergic neurons, but also by expressing it selectively in glutamatergic neurons or even in glia. Regardless of its source, secreted Hig diffused and localized to cholinergic synapses.

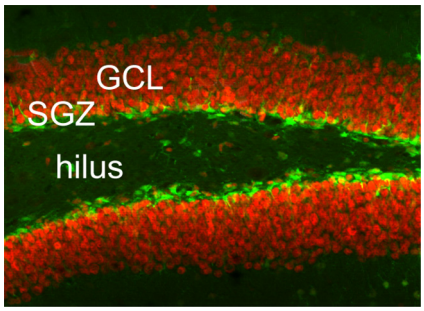
Development/Plasticity/Repair

Fezf2 Suppresses Stem Cell Proliferation and Differentiation

Michael A. Berberoglu, Zhiqiang Dong, Guangnan Li, Jiashun Zheng, Luz del Carmen G. Trejo Martinez, et al.

(see pages 13911–13923)

Neurons generated in adult brains can replace injured neurons, help maintain existing circuits, and/or contribute to learning. Ongoing neurogenesis requires maintenance of neural stem cell (NSC) populations in neurogenic niches, but how NSCs are kept quiescent until new neurons are needed is not fully understood. Berberoglu et al. report that the transcription factor fezf2 has a role in this process. Expressing green fluorescent protein under the control of the *fezf2* promoter in zebrafish revealed that quiescent



fezf2 (green) is expressed in most neural stem cells in the subgranular zone (SGZ) and a few granule cells (red) in the granule cell layer (GCL) of mouse dentate gyrus, indicating that Fexf2 function may be conserved between fish and mice. See the article by Berberoglu et al. for details.

putative NSCs had high *fezf2* expression levels, proliferating NSCs had low expression levels, and differentiating cells lacked detectable expression of *fezf2*. Loss of fezf2 function increased the proportion of proliferative relative to quiescent NSCs and increased the number of adult-born neurons in the telencephalon. Analysis of chimeric animals indicated that fezf2 acts both cell autonomously and nonautonomously to suppress NSC proliferation and differentiation. Fezf2 appeared to regulate these processes by promoting Notch signaling, that is, by regulating expression of several members of this pathway.

Systems/Circuits

Optical Imaging Responses Correlate with Spiking Activity

Bruss Lima, Mariana M. B. Cardoso, Yevgeniy B. Sirotin, and Aniruddha Das

(see pages 13878 –13891)

Intrinsic-signal optical imaging and blood-oxygen-level-dependent signals obtained with functional magnetic resonance imaging detect local changes in blood volume and oxygenation, from which researchers can infer changes in neuronal activity. What component of neuronal activity is best reflected by these measures remains a matter of debate, however. Some studies found that functional imaging correlates with local field potentials (LFPs) and likely reflects metabolic demand resulting from ionic currents downstream of synaptic inputs. But other studies suggest that neuroimaging is sensitive to glutamate release and reflects local spiking. Lima et al. argue that previous investigations of this question were confounded by inclusion of task-related imaging components (which are not correlated with LFPs or spiking) along with stimulus-related components and by not comparing neuroimaging and electrophysiological measures over a wide enough range of stimulus intensities. Avoiding these confounds, the authors found that the linearity and shape of intrinsic imaging responses in primary visual cortex of monkeys best matched those of spiking.

Behavioral/Cognitive

Lateral Amygdala Neurons Store Context–Cocaine Memory

Hwa-Lin (Liz) Hsiang, Jonathan R. Epp, Michel C. van den Oever, Chen Yan, Asim J. Rashid, et al.

(see pages 14115–14127)

With repeated exposure, cocaine users learn to associate certain cues or environments with drug use. Later re-exposure to these cues or environments induces craving and often leads to relapse. Hsiang et al. propose that these relapse-inducing associations are stored by neurons in the lateral amygdala (LA) that happen to be activated during cocaine exposure. Overexpressing CREB in ~10% of neurons in mouse LA made these neurons more likely than other LA neurons to be activated in a chamber associated with cocaine administration, suggesting these neurons helped form the contextual memory. Selectively ablating or silencing CREB-overexpressing neurons just before testing reduced conditioned place preference (CPP) for the cocaine-associated chamber. Furthermore, silencing CREB-overexpressing neurons immediately after training—which was expected to impair memory consolidation—eliminated CPP. Together, the data suggest that the context–cocaine association is stored in a subset of LA neurons that exhibit high CREB expression during cocaine exposure, and that reactivation of these neurons after training is required to consolidate the memory.