This Week in The Journal

● Cellular/Molecular

CRMPs May Regulate Development of Neuronal Polarity

Sébastien Brot, Véronique Rogemond, Valérie Perrot, Naura Chounlamountri, Carole Auger, et al.

(see pages 10639–10654)

Most neurons develop one axon and several dendrites. Cultured rat hippocampal neurons initially extend several short neurites that grow and retract for several hours before one of them extends rapidly and acquires axonal characteristics. The other neurites remain quiescent for another day before becoming dendrites. Several studies suggest that this initial restriction of growth to a single process is essential for establishing neuronal polarity, and collapsin response mediator proteins (CRMPs) might contribute to this process. Overexpression of CRMP2 increases axon growth and causes production of multiple axons. Brot et al. show that CRMP2 also enhances dendritic growth, but CRMP5 appears to counteract this effect by reducing CRMP2 interactions with tubulin. Overexpression of CRMP5 reduced dendritic growth without affecting axons, whereas CRMP5 knockdown increased dendrite length and number. Intriguingly, CRMP5 was expressed preferentially in future dendrites when the axon was undergoing rapid growth, and its expression decreased as the dendrites began growing, suggesting that it spatially restricts the growth-promoting effects of CRMP2.

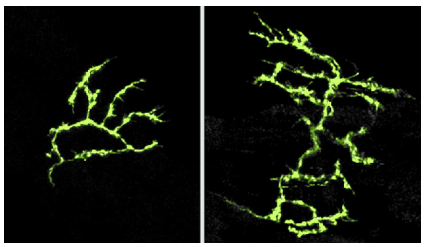
▲ Development/Plasticity/Repair

RGC Activity Autonomously Regulates Filopodial Extension

Naila Ben Fredj, Sarah Hammond, Hideo Otsuna, Chi-Bin Chien, Juan Burrone, et al.

(see pages 10939–10951)

Retinal ganglion cell (RGC) axons initially form extensive arbors in their target areas, and these arbors are later refined by retraction of exuberant branches to form a precise retinotopic map. Spontaneous RGC activity is required for this refinement, but whether the activity acts autonomously within axons or requires communication with postsynaptic targets is not clear. To address this question, Ben Fredj et al. expressed tetanus toxin in single developing zebrafish RGCs to block vesicle release without blocking intrinsic electrical activity. This greatly increased the number of transient filopodia extensions from axons in the tectum and increased the total length of axonal arbors, but did not alter the number of stable axonal branches. These data suggest that RGC acts autonomously to promote filopodial extension, but formation of functional synapses is required for these filopodia to become stable branches and for growth of axonal branches to stop within the tectum.



The axonal arbors of RGCs that express tetanus toxin (right) are much longer than those of controls (left). See the article by Ben Fredj et al. for details.

■ Behavioral/Systems/Cognitive

Dopamine Neurons Encode Ongoing Changes in Reward Expectation

Kensaku Nomoto, Wolfram Schultz, Takeo Watanabe, and Masamichi Sakagami

(see pages 10692–10702)

Midbrain dopaminergic neurons appear to encode reward prediction error—the difference between the value of a reward and the value expected. If an unexpected reward is received, dopamine neuron activity increases. If an animal learns that a cue predicts a reward, activity increases when the cue appears, but not when the expected reward is delivered. If the reward is not received when expected, however, activity decreases. Previous studies paired simple cues with reward, leading to immediate anticipation of reward. Nomoto et al. now show that in monkeys, dopaminergic neuronal activity changes throughout complex discrimination tasks that require additional processing to accurately predict reward magnitude and likelihood. Stimulus presentation caused an increase in firing that probably reflected an expectation of some reward. Once the stimulus was discriminated, neuron activity increased only if the monkey's choice indicated it expected a larger-than-normal reward. If a feedback cue indicated that the monkey incorrectly discriminated the stimulus and would not receive a reward, neuron activity decreased.

♦ Neurobiology of Disease

Excess PI3K May Underlie Some Effects of FMRP Loss

Christina Gross, Mika Nakamoto, Xiaodi Yao, Chi-Bun Chan, So Y. Yim, et al.

(see pages 10624–10638)

Fragile X mental retardation protein (FMRP) is an mRNA binding protein thought to inhibit local translation until appropriate extracellular stimuli occur. Loss of FMRP results in excessive baseline production of proteins, and thus occludes stimulus-induced increases in translation. For example, activation of metabotropic glutamate receptors (mGluRs) appears to produce long-term depression (LTD) by releasing FMRP-mediated translational repression of specific mRNAs involved in AMPA receptor internalization: in FMRP-null mice, LTD and AMPA receptor internalization are enhanced and occur in the absence of new protein synthesis. Gross et al. show that these effects might be mediated by dysregulated translation of phosphoinositide 3-kinase (PI3K). FMRP associated with PI3K, and PI3K translation at synapses was elevated in FMRP-null mice. Whereas mGluR activation normally induced translation and activation of PI3K, these were insensitive to mGluR activation in mice lacking FMRP. Moreover, blocking PI3K, like blocking mGluRs, reduced overall increases in protein translation, AMPA receptor internalization, and spine formation in FMRP-null mice.