A Role for "Local" Protein Synthesis in Synaptic Plasticity, Learning & Memory

David G. Wells

Department of Molecular, Cellular, and Developmental Biology, Yale University, New Haven, Connecticut 06520-8103, USA.

Information is transmitted in the nervous system through specialized connections called synapses. Neurons can receive thousands of synaptic connections, potentially from thousands of different neurons; yet, remarkably, each synapse can be modified – the strength of the signal can be increased or decreased – independently. These changes in strength can occur over many time scales, from seconds to hours and possibly days and months. The long-term changes in synaptic strength are widely thought to be the cellular encoding of information or memory. Long-term changes in synaptic strength (plasticity) are dependent upon synthesis of new proteins and there is growing evidence that a cohort of mRNAs appear to be translated locally at or near the synapse. My talk will focus on a molecular mechanism capable of regulating mRNA translation in neuronal dendrites.

Some dendritically targeted mRNAs contain cytoplasmic polyadenylation element (CPE) sequences in their 3' untranslated region (UTR). The *trans*-acting CPE-binding protein CPEB may mediate the translation of these mRNAs. I will present our findings that CPEB-mediated protein synthesis is occurring in neurons from different regions of the brain, including cortex, hippocampus and cerebellum. I will focus on recent work showing that tissue plasminogen activator is synthesized and released in the dendrites of hippocampal neurons. I will conclude the talk with evidence indicating that CPEB-mediated protein synthesis plays a role in cerebellar synaptic plasticity and show that a disruption of this process leads to ataxia.