

# Stored mRNA in Brain Cells

One of the most important areas of local translational regulation may be in the brain. The storage of long-term memory requires new protein synthesis, and the local translation of mRNAs in the dendrites of brain neurons has been proposed as a control point for increasing the strength of synaptic connections (Martin 2000; Klann et al. 2004; Wang and Tiedge 2004). The ability to increase the strength of the connections between neurons is critical in forming the original architecture of the brain and also in the ability to learn. Indeed, in recent studies of mice, Kelleher and colleagues (2004) have shown that neuronal activity-dependent memory storage depends on the activation of eIF4E and other components of protein synthesis.

Several mRNAs appear to be transported along the cytoskeleton to the dendrites of neurons (the “receiving portion” of the neuron, where synapse connections are formed with the other neurons). These messages include those mRNAs encoding receptors for neurotransmitters (needed to transmit the signals from one neuron to another); activity-regulated enzymes; and the cytoskeletal components needed to build a synapse. As we will see in later chapters of the textbook, one of the proteins responsible for constructing specific synapses is brain-derived neurotrophic factor, or BDNF. BDNF regulates neural activity and appears to be critical for new synapse formation. Takei and colleagues (2004) have shown that BDNF induces local translation of these neural messages in the dendrites.

Another indication of the importance of dendritic mRNA translation comes from studies of a leading cause of human mental retardation, fragile X syndrome. Fragile X syndrome is caused by loss-of-function mutations in the X-linked *FMR1* gene. The FMR1 protein (FMRP) appears to prevent the translation of several mRNAs that are being transported to the dendrites along microtubules in response to stimulation by glutamic acid (Dictenberg et al. 2008; Wang et al. 2008b). In the absence of functional FMRP, these mRNAs are expressed in the wrong amounts, leading to signaling abnormalities that are believed to cause problems in cognition and learning. Indeed, a subset of the mRNAs regulated by FMRP have been linked to autism and new synapse formation, and autism is often seen in patients with Fragile X syndrome (Darnell et al. 2011; Darnell and Richter 2013) Thus, translational regulation in neurons might be important not only for their initial development but also for their continued ability to learn and change.

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