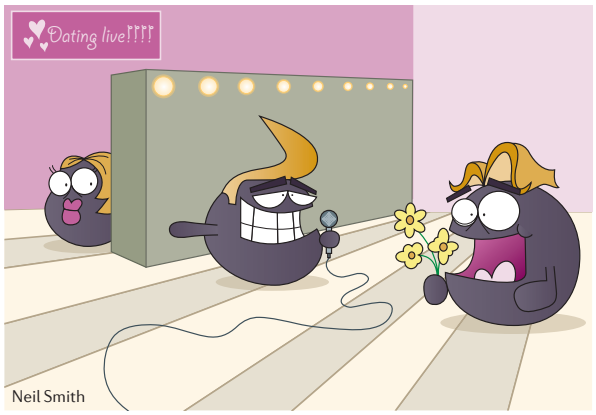
SYNAPTIC PLASTICITY

Pulling power of CAMK2α

Synaptic plasticity relies in part on protein degradation by proteasomes, which move from the dendritic shaft to spines and are activated following synaptic excitation. Sheng and colleagues now shed light on the molecular mechanisms that underlie proteasome redistribution and reveal that Ca^{2+}–calmodulin-dependent protein kinase 2α (CAMK2α) acts as a scaffold for proteasomes at synapses.

CAMK2α and CAMK2β are expressed in neurons, and their kinase activity contributes to synaptic plasticity. Upon neuronal activation, both isoforms move from the dendritic shaft to spines. The abundance of CAMK2 at synapses suggests that it may have an additional, structural role. Indeed, CAMK2β had been shown to mediate the reorganization of the actin cytoskeleton, but a structural role for CAMK2α had not been demonstrated.



Neil Smith

In co-precipitation studies followed by mass spectrometry, the authors identified CAMK2α as a brain proteasome-associated protein. After demonstrating that CAMK2α and proteasomes colocalize in cultured rat hippocampal neurons, they showed in time lapse imaging studies that overexpression of CAMK2α enhanced NMDA (*N*-methyl-D-aspartate)-dependent recruitment of proteasomes to spines. By contrast, downregulation of CAMK2α expression by RNA interference or expression of mutant forms of CAMK2α that are deficient in activity-dependent translocation impaired this proteasome accumulation, suggesting a crucial role for CAMK2α in proteasome redistribution.

Next, the authors developed an ingenious system in which rapamycin was used to induce binding of CAMK2α to postsynaptic density protein 95, rendering CAMK2α translocation to the postsynaptic density independent of neuronal stimulation or kinase activity. Using this system, they showed that translocation of CAMK2α was sufficient to accumulate proteasomes in spines.

Mutant forms of CAMK2α that were unable to translocate did not affect postsynaptic ubiquitination (which marks proteins for degradation), but impaired activity-dependent protein degradation, suggesting that CAMK2α translocation is required for the degradation of ubiquitinated proteins in response to synaptic stimulation.

This study provides evidence that, apart from its well-known kinase activity-dependent function in synaptic plasticity, CAMK2α has a structural role in localizing proteasomes to dendritic spines.

Claudia Wiedemann

ORIGINAL RESEARCH PAPER Bingol, B. *et al.* Autophosphorylated CaMKIIα acts as a scaffold to recruit proteasomes to dendritic spines. *Cell* **140**, 567–578 (2010)
FURTHER READING Tai, H.-C. & Schuman, E. M. Ubiquitin, the proteasome and protein degradation in neuronal function and dysfunction. *Nature Rev. Neurosci.* **9**, 826–838 (2008)