Neuronal plasticity regulated by the cytoskeletal-associated proteins Eml1, Eml4 and synaptopodin

Houtman SH, De Zeeuw CI, French PJ
Department of Neuroscience, Erasmus MC, Rotterdam

Microtubules are polymers made up of α and β-tubulin subunits that provide architectural support for eukaryotic cells. In neurons, they are required for the growth and maintenance of neuronal processes. Furthermore, microtubules act as pathways for transport of cytoplasmic constituents. Structural binding proteins control the dynamics of microtubules by regulating the growth and shrinkage at the plus ends. In dividing sea-urchin (Strongylocentrotus purpuratus) eggs, a 77 kDa echinoderm microtubule associated protein (EMAP) is the major microtubule binding protein. Several mammalian homologues of EMAP, EML_{1-5} (EMAP like proteins 1-5), have been identified, and a growing picture is emerging that the EML protein family are a novel class of microtubule destabilizing proteins. Interestingly, the presence of tubulin and associated proteins has been reported within dendritic spines and it has been suggested that microtubules can contribute to changes in their morphology. We are currently examining whether Eml proteins support morphological changes in neurons and dendritic spines. Furthermore, recent observations have demonstrated an association between rat-Eml2 and the δ2 glutamate receptor, a protein known to be required for the expression of cerebellar long-term depression. The δ2-interacting domain of Eml2 is highly conserved among other Eml proteins and we are exploring the possibility that Eml proteins, by their putative association of glutamate receptors, are involved molecular mechanisms that support changes in synaptic efficacy.
Morphological changes of dendritic spines may also be induced by changes of the actin-cytoskeleton. Synaptopodin is a protein that associates with the actin cytoskeleton and is upregulated following electrical stimulation (e.g. induction of LTP). Since synaptopodin is localized to the spine-neck, it can be hypothesized that synaptopodin is involved in the morphological changes of dendritic spines after the induction of LTP. Indeed, our results demonstrate that synaptopodin, by modifying the actin-cytoskeleton, can induce morphological changes in transiently transfected Cos7 cells.

Simone H. Houtman, Department of Neuroscience, Erasmus MC, P.O. Box 1738, 3000 DR Rotterdam, t 010-4087407, e-mail s.houtman@erasmusmc.nl

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