How Myosin-Va Targets the Endoplasmic Reticulum Calcium-Store to the Dendritic Spines of Purkinje Neurons

by Wolfgang Wagner

National Health Lung and Blood Institute, NIH, Bethesda, USA

Abstract:

The intracellular localization of organelles and membrane-bound compartments to the right place at the right time is of fundamental importance for the function of eukaryotic cells. A striking example for this notion is the distribution of the endoplasmic reticulum (ER) calcium store within Purkinje neurons. These neurons are central signal integrators within the cerebellum, a part of the brain that is important for movement coordination and fine-tuning. Synaptic plasticity (a use-dependent change in synaptic efficacy) in the form of synaptic long-term depression (LTD) expressed in Purkinje neurons was postulated to underlie cerebellar motor learning.

Purkinje neurons receive excitatory input via synapses on small, actin-filament rich protrusions called dendritic spines. Importantly, the presence of tubular extensions of the ER within the Purkinje neuron spines is required for the postsynaptic calcium signaling that induces LTD. Interestingly, mutations in myosin-Va abolish the localization of ER to spines of Purkinje neurons and, consequently, cerebellar LTD. Myosin-Va is a cytoskeletal motor that moves processively along actin filaments in vitro.

To define how the myosin is responsible for ER localization in Purkinje neurons, we used live cell microscopy of cerebellar cultures as well as molecular and genetic tools, including a novel, efficient method that we developed to express cDNAs in cultured Purkinje neurons. We demonstrated that myosin-Va is a cargo transporter that associates with ER to move the organelle along actin filaments into the spines of Purkinje neurons.

Furthermore, using two-photon laser glutamate uncaging, we determined at the single spine level that myosin-Va-mediated ER targeting is essential for a metabotropic glutamate receptor-dependent calcium transient that is locally restricted to the Purkinje neuron spine. Taken together, our work provided novel insight into the basic function of myosin-Va in mammalian cells by showing that this myosin acts as a point-to-point cargo transporter. By providing direct evidence that myosin-Va transports the ER, we also defined a novel mechanism of ER motility in mammalian cells. We are currently investigating how myosin-Va is physically linked to the spine ER in Purkinje neurons.

Thursday, May 26th, 2011, 13:00

Room 813, LMU

Institut für Zelluläre Physiologie

Schillerstr. 44, 80336 München

Contact:

Claudia Veigel, claudia.veigel@med.uni-muenchen.de , phone: 089 / 2180-75510