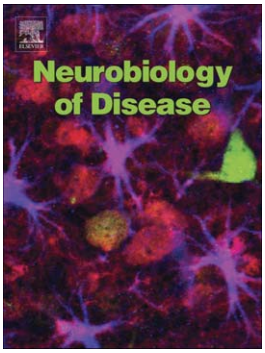

Miro sculpts mitochondrial dynamics in neuronal health and disease

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Miro sculpts mitochondrial dynamics in neuronal health and disease

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Key words

Mitochondria; Miro; mitophagy; trafficking; Calcium sensing

Abstract

Neurons are highly polarised cells with an elaborate and diverse cytoarchitecture. But this complex architecture presents a major problem: how to appropriately distribute metabolic resources where they are most needed within the cell. The solution comes in the form of mitochondria: highly dynamic organelles subject to a repertoire of trafficking, fission/fusion and quality control systems which work in concert to orchestrate a precisely distributed and healthy mitochondrial network. Mitochondria are critical for maintaining local energy supply and buffering Ca2+ flux within neurons, and are increasingly recognised as being essential for healthy neuronal function. Mitochondrial movements are facilitated by their coupling to microtubule-based transport via kinesin and dynein motors. Adaptor proteins are required for this coupling and the mitochondrial Rho GTPases Miro1 and Miro2 are core components of this machinery. Both Miros have Ca2+-sensing and GTPase domains, and are therefore ideally suited to coordinating mitochondrial dynamics with intracellular signalling pathways and local energy turnover. In this review, we focus on Miro's role in mediating mitochondrial transport in neurons, and the relevance of these mechanisms to neuronal health and disease.

Introduction

A disproportionate amount of the body's resting energy production is used by the nervous system, primarily to reverse the ion fluxes that underlie action potential generation and synaptic transmission (Harris et al., 2012). Mitochondria play a pivotal role in producing cellular energy in the form of ATP, but they also buffer and sequester intracellular Ca2+ and thus their localisation can influence the dynamics of intracellular Ca2+ signalling. Neurons are highly complex in terms of their spatial configuration and they can be very large in size -- human motor neuron axons can be up to a metre