How the stress-induced protein DRR1 modulates actin dynamics

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Abstract

Being previously known as a potential tumor suppressor, DRR1 was recently characterized as a direct link between stress, actin dynamics, synaptic efficacy and complex behaviour at our institute. It was shown to localize to actin-rich cellular structures and primarily to synapses in neurons. While it decreases neurite outgrowth, reduces LTP magnitude and spine density and enhances paired-pulse facilitation in CA3-CA1 hippocampal neurons, mice with viral DRR1-overexpression show enhanced cognitive performance (Schmidt et al., 2011). These findings suggest a protective function of DRR1 during stress as a counterbalance of adverse stress effects. Its relevance becomes evident as failing of stress coping imposes an increased risk for depression, anxiety or post-traumatic stress disorder.

Currently we are dissecting the molecular mechanism, cellular and synaptic function of this intriguing protein with *in vitro* and *ex vivo* studies. It exerts a three-fold effect on actin dynamics by bundling filaments, inhibiting their elongation but also enhancing nucleation of new filaments. Altogether, these effects increase the overall cellular F-actin content. As the most prominent cytoskeletal component at the synapse, actin is a major player in many processes impacting on synaptic transmission: synaptic shape, neurotransmitter vesicle release and post-synaptic receptor distribution. However, up to now, a profound mechanistic understanding of the pathway from stress to neuronal reorganization and cognitive performance remains elusive. A better understanding of this pathway may help in identifying novel treatment strategies for stress-associated psychiatric disorders.

Assuming that the mechanism of DRR1 is not only significant for coping with chronic stress but also during tumor development and progression, elucidating DRR1's mechanism of action could contribute to several physiologically relevant processes.