Journal club

SRF REGULATION — ACTIN BRANCHES OUT

Almost 20 years ago, Caroline Hill and Richard Treisman published evidence suggesting that the transcription factor serum response factor (SRF) is activated by RHO-mediated cytoskeletal actin dynamics (Hill *et al.*), a concept that is now fully accepted.

The SRF cofactors of the myocardin-related transcription factor (MRTF) family sense cytoplasmic actin polymerization by reversibly binding monomeric G-actin. The incorporation of monomeric G-actin into F-actin filaments in the cytoplasm releases MRTF, which translocates to the nucleus to elicit SRF-directed transcription. As SRF and its cofactors regulate the transcription of genes that are involved in cell proliferation, cell motility and cell adhesion, these cellular processes are controlled by this autoregulatory circuit.

It was thought that the sequestration of MRTF proteins in the cytoplasm by monomeric G-actin

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regulated MRTF-mediated activation of nuclear SRF. However, new evidence suggests that this scenario is fine-tuned by both cytoplasmic and nuclear actin dynamics. Nuclear forms of actin were identified and found to determine the persistence and activity of MRTF in the nucleus. First, the nuclear export of MRTF and the associated termination of MRTF–SRF-dependent transcription are guided by nuclear G-actin (Vartiainen *et al.*). Second, the formin-dependent polymerization of actin in the nucleus, which probably reduces the levels of nuclear G-actin that can engage in MRTF export, leads to the activation of SRF (Baarlink *et al.*). Third, using the MRTF–SRF paradigm, a functional link between nuclear actin dynamics and the nuclear lamina was described (Ho *et al.*). Fourth, the nuclear protein MICAL2, which promotes the depolymerization of nuclear actin upon redox stimuli, also facilitates the depletion of nuclear G-actin, which enables MRTF to accumulate in the nucleus and to stimulate MRTF–SRF-dependent gene expression (Lundquist *et al.*).

Collectively, these papers have refined our understanding of nuclear actin dynamics and deepened our insight into how actin controls gene expression. Already, interesting new links between nuclear architecture, gene control and disease formation have been indicated (Ho *et al.*), which hold promise as therapeutic targets that could be pharmacologically modulated to regulate gene expression.

Alfred Nordheim

Department of Molecular Biology,
Interfaculty Institute of Cell Biology,
Eberhard Karls University Tübingen,
Auf der Morgenstelle 15, 72076 Tübingen,
Germany

e-mail:

alfred.nordheim@uni-tuebingen.de
The author declares no competing interests.

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