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Editorial

Signaling towards actin nucleation: evolutionary aspects

Actin microfilaments fulfill a crucial role for intracellular dynamics and architecture. De novo nucleation of microfilaments often heralds the morphogenetic response to external and internal signals and the molecular components of actin nucleation have therefore attracted considerable attention during the last years. The organization of microfilaments into different arrays that fulfill specific functions differs between different organisms and that would argue for considerable diversity in terms of molecular components.

In their recent review article, Cvrčková et al. (Protoplasma 224: 15–31, 2004) have surveyed this issue by taking into account recent findings from the slime mold *Dictyostelium discoideum* and plants. They have demonstrated that most components of actin nucleation are fairly conserved in terms of sequence – beginning with the actins themselves, which despite the existence of several isoforms, are almost identical, and extending to the core machinery of nucleation either through the Arp2/3 complex or through the formins.

One would therefore expect that the regulatory chains linked to this core machinery should be quite diverse. But even at this level, certain aspects have been shown to be conserved. For instance, the involvement of Rho-related small GTPases seems to be a common theme of actin regulation. By comparing the domain structure rather than the sequence similarity of the proteins involved, those authors have even come to the conclusion that the formin-mediated nucleation and the WASP-activated Arp2/3-mediated nucleation of actin microfilaments share a number of functional and regulatory elements.

The work of Kłopocka et al. in this issue (pp. 77–84) can be read as case study for the evolution of actin nucleation. Using *Amoeba proteus* as a model, they investigate the role of the myosin I heavy chain kinase (MIHCK) in this primitive organism. They use microinjection of antibodies against the catalytic domain of *Acanthamoeba castellanii* MIHCK and observe that to some extent the resulting phenotype resembles that of cells microinjected with antibodies against the small GTPase Rac antibodies. Moreover, MIHCK and Rac show a similar subcellular localization in *A. proteus*. The authors go on to show that a high-speed supernatant of *A. proteus* has an enhancing effect on the polymerization of fluorescently labelled actin, an effect that can be blocked by preincubation with anti-Rac1 antibodies. These observations suggest that MIHCK may be one of the effectors for Rac in these extremely large cells. Previous work has shown that mammalian Cdc42 (a further member of the Rho-type superfamily of GTPases) can control the nucleation of *Acanthamoeba castellanii* actin via the Arp2/3 complex (R. D. Mullins, T. D. Pollard, Curr. Biol. 9: 405–415, 1999). The sequence of events is consistent with the usual pattern in which active Cdc42 binds to WASP/Scar proteins and this complex in turn activates Arp2/3 proteins initiating actin nucleation and/or filament branching. Thus, already at the base of evolution the basic players in the game of actin nucleation seem to be not only present but also functionally equivalent.

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