# Actin dynamics

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The figure shows the dendritic nucleation hypothesis for the assembly of actin filament networks at the leading edge of motile cells (Pollard et al., 2000). In this model, the actin-monomer-binding protein profilin (shown in black), with help in vertebrate cells from thymosin β4 (not shown), maintains a pool of unpolymerized ATP-actin subunits (shown in lighter blue). Extracellular stimuli such as chemotactic factors bind to plasma membrane receptors, activating intracellular signalling molecules including Rho family GTPases. These GTPases bind to and activate WASP/Scar family proteins (shown in green) by freeing them from autoinhibition. Active WASP/Scar proteins bring together an actin monomer and Arp2/3 complex (shown in red), an assembly of seven subunits including two actin-related proteins. Arp2/3 complex then initiates the growth of a new actin filament as a branch on the side of an older actin filament. The branch grows rapidly at its barbed end by addition of actin-profilin complexes. As it grows, it pushes the plasma membrane forward. The new filament elongates for a second or two until it is capped by capping protein (shown in yellow).

Incorporation of ATP-actin into a filament promotes hydrolysis of the bound ATP, a reaction with a half-time of a few seconds. Gamma phosphate dissociates slowly from polymerized ADP-P-actin subunits with a half time of 6 minutes, unless an ADF/cofilin protein (shown in gray) binds to a subunit and accelerates phosphate dissociation. Dissociation of phosphate promotes dissociation of branches from Arp2/3 complex and binding of ADF/cofilin to ADP-actin subunits (shown in darker blue). ADF/cofilin bound to filaments promotes severing of the filaments and dissociation of ADP-actin bound to ADF/cofilin. Profilin is the nucleotide-exchange factor for actin and promotes the exchange of ADP for ATP. Profilin then binds tightly to ATP-actin monomers, refilling the actin monomer pool. Rho family GTPases also activate p21-activated protein kinase (PAK), which stimulates LIM kinase to phosphorylate ADF/cofilin. Phosphorylation inactivates ADF/cofilin and slows down the rate of filament disassembly.

## REFERENCE

**Pollard, T. D., Blanchoin, L. and Mullins, R. D.** (2000). Biophysics of actin filament dynamics in nonmuscle cells. *Annu. Rev. Biophys. Biomolec. Struct.* **29**, 545-576.

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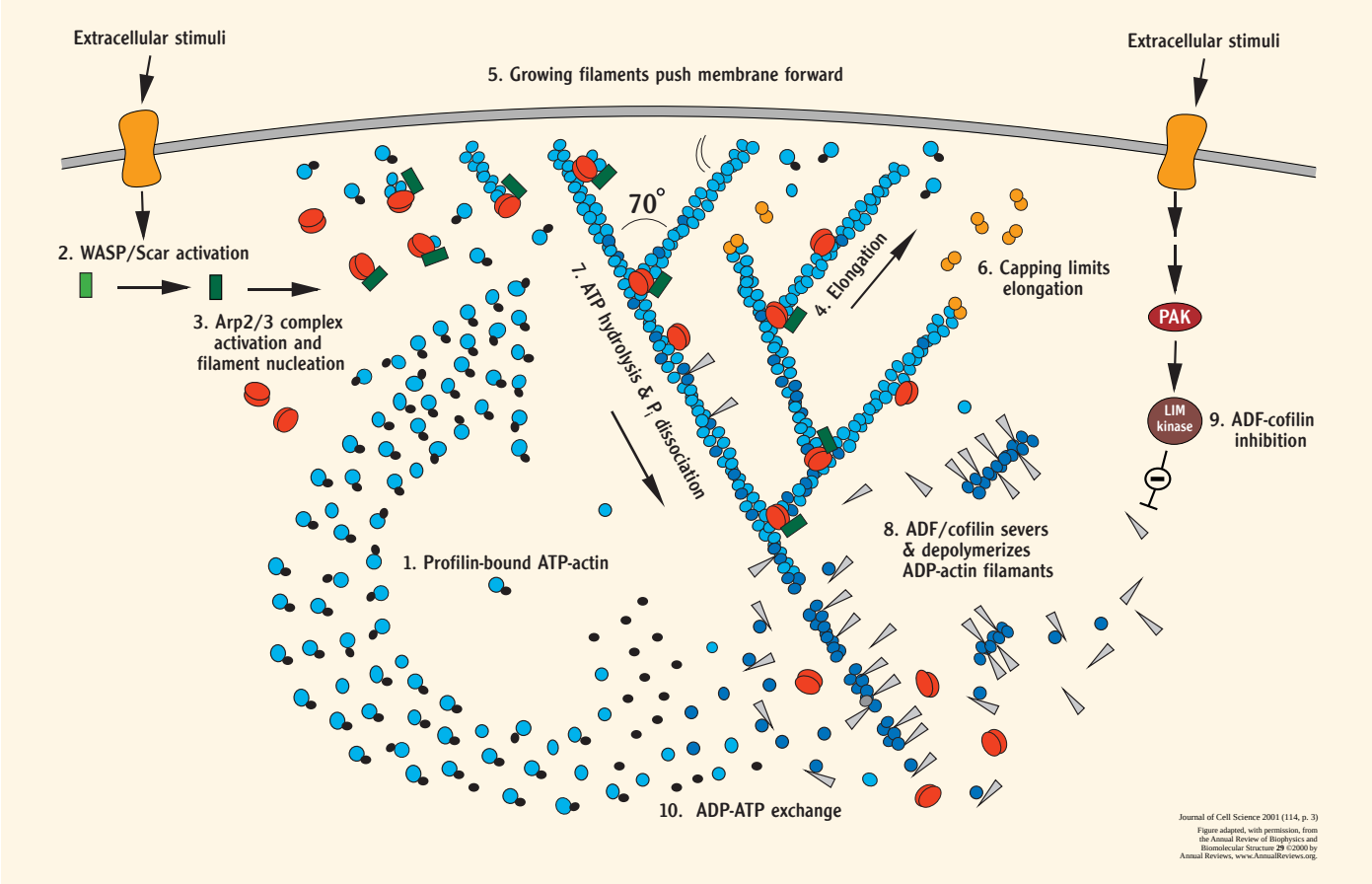


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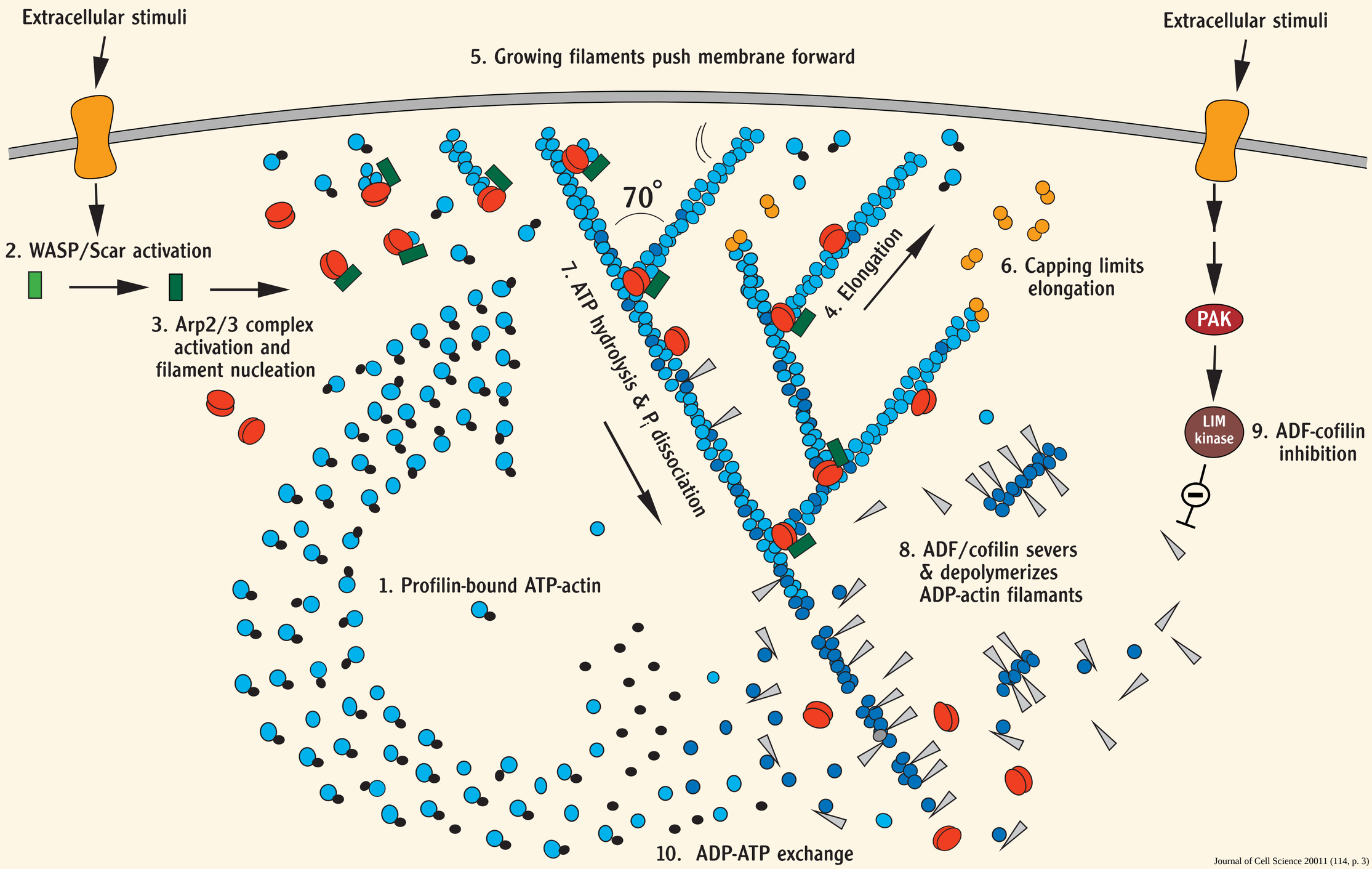


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