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Mechanism of formin-associated actin filament elongation DIMITRIOS VAVYLONIS, Columbia University, Yale University, DAVID R. KOVAR, University of Chicago, BEN O'SHAUGHNESSY, Columbia University, THOMAS D. POLLARD, Yale University — Formins control the kinetics of actin filament polymerization by remaining processively attached at the growing filament end. The FH2 formin domain associates with the barbed end while FH1 interacts with profilin and is thought to mediate profilin-actin polymerization. We combined TIR microscopy (Kovar et al., Cell, in press) with theoretical modeling to study the dependence of the rate of formin-associated actin filament elongation on profilin and actin concentrations. We assume a transfer mechanism of profilin-actin from FH1 to the barbed end, gated by FH2 as described by the gating parameter p measuring the accessibility of the barbed end. The model explains the main experimental trends and rationalizes (i) how filaments associated with formin mDia1 elongate more rapidly than formin-free filaments due to the the large number of profilin binding sites and p 1, and (ii) how filaments associated with formins with p¡1 elongate slowly in the absence of profilin but more rapidly in the presence of profilin. High profilin concentrations suppress elongation and in the model this is attributed largely to the saturation of FH1 by profilin. Consistent with our ADP-actin experiments, the proposed mechanism does not require ATP hydrolysis though we cannot exclude the possibility that formin translocation accelerates ATP hydrolysis for ATP-actin.

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