# Title

Mechanical stimulation induces formin-dependent assembly of a perinuclear actin rim

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# Abstract

Cells constantly sense and respond to mechanical signals by reorganizing their actin cytoskeleton. Although a number of studies have explored the effects of mechanical stimuli on actin dynamics, the immediate response of actin following force application has not been studied. We designed a method to monitor the spatiotemporal reorganization of actin following cell stimulation by local force application. We found that force could induce reversible actin polymerization in the perinuclear region within ~ 2 minutes. This actin reorganization was triggered by an intracellular Ca2+ burst induced by force application. Treatment with the calcium ionophore A23187 recapitulated the force induced perinuclear actin remodeling. Blocking of either actin polymerization or depolymerization inhibited perinuclear actin remodeling. Overexpression of KASH domain to displace nesprin from the nuclear envelope did not abolish Ca2+-dependent perinuclear actin assembly. However, the ER and nuclear membrane-associated inverted formin-2 (INF2), a potent actin polymerization activator, was found to be required for perinuclear actin assembly. The perinuclear actin rim structure co-localized with INF2 upon stimulation, and INF2 depletion resulted in attenuation of the rim formation. Experimental results, together with numerical simulation, suggest a scenario, where force-induced Ca2+ burst triggers actin depolymerization and a transient increase in G-actin level, which in turn activates INF2 and leads to perinuclear actin assembly. Our work suggests that cells can respond to external force immediately by remodeling perinuclear actin in a unique Ca2+- and INF2-dependent manner.

**Key words:** force, mechanotransduction, calcium, formin, perinuclear actin rim