Crosstalk between myosin IIA filaments, integrin-mediated cell-matrix adhesions, and microtubules

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Actomyosin cytoskeleton and cell-matrix adhesions are the key elements determining cell morphogenesis. Transmembrane integrin receptors trigger the assembly of various types of actin filament-based adhesion structures, such as focal adhesions, filopodia, and podosomes. These structures are all myosin-IIA-dependent but their dynamics and function are controlled by myosin-IIA-filaments in a differential manner. In particular, assembly of myosin-IIA-filaments promotes growth of focal adhesions but disrupts podosomes. A feedback response from the integrin adhesions to the myosin IIA filaments is in part mediated by another essential cytoskeletal system, microtubules. Guanine nucleotide exchange factor GEF-H1 is trapped and inactivated by microtubules when they are coupled with integrin adhesions via KANK family proteins. Uncoupling microtubules from the integrin adhesions allows the release and activation of GEF-H1 followed by triggering Rho/Rho kinase (ROCK) pathway, and thereby the assembly of myosin IIA filaments, which in turn remodel the adhesions. These regulatory processes may play a role in cell migration and angiogenesis.

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