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Spatiotemporal control of the forces that drive cell rearrangements within multicellular tissues

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The local rearrangements of cells within multicellular tissues are actively driven by forces generated in the actin-myosin cytoskeleton. During development, these forces are patterned to bias or orient cell rearrangements, resulting in changes in tissue shape and structure that build functional tissues and organs. We use the fruit fly embryo as a model system, where polarized patterns of myosin activity are required for oriented cell rearrangements that drive rapid tissue elongation along the head-to-tail axis. To uncover mechanisms of how active, myosin-generated forces drive cell rearrangement, we quantify how perturbations to myosin activity influence the number, speed, and orientation of rearrangements. First, to investigate microscopic mechanisms by which myosin drives contraction of cell edges to initiate rearrangement, we generated myosin variants predicted to alter the speed at which myosin translocates actin filaments. These myosin variants display slowed turnover dynamics at cell edges and result in decreased numbers of cell rearrangements, indicating a role for myosin-driven actin sliding during rearrangement. Next, to study how myosin activity levels influence cell rearrangements, we generated myosin variants that mimic the active, phosphorylated state of myosin. These variants accelerate rearrangements but, surprisingly, also alter the spatial pattern of forces in the tissue and result in reduced tissue elongation. These myosin variants increase the rate of cell edge contraction but cause defects in the formation of new contacts between cells. Finally, we discuss how higher-order, collective cell rearrangements called rosettes are influenced by these perturbations to myosin activity. *This work is in collaboration with D. Farrell and J. Zallen at the Sloan Kettering Institute.*