Morphogenesis in *Drosophila* requires nonmuscle myosin heavy chain function

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We provide the first link between a known molecular motor and morphogenesis, the fundamental process of cell shape changes and movements that characterizes development throughout phylogeny. By reverse genetics, we generate mutations in the *Drosophila* conventional nonmuscle myosin (myosin II) heavy chain gene and show that this gene is essential. We demonstrate that these mutations are allelic to previously identified, recessive, embryonic-lethal *zipper* mutations and thereby identify nonmuscle myosin heavy chain as the *zipper* gene product. Embryos that lack functional myosin display defects in dorsal closure, head involution, and axon patterning. Analysis of cell morphology and myosin localization during dorsal closure in wild-type and homozygous mutant embryos demonstrates a key role for myosin in the maintenance of cell shape and suggests a model for the involvement of myosin in cell sheet movement during development. Our experiments, in conjunction with the observation that cytokinesis also requires myosin, suggest that the processes of cell shape change in morphogenesis and cell division are intimately and mechanistically related.

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The development of metazoan form is characterized by complex cell shape changes and cell sheet movements, whose molecular basis has not been established. A number of studies suggest a key role for the cytoskeleton, the cell surface, and the extracellular matrix in morphogenesis (for review, see Armstrong 1985; Ettensohn 1985; Fristrom 1988; Fessler and Fessler 1989). To date, the most compelling evidence that microfilaments participate in these developmental processes comes from pharmacological studies. For example, cytochalasins can disrupt global morphological changes during neural tube formation in vertebrates (e.g., Burnside 1971), embryo elongation in nematodes (Priess and Hirsh 1986), and epiboly in teleosts (Betchaku and Trinkaus 1978). In addition, these drugs abolish neurite elongation and the establishment of neuron polarity—extreme examples of individual cell shape changes (e.g., Letourneau et al. 1987). Such studies suggest that a detailed understanding of morphogenesis will require a catalog of the molecular motors responsible for cell movement and cell shape change, the molecular switches that regulate the function of such motors, and the cytoskeletal elements with which they interact to produce and transmit force.

Myosins are molecular motors with widespread expression in both muscle and nonmuscle cells where they participate in diverse processes. Conventional myosins (myosins II) are molecular motors composed of two identical heavy chains and two pairs of light chains (Warrick and Spudich 1987; Korn and Hammer 1988; Spudich 1989; Kiehart 1990; Kiehart et al. 1990). Myosin heavy chains, in concert with a filamentous actin substrate, alone may be sufficient for chemomechanical force production, whereas the light chain subunits apparently function to regulate and modify heavy chain activity. Nonmuscle (or cytoplasmic) myosins II are required for cytokinesis in dividing cells: Microinjection of anti-myosin II antibody blocks cytokinesis in echinoderms (Mabuchi and Okuno 1977; Kiehart et al. 1982), gene disruption and antisense experiments show that myosin II is required for cytokinesis in *Dictyostelium* (De Lozanne and Spudich 1987; Knecht and Loomis 1987; for review, see Spudich 1989), and a mutation in the nonmuscle myosin regulatory light chain [*spaghetti-squash* (*sqh*)] blocks cytokinesis in *Drosophila* (Karess et al. 1991). However, in metazoans, myosins II are also conspicuous components of postmitotic cells, suggesting that there are key roles for this protein beyond its contribution to cell division. Antibody microinjection experiments in *Drosophila*, for example, demonstrate that myosin II may participate in nuclear migration and in the maintenance of the cell (embryo) cortex (Kiehart et al. 1990; D. Lutz and D.P. Kiehart, unpubl.). In addition, studies on lower eukaryotes have shown that conventional myosin is required for nuclear migration in yeast (Watt et al. 1987) and for the distribution of cell-surface receptors and development in *Dictyostelium* (Spudich 1989).

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