

Fly Division

Kathryn G. Miller* and Daniel P. Kiehart[‡]

*Department of Biology, Washington University, St. Louis, Missouri 63130, and[‡]Department of Cell Biology, Duke University Medical Center, Durham, North Carolina 27710

STUDIES in animal cells (reviewed by Rappaport, 1986; Satterwhite and Pollard, 1992; Fishkind and Wang, 1995) provide a view of cytokinesis whereby in each dividing cell, a contractile ring of interdigitated anti-parallel actin and bipolar myosin (nonmuscle myosin II) filaments forms in the equatorial region of the cell cortex, and then constricts, in purse string-like fashion, to pinch the cell in two. A number of key questions about this process remain unresolved. An understanding of the signal(s?) that spatially and temporally orchestrate ring formation is lacking. A comprehensive catalog of the proteins that act in concert with actin and myosin to form the ring is also not yet available. In addition, our knowledge of how the ring is integrated into the cortex at large and is associated with the plasma membrane is only rudimentary. Finally, molecular mechanisms by which each protein contributes to the assembly of the complex, supramolecular structure of the ring and functions in chemomechanical force production are far from clear.

The multidisciplinary approaches that are being applied in *Drosophila* are likely to provide insight into the many aspects of furrow function that remain poorly understood. Recently, genetic approaches have identified several new proteins that are required for cytokinesis and cell biological and biochemical methods have revealed proteins that localize in cytokinetic structures. Together, these findings have expanded the list of the molecules implicated in cytokinesis and are harbingers of a new understanding of cytokinesis at the molecular level.

Drosophila as a Model System for Studies of Cytokinesis

A unique feature of the life cycle of the fly are the three distinct cortical contractile events (cytokinetic events) that are coupled with the cell cycle (see Fig. 1). Typical cytokineses, complete with actomyosin contractile rings, typify many cell divisions in the organism (panel A). There is every reason to believe that such cytokineses provide a "perfect" model for animal cytokinesis. Two additional cortical structures, formation of which is precisely coordinated with the cell cycle are not found in most organisms. These are the metaphase furrows in the pre-cellular (syncytial)

blastoderm (panel B), and the furrow canals of the cellularizing embryo (panel C). Metaphase furrows (or pseudo-cleavage furrows) are transient membrane invaginations that occur during late prophase to anaphase of mitotic cycles 11 to 13. The invaginations isolate individual mitotic apparatuses and prevent aberrant chromosomal attachments and "colliding mitoses." Metaphase furrows contain actin, myosin, and at least some of the other components typically found in cleavage furrows of true cytokinesis; however, they fail to effect cleavage and instead, regress during late anaphase. Later, during G1 of interphase of mitotic cycle 14, comparable furrowing occurs, but, in contrast, continues deep into the cortical cytoplasm. In this process of "cellularization" the furrows proceed beyond the nuclei, finally undergoing a complex and unusual shape change that packages each of the nuclei into an individual, columnar epithelial cell. This furrowing event lasts for almost an hour, making study of it much easier than study of conventional furrows, which are short-lived. Like the metaphase furrows, the furrow canals are associated with a cup of actin and myosin that are positioned to provide force for cortical and membrane invagination. Both metaphase furrowing and cellularization share many fundamental features with typical animal cytokinesis. Nevertheless, their complex geometry and precise timing with respect to the cell cycle indicate that they are likely to differ in molecular detail from more typical cytokineses. The ring canals that form during oogenesis (Knowles and Cooley, 1994) are additional cortical structures that contain actin and myosin II. However, they will not be considered here, since they are not contractile.

Each of the cytokinetic events described above is amenable to a number of complementary approaches. Reverse genetics (i.e., starting with a protein and using appropriate strategies to generate mutants) has been useful for investigating the function of known molecular players (e.g., myosin II). Biochemical approaches have been used to identify key components of the contractile apparatus through a general search for actin binding proteins (Miller et al., 1989). Studies demonstrating that one of these, anillin, is a novel furrow component are presented in this issue (Field and Alberts, 1995). These approaches complement those based on the awesome power of fly genetics; that is, a forward genetic screen for mutants with defects in cell division (forward or "classical" genetics defined as starting with a phenotype and molecularly characterizing the gene in which there is a defect).

Classic genetic strategies capitalize on specific features

Address correspondence to K. G. Miller, Dept. of Biology, Box 1229, Washington University, 1 Brookings Drive, St. Louis, MO 63130. Tel.: (314) 935-7305. Fax: (314) 935-5125. E-mail: miller@biodec.wustl.edu.; or to D. P. Kiehart, Dept. of Cell Biology, Box 3709, Duke University Medical Center, Durham, NC 27710. Ph.: (919) 681-8079. Fax: (919) 684-5481. E-mail: dan_kiehart@cellbio.duke.edu.

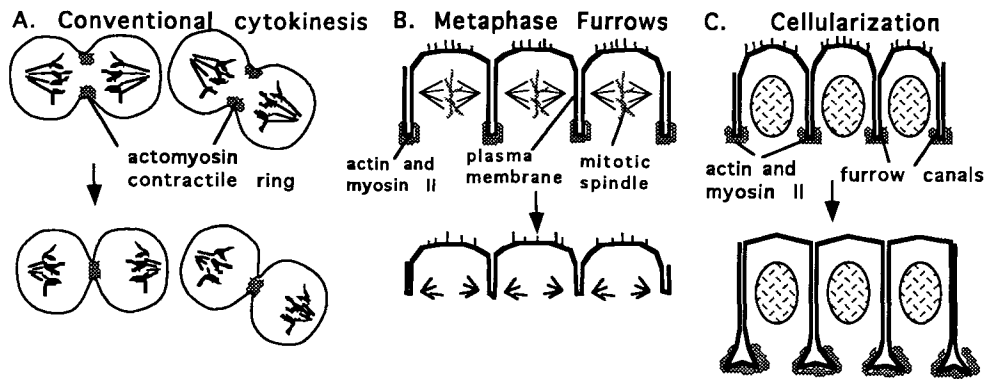


Figure 1. Schematic representation of the three cytokinetic events that occur during the *Drosophila* life cycle. The shading represents regions where actin and myosin II colocalize.

of *Drosophila* biology and the timing of these different cytokinetic events during development. A majority of gene products required for cytokinesis are maternally loaded. Specifically, this means that even in animals whose zygotic genotype is mutant for a component required for cell division, wild type gene product is contributed by the heterozygous mother during oogenesis. This wild type gene product can support cell division through cellularization of the blastoderm. Subsequently there is minimal proliferation of cells during embryonic and larval stages, so animals with mutations in many of these components can survive with only maternally provided protein until pupation. Imaginal cells fated to contribute to the adult proliferate during larval life, but are not required until metamorphosis. Mutants that have cell division defects lack this imaginal tissue and fail to progress beyond late larval or early pupal stages (e.g., Gatti and Baker, 1989; Karess et al., 1991). Contrasting with screens for defects in imaginal cells are screens for maternal effect mutations in which the embryonic mutant phenotype depends only on the genotype of the mother. This type of screen can identify maternally contributed proteins that are required for metaphase furrow formation and cellularization (e.g., Sullivan et al., 1993). Moreover, because such screens can identify partial loss-of-function alleles whose most severe effects are on early cytokinetic events, genes that contribute to all three contractile events can be recovered. A variety of other genetic screens are also revealing new components involved in cytokinesis (for examples see Hime and Saint, 1992; Lehner, 1992; Castrillon and Wasserman, 1994; Neufeld and Rubin, 1994; Edwards et al., 1994; for a review of techniques see Wolfner and Goldberg, 1994).

Myosin II Is a Key Motor That Acts on Actin Filaments to Catalyze Cleavage

The metaphase furrows, furrow canals of the cellularizing embryo and the contractile rings that typify cytokinesis for pole cell formation, and cell division later in the life of the fly each are rich in nonmuscle isoforms of both actin and myosin II. Genetic analysis of actin isoforms has not been performed in flies. Reverse genetic studies showed that myosin II is necessary for cell shape changes for both cytokinesis and cellular morphogenesis (Karess et al., 1991; Young et al., 1993; Wheatley et al., 1995; Edwards, K., and D. P. Kiehart, unpublished results) and that cytokinesis can be treated as a myosin-driven shape change that is closely coordinated with the cell cycle. Partial loss-of-function of the *spaghetti squash* (*sqh*) gene that encodes the regulatory light chain of *Drosophila* nonmuscle myosin II

(Karess et al., 1991) causes a failure in cytokinesis of imaginal tissue and, like other such mutants, *sqh* animals die as early pupae. In contrast, complete loss-of-function of the *zipper* gene that encodes the myosin heavy chain causes defects in tissue morphogenesis that result in embryonic death, independent of myosin's role in cytokinesis (Young et al., 1991, 1993). Two tools allow investigation at the cellular level of lethal mutations at other times in the life of the fly: clonal analysis, which produces a small patch of mutant tissue on an otherwise phenotypically wild type fly; and selective conditional expression of wild type alleles on a mutant background. Clonal analysis of *zipper* mutations and conditional expression of wild type *sqh* rescue constructs in a *sqh* mutant background confirm that both the myosin heavy and regulatory light chains are required for cytokinesis at a number of different stages of fly development (Edwards, K. A., R. A. Montague, and D. P. Kiehart, unpublished results). Further studies of these mutants using reagents and tools available in *Drosophila* promise to reveal the mechanisms by which myosin in the ring is regulated and the proteins with which it interacts.

New Molecules Involved in Animal Cell Cytokinesis

Three new proteins have been identified that localize to the sites of contractile activity during all three cleavage events: Anillin (Field and Alberts, 1995; the subject of an article in this issue), Pnut (Neufeld and Rubin, 1994), and SEP1 (Fares, H., M. Peifer, and J. R. Pringle, personal communication). They colocalize with myosin II; however, they all persist in the furrow region (at least during cytokinesis) after myosin disappears. During cytokinetic events, they are all specific for the furrow and do not associate with other parts of the actin cytoskeleton. There is no evidence that these proteins bind to myosin II, although anillin does bind to actin. Together, myosin II and these three proteins appear to define an important functional domain of the actin cytoskeleton. Anillin does not colocalize with myosin II during other cell shape changes in which myosin II plays an important role, while Pnut and SEP1 do. Thus, anillin may be important for generating or stabilizing furrow-specific actin structures, while Pnut and SEP1 may be more generally involved in myosin-based contractile structures.

A novel feature of anillin is that after cellularization, it cycles between the cortex and the nucleus. This behavior is unlike other proteins associated with the actin cytoskeleton and potentially provides a direct link between the mitotically active, cycling nucleus and the actin cortex which must effect cytokinesis in phase with mitosis. It is not clear

whether anillin has a function in the nucleus, but the authors speculate that its nuclear localization may prevent it from actively modulating the structure or function of the actin cytoskeleton inappropriately during interphase. Anillin's predicted amino acid sequence is not particularly revealing; however, it does have sequence motifs that are shared by other cytoskeletal proteins such as paxilin, radixin and zyxin. Anillin has not yet been identified in other organisms and no genetic data is yet available for anillin. Reverse genetic studies should be straightforward.

Pnut and SEP1 are members of the septin family of proteins. Septins were first discovered in yeast, where they are present at the bud neck and are required for cytokinesis. The *peanut* gene (Neufeld and Rubin, 1994) is also required for cytokinesis in fly. Complete loss-of-function mutations are lethal, again causing death in pupae due to the failure of imaginal tissue to proliferate. Additional *Drosophila* septins, *sep1* and *sep2* were recovered in a PCR screen for genes with sequence similarity to the yeast septins (Pringle, J. R., personal communication), but only *sep1* has been further characterized. The defect in cytokinesis due to loss of *peanut* function and protein localization to the furrows suggest that there may be conservation of function during completion of cytokinesis between yeast and animal cells, despite the fact that other aspects of the mechanisms of cell division appear quite distinct (for discussion see Sanders and Field, 1994).

Further support for the idea that mechanisms of cell division in yeast and animal cells might be similar comes from studies on *diaphanous* (Castrillon and Wasserman, 1994). Complete loss-of-function *diaphanous* mutants have defects in cytokinesis and a terminal phenotype similar to that described for *sqh* and *peanut* (animals die as pupae with imaginal tissue that fails to proliferate). Molecular studies on *diaphanous* reveal that it encodes a protein with homology to the budding yeast protein BNI1, which was identified through its genetic interaction with a budding yeast septin (CDC12). Interestingly, the *diaphanous* protein also has a homolog in fission yeast (ironically also called CDC12) that is essential for actin ring formation and cytokinesis and is localized in the contractile ring but not in other actin structures (Chang, F., and P. Nurse, personal communication). Another related protein is the product of the mouse *limb-deformity* gene, which may also have effects on cell proliferation. Together, the data from yeast and *Drosophila* suggests that *diaphanous* and one or more of the *Drosophila* septins collaborate in the formation and function of the contractile ring. The unique tools available in *Drosophila* should allow an analysis of the molecular basis of this interaction and its functional significance.

Other Known Molecular Players May Contribute to Cytokinetic Cortical Shape Changes in Drosophila

Some of the proteins that have been identified in other animal cells as furrow components or as required for cytokinesis have been identified in *Drosophila*. Both fission yeast and *Dictyostelium* cells lacking profilin cannot undergo cytokinesis (Balasubramanian et al., 1994; Haugwitz et al., 1994), indicating that its function is essential for this process. Mutants that affect profilin function in *Drosophila* have a wide range of defects, some of which are consistent with an effect on cell proliferation during both oogen-

esis and spermatogenesis (Verheyen and Cooley, 1994). Profilin's role may stem from its regulation of actin polymerization, but detailed investigations of why cleavage is defective have not yet been performed.

Another regulator of actin assembly, cofilin, concentrates in the cleavage furrow of mammalian cells in culture and is required for cell division in budding yeast (Moon et al., 1993 and references therein; Nagaoka et al., 1995). Cofilin's known filament severing and monomer buffering functions in vitro suggest that it may play an important role in modulating contractile ring structure. Fly cofilin (Edwards et al., 1994) is the product of the *twinstar* gene (Gunsalus et al., 1995). The examination of the *twinstar* phenotype reveals failure in the formation and function of normal contractile rings and as a result, defects in cytokinesis. Preliminary localization of the *twinstar* protein in developing embryos suggests that it is concentrated in metaphase furrows and furrow canals, but trails the very leading edge of the invagination in a pattern more like spectrin than myosin II (see below; Gunsalus, K., and M. Goldberg, personal communication).

Proteins from two families, the spectrin and the MER or ERM (moesin, ezrin, and radixin) families are key components of the membrane skeleton that mediate interactions between the cytoskeleton and the plasma membrane and are therefore potential candidates for providing a link between the contractile ring and the plasma membrane during cytokinesis. The spectrins are localized in cellularizing furrows, just behind the site at which actin and myosin likely conspire to drive cellularization and therefore may play a role in stabilizing newly formed cell surfaces (Pescrreta et al., 1989; Thomas and Kiehart, 1994 and references therein). Mutations in both α -spectrin and β -spectrin have been recovered and, to date, no effects on metaphase furrowing, cellularization, or conventional cytokinesis have been observed (Lee et al., 1993; Thomas, G. H., and D. P. Kiehart, personal communication). However, a proper search for such phenotypes has not been performed. Vertebrate furrows also contain radixin, a member of the MER family, but this membrane-cytoskeletal linker appears in the cleavage furrow due to its association with microvilli in the furrow and not the contractile ring per se (Yonemura et al., 1993). A fly MER-like protein has been identified that is similar to all three of the vertebrate proteins (Edwards et al., 1994; McCartney, B., and R. Fehon, personal communication). It is not localized with myosin II in furrow canals during cellularization (it essentially colocalizes with the spectrins) nor does it localize to furrows in post-blastoderm divisions (Montague, R., J. Crawford, and D. P. Kiehart, personal communication). Finally, filamin, another furrow component in vertebrates, was identified among the *Drosophila* proteins that bind to F-actin affinity columns (see Discussion in Field and Alberts, 1995), but it has not been characterized further. Additional localization and genetic studies of this group of proteins will be important to determine their precise contributions to furrow structure and function.

Certain Molecules Distinguish among Cytokinetic Events in Drosophila

The similarity among metaphase furrows, the furrow canals during cellularization and contractile rings in conventional cytokinesis is underscored by their common com-

ponents, which include, for example, actin, myosin II, anillin, and Pnut. Nevertheless, there are emerging molecular differences among them that may explain their structural and functional differences. Remarkably, zygotic expression of only three genes is required for cellularization: *nullo*, *bottleneck*, and *serendipity-α* (Merrill et al., 1988; Wieschaus and Sweeton, 1988). Their products are expressed only in a narrow window around the time of cellularization and mutations in them only affect cellularization (Schweisguth et al., 1990; Simpson and Wieschaus, 1990; Schejter and Wieschaus, 1993a,b). These may well be the only gene products that are not maternally provided that contribute to cellularization, since in the study that identified them, almost the entire genome's contribution was assessed. These proteins are thought to be required to modify the metaphase furrow structures to accomplish this novel cytokinesis.

All three proteins are localized to the actin-rich region of the advancing furrow canal early in the process of invagination (Postner and Wieschaus, 1994; Schejter and Wieschaus, 1993a,b). *nullo* and *serendipity-α* mutants have very similar phenotypes—the actin network formed is uneven with some regions thicker and some thinner than normal. Cellularization occurs, but furrow canals are not present between all nuclei. Often several nuclei end up within one domain of invaginating membrane. These proteins are hypothesized to stabilize the initial actin structures formed as the membrane begins to invaginate. In the mutants, the structure fails in some positions, causing the multinucleate cellularization seen. *nullo* function is required for proper localization of *serendipity-α* protein, suggesting that these two proteins might interact. *bottleneck* mutants, in contrast, appear to begin the late, fast phase of cellularization too soon. Rings of actin, which normally form and begin to contract to pinch off the forming cells at their base only after the furrow canals have invaginated deeply into the embryo, instead form and contract prematurely. Thus, *bottleneck*'s role is thought to be in regulating the transition from the hexagonal structure seen early in furrow invagination to the actin rings seen later. It may play a role in resisting contractile force of the actin rings until the appropriate developmental time.

The function of an unconventional myosin (95F myosin) is required for particle transport and metaphase furrow formation (Mermall et al., 1994; Mermall and Miller, 1995). Such transport may be important for delivery of proteins and lipid bilayer components to the invaginating furrows. Whether 95F myosin has a role in other cytokinetic events is not known. Several other as yet uncharacterized proteins, identified biochemically as actin-binding proteins in the early embryo, are also present in the mitotic furrows and enriched at the cellularization front (Miller et al., 1989). It is not yet known whether these proteins participate in conventional cleavage, nor is any molecular information available on them.

One Mutant has a Defect in Postblastoderm Cytokinesis

pebble mutants contrast with the cellularization mutants described above: so far, abnormalities have been seen only in cytokineses following the first round of post-blastoderm mitosis (Hime and Saint, 1992; Lehner, 1992). Thus, *pebble* is required specifically for cytokinesis during the postblastoderm divisions. Because early cleavage events

through cellularization of the blastoderm are completely unaffected, and all postblastoderm cytokineses fail absolutely, it seems highly unlikely that the defects in postblastoderm cytokineses are the result of a sudden lack of maternal product. This phenotype also contrasts with that of the previously described cell division mutants, which manifest defects only during later development when proliferation of imaginal discs occurs.

Maternal Effect Mutations Identify Genes Required in Early Cytokinetic Events

So far, three maternal effect mutations (embryonic phenotype depends on the genotype of the mother, see above) have been studied that cause defects in early embryonic cytokinetic events: *sponge*, *nuclear-fallout*, and *scrambled*. Embryos from *sponge* mutant mothers (*sponge* embryos) were found to lack the actin structures typical of the syncytial blastoderm, including metaphase furrows (Postner et al., 1992). In *sponge* embryos, most actin-binding proteins' organizations were disrupted, as might be expected from the lack of normal actin structures. However, one actin-binding protein (13D2 antigen) was organized normally. This suggests that *sponge* functions downstream of 13D2 antigen in cortex organization, but upstream of actin. This type of experiment is analogous to genetic epistasis analysis and is very powerful in establishing dependency relationships among proteins in the same structures. *sponge* is not required for cellularization and is unlikely to be involved in conventional cytokinesis. These data confirm that organization of the cytoskeletal structures of the syncytial blastoderm requires some unique gene functions.

scrambled (*sced*) and *nuclear-fallout* (*nuf*) cause defects in metaphase furrow formation and during cellularization (Sullivan et al., 1993), suggesting they are components common to these two processes. In *sced* mutant embryos, no metaphase furrows are apparent. In *nuf* mutant embryos, metaphase furrows are formed, but are not continuous around each mitotic spindle. While cellularization proceeds in both these mutants, it is not normal. *sced* affects the organization of actin structures of the furrow canals. In contrast, *nuf* animals have a cellularization phenotype similar to the cellularization mutants, *nullo* and *serendipity-α*, described in the preceding section. Thus, *nuf* might be a maternally provided protein that is required for *nullo* and *serendipity-α*'s activity, but this remains to be tested. The similarity in phenotype of this maternally required and the zygotically required cellularization genes supports the idea that the cellularization-specific gene products modify the structures that are present in the syncytial stage to effect this new process. While the expression of *nullo* and *serendipity-α* is restricted to cellularization, the expression pattern of *sced* and *nuf* and the molecular nature of their gene products are not known, so their contribution to later cytokineses is not clear. More complete characterization of these genes through molecular cloning should be relatively straightforward, since the mutations are transposon induced.

Conclusion/Future Prospects

Recent studies in *Drosophila* have identified new proteins whose localization to cytokinetic structures implicate their function in cell division and other new players whose mu-

tant phenotypes demonstrate that they are required for cytokinesis. Important new opportunities are provided by these mutants and the new reagents that recognize furrow components for additional cell biological, molecular and genetic studies of the problem of how furrow components collaborate to execute successful cytokinesis. Specifically, further analysis of mutant animals, using antibodies to furrow components and various genetic techniques that allow disruption of gene function in particular tissues will likely result in a more complete understanding of each protein's role. The forward genetic methods that have been used to identify maternally contributed proteins required for early events and zygotic functions involved in true cytokinesis have not been exploited to saturation, so many genes involved in these cytokinetic events remain to be discovered. A combination of genetic and biochemical analyses in *Drosophila* is likely to reveal significant new information about the process of cytokinesis in the near future. In particular, identification of the signals from microtubules and/or chromosomes that position the furrow and that coordinate its timing with the cell cycle, the additional components that anchor the ring to the membrane, the elements that control actin polymerization, the mechanism by which the organization of the ring is generated and the molecules and mechanisms that drive the process of final separation of cells are all amenable to these approaches. There is every reason to believe that the lessons we learn in *Drosophila* about cytokinesis, as in other areas, will be widely applicable and significantly enhance our appreciation and understanding of one of the amazing and complex processes that is required for all life.

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References

- Balasubramanian, M. K., B. R. Hirani, J. D. Burke, and K. L. Gould. 1994. The *Schizosaccharomyces pombe* cd3+ gene encodes a profilin essential for cytokinesis. *J. Cell Biol.* 125:1289–1301.
- Castrillon, D. H., and S. A. Wassermann. 1994. *diaphanous* is required for cytokinesis in *Drosophila* and shares domains of similarity with the products of the *limb deformity* gene. *Development.* 120:3367–3377.
- Edwards, K., R. Montague, S. Shepard, B. Edgar, R. Erikson, and D. Kiehart. 1994. Identification of *Drosophila* cytoskeletal proteins by induction of abnormal cell shape in fission yeast. *Proc. Natl. Acad. Sci. USA.* 91:4589–4593.
- Field, C. M., and B. M. Alberts. 1995. Anillin, a contractile ring protein that cycles from the nucleus to the cell cortex. *J. Cell Biol.* 131:165–178.
- Fishkind, D. J., and Y.-I. Wang. 1995. New horizons for cytokinesis. *Curr. Opin. Cell Biol.* 7:23–31.
- Gatti, M., and B. S. Baker. 1989. Genes controlling essential cell-cycle functions in *Drosophila melanogaster*. 3:438–453.
- Gunsalus, K. C., S. Bonaccorsi, E. Williams, F. Verni, M. Gatti, and M. L. Goldberg. 1995. Mutations in *twinstar*, a *Drosophila* cofilin/ADF homolog, result in defects in centrosome migration and cytokinesis. *J. Cell Biol.* In press.
- Haugwitz, M., A. Noegel, J. Karakesisoglou, and M. Schleicher. 1994. *Dictyostelium* amoebae that lack G-actin-sequestering profilins show defects in F-actin content, cytokinesis, and development. *J. Cell Biol.* 79:303–314.
- Hime, G., and R. Saint. 1992. Zygotic expression of the *pebble* locus is required for cytokinesis during the postblastoderm mitoses of *Drosophila*. *Development.* 114:165–171.
- Karess, R. E., X.-j. Chang, K. A. Edwards, S. Kulkarni, I. Aguilera, and D. P. Kiehart. 1991. The regulatory light chain of nonmuscle myosin is encoded by *spaghetti-squash*, a gene required for cytokinesis in *Drosophila*. *Cell.* 65:1177–1189.
- Knowles, B. A., and L. Cooley. 1994. The specialized cytoskeleton of the *Drosophila* egg chamber. *Trends Genet.* 10:235–240.
- Lee, J. K., R. S. Coyne, R. R. Dubreuil, L. S. B. Goldstein, and D. Branton. 1993. Cell Shape and interaction defects in α -spectrin mutants of *Drosophila melanogaster*. *J. Cell Biol.* 123:1797–1810.
- Lehner, C. F. 1992. The *pebble* gene is required for cytokinesis in *Drosophila*. *J. Cell Sci.* 103:1021–1030.
- Mermall, V., and K. G. Miller. 1995. The 95F unconventional myosin is required for proper organization of the *Drosophila* syncytial blastoderm. *J. Cell Biol.* 129:1575–1588.
- Mermall, V., J. G. McNally, and K. G. Miller. 1994. Transport of cytoplasmic particles catalysed by an unconventional myosin in living *Drosophila* embryos. *Nature (Lond.)* 369:560–562.
- Merrill, P. T., D. Sweeton, and E. Wieschaus. 1988. Requirements for autosomal gene activity during precellular stages of *Drosophila melanogaster*. *Development.* 104:495–510.
- Miller, K. G., C. M. Field, and B. M. Alberts. 1989. Actin-binding proteins from *Drosophila* embryos: a complex network of interacting proteins detected by F-actin affinity chromatography. *J. Cell Biol.* 109:2963–2975.
- Moon, A., P. Janmey, K. Louie, and D. Drubin. 1993. Cofilin is an essential component of the yeast cortical cytoskeleton. 120:421–435.
- Nagaoka, R., H. Abe, K. Kusano, and T. Obinata. 1995. Concentration of cofilin, a small actin-binding protein, at the cleavage furrow during cytokinesis. *Cell Motil. Cytoskeleton.* 30:1–7.
- Neufeld, T. P., and G. M. Rubin. 1994. The *Drosophila* *peanut* gene is required for cytokinesis and encodes a protein similar to yeast putative bud neck filament proteins. *Cell.* 77:371–379.
- Pesacreta, T. C., T. J. Byers, R. Dubreuil, D. P. Kiehart, and D. Branton. 1989. *Drosophila* spectrin: the membrane skeleton during embryogenesis. *J. Cell Biol.* 108:1697–1709.
- Postner, M. A., and E. F. Wieschaus. 1994. The *nullo* protein is a component of the actin-myosin network that mediates cellularization in *Drosophila* melanogaster embryos. *J. Cell Sci.* 107:1863–1873.
- Postner, M. A., K. G. Miller, and E. F. Wieschaus. 1992. Maternal effect mutations of the *sponge* locus affect actin cytoskeletal rearrangements in *Drosophila melanogaster* embryos. *J. Cell Biol.* 119:1205–1218.
- Rappaport, R. 1986. Establishment of the mechanism of cytokinesis in animal cells. *Int. Rev. Cytol.* 105:245–281.
- Sander, S. L., and C. M. Field. 1994. Septins in common? *Curr. Biol.* 4:907–910.
- Satterwhite, L. L., and T. D. Pollard. 1992. Cytokinesis. *Curr. Opin. Cell Biol.* 4:43–52.
- Schejter, E. D., and E. Wieschaus. 1993a. *bottleneck* acts as a regulator of the microfilament network governing cellularization of the *Drosophila* embryo. *Cell.* 75:373–385.
- Schejter, E. D., and E. Wieschaus. 1993b. Functional elements of the cytoskeleton in the early *Drosophila* embryo. *Ann. Rev. Cell Biol.* 9:67–99.
- Schweiguth, F., J. A. Lepesant, and A. Vincent. 1990. The *serendipity alpha* gene encodes a membrane associated protein required for the cellularisation of the *Drosophila* embryo. *Genes & Dev.* 4:922–931.
- Simpson, L., and E. Wieschaus. 1990. Zygotic activity of the *nullo* locus is required to stabilize the actin-myosin network during cellularization in *Drosophila*. *Development.* 110:851–863.
- Sullivan, W., P. Fogarty, and W. Theurkauf. 1993. Mutations affecting the cytoskeletal organization of syncytial *Drosophila* embryos. *Development.* 118:1245–1254.
- Thomas, G. H., and D. P. Kiehart. 1994. β_{heavy} -spectrin has a restricted tissue and subcellular distribution during *Drosophila* embryogenesis. *Development.* 120:2039–2050.
- Verheyen, E. M., and L. Cooley. 1994. Profilin mutations disrupt multiple actin-dependent processes during *Drosophila* development. *Development.* 120:717–728.
- Wheatley, S., S. Kulkarni, and R. Karess. 1995. *Drosophila* nonmuscle myosin II is required for rapid cytoplasmic transport during oogenesis and for axial nuclear migration in early embryos. *Development.* 121:1937–1946.
- Wieschaus, E., and D. Sweeton. 1988. Requirements of X-linked zygotic gene activity during cellularization of early *Drosophila* embryos. *Development.* 104:483–493.
- Wolfner, M. F., and M. L. Goldberg. 1994. Harnessing the power of *Drosophila* genetics. *Methods Cell Biol.* 44:33–80.
- Yonemura, S., A. Nagafuchi, N. Sato, and S. Tsukita. 1993. Concentration of an integral membrane protein, CD43 (leukosialin, sialophorin), in the cleavage furrow through the interaction of its cytoplasmic domain with actin-based cytoskeletons. *J. Cell Biol.* 120:437–449.
- Young, P. E., T. C. Pesacreta, and D. P. Kiehart. 1991. Dynamic changes in the distribution of cytoplasmic myosin during *Drosophila* embryogenesis. *Development.* 111:1–14.
- Young, P. E., A. M. Richman, A. S. Ketchum, and D. P. Kiehart. 1993. Morphogenesis in *Drosophila* requires nonmuscle myosin heavy chain function. *Genes & Dev.* 7:29–41.