# The Molecular Requirements for Cytokinesis

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After anaphase onset, animal cells build an actomyosin contractile ring that constricts the plasma membrane to generate two daughter cells connected by a cytoplasmic bridge. The bridge is ultimately severed to complete cytokinesis. Myriad techniques have been used to identify proteins that participate in cytokinesis in vertebrates, insects, and nematodes. A conserved core of about 20 proteins are individually involved with cytokinesis in most animal cells. These components are found in the contractile ring, on the central spindle, within the RhoA pathway, and on vesicles that expand the membrane and sever the bridge. Cytokinesis involves additional proteins, but they, or their requirement in cytokinesis, are not conserved among animal cells.

Cell multiplication involves cell growth and an ordered sequence of events: replication of the genome, chromosome segregation, and cell division. Although many aspects of cell growth, cell cycle regulation, and chromosome replication and segregation are understood at the molecular and, increasingly, the atomic level, cell division, also called cytokinesis, is less well understood. However, a molecular outline is emerging. Animal cells use a contractile ring that is attached to the plasma membrane to create a cleavage furrow that partitions the cell into two lobes (Fig. 1A). The contractile ring is a network of actin and myosin filaments, and the motor activity of myosin translocates actin filaments to drive its constriction. Contractile ring assembly is directed by the RhoA guanosine triphosphatase (GTPase), which induces actin nucleation and activates myosin. The contractile ring assembles in a position dictated by the position of the anaphase spindle, perhaps through local regulation of RhoA activity. The contractile ring and the central spindle probably sterically hinder simple fission of the plasma membrane. Instead, vesicle insertion appears to be necessary ultimately to achieve division of the plasma membrane.

Here, I introduce the core protein machines that are important for animal cell cytokinesis in divergent animal species (e.g., vertebrates, nematodes, and insects). The well-characterized machines that regulate cytokinesis fall into five broad categories (Fig. 1B): (i) components of the central spindle, (ii) RhoA and its regulators and direct effectors, (iii) nonmuscle myosin II, (iv) actin and direct regulators of its assembly into filaments, and (v) factors required for trafficking and fusion of membrane vesicles. As might be expected for a process that requires the coordinated action of microtubules, actomyosin, and membrane fusion, some proteins required for cytokinesis fall into more than one category. Some, but not all, of these machines also regulate cytokinesis in fungi and *Dictyostelium*.

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## The Cytokinetic Machinery

*The central spindle: a set of microtubule-based machines.* Anaphase onset marks the beginning of cytokinesis. The proteolytic destruction of cyclins inactivates mitotic kinases and permits dephosphorylation and activation of several proteins that are critical for assembly of the central spindle, a set of antiparallel microtubules that become bundled between the separating chromosomes during anaphase and serve to concentrate key regulators of cytokinesis (Fig. 2). The components of the central spindle have acquired a bewildering nomenclature that is summarized in Fig. 2. One of these proteins, PRC1, is a microtubule-associated protein (MAP) with microtubule-bundling activity. PRC1 localizes primarily to the central spindle and is required for central spindle organization and cytokinesis in most animal cells (*1*–*3*). The kinesin-4 family member, KIF4, interacts with PRC1 and restricts the localization of PRC1 to a narrow region in the center of the anaphase spindle (*4*). During metaphase, PRC1 is inhibited from binding to microtubules by phosphorylation on Cdk1 sites (*1*). Cdk1/cyclin B also inhibits microtubule bundling by the centralspindlin complex, which consists of the kinesin-6 family member MKLP1 and the Rho family GTPase activating protein (GAP), CYK-4 (*5*). During anaphase, centralspindlin becomes highly concentrated in the central spindle, apparently where microtubule plus ends overlap (*6*–*8*). Central spindle assembly requires complex formation between MKLP1 and CYK-4, and the MKLP1/CYK-4 complex but not the individual subunits has microtubule bundling activity in vitro (*6*).

Localization of centralspindlin depends on another complex that concentrates on the central spindle, the aurora B kinase complex (*9*, *10*). Aurora B function requires interactions with incenp, survivin, and a poorly conserved subunit, CSC-1 (*11*–*16*). Inhibition of aurora B kinase activity results in cytokinesis defects that are similar to those caused by depletion of MKLP1. Centralspindlin localization may not be the sole function of aurora B. A combination of the strong phenotype caused by defects in central spindle assembly and the existence of parallel pathways for furrow formation may obscure an early, central spindle–independent role for aurora B. The relevant substrates of aurora B remain to be identified, although aurora B can phosphorylate CYK-4 in vitro and this phosphorylation may indirectly affect its GTPase activation function (*17*).

Numerous proteins become concentrated on the central spindle during anaphase and telophase. These include proteins, such as NuSAP (nucleolar spindle-associated protein), orbit, and the tumor suppressor BRCA2, that affect the organization of the central spindle and/or progression of cytokinesis (*18*–*20*). Currently, it is not clear whether these are core components that are required for cytokinesis in diverse species.

Activation of central spindle assembly in early anaphase has implications for formation of the contractile ring. In *Drosophila*, for example, cells lacking the MKLP1 subunit of centralspindlin do not form a contractile ring (*21*). This phenotype may reflect interactions of components of centralspindlin with factors that regulate RhoA activation. However, depletion of the orthologous protein in *Caenorhabditis elegans* or human cells does not prevent furrow formation; in *C. elegans*, this difference is caused by a redundant pathway for furrow formation (*22*).

*The RhoA pathway: the key switch for cytokinesis.* A central player in contractile ring assembly is the RhoA GTPase module (Fig. 3). RhoA, like most ras-related GTPases, is regulated by factors that promote nucleotide exchange [guanine nucleotide exchange factors (GEFs)] and nucleotide hydrolysis (GAPs). There appears to be one critical GEF for RhoA in cytokinesis, known as ECT2 (*23*, *24*).

Depletion of ECT2 blocks furrow formation as does depletion of RhoA, although in vitro this GEF is not RhoA specific (*22*, *23*). The identity of the GAP for RhoA in cytokinesis is not completely clear. CYK-4 is an attractive candidate, because it is localized to the midbody at a late stage in cytokinesis, a site where inactivation of RhoA could be required for the final steps of cytokinesis (*25*). However, genetic evidence suggests that CYK-4 regulates Rac proteins (*26*). Perhaps CYK-4 regulates both GTPases; indeed, it has GAP activity for RhoA, Rac, and Cdc42 in vitro (*25*). Interestingly, an interaction has been detected between the *Drosophila* orthologs of the GEF and the putative GAP for RhoA, namely ECT2/Pebble and CYK-4/RacGAP50C (*8*). Localization of this RhoGEF may direct local RhoA activation to sites in the cell cortex adjacent to the central spindle (*8*). This complex is reminiscent of the breakpoint cluster region protein in that it contains both RhoGAP and RhoGEF domains. Localization of ECT2 to the central spindle may not be essential to activate RhoA, because RhoA activation apparently occurs in cells depleted of MKLP1 (*27*–*29*). Nevertheless, central spindle localization of ECT2 activity could contribute to RhoA activation.

*Myosin: the engine of cytokinesis.* RhoA•GTP activates downstream pathways that lead to actin polymerization and myosin II activation. Nonmuscle myosin II is one of the central machines in cytokinesis, because its activity is required for furrow formation (*30*–*32*). This motor consists of a parallel dimer of heavy chains, each bound to an essential light chain and a regulatory light chain (rMlc). These hexamers assemble into filaments that translocate actin filaments and drive constriction of the contractile ring. In animal cells, nonmuscle myosin II is regulated by phosphorylation of the rMlc, which binds between the motor domain and the coiled coil. Phosphorylation of rMlc releases myosin II from an auto-inhibited state, allowing it to assemble into filaments and activating its actin-stimulated adenosine triphosphatase (ATPase) activity (Fig. 3). Phosphorylation of rMlc appears to be critical for cytokinesis, because a phosphomimetic allele of rMlc can substantially substitute for rMlc in *Drosophila,* whereas a nonphosphorylatable rMlc results in severe cytokinesis defects (*33*). RhoA regulates the phosphorylation state of rMlc by several mechanisms. RhoA activates Rho kinase (ROCK), which phosphorylates rMlc (*34*) and regulates cytokinesis (*35*, *36*). In addition, ROCK phosphorylates myosin phosphatase–targeting (MYPT) subunit, thereby inhibiting myosin phosphatase and indirectly promoting rMlc phosphorylation (*37*). Genetic interactions indicate that rMlc is one of the most important substrates for ROCK (*38*). However, several additional kinases phosphorylate rMLC, including the RhoA-activated citron kinase (*39*). However, citron kinase–depleted cells progress to a later stage of cytokinesis than would be expected if it were a major rMlc kinase (*39*–*41*).

*Actin assembly: the formin-profilin machine.* The mechanochemical activity of myosin is latent until it interacts with actin filaments, a second major constituent of the contractile ring. Actin filaments in the contractile ring often appear in parallel bundles, as opposed to the dendritic meshwork observed in the leading edge of a migrating cell. The organization of the filaments can be ascribed, at least in part, to the different nucleating complexes that generate these structures. The ARP2/3 complex generates branched filaments and is critical for cell migration but is only weakly involved in contractile ring assembly (*42*, *43*). Rather, formins nucleate unbranched filaments and are essential for contractile ring assembly in animal cells (Fig. 3) (*44*–*46*). Formins cap the barbed end of the actin filament but allow filament growth (*47*–*49*). Together with profilin, the central region of formin, containing the conserved FH1 (profilin-binding) and FH2 (actin-binding) domains, induces ATP hydrolysis by actin and uses the released free energy to favor processive growth of actin filaments (*50*). In vivo, however, formin is autoinhibited because of intramolecular binding of the N and C termini. Active RhoA binds the N terminus and relieves this autoinhibition (*51*). Thus, spatially restricted RhoA activation could induce local activation of myosin activity and actin filament assembly.

Another actin-binding protein that is required for cytokinesis is the actin-severing protein cofilin/ADF (*52*, *53*). In vitro, cofilin can antagonize filament growth by severing and destabilizing filaments as well as promote growth by increasing the number of elongation competent barbed ends. The net effect of cofilin activation depends on the concentration of actin monomers and other factors that regulate filament ends. In cytokinesis, it seems that the primary role of cofilin is to destabilize actin filaments, because in cofilin mutants the contractile ring

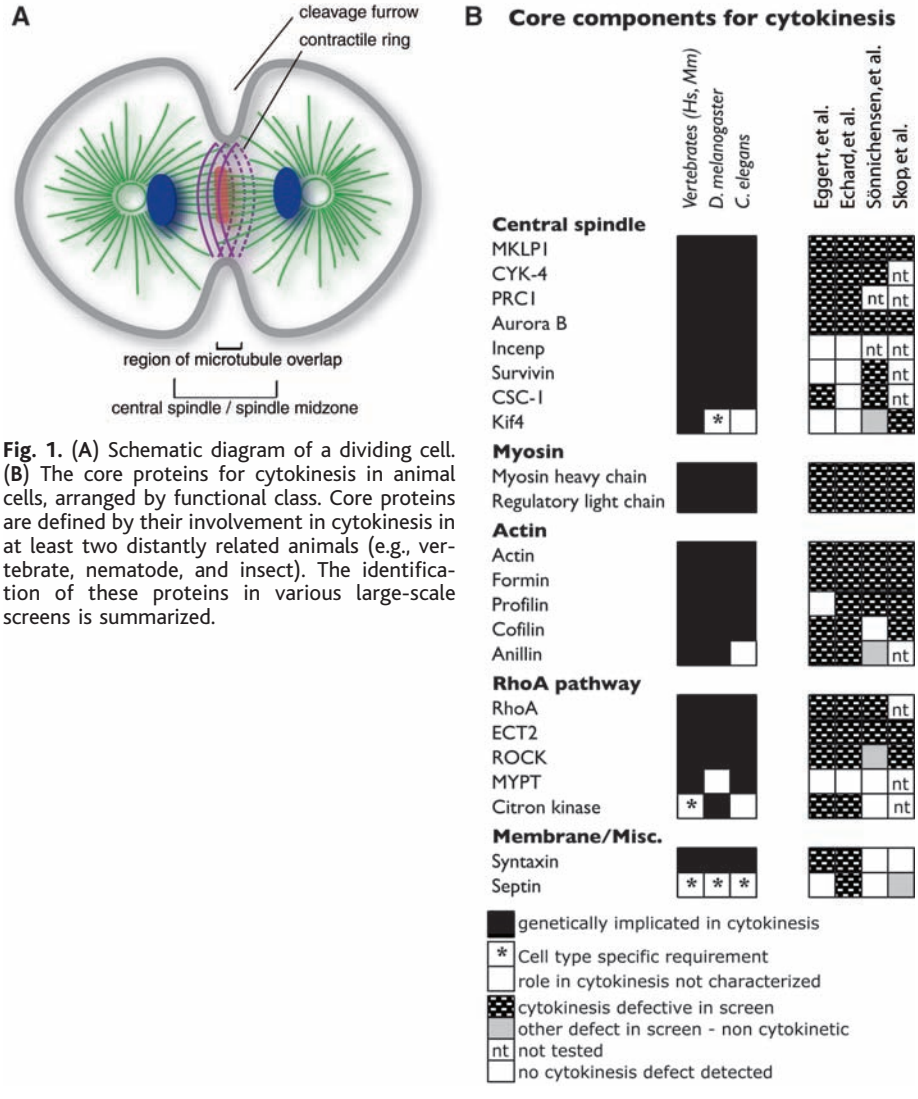
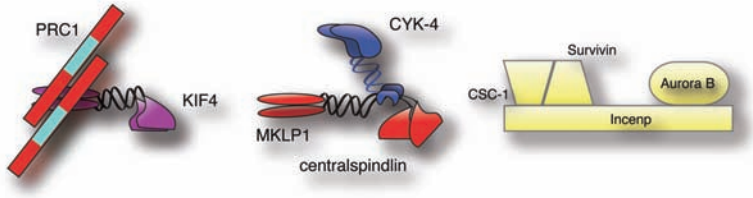



**Fig. 1.** (**A**) Schematic diagram of a dividing cell. (**B**) The core proteins for cytokinesis in animal cells, arranged by functional class. Core proteins are defined by their involvement in cytokinesis in at least two distantly related animals (e.g., vertebrate, nematode, and insect). The identification of these proteins in various large-scale screens is summarized.

contains an overabundance of actin filaments at late stages of cytokinesis.

Lastly, another actin-binding protein, anillin, has been genetically implicated in cytokinesis. This multidomain protein is tightly localized to the cleavage furrow and interacts with myosin and septins, but its biochemical function in the context of cytokinesis is not fully defined (*54*). Anillin-depleted animal cells have late defects in cytokinesis; contractile ring formation and ingression are not abolished (*36*, *55*, *56*).

*The membrane fusion machinery.* The actomyosin system is not sufficient to fully execute cytokinesis. Ultimately, each daughter cell must be surrounded by an independent plasma membrane, and the contractile ring, being linked to the inner cytoplasmic face of the membrane, is not in an appropriate location to promote membrane fusion. The final step of cytokinesis, membrane fusion, requires delivery of membrane vesicles that bridge the space remaining after full ingression of the contractile ring (*57*). Membrane addition may also be required to provide the membrane surface necessary to surround the two daughter cells. The machinery involved in membrane insertion during cytokinesis includes syntaxins, syntaxin-associated proteins, coatomer complex members, rab family GTPases, and subunits of the exocyst complex (*36*, *57*–*59*). Conventional kinesin may help to deliver membranes to the midbody region (*60*).




**Nomenclature of the central spindle**

| | *H. sapiens* | *D. melanogaster* | *C. elegans* | ref. |
|---|---|---|---|---|
| Microtubule Associated Protein | | | | |
| PRC1 | PRC1 | Fascetto | SPD-1 | (*1-4*) |
| KIF4 | KIF4 | KLP3A | KLP-19 | |
| Centralspindlin complex | | | | |
| CYK-4 | MgcRacGAP | RacGAP50C | CYK-4 | (*6-8*) |
| MKLP1 | MKLP1 | Pavarotti | ZEN-4 | |
| Aurora kinase complex | | | | (*9-16*) |
| Aurora B | Aurora B | Aurora B | AIR-2 | |
| Incenp | Incenp | Incenp | ICP-1 | |
| Survivin | Survivin | Deterin | BIR-1 | |
| CSC-1 | Dasra/Borealin | Borealin | CSC-1 | |
| RhoGEF | | | | (*23, 24*) |
| ECT2 | ECT2 | Pebble | LET-21 | |

**Fig. 2.** Guide to the nomenclature of proteins that organize and concentrate on the central spindle. Also shown are schematic models for the molecular organization of a subset of these complexes: PRC1/KIF4, centralspindlin, and aurora B kinase.

## Evolutionary Conservation of the Cytokinesis Machinery

In addition to animal cells, cytokinesis has been intensively studied in budding and fission yeast as well as in *Dictyostelium*. There are both similarities and differences in the genetic requirements for the major cytokinetic machines in eukaryotes [see (*61*) for more details].

Some of the components of the central spindle are widely conserved, whereas others appear to be specific for metazoans. For example, the microtubule-bundling protein PRC1 has a clear ortholog in budding yeast, Ase1p, and although it plays role in late mitotic events in budding yeast, it is not required for cytokinesis (*62*). Genes weakly related to PRC1 also exist in the *S. pombe* and *Dictyostelium* genomes, but their involvement in cytokinesis have not yet been evaluated. A kinesin-6 exists in the *Dictyostelium* genome and it plays a role in cytokinesis (*63*), but it does not share all the sequence features characteristic of vertebrate MKLP1 and there is no protein clearly related to CYK-4 in the *Dictyostelium* genome. Neither budding nor fission yeast contain proteins that resemble MKLP1 or CYK-4. On the other hand, aurora B kinase and most of its associated subunits are widely conserved and are found in budding and fission yeast and *Dictyostelium*.

Although actomyosin contractile rings form in budding yeast, fission yeast, and *Dictyostelium*, they are not strictly essential in budding yeast nor in *Dictyostelium*. In both of these systems, redundant pathways mediate cell division in the absence of myosin. For example, in budding yeast, there is a pathway that can build a septum sufficient to divide the cell in the absence of myosin II (*64*).

Myosin II is dispensable for cytokinesis in *Dictyostelium* cells cultured on a surface, although it is required for these cells to grow in suspension (*65*, *66*). Remarkably, the division of myosin II–deficient *Dictyostelium* cells on a surface is morphologically similar to that of wild-type cells. If translocation of actin filaments by myosin II normally provides the force for furrow ingression, what substitutes in its absence? Two genes are proposed to act in a parallel, myosin-independent pathway, *amiA* and *coronin* (*67*). These genes are not required for myosin-driven division in suspension, but mutations in either of these genes synergize with myosin II mutations and either double mutant fails to divide on a surface. This may reflect a direct role in substrate-mediated division or an indirect one in maintaining the substrate contacts required for myosin-independent division. Two other important factors are the actin-bundling proteins cortexillin I and II, which are highly concentrated in the equatorial region (*68*). These related proteins regulate cytokinesis in a partially redundant fashion (*69*). Their concentration to the equatorial region is thought to locally modulate cortical tension, thereby promoting furrow ingression.

The Rho family of GTPases is ancient. It consists of three major branches—Rho, Rac, Cdc42—and several members that do not fit into these major groupings. *Dictyostelium* has at least 15 Rho family members. Although none of these genes are closely related to RhoA or Cdc42, there are several Rac-related genes and a large number of outliers not highly related to RhoA, Rac1, or Cdc42. This latter class includes RacE, which is an important regulator of cytokinesis in this system (*70*). Both *S. pombe* and *S. cerevisiae* contain true Rho orthologs that participate in cytokinesis, primarily by regulating deposition of cell wall material. In addition, *S. pombe* contains the Spg1 GTPase, which is an extremely divergent member of the Ras superfamily and a critical regulator of cytokinesis, being necessary and sufficient for septum formation (*71*).

The effectors regulated by RhoA in animal cells are not universally required for cytokinesis in other eukaryotes. Phosphorylation of rMlc is not essential in *S. pombe* or *Dictyostelium* (even in suspension growth) (*72*, *73*). However, formins are essential for cytokinesis in budding and fission yeast, and in the former case they are known to be activated by Rho family GTPases, primarily Rho3p and Rho4p (*74*). The GAPs and GEFs that regulate cytokinesis in yeast, *Dictyostelium*, and animals cells do not appear to be orthologous.

The *S. pombe* ortholog of the actin-binding protein anillin, Mid1, controls division plane positioning in fission yeast. It is the first protein known to localize to the furrow in *S. pombe*, and mutants have severe ring-positioning defects (*75*, *76*). Although anillin is an early marker of the division plane in

animal cells, anillin-depleted cells form furrows that fail to complete, indicating that anillin is not essential for division plane positioning in animal cells (*36*, *55*, *56*).

Some factors required for trafficking and fusion of membrane vesicles appear to have a conserved requirement for cytokinesis in both metazoans and unicellular eukaryotes. These include the exocyst complex and syntaxins (*77*). Whereas in metazoans microtubules and kinesins appear to play the primary delivery role for membrane deposition during cytokinesis (*60*), in yeast this function is primarily mediated by actin filaments and myosin (*78*).

Thus, a number of related molecules mediate cytokinesis in divergent eukaryotes. However, differences do exist, particularly in the regulatory mechanisms and the degree of reliance on particular pathways. Nevertheless, many insights obtained into cytokinesis in unicellular eukaryotes have been transferable to multicellular eukaryotes. The apparent differences in these systems may be obscuring common biochemical mechanisms of cytokinesis.

## Toward a Comprehensive List of Core Cytokinesis Genes

Identification of the proteins required for cytokinesis is a critical step that provides the starting material for the biochemical, biophysical, and structural investigations required to understand the molecular basis of cytokinesis. With the use of forward and/or reverse genetics, ~20 core components required for cytokinesis in vertebrates, insects, and nematodes have been identified. These data can be compared to the results of four large-scale RNAi screens using *Drosophila* or *C. elegans* (Fig. 1B) (*36*, *58*, *79*, *80*). RNAi allows efficient depletion of individual genes and is a useful method to functionally dissect cytokinesis. Defects in cytokinesis cause a readily recognizable phenotype that is not lethal to cells over short time periods. These data have been tabulated (Fig. 1B). A criterion that can aid the evaluation of these data is whether an individual gene scored positive in multiple independent screens. Of the core cytokinesis genes, 17 of 22 were identified in at least two of the three largely comprehensive screens (*36*, *79*, *80*), suggesting that, collectively, these screens did not suffer from a large number of false negatives. Conversely, the genes identified in multiple screens largely overlaps with those defined by conventional genetics, implying that there exists a relatively small set of core cytokinesis genes that are each essential for cytokinesis.

Genes not previously implicated in cytokinesis scored positive in each of these screens. Of the 40 novel genes identified in one proteomic screen (*58*), 7 may be explained by other primary defects (such as osmosensitivity, microtubule defects, and chromosome segregation), 13 have been tested in at least two other screens and no phenotypes were observed (*80*) (www.wormbase.org), and the remaining 20 were previously found to cause a detectable, although noncytokinetic, phenotype. Of the 214 genes identified in a *Drosophila* cell culture screen (*79*), 16 genes are among those listed in Fig. 1B, 12 are involved in membrane trafficking, and 116 have known functions in transcription, translation, chromatin, or cell cycle control. Most of the other genes caused weakly penetrant phenotypes, and there is insufficient information available for these genes to assess whether they are directly involved in cytokinesis. The novel genes from these large-scale screens do not overlap extensively, suggesting that they need to be studied in further detail to verify their direct involvement in cytokinesis.

One exception could be proteins involved in membrane trafficking. This class of proteins was found more frequently in the new screens as compared with previous studies. Even though the same genes were not generally found in multiple screens, factors involved in this process were identified in independent screens, so this class can be considered a robust hit.

Are there additional factors involved in cytokinesis that remain to be identified? The list of actin-binding proteins among the cytokinesis genes is remarkably short: myosin, formin, profilin, cofilin, and anillin. Are no additional actin-bundling proteins required for animal cell cytokinesis? What is responsible for linking the contractile ring to the plasma membrane? Are there structural proteins that stabilize the interaction between the contractile ring and the central spindle? What are the critical molecules through which spindle position directs contractile ring assembly? Are there myosin-independent pathways that can contribute to cytokinesis in animal cells as in *Dictyostelium* and budding yeast?

Genetic redundancy may have impaired the identification of genes that are critical for cytokinesis. Functionally redundant genes will not be identified in screens in which single genes are inactivated. Although cytokinesis is largely dependent on the same machinery in most animal cells, the molecular requirements for cytokinesis do vary somewhat in different organisms. For example, vertebrates have multiple kinesin-6 family members that are each involved in cytokinesis (*81*), whereas there is only one such family member in *C. elegans*. Similarly, KIF4 is required for cytokinesis in vertebrate cells and in *Drosophila* spermatocytes; it is not apparently required in somatic cells in *Drosophila*. More surprising is the case of citron kinase. In cultured human cells, overexpression of a kinase-defective mutant causes cytokinesis defects (*82*). Likewise, *Drosophila* citron kinase is essential for cytokinesis in cell culture and in the larval brain (*26*, *36*, *40*, *41*). These data suggest citron kinase is a core part of the cytokinetic machinery. However, the most closely related gene in the *C. elegans* genome has not been implicated in cytokinesis. More strikingly, mice homozygous for a deletion of the citron kinase gene are viable, and tissues other than brain and testis do not show cytokinesis defects (*83*, *84*). Redundancy at the process level as opposed to the molecular level also impedes genetic analysis of cytokinesis. For example, in some organisms, parallel pathways regulate furrow

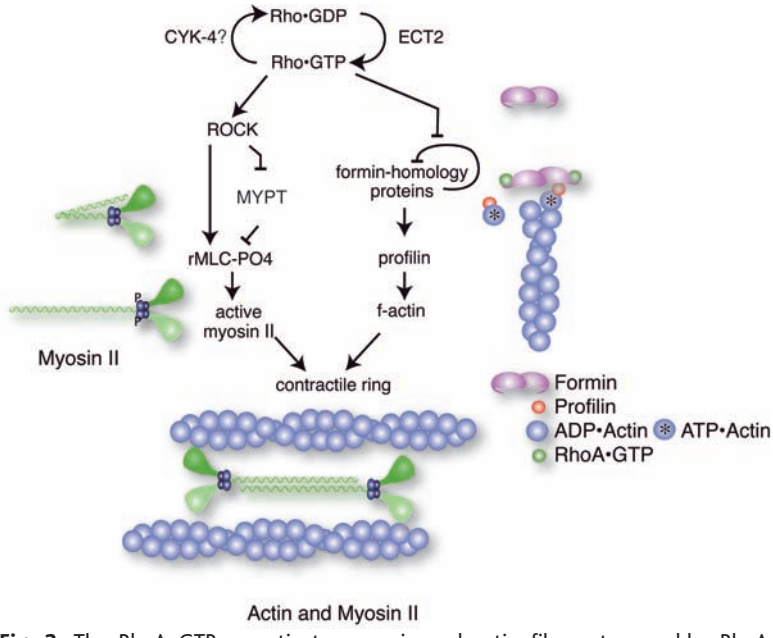



**Fig. 3.** The RhoA GTPase activates myosin and actin filament assembly. RhoA induces phosphorylation of the regulatory light chain of myosin (blue) and induces a conformational change permissive for filament assembly. Formin autoinhibition is relieved by RhoA•GTP and allows the processive elongation of the barbed end of actin filaments, a reaction that is profilin dependent.

positioning. In *Drosophila*, central spindle components are essential for cleavage furrow formation. However, *C. elegans* embryos lacking central spindle components do form furrows (*22*); similar results have been observed in vertebrate cells (*1*, *29*). Thus, although there is a significant degree of conservation in the mechanism of cytokinesis in animal cells, there is genetic variability in the requirements for cytokinesis. Because our understanding of cytokinesis is emerging from analyses of different experimental systems, these evolutionary changes vex efforts to derive a consensus mechanism. In addition, various kinds of functional redundancy may preclude a full account of the genes required for cytokinesis.

For the sake of comparison, although ~4700 out of ~6000 genes are nonessential in budding yeast, systematic synthetic lethal screens indicate that a sizable fraction (probably >50%) of these nonessential genes have an easily detected phenotype when combined with a second mutation (*85*). Three general strategies will be useful for teasing apart the underlying mechanisms of cytokinesis. First, by developing more sensitive assays, it is possible to determine whether a gene participates in cytokinesis, even when it is not strictly essential for the process. Second, it is likely that the pattern of genetic redundancy will vary in different systems, and therefore some pathways will be accessible in some systems but not others. Third, sensitized strains in which cytokinesis is less robust may be useful for second-generation screens and for analyzing factors identified by biochemistry and bioinformatics.

The average human consists of about $10^{14}$ cells. How do cells maintain their integrity through so many multiplication cycles? DNA replication is nearly error-free, producing an average of three mutations each time a human-sized genome is replicated. To ensure equal segregation of the replicated sister chromatids, the spindle checkpoint delays mitotic exit until all sister chromatids are bioriented and under tension. It is not clear whether there are mechanisms that prevent or correct errors in cytokinesis. After anaphase onset, mammalian cells have a 1-hour window in which to complete cytokinesis (*86*). After that time, cells will exit mitosis and either arrest in G1 or continue to cycle. If they fail cytokinesis, the resulting polyploid cells have four possible fates. They can either undergo apoptosis, remain polyploid, rectify the situation by extruding a nucleus, or, if the two sets of chromosomes remain independent until the next mitosis and align on independent mitotic spindles, the cell could then cleave into four karyotypically normal cells. The relative frequencies of these alternate fates are unknown, particularly in vivo. There is evidence that the tumor suppressor p53 can block S-phase entry in cleavage-defective cells (*87*, *88*). However, multinucleation per se is not sufficient to arrest the cell cycle, and the G1 arrest may be due to general perturbations of the actin cytoskeleton (*89*, *90*). In any case, a G1 arrest after cytokinesis failure would not correct the defect; it would merely reduce its potential to cause harm. Perhaps redundant mechanisms for cytokinesis exist to prevent defects in cytokinesis, because the repair processes may not be sufficiently robust.

The molecular mechanism of cytokinesis is coming into focus, but a number of blind spots persist. Although it will be important to identify additional components, the challenge for the future will be to analyze the underlying biochemistry and cell biology of this dynamic and dramatic event in the life of a cell.

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