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Signal to forces: Central themes in cytokinesis

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Records dating back three-hundred years show an anonymous British naturalist observing that an organism divided into two units. The observation was apparently made on a ciliated organism collected from pond water in his backyard, by using a hand-made microscope (1). The author reported that “*I have likewise seen them double ... and go forward so, as Flies in copulation...*”. The first study on amoeboid locomotion can be traced back to 1805, when a French scientist made a prediction that the amoeba moves by a similar mechanism to muscle contraction (2). It appears that, during the past century, the biologists’ interests were primarily focused on identification and characterization of the protein components and gene regulation (3). At this turning of the millennium, the integrated mechanism of cytokinesis still remains to be elucidated.

Currently two central themes are most intensively being studied. First, the exact mechanochemical problems operating constriction of the cleavage furrow; second, the chemical signals that put the spatial and temporal information together (4, 5). Such biological techniques as green fluorescence protein (GFP)-fusion protein and gene knock-out work well with modern computer technology (6, 7). While video microscopy has an advantage in long term real-time image recording (8), the digital imaging technique is superior in its flexibility in image acquisition, spatiotemporal resolution, and most importantly, simplicity in hardware connections. It must also be pointed out that the method of publication has been changing in the last several years, and publishing dynamic image sequences through the Internet is becoming the primary method of publication.

This issue of Microscope Research and Technique entitled “The Biology of Cytokinesis” contains review as well as original articles focusing on the signaling and force generation mechanisms in cytokinesis in various systems. Note that this issue primarily focuses on simple unicellular systems such as yeast (*Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*), cellular slime mold (*Dictyostelium discoideum*), ciliate (*Tetrahymena pyriformis*), and vertebrate tissue cultured cells (HeLa, 3T3, and PtK1), while marine eggs and multicellular systems are mostly excluded. The papers were contributed from internationally established groups that have been making valuable contributions to the mechanism of cytokinesis.

In the first part of this issue, Chang and Lu present intriguing original works demonstrating multiple calcium transients in zebrafish embryos, each of which seems playing distinctive role for cytokinesis. The dynamic image sequence of the calcium transient is phenomenal as generated by use of the state-of-the-art laser confocal microscope system. This article is followed by an article by Madaule from Narumiya’s laboratory, reviewing a role of recently identified novel Rho target protein “citron” in HeLa cells. Numata and colleagues’ article is a unique review on the structure and composition of the contractile ring in *Tetrahymena pyriformis*, particularly about a novel Ca^{2+} /calmodulin target protein *Tetrahymena* p85, and two actin-binding proteins, fimbrin and EF-1 α . This review comes with image data of localization of p85 into the cleavage furrow. Uyeda and Yumura focus on reviewing the molecular biological approaches, examining the mechanism of how conventional myosin assembles into the contractile ring in *Dictyostelium*, which represents the best studied organisms for dissecting myosin functions (9).

The second part of this issue focuses on *in vivo* dynamics of signal molecules during cytokinesis in yeast and *Dictyostelium*. First, Laroche and colleagues review

genetic targeting studies of a small G-protein *racE* and the effect of gene knock-out on actin filament organizations in *Dictyostelium*. An interesting consequence of *RacE* knock-out is demonstrated in dynamic phase-contrast image sequence. Mulvihill and colleagues present a review on novel yeast myosins, *Myo2* and *Myp2*, as well as signal components in contractile ring and septum formation in *S. pombe*. Chang discusses about microtubule and actin-based movement of the formin *cdc12p* in *S. pombe*. This article illustrates the architectural dynamics of GFP-*cdc12*. The article by Lippincott and Li is a review about “pombe *Cdc15* homology” proteins in budding yeast *S. cerevisiae*. This article demonstrates a stunning detail of the assembly into septin rings by Delta Vision Microscopy.

The third and final part of this issue is intended to focus on the global mechanism of cytokinesis using various microscopic techniques. In the article by Goto and colleagues, the authors suggest a regulatory role of rho-kinases in intermediate filament organization in vertebrate 3T3 cells. In the original article by Fukui, the author suggests a biphasic mode of the cytokinetic mechanism in *Dictyostelium*, based on high-resolution image analysis. The last two articles of this topical issue focus on the key issue in the studies on cytokinesis; i.e., the mechanism how the contractile ring is formed precisely at the center of equator. Sanger and Sanger hypothesize a role of microtubule-based signals responsible for the assembly of the contractile ring, based on spatial and temporal patterns of accumulation of actin and myosin II into the cleavage furrow. Finally, Gatti and colleagues suggest a possible contribution of midzone of the central spindle in providing signals for contractile ring positioning, as opposed to the microtubule asters (4). This article is also an updated review about cytokinetic stimuli in multicellular embryos such as *Xenopus*, *Drosophila*, and *Caenorhabditis elegans*. It must be pointed out that the last two articles both suggest a possible signal transmission mechanism via microtubule-based molecules to the F-actin system organizing into the contractile ring.

While recent technical advances in gene targeting and imaging of fluorescently tagged cellular components are noteworthy, it appears that central dogmas on the mechanism of cytokinesis have not been changed; i.e., signal and forces. We have just begun drawing a crude blueprint into which significant architectural components and their interactions are not yet incorporated. Yeast two-hybrid system (10, 11) appears to be a powerful tool for identifying partners of those components, particularly between signal molecules and cytoskeletal components, and also between actin, microtubule, and intermediate filaments systems.

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