Meetings

Microtubules and Microfilaments in Division and Development

The completion of the Kewalo Marine Laboratory of the University of Hawaii's Pacific Biomedical Research Center was the occasion for the scheduling of the Second International Conference of the International Society of Developmental Biologists (ISDB, a subdivision of the International Union of Biological Sciences). The laboratory, constructed with funds provided by the National Science Foundation and the state of Hawaii, has been established for studies in those areas of basic biomedical research for which marine animals provide the most useful experimental material. The laboratory will emphasize cellular and developmental biology, for marine animals have long provided the "classic" material for studies in these fields—as evidenced by the utilization of the gametes of the sea urchin in current developmental biology, and the use of gametes of marine animals in studies of mitosis and cytokinesis—and will exploit advantages provided by Hawaii for year-round research for both resident and visiting scientists.

In line with the ISDB guidelines for these conferences, the topic of this meeting, "Microtubules and Microfilaments in Division and Development," was chosen because it relates directly to the research interests of the sponsoring laboratory, and it is also a research area that illustrates the importance of marine animals as experimental material. The process of cell division is also an example of the roles of microtubules and microfilaments at the cellular level, as microtubules are directly related to chromosome movement, and microfilaments have been implicated in the functioning of the cleavage furrow.

The conference, organized by R. E. Kane (University of Hawaii), was held 27–29 May 1972. The session on the biochemistry of microtubules and microfilaments was opened by its chairman, R. E. Stephens (Brandeis University), with a discussion of two types of microtubular polymerization: the thermodynamic parameters of the reversible in vivo assembly of the microtubules of the mitotic apparatus, and the in vitro assembly of stable structures from A and B tubulins. The latter subject was extended by M. Shelanski (NIH), with a presentation of the in vitro assembly of paracrystals of tubulin as induced by vinblastine, and the role of nucleotides in this assembly process. I. R. Gibbons (University of Hawaii) presented evidence for a sliding filament mechanism in the production of motion by microtubules in flagella. V. Nachmias (Haverford College) presented her work on the properties of the myosin-like protein from *Physarum polycephalum*, and K. E. Wohlfarth-Botterman (University of Bonn) discussed the fine structure of this organism, and the interaction of its contractile proteins by a sliding filament mechanism. This discussion of contractile proteins of primitive motile systems was supplemented by the results of T. D. Pollard (NIH) on the contractile proteins of *Acanthamoeba*, in which actin and myosin-like proteins and a new cofactor are implicated.

Although many aspects of the biochemistry of microtubules are now becoming understood, and the mechanism of their action in such organelles as the flagellar axoneme is beginning to be clarified, no such understanding has yet emerged from the studies of chromosome movement in mitosis. J. R. McIntosh (University of Colorado), who recently presented a theory of the role of microtubules in mitosis based on a sliding mechanism, was chairman of a session that brought together, physically if not intellectually, a number of researchers in the field of chromosome movement. McIntosh's sliding mechanism theory for mitosis has not received support from those investigators concerned with the dynamic properties of the spindle in living cells, and S. Inoue (University of Pennsylvania) and R. Dietz (Max Planck Institute for Cell Biology) presented their evidence for the role of microtubules in chromosome movement based on the assembly and disassembly of the microtubular subunits in a thermodynamic equilibrium. B. R. Brinkley (University of Texas) presented evidence from electron microscopy that the chromosomal and the continuous microtubles of the spindle could be distinguished by use of the mitotic inhibitor nitrous oxide, which appears to act in a manner opposite to that of the classical colchicine inhibition. A. Bajer (University of Oregon) showed elegant motion pictures of mitosis in *Haemanthus*, and he discussed the role of microtubules in chromosome movement and phragmoplast formation. More general transport mechanisms in the mitotic spindle, presumably based on microtubular activity but not by a sliding mechanism, were discussed by G. Ostergren (Agricultural College of Sweden). One can conclude from these discussions that at the present time the proposed mechanisms of chromosome movement appear to be influenced by the method of observation (birefringence, phase microscopy, electron microscopy), and by the material investigated, and that no single mechanism seems able to fit the great variety of experimental data available.

In contrast to this, current studies of cytokinesis seem to be moving toward elucidating some general mechanisms, at least in animal cells. The session chairman, R. Rappaport (Union Col-

lege), presented his results on the micromanipulation of dividing cells which show clearly that the mitotic apparatus, and more specifically the asters, are responsible for the localization of the furrow, and that the furrow acts by a contractile mechanism. The nature and origin of the cleavage force, as determined by direct surface measurement, was discussed by Y. Hiramoto (Tokyo Institute of Technology). These micromanipulation studies received direct support from electron microscopy of a variety of cleaving cells. Studies on the cleavage of HeLa and sea urchin cells (T. Schroeder, University of Washington), on the unilateral cleavage of the jellyfish egg (D. Szollosi, University of Washington), and on the telolecithal egg of the cephalopods (J. M. Arnold, University of Hawaii) all indicate the presence of a band of microfilaments forming a contractile ring that mechanically accomplishes the furrow. Further work may relate the activity of this microfilamentous band more directly to the primitive motile systems discussed above. Its apparent induction by the asters of the mitotic apparatus provides an interesting link between the microfilament and microtubular systems.

The final day of conference was devoted to a consideration of the role of these organelles in the process of development. R. A. Cloney (University of Washington) chaired this session, and described his research on the role of microfilaments in the resorption of the ascidian tail, which was one of the first demonstrated instances of the contractile role of microfilaments in a developmental process. P. C. Baker (University of California, Berkeley) reviewed the work on microtubules and microfilaments in amphibian gastrulation and presented her investigations on the role of microfilaments in the change of cell shape associated with gastrulation, and on the reduction of the external membrane during such shape changes by the sequestering of plasmalemma in specialized regions of the cell. The role of microtubules in the invagination of the chick primitive streak was discussed by N. H. Granholm (South Dakota State University). Studies by B. Burnside (Harvard University) on neurulation of amphibia indicate that microtubules are implicated in the elongation of cells of the neural plate, and microfilaments are active in cells undergoing apical constriction to form the neural tube.

The meeting closed with an afternoon of general discussion which in-

cluded a consideration of some recent controversies on the action of cytochalasin B on microfilaments, and on the role of microtubules in chromosome movement. The small size of this meeting provided an opportunity for the informal discussion of current developments by all the participants and, in the opinion of the writer, such conferences can contribute much to clarifying—if not resolving—conflicting points of view.

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Arene Oxides: Biochemistry and Metabolism

Although arene oxides (epoxides of aromatic compounds) were proposed as reactive intermediates in the metabolism of polycyclic aromatic compounds some 25 years ago by E. Boyland, the first symposium on this subject was held at the Roche Institute of Molecular Biology, Nutley, New Jersey, on 6 and 7 April 1972. Arene oxides have become the focal point of interest in laboratories around the world because of the possibility of obtaining them synthetically in sufficient amounts for studying their chemical, physical, and biological properties. It has become possible to demonstrate that they are in fact the primary oxidation products of catalytically hydroxylated—for example by aryl hydroxylase (cytochrome P-450)—aromatic compounds. Naphthalene and dibenz(*a,h*)anthracene (directly) and brombenzene and benzo(*a*)pyrene (indirectly) yield the corresponding arene oxides as primary oxidation products on treatment with cytochrome P-450. The oxides are highly reactive electrophiles with a lifetime of minutes under physiological conditions. They rearrange to phenols, which react with glutathione to yield adducts that are then converted to mercapturic acid. With a water molecule arene oxides give rise to corresponding dihydrodiols. The rearrangement and hydration are presumably catalyzed by enzymes.

Of special interest is the cytotoxicity of arene oxides resulting from covalent binding to proteins and nucleic acids. Direct evidence was presented relating cytochrome P-450–catalyzed arene oxide formation to cytotoxicity, mutagenicity, and carcinogenicity of