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Mechanism of Cytokinesis in Animal Cells

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Since cell division is an indispensable process for living organisms, it has been a great topic in biology. The animal cell divides into two by constriction of the cleavage furrow. It has been apparent that the cleavage furrow actively exert a force for the constriction. The structure called the contractile ring or the contractile arc has been found in equilateral cleavage or in unilateral cleavage, respectively, and shown to be mainly composed of actin filaments. We have been studying at a molecular level the mechanisms by which the force for the constriction is produced and the contractile apparatuses are formed.

The interaction between actin and myosin filaments has been known long to produce the contractile force in skeletal muscle. In non-muscle cells, however, even the presence of these proteins had not been established in the early 1970s except *Physarum* plasmodium and blood platelet. We studied ATPases in sea urchin eggs to clarify motor proteins for cleavage, and found myosin. We produced antibodies against starfish egg myosin which abolished the interaction between actin and myosin. When the antibodies were microinjected into live starfish blastomeres, cleavages of these cells were inhibited. This was the first evidence that myosin is involved in cytokinesis. On the other hand, this experiment exploited a novel approach to function of proteins in the cell. The involvement of myosin in cytokinesis has recently been re-confirmed in yeast and *Dictyostelium discoideum,* by gene targeting.

Next we became interested in the dynamic property of the contractile ring. This structure had been reported to appear at the onset of furrowing, reduce its volume during contraction and finally disappear after cleavage. This dynamics could not be explained solely from the property of actin itself. We searched for factors which regulate supramolecular structure of actin in the echinoderm eggs, and found nine proteins which modulate assembly properties of actin *in vitro.* Among these proteins, alpha-actinin was shown to be concentrated in sperm-reception cones in immature oocytes, fertilization cone and cortical layer in fertilized eggs, and the cleavage furrow.

Even after these studies, both the dynamics and the mode of contraction of the contractile ring or arc were still mysterious. Perhaps the most important approach to these problems is isolation of the contractile apparatus. This had not been successful for many years. Recently, we have been able to isolate the cleavage furrow from newt eggs by a surgical method. The isolated furrow was contractile *in vitro* in the presence of ATP. The contraction was inhibited by various actin- and -SH poisons which re-confirmed the role of the actin-myosin system in the furrowing. The ultrastructure of the contractile arc was also investigated in detail at the first time. Evidence that the arc filaments are formed by bundling of the unorganized cortical actin filaments was obtained. Furthermore, interestingly, the isolated furrow fraction contained some unique proteins. We have also succeeded in isolating the cleavage furrow from sand dollar (*Clypeaster japonicus*) eggs and found that the fraction contained unique proteins. Currently we are trying to identify these proteins. This approach should lead us to further understanding of the mechanism of cleavage.