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# SIGNAL TRANSDUCTION MECHANISMS FOR THE REGULATION OF SPERM MOTILITY

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Much evidence has accumulated suggesting that the basic mechanochemical mechanism of flagellar motility is ATP-induced sliding of microtubules. Since Morisawa et al. (1980,1983) first found the physiological factors triggering the initiation of sperm motility in teleosts, studies on spermatozoa have been focused on the signal transduction mechanism for regulation of motility. Completely immotile sperm in the male reproductive organ start to become motile on spawning or ejaculation. Activation of sperm motility and attraction of sperm to eggs in response to substances released from the egg occur after the initiation of motility. I and my colleagues have showed the possible regulatory mechanisms for sperm motility with two different types of trigger, *i.e.* change in the external environment and ligand-receptor binding.

Initiation of sperm motility is triggered by signals in many cases from the environment. Spermatozoa of salmonid fishes such as rainbow trout are completely quiescent by a high concentration of $K^+$ contained in the seminal plasma. Release from the suppression of $K^+$ on spawning in fresh water causes the reduction of the $K^+$ surrounding sperm and then induces the efflux of $K^+$ through the $K^+$ channel, hyperpolarization of the plasma membrane and increase in intracellular $Ca^{2+}$. Cyclic AMP synthesized by adenylyl cyclase, which may be activated by the increased intracellular $Ca^{2+}$, induces activation of cAMP-dependent protein kinase and tyrosine kinase. Phosphorylation of tyrosine residues of Motility Initiating Phospho-Protein (MIPP) with a molecular weight of 15,000 which is located in the basal region of the sperm flagellum causes the conversion of sliding to bending of microtubules in the axoneme, resulting in the initiation of sperm motility. The cell signalling systems that are involved in the control of flagellar movement are located in the basal region of flagellum in salmonid fishes.

Spermatozoa of marine teleosts, such as the puffer fish and freshwater cyprinid teleosts, such as the goldfish and of amphibians, such as frogs are quiescent by the osmolality isotonic to the seminal plasma (almost 300 mOsm $kg^{-1}$), but become motile when the sperm are diluted with a hypotonic fresh water for freshwater teleosts and amphibians and with a hypertonic seawater for marine teleosts. The $K^+$-dependent and osmolality-dependent initiation of sperm motility mimic the motility initiation on spawning of sperm in the natural environment.

Shrinkage or swelling of sperm cells by change of the environmental osmolality occurs and causes increase or decrease in intracellular $K^+$ which triggers the initiation of axonemal movement. Possible contributions of $Ca^{2+}$ and intracellular pH to the phenomenon are proposed in marine teleosts.

After sperm initiate motility, the motility is sometimes increases in response to secretions from the eggs. Spermatozoa of the herring that are immotile in seawater, start to move actively, when they reach the egg surface, by herring sperm activating peptides(HSAPs) with the molecular weight of 8.1 kDa which are released from the eggs. The HSAPs are homologous to Kazal type trypsin inhibitor, suggesting the contribution of interaction of enzyme and its inhibitor to sperm activation. Prolyl endopeptidase extracted from herring sperm with Triton X-100 was remarkably activated by HSAPs. Activation of the protease and activation of sperm motility by HSAPs are inhibited by a specific protease inhibitor, suggesting that prolyl endopeptidase is related to HSAPs-induced sperm activation. It is possible that the interaction of a protease and its inhibitor plays a key role in sperm activation.

Sperm chemotaxis toward eggs occurs under the influence of a chemo-attractant released from the egg to complete fertilization. Our recent study showed that a sperm-activating and -attracting factor(SAAF) requires $Ca^{2+}$ for the modulation of chemotactic behavior of the sperm as well as for induction of activation. However, cAMP, an intracellular factor for activation of *Ciona* sperm, is independent of sperm chemotaxis. Thus it seems that one kind of molecule mediates two different pathways: $Ca^{2+}$- and cAMP-dependent sperm activation and sperm attraction which is regulated by $Ca^{2+}$ alone.

Internal cascade systems for the regulation of sperm motility are triggered by several factors, mainly second messengers, such as cyclic nucleotides, $Ca^{2+}$, and seem to converge upon the phosphorylation of proteins through several kinds of protein kinases which would be related to the axonemal movement. For initiation and activation of sperm motility, the main cell signaling pathway is cyclic nucleotide-dependent, whereas the chemotactic behavior of sperm may be modulated by $Ca^{2+}$ rather than cAMP. Efforts to identify the molecular mechanisms of the regulation of sperm motility will contribute to understanding of general signal transduction mechanisms in cells.