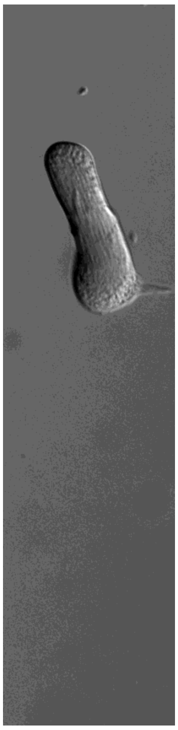
Mitochondria shape cell morphology

May 9, 2011 – Animals employ a surprising array of tricks to ensure their reproductive chances, and successful innovations, such as the feathers in a male peacock's tail, can drive evolutionary change. In another remarkable example, some species of *Drosophila* develop sperm as long as 6 cm, around 30 times the length of the fly itself. Such elongated sperm are more successful in reaching eggs, resulting in the genes of their possessors being evolved through natural selection. But how are such dramatic cellular morphologies achieved?

Tatsuhiko Noguchi and colleagues in the Laboratory for Morphogenetic Signaling (Shigeo Hayashi, Group Director) have now shown in the fruit fly, *Drosophila melanogaster*, how mitochondria play a critical role in sperm elongation in this species. The report, published in Current Biology, reveals that interactions between giant mitochondria and microtubules underlie and maintain the sperm's extraordinary stretch.



Drosophila melanogaster sperm cells undergo changes in shape during their maturation that leave them 200 times longer without any increase in volume. Four primary structures run along the sperm's longitudinal axis: the flagellar axoneme, cytoplasmic microtubules, giant mitochondria, and cables of F-actin. It has previously been shown that the axoneme is not required for sperm elongation, but the role of the other components has remained unknown. In their recent work, Noguchi et al. extracted intact sperm cells and maintained them in culture, allowing them to apply live imaging techniques to get to the bottom of these questions.

The group began by chemically interfering with actin and microtubule function, which revealed that while actin was dispensable, microtubules were necessary for sperm tail elongation. They followed up by inhibiting microtubule growth in a localized fashion, and found indications that the sperm tail end is the focus of elongation activity. They looked next at the role of mitochondria. Giant mitochondria form from the fusion of multiple smaller mitochondria, but Noguchi found that when he inhibited this fusion, sperm elongation was markedly reduced. Even more interestingly, the crucial property of these organelles was shown to be their length and shape, rather than their better-known energy-generating respiratory activity.

The discovery that both microtubules and mitochondria are essential for sperm elongation naturally suggested the next experiment, in which the group asked if they act on each other. When microtubules were destroyed in the absence of axoneme, giant mitochondria reverted from their elongated form to a rounded shape. When mitochondrial fusion was inhibited, microtubules assembled preferentially on fragmented mitochondria. Electron microscopic imaging further revealed structures cross-linking both between microtubules and between microtubules and mitochondria.

In loss-of-function mutants for Milton, a protein cross-linking mitochondria to microtubule motor kinesisn, this sliding action, and consequently sperm elongation, were lost, suggesting a role for this motor protein in the process. Further experiments in which microtubules were transiently depolymerized and allowed to regrow indicated that these cytoskeletal structures use the mitochondrial surface as a substrate for growth.

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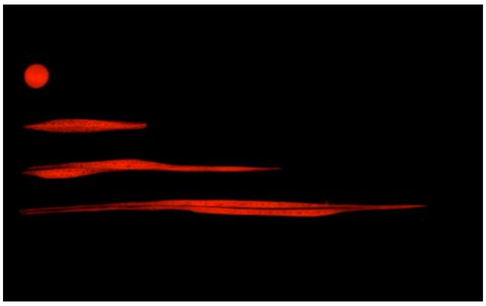

Elongation of giant mitochondria showing increase in length while volume remains constant.

Given these findings, the group proposes that sperm elongation plays out as follows. First, microtubules form at the surface of giant mitochondria in the sperm tail, after which microtubules pair up by cross-linking and slide along the mitochondrial surface, causing them to lengthen and thin, creating a foothold for more microtubules to accumulate and continue the elongation process, as well as to stabilize the structure.

These results represent the first finding that mitochondria can contribute to cell morphogenesis. “The discovery that the mitochondria that occupy our cells can act not only as cellular power plants, but in germ line development as well is intriguing,” says Hayashi. “Mitochondria have a strong bi-layered membrane, and can additionally provide the energy needed for flagellar motion, so the fact that they are used as a scaffold in this context makes perfect sense.”