Nature Reviews Molecular Cell Biology | AOP, published online 16 November 2011; doi:10.1038/nrm3234

DEVELOPMENT

Autophagy eliminates paternal mitochondria

Mitochondrial DNA (mtDNA) is thought to be maternally inherited, with paternal mtDNA being eliminated from fertilized oocytes by an unknown mechanism. Two groups now show that, in *Caenorhabditis elegans*, paternal mitochondria are degraded by fertilization-induced autophagy.

Both groups monitored fluorescently labelled paternal mitochondria and the autophagosome marker LGG-1, a homologue of mammalian LC3, in *C. elegans* embryos. They found that, after fertilization, LGG-1-positive structures accumulated around paternal mitochondria in early embryos, but disappeared by the 16-cell stage (Sato and Sato) or after the first mitotic divisions (Al Rawi *et al.*). Al Rawi *et al.* also observed mitochondria in double-membrane vesicles (which are indicative of autophagosomes) after fertilization. Thus, autophagosome formation coincides with the localization, and disappearance, of paternal mitochondria.

But do autophagosomes eliminate paternal mitochondria? Both groups found that the formation of these structures was triggered by spermatozoon entry into the ooplasm. Sato and Sato also discovered that paternal mitochondria were not degraded in embryos depleted of the small GTPase RAB-7, which is required for autophagosome–lysosome fusion and thus for the degradation of autophagosome components. Furthermore, both groups found that paternal mitochondria were not degraded in *lgg-1*-depleted embryos. Thus, spermatozoon-triggered autophagy degrades paternal mitochondria, eliminating paternal mtDNA.

Next, as the mitochondria of mammalian spermatozoa are ubiquitylated, both groups tested whether ubiquitin might target spermatozoan mitochondria for autophagy-mediated degradation in *C. elegans*. They found that spermatozoan mitochondria were not ubiquitylated either in mature spermatozoa or after their entry into the ooplasm, although spermatozoan membranous organelles (specialized vesicular structures) were rapidly ubiquitylated after ooplasm entry. Despite this differential ubiquitylation, spermatozoan membranous organelles and mitochondria are both degraded by autophagy.

Finally, Al Rawi *et al.* stained fertilized mouse oocytes with antibodies against ubiquitin and LC3, observing that mitochondria are ubiquitylated in the midpiece of spermatozoa after fertilization, where LC3 staining is also present. This suggests that the autophagy-mediated degradation of paternal mitochondria might be evolutionarily conserved, even if the dependence on ubiquitylation is not.

Together, these studies explain why paternal mtDNA is not inherited and reveal a novel physiological role for autophagy.

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ORIGINAL RESEARCH PAPERS Sato, M. & Sato, K. Degradation of paternal mitochondria by fertilization-triggered autophagy in *C. elegans* embryos. *Science* 13 Oct 2011 (10.1126/science.1210333) | Al Rawi, S. *et al.* Postfertilization autophagy of sperm organelles prevents paternal mitochondrial DNA transmission. *Science* 27 Oct 2011 (10.1126/science.1211878)