Nature Reviews Molecular Cell Biology | Published online 21 Jul 2016; doi:10.1038/nrm.2016.99

DEVELOPMENT

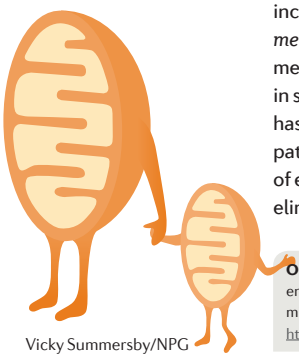
Eliminating paternal mitochondria

In most animals, mitochondria are inherited maternally, whereas paternal mitochondria are eliminated; however, the mechanisms underlying selective paternal mitochondrial elimination (PME) are still largely unclear. Zhou *et al.* now report that, in *Caenorhabditis elegans*, the endonuclease CPS-6 mediates the degradation of paternal mitochondrial DNA (mtDNA) and its activity promotes efficient PME through autophagy.

To identify mitochondrial factors involved in PME, the authors performed an RNAi screen against 217 *C. elegans* nuclear genes that are predicted to encode mitochondrial proteins, and looked at the effects of gene knockdown on paternal mtDNA removal during embryogenesis. RNAi of *cps-6*, which encodes a homologue of human mitochondrial endonuclease G, resulted in persistence of paternal mtDNA to the late stages of embryogenesis, whereas normally paternal mtDNA disappears early, at around 64-cell stage embryos. PME occurred at the same time as paternal mtDNA clearance and was delayed when *cps-6* was lost. Moreover, the authors found that paternal (but not maternal) *cps-6* is required to promote PME and, by analysing the effects of a *cps-6* mutation that removes the catalytic site of CPS-6, they found that CPS-6 enzymatic activity is required for PME.

When observing paternal *C. elegans* mitochondria by electron microscopy, the authors found that they self-initiate internal breakdown, seen by the formation of mitochondrial matrix aggregates. This internal damage occurred shortly after fertilization, concurrent with mitochondria depolarization, and led to the release of CPS-6 from the intermembrane space into the matrix and thus to paternal mtDNA degradation. This is normally followed by autophagosomal degradation, but loss of *cps-6* reduced the formation of autophagosomes on paternal mitochondria.

> “the role of endonuclease G in paternal mtDNA elimination may be conserved”



Vicky Summersby/NPG

This study shows that, following fertilization, CPS-6 is required for the rapid degradation of paternal mtDNA and internal breakdown of paternal mitochondria. This ‘self-destruction’ process is important for the efficient recruitment of autophagosomes to paternal mitochondria and their degradation. Interestingly, Zhou *et al.* also report that PME is important for animal fitness, as loss of paternal *cps-6* compromised animal development and increased embryo lethality. As *Drosophila melanogaster* endonuclease G also mediates the degradation of mtDNA in sperm during spermatogenesis and has been proposed to play a part in paternal mtDNA elimination, the role of endonuclease G in paternal mtDNA elimination may be conserved.

Kim Baumann

ORIGINAL ARTICLE Zhou, Q. *et al.* Mitochondrial endonuclease G mediates breakdown of paternal mitochondria upon fertilization. *Science* http://dx.doi.org/10.1126/science.aaf4777 (2016)

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