The incredible shrinking organelle

Michael W. Gray

Considering its central role in energy metabolism in almost all eukaryotes, the mitochondrion is an amazingly plastic organelle, both evolutionarily and functionally. The few genes that the mitochondrial genome (mitochondrial DNA; mtDNA) encodes are clearly bacterial in origin—emanating from the α-proteobacterial lineage—supporting the widely held view that the mitochondrion is the evolutionary remnant of a bacterial symbiont (Gray *et al*, 2001). However, contemporary mitochondria are nothing like contemporary bacteria. For one thing, even the most gene-rich mtDNA encodes far less genetic information than the most gene-poor bacterial genome, and mitochondrial genomes are different from bacterial genomes in form, organization and mode of expression; these features vary tremendously among diverse eukaryotes. Mitochondrial genomes might be circular, linear or even highly fragmented, and they might contain highly fragmented and rearranged genes. Only within a poorly studied group of eukaryotic microbes—protists—known as jakobid flagellates does the mtDNA resemble a typical, albeit highly reduced, bacterial genome.

In addition, the mitochondrial proteome is not only overwhelmingly (>90%) encoded in the nucleus, but only a small proportion (10–15%) is demonstrably α-proteobacterial in evolutionary affiliation. Thus, in the evolutionary transition from bacterial symbiont to integrated organelle, the mitochondrion has undergone an impressive degree of re-tailoring, shedding the bulk of its genetic information and taking on proteins of diverse evolutionary origins. Moreover, this re-tailoring is highly variable within different eukaryotic lineages, with an intriguing chunk of the mitochondrial proteome seeming to be organism-specific—lacking demonstrable sequence homologues other than in very close evolutionary relatives.

Although the evolutionary shrinkage of the mitochondrial genome is well-documented, what is less widely appreciated is the wholesale shrinkage of the organelle itself in certain anaerobic eukaryotes. Taken to its extreme, such shrinkage involves complete loss of the mitochondrial genome, with a consequent reduction in the structural complexity and biochemical versatility of the organelle. This simplification might include elimination of the electron-transport chain (ETC) and thus lead to inability of the resulting mitochondrion-related organelle (MRO) to carry out a key function of aerobic mitochondria: ATP synthesis through coupled oxidative phosphorylation (for a full account, see Hjort *et al*, 2010).

One such MRO, the hydrogenosome, is a hydrogen-producing organelle that was originally characterized in an anaerobic protist, *Trichomonas vaginalis*. The *T. vaginalis* hydrogenosome lacks mtDNA as well as components of the classic mitochondrial ETC, relying instead on substrate-level phosphorylation to generate ATP. Initially, the resemblance between the anaerobic biochemistry of the *T. vaginalis* MRO and that of anaerobic bacteria such as *Clostridia* raised the possibility that the hydrogenosome might have a different evolutionary origin than the classic aerobic mitochondrion. However, studies of hydrogenosomal proteins have demonstrated that the hydrogenosome is an evolutionarily derived (remnant) mitochondrion. Hydrogenosomes have been found in eukaryotes that are widely separated in phylogenetic trees, and in such trees, anaerobic, hydrogenosome-containing eukaryotes are often interspersed with close relatives that grow aerobically and contain conventional mitochondria. This punctate phylogenetic distribution suggests that the transition from mitochondrion to hydrogenosome has happened repeatedly and independently throughout eukaryotic evolution.

The mitosome, an even more shrunken MRO that has not only dispensed entirely with a genome, but also has no ATP-generating capacity. This MRO was discovered in anaerobic eukaryotes that were initially thought to lack mitochondria entirely, the postulate being that they diverged away from the main line of eukaryotic evolution prior to the symbiosis that led to the mitochondrion. However, in all supposedly amitochondriate protists that have been examined, a candidate mitosome has been identified. As with hydrogenosomes, a punctate phylogenetic distribution of mitosomes is emerging.

Recently, intermediate forms of 'shrinking organelle' have been identified in the anaerobic protists *Nyctotherus ovalis*, *Blastocystis* sp. and *Proteromonas lacertae* (Hjort *et al*, 2010; Pérez-Brocal *et al*, 2010; de Graaf *et al*, 2011), relatives of brown algae and diatoms. In these cases, regions of the mtDNA that code for terminal portions of the ETC and for the mitochondrial ATP synthase have been discarded. The remaining DNA specifies genes for components of a mitochondrial translation system, as well as subunits of a proton-pumping complex I (NADH:ubiquinone oxidoreductase); a remarkable example—comparing the ciliate *Nyctotherus* with the stramenopiles *Blastocystsis* or *Proteromonas*—of convergent mtDNA evolution. These observations suggest that the transitional MROs of *Nyctotherus*, *Blastocystis* and *Proteromonas* retain a partial ETC, as well as the ability to synthesize protein, whereas other data (EST surveys) indicate that they are metabolically more complex than either hydrogenosomes or mitosomes. The discovery of these particular MROs is important because their existence argues that the transition from fully fledged aerobic mitochondrion to fully fledged anaerobic mitosome proceeds through, and might stop at, several intermediate stages: a realization that not only dramatically emphasizes the evolutionary and functional versatility of the mitochondrion, but also opens the possibility that we might yet uncover still other variations of this incredible shrinking organelle.

REFERENCES

de Graaf RM *et al* (2011) *Mol Biol Evol* **28:** 2379–2391

Gray MW *et al* (2001) *Genome Biol* **2:** 10181–10185

Hjort K *et al* (2010) *Phil Trans R Soc Lond B Biol Sci* **365:** 713–727

Pérez-Brocal V *et al* (2010) *Genome Biol Evol* **2:** 257–266

Michael W. Gray is at the Centre for Comparative Genomics and Evolutionary Bioinformatics, Department of Biochemistry and Molecular Biology, Dalhousie University, Halifax, Nova Scotia, Canada.
E-mail: m.w.gray@dal.ca

EMBO *reports* (2011) **12,** 873.
doi:10.1038/embor.2011.168