

## EVOLUTION

## From organelle to nucleus

In a reconstruction of events that took place early in the evolution of eukaryotic cells, a new study has shown how the transfer of DNA from an organelle to the nucleus can give rise to functional genes.

After the initial uptake of endosymbiotic bacteria that led to eukaryotic evolution, DNA transfer took place between newly formed organelles and host nuclear genomes. Stegemann and Bock used cultured tobacco cells carrying a construct that represents the transfer of a plastid gene to a position next to a nuclear gene. The construct was moved from transgenic chloroplasts to the nuclear genome and consists of one gene, *aadA*, in a cassette with sequences that drive its expression only in plastids, plus an upstream gene, *nptII*, which is flanked by eukaryotic promoter and termination signals.

By growing large numbers of cells in the presence of the two antibiotics to which *aadA* encodes resistance, the authors selected lines in which *aadA* had become functional, with expression from the nuclear genome. In all cases, rearrangements had placed *aadA* under the control of the *nptII* promoter; however, the signals that were needed for mRNA 3' end formation had been provided by the plastid 3' flanking sequences. The authors postulate that the AT-richness of plastid non-coding regions might make it easier for chloroplast genes to take on eukaryotic-type mRNA cleavage and polyadenylation.

Although other outcomes and functionalization processes are possible, this study provides an important insight into how organellar gene functions can be taken over by the nucleus — a process that might have fundamentally shaped the biology of eukaryotic cells.

Louisa Flintoft

**ORIGINAL RESEARCH PAPER** Stegemann, S. & Bock, R. Experimental reconstruction of functional gene transfer from the tobacco plastid genome to the nucleus. *Plant Cell* 3 November 2006 (doi:10.1105/tpc.106.046466)

## GENE THERAPY

## Getting into mitochondria

“...this approach could potentially be used to treat several other diseases that are caused by mitochondrial tRNA mutations.”

Gene therapy options for diseases that are caused by mutations in mitochondrial DNA are limited for several reasons, not least the difficulty of getting therapeutic molecules into the organelle. A recent study shows how this problem can be overcome by co-opting a mitochondrial import mechanism from protozoan parasites.

*Leishmania* parasites use a specialized protein complex to import tRNAs into mitochondria. Mahata and colleagues investigated whether this complex, RIC (RNA import complex), could be used to restore mitochondrial function in cells from patients with myoclonic epilepsy with ragged red fibres (MERFF) and Kearns–Sayre syndrome (KSS). In these conditions,

the *MTTK* gene, which encodes mitochondrial tRNA<sup>Lys</sup>, is mutated or deleted, resulting in decreased translation of mitochondrial mRNAs.

The authors used ‘cybrid’ cell lines that were made by fusing cytoplasts (enucleated cells) from MERFF and KSS patients with a cell line that lacks mitochondrial DNA. When these cells were incubated with RIC, the complex was taken up and transported into mitochondria. Using RT-PCR to detect tRNA<sup>Lys</sup> in different cellular compartments, Mahata and colleagues showed that, as hoped, RIC mediates mitochondrial import of cytoplasmic tRNA<sup>Lys</sup>.

Is RIC-mediated tRNA import sufficient to restore mitochondrial

## EVOLUTION

## Good mothers have bad sons

When a gene affects a trait that has an optimum value that differs between the sexes, its alleles can have opposing effects on fitness in males and females. Such intralocus sexual conflict predicts that the sons of high-fitness females and the daughters of high-fitness males will be of low fitness, undermining the effect of sexual selection. Pischedda and Chippindale directly measured fitness in *Drosophila melanogaster* to demonstrate the extent of intralocus sexual conflict and showed that it occurs mainly in X-chromosomal genes.

Many genes that affect sexually dimorphic phenotypes have evolved to be imprinted, expressed in a sex-limited manner, or inherited preferentially by the same sex. This reduces the problem of alleles that increase the fitness of one sex interfering with the fitness of the other. However, many loci are not

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modified in these ways and there is mounting evidence that some are the focus of intralocus sexual conflict.

After screening the *D. melanogaster* genome for genetic variation in fitness, the authors selected lines of high-fitness and low-fitness males and females, and directly measured the fitness of their male and female offspring. High-fitness females produced fitter daughters but less fit sons than low-fitness females, and high-fitness males produced less fit daughters than low-fitness males. However, the sons of high-fitness males did not inherit the fitness of their fathers, which is consistent with most of the sexually antagonistic loci being on the X chromosome.

These results help explain why strong sexual selection does not eliminate variation for fitness in populations. Moreover, they might explain why the results of sexual selection are more pronounced



translation and correct respiratory defects? The authors used cycloheximide treatment to block cytoplasmic mRNA translation, allowing them to monitor mitochondrial protein synthesis. RIC treatment restored mitochondrial translation to almost wild-type status in MERFF and KSS cells. Furthermore, mitochondrial respiration was restored by RIC in MERFF cells (this is not possible in KSS cells as other genes that are essential for respiration are deleted in addition to *MTTK*). This rescue of respiration was dependent on the ability of RIC to import cytoplasmic tRNA<sup>Lys</sup>.

*Leishmania* mitochondria import several other cytosolic tRNAs as well as tRNA<sup>Lys</sup>, indicating

that this approach could potentially be used to treat several other diseases that are caused by mitochondrial tRNA mutations. The authors point out that RIC also mediates the translocation of small RNAs, raising the exciting possibility of using this approach for a wider range of conditions by manipulating the expression of mitochondrial genes.

Louisa Flintoft

**ORIGINAL RESEARCH PAPER** Mahata, B. *et al.* Functional delivery of a cytosolic tRNA into mutant mitochondria of human cells. *Science* **314**, 471–474 (2006)

**FURTHER READING** Taylor, R. W. & Turnbull, D. M. Mitochondrial DNA mutations in human disease. *Nature Rev. Genet.* **6**, 389–482 (2005)

**WEB SITE**  
Indian Institute of Chemical Biology:  
<http://www.iicb.res.in>

in birds and butterflies, in which males are the homogametic sex. In these species, sex-linked fitness variation can be passed from fathers to sons, allowing females to select for exaggerated male secondary sexual features more efficiently.

Several field studies indicate that intralocus sexual conflict is taxonomically widespread, but more work must be done to directly measure it outside laboratory populations of *D. melanogaster*. It can occur in any trait that is differentially selected between the sexes but is genetically constrained from diverging. Research on this topic therefore affects areas such as the evolution of imprinting, the maintenance of polymorphism, the existence of evolutionary constraints and the cost of sex.

Patrick Goymer



**ORIGINAL RESEARCH PAPER** Pischedda, A. & Chippindale, A. K. Intralocus sexual conflict diminishes the benefits of sexual selection. *PLoS Biol.* **4**, e356 (2006)

**FURTHER READING** Chenoweth, S. F. & Blows, M. W. Dissecting the complex genetic basis of mate choice. *Nature Rev. Genet.* **7**, 681–692 (2006)

## IN BRIEF

### GENOME EVOLUTION

Natural selection on human microRNA binding sites inferred from SNP data.

Chen, K. & Rajewski, N. *Nature Genet.* 29 October 2006 (doi:10.1038/ng1910)

Using SNP genotype data from three human populations to study cis-regulatory sites in the human genome, these authors show that negative selection is stronger on computationally predicted microRNA (miRNA) binding sites than on other conserved 3' UTR sequence motifs. This finding provides evidence for the contribution of miRNAs to fitness. This approach, which can be extended to other types of cis-regulatory sites, indicated that 30–50% of unconserved miRNA binding sites can be functional. The probably deleterious effects of polymorphisms in predicted miRNA binding sites make them candidates for disease-causing variants.

### GENOMICS

The genome of the sea urchin *Strongylocentrotus purpuratus*.

Sea Urchin Genome Sequencing Consortium. *Science* **314**, 941–952 (2006)

Sea urchin embryos have been extensively used in developmental, molecular, evolutionary and cell biology. The sequencing and analysis of the sea urchin genome has now been reported. The 814 Mb genome was sequenced at ~8× coverage using shotgun cloning and BAC sequences, and is estimated to contain ~23,300 genes. Genome analysis revealed a wealth of information about sea urchin biology (including a surprisingly sophisticated immune system), as well as vertebrate and chordate genome evolution.

### CANCER GENETICS

The BRCA1/BARD1 heterodimer modulates RAN-dependent mitotic spindle assembly.

Joukov, V. *et al. Cell* **127**, 539–552 (2006)

The tumour suppressor BRCA1 functions in maintaining genomic integrity, but the details of how it does so have not been completely determined. Using *Xenopus laevis* egg extracts and human cells, this study demonstrates a previously unknown role of BRCA1 in mitotic spindle assembly. Heterodimers of BRCA1 and BARD1 work downstream of the RAN pathway to modulate the activity of spindle-pole proteins, probably through their E3 ubiquitin ligase activity. Defects in spindle-pole formation that lead to chromosome-segregation defects and aneuploidy might contribute to the genomic instability that is observed in BRCA1-deficient tumour cells.

### DNA REPAIR

Age-dependent usage of double-strand-break repair pathways.

Preston, C. R. *et al. Curr. Biol.* **16**, 2009–2015 (2006)

Cells have evolved different mechanisms of DNA repair to preserve genetic information. The authors analysed the amount and quality of DNA double-strand break repair in *Drosophila* premeiotic germ cells and found that the relative use of different repair pathways changes as the organism ages. In particular, cells in old individuals use slow but accurate homologous recombination, whereas cells in younger flies opt for faster but error-prone repair mechanisms. This might contribute to the accumulation of genetic damage that takes place during ageing.