

# Does endosymbiosis explain the origin of the nucleus?

*To the editor* — Horiike *et al.*<sup>1</sup> give an excellent bioinformatic analysis showing relationships between yeast genes that function in the nucleus and archaeal genes, and between yeast genes that function in the cytoplasm and bacterial genes. However, their conclusion that the nucleus originated as an archaeal endosymbiont fails to explain the following features of the nucleus: the structure of the nuclear envelope; the nuclear pore complex; linear chromosomes; absence of phagocytic bacteria; the preservation of RNA-world relics in eukaryotes, and reduction of these in prokaryotes. Furthermore, their explanation contradicts the general trend of gene loss reported in parasitic, endosymbiotic and organellar genomes<sup>2</sup>.

Clear parallels exist between bacterial, mitochondrial, hydrogenosomal and chloroplast membranes. No such parallel exists for the nuclear envelope where the inner and outer membranes are continuous. Likewise, the nuclear pore complex bears no resemblance to prokaryotic transmembrane pores. Hence, unlike for other organelles, ultrastructure does not favour endosymbiotic origins<sup>3</sup>.

The nucleus contains linear chromosomes with telomeres, which have not been found in archaea and arguably predate circular chromosomes. Forterre's thermoreduction hypothesis<sup>4</sup>, that prokaryotes arose through reductive evolution at high temperature, argues for circularization being derived; circular DNA is more thermostable than linear. Maintenance of telomeres by telomerase probably originated in the RNA world, before modern cells<sup>5</sup>; telomerase has an RNA core and is highly conserved among eukaryotes. Using RNA relics to root the tree of life argues that some eukaryote nuclear traits are ancestral, having been lost through reductive evolution in prokaryotes<sup>5</sup>; thermoreduction explains this pattern because RNA is thermolabile<sup>4,5</sup>. If some eukaryote nuclear traits predate archaeal traits, these cannot be explained by an archaeal endosymbiont.

The conclusion of Horiike and colleagues<sup>1</sup> requires that the endosymbiont

gained genes from its host, which is counter to known examples of endosymbiosis (including eukaryotic organelles) and intracellular parasitism, where the unifying feature is gene loss. Intracellular existence makes primary synthetic pathways redundant<sup>2</sup>. Furthermore, the yeast cytoplasmic–bacterial gene relationship described<sup>1</sup> can be explained by Muller's ratchet — the irreversible accumulation of mutations in small asexual populations. Relocation of organellar genes to the nucleus results in escape of the effects of the ratchet<sup>2,3</sup> but extensive transfer from host to endosymbiont would place genes under greater mutational pressure.

Neither reductive evolution nor endosymbiosis explains nuclear origins. The former, however, explains RNA-world relics and linear chromosomes in eukaryotes, is consistent with Horiike and colleagues' results<sup>1</sup> and argues against an archaeal origin for the nucleus.

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*To the editor* — Horiike *et al.*<sup>1</sup> found that yeast proteins involved in transcription, translation, DNA replication and the like are more similar to archaeobacterial homologues, whereas those involved in metabolism are more similar to eubacterial homologues. They conclude that such findings "strongly support" the notion of an origin of eukaryotic nuclei through endosymbiosis of an archaeobacterium in a eubacterial host<sup>1</sup>. Their observations are valid but the inferences about cell evolution drawn from them are flawed.

First, their conclusions hinge upon the existence of a correlation between protein compartmentation and gene origin in eukaryotes. But each functional category of genes studied, particularly the ones specific to cell compartments, contained proteins of eubacterial and archaeobacterial origins<sup>1</sup>. At the genome-wide level, protein compartmentation is a poor indicator of gene origin<sup>6</sup>. Indeed, eukaryotic ribosomes are archaeobacterial but are localized in the cytosol, whereby nuclear symbiotic models<sup>1</sup> would predict them to be nuclear.

Second, all nuclear symbiotic hypotheses<sup>3</sup> derive a primitively amitochondriate, nucleus-bearing cell — an archaeozoon — as the host for mitochondria. But all mitochondrion-lacking eukaryotes studied so far possessed a mitochondrion in their

past<sup>7,8</sup>, so they can hardly be descendants of that host. If all nucleus-bearing cells also possess(ed) mitochondria, how can we tell what came first? Inferences that the origin of the nucleus has been revealed and that this involved an archaeobacterial symbiont<sup>1</sup> are unsubstantiated.

Third, models for endosymbiotic nuclear origins draw upon the finding that the nucleus contains DNA (as do chloroplasts and mitochondria) and from the superficial similarity that can be construed (if the nuclear membrane is depicted incorrectly<sup>1</sup>) between its membrane and the double membranes surrounding chloroplasts and mitochondria. The nucleus is bounded by a single, folded membrane (no free-living cells are bounded similarly)<sup>3</sup>, its pores are permeable to molecules of relative molecular mass 5,000 (not true for any prokaryote)<sup>3</sup>, and it disintegrates at open mitosis (no compartment of demonstrably endosymbiotic origin does anything vaguely similar)<sup>3</sup>.

The new report<sup>1</sup> underscores "the archaeobacterial nature of the eukaryotic genetic apparatus and the eubacterial nature of eukaryotic energy metabolism"<sup>9</sup> — the focus of an alternative model<sup>9</sup> for the origin of eukaryotes that derives the nucleus in a mitochondrion-bearing cell<sup>3</sup> and directly accounts for eubacterial lipids and importers<sup>1</sup> in the eukaryotic plasma membrane<sup>3,9</sup>.

Not everything in a eukaryotic cell is a direct inheritance from prokaryotes — Darwin's principle of descent with modification includes the possibility of invention. After all, there must have been a time when the ancestor of eukaryotes did not possess a nucleus; the question is whether that cell possessed a mitochondrion or not.

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*Reply* — We should consider the differences in the strategies<sup>10</sup> used by eukaryotic and prokaryotic cells, and also in the structures of these cells between the past and the present: the differences in chromosomal structure and the relics of the "RNA world" between eukaryotic and prokaryotic cells must have originated from the differences in strategies between eukaryotic cells (accumulation of DNA, enlargement of cell with complex structure and functions) and prokaryotic cells (rapid growth and many populations with a high ability to adapt).

The stable conditions of the cytoplasm over long periods, which are different