

EVOLUTION

## Steps on the road to eukaryotes

**A new archaeal phylum represents the closest known relatives of eukaryotes, the group encompassing all organisms that have nucleated cells. The discovery holds promise for a better understanding of eukaryotic origins.**

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There are many competing hypotheses<sup>1</sup> for how eukaryotic cells, which contain a nucleus and other membrane-bound organelles, evolved from their prokaryotic ancestors, whose cells lack a nucleus. But testing these theories has been difficult owing to a lack of known intermediate stages in the prokaryote-to-eukaryote transition. In an article published on *Nature's* website today, Spang *et al.*<sup>2</sup> describe a prokaryotic lineage that is more closely related to eukaryotes than any yet sampled and that shares with eukaryotes several genes previously thought to define aspects of eukaryotic biology. This technically outstanding paper has far-reaching implications for how we view early eukaryotic evolution, including our own deep ancestry.

In most textbooks the cellular world is

divided into three domains<sup>3</sup>: the eukaryotes (Eukarya) and two distinct prokaryotic groups, the Bacteria and the Archaea. In the classical three-domains tree, the eukaryotes are separated from a common prokaryotic ancestor that they share with Archaea by a long branch that has been variously interpreted as representing a long period of time with unsampled diversity, a high rate of evolution in the eukaryotic ancestor, or the extinction of intermediate forms. Surveys of environmental microbial diversity using the tools of molecular biology have sought to populate this long branch, but have so far failed to identify any fundamentally new eukaryotic groups. In the three-domains tree, the eukaryotes appear fully formed, with almost all of the cellular complexity that we associate with modern eukaryotes already in place<sup>1</sup>.

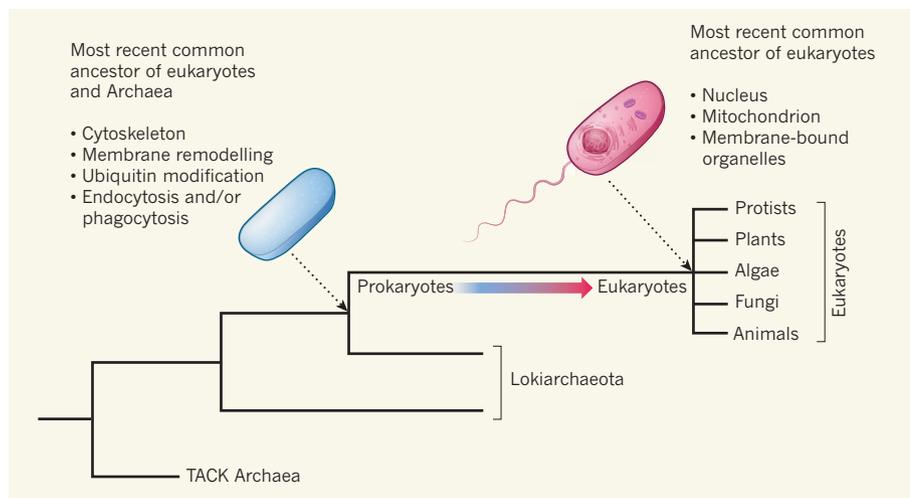
The three-domains tree is the most visible

image depicting the diversity of cellular life, but it has not gone unchallenged. An alternative two-domains tree, in which the eukaryotic lineage originated within the archaeal domain, has gathered support from recent phylogenetic analyses<sup>4–6</sup> and is now arguably the favoured hypothesis. In this tree, the eukaryotes are related to a diverse group of Archaea called the TACK superphylum<sup>7</sup>. Thus, unlike the three-domains tree, the two-domains tree includes an explicit prediction about where we should look for closer relatives of the eukaryotic ancestral lineage. Spang *et al.* report the first spectacular results of that search.

The authors sequenced the combined genomes (metagenomes) from samples of marine sediments that had been enriched for members of the Deep-Sea Archaeal Group, a lineage related to the TACK Archaea that has not been cultured in the laboratory. Using cutting-edge computational methods, Spang *et al.* reconstructed one largely complete and two partial genomes from closely related members of the Deep-Sea Archaeal Group, for which they propose the new name Lokiarchaeota. Using slowly evolving marker genes, the authors constructed phylogenetic trees that place eukaryotes within the Lokiarchaeota at the base of the TACK superphylum, suggesting that Lokiarchaeota are the closest prokaryotic relatives of eukaryotes yet discovered (Fig. 1).

Consistent with the relationship implied by the authors' trees, the Lokiarchaeum genome contains more eukaryotic signature genes than do other prokaryotes, including genes encoding actin proteins, components of a primordial vesicle-trafficking complex, a ubiquitin-modifier system and a diverse array of small GTPase enzymes belonging to the Ras superfamily. Making reliable evolutionary trees for ancient relationships is difficult<sup>5</sup>, especially given that the split between eukaryotes and the Lokiarchaeota may have occurred more than 2 billion years ago. So it is this combination of enhanced 'eukaryote-like' genome content and the phylogeny that make the case for a close relationship between eukaryotes and Lokiarchaeota so convincing.

In the absence of cultured Lokiarchaeota, the cellular manifestation of this enhanced protein repertoire can be only indirectly inferred. Nevertheless, the genome hints at an organism that has a dynamic, actin-based cytoskeleton, vesicular-trafficking and membrane-remodelling capabilities, and the potential for uptake of materials from the environment by endocytosis and/or phagocytosis. These are all traits that could have enabled the common ancestor of all eukaryotes to engulf the bacterial symbiont that became the progenitor of the mitochondrion, a vital



**Figure 1 | Lokiarchaeota are the closest known prokaryotic relatives of eukaryotes.** Phylogenetic trees presented by Spang *et al.*<sup>2</sup> place eukaryotes within the Lokiarchaeota — a new group of Archaea described by the authors. The genomes of these Archaea contain more eukaryotic-like genes than other known Archaea. This finding implies that some of the defining features of eukaryotes — including a cytoskeleton, membrane remodelling, ubiquitin modification and the capacity for endocytosis and/or phagocytosis — might have already evolved in the last common ancestor of eukaryotes and Archaea. Spang and colleagues' findings suggest that it is likely that other new lineages will be found to further close the evolutionary gap between Archaea and eukaryotes, increasing the precision with which we can identify when key cellular innovations such as the nucleus, mitochondrion and endoplasmic reticulum first evolved.

organelle of modern eukaryotes<sup>1</sup>. The presence of these genes in an otherwise unambiguously archaeal genome is consistent with hypotheses proposing that an archaeon was the host for that fundamental event in the development of eukaryotic cells<sup>1,8</sup>.

The discovery of the Lokiarchaeota provides strong evidence that phylogenetics can be used to infer ancient relationships and, in combination with single-cell and metagenomic sequencing, provides a powerful toolkit for testing ideas about the origins of the component parts of eukaryotic cells<sup>1,5,6</sup>. The same techniques can be applied in future studies to pinpoint the source of the mitochondrial endosymbiont, and to investigate the origins of the many bacterial genes that comprise a major component of eukaryotic genomes. The sequences of genes encoding ribosomal RNA molecules, which are commonly used for taxonomic classification, can help to identify environmental samples enriched in Lokiarchaeota

and its relatives. This will facilitate the isolation and cultivation of such cells for detailed study of their biology and metabolism.

The identification of Lokiarchaeota so early in the history of this nascent field suggests that more-closely related archaeal relatives of eukaryotes will soon be discovered. Some of these may be related to the Deep-Sea Archaeal Group<sup>9</sup>, an enormously diverse and abundant radiation of Archaea for which the Lokiarchaeota genomes are the first available. The genomes and cellular features of these relatives may provide a more detailed picture of the most recent common ancestor of eukaryotes and Archaea, and may help to resolve the timing of the innovations that are used to define eukaryotes. Not least, the discovery of Lokiarchaeum, and the promise of further discoveries from the vast, unexplored world of prokaryotic diversity, raises the tantalizing prospect that the investigation of eukaryotic origins can now enter the realm of testable science. ■

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