Meet the relatives of our cellular ancestor

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Microorganisms related to lineages of the Asgard archaea group are thought to have evolved into complex eukaryotic cells. Now the first Asgard archaeal species to be grown in the laboratory reveals its metabolism and cell biology.

Complex life forms including plants, animals and fungi are known as eukaryotes. These organisms are composed of cells that contain membrane-bound internal compartments such as nuclei and other organelles. Writing in Nature, Imachi et al. report that a type of microorganism called an Asgard archaeon, which might shed light on how early eukaryotic cells evolved, has finally been cultured in the laboratory. The achievement will enable detailed metabolic and cellular investigation of microbes that represent the closest Archaeal relative of eukaryotes cultured so far.

It is thought that eukaryotes arose when two types of single cell merged, with one engulfing the other. A cell from the domain archaea is proposed to have engulfed a bacterial cell of a type known as an alphaproteobacterium, and the engulfed bacterium evolved into eukaryotes’ energy-generating organelles — mitochondria.

However, the nature of the ancestral cell that engulfed this bacterium is unclear. Genomic analyses have strengthened the idea that this cell traces back to archaea because many archaeal genes involved in central biological processes such as transcription, translation and DNA replication share a common ancestry with (are phylogenetically related to) the corresponding eukaryotic genes. Was the alphaproteobacterium engulfed by a bona fide archaeal cell, or by an archaeal cell that had already acquired some eukaryotic characteristics, such as a nucleus? No fossils have been found that could shed light on the early eukaryotic ancestors. However, investigation of archaeal lineages has offered a way forward.

Since 2015, on the basis of genomic and phylogenetic analyses, archaea of a newly discovered phylum termed Lokiarchaeota (after the Norse god Loki) have been proposed as the closest living relatives of the ancient archaeal host cells from which eukaryotes are thought to have evolved. Subsequent genomic research revealed yet more such lineages, for which other Norse gods have provided names (Thor, Odin, Heimdall and Hel), and which are now grouped together with Lokiarchaeota into what are collectively termed Asgard archaea (Fig. 1). Intriguingly, all of these lineages contain an unprecedentedly large number of genes that encode what are called eukaryotic signature proteins (ESPs), which are usually found only in eukaryotes. Heimdallarchaeota currently represent the predicted closest Archaeal relative of eukaryotes on the basis of phylogenetic analysis and the ESP content of their genomes. However, all members of the Asgard archaea were previously unidentified, and their metabolism predicted, solely by their DNA sequences, and thus their cellular features have remained unknown until now.

Imachi and colleagues report that they have cultured in the laboratory an Asgard archaeon from the Lokiarchaeota phylum that they propose to call ‘Prometheoarchaeum syntrophicum’, which was obtained from deep-ocean sediments. The unusual shape and metabolism of Prometheoarchaeum prompt the authors to propose a new model for the emergence of the first eukaryotic cell. This event, predicted to have occurred between 2 billion and 1.8 billion years ago, is one of the key cellular transitions in evolutionary biology, and is also a major biological mystery.

More than six years before Asgards were even identified, Imachi and colleagues had...
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already started to generate enrichment cultures of microorganisms found in deep marine sediments. Their original goal was to find organisms that could degrade methane, and the authors searched for such microbes at a site about 2.5 kilometres below the ocean surface off the coast of Japan.

Imachi et al. set up a flow bioreactor device that mimicked the temperature (10 °C) and the low-oxygen and low-nutrient conditions at this underwater site. Within five years of starting this bioreactor work, a highly diverse consortium of active bacteria and archaea, including Lokiarchaeota, were obtained. Small subcultures were then used to gradually enrich for cultures in which archaeal cells were the dominant component, and Prometheoarchaeum was successfully enriched in this way after seven more years of work. These optimizations revealed that Prometheoarchaeum grows best in conditions that do not directly reflect its original habitat: at 20 °C and supplemented with amino acids, peptides and even baby-milk powder.

The authors report that Prometheoarchaeum’s growth depends on the presence of other microbial partners that in turn rely on Prometheoarchaeum for their survival — a relationship called a syntrophy. The partners scavenge hydrogen released by Prometheoarchaeum, a metabolic product that was correctly predicted to be generated by Asgard archaea on the basis of genomic data. The authors found that Prometheoarchaeum could be enriched to make up more than 80% of the cells in the culture, even though it grows extremely slowly, taking 2 to 4 weeks to replicate and divide. From preliminary studies using isotope analysis, the authors report that this organism can degrade externally supplied amino acids. However, that does not exclude the possibility that it also thrives on other nutrients in the growth medium.

Prometheoarchaeum cells are relatively small (300–750 nanometres in diameter), have lipids characteristic of other archaea, and show no evidence for eukaryotic-like organelles. However, the organism forms intriguing structures on its cellular surface that include long and often branching protrusions.

On the basis of its cell shape and small size, and on evidence that Prometheoarchaeum produces and syntrophically transfers hydrogen and formate molecules to other organisms, the authors propose a new model for the emergence of eukaryotic cells — one involving three partners. In this model, a free-living bacterial ancestor that would give rise to mitochondria became entangled with, and was then engulfed by, an archaeal host cell that itself was in a syntrophic relationship with a bacterial partner.

This model is consistent with earlier suggestions about the engulfment process in eukaryotic evolution, and emphasizes the importance of membrane-mediated processes in the origin of eukaryotes. However, extensive cellular protrusions are not found exclusively in this Asgard archaeon. It would therefore be of interest to investigate to what extent these protrusions differ from those of branched cellular extensions previously observed in other archaea such as Pyrodictium or Thermococcus species. In addition, it will be interesting to determine whether the ESPs potentially involved in membrane remodelling are localized in these structures in Prometheoarchaeum.

The syntrophic interactions that Imachi and colleagues propose in their model for the origin of mitochondria are based on the need for the host cell to adapt to oxygen use (as a consequence of rising oxygen levels on the ancient Earth). These ideas differ from the ‘reverse hydrogen flow’ model, which suggests instead that hydrogen produced by the archaeon is consumed directly by the bacterial mitochondrial ancestor, with no need to invoke a hypothetical third partner. Considering that Prometheoarchaeum does not directly represent the ancestral ancestor of eukaryotes (nor does any other currently existing archaeon), other suggested metabolic exchanges between the archaeal host and bacterial mitochondrial ancestor, such as hydrogen consumption from the archaeal or the bacterial side, remain plausible as initial drivers of a syntrophic relationship. In any case, the many models for the origin of eukaryotes highlight the importance of initial syntrophic associations and membrane-mediated processes. Interestingly, albeit for different reasons, both syntrophy and membranes were crucial aspects in an engineered synthetic relationship in which an Escherichia coli bacterium was maintained inside a yeast cell for more than 120 days. Imachi and colleagues’ success in culturing Prometheoarchaeum after efforts spanning more than a decade represents a huge breakthrough for microbiology. It sets the stage for the use of molecular and imaging techniques to further elucidate the metabolism of Prometheoarchaeum and the role of ESPs in archaeal cell biology. This, in turn, could guide the direction of future work investigating how eukaryotic cells emerged.

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