

EDITORIAL

Burning Questions

Is an archaeon the ancestor of eukaryotes?

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Abstract

The origin of complex cellular life is a key puzzle in evolutionary research, which has broad implications for various neighbouring scientific disciplines. Naturally, views on this topic vary widely depending on the world view and context from which this topic is approached. In the following, I will share my perspective about our current scientific knowledge on the origin of eukaryotic cells, that is, eukaryogenesis, from a biological point of view focusing on the question as to whether an archaeon was the ancestor of eukaryotes.

CELLULAR LIFE AND HISTORICAL VIEW ON THE ORIGIN OF EUKARYOTES

Based on our current understanding, cellular life can be divided into three distinct major domains: the Bacteria, Archaea and Eukaryota (Woese et al., 1990). Despite fascinating and important exceptions (Greening & Lithgow, 2020; Volland et al., 2022), Bacteria and Archaea share various cellular features such as their generally small cells that are enclosed by membranes and comprise genetic material but few internal structures with membranes discontinuous from the outer cell membrane. In contrast, eukaryotic cells are often larger and characterized by a diversity of internal membrane-bound organelles such as the nucleus, mitochondria, Golgi apparatus, endoplasmic reticulum, and chloroplasts present in photosynthetic eukaryotes.

The idea that at least some of these organelles originated through endosymbiosis and/or the uptake of formerly free-living bacteria goes back to the end of the 19th and early 20th century, with Konstantin Mereschkowsky and subsequently Ivan Wallin proposing that chloroplasts and mitochondria are derived from cyanobacteria (Mereschkowsky, 1905, 1910) and alphaproteobacteria (Wallin, 1927), respectively. Decades later, Lynn Margulis elaborated on these ideas in her serial endosymbiosis hypothesis (Margulis, 1981, 1996; Sagan, 1967). Specifically, upon the discovery of the Archaea as a domain distinct from Bacteria (Woese et al., 1990; Woese & Fox, 1977) and the finding that archaeal cells harbour a simplified informational machinery resembling that of eukaryotes (e.g. transcription and translation), she and other authors put forth the hypothesis that an archaeon may have been the symbiotic partner of the bacterial endosymbiont(s) (Lopez-Garcia et al., 2017; Margulis, 1981, 1996; Searcy, 1992).

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STATE-OF-THE-ART VIEW ON EUKARYOGENESIS AND THE DISCOVERY OF ASGARD ARCHAEA

The suggestion that eukaryotic cells may have originated through the merging of an archaeal host and bacterial symbionts, while not very popular initially, has obtained increasing support over the recent years (Eme et al., 2017; Guy et al., 2014; Koonin & Yutin, 2014; Lopez-Garcia et al., 2017; Lopez-Garcia & Moreira, 2020; Martin et al., 2015) and led to the proposal that eukaryotes represent a secondary domain of life (Williams et al., 2013). Particularly, improved phylogenetic approaches combined with a better genomic representation of genome-sequenced organisms have allowed to improve our view of the tree of life (TOL) and microbial genomic diversity, with several implications for our understanding of eukaryogenesis. While Archaea were initially thought to represent the sister lineage to an independent (autogenously evolving) lineage leading to eukaryotes (Woese et al., 1990), with few exceptions (Da Cunha et al., 2017; Da Cunha et al., 2018), the majority of phylogenetic analyses today, based on concatenated universally conserved single-copy marker genes, indicate that the branch leading to eukaryotes emerges from within the Archaea (Cox et al., 2008; Foster et al., 2009; Guy & Ettema, 2011; Raymann et al., 2015; Spang et al., 2015, 2018; Williams et al., 2011, 2020; Zaremba-Niedzwiedzka et al., 2017) as originally suggested by Lake and coworkers (Lake et al., 1984). Specifically, the discovery of the Asgard archaea (Seitz et al., 2016; Spang et al., 2015; Zaremba-Niedzwiedzka et al., 2017), which appear to be more closely related to eukaryotes than any of the previously known archaeal lineages, increased support for the placement of the eukaryotic branch within Archaea, that is, as a sister to or within the Heimdall–/ Gerd–/ Kari–/ Hod–/ Wukongarchaeota clade (Cai et al., 2020; Liu et al., 2021; Seitz et al., 2019; Zaremba-Niedzwiedzka et al., 2017). Asgard archaea were found to encode various so-called eukaryotic signature proteins, that is, proteins generally absent from genomes of Archaea and Bacteria and/or encoding domains underlying key aspects of eukaryotic cellular complexity such as an active actin cytoskeleton consisting of actins, profilins and gelsolins, a ubiquitin system as well as cell division and trafficking components (incl. homologues of endosomal sorting complexes required for transport (ESCRT) systems) (Liu et al., 2021; Spang et al., 2015; Zaremba-Niedzwiedzka et al., 2017). Subsequent experimental work on some of these proteins has confirmed a conservation in function. For instance, it has been demonstrated that Asgard profilins can regulate mammalian actin (Akil & Robinson, 2018), with heimdallarchaeal profilins inhibiting both eukaryotic and heimdallarchaeal actin polymerization, and binding being regulated by

polyproline motifs (Surgery et al., 2021). Furthermore, certain Asgard archaeal gelsolins were shown to enhance filament disassembly in eukaryotic cells in a calcium-regulated manner (Akil et al., 2020). Remarkably, the cultivation of the first representatives of the Asgard archaea, that is of the Lokiarchaeota (Imachi et al., 2020; Rodrigues-Oliveira et al., 2022), indicates that extant members of this group harbor complex cellular features including protrusions supported by cytoskeletal filaments comprising lokiactins (Rodrigues-Oliveira et al., 2022). This suggests that the last common ancestor of eukaryotes and the Asgard archaeal sister lineage might already have harboured a complex cytoskeleton. Notably, another study has recently revealed that Asgard archaeal proteins with domains homologous to eukaryotic ESCRT-I, II and III and ubiquitin system components, comprise a ubiquitin-coupled ESCRT system functioning in a similar manner as in eukaryotes (Hatano et al., 2022).

Together, this strongly indicates that certain building blocks essential for the evolution of complex eukaryotic cells have originated in a lineage of the Archaea and were directly inherited by eukaryotes from their archaeal ancestry. In turn, while the origin of the nucleus remains unresolved (Eme et al., 2017), recent research seems to unequivocally support a symbiogenetic origin of the eukaryotic cell from an archaeon contributing key informational and cellular machinery and bacterial symbionts underlying the origin of mitochondria (Fan et al., 2020; Martijn et al., 2018; Muñoz-Gómez et al., 2022; Roger et al., 2017) and chloroplasts (Sibbald & Archibald, 2020), respectively.

DOES THIS IMPLY THAT AN ARCHAEOON IS THE ANCESTOR OF EUKARYOTES?

Recent findings leave little doubt that archaea account for at least part of eukaryotic ancestry. However, to fully resolve to what extent eukaryotes are archaea, it is important to agree on a definition as to what eukaryotes are and at which point during eukaryogenesis they would have been eukaryotic in nature. Part of the current discussion and controversy around this question may arise from distinct views on the essential features of a eukaryote. Is a cell with either a nucleus or an endomembrane system a eukaryote? What about prokaryotes that harbour nucleus-like structures (Avcı et al., 2021; Katayama et al., 2020), endosymbionts (Husnik et al., 2013; von Dohlen et al., 2001) or internalized cells (Shiratori et al., 2019)? On the other hand, did the host cell only become a eukaryote once it engulfed symbionts to power its metabolism? What about eukaryotes that secondarily lost mitochondria altogether?

Etymologically, the word eukaryote is derived from Greek εὖ (eu) and κάρυον (karyon) meaning ‘true kernel’

and places emphasis on the presence of a nucleus enclosing the genome as the defining feature of eukaryotes. In this context, it may be argued that neither the evolution of an endomembrane system nor of mitochondria mark the boundary between a prokaryotic and eukaryotic cell. Unfortunately, it remains unclear whether the nucleus has symbiogenetic origins or evolved autogenously before or after the endosymbiosis of an alphaproteobacterial cell within an archaeal host. For instance, in a recent perspective, Lopez-Garcia and Moreira updated their original syntrophy hypothesis (Lopez-Garcia & Moreira, 2020) proposing that three rather than two partners were involved in the origin of the eukaryotic cell, that is, a hydrogen-producing Asgard archaeon was suggested to have been engulfed within a complex sulfate-reducing deltaproteobacterium and stood at the basis of the evolution of a nucleus with the mitochondrion evolving later upon the acquisition of alphaproteobacterial endosymbiont(s) by this deltaproteobacterial/archaeal hybrid organism. Others have suggested that a virus may be at the origin of the nucleus (Bell, 2022; Takemura, 2020). However, the most common hypotheses envision an autogenous origin of the nucleus (reviewed by Baum & Baum, 2014; Guy et al., 2014; Imachi et al., 2020; Koonin & Yutin, 2014; Lopez-Garcia et al., 2017; Martin et al., 2015), though the timing of its origin relative to other eukaryotic cellular features remains unknown (Eme et al., 2017; Pittis & Gabaldon, 2016; Vosseberg et al., 2021).

If the nucleus evolved autogenously in a hypothetical archaeal ancestor prior to the acquisition of an endosymbiont and is chosen as the defining feature of eukaryotes, an archaeon is not only the ancestor of eukaryotes, but eukaryotes could be regarded as a clade of Archaea.

Alternatively, if the acquisition of alphaproteobacterial symbionts is seen as key or at least similarly important for eukaryogenesis, eukaryotes are a symbiosis of at least two partners and as much bacterial as they are archaeal. The nucleus could have evolved autogenously prior or after this event or be the result of an additional symbiosis event. Considering that phylogenetic analyses suggest that all extant eukaryotic proteomes comprise more proteins derived from bacterial rather than archaeal ancestry (Brueckner & Martin, 2020; Pisani et al., 2007; Rochette et al., 2014), that all but the most reduced amitochondriate eukaryotes (Karnkowska et al., 2016) contain a legacy of genes tracing back to alphaproteobacterial origins (Embley et al., 2003; Hjort et al., 2010; Müller et al., 2012; Philippe et al., 2000; Stechmann et al., 2008), and that mitochondria, if not essential (Lynch & Marinov, 2017), may have been key for eukaryotic diversification (Schavemaker & Muñoz-Gómez, 2022), it may seem worth reconsidering the strict etymological definition of eukaryotes based on the presence of a nucleus alone.

In the latter case, however, one may wonder whether photosynthetic eukaryotes with plastids should be defined as yet additional domains of life, considering that they too, emerged through a symbiosis event that led to a new cellular organelle.

While it may be difficult to reach a consensus regarding the definition of eukaryotes and answer the question to what degree eukaryotes are archaea, contemplating this topic can guide prospective research avenues. Future progress on our understanding of eukaryogenesis will in part rely on the further exploration of Asgard archaeal phylogenetic diversity and the study of their cell biological features and lifestyles as this may allow to better constrain the order of events in which eukaryotic cellular complexity has evolved (Eme et al., 2017). For example, will we discover (Asgard) archaea with a true nucleus (Avcı et al., 2021)? Furthermore, a better characterization of the origin of eukaryotic proteins and cellular features, particularly those which currently lack homologues in both the putative Asgard archaeal host and alphaproteobacterial endosymbiont, will help to determine whether additional partners were involved.

The ever-increasing genomic sampling of archaeal diversity combined with profound technological developments in phylogenetics, and microscopy, will without doubt lead to many new and fascinating discoveries in the coming years, which promise to further illuminate the deep origin of the eukaryotic cell and might require us to reconsider our definition of cellular life and eukaryotes.

AUTHOR CONTRIBUTION

A.S has designed and written this perspective article.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

DATA AVAILABILITY STATEMENT

No data has been analysed.

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