

Genomic analyses of the closest isolated archaeal relative of eukaryotes reveals novel insights into eukaryogenesis

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The origin of eukaryotes remains enigmatic. Recent data suggest that eukaryotes may have evolved from an archaeal lineage known as “Asgard archaea”. Despite the eukaryote-like genomic features in these archaea, the evolutionary transition from to eukaryotes remains unclear due to the lack of cultured representatives and corresponding physiological insight. By obtaining an archaeon representing the closest isolated prokaryotic relative of eukaryotes “*CandidatusPrometheoarchaeum syntrophicum* strain MK-D1”, characterizing the strain and its genome, and further performing comparative genomic analyses, we obtain novel insight into ancestral features of Asgard archaea and eukaryogenesis.

The isolated strain MK-D1 degrades amino acids (AAs) through syntrophic interaction (H_2 and formate transfer) with methanogenic and sulfate-reducing partners. The strain was also predicted to lack various biosynthetic machinery and depend on the above partners for biosynthesis. A survey of the publicly available Asgard archaea genomes reveals that most also encode AA catabolism and H_2 metabolism and lack many biosynthetic pathways. Exhaustive comparative genomics revealed several genes related to AA catabolism and fermentative metabolism conserved across the phylum (*i.e.*, those that form monophyletic clusters in gene trees). In total, we provide the first evidence that Asgard archaea are capable of syntrophic AA degradation, dependent on symbiotic interactions for both catabolism and anabolism (*e.g.*, H_2 , formate, and metabolite transfer), and conserve related metabolic features across the superphylum, suggesting that the Asgard archaea ancestor possessed such capacities.

Evolution of this ancestral organism, possibly intracellularly simple (*i.e.*, as observed for MK-D1), towards the last eukaryotic common ancestor likely involved (i) transition from anaerobiosis towards aerobiosis, (ii) acquisition of an endosymbiont capable of O_2 respiration and ATP transfer (*i.e.*, mitochondrion), and (iii) transformation to develop elaborate intracellular structures. Based on insight from the isolate and comparative genomics, we propose a new theory for eukaryogenesis –the “Entangle-Engulf-Endogenize (E^3) model” –that sheds light on potential evolutionary scenarios that may have addressed these obstacles and led to emergence of an aerobic organotroph possessing an O_2 -respiring ATP-generating endosymbiont.

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