Proceedings of ICBioMed 2025 Symposium: Computational Modelling and Simulation for Biology and Medicine
DOI: 10.54254/2753-8818/2025.LD24436

The Origin of Mitochondria and Its Role in the Cellular Energy Revolution of Life

Hongjie Zhao

School of Life Science and Engineering, Southwest Jiaotong University, Chengdu, China
a1005649516@163.com

Abstract. The endosymbiotic origin of mitochondria is widely regarded as a defining moment in eukaryotic evolution, though its details and broader implications remain subjects of debate. This dissertation investigates the mitochondrial genesis and its pivotal function in transforming cellular energy dynamics and complexity, utilizing phylogenetic, bioenergetic, and theoretical paradigms. It tackles ongoing controversies, including the phylogenetic placement of mitochondria within Alphaproteobacteria and the relationship between enhanced energy availability and eukaryotic complexity. The analysis confirms mitochondria arose from an alphaproteobacterial endosymbiont, with a chimeric proteome blending contributions from both the symbiont and a pre-existing host premitochondrion. This endosymbiotic occurrence transcended the bioenergetic limitations inherent to prokaryotes, thereby catalyzing genomic proliferation and the emergence of advanced eukaryotic characteristics. Empirical data indicate that the host organism was probably an archaeon, potentially a hydrogen-dependent methanogen, with this pivotal event transpiring approximately 1.5 billion years ago. By resolving these debates, the thesis discussed how endosymbiosis triggered a cellular energy revolution, distinguishing eukaryotes from prokaryotes. This work highlights endosymbiosis as the key to unlocking eukaryotic genomic and functional complexity, laying a foundation for future studies into the evolutionary dynamics of life.

Keywords: Mitochondria origin, Endosymbiosis, Eukaryotic Evolution, Phylogenomics, Alpha-proteobacteria

1. Introduction

The endosymbiotic origin of mitochondria is a foundational event in eukaryotic evolution, yet its specifics remain under scrutiny. The prevailing view is that mitochondria arose from an alphaproteobacterium engulfed by a host cell, likely an archaeon akin to the Asgard group[1] However, the exact lineage of this bacterial ancestor is contested, with phylogenomic evidence suggesting it may diverge from known alphaproteobacterial clades, possibly representing an unsampled lineage[2]. Before this event, the nature of the host cell also sparks debate—did it already possess complex features, or were these traits a consequence of endosymbiosis [3]? A critical question emerges: how did mitochondrial acquisition, with its energy-generating prowess, propel the development of complex eukaryotic life? This phenomenon, often dubbed a cellular

© 2025 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/2025.LD24436

energy revolution, is tied to increased energy availability, though the precise mechanisms are still being unraveled [4,5].

This research examines the endosymbiotic theory of mitochondrial genesis and its fundamental role in cellular bioenergetics and organismal complexity. Through an integrated analysis of phylogenomic data, bioenergetic mechanisms, and theoretical frameworks, this research seeks to illuminate the characteristics and evolutionary implications of this pivotal endosymbiotic event. The investigation critically evaluates two central controversies: the phylogenetic positioning of mitochondria within the bacterial tree of life, with particular emphasis on the alphaproteobacterial hypothesis versus alternative evolutionary scenarios, and the mechanistic relationship between bioenergetic capacity and cellular sophistication [5]. It contends that mitochondrial endosymbiosis was the linchpin that unlocked eukaryotic genomic and energetic expansion.

The thesis unfolds as follows: Section 2 delves into mitochondrial origins, Section 3 traces the evolution of the mitochondrial proteome, Section 4 examines endosymbiosis and genomic complexity, Section 5 explores host cell types and timing, and the conclusion synthesizes these insights to illuminate eukaryotic evolution. The significance of this research lies in its integrative approach, clarifying how mitochondrial endosymbiosis catalyzed a cellular energy revolution. Resolving controversies and linking energy availability to eukaryotic complexity underscores endosymbiosis as the pivotal event distinguishing eukaryotes from prokaryotes, enabling genomic and functional sophistication.

2. The bacterial origin of mitochondria

2.1. Evidence for the origin of mitochondria from proteobacteria

The hypothesis that mitochondria originated from an alphaproteobacterial endosymbiont is bolstered by compelling phylogenomic, genomic, and biochemical evidence [1,6]. Phylogenetic analyses consistently classify mitochondria within the Alphaproteobacteria, revealing significant affiliations with obligate intracellular lineages such as Rickettsiales and uncultured marine taxa[6]. However, challenges such as long-branch attraction (Long-branch attraction refers to an artefact in phylogenetic trees where rapidly evolving lineages appear closely related) and compositional biases have muddied precise placements, occasionally aligning mitochondrial sequences with fast-evolving lineages like Pelagibacterales due to convergent genomic streamlining[1]. The investigators implemented rigorous sampling protocols coupled with Bayesian statistical frameworks to address phylogenetic bias inherent in antecedent studies, thereby resolving the longstanding debate concerning mitochondrial evolutionary origins. Their findings definitively establish mitochondrial lineage within the α-proteobacterial clade, demonstrating shared ancestral derivation with Rickettsiales and specific pelagic microbial assemblages.[6] .

Genomic and proteomic data reinforce this lineage. Though reduced to ~60–70 genes, mitochondrial genomes predominantly encode oxidative phosphorylation and translation components with apparent alphaproteobacterial homology[1]. About 10–20% of the mitochondrial proteome traces directly to this ancestry, while the remainder reflects host contributions or lateral acquisitions [6]. The transition from a free-living bacterium to an organelle entailed substantial genomic reduction and the evolution of protein import mechanisms, reflecting characteristics of contemporary intracellular bacteria [1]. The retention of specific genes likely stems from selective pressures for localised redox regulation in the electron transport chain [1].

DOI: 10.54254/2753-8818/2025.LD24436

2.2. Other alternative bacterial lineages

Despite the robust case for an alphaproteobacterial origin, its exact phylogenetic ties remain uncertain. [2] employed sophisticated phylogenomics to counter biases, analyzing twelve divergent alphaproteobacterial clades and a sister group. Their findings suggest mitochondria branched off before the diversification of sampled alphaproteobacteria, questioning a direct Rickettsiales-like ancestry and hinting at a deeper proteobacterial root [2]. Gray notes that only 10–20% of the mitochondrial proteome aligns with alphaproteobacteria, with the rest suggesting contributions from other bacteria or eukaryotic innovations [3]. While these alternative hypotheses warrant further exploration, the alphaproteobacterial origin remains the most substantiated, pending broader taxonomic sampling.

3. The evolution of the mitochondrial proteome

3.1. The frontal mitochondrial hypothesis

The Frontal Mitochondrial Hypothesis, often referred to as the pre-endosymbiont hypothesis, proposes that the host cell contained a premitochondrion—a membrane-bound organelle—before the endosymbiotic event that introduced the alphaproteobacterial ancestor of mitochondria [3]. This premitochondrion likely served as a compartment for critical metabolic processes, such as amino acid biosynthesis, Fe-S cluster assembly, and lipid metabolism, functions that persist in modern mitochondria. Equipped with a protein import system and various metabolite transporters, it exhibited a sophistication that preceded the arrival of the endosymbiont. The hypothesis posits that this pre-existing organelle established a structural and functional basis for the seamless incorporation of the alphaproteobacterial symbiont. A critical result of this integration was a bioenergetic transition: the premitochondrion, initially an ATP-importing organelle, evolved into an ATP-exporting entity by assimilating the symbiont's oxidative phosphorylation apparatus [7]. This change significantly boosted the host cell's energy capacity, paving the way for the complexity seen in eukaryotic cells. Evidence for this hypothesis includes mitochondrial proteins and functions lacking clear alphaproteobacterial origins, implying they were inherited from the host's premitochondrion.

3.2. The origin of non-α-proteobacterial proteins

The mitochondrial proteome is a complex mosaic, with only 10–20% of its proteins, known as the alphaproteobacterial component (APC), directly linked to the endosymbiont [3]. The predominant non-alphaproteobacterial component (NPC) comprises proteins from various archaeal, bacterial, and eukaryotic lineages. This heterogeneity challenges traditional endosymbiotic models that emphasize the alphaproteobacterial contribution alone. The pre-endosymbiont hypothesis suggests that the NPC originated from the pre-existing protein complement of the premitochondrial ancestor. Following the integration of the alphaproteobacterial symbiont, its ancestral protein import machinery APCbecame incorporated into the host-derived NPC, culminating in a composite proteome of dual origin.

This blending is apparent in metabolic pathways like the TCA cycle, where enzymes from both the NPC and APC collaborate to sustain mitochondrial function [3]. Unlike alternative theories that rely on extensive lateral gene transfer to explain the NPC's presence, the pre-endosymbiont hypothesis provides a more straightforward explanation. These proteins were already part of the host

DOI: 10.54254/2753-8818/2025.LD24436

cell's organelle, reducing the need for multiple gene acquisitions. This model elegantly accounts for the mitochondrial proteome's chimeric nature through a single endosymbiotic event enhanced by the host's pre-existing components.

4. Endosymbiotic events and the expansion of eukaryotic genomes

Having established the energy surplus from mitochondria, this paper now explores how this fueled genomic expansion. A critical outcome of endosymbiosis was endosymbiotic gene transfer (EGT), the process by which numerous mitochondrial genes migrated to the nuclear genome, profoundly influencing the host cell's genetic architecture and evolution. This transfer led to pronounced genomic asymmetry: the mitochondrial genome contracted to a minimal set of essential respiratory genes, whereas the nuclear genome underwent substantial expansion [8]. EGT has not only facilitated the accretion of genetic material to the nuclear genome but has also refined the regulatory architectures that underpin mitochondrial functionalities, thereby potentiating the evolutionary trajectory toward sexual reproduction. Cumulatively, these genetic and regulatory modifications accentuate the pivotal role of mitochondrial gene migration in modulating the genomic complexity and evolutionary ascendancy of the recipient host cell[5]. This shift enhanced cellular efficiency and adaptability, aligning mitochondrial performance with the host's broader metabolic needs.

The migration of mitochondrial genes had far-reaching effects on eukaryotic evolution. By integrating mitochondrial DNA into the nucleus, the host cell faced increased genetic instability, likely driving the development of recombination-based repair mechanisms [4]. This pressure is thought to have contributed to the origin of meiotic sex, which offered a systematic way to repair DNA damage and enhance genetic diversity, key factors in eukaryotic adaptability. Additionally, relocating genes to the nucleus reduced the mitochondrial genome's vulnerability to mutations caused by reactive oxygen species generated during respiration, a risk inherent to its proximity to the respiratory chain [7]. EGT not only augmented the nuclear genome but also enhanced regulatory oversight of mitochondrial functions, thereby promoting the evolution of sexual reproduction. Collectively, these alterations highlight the role of mitochondrial gene migration in shaping the genomic complexity and evolutionary success of the host cell [1].

5. Host cell types and endosymbiotic timing

5.1. Selective pressure on the host cell

The identity of the host cell in the mitochondrial endosymbiosis event is pivotal to understanding eukaryotic evolution, shaped by distinct metabolic and environmental pressures. Current evidence, notably from [11] in "Endosymbiotic theories for eukaryote origin," supports an archaeal host, potentially a hydrogen-dependent methanogen, as proposed by the hydrogen hypothesis. This model suggests that the host relied on a bacterial symbiont—likely an alphaproteobacterium—for hydrogen, establishing a metabolic symbiosis that drove the partnership [9]. Unlike phagocytic models, this archaeal host lacked engulfment capabilities, relying instead on intimate metabolic exchange, as highlighted in Lane's Bioenergetic Constraints on the Evolution of Complex Life. The selective pressure favoring this symbiosis was bioenergetic: the archaeon, constrained by limited energy from its plasma membrane-bound respiration, gained a transformative advantage through the symbiont's oxidative phosphorylation capacity [7]. The energy enhancement elucidated by Lane and Martin facilitated the host's transcendence of prokaryotic energetic constraints, thereby underpinning

DOI: 10.54254/2753-8818/2025.LD24436

the emergence of intricate eukaryotic characteristics [8]. The compatibility between host and symbiont, rather than physical engulfment, emerges as a critical driver, aligning with phylogenomic data linking eukaryotes to the Asgard archaea [1].

5.2. Timing of mitochondrial endosymbiosis

The timing of mitochondrial endosymbiosis is fundamental to tracing eukaryotic origins. [9] Propose an early event, potentially over 1.5 billion years ago (Ga), coinciding with methanogenic archaea in anaerobic environments like hydrothermal vents. This early acquisition, as Lane argues, provided an immediate energy surplus via mitochondrial respiration, catalyzing the development of eukaryotic complexity [7]. TThe lack of distinct prokaryotic-to-eukaryotic intermediates, as highlighted by Martin et al. and Lane, substantiates the notion of this occurrence as a unique, foundational event. The subsequent plastid endosymbiosis within photosynthetic lineages further elaborated upon this mitochondrial framework, thereby enhancing eukaryotic diversity [9]. Lane and Martin emphasize that this early timing fixed the eukaryotic lineage by unlocking genomic expansion and cellular sophistication, unattainable in prokaryotes due to bioenergetic constraints [8]. Thus, the mitochondrial endosymbiosis likely marked the inception of eukaryotic evolution, with its energetic legacy enabling later innovations.

6. Conclusion

This thesis elucidates the origin of mitochondria and their transformative role in eukaryotic evolution, addressing key research questions through phylogenetic, bioenergetic, and theoretical lenses. Primarily, the endosymbiotic origin of mitochondria is strongly substantiated within the clade of Alphaproteobacteria, with phylogenetic analyses demonstrating a close alignment with Rickettsiales and marine planktonic taxa, notwithstanding complications such as long-branch attraction. Secondly, the mitochondrial proteome's evolution reveals a chimeric nature, with 10–20% of proteins tracing to the alphaproteobacterial endosymbiont and the majority likely derived from a pre-existing premitochondrion in the host, as posited by the Frontal Mitochondrial Hypothesis. Furthermore, the establishment of mitochondrial endosymbiosis transcended the bioenergetic constraints inherent to prokaryotic systems, facilitating both genomic expansion and architectural complexity through enhanced metabolic capacity and horizontal gene transfer mechanisms, specifically the translocation of mitochondrial genetic material to the nuclear genome. Lastly, the host cell, likely an archaeon such as a hydrogen-dependent methanogen, engaged in metabolic syntrophy with the symbiont, with endosymbiosis occurring early, around 1.5 billion years ago, marking the onset of eukaryotic evolution.

Limitations include reliance on existing phylogenomic datasets, potentially skewed by incomplete taxon sampling or methodological biases. Future improvements could involve broader alphaproteobacterial and eukaryotic diversity sampling to refine phylogenetic inferences. Experimental models simulating endosymbiosis or metabolic interactions could also yield functional insights. Directions for future research include deeper investigation of the premitochondria's role, the mechanisms and selective pressures of EGT, and the bioenergetic advantages across eukaryotic lineages. This thesis reaffirms mitochondria's alphaproteobacterial roots and their energetic legacy, setting the stage for further exploration of eukaryotic evolution's intricate dynamics.

DOI: 10.54254/2753-8818/2025.LD24436

References

[1] Roger, A. J. , Muñoz-Gómez, S. A. , & Kamikawa, R. (2017). The origin and diversification of mitochondria. Current Biology, 27(21), R1177-R1192.
[2] Martijn, J. , Vosseberg, J. , Guy, L. , Offre, P. , & Ettema, T. J. (2018). Deep mitochondrial origin outside the sampled alphaproteobacteria. Nature, 557(7703), 101-105.
[3] Gray, M. W. (2014). The pre-endosymbiont hypothesis: a new perspective on the origin and evolution of mitochondria. Cold Spring Harbor perspectives in biology, 6(3), a016097.
[4] Lane, N. (2011). Energetics and genetics across the prokaryote-eukaryote divide. Biology Direct, 6, 1-31.
[5] Lane, N. (2020). How energy flow shapes cell evolution. Current Biology, 30(10), R471-R476.
[6] Fan, L. , Wu, D. , Goremykin, V. , Xiao, J. , Xu, Y. , Garg, S. , . . . & Zhu, R. (2020). Phylogenetic analyses with systematic taxon sampling show that mitochondria branch within Alphaproteobacteria. Nature ecology & evolution, 4(9), 1213-1219.
[7] Lane, N. (2014). Bioenergetic constraints on the evolution of complex life. Cold Spring Harbor perspectives in biology, 6(5), a015982.
[8] Lane, N. , and Martin, W. (2010). The energetics of genome complexity. Nature 467, 929–934.
[9] Martin, W. F. , Garg, S. , & Zimorski, V. (2015). Endosymbiotic theories for eukaryote origin. Philosophical Transactions of the Royal Society B: Biological Sciences, 370(1678), 20140330.