Journal of Theoretical Biology 000 (2017) 1–10

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/jtbi

Revisiting the theoretical basis of the endosymbiotic origin of plastids in the original context of Lynn Margulis on the origin of mitosing, eukaryotic cells

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ARTICLE INFO

Article history:
Received 13 July 2017
Revised 29 August 2017
Accepted 31 August 2017
Available online xxx

Keywords:
Chloroplast
Cyanobacterium
Endosymbiosis
Mitosis
Centriole

ABSTRACT

Fifty years ago, Lynn Margulis proposed a comprehensive hypothesis on the origin of eukaryotic cells with an emphasis on the origin of mitosis. This hypothesis postulated that the eukaryotic cell is a composite of different parts as a result of the symbiosis of various different bacteria. In this hypothesis, she integrated previously proposed ideas that mitochondria and chloroplasts were descendants of endosymbionts that originated from aerobic bacteria and blue-green algae (now cyanobacteria), respectively. However, the major part of her hypothesis, which she believed to be original, was the origin of mitosis. The core of her postulate involved a chromosome partition mechanism dependent on DNA-microtubule binding, which originated from a hypothetical centriole-DNA complex, with an ability to replicate. Surprisingly, her complete lack of real experimental works in the cytoskeleton, cell motility, or paleontology did not prevent this 29-year-old junior scientist from assembling archival knowledge and constructing a narrative on the evolution of all organisms. Whether the centriole-DNA complex originated from a spirochete or not was a minor anecdote in this initial postulate. Unfortunately, this hypothesis on the origin of mitosis, which she believed to be a holistic unity, testable by experiments, was entirely refuted. Despite falsification of her original narrative as a whole, her success as a founder of endosymbiotic theory on the origin of mitochondria and chloroplasts is undoubted. We will discuss the reasons for her success in terms of the historical situation in the latter half of the 20th century.

1. Introduction

Fifty years ago, Lynn Margulis (1938–2011; her maiden name was Alexander, and her family name in 1967 was Sagan; we use Margulis throughout this article) published epoch-making works on the endosymbiotic origin of eukaryotic cells: a hypothesis paper "On the origin of mitosing cells" in the *Journal of Theoretical Biology* in 1967 (Sagan, 1967) and the comprehensive book "Origin of Eukaryotic Cells" in 1970 (Margulis, 1970). Criticized vigorously at first, these works became accepted by the scientific community over time, and gained support from the then novel technology of molecular phylogeny. Her original works are difficult to understand, however, because more than a half of their pages were devoted to her unusual, incomprehensible views on the origin of eukaryotic cells that proliferate by mitosis, which was, in fact, represented by the titles of the works and which I believe was the principal subject of her studies at the time. Endosymbiotic origins of mitochondria and plastids, although described briefly as existing hypotheses, were not indeed part of her main, original proposal. The main postulate of her works has been, however, simply neglected by researchers of the time and later, because it was difficult to understand, and included the "spirochete anecdote", which nobody accepted. In the present article, we will decipher the logic inherent in her seminal works, and analyze the changing status of her hypothesis, which has gained scientific popularity during the last 30 years. Some of my descriptions in the present article may appear highly critical of Margulis, but I believe this is a sincere, scholarly quest for the truth in the history of biological thought, which, in turn, will uncover the previously unrecognized originality of Margulis.

2. Brief overview

Endosymbiosis of organelles or symbiogenesis is currently widely accepted as the mechanism of the origin of chloroplasts and mitochondria (Archibald, 2015). Statements such as "chloroplasts originated from ancestral cyanobacteria" or "chloroplasts are de-

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http://dx.doi.org/10.1016/j.jtbi.2017.08.028
0022-5193/

scendants of a cyanobacterial endosymbiont" are commonly found in the biological literature. Is this a valid scientific fact? Or is this just an assumption used to explain the results of comparisons of chloroplasts and cyanobacteria? An "origin story" describes a past history that we cannot observe directly and that all what we can do is construct plausible hypotheses on what happened to the objects in which we are interested (Margulis, 1970; Sapp, 1994). The endosymbiotic origin of plastids seemed "established" in the 1980s in the sense that the discourses of opponents faded out in this decade (Gray, 1982; Margulis and Bermudes, 1985). In contrast, the origin of mitochondria remained discussed for a further 10 years. The year 1986 marked the beginning of a new era due to publication of the complete nucleotide sequences of the chloroplast genomes of tobacco (*Nicotiana tabacum*) and *Marchantia polymorpha*, which facilitated genome-based phylogenetic studies on the chloroplasts. Genome sequencing of cyanobacteria began 10 years later, with the genomes of *Synechocystis* sp. PCC 6803 and *Anabaena* sp. PCC 7120. The publication of these genomes, intentionally or unintentionally, contributed strong support to the endosymbiotic origin of plastids.

The International Society of Endocytobiology (ISE) was established in 1980 to discuss cellular symbiosis in general, but more specifically, the endosymbiotic origin of organelles. Lynn Margulis was awarded the first Miescher-Ishida medal of the society for "Resurrection and Expansion of the Endosymbiotic Hypothesis to Endocytobiosis and Cell Research" (see the ISE website: http://www.endocytobiology.org/miescher-ishida-prize.html). Curiously, this was not given for her original postulate on the origin of eukaryotic cells, but for her contribution to the re-establishment of the endosymbiotic theory. In contrast, Mereschkowsky (1905) was identified by the historians as the scientist that first proposed the endosymbiotic origin of plastids (chloroplasts) (see Martin and Kowallik, 1999 for the English translation of the 1905 paper in German, which I translated into Japanese: Sato, 2016). For mitochondria, Portier (1918) stated the similarity of bacteria and mitochondria, but his cultivation of mitochondria was obviously a result of contamination. Wallin (1927), on the other hand, summarized his own works on the endosymbiotic origin of mitochondria, which he had performed during the preceding 5 years. Various papers formulating endosymbiotic origins of these organelles appeared during the 1960s (Ris and Plaut, 1962; Echlin, 1966; Goksøyr, 1967; Edelman et al., 1967; Loening, 1968, Raven, 1970). This is somewhat different from what is believed to be Margulis' contribution in contemporary textbooks. Several lines of evidence suggest that the scientific community of the time (1986) did not recognize Margulis as the founder of the endosymbiotic hypothesis of the origin of plastids and mitochondria, but rather as one of its advocates, or even doubted her originality. In this context, we are interested in the change of Margulis' status within the endosymbiotic theories.

As we decipher her texts, we are led to understand that the endosymbiotic origin of plastids and mitochondria was not her primary concern. Her originality resided in her proposal of a new "theory" on the origin of eukaryotic cells, notably the origin of mitosis. She tried to explain the origin of mitosis by endosymbiotic microtubular structures associated with the endosymbiont genome (centriole-DNA complex). Her strange association of these structures with a specific bacterium such as a spirochete (which I call the 'spirochete anecdote') made the whole story incomprehensible to most scientists. Many reviews published recently to commemorate the 50th anniversary of Margulis' 1967 paper also ignore the core of her theory on the origin of mitosing eukaryotic cells (Martin, 2017; López-García et al., 2017; Lazcano and Peretó, 2017). Martin (2017; first paragraph in Section 3) states:

> That (cyanobacterial origin of plastids and the single bacterial origin of mitochondria) is possibly the only thing that Margulis maintained in her 1967 paper upon which everyone would still agree today.

But I believe that we cannot separate the 'dark' part related to mitosis from the endosymbiotic origin of plastids and mitochondria within the framework of Margulis' thoughts. In other words, it is crucial to assess her thought processes to identify the founder of the endosymbiotic origin of plastids, a mantle that she claimed only later (Margulis, 1998). She considered that her theory could resolve several problems at a time:

> The theory developed in the course of this narrative seems, at least to the author, to simultaneously explain three problems of cellular evolution, each previously considered to be the domain of an independent discipline. They are (1) the cellular discontinuity between pro- and eukaryotic cells; (2). the fossil discontinuity between the Precambrian and Phanerozoic, and (3) the observable trends in DNA base ratios.
>
> (Margulis, 1970, p. 44)

We noted that she repeatedly presented her theory as a "testable" or "verifiable" hypothesis (Sagan, 1967; Margulis, 1970). Especially in Margulis (1975, p. 21), she wrote on the philosophical context of scientific theories as follows:

> a specific historical theory may be extremely useful for the integration of many observations into a *coherent whole*.
>
> (Emphasis by NS)

She continued:

> the extreme endosymbiotic view (Margulis, 1970) has the advantage of being holistic and relatively complete. That is, it provides the most comprehensive, explicit, and *testable* framework of necessarily interrelated evolutionary postulates.
>
> (Margulis, 1975, p. 22. Emphasis by NS)

For Margulis, her theory must be considered a single entity, not a composite of three different endosymbiosis stories related to plastids, mitochondria, and flagella. This is the basic standpoint of the present article.

For this purpose, I will provide three major arguments in the following sections. First, we will analyze Margulis' hypothesis on the origin of mitosing, eukaryotic cells, which was described in detail in her 1967 paper and 1970 book, which included the role of the centriole in mitosis, the role of the basal body in flagellar motion, and the relationship between the centriole and basal body. Second, we will examine various forms of the concept of endosymbiosis, presenting various different types of possible endosymbiosis, and will point out that the meaning of endosymbiosis changed over time. Then, we will examine the role or scientific contribution of Margulis to the development of the endosymbiotic theory of plastid origin. Finally, we will discuss various reasons for the success of Margulis.

3. Origin of mitosing, eukaryotic cells: centriole, basal body, and microtubular structures

None of the previous articles or reviews on Margulis seriously addressed this 'dark' aspect of her theory. The spirochete origin of the flagellum that was not accepted was only an anecdote of this unique, fundamental hypothesis on the origin of mitosing, eukaryotic cells. The declaration of the absence of DNA in the basal body (Johnson and Rosenbaum, 1991) seemed to be the final, decisive attack on this hypothesis. Proteomic analyses of centrioles (e.g., Li et al., 2004) could also represent an additional attack, although this was not clearly stated in the text. I begin by explaining the theory of Margulis on the origin of mitosing cells as I understand it. Sagan (1967) declared to propose a novel hypothesis:

Please cite this article as: N. Sato, Revisiting the theoretical basis of the endosymbiotic origin of plastids in the original context of Lynn Margulis on the origin of mitosing, eukaryotic cells, Journal of Theoretical Biology (2017), http://dx.doi.org/10.1016/j.jtbi.2017.08.028