

"On the Origin of Mitosing Cells" (1967), by Lynn Sagan

"On the Origin of Mitosing Cells" by Lynn Sagan appeared in the March 1967 edition of the *Journal of Theoretical Biology*. At the time the article was published, Lynn Sagan had divorced astronomer Carl Sagan, but kept his last name. Later, she remarried and changed her name to Lynn Margulis, and will be referred to as such throughout this article. In her 1967 article, Margulis develops a theory for the origin of complex cells that have enclosed nuclei, called eukaryotic cells. She proposes that three organelles: mitochondria, plastids, and basal bodies, which are all parts of eukaryotic cells, were once free-living cells that took residence inside primitive eukaryotic cells. This process Margulis called endosymbiosis. Margulis' theory explained the origin of eukaryote cells, which are the fundamental cell type of most multicellular organisms and form the basis of embryogenesis. After fertilization, embryos develop from a single eukaryotic cell that divides by mitosis.

When the *Journal of Theoretical Biology* published her article in 1967, Margulis was a professor at Boston University in Boston, Massachusetts. Margulis independently proposed ideas similar to those proposed by biologists in the late nineteenth and early twentieth centuries. At the end of the nineteenth century, several researchers advanced theories similar to symbiosis, two of whom were Richard Altmann of Leipzig, Germany, and Peter Kropotkin who was exiled from Russia and living in England. At the beginning of the twentieth century, researchers such as Boris Kozo-Polyansky in Russia and Ivan Wallin, a professor at the University of Colorado in Boulder, Colorado, also proposed theories similar to that of endosymbiosis.

These earlier biologists theorized that the energy-producing mitochondria, and the photosynthesizing plastids of algae and plants, resulted from a symbiotic relationship between different types of free-living cells. In addition, several of the researchers also hypothesized that the sub-cellular organelles contained hereditary information similar to that found in the nucleus. However, when earlier biologists put forth theories of symbiosis, they lacked the technological resources to test them. By the time Margulis proposed her theory, evidence for symbiosis theories was available from microscope studies of cells, electron microscopy, genetics, and molecular biology. Such evidence enabled Margulis to support her theories with experimental data.

"On the Origin of Mitosing Cells" has four main sections: an "Introduction," followed by sections titled, "Hypothetical Origin of Eukaryotic Cells," in which Margulis presents a theory for the origin of eukaryotic cells; "Evidence from the Literature," in which she reviews the literature that supports the sequence of the origin of eukaryotic cells; and "Some Predictions," in which she presents experimental evidence that support predictions made based on her theory.

In the "Introduction," Margulis states that all free-living organisms are made of cells. She describes differences between eukaryotic cells, which have distinct nuclei, and prokaryotic cells, which lack distinct nuclei. Researchers didn't note those differences until the 1960s, shortly before Margulis published her paper. Margulis focuses on three sub-cellular organelles of eukaryotic cells, the mitochondria, chloroplasts, and (9+2) basal bodies, which she asserts were once free-living prokaryotic cells. (9+2) basal bodies are organelles found at the base of eukaryotic whip-like structures, such as the flagellum of sperm cells.

Margulis begins her argument with a section titled, "Hypothetical Origin of Eukaryotic Cells," which has multiple subsections. She describes the state of prokaryotic cells of two billion years ago, before the accumulation of free oxygen in the atmosphere. At that time, prokaryotic cells contained DNA, they synthesized proteins on structures made of RNA, called ribosomes, and they used messenger RNA (mRNA) to help build those proteins from DNA. With oxygen accumulating in the atmosphere,

prokaryotic cells developed nucleotide sequences, or genes, that coded for molecules that could bind with metals and oxygen, called porphyrins. This mutation provided a protective advantage from the harmful effects of oxidization. Margulis explained that these cells evolved to contain mechanisms that used oxygen to produce the molecule that stores energy in cells, adenosine-5'-triphosphate (ATP), and other nucleotides that used solar energy, which the chlorophyll-like porphyrins absorbed and used to produce complex sugars. In contrast, more primitive cells, called heterotrophs, fermented ATP from simple sugars. Additionally, some porphyrins used oxygen to release and to store ATP in the absence of light, a process called aerobic respiration.

Next, Margulis discusses how eukaryotic cells evolved from prokaryotic cells via endosymbiosis. Margulis suggests the emergence of eukaryotes was a response to the new oxygen-containing atmosphere. From geological evidence, oxygen became present in the atmosphere as early as 2.7 billion years ago, however the atmosphere became oxygen rich 1.2 billion years ago. Margulis argues that to survive and reproduce, cells had to adapt to the oxygen rich environment or find a specialized environment lacking oxygen. She suggests the eukaryotes originated when an anaerobic heterotroph living on organic matter ingested an aerobic microbe. The ingested microbe became obligate and resulted in, as Margulis calls it, the first aerobic amoeboid organism. Margulis hypothesizes that some of these amoeboid organisms ingested motile prokaryotes (flagellates) that became symbiotic with their host, and thus classical mitosis evolved. Mitosis is a process by which a non-reproductive cell divides into two genetically identical cells, thus passing all of its genetic information to the two daughter cells.

Margulis next discusses the evolution of mitosis in protists and hypothesizes that a motile spiral shaped bacteria was one of the prokaryotes ingested by the large amoeboids, and that the amoeboids became hosts to the motile parasites. Amoeboids benefited from this endosymbiont relationship, as the motility of the parasite gave the host the ability to pursue food before mitosis evolved. Margulis then proposes that the endosymbiont genes, which give rise to the (9+2) substructure, evolved over generations to form chromosomal centromeres, the structures that link together the individual chromatids from duplicated chromosomes. She also claims that the endosymbiotic genes contributed to the small centrioles that facilitate cell mitosis in animals. Margulis hypothesized that the motile prokaryote parasite was the ancestor of the flagellum found in later eukaryotic cells.

Margulis two further topics in the first section of her paper. First, she recreates the steps in evolution of the centromeres, centrioles, and the (9+2) flagella basal bodies from steps for which she had found support in other publications. Then she discusses the evolution of eukaryotic plants, a process she attributes to symbiotic relationships between protozoans and prokaryotic algae. Margulis asserts that the process of mitosis took millions of years to evolve, and she claims that the process evolved millions of years after the evolution of photosynthesis. Margulis then argues that her hypothesis on the origin of eukaryotes is inconsistent with the theory that eukaryotic plant cells first evolved photosynthesis, which eliminates oxygen from plants, and then structured that process into membrane-bound plastids. Instead, Margulis proposes that plants acquired photosynthetic plastids through multiple symbiotic relationships that occurred over time, each of which led to endosymbiosis.

In the next section of her paper, "Evidence from the Literature," Margulis supports her theory by discussing publications on the subject up through 1967. Margulis considers the claim that the more traits two organisms share, the more closely related those organisms are. She says that the hypothesis holds for some organisms, but not for single celled microbes. Margulis acknowledges that she had inadequate data to support that claim, but she contends that the recent studies in molecular biology confirm her theory. Margulis then proposes to use methods from molecular biology to address issues in taxonomy. She next proposes that photosynthesis evolved separately in several diverse organisms. Then, Margulis reviews the general properties of symbiosis, and she says that the origin of eukaryotic cells indicates that larger cells acquired mitochondria, the genome of the (9+2) complex flagellum, and the photosynthetic plastids by endosymbiosis.

Margulis reports that the literature lists six general criteria for organelles derived by endosymbiosis. She applies these criteria to the three organelles, mitochondria, plastids, and the basal bodies, and she concludes that they could have evolved by endosymbiosis, but that the eukaryotic cell nucleus could not have. In the remaining sections of her literature review, Margulis concentrates

on the origin of the prokaryotic cells, which she argues evolved into the organelles of eukaryotic cells. Margulis describes the evolution of photosynthesis in cells, the accumulation of oxygen in the atmosphere, and the evolution of aerobic cells. She then discusses research on how mitochondria self-replicate, and she includes a table with a list of mechanisms by which eukaryotic cells, throughout mitosis and their life cycles, retain mitochondria and chloroplasts.

Margulis concludes with the third and final section of the paper, "Some Predictions." She suggests that some of the classifications presented in the phylogenetic tree put forth by previous scientists were likely in error. But if her hypothesis about the origination of the three organelles is correct, so too should be her classification of all eukaryotes. However, Margulis predicts that if these three organelles—mitochondria, plastids, and basal bodies—did originate as free-living microbes, then new technologies would provide researchers the tools required to grow those organelles in vitro. Mitochondria and chloroplasts cannot grow outside of cells, because they have lost too many genes to be free living again. Margulis concludes that all eukaryotic cells must be regarded as multi-genome systems. She says that the evolution of mitosis in primitive eukaryotic cells enabled genes to pass independently from one generation to the next.

Margulis submitted "On the Origin of Mitosing Cells" to at least fifteen journals before it was accepted and published in June 1967. She later expanded on the theory of endosymbiosis in a book titled, *Origin of Eukaryotic Cells*, published in 1970. In 1981, Margulis published a revised edition titled, *Symbiosis in Cell Evolution*, which included molecular data to support her findings. In 1993 she published another edition of *Symbiosis in Cell Evolution* claiming that the difference between prokaryotes and eukaryotes is the most significant division in biology.

By the 1990s, Margulis' theory on the origin of eukaryotes had influenced many scientists. In 2011, John M. Archibald, a professor and researcher at Dalhousie University, in Nova Scotia, Canada, said that Margulis' *Origin of Eukaryotic Cells* influenced scientists to accept the process of endosymbiosis in the evolution of cells.

Sources

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