Endosymbiotic Theory

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Glossary

Alveolata A monophyletic taxon composed primarily of dinoflagellates (half of them containing the peridinin plastid), parasitic apicomplexans (with a nonphotosynthetic plastid known as the apicoplast), and ciliates (completely aplastidal); a common feature of alveolates is the presence of alveoli, flattened membranous sacs that subtend their plasma membrane and fulfill cytoskeletal functions.

Archaea One of three domains of life, parallel to Bacteria and Eucarya (Eukaryota); it contains unicellular microorganisms devoid of a nucleus. These organisms formerly were classified under the name Archaebacteria along with Bacteria (previously Eubacteria) as prokaryotes; however, archaeons differ from bacteria in the biochemistry of their cell walls and membranes, and many of their informational genes (i.e., those encoding DNA replication, transcription, and translation components) are more closely related to eukaryotes than to bacteria.

Archaeplastida A eukaryotic kingdom (also known as Plantae) comprising three groups of eukaryotes harboring primary plastids, that is, glaucophytes, red algae, and green plants (including green algae and higher plants). Their plastids are surrounded by two membranes and contain phycobiliproteins (glaucophytes, red algae) or chlorophyll *b* (green plants) in addition to chlorophyll *a*; moreover, glaucophyte plastids still retain the bacterial cell wall (of peptidoglycan) of their cyanobacterial ancestor, a conserved ancient trait in the evolution of primary plastids.

Cell organelles Intracellular structures surrounded by a membrane or membranes and fulfilling specific metabolic functions. Some organelles, such as mitochondria and plastids, have an endosymbiotic origin; their genomes encode only a very restricted pool of proteins, with the remaining proteins encoded in the host nuclear genome (some originally from the endosymbiont and others from the host) and imported into the organelles through translocons in their envelope membranes.

Chromista A historic term for a eukaryotic kingdom containing algae with red alga-derived plastids, such as cryptophytes, heterokonts, and haptophytes. Their plastids contain chlorophyll *c* and are surrounded by four membranes, the outermost bearing ribosomes.

Endosymbionts Organisms residing in the cells or tissues of other organisms, which can come from either eukaryotic or prokaryotic lineages; in contrast to cell organelles, their genomes encode all their required proteins and, in the case of obligatory endosymbionts, they are integrated with their host cells only at the metabolic level.

Endosymbiotic gene replacement There are two kinds of such replacement: one is when a host gene present in the nucleus, takes over the function of an endosymbiont gene, resulting in loss of the latter. The second is when a host nuclear gene is replaced by an endosymbiont gene transferred to the host nucleus. In the first case, this process generally is accompanied by duplication of a host nuclear gene, followed by one copy is acquiring a proper endosymbiont/organelle-targeting signal.

Endosymbiotic gene transfer Gene transfer occurring during endosymbiosis in which a gene from an endosymbiont or organelle genome is transferred and integrated into the host's nuclear genome.

ERAD system The *e*ndoplasmic *r*eticulum-*a*ssociated *d*egradation (ERAD) transport system characteristic of all eukaryotes; it participates in the export of misfolded proteins from the lumen of the endoplasmic reticulum into the cytosol, where they are degraded by the proteasome. ERAD-like translocons also operate in peroxisomes and secondary plastids.

Hydrogenosomes Anaerobic forms of mitochondria that perform H_2-producing fermentation reactions to synthesize ATP via substrate-level phosphorylation; they occur in some anaerobic protists.

Mitosomes Highly reduced mitochondria of several anaerobic and parasitic protozoan lineages; they have lost all bioenergetic functions characteristic of mitochondria and hydrogenosomes. The only functions known for mitosomes are sulfate metabolism and Fe–S cluster biogenesis.

Primary plastids Plastids derived directly from cyanobacteria; they are found in all representatives of the Archaeplastida.

Introduction

The endosymbiotic theory posits that at least some organelles in eukaryotic cells, mitochondria and plastids, in particular, evolved from free-living organisms that were enslaved by other cells functioning as their hosts (Figure 1). The endosymbiotic (or exogenous) origin of mitochondria and plastids was proposed by several scientists (C. Mereschkovsky, A. F. W. Schimper, I. E. Wallin) toward the end of the nineteenth and the beginning of the twentieth century. Although initially abandoned, the idea was revived after the discovery of DNA molecules in mitochondria and plastids in the 1960s. In 1967, Lynn Margulis suggested not only the endosymbiotic origin of mitochondria and plastids, but also an endosymbiotic origin of the eukaryotic cell itself. In her model, eukaryotic cells originated in a series of endosymbioses involving distinct bacterial cells. A hallmark of this scenario was a

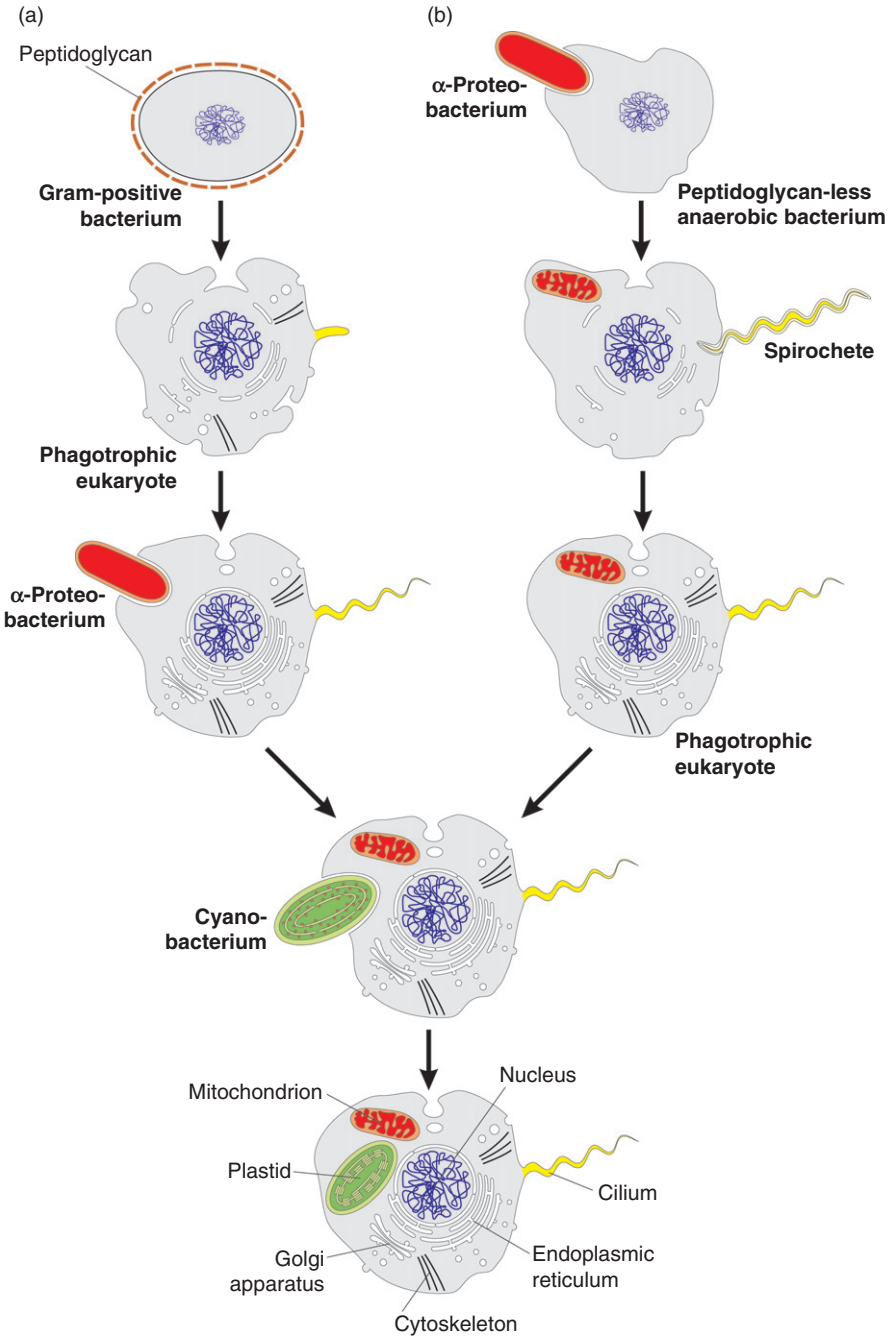

Figure 1 Two main models explaining the origin of the eukaryotic cell. (a) The non-symbiotic model posits that the characteristic organelles and structures of the eukaryotic cell are not mitochondria and plastids, but the endomembrane system (including peroxisomes), the nucleus, and the cilium along with cytoskeleton. It is hypothesized that all these structures evolved autogenously (= endogenously) from a Gram-positive bacterial ancestor (termed the neomuran) after loss of its peptidoglycan wall, and were driven by endo- and exocytosis. In this model, only an already phagocytotic eukaryotic cell could engulf the bacterial progenitors of mitochondria and plastids. Consequently, endosymbioses only resulted in the diversification of the eukaryotic cell, but not in its origin. (b) By contrast, the endosymbiotic model postulates that the eukaryotic cell originated by a series of endosymbioses occurring between distinct bacterial cells. Its original version, formulated by L. Margulis, stated that the first endosymbiosis involved an anaerobic bacterial host devoid of cell wall and an aerobic bacterium as an endosymbiont. The nucleus evolved autogenously after this endosymbiosis and such a proto-eukaryotic cell could then acquire a cilium and cytoskeleton from a spirochete (a kind of ectosymbiosis). According to this model, the last endosymbiosis involved a cyanobacterium as the source of primary plastids. Some versions of the endosymbiotic scenario suggest an endosymbiotic origin for almost all organelles (including even the endoplasmic reticulum) within the eukaryotic cell.

spirochete origin of the eukaryotic cytoskeleton and cilium. Thus, there are two main versions of the endosymbiotic theory: one proposes that some cell organelles evolved by endosymbiosis within an already established eukaryotic host, whereas the second suggests the eukaryotic cell initially assembled through a process of endosymbiosis (Figure 1).

Bacterial Origins for Mitochondria and Primary Plastids

Mitochondria and primary plastids almost certainly evolved from α-proteobacteria and cyanobacteria, respectively (Figure 2), but a more exact determination of their bacterial sources remains elusive. In the case of mitochondria, it has been suggested they evolved from *Rickettsia*-, *Pelagibacter*-, or *Rhodospirillum*-like species. A similar uncertainty concerns primary plastids, with proposal of an *Anabena*-like species versus an unknown ancient cyanobacterial lineage. A major to resolving these controversies is the chimerism of bacterial genomes; it probably results from horizontal gene transfers between distinct bacterial lineages on the one hand, and lineage-specific gene duplications and losses on the other hand.

α-Proteobacteria and cyanobacteria are Gram-negative bacteria, which means the ancestors of mitochondria and primary plastids were very likely surrounded by two membranes, a plasma membrane and an outer membrane, with a peptidoglycan wall between them.

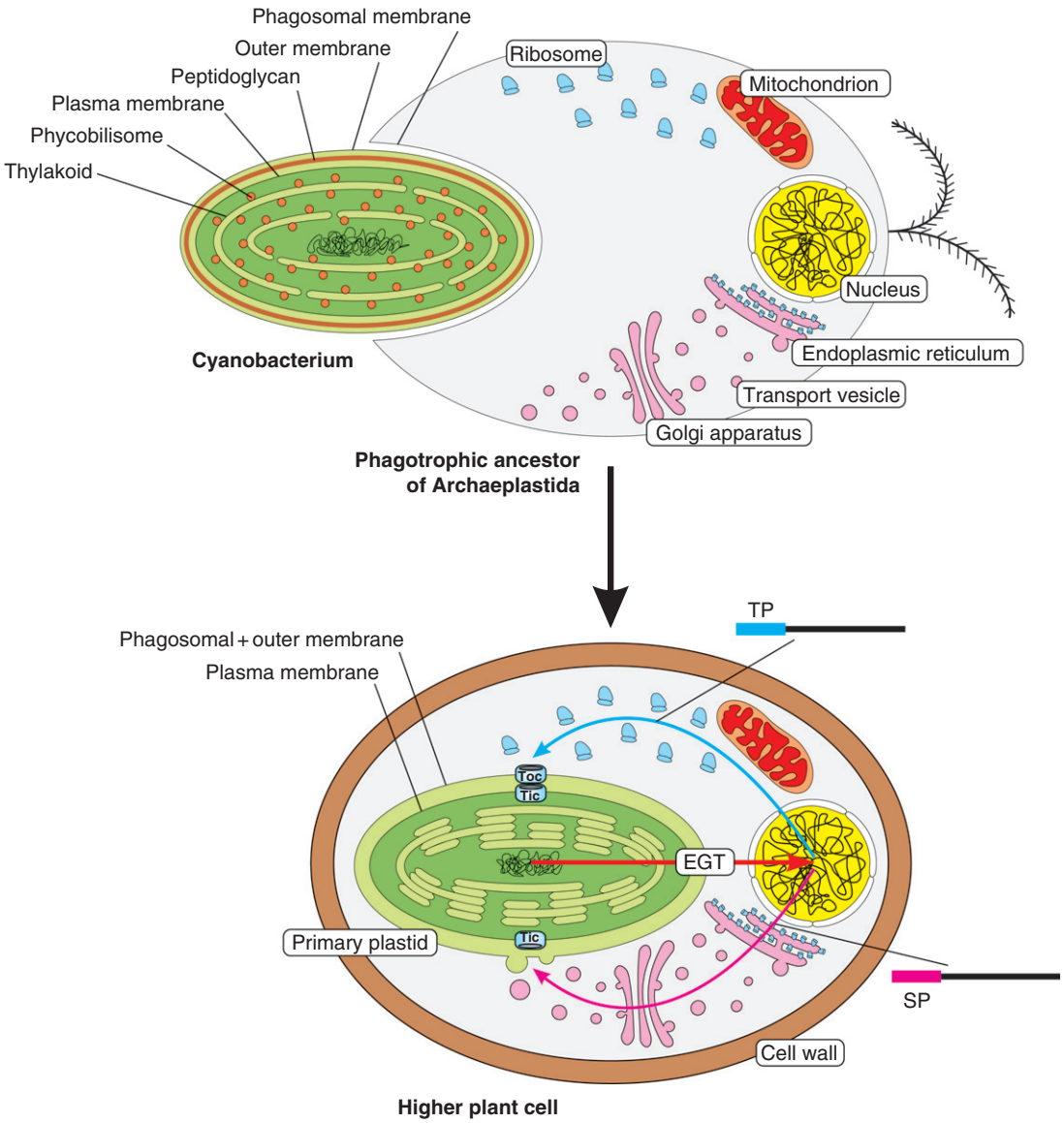

Figure 2 Evolution of primary plastids. Primary plastids evolved from cyanobacteria that were engulfed by phagotrophic protozoans. Driving forces behind the establishment of primary plastids could have been photosynthesis, as well as nonphotosythetic functions such as nitrogen fixation or fatty acid synthesis. Numerous genes of the cyanobacterial endosymbiont have moved to the host nucleus via the endosymbiotic gene transfer (EGT). Almost all their protein products are equipped with transit peptides (TPs) and imported into the plastid with the help of Toc and Tic translocons; however, some plastid pre-proteins carry signal peptides (SPs)(e.g., α-carbonic anhydrase) that deliver them to primary plastids via the endoplasmic reticulum and/or the Golgi apparatus. The inner membrane of primary plastids is certainly derived from the endosymbiont plasma membrane, but the origin of their outer membrane is still controversial. This membrane could have come from the host phagosomal membrane (as demonstrated by the endomembrane system-mediated targeting of some proteins) or the outer membrane of the cyanobacterial endosymbiont (the membrane contains porin-like proteins such as the Toc75 channel). It is possible, however, that the outer membrane of primary plastids has a chimeric eukaryotic–bacterial origin, because the engulfed cyanobacteria (with their outer and plasma membranes) must initially have been surrounded by a phagosomal membrane, and, after its disruption, their outer membrane could have acquired features of the host phagosomal membrane.

Transformation of Endosymbionts into Organelles

The first step in the evolution of mitochondria and primary plastids was establishment of permanent endosymbioses between their bacterial ancestors and eukaryotic (or prokaryotic) host cells. Under the traditional model, these bacteria were initially engulfed as food by eukaryotic cells and digested in phagosomes. Therefore, establishment of stable α-proteobacterial and cyanobacterial endosymbioses required disturbing the digestion process by disrupting the phagosomal membrane or modifying the endocytotic pathway. Bacteria are known (mainly parasitic in these cases, but similar to bacteria suggested as the mitochondrial ancestor) that invade eukaryotic cells without formation of phagosomes and/or secrete proteins that modify endocytotic pathways. In contrast, the mechanisms by which bacteria integrate inside their prokaryotic host cells are unknown.

After the establishment of permanent endosymbioses, the acquired bacteria began to undergo transformation into true cell organelles. Such transformations involved two processes: gene transfer from the endosymbiont to the host nuclear genome, and the origin of translocons in the endosymbiont envelope that could import proteins encoded by these transferred genes. Known genomes of mitochondria and plastids contain from 3 to 273 protein-encoding genes, whereas those of modern α-proteobacteria and cyanobacteria encode, for example, 3788 (*Rhodospirillum rubrum*) and 5043 (*Anabaena variabilis*), respectively. Numerous endosymbiont genes required by free-living bacteria were lost completely, while most others were transferred (or 'escaped') to the host nuclear genome via endosymbiotic gene transfer. Various hypotheses have been advanced to explain this process, for example, that such transfers protected endosymbiont genes from mutations induced by free radicals generated during redox reactions occurring in mitochondria and plastids.

After transfer to the nucleus, each prokaryotic endosymbiont-derived gene needed to acquire nuclear promoter and polyadenylation signals. Acquistions of these signals by the transferred genes enabled their expression in the host cytosol and sometimes resulted in the replacement of a host gene by a bacterial homolog, a process known as endosymbiotic gene replacement. In a next evolutionary stage, transferred genes acquired sequences encoding targeting signals (e.g., via exon shuffling) that allowed their protein products to be imported into the mitochondrion or the primary plastid. Most proteins targeted to mitochondria and primary plastids carry N-terminal transit peptides that are later removed in the organelle matrix.

Mitochondria and primary plastids are surrounded by two membranes. Consequently, their import machineries are composed of two translocons: one for the outer membrane and the other for the inner membrane; these are Tom and Tim (mitochondria) and Toc and Tic (primary plastids), respectively (**Figure 2**). Each of these translocons is built from multiple proteins fulfilling channel, receptor, and regulatory functions. Some of these components can be traced to the endosymbiont, whereas others are evolutionary inventions of the host lineage, suggesting that the import machineries of mitochondria and primary plastids evolved via molecular tinkering. Proteins initially imported into mitochondria and primary plastids probably were host-derived metabolic carriers devoid of N-terminal targeting signals. These could cross the outer membrane through pre-existing porin-like channels and then insert spontaneously into the inner membrane. Perhaps to improve efficiency of their membrane insertion, they acquired N-terminal targeting signals permitting them to use insertion machinery. In a last step, these pathways, along with an amino acid pre-existing channel in the inner endosymbiont membrane, could have given rise to the import of proteins with N-terminal targeting signals into the endosymbiont matrix (or stroma).

Under the classical view, the outer membrane of mitochondria and primary plastids corresponds strictly to the outer membrane of Gram-negative bacteria. In higher plants, however, a small number of nuclear-encoded plastid proteins carry signal peptides and are imported via the endoplasmic reticulum (ER) and/or Golgi apparatus. This suggests that the outer plastid membrane could have a chimeric eukaryotic–bacterial origin.

Complex Evolutionary Pathways of Plastids: Eukaryotic Alga-Derived Plastids and Disappearing Nuclei

The evolution of plastids is much more complicated than that of mitochondria. Primary plastid endosymbiosis resulted in the plastids of glaucophytes, red algae, and green plants (**Figure 2**), which constitute the kingdom Archaeplastida; however, this was only the starting point for the further reticulate plastid evolution. In a second layer of plastid endosymbioses, both red and green algal plastids were acquired independently by different heterotrophic lineages, creating secondary plastids surrounded by three or four envelope membranes (**Figure 3**). Green alga-derived secondary plastids are present in euglenids, some dinoflagellates (e.g., *Lepidodinium viride*), and chlorarachniophytes, whereas those descended from red algae occur in cryptophytes, heterokonts, and haptophytes (the former kingdom Chromista), as well as in most plastid-bearing dinoflagellates and apicomplexans (in the supergroup Alveolata). In a third layer of plastid endosymbioses, secondary plastid-containing algae (e.g., cryptophytes and haptophytes) were enslaved by additional eukaryotic hosts belonging to the dinoflagellates. Good examples of tertiary endosymbioses are the fucoxanthin plastids of *Karenia brevis* and *Karlodinium micrum*, which evolved from a haptophyte alga.

A 'missing-link' stage in the evolution of eukaryotic alga-derived plastids is exemplified by chlorarachniophytes and cryptophytes. These algae preserved remnants of the cytoplasm of the eukaryotic alga, including its vestigial nucleus known as the nucleomorph (**Figure 3**). Although nucleomorph genomes have undergone drastic reduction, they preserve several typical eukaryotic features, including linear chromosomes with telomeres and spliceosomal introns. Moreover, molecular phylogenetic analyses of nucleomorph genes clearly demonstrate that they are derived from green algal (chlorarachniophytes) and red algal (cryptophytes) nuclei.

Modifications, Reductions, and Losses of Endosymbiont-Derived Organelles

Although most eukaryotes contain mitochondria, there are several lineages (e.g., diplomonads, some amoebozoans, microsporidians) that are devoid of typical mitochondria. In the 1980s, Cavalier-Smith erected the superkingdom Archezoa, whose members were proposed never to have contained mitochondria; in other words, they represented a premitochondrial stage in the evolution of eukaryotic cell. A characteristic

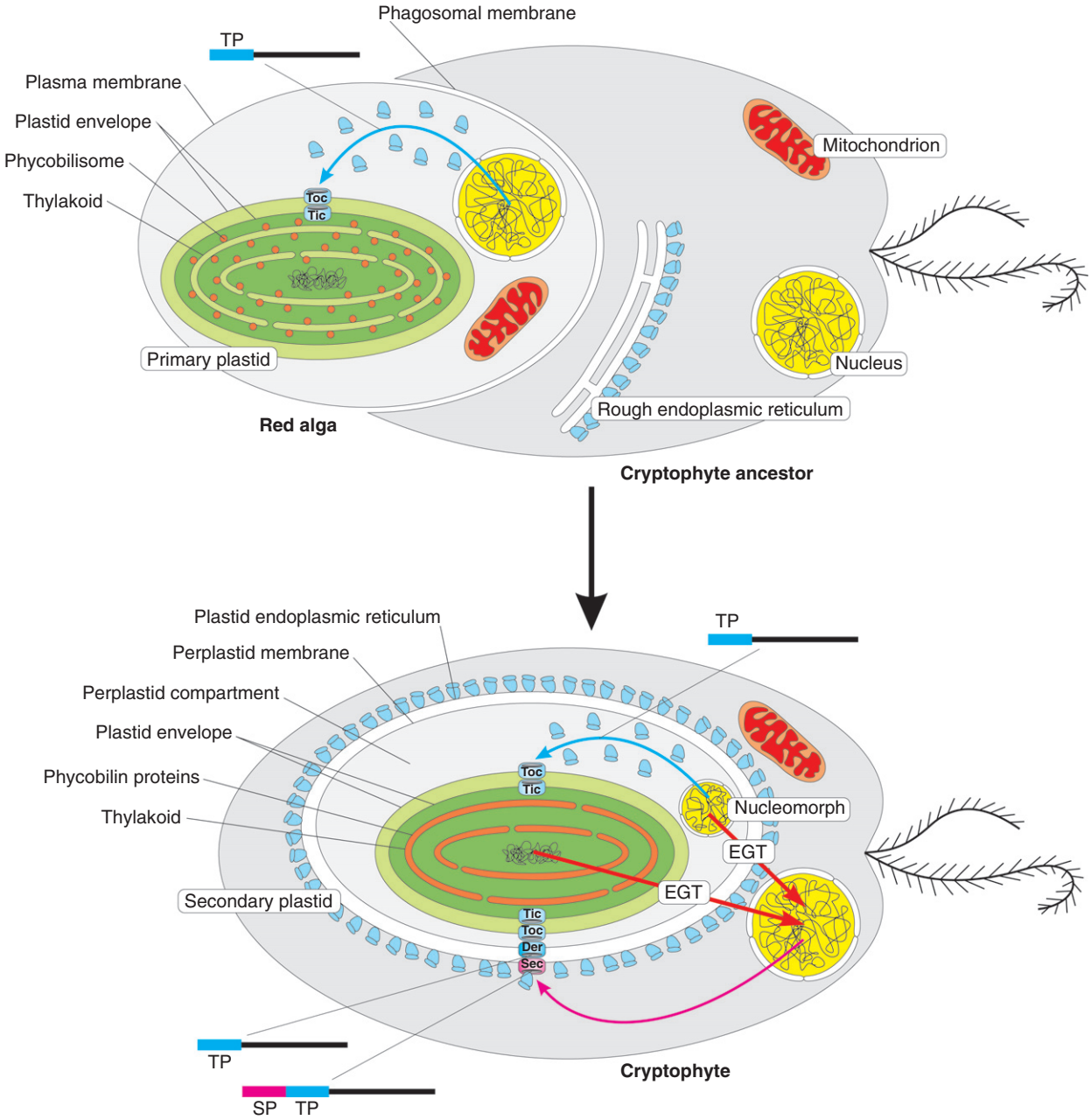

Figure 3 Evolution of secondary plastids in cryptophyte algae. Cryptophytes are a peculiar group of algae containing secondary plastids of red algal origin. Their plastids are surrounded by four membranes: the two innermost membranes (or plastid envelope) originated from the envelope membranes of the endosymbiont primary plastid, the third (or periplastid) membrane from the endosymbiont plasma membrane, and the outermost membrane from the phagosomal membrane of the host. Since the outermost membrane is covered with ribosomes, it is suggested that the phagosomal membrane underwent fusion with the ER, resulting in the plastid ER membrane. Cryptophyte plastids still retain the vestigial cytoplasm of the red algal endosymbiont (the periplastid compartment) along with its reduced nucleus known as the nucleomorph. The nucleomorph genome encodes some plastid proteins with transit peptides that are imported into the stroma with the help of Toc and Tic translocons. During secondary endosymbiosis, most endosymbiont genes were transferred out of the endosymbiont's nucleus (subsequently reduced to the nucleomorph) via endosymbiotic gene transfer (EGT). Host nucleus-encoded, plastid-targeted proteins of cryptophytes carry bipartite presequences composed of a signal peptide followed by a transit peptide. The signal peptide is responsible for protein translocation across the outermost membrane containing the Sec translocon, whereas the transit peptide enables passage across the three remaining membranes that are equipped with the Der translocon (in the periplastid membrane), and the Toc and Tic translocons (in the plastid envelope). The Der translocon is derived from the ERAD system and was probably relocated from the endosymbiont's ER.

representative of this clade was the diplomonad *Giardia lamblia*; however, further studies identified mitochondrion-related organelles, such as hydrogenosomes and mitosomes, in each eukaryotic supergroup (including all archezoan lineages), tracing the origin of mitochondria back to the eukaryotic common ancestor. Hydrogenosomes and mitosomes are specialized mitochondria that arose as adaptations to anaerobic conditions. They are usually devoid of a genome, although the hydrogenosome of the ciliate *Nyctotherus ovalis* still retains its DNA. Formation of Fe–S clusters is a common and vital feature

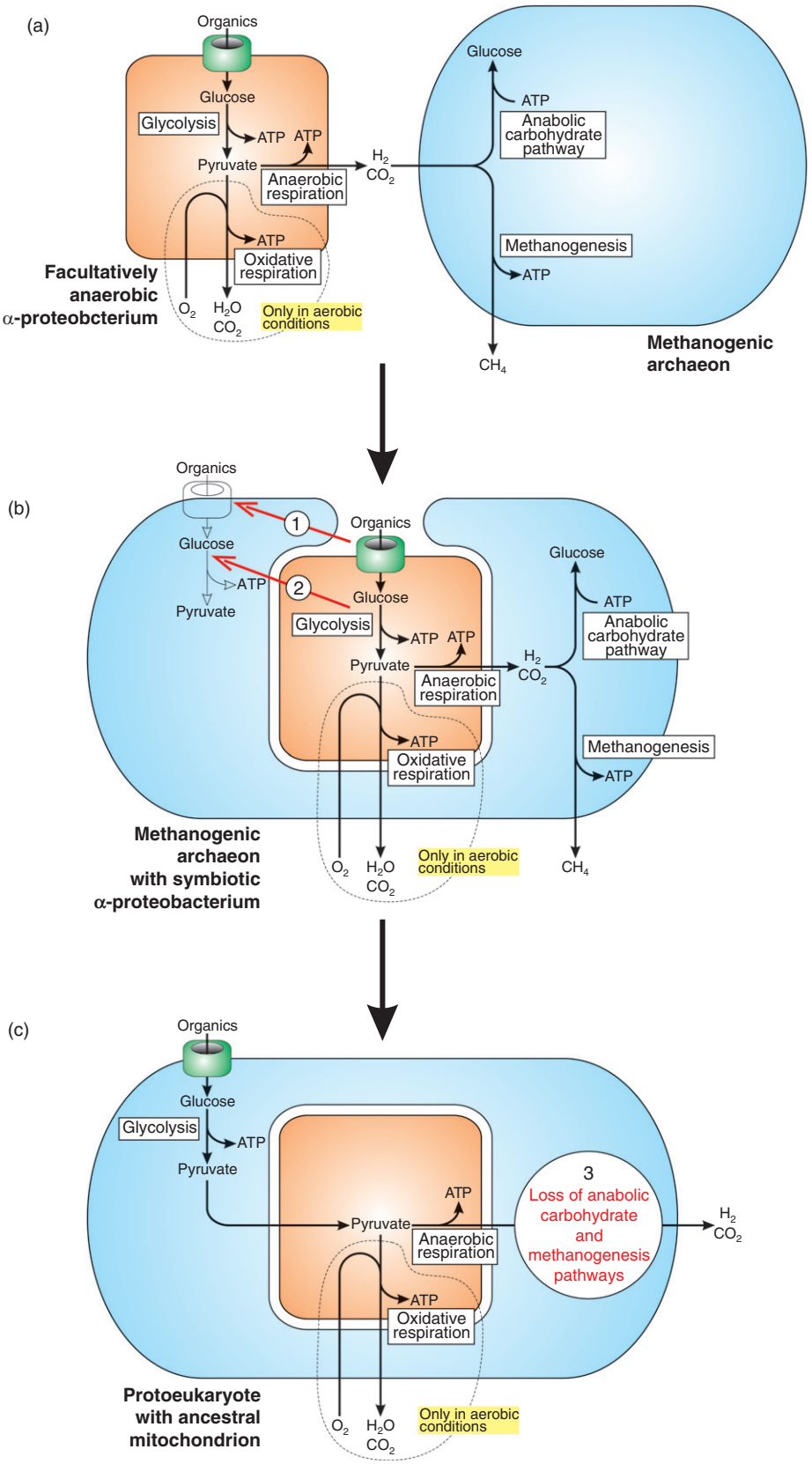

Figure 4 *(Continued)*

of typical mitochondria, hydrogenosomes, and mitosomes, and apparently the main reason they are maintained by all eukaryotic cells.

Plastids are known mainly as photosynthetic organelles, but they also fulfill numerous vital nonphotosynthetic functions, such as the biosynthesis of fatty acids, heme groups, and amino acids. Consequently, they are retained by their hosts even when photosynthesis is lost. In addition to higher plants, there are several well-characterized examples of nonphotosynthetic plastids in euglenids (e.g., *Euglena (Astasia) longa*), cryptophytes (e.g., *Cryptomonas paramecium*), and heterokonts (e.g., *Pteridomonas danica*). Interestingly, such plastids are found even in parasitic organisms, such as the green alga *Helicosporidium* sp., most apicomplexans (e.g., *Plasmodium falciparum* and *Toxoplasma gondii*) and the apicomplexa-related perkinsid *Perkinsus marinus*. They are considered good targets for the development of efficient drugs against diseases caused by these parasites.

As with mitochondria, there are no known examples of complete plastid loss from algae with primary plastids. The possibility of such losses is still debated in the cases of several protist lineages (e.g., ciliates, goniomonads) that are closely related to algae containing secondary plastids. Plastid loss is highly unlikely in such free-living organisms, however, because of numerous plastid nonphotosynthetic functions. It appears more likely to have occurred in parasitic forms (e.g., in the apicomplexan *Cryptosporidium parvum*) that receive abundant different compounds from their host cells.

Cyanobacterial Endosymbionts of *Paulinella chromatophora*: An Interesting Example of Cell Organelles in Progress

The thecate amoeba *P. chromatophora* harbors two cyanobacterium-derived endosymbionts that are deeply integrated with the host cell; for example, they divide synchronously with the host cell. Moreover, the genomes of these endosymbionts have lost ~75% of their initial coding capacity. Interestingly, this process was accompanied by the efficient transfer of at least 32 endosymbiont genes to the host nucleus, including some that encode N-terminal targeting signals. For example, an N-terminal extension of nucleus-encoded PsaE from *Paulinella* strongly resembles signal peptides (and it is absent from homologous cyanobacterial proteins), suggesting protein import into these endosymbionts via the endomembrane system. All these data indicate that *Paulinella* endosymbionts are undergoing transformation into true cell organelles.

Number of Endosymbiotic Origins of Mitochondria and Plastids

Available data clearly demonstrate that all mitochondria, along with their hydrogenosomal and mitosomal derivatives, evolved from a single α-proteobacterial endosymbiosis. A single cyanobacterial origin seems to have given rise to the primary plastids of glaucophytes, red algae, and green plants, but independent primary endosymbioses and even secondary origin of some of these plastids are still considered possible.

Available evidence indicates that the green algal plastids of euglenids, some dinoflagellates (e.g., *L. viride*), and chlorarachniophytes resulted from separate secondary endosymbioses. In addition, the tertiary plastids found in several dinoflagellate lineages certainly evolved via independent endosymbioses. More controversy surrounds the origin of chromist and alveolate plastids, termed collectively chromalveolate plastids. One model posits that all these plastids are derived from a single red algal secondary endosymbiosis; however, an increasing number of data favor an alternative scenario involving a secondary origin specifically in cryptophytes, with the remaining chromalveolate plastids evolving by multiple tertiary (or serial) endosymbioses.

Endosymbiotic Origin of the Eukaryotic Cell: Nucleus or Mitochondrion First?

There are two kinds of models for the endosymbiotic origin of the eukaryotic cell, those suggesting that the nucleus was the first endosymbiont-derived organelle to evolve and those assuming that the first endosymbiotic organelle was the mitochondrion.

Under the 'nucleus first' models (as in non-symbiotic models for the origin of eukaryotic cells), the mitochondrion could only be acquired by a complex (eukaryotic) cell with a developed nucleus, an endomembrane system, and cytoskeleton along with phagocytotic abilities they conferred. The evolution of all these features must have been extremely expensive energetically (it required the origin and expression of ~3000 new protein families), however, and thus could not have happened without an energy source to satisfy these needs. Thus, it now appears that only the acquisition of a mitochondrion by a prokaryotic host, with subsequent expansion of its inner membrane and massive transfer and/or loss of its non-bioenergetic genes could provide sufficient energy sources to support, in energetic terms, the origin of typical eukaryotic features. Consequently, the alternative 'mitochondrion first' models are much more probable based on the idea of syntrophy between an archaeal (= archaebacterial) host and an α-proteobacterial symbiont (**Figure 4**).

Figure 4 The hydrogen hypothesis for the origin of the first eukaryotic cell by a syntrophic symbiosis between an α-proteobacterium (the symbiont) and a methanogenic archaeon (the host). (a) The methanogen was an obligate autotroph dependent on H_2 (used in the synthesis of ATP via methanogenic respiration) and CO_2 (incorporated into carbohydrates in the anabolic carbohydrate pathway). The α-proteobacterium was a facultative anaerobe capable of carrying out both oxidative and anaerobic respiration. Because the methanogen was an obligate anaerobe, these bacteria could only meet in an anoxygenic environment, where the symbiont produced H_2 and CO_2 and the host utilized them. (b) After the disappearance of the geological source of H_2, the methanogen became strictly dependent on the α-proteobacterium and the selection favored its enclosure by the host to increase the diffusion of H_2. These changes decreased the influx of organic compounds into the α-proteobacterium, and later could have triggered the relocation of organic importers to the host plasma membrane (1). At this stage, the methanogen imported organic compounds and transported them into the α-proteobacterium, but most were certainly incorporated by its anabolic carbohydrate pathway. A subsequent evolutionary step would have been relocation of glycolysis to the host cytosol (2). (c) The presence of two carbohydrate pathways (anabolic and catabolic) in the methanogen cytosol operating in opposite directions resulted in a futile carbon cycle, and selection eliminated the anabolic pathway (3). The resulting proto-eukaryotic cell was a heterotroph, with proto-mitochondrion having features of both mitochondria (oxidative respiration) and hydrogenosomes (anaerobic respiration).

An obstacle faced by all endosymbiotic models for the origin of the eukaryotic cell is the inability of known bacterial or archaeal cells to employ phagotrophic feeding and, therefore, to be able to incorporate potential endosymbionts. There do exist predatory bacteria that are able to invade other bacterial cells (e.g., *Bdellovibrio*), however, and examples are known of bacterial endosymbiosis (e.g., the γ-proteobacterium *Moranella* inside the β-proteobacterium *Temblaya*). Thus, it is important to note that α-proteobacteria, the ancestors of mitochondria, include *Bdellovibrio*-like species such as *Midichloria mitochondrii*.

Cilium, Nucleus, and Peroxisomes: Symbiotic versus Autogenous Origins

The motility symbiosis between the parabasalid *Mixotricha paradoxa* and spirochetes attached to its plasma membrane is sometimes regarded as a model for symbiotic origin of the eukaryotic cilium and cytoskeleton. The movement of spirochetes is driven by typical bacterial flagella, however, which are absent from eukaryotic cilia. Although these bacteria have microtubule-like structures in their cytosol, they are neither composed of tubulins nor involved in cell movement. Moreover, spirochetes are surrounded by two membranes (with flagella located between them) and it is difficult to imagine how they could be transformed into cilia that are not even completely bound by a single membrane. Finally, tubulins probably evolved from the bacterial FtsZ proteins, which are involved in bacterial cell division.

Eukaryotic informational genes encoding replication, transcription, and translation components predominantly have an archaeal origin. Based on this finding, it was proposed that the nucleus evolved from an archaeal endosymbiont; however, the nuclear envelope contains highly permeable pore complexes and disintegrates during open mitosis, unique features absent from all prokaryotic cells and endosymbiont-derived organelles. Moreover, it originates from the endomembrane system during the eukaryotic cell cycle. Available data clearly indicate that the host component of eukaryotic cells evolved from an archaeon, whereas the transformation of its genome to the eukaryotic nucleus could have been driven by the endosymbiosis with an α-proteobacterium (later mitochondrion). Transfer of group II self-splicing introns from the α-proteobacterium to the archaeal host genome, and their subsequent evolution into spliceosomal introns, would have resulted in the direct translation of these foreign sequences to nonfunctional chimeric proteins. Only spatial separation of translation from intron excision by the formation of a nuclear envelope could solve these problems.

Considering their ability to divide and import matrix proteins posttranslationally, it was suggested that peroxisomes, which are surrounded by a single membrane, also have an endosymbiotic origin. Most proteins responsible for their biogenesis, however, are imported into them cotranslationally via the ER. Moreover, the peroxisome membrane possesses an ER-derived translocon (or ERAD system) involved in protein import, but is devoid of bacterial porin-like proteins characteristic of the outer membranes of mitochondria and plastids. It was also demonstrated that, unlike plastids and mitochondria, peroxisomes can develop *de novo* from the ER after they are lost, providing additional support for their autogenous (or endomembrane) origin.

Perspectives

The endosymbiotic theory is usually used to explain the origin of eukaryotic cells, but it can also be applied to bacterial cells. For example, Gram-negative bacteria could have evolved via an endosymbiosis between a clostridium and an actinobacterium, implying that their inner membrane is derived from the plasma membrane of the endosymbiotic bacterium, whereas the outer membrane originated from the plasma membrane of the bacterial host.

Darwin did not consider the significance of symbiotic associations in his theory of evolution. Moreover, endosymbiosis-mediated fusion of evolutionarily distinct lineages (netlike or reticulate evolution) contrasts with his idea of bifurcating divergence from common ancestors (treelike evolution). Thus, endosymbiotic associations are sometimes treated as examples of non-Darwinian evolution via the inheritance of acquired characteristics (e.g., acquisition of new genes and membranes) or macrogenesis involving 'hopeful monsters' (e.g., protozoans containing red or green algal endosymbionts). Nevertheless, each endosymbiotic association comes under natural selection, resulting in the survival (and reproduction) of only those best adapted to their environments.

Regardless of these general evolutionary considerations, available data clearly indicate that endosymbioses have had an enormous impact on the evolution of biosphere of our planet. It seems that a special role in this process was played by the mitochondrial endosymbiosis, which not only enabled the origin of the first eukaryotic cell but also facilitated a dramatic increase in the complexity of the eukaryotic world through the evolution of multicellularity.

See also: Archaea; Archaeal Genetics; Bacteria; Chloroplasts, Genetics of; Cytoskeleton; Eukaryotes; Evolution: Eukaryotes; Flagella; Gene Duplication; Mitochondria, Genetics of; Glycolysis; Horizontal Gene Transfer; Introns and Exons; Mitochondria; Mitochondrial Genetics/Evolution; Mitochondrial DNA; Mitochondrial Genome; Nuclear Envelope, Transport; Nuclear Pores; Nucleomorph Genomes; Nucleus; Organelles; Progenote; Prokaryotes; Signal Sequence; Splicing; Symbionts, Genetics of; Symbiosome.

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