# Endosymbiotic Theory

**S Garg, V Zimorski, and WF Martin,** Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany



## Glossary

**Aerobic organisms** Aerobic organisms live in oxic environments. Obligate aerobes are strictly dependent on oxygen and need it to grow. Aerobes usually use oxygen as the terminal electron acceptor in energy metabolism.

**Alveolates** The alveolates are a group of unicellular eukaryotes, including dinoflagellates, apicomplexans, and ciliates.

**Amoebozoa** The Amoebozoa are one eukaryotic supergroup containing ameboid microorganisms.

**Anaerobic organisms** Anaerobic organisms do not require oxygen for growth. For obligate anaerobes oxygen is harmful, because various enzymes of anaerobes are readily inactivated by oxygen.

**Apicomplexa** Apicomplexa are a large group of obligate parasitic, unicellular eukaryotes belonging to the supergroup Chromalveolata.

**Archaeplastida** The Archaeplastida are one eukaryotic supergroup containing glaucophyta, rhodophyta, and chlorophyta (with land plants).

**Autotrophy** Autotrophic organisms are able to produce organic compounds (food/energy-source) from inorganic ones using light or chemical reactions.

**Chlorarachniophytes** Chlorarachniophytes are ameboid eukaryotes belonging to the rhizaria. They possess secondary (green) plastids with four membranes and a nucleomorph.

**Chlorophytes** The lineage of Archaeplastida having green primary plastids.

**Endosymbiosis** One cell living in stable symbiosis within another.

**Facultative anaerobic organisms** Facultative anaerobes are able to grow with or without oxygen.

**Fermentation** Enzymatic conversion of organic compounds (sugars) into acids, gases, or alcohol.

**Functional redundancy (through endosymbiosis)** The retention of divergent but homologous gene copies donated both by host and endosymbiont at organelle origin for the same functions (e.g., ribosomal proteins of chloroplasts, mitochondria, and the cytosol).

**Glaucophytes** A group of unicellular algae with plastids that still possess a rudimentary peptidoglycan wall and that together with the rhodophytes and the chlorophytes comprise the eukaryotic supergroup Archaeplastida.

**Heterocyst** Differentiated cells of some cyanobacteria that are specialized for nitrogen fixation.

**Heterotrophy** Heterotrophic organisms use reduced organic substances as their source of carbon.

**Hydrogenosome** Hydrogenosomes are anaerobic mitochondria that have a double membrane and synthesize ATP via hydrogen-producing fermentations. They lack cytochromes, a membrane-associated electron transport chain, and (except in rare cases) a genome. Hydrogenosomes arose several times independently in evolution and can be found in trichomonads, anaerobic ciliates, and some fungi.

**Methanogen** Methanogens are archaea that produce methane as a metabolic byproduct of core energy metabolism.

**Mitosome** Mitosomes are organelles of mitochondrial origin that do not produce ATP. They have retained components of FeS cluster assembly or sulfate activation.

**Nucleomorph** Found only in some groups of eukaryotic algae whose plastids stem from secondary endosymbiosis, the nucleomorph is the highly reduced nucleus of the eukaryotic endosymbiont, it is located inside the periplastidal compartment. The nucleomorph is lost in most algae with secondary plastids but still can be found in chlorarachniophytes and cryptophytes.

**Opisthokonts** Another name for the group consisting of animals and fungi.

**Periplastidal compartment** The periplastidal compartment can be found in plastids of secondary origin within the chlorarachniophytes and cryptophytes. It corresponds to the cytosol of the eukaryotic endosymbiont.

**Phagocytosis** Phagocytosis is the engulfment of cells or particles by living cells.

**Primary plastids** Designates plastids that stem from a symbiotic association of a cyanobacterium with a eukaryotic host.

**Proteobacteria** Proteobacteria are a major group of bacteria. They are Gram-negative.

**Pseudogene** Pseudogenes are DNA segments resulting from multiple mutations, which look like genes, but are dysfunctional.

**Rhodophytes** Red algae, a group of Archaeplastida.

**Ribosome** Ribosomes are cellular particles composed of proteins and rRNA, where proteins are synthesized. They can be found in the cytosol, in mitochondria, and in plastids. In algae with a nucleomorph, a fourth set of ribosomes occurs in the periplastidal compartment.

**SAR** An eukaryotic group of organisms including stramenopiles (heterokonts), alveolates, and rhizaria.

**SCH** An eukaryotic group including stramenopiles, cryptophytes, and hacrobia.

**Secondary plastids** Designates plastids that stem from secondary endosymbioses in which the product of the primary endosymbiosis (a green- or a red-algae) came to reside into a heterotrophic, eukaryotic host.

**Symbiosis** Living together. When symbiosis involves benefit for both partners, it is mutualism.

**Syntrophy** 'Eating together,' designates a kind of metabolic association in which one cell is dependent upon a metabolic endproduct of another. The metabolic endproduct is often molecular hydrogen.

## Introduction

Endosymbiotic theory designates a class of hypotheses that view various organelles in eukaryotic cells as descendants of endosymbionts: cells that came to live inside another cell (a host). In its oldest and most familiar versions, endosymbiotic theory posits that mitochondria and plastids were once free-living cells: mitochondria (the powerhouses of eukaryotic cells) stemming from free-living proteobacteria and plastids (the chlorophyll-containing solar panels of plant cells) stemming from cyanobacteria. The Russian botanist Constantin Mereschkowsky is generally credited with the first formulation of endosymbiotic theory. He described plastids as reduced cyanobacteria that entered into a symbiosis with a heterotrophic host, which itself originated via a symbiosis between a heterotrophic host cell and a smaller endosymbiont that, in his view, gave rise to the nucleus (Mereschkowsky, 1905). Mereschkowsky's reasoning was remarkably modern with regard to the origin of plastids. He did not consider that mitochondria might also be of endosymbiotic origin (Mereschkowsky, 1910). That idea probably traces back to the French biologist Paul Portier (1918), who developed ideas about the relationship between bacteria and mitochondria. But Portier proposed that mitochondria could be cultured outside their host cells, and this precipitated considerable criticisms from peers (Archibald, 2014). The American biologist Ivan Wallin developed endosymbiotic theory further for mitochondria (Wallin, 1927). He was convinced that mitochondria are descendants of endosymbiotic bacteria, but he did not expound upon the ancestry of the host that acquired them (Wallin, 1927). Like Portier, he thought that the cultivation of mitochondria outside their host should be possible. Though initially quite popular in the early 1900s, endosymbiotic theories endured scathing criticism in a leading college textbook of the day (Wilson, 1928), whereupon they fell into disrepute for decades.

Endosymbiotic theory was revived in 1967 when Lynn Sagan (later named Margulis) argued that chloroplasts and mitochondria had descended from separate endosymbionts. Sagan envisaged as a host for the origin of mitochondria a heterotrophic anaerobic prokaryote, in whose cytoplasm an aerobic prokaryotic microbe had taken up residence. The resulting heterotrophic protozoan later engulfed a cyanobacterium, resulting in the origin of plastids (Sagan, 1967). However, germane to all of Margulis's versions of endosymbiotic theory, from 1967 onward, is the notion that the eukaryotic flagellum arose from a symbiotic spirochete (Margulis, 1970; Margulis *et al.*, 2006) – a view that never received reproducible experimental support and that remained outside the mainstream of developments surrounding endosymbiotic theory. Since Margulis's revival of the idea, more than 30 different versions of endosymbiotic theory, with varying degrees of detail, and with different areas of focus, have been put forward (reviewed in Martin *et al.*, 2015). Some versions introduce new ways to imagine the origin of mitochondria and chloroplasts, other versions suggest endosymbiotic origins for other cell compartments like peroxisomes or the nucleus, or aim to account for the origin of various eukaryotic traits. In the main, however, endosymbiotic theory is about the origin of chloroplasts and mitochondria.

## Mitochondria

Early models for the origin of mitochondria have a primitive mitochondrion-lacking (amitochondriate) microbe as the hosts of an aerobic bacterium (De Duve, 1969). Following the discovery of archaebacteria (archaea), an archaeon was often viewed as the host that acquired the mitochondrion (Van Valen and Maiorana, 1980; Doolittle, 1980). The model of Vellai and Vida (1999) operates with a prokaryotic host, as does the sulfur cycling theory of Searcy (1992). López-García and Moreira (2006) proposed a three-partner endosymbiosis between a fermenting, heterotrophic, hydrogen-producing ancestral myxobacterium (delta-proteobacterium) that serves as the host, a strictly anaerobic, methanogenic archaeon that becomes the nucleus, and an alpha-proteobacterium that was then surrounded by the syntrophic couple and became the mitochondrial ancestor. The model presented by Martijn and Ettema (2013), like that put forward by Yutin *et al.* (2009), suggests a phagocytosing archaeal host, which engulfed an alpha-proteobacterium.

Most models for the origin of mitochondria posit that the mitochondrial endosymbiont was an aerobic bacterium, if they take a stance on its physiology at all. But various anaerobic forms of mitochondria like hydrogenosomes also occur among eukaryotes (Müller *et al.*, 2012) and these also need to be accounted for under endosymbiotic theory. One variant of endosymbiotic theory, called the hydrogen hypothesis, accounts for these anaerobic mitochondria. It posits a symbiotic association of an anaerobic, strictly hydrogen-dependent and autotrophic archaebacterium as the host with a facultatively anaerobic, heterotrophic bacterium as the endosymbiont, with specialization and differential loss leading to aerobic and anaerobic forms of mitochondria (Martin and Müller, 1998). Today, some models for the origin of mitochondria entail the assumption that the host that acquired the mitochondrial symbiont was already a eukaryote, others operate on the premise that the host was a prokaryote and that the origin of eukaryote cell complexity came later (reviewed in Martin *et al.*, 2015). Present data tend to favor the view that the host was a prokaryote, specifically an archaeon in most current views (Lane and Martin, 2010; Williams *et al.*, 2013; Bolte *et al.*, 2015; Raymann *et al.*, 2015; Spang *et al.*, 2015). The endosymbiotic origin of mitochondria in an archaeal host is illustrated in **Figure 1**.

## Plastids

All models for the origin of chloroplasts propose that the host was already a eukaryote. The nature of the symbiotic association between host and plastid symbiont varies across models. Today, plastids are involved in photosynthesis, carbon fixation, amino acid biosynthesis, lipid and cofactor biosynthesis as well as nitrogen metabolism. This gives rise to several hypotheses about the physiological context for the establishment of the plastids. In Mereschkowsky's version of endosymbiotic theory, the production of carbohydrates for the host was the key contribution by the cyanobacterial endosymbiont right from the start (Mereschkowsky, 1905). Another reason for the establishment of the symbiosis could

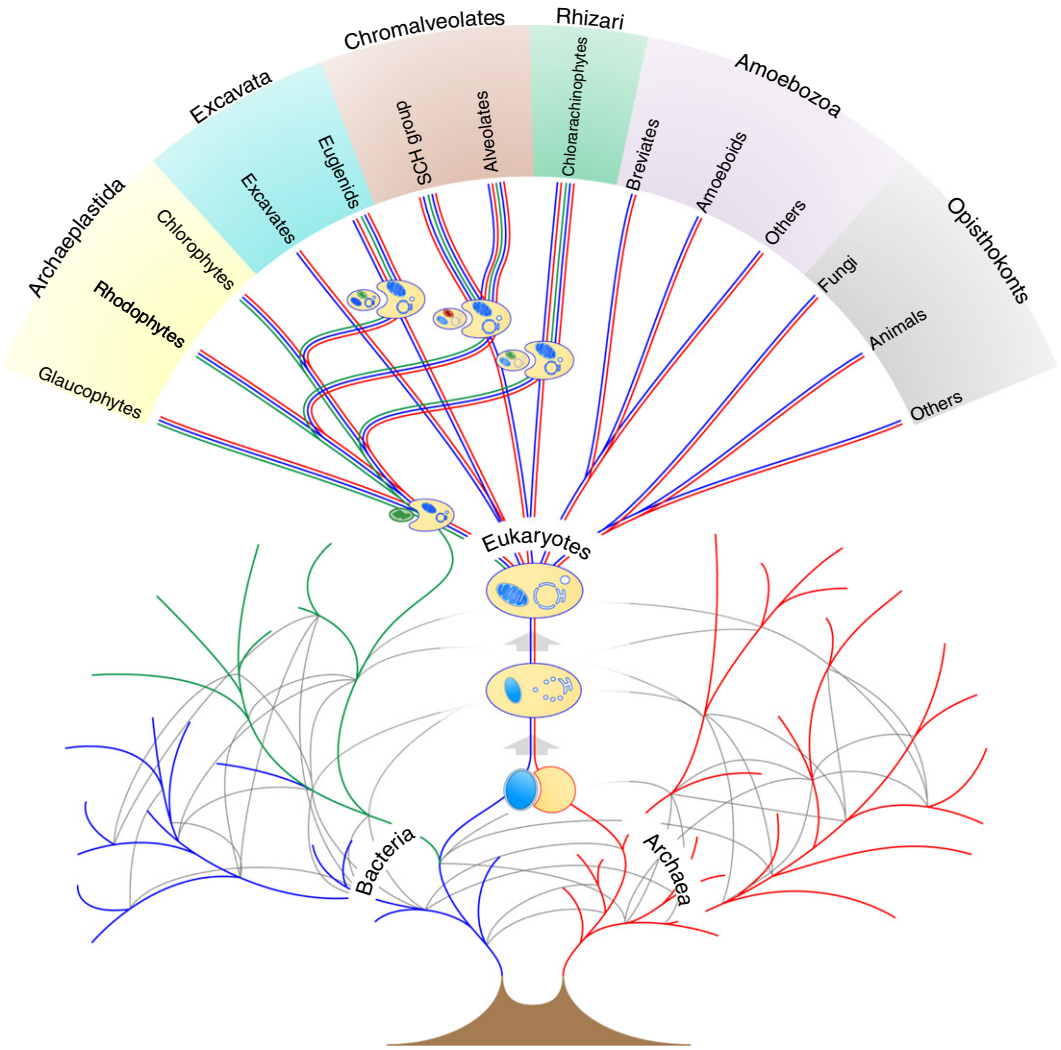


**Figure 1** A schematic representation of the origin of the three domains of life and their relationships: The bacteria are shown in blue while the archaea are shown in red. Each colored line serves to show the number of genomes involved in shaping that lineage while also indicating phylogenetic relationships between the various groups. Life arose from alkaline hydrothermal vents as the two bacterial kingdoms the bacteria and the archaea. Prokaryotic evolution is rampant with Lateral Gene Transfers (LGT) – shown in dotted gray lines between the various groups – that shape the various prokaryotic lineages. A symbiotic association of an archaea and bacteria gave rise to eukaryotes where genome evolution is dominated by endosymbiotic events rather than LGT. The taxonomic groups shown correspond to those recognized by Adl *et al.* (2005). The term SCH-group is introduced here to designate Stramenopiles, Cryptomoads, and Haptophytes, whose plastids appear to share a single common origin (Zimorski *et al.*, 2014; Gould *et al.*, 2015).

have been the low concentration of oxygen in the air at the time of endosymbiosis, such that the oxygen produced by the symbiont subversed the host's mitochondrial respiration (Martin and Müller, 1998). However, if we look at modern symbioses involving cyanobacteria, they mostly involve cyanobacterial nitrogen fixation (Kneip *et al.*, 2007; Ran *et al.*, 2010). Today's plastids do not fix nitrogen. Possibly they have lost this attribute (and the associated genes) as a consequence of the evolution of the nitrogen cycle (there is more nitrate in the environment today because of environmental $O_2$). This aspect of endosymbiotic theory for plastid origin (nitrogen fixation) is not directly supported by data, but is congruent with recent analyses that today's filamentous, heterocyst-forming and nitrogen fixating cyanobacteria (sections IV and V) are most similar, from the genomic perspective, to the plastid ancestor (Deusch *et al.*, 2008; Dagan *et al.*, 2013).

In recent literature, a proposal for the origin of plastids involving chlamydia continues to surface. It posits that a chlamydial endosymbiont was involved as a kind of metabolic helper in the origin of plastids (Ball *et al.*, 2013), a kind of preplastidial infection that the cyanobacterial symbiosis somehow cured. That suggestion, though published in prominent journals, is problematic, because the observations upon which it is founded (phylogenetic trees) are subject to simpler alternative interpretations that do not require the participation of any symbionts other than a cyanobacterium at the origin of plastids (Deschamps, 2014; Zimorski *et al.*, 2014;

Domman *et al.*, 2015). Moreover, the chlamydia story has the problem that if one infers the existence of a symbiont from a few gene trees (which is how the chlamydia symbiosis narrative operates), then for every unexpected branch that we observe in phylogenetic trees we would have to infer a new endosymbiont, and that kind of reasoning in endosymbiotic theory simply does not work (Ku *et al.*, 2015).

A member of the rhizaria, the ameba *Paulinella chromatophora*, harbors within its cytoplasm cyanobacteria of the genus *Synechococcus* (Marin *et al.*, 2005; Yoon *et al.*, 2006). These endosymbiotic cyanobacteria have been known for over 100 years and are called chromatophores (Mereschkowsky, 1905; Melkonian and Mollenhauer, 2005). Their genome is reduced compared to their closest free-living relatives, but is larger than typical plastid genomes (Nowack *et al.*, 2008). Some authors refer to this classical cyanobacterial endosymbiont as a 'photosynthetic organelle' (Marin *et al.*, 2005, Nowack and Grossman, 2012).

The timing in Earth history of mitochondrial and plastid origin cannot be pinpointed, but plausible ranges are often cited that stem from fossil evidence. The oldest eukaryotic microfossils are about 1.8 billion years old (Knoll, 2014). Because mitochondria arose only once in eukaryote evolution (Lane and Martin, 2010), this age can also be seen as a minimum age for mitochondria. The origin of plastids has been estimated at about 1.5 billion years ago (Parfrey *et al.*, 2011), the minimum age for plastids is 1.2 billion years ago because a fossil red alga called *Bangiomorpha* (Butterfield, 2000) is found in rocks of that age. The origin of plastids is sketched in **Figure 1**.

## Secondary Endosymbiosis

Mitochondria and chloroplasts can take on a diversity of form and function across different eukaryotic groups. But they have one attribute in common: chloroplasts and mitochondria are always surrounded by two membranes. This is a telling character that betrays their endosymbiotic origin. The two membranes surrounding chloroplasts and mitochondria correspond, in terms of homologies, to the plasma membrane and lipopolysaccharide layer of the Gram-negative bacteria from which the organelles arose (Lister *et al.*, 2005; Schleiff and Becker, 2011). Yet there are photosynthetic eukaryotes whose plastids are surrounded by three or even four membranes (Gould *et al.*, 2008; Stoebe and Maier, 2002; Van Dooren *et al.*, 2001), such organelles are often called 'complex plastids.' The plastids of euglenids and dinoflagellates are surrounded by three membranes. The plastids of the chlorarachniophytes, the cryptophytes, the diatoms, the brown algae, and relatives are surrounded by four membranes.

How did these algae obtain their plastids? Under endosymbiotic theory, these additional membranes are explained as a result of secondary symbiosis. That is, the plastids of these algal groups stem from secondary endosymbiosis: symbioses between a eukaryotic host and a eukaryotic alga. In contrast to the single endosymbiotic origin of primary plastids from cyanobacteria, these secondary symbioses have occurred at least three times independently in evolution: once in the euglenid lineage, once in the chlorarachniophyte lineage, and (at least) once in the 'chromalveolate' lineage (for a discussion of what chromalveolates are, see Zimorski *et al.* (2014) and Gould *et al.* (2015)). The euglenid and chlorarachniophyte lineages acquired their plastids from green algae, the chromalveolate lineages acquired their plastids from a red alga (or red algae).

The uncertainty about the number of secondary endosymbiotic events in the red algae has to do with the conflicting data from molecular phylogenies (gene trees). The gene trees that would address the question of how many secondary endosymbiosis took place among the chromalveolates conflict with one another, giving rise to many suggestions for independent origins of the red secondary plastids. Considerations relating to protein import into red secondary plastids argue for a single secondary endosymbiotic event at the origin of this group (Zimorski *et al.*, 2014; Gould *et al.*, 2015). The additional two membranes surrounding red secondary plastids are most easily interpreted as the inner and outer leaves of the endoplasmic reticulum (ER) of the host that acquired the red algal endosymbiont (Zimorski *et al.*, 2014; Gould *et al.*, 2015). The workings of secondary endosymbiosis in algal evolution are shown in **Figure 1**.

The number and nature of secondary hosts involving the origin of red secondary plastids remain unclear – some red secondary plastids are been suggested to be of tertiary or even quaternary endosymbiotic origin (Stiller *et al.*, 2014). Lineages with secondary red plastids include the nucleomorph-bearing cryptophytes, the haptophytes, the diatoms (stramenopiles), some dinoflagellates, the chromerids, and the perkensids and some apicomplexans (McFadden, 2014), which secondary lost their photosynthetic ability – all lineages of the SCH-group and alveolates. Within these lineages the dinoflagellates are the only organisms with three-membrane bound plastids. Considerations relating to protein import suggest that it was the second outermost membrane (corresponding to the host's distal ER leaf) that was lost in the dinoflagellates (Zimorski *et al.*, 2014; Gould *et al.*, 2015), all other secondary plastids derived from red algae are surrounded by four membranes. In the context of membrane homologies in endosymbiotic theory, there have been several suggestions that the nucleus was once an endosymbiont (reviewed in Martin, 2005). However, such theories often state that the nucleus is surrounded by two membranes (or a double membrane), which is incorrect: the nucleus is surrounded by one folded membrane that is contiguous with the ER (Martin, 1999).

## The Rationale Behind Mitochondrial Ubiquity

Because plastids arose more recently in evolution than mitochondria, we know a bit more about the host of plastids than we do about the host of mitochondria. It is a particularly curious aspect of endosymbiotic theory that ideas about the bacterial ancestry of mitochondria developed historically long before concepts about the host for the origin of mitochondria appeared. Ideas about the nature of the mitochondrial host came as a necessary afterthought in the wake of the more pressing debate about whether endosymbiosis for organelle origins was a good idea or not. In the early 1970s and well into the 1990s it was customary to view the mitochondrial host as a mitochondrion-lacking eukaryote – a cell that had mastered the evolutionary transition from being a prokaryote to one that had

a nucleus, a cell cycle, and all the other myriad attributes that separate eukaryotes from prokaryotes (for a long list of such attributes see Cavalier-Smith, 2002). In that view, summarized succinctly by Doolittle (1998), the mitochondrial host became eukaryotic more or less by point mutation, and eukaryotes that were then known to lack mitochondria were most simply seen as descendants of that host.

It turned out, however, that all of the eukaryotes that then appeared to lack mitochondria actually had mitochondria after all, albeit sometimes in highly reduced forms (Tovar *et al.*, 1999, 2003; Williams *et al.*, 2002). That placed the origin of mitochondria at the very base of eukaryote evolution (Embley and Martin, 2006). All the while it should have been evident that the host for the origin of mitochondria was related to archaea (or was an archaeon outright), because the eukaryotic cytosol harbors archaeal ribosomes (Esser *et al.*, 2004). Improvements in phylogenetic methods have gradually brought forth a picture in which the host for the origin of mitochondria branched within the archaea (Cox *et al.*, 2008; Williams *et al.*, 2013; Spang *et al.*, 2015), not as a sister to the archaea, as the older rRNA tree of life implied (Pace, 2006). That suggests that the mitochondrion was acquired by an archaeon (a prokaryote), as some of the endosymbiotic models had suggested. As a consequence, the origin of eukaryotic-specific traits might have come in the wake of mitochondrial symbiosis.

In line with that view, the nucleus could have arisen in the wake of mitochondrial endosymbiosis, the proliferation of (rapidly self spliced) group II introns and their transformation into (slowly spliced) spliceosomal introns may have caused the need for a nuclear membrane to separate splicing from translation (Martin and Koonin, 2006). Also in agreement with the view that eukaryote complexity emerged in the wake of the mitochondrial endosymbiosis is the comparatively recent recognition that the many evolutionary inventions that separate eukaryotes from prokaryotes did not come for free, they came at an energetic price. The configuration of bioenergetic membranes that mitochondria conferred upon the ancestor of the eukaryotic lineage allowed it to do the evolutionary inventing required to forge the eukaryotic lineage (Lane and Martin, 2010). Such bioenergetic considerations would readily explain why mitochondria are ubiquitous among eukaryotes (they were required for eukaryote origin) and why no prokaryote on its own ever made the leap to eukaryote-like complexity: without a mitochondrial endosymbiont, it lacked the energy per gene to do so (Lane and Martin, 2010; Lane, 2014). Thus, the ubiquity of mitochondria among eukaryotes, including among anaerobic eukaryotes (Müller *et al.*, 2012), is perhaps best seen as evidence that endosymbiosis really was important, not just in terms of making eukaryotes more efficient at what they do, but bringing them into existence in the first place.

## Endosymbiotic Gene Transfer

One of the important aspects of endosymbiosis is that it can, and does, lead to gene transfer from organelles to the nucleus (Martin *et al.*, 1998; Martin and Herrmann, 1998; Timmis *et al.*, 2004). Ninety years ago, even Wallin sensed that somehow the process of endosymbiosis should be connected to a transfer of genetic material from the organelle to the host. He wrote: "It appears logical, however, that under certain circumstances, [...] bacterial organisms may develop an absolute symbiosis with a higher organism and in some way or another impress a new character on the factors of heredity. The simplest and most readily conceivable mechanism by which the alteration takes place would be the addition of new genes to the chromosomes from the bacterial symbiont" (Wallin, 1925; p. 144). That is a fairly modern formulation of a process that is now called endosymbiotic gene transfer (Martin *et al.*, 1993). About 15–18% of the genes in a higher plant's nuclear genome come from the cyanobacterial antecedent of plastids (Martin *et al.*, 2002; Deusch *et al.*, 2008), and in eukaryotes that lack plastids, such as yeast, the vast majority of genes having prokaryotic homologues come from bacteria, not archaea (Esser *et al.*, 2004; Cotton and McInerney, 2010; Thiergart *et al.*, 2012). The simplest interpretation is that these bacterial genes in nonphotosynthetic eukaryotic lineages come from the mitochondrial ancestor (Pisani *et al.*, 2007; McInerney *et al.*, 2014).

The process of endosymbiotic gene transfer entails the integration of bulk chunks of organellar chromosomes, or in some cases even a whole organelle genome spanning more than 100 kb (Huang *et al.*, 2005). The evidence that this has happened can be seen at the computer by comparing organelle genomes to nuclear genomes (Hazkani-Covo and Covo, 2008) and in laboratory experiments where organelles are transformed with constructs that only become active in the nucleus (Huang *et al.*, 2003, 2004). The mechanism of DNA insertion entails nonhomologous end joining and most eukaryotic genomes are replete with such recent organelle insertions (Hazkani-Covo and Covo, 2008). One might wonder how organelle DNA gets to the nucleus in the first place so that it can recombine. The most likely mechanism is simply stress induced organelle lysis, and there is some evidence for this in plants (Lane, 2011; Wang *et al.*, 2012). Importantly, organelle lysis means that there has to be more than one organelle copy in the cell, one to lyse and one for progeny, and this is the crux of the 'limited window' hypothesis (Barbrook *et al.*, 2006).

There is another important aspect to gene transfer to the nucleus. Both at the origin of mitochondria and at the origin of plastids, host, and symbiont possessed a large number of genes for homologous functions. Such genes would include ribosome biogenesis, amino acid biosynthesis, nucleotide biosynthesis, core carbon and energy metabolism, cofactor biosynthesis, and the like. Chloroplasts and mitochondria have both retained their own ribosomes, for example, and divergent members of homologous gene families for ribosomal proteins as one example, but other examples have been well studied, including core carbohydrate metabolism. This phenomenon is called 'functional redundancy through endosymbiosis' (Martin and Schnarrenberger, 1997). It generates highly divergent copies of genes homologous to prokaryotes even though they reside on eukaryotic chromosomes.

## Protein Import

The origin of organellar protein import machineries played an important role in the evolution of mitochondria (Dolezal *et al.*, 2006) and plastids (Schleiff and Becker, 2011), because

it allowed the genetic integration of host and endosymbiont while allowing the endosymbiont to maintain its biochemical identity. In the early phases of organelle evolution, before the invention of the protein import apparatus that allowed plastids and mitochondria to import proteins from the cytosol, the transferred genes either became pseudogenes or became expressed as cytosolic proteins. In this way, endosymbionts can easily transfer whole pathways from the organelle to the cytosol. The transfer of whole pathways from the cytosol to an organelle is also possible, but the mechanisms are different (Martin, 2010).

With the advent of organelle protein import, however, transferred genes had the opportunity to obtain the necessary expression and targeting signals to be targeted back to the organelle from which the nuclear gene was acquired. This process has resulted in an expansion of the eukaryotic nuclear gene repertoire and in reductive genome evolution in the organelle. While it has long been known that the genes retained most tenaciously by plastids and mitochondria encode for proteins involved in the electron transport chain of the bioenergetic organelle or for the ribosome required for their synthesis (Allen, 2003, 2015), only recently was it recognized that even within the ribosome, the same core of proteins has been retained independently by plastids and mitochondria, probably owing to constraints imposed by the process of ribosome assembly (Maier *et al.*, 2013).

## Conclusion

Endosymbiotic theory explains why some organelles of eukaryotic cells are so similar to prokaryotic cells. It is a fairly powerful theory in that it can explain a number of disparate observations within a single unifying framework. Mutation theory, population genetics and selection can explain many aspects of evolutionary divergence among cells, but they cannot explain how mitochondria, chloroplasts, and complex plastids arose; for those major events in evolutionary cell biology, endosymbiotic theory is the only explanatory tool available. It works quite well, but it works best when used sparingly and in close conjunction with neighboring disciplines like microbial physiology and genetics.

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*See also*: Mitochondrial and Nuclear Genome Coevolution. Symbiogenesis, History of. Symbiosis, Introduction to

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