The Scientist
www.the-scientist.com

SIGMAPLOT
Exact Graphs for Exact Science
The Technical Graphing Standard

Research
Volume 18 | Issue 9 | 33 | May. 10, 2004 Previous | Next

Research Vision | Evolutionary Teamwork

Constructing eukaryotes through endosymbiosis | By Frederic D. Bushman

Courtesy of Frederic D. Bushman

The endosymbiotic theory, which posits that organelles such as chloroplasts and mitochondria descended from formerly independent cells, has received wide acceptance in the last third of the 20th century. But recent findings suggest that endosymbiotic processes may have contributed still more cellular components, chloroplasts and mitochondria being simply the most easily identified examples.

Genomic analyses across a broad spectrum of organisms have solidified the case for mitochondria and chloroplasts and suggested that less well known organelles, the hydrogenosome and mitosome, are remnants of genome-depleted mitochondrial descendants. These findings raise questions as to whether still other structures in eukaryotic cells, now lacking their own DNA, might also have originated through endosymbiosis.

THE FEELING IS MUTUAL According to the presently favored views on endosymbiosis, an anaerobic cell engulfed a respiring α-proteobacterium, allowing respiration in the resulting consortium. This may have taken place during early evolution concomitant with Earth's planetary transition from a reducing to an oxidizing atmosphere. Later, some descendents of this fused cell captured a cyanobacterium capable of photosynthesis. The α-proteobacterium evolved to become modern mitochondria, and the cyanobacterium gave rise to chloroplasts.[1-3]

The endosymbiotic theory became topical early in the 20th century, largely because mitochondria looked like bacteria inside larger cells. But

Search
::Go
Advanced Search

Edit account preferences ::Go

Tools
Comment
E-mail article

Ads by Google

Sequence analysis tools
Simplify DNA and protein sequence analysis. Try new Vector NTI 9 free
www.informaxinc.com

Analyze DNA Sequences
View, edit and analyze DNA sequence data. Design and evaluate primers.
www.stratagene.com

Genome Sequencing Center
Agencourt announces publication of the rat genome sequence
www.agencourt.com

Human Genome Project
Stanford genomics courses. Latest research. Leading experts.
scpd.stanford.edu

DNA Vault
DNA Vault for Human Genome By getting your personal Replica
www.ZORNEX.com

2004 BEST places to work POSTDOCS The Scientist

BioMed Central

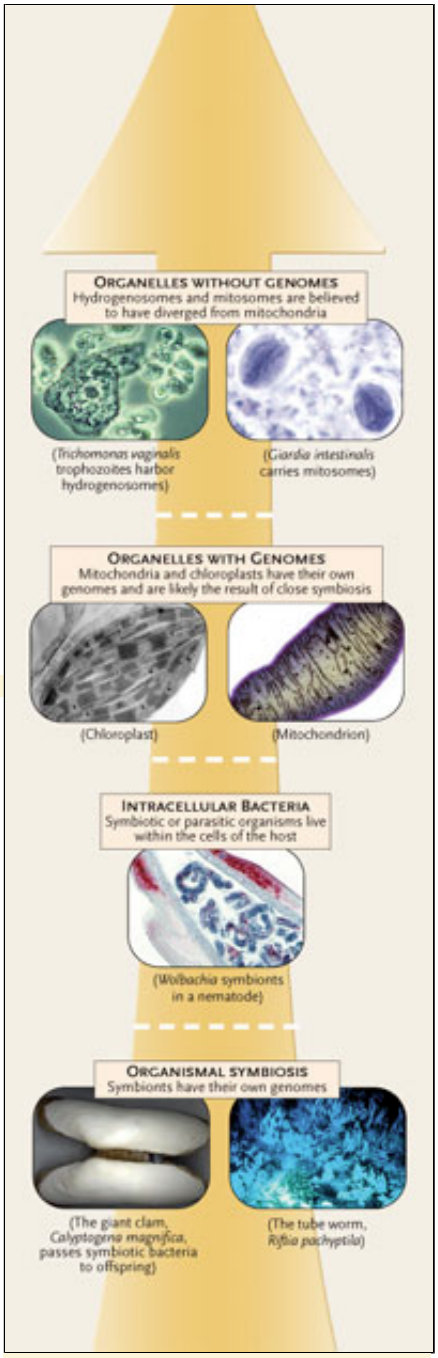
the theory lost favor after many unsuccessful attempts to cultivate mitochondria outside the host cell. In the 1960s and 1970s Lynn Margulis revitalized the idea when she articulated a case for endosymbiosis that didn't rely on independent cultivation but on biochemical and molecular data.[1] More recently, genome sequence comparisons have supported this idea: Mitochondrial genes closely match α-proteobacteria such as *Rickettsia*, and chloroplast genes match cyanobacteria such as *Prochlorococcus marinus*.

Mutualistic relationships today may illustrate some of the steps involved in forming a eukaryote/ prokaryote endosymbiosis. Our guts, for example, are thought to harbor some 500 bacterial species that aid in digestion
and obstruct colonization by pathogens. The giant tubeworm, *Riftia pachyptila*, which crowds about hydrothermal vents, also associates with bacterial mutualists that provide the sole source of nutrition to the animal by chemolithotrophic energy generation from hydrogen sulfide. The giant vent clam, *Calyptogena magnifica*, demonstrates an even closer relationship: The chemolithotrophic bacteria are inherited by descent, rather than captured from seawater as with *Riftia*. Similarly many insect species harbor intracellular
bacteria, including *Wigglesworthia*, *Buchnera*, and others, that carry out reactions essential for host nutrition. Some of these bacteria are unable to live outside the insect host; such obligate mutualists are close to qualifying as new organelles, though they do apparently still move between cells in some cases.

The progression from gut bacteria to required mutualist to obligate endosymbiont describes increasingly intimate cohabitation. Complete loss of the capacity for independent life, together with cell-to-cell transmission through the germ line, completes the conversion of a bacterial mutualist to an organelle.

GENES LOST AND FOUND ... Mitochondria and chloroplasts differ from bacterial progenitors in that their genomes are greatly reduced, which explains failed attempts at independent cultivation. *Rickettsia* has about 800 genes; mitochondria have between 3 and 97, depending on the organism. A relatively minimal cyanobacterium has 1900 genes; chloroplasts have no more than 250. Many of these genes aren't lost, it turns out, but rather have relocated. Eukaryotic genome sequences reveal that some of the missing organellar genes can be found in the nuclear DNA, indicating a transfer of information.

Indeed, this gene transfer from organelles to the nucleus is so active that it can readily be measured in the laboratory. Several studies have introduced marker genes into mitochondria and chloroplasts and monitored their rate of appearance in the nuclear genome. Results indicate that the transfer is quite high. And, with an active process it becomes possible to envision a ratchet mechanism for gene swapping. Organellar genes that take care of an overall cellular function can replace their counterparts in the genome as one gene becomes deleted by random mutation.



Similarly, genes needed for organellar function can become transferred to the nuclear genome and incorporated there, provided the encoded protein acquires the signal needed to traffic it back to the organelle. Over eons, the process has reduced the mitochondrial and chloroplast genomes but not completely eradicated them. The same might not be said for other organelles.

... AND LOST AGAIN Remarkably, two structures appear to have evolved from mitochondria by losing all their DNA, either by deletion or transfer to the nuclear genome. Each of these organelles, the hydrogenosomes and mitosomes, appear in eukaryotic parasites that live in anaerobic environments and no longer need the mitochondria's respiratory functions.[4-6]

The hydrogenosome was the first organelle proposed to be a mitochondrial descendent lacking its own genome.[4] This organelle, found in some trichomonads, ciliates, and fungi, morphologically resembles mitochondria. Hydrogenosomes are surrounded by a double membrane and participate in energy metabolism, yet they lack a genome, have some differences in membrane architecture, and do not

participate in respiration. Instead, hydrogenosomes direct substrate-level phosphorylation, an anaerobic form of energy generation.

Despite these differences, the case for mitochondria as the hydrogenosome's precursor is strong. The genes that encode organelle proteins can be traced to mitochondrial relatives that now reside in the nuclear genome. The encoded proteins traffic back to the organelles, directed by short peptides that resemble mitochondrial trafficking signals. These sequences are functionally interchangeable in the laboratory.

Some organisms, including the anaerobic parasitic amoeba, *Giardia intestinalis*, possess another organelle called the mitosome. Like hydrogenosomes, mitosomes are enclosed in a double membrane and lack any organelle-associated genome. Mitosomes do not carry out respiration, but retain another function of mitochondria, the capacity to synthesize iron-sulfur clusters that become assembled into cellular proteins. Studies in yeast reveal that iron-sulfur protein formation in mitochondria is indispensable for growth, whereas respiratory function is not required under some conditions.

The complete sequence of *Encephalitozoon cuniculi*, a mitosome-containing parasite, provides a detailed picture of the genes involved.[5] The sequence reveals five genes for iron-sulfur cluster formation and their subsequent assembly into proteins, all of which are encoded in the nuclear genome. Some of these proteins have been shown to be localized in the mitosomes of other parasites, *G. intestinalis* and *Trach-ipleistophora hominis*. The signals for postsynthetic protein sorting again resemble mitochondrial sorting signals. Together these findings support the idea that mitosomes, like hydrogenosomes, are reduced mitochondrial descendents.

LIFTING THE LID Endosymbiosis might have played a larger role in eukaryotic evolution than is currently appreciated. Once you allow that cellular structures lacking their own DNA may indeed be relics of former bacterial mutualists, the lid is off. Margulis and coworkers have proposed that the cellular microtubule network, together with its associated kinetochores and centrioles, might have arisen by capture of a spirochete bacterium.[1] In another example, the peroxisome, a membrane-enclosed compartment for specialized oxidative reactions, has been proposed to have arisen from a captured bacter-ium capable of this chemistry.

But these just scratch the surface with regards to organelle diversity. As the number of complete genome sequences grows, and computational tools become more sensitive, we can investigate proteins in many

organelles or subcellular structures for weak genetic signatures of endosymbiotic origin. There still might be some resemblance between microtubule network or peroxisome proteins and genes in modern bacteria. And eukaryotic genes that closely resemble bacterial counterparts might suggest new cellular structures to investigate as potential endosymbiotic products.

A related set of questions surrounds formation of new organelles. Was this process completed eons ago? It seems that gene transfer from mitochondria to the nucleus and stable incorporation into the germ line has largely stopped in metazoan animals, but for other lineages and other organelles it may well be ongoing. In plants, for example, transfer of genes from the chloroplast to the nucleus appears much more dynamic and potentially continues today.

Looking ahead, we can expect more genome sequences to be determined for partners engaged in mutualistic lifestyles. It should be possible to clarify how often genes are transferred from endosymbionts to their hosts, and analyze this as a function of the intimacy of the mutualistic association.
For example, do the mutual interactions seen in *Riftia*, *C. magnifica*, or *Wigglesworthia* result in gene transfer to the nucleus? We should soon be able to answer these questions, allowing a detailed look at the roles of endosymbiosis in the formation and ongoing evolution of eukaryotes.

Frederic D. Bushman, professor of microbiology at the University of Pennsylvania School of Medicine, studies the transfer of genetic information between cells and organisms by integrating viruses. He has published more than 80 scientific papers and a book, Lateral DNA Transfer: Mechanisms and Consequences. He can be contacted at bushman@salk.edu.

Selected References

1. L. Margulis, *Origin of Eukaryotic Cells*, New Haven: Yale University Press, 1970.

2. F.D. Bushman, *Lateral DNA Transfer: Mechanisms and Consequences*, New York: Cold Spring Harbor Laboratory Press, 2001.

3. J.N. Timmis et al., "Endosymbiotic gene transfer: Organelle genomes forge eukaryotic chromosomes," *Nat Rev Gen*, 5:123-36, 2004.

4. S.D. Dyall, P.J. Johnson, "Origins of hydrogenosomes and mitochondria: evolution and organelle biogenesis," *Curr Opin Microbiol*, 3:404-11, 2000.

5. M.D. Katinka et al., "Genome sequence and gene compaction of the eukaryote parasite *Encephalitozoon cuniculi*," *Nature*, 414:450-3, 2001.

6. B.A. Williams
et al., "A mitochondrial remnant in the microsporidian *Trachipleistophora hominis*," *Nature*, 418:865-9, 2002.

Vote

Please indicate on a 1 - 5 scale how strongly you would recommend this article to your colleagues?

Not recommended 1 2 3 4 5 Highly recommended

Please register your vote

Vote

© 2004, The Scientist LLC, All rights reserved.

Previous | Next